REPORTS OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

The following reports were presented by David J. Welsh, MD, MBA, Chair:

1. COUNCIL ON SCIENCE AND PUBLIC HEALTH SUNSET REVIEW OF 2014 HOUSE POLICIES

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED

Policy G-600.110, "Sunset Mechanism for AMA Policy," calls for the decennial review of American Medical Association (AMA) policies to ensure that our AMA's policy database is current, coherent, and relevant. This policy reads as follows, laying out the parameters for review and specifying the needed procedures:

1. As the House of Delegates adopts policies, a maximum ten-year time horizon shall exist. A policy will typically sunset after ten years unless action is taken by the House of Delegates to retain it. Any action of our AMA House that reaffirms or amends an existing policy position shall reset the sunset "clock," making the reaffirmed or amended policy viable for another 10 years.

2. In the implementation and ongoing operation of our AMA policy sunset mechanism, the following procedures shall be followed: (a) Each year, the Speakers shall provide a list of policies that are subject to review under the policy sunset mechanism; (b) Such policies shall be assigned to the appropriate AMA councils for review; (c) Each AMA council that has been asked to review policies shall develop and submit a report to the House of Delegates identifying policies that are scheduled to sunset; (d) For each policy under review, the reviewing council can recommend one of the following actions: (i) retain the policy; (ii) sunset the policy; (iii) retain part of the policy; or (iv) reconcile the policy with more recent and like policy; (e) For each recommendation that it makes to retain a policy in any fashion, the reviewing council shall provide a succinct, but cogent justification (f) The Speakers shall determine the best way for the House of Delegates to handle the sunset reports.

3. Nothing in this policy shall prohibit a report to the HOD or resolution to sunset a policy earlier than its 10-year horizon if it is no longer relevant, has been superseded by a more current policy, or has been accomplished.

4. The AMA councils and the House of Delegates should conform to the following guidelines for sunset: (a) when a policy is no longer relevant or necessary; (b) when a policy or directive has been accomplished; or (c) when the policy or directive is part of an established AMA practice that is transparent to the House and codified elsewhere such as the AMA Bylaws or the AMA House of Delegates Reference Manual: Procedures, Policies and Practices.

5. The most recent policy shall be deemed to supersede contradictory past AMA policies.

6. Sunset policies will be retained in the AMA historical archives.

RECOMMENDATION

The Council on Science and Public Health recommends that the House of Delegates policies listed in the appendix to this report be acted upon in the manner indicated and the remainder of this report be filed.

APPENDIX: RECOMMENDED ACTIONS

Policy Number	Title	Text	Recommendation
D-120.946	Modification to the USP Chapter 797 Guidelines	1. Our AMA will inform physicians on the far-reaching effects of the immediate-use exception to practice and patient safety.	Rescind, completed. AMA's stance on USP Chapter 797 policy can be found in Policy H-120.930, "USP Compounding Rules."

	as Currently Written	2. Our AMA will encourage and facilitate as a convener for all state, medical school, and specialty organization delegates to the United States Pharmacopeial Convention to protest the "immediate-use" exception to the USP Chapter 797 guidelines as currently written, including the "one-hour-rule," and seek reasonable accommodation and modification of Chapter 797 guidelines with interested stakeholders. 3. Our AMA will encourage and facilitate as a convener for all state, medical school, and specialty organization delegates to the United States Pharmacopeial Convention to protest the USP Chapter 797 guidelines as currently written, including the prohibition to enter a container no more than twice, and seek reasonable accommodation and modification of Chapter 797 guidelines with interested stakeholders. 4. Our AMA will urge The Joint Commission and other deeming organizations to suspend the enforcement of the "immediate-use" exception to USP Chapter 797 as currently written, including the "one-hour-rule" until the reconvening of the USP in June 2015. 5. Our AMA will urge the USP to employ evidence-based methods to survey current medical practice as it relates to USP Chapter 797 guidelines. (Res. 520, A-14)	
D-125.987	Biosimilar Product Naming and Labeling	Our AMA urges the FDA to finalize Guidance on the naming and labeling conventions to be used for biosimilar products, including those that are deemed interchangeable. Any change in current nomenclature rules or standards should be informed by a better and more complete understanding of how such changes, including requiring a unique identifier for biologic USANs would impact prescriber attitudes and patient access, and affect post marketing surveillance. Actions that solely enhance product identification during surveillance but act as barriers to clinical uptake are counterproductive. However, because of unique product attributes, a relatively simple way to identify and track which biosimilar products have been dispensed to individual patients must be established. If unique identifiers for biosimilar USANs are required to support pharmacovigilance, they should be simple and the resulting names should reinforce similarities by using the same root name following standards for nonproprietary names established by the USAN Council. (CSAPH Rep. 4, A-14)	Retain, still relevant. Note: May be modified by CSAPH5-A-24, “Biosimilar/Interchangeable Terminology
D-125.989	Substitution of Biosimilar Medicines and Related Medical Products	Our AMA urges that State Pharmacy Practice Acts and substitution practices for biosimilars in the outpatient arena: (1) preserve physician autonomy to designate which biologic or biosimilar product is dispensed to their patients; (2) allow substitution	Retain as amended. Amendments noted here are consistent with those currently proposed in CSAPH 5-A-24,

		when physicians expressly authorize substitution of a biologic or biosimilar ~~an interchangeable~~ product; (3) ~~limit the authority of pharmacists to automatically substitute only those biosimilar products that are deemed interchangeable by the FDA~~ in the absence of express physician authorization to the contrary, allow substitution of the biologic or biosimilar product when (a) the biologic product is highly similar to the reference product, notwithstanding minor differences in clinically inactive components; and (b) there are no data indicating clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. (Res. 918, I-08; Modified: CSAPH Rep. 1, I-11; Modified: CSAPH Rep. 4, A-14)	"Biosimilar/Interchangeable Terminology"
D-135.973	Safer Chemical Policies	Our AMA will review the recommendations of the National Academies of Sciences, Engineering, and Medicine with respect to chemical policy reform. (Res. 415, A-14)	Retain as amended to update terminology.
D-135.985	Air Pollution and Public Health	Our AMA: (1) promotes education among its members and the general public and will support efforts that lead to significant reduction in fuel emissions in all states; and (2) will declare the need for authorities in all states to expeditiously adopt, and implement effective air pollution control strategies to reduce emissions, and this position will be disseminated to state and specialty societies. (Res. 408, A-08; Reaffirmation A-14)	Retain; still relevant.
D-135.992	Mercury Pollution	Our AMA: (1) recognizes that the trading of air pollutants is potentially harmful for vulnerable populations~~, and that the Clean Air Mercury Rule is inconsistent with our AMA's health-protective approach to air pollution~~; (2) encourages state governments to be proactive in protecting citizens from harmful mercury emissions; (3) encourages reduction in mercury use in manufacturing wherever possible, and recognize that more must be done using available and emerging technology to reduce mercury emissions; (4) recommends increased vigilance, monitoring and tracking of mercury use and emissions in chlor-alkali facilities that use mercury in manufacturing processes; (5) encourages the US government to assume a leadership role in reducing the global mercury burden and work toward promoting binding, health-protective international standards; (6) supports the Environmental Protection Agency's national mercury emissions standards for cement kilns at limits based on the latest pollution control technology; and	Retain as amended. Mercury air pollution is regulated under the Mercury & Air Toxics Standards, which was passed in 2012. The Clean Air Mercury Rule is no longer relevant.

		(7) supports modern and strict source monitoring of mercury emissions from cement plants. (CSAPH Rep. 1, I-06; Appended: Res. 501, A-11; Reaffirmation A-14)	
D-150.973	Powdered Caffeine and Easy Unintentional Overdose	Our AMA ~~will: (1) seek~~ supports regulation or legislation ~~to~~ banning the sale of powdered caffeine to minors~~; and (2) issue a statement condemning the sale of powdered caffeine in packaging so concentrated, so difficult to measure, and in sufficient quantity that misuse and overdose is too common~~. (Res. 217, I-14)	Retain as amended to remove the portion of the directive that has been accomplished; convert to H-policy.
D-150.983	Food Stamp Incentive Program	Our AMA supports legislation to provide a meaningful increase in the value of SNAP ~~food stamps~~ when used to purchase fruits and vegetables. (Res. 405, A-07; Reaffirmation A-13; Reaffirmation A-14)	Retain as amended to update terminology.
D-190.972	Physician Credit Card Payments by Health Insurance Companies	Our AMA will consider legislation on behalf of physicians that any credit card transaction/bank fees are paid by the insurer and not the health care provider. (Res. 225, I-14)	Retain; still relevant.
D-20.993	Promotion of Rapid HIV Test	Our AMA will work with any and all local and state medical societies, and other interested US and international organizations, to increase access to and utilization of Food and Drug Administration-approved rapid HIV testing in accordance with the quality assurance guidelines for rapid HIV testing developed by the Centers for Disease Control and Prevention. Additionally, pre- and post-test counseling should be performed in accordance with guidelines established by the CDC. (Res. 511, A-05; Modified: CCB/CLRPD Rep. 2, A-14)	Retain; still relevant.
D-440.943	Obstructive Sleep Apnea	Our AMA: (1) recognizes Obstructive Sleep Apnea (OSA) as a major public health issue; (2) encourages a national public education campaign by appropriate federal agencies and relevant advocacy groups; (3) encourage research into the association of OSA with metabolic, cardiovascular, respiratory, and other diseases; and (4) encourages that all physicians become knowledgeable about the diagnosis and management of OSA. (Res. 521, A-09; Reaffirmed: Res. 107, A-14)	Retain; convert to H-policy.
D-450.988	Performance Measures for Evidence-Based Medicine	Our AMA will continue to ensure the quality of medical care through the appropriate use of evidence-based clinical performance measures. (Res. 506, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; convert to H-policy.
D-460.969	Navajo Birth Cohort Study	1. Our AMA recognizes the public health importance of the Navajo Birth Cohort Study for our Native American population and other populations exposed to uranium. ~~2. Our AMA will urgently endeavor to convene key stakeholders involved with the Navajo Birth Cohort Study and appropriate high-level officials~~	Retain as amended; convert to H-Policy. The study is ongoing, so funding issues appear to have been addressed.

		~~of the Centers for Disease Control and Prevention, with the goal of achieving a resolution of any issues that have prevented the release of full funding to the university contracted to perform this study, as mandated by Congress.~~ (Res. 932, I-14)	
D-460.979	Physicians and Clinical Trials	Our AMA supports elimination of the use of restrictive covenants or clauses that interfere with scientific communication in agreements between pharmaceutical companies or manufacturers of medical instruments, equipment and devices, and physician researchers. (Res. 610, I-04; Modified: CSAPH Rep. 1, A-14)	Retain; convert to H-policy.
D-485.999	Unrealistic Expectations from Surgery on Television	Our AMA opposes television programs that minimize the seriousness and risks of surgery and distort patient expectations. (Res. 609, I-04; Modified: CSAPH Rep. 1, A-14)	Retain; convert to H-policy.
D-60.969	Legal Protection and Social Services for Commercially Sexually Exploited Youth	Our AMA will work with state medical societies and specialty societies to: (1) where appropriate, advocate for legal protection and alternatives to incarceration for commercially sexually exploited youth as an alternative to prosecution for crimes related to their sexual or criminal exploitation; and (2) encourage the development of appropriate and comprehensive services as an alternative to criminal detention in order to overcome barriers to necessary services and care for commercially sexually exploited youth. (Res. 4, I-14)	Rescind. Addressed in current policies H-60.912 and H-65.948.
D-60.976	Childhood Anaphylactic Reactions	Our AMA will: (1) urge all schools, from preschool through 12th grade, to: (a) develop Medical Emergency Response Plans (MERP); (b) practice these plans in order to identify potential barriers and strategies for improvement; (c) ensure that school campuses have a direct communication link with an emergency medical system (EMS); (d) identify students at risk for life-threatening emergencies and ensure these children have an individual emergency care plan that is formulated with input by a physician; (e) designate roles and responsibilities among school staff for handling potential life-threatening emergencies, including administering medications, working with EMS and local emergency departments, and contacting families; (f) train school personnel in cardiopulmonary resuscitation; (g) adopt the School Guidelines for Managing Students with Food Allergies distributed by FARE (Food Allergy Research & Education); and (h) ensure that appropriate emergency equipment to deal with anaphylaxis and acute asthmatic reactions is available and that assigned staff are familiar with using this equipment; (2) work to expand to all states laws permitting students to carry prescribed epinephrine or other medications prescribed by their physician for asthma or anaphylaxis; (3) support increased research to better understand the	Retain; still relevant.

		causes, epidemiology, and effective treatment of anaphylaxis; (4) urge the Centers for Disease Control and Prevention to study the adequacy of school personnel and services to address asthma and anaphylactic emergencies; (5) urge physicians to work with parents and schools to ensure that all their patients with a food allergy have an individualized emergency plan; and (6) work to allow all first responders to carry and administer epinephrine in suspected cases of anaphylaxis. (CSAPH Rep. 1, A-07; Modified: CCB/CLRPD Rep. 2, A-14)	
H-10.963	Safe In-Line Skating	1. Our AMA encourages physicians to counsel patients, and their parents when appropriate, that full protective equipment should be worn and appropriate safety measures be taken to prevent in-line skating injuries. Consistent with recommendations of the American Academy of Pediatrics, prevention efforts should include the following: (a) Full protective gear should be worn at all times. This would include wrist guards, elbow pads, kneepads, and a helmet. The helmet should be certified by the ASTM, the ANSI, or the Snell Foundation. (b) Unsafe activities such as hitching or truck surfing, which is latching onto a moving vehicle, should be avoided. (c) Training for beginners should be encouraged, and novice skaters should start in an indoor or outdoor rink rather than on the street. (d) Skaters should not skate in the dark and should learn to look for road debris or defects that could cause them to lose their balance. (e) Skaters, especially children with balance problems, physical disabilities, or uncorrected vision or hearing problems should do so in a rink or another protected place. 2. Our AMA encourages federal agencies and industries to support research on patterns of equipment use and frequency of protective equipment use for in-line skating. 3. Our AMA will continue to work with the Consumer Product Safety Commission, Centers for Disease Control and Prevention, national in-line skating organizations, and medical specialty societies, the AMA Alliance and the Federation to encourage in-line skaters to wear protective equipment. 4. Our AMA encourages medical specialty societies and state and local medical societies to advocate for state and local legislation to improve the safety of in-line skating through: (a) the use of appropriate protective equipment (especially helmets); (b) the designation of protected areas for in-line skating; (c) prohibitions against hitching a ride behind a moving vehicle; (d) the assurance that protective equipment is available at skating rental shops; and (e) the provision of training and educational materials. Such legislation should	Retain; still relevant.

		include a surveillance component to monitor compliance. (CCB/CLRPD Rep. 3, A-14)	
H-10.964	Helmets for Riders of Motorized and Non-motorized Cycles	General Helmet Use: Our AMA: (1) encourages physicians to counsel their patients who ride motorized and non-motorized cycles to use approved helmets and appropriate protective clothing while cycling; (2) encourages patients and families to inform and train children about safe cycle-riding procedures, especially on roads and at intersections, the need to obey traffic laws, and the need for responsible behavior; (3) encourages community agencies, such as those involving law enforcement, schools, and parent-teacher organizations, to promote training programs for the responsible use of cycles; (4) urges manufacturers to improve the safety and reliability of the vehicles they produce and to support measures to improve cycling safety; (5) advocates further research on the effectiveness of helmets and on the health outcomes of community programs that mandate their use; (6) encourages efforts to investigate the impact of helmet use by riders of motorcycles and all bicycles, in order to establish the risk of major medical trauma from not wearing helmets, the costs added to the health care system by such behavior, and the payers of these added costs (i.e., private insurance, uncompensated care, Medicare, Medicaid, etc.); (7) supports the exploration of ways to ensure the wearing of helmets through the use of disincentives or incentives such as licensing fees, insurance premium adjustments and other payment possibilities. Bicycles: Our AMA: (1) actively supports bicycle helmet use and encourages physicians to educate their patients about the importance of bicycle helmet use; (2) encourages the manufacture, distribution, and utilization of safe, effective, and reasonably priced bicycle helmets; and (3) encourages the availability of helmets at the point of bicycle purchase. Scooters: Our AMA: (1) recommends the use of protective gear (certified helmets, elbow and knee pads, closed-toe shoes) for riders of scooters, especially children and adolescents; (2) encourages physicians to counsel patients, and their parents when appropriate, that full protective equipment should be worn and appropriate safety measures should be taken to prevent scooter injuries (e.g., riding away from traffic, and close supervision of riders under the age of eight); and (3) urges companies that manufacture or sell scooters to include appropriate information about the safe use of scooters on the scooters themselves, on or inside scooter packaging, on their web sites, and at the point of sale.	Retain; still relevant.

		Motorcycles: Our AMA: (1) encourages physicians to be aware of motorcycle risks and safety measures and to counsel their patients who ride motorcycles to wear appropriate protective gear and helmets that meet federal safety standards, receive appropriate training in the safe operation of their motorcycle, comply with state licensing laws, and avoid riding a motorcycle while under the influence of alcohol and other drugs; (2) endorses the concept of legislative measures to require the use of helmets when riding or driving a motorcycle; (3) supports federal regulatory rules to make the receipt of federal highway funds by a state dependent on passage of mandatory motorcycle helmet laws by that state; (4) urges constituent societies to support the enactment or preservation of state motorcycle helmet laws; and (5) supports rider education legislation, which is more easily implemented and more effective than legislation requiring manufacturers to emphasize the dangers of operating motorcycles. (CCB/CLRPD Rep. 3, A-14)	
H-120.936	Improve Safety of Mail-Ordered Medication	Our AMA supports the establishment of national guidelines for mail-order pharmacies to ensure that medications reach patients in a safe and timely manner with full potency, and that when medication is damaged or loses potency during shipment, it should be replaced by the pharmacy at no cost to the patient. (Res. 917, A-14)	Retain; still relevant.
H-120.962	National Mail Order Pharmacy Practices	1. The AMA insists that mail-order pharmacy companies respect the prescribing authority of physicians and dispense prescription medications only in the amounts prescribed; and recommends that mail order pharmacy companies charge only a reasonable and small shipping and handling fee per shipment in order not to encourage patients to request amounts of medications greater than those warranted by their physician's best judgment. 2. Our AMA opposes charging patients more than one co-pay for multiple prescriptions of the same or varying doses of a long-term medication within a 90-day period when evidence-based medicine dictates that less than 90-day prescriptions should be written during the initialization and dose stabilization of a newly prescribed long-term medication or during change in dosing of a long-term medication currently being taken. ~~3. Our AMA will make traditional pharmacies, including national chains, mail-order pharmacies, appropriate insurance carriers, and pharmaceutical benefit management companies aware of its policy opposing the charging of patients more than one co-pay for multiple prescriptions of the same or varying doses of a long-term medication within a 90-day period when evidence-based medicine dictates that less than 90-day prescriptions should~~	Retain as amended to remove clause that has been accomplished.

		~~be written during the initialization and dose stabilization of a newly prescribed long-term medication or during change in dosing of a long-term medication currently being taken.~~ (Sub. Res. 506, I-96; Reaffirmed: CSAPH Rep. 3, A-06; Appended: Res. 121, A-07; Reaffirmed: BOT Rep. 8, A-11; Reaffirmation A-14)	
H-120.968	Medication (Drug) Errors in Hospitals	(1) Our AMA encourages individual physicians to minimize medication errors by adhering to the following guidelines when prescribing medications: (a) Physicians should stay abreast of the current state of knowledge regarding optimal prescribing through literature review, use of consultations with other physicians and pharmacists, participation in continuing medical education programs, and other means. (b) Physicians should evaluate the patient's total status and review all existing drug therapy before prescribing new or additional medications (e.g., to ascertain possible antagonistic drug interactions). (c) Physicians should evaluate and optimize patient response to drug therapy by appropriately monitoring clinical signs and symptoms and relevant laboratory data; follow-up and periodically reevaluate the need for continued drug therapy. (d) Physicians should be familiar with the hospital's medication-ordering system, including the formulary system; the drug use review (DUR) program; allowable delegation of authority; procedures to alert nurses and others to new drug orders that need to be processed; standard medication administration times; and approved abbreviations. (e) Written drug or prescription orders (including signatures) should be legible. Physicians with poor handwriting should print or type medication orders if direct order entry capabilities for computerized systems are unavailable. (f) Medication orders should be complete and should include patient name; drug name (generic drug name or trademarked name if a specific product is required); route and site of administration; dosage form (if applicable); dose; strength; quantity; frequency of administration; and prescriber's name. In some cases, a dilution, rate, and time of administration should be specified. Physicians should review all drug orders for accuracy and legibility immediately after they have prescribed them. (g) Medication orders should be clear and unambiguous. Physicians should: (i) write out instructions rather than use nonstandard or ambiguous abbreviations (e.g., write "daily" rather than "qd" which could be misinterpreted as "qid" or "od"); (ii) not use vague instructions, such as "take as directed"; (iii) specify exact dosage strengths	Retain; still relevant.

		(such as milligrams) rather than dosage form units (such as one vial) (an exception would be combination products, for which the number of dosage form units should be specified); (iv) prescribe by standard nomenclature, using the United States Adopted Names (USAN)-approved generic drug name, official name, or trademarked name (if a specific product is required) and avoid locally coined names, chemical names, unestablished abbreviated drug names (e.g., AZT), acronyms, and apothecary or chemical symbols; (v) always use a leading "0" to precede a decimal expression of less than one (e.g., 0.5 ml), but never use a terminal "0" (e.g., 5.0 ml); (vi) avoid the use of decimals when possible (e.g., prescribe 500 mg instead of 0.5 g); (vii) spell out the word "units" rather than writing "u"; (viii) and use the metric system. Instructions with respect to "hold" orders for medications should be clear. (h) Verbal medication orders should be reserved only for those situations in which it is impossible or impractical for the prescriber to write the order or enter it in a computer. Verbal orders should be dictated slowly, clearly, and articulately to avoid confusion. The order should be read back to the prescriber by the recipient (e.g., nurse, pharmacist); when read back, the recipient should spell the drug name and avoid abbreviations when repeating the directions. A written copy of the verbal order should be placed in the patient's medical record and later confirmed by the prescriber in accordance with applicable state regulations and hospital policies. (2) Our AMA encourages the hospital medical staff to take a leadership role in their hospital, and in collaboration with pharmacy, nursing, administration, and others, to develop and improve organizational systems for monitoring, reviewing, and reporting medication errors and, after identification, to eliminate their cause and prevent their recurrence. (BOT Rep. 11, A-94; Reaffirmed by Sub. Res. 508, I-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-120.975	Certifying ~~Indigent~~ Patients Unable to Pay for Pharmaceutical Manufacturers' Free Drug Programs	Our AMA: (1) supports Pharmaceutical Research and Manufacturers of America (PhRMA) programs for ~~indigent~~ patients unable to pay and the development of a universal application process, eligibility criteria and form for all prescription drug patient-assistance programs to facilitate enrollment of patients and physicians; (2) encourages PhRMA to provide information to physicians and hospital medical staffs about member programs that provide pharmaceuticals to ~~indigent~~ patients unable to pay; (3) urges drug companies to develop user-friendly and culturally sensitive uniform centralized policies and procedures for certifying ~~indigent~~	Retain as amended to include person-first language.

		~~patients~~ ~~for~~ free or discounted medications for patients unable to pay; and (4) opposes the practice of charging patients to apply for or gain access to pharmaceutical assistance programs. (Sub. Res. 105, I-92; Sub. Res. 507, A-96; Appended: Sub. Res. 513, I-97; Reaffirmation I-98; Reaffirmation I-00; Reaffirmation A-01; Amended: Res. 513, A-02; Reaffirmed and Appended: Sub. Res. 705, I-03; Reaffimed and Modified: BOT Rep. 13, A-04; Reaffirmation I-04; Modified: CSAPH Rep. 1, A-14)	
H-125.980	Abbreviated Pathway for Biosimilar Approval	Our AMA supports FDA implementation of the Biologics Price Competition and Innovation Act of 2009 in a manner that 1) places appropriate emphasis on promoting patient access, protecting patient safety, and preserving market competition and innovation; 2) includes planning by the FDA and the allocation of sufficient resources to ensure that physicians understand the distinctions between biosimilar products that are considered highly similar, and those that are deemed interchangeable. Focused educational activities must precede and accompany the entry of biosimilars into the U.S. market, both for physicians and patients; and 3) includes compiling and maintaining an official compendium of biosimilar products, biologic reference products, and their related interchangeable biosimilars as they are developed and approved for marketing by the FDA. (Res. 220, A-09; Reaffirmation A-11; Modified: CSAPH Rep. 1, I-11; Modified: CSAPH Rep. 4, A-14)	Retain; still relevant. Note: May be modified by CSAPH5-A-24, "Biosimilar/Interchangeable Terminology.
H-130.936	Tornado Safety and Manufactured Homes	Our AMA believes that: 1. Owners of manufactured home parks should provide a plan, developed with and approved by local authorities, for the evacuation and sheltering of residents of the park in severe weather events such as tornadoes, high winds, or floods. The plan should advise residents of the vulnerability of manufactured homes in tornadoes and other extreme wind events and that evacuation to a safer location is necessary. The shelter or evacuation plan should be posted conspicuously in the park and the park owner should provide each resident with a copy of the approved shelter or evacuation plan. 2. State and local government authorities in regions at increased risk for tornadoes and other extreme wind events should enact measures to either provide, or require owners of manufactured home parks in their jurisdiction to provide, as appropriate, an approved common storm shelter or safe room for all residents of manufactured homes in the park as protection against tornadoes and other extreme wind events. 3. Research is needed to enhance the design and construction of manufactured homes and	Retain; still relevant.

		manufactured home tie down/anchoring systems to withstand extreme wind forces and wind-blown debris. 4. Federal, state, regional, and local authorities should coordinate policies, processes, and procedures to ensure that manufactured homes are installed and inspected in accordance with established guidelines and standards, including requirements for the installation and inspection of tie down/anchoring systems. 5. Incentives should be developed for all homeowners (including those who live in manufactured homes), businesses, and local governments in regions at increased risk for tornadoes and other extreme wind events for the installation of home or community safe rooms and storm shelters, in accordance with federal and professional guidelines and standards. 6. All citizens should consider purchasing a NOAA Weather Radio All Hazards public alert radio for use in disasters and other emergency situations. Citizens also should develop a plan for where they will go and what they will do when a severe weather alert is issued. (CSAPH Rep. 3, I-14)	
H-135.991	Clean Air	(1) The AMA supports setting the national primary and secondary ambient air quality standards at the level necessary to protect the public health. ~~Establishing such standards at the level necessary to protect the public health.~~ Establishing such standards at a level "allowing an adequate margin of safety," as provided in current law, should be maintained, but more scientific research should be conducted on the health effects of the standards currently set by the EPA. (2) The AMA supports continued protection of certain geographic areas (i.e., those with air quality better than the national standards) from significant quality deterioration by requiring strict, but reasonable, emission limitations for new sources. ~~(3) The AMA endorses a more effective hazardous pollutant program to allow for efficient control of serious health hazards posed by airborne toxic pollutants.~~ (43) The AMA believes that more research is needed on the causes and effects of acid rain, and that the procedures to control pollution from another state need to be improved. (5) The AMA believes that attaining the national ambient air quality standards for nitrogen oxides and carbon monoxide is necessary for the long-term benefit of the public health. Emission limitations for motor vehicles should be supported as a long-term goal until appropriate peer-reviewed scientific data demonstrate that the limitations are not required to protect the public health.	Retain as amended. The deleted sentence in first clause is not a complete sentence and does not add value to the policy as written. The third resolve recommended for deletion is redundant with existing and newer AMA policy H-135.949, with the newer resolve having more specific language on encouraging regulations that reduce hazardous emissions.

		(BOT Rep. R, A-82; Reaffirmed: CLRPD Rep. A, I-92; Amended: CSA Rep. 8, A-03; Reaffirmation I-06; Reaffirmed in lieu of Res. 509, A-09; Reaffirmation I-09; Reaffirmation A-14)	
H-145.977	Use of Conducted Electrical Devices by Law Enforcement Agencies	Our AMA: (1) recommends that law enforcement departments and agencies should have in place specific guidelines, rigorous training, and an accountability system for the use of conducted electrical devices (CEDs) that is modeled after available national guidelines; (2) encourages additional independent research involving actual field deployment of CEDs to better understand the risks and benefits under conditions of actual use. Federal, state, and local agencies should accurately report and analyze the parameters of CED use in field applications; and (3) policy is that law enforcement departments and agencies have a standardized protocol developed with the input of the medical community for the evaluation, management and post-exposure monitoring of subjects exposed to CEDs. (CSAPH Rep. 6, A-09; Modified: Res. 501, A-14)	Retain; still relevant.
H-15.950	Child Safety Seats - Public Education and Awareness	Our AMA supports efforts to require child safety seat manufacturers to include information about the importance of rear-facing safety seats until children are ~~two~~ at least four years of age or until they reach the maximum height or weight specifications of their car seat, at which time they should be placed in a forward-facing child safety system with a harness as recommended by the American Academy of Pediatrics. (Res 922, I-14)	Retain as amended to bring the age recommendation in line with current AAP recommendations.
H-15.951	All-Terrain Vehicles	Our AMA: supports publicizing the dangers of all-terrain vehicles, especially to persons unlicensed to drive other vehicles; encourages manufacturers and dealers of ATVs to provide information regarding the safe operation of such vehicles; and seeks federal legislation to require sellers of all-terrain vehicles in the United States to promote the sale and use of suitable helmets to be used when operating or riding as a passenger on ATVs; and federal and state legislation and/or regulation to maximize safety of ATV operation including but not limited to (a) wearing suitable helmets and protective gear when operating or riding as a passenger on an ATV, (b) providing some safety instruction and training to all operators of ATVs, and (c) ensuring appropriate licensure for all operators of ATVs. (CCB/CLRPD Rep. 3, A-14)	Retain; still relevant.
H-15.986	Automatic (i.e., Passive) Restraints to Prevent Injuries and Deaths from Motor Vehicle Accidents	The AMA (1) supports legislation to promote availability of effective seat belts in school buses in the U.S.; and (2) supports legislative action to promote availability of effective seat belts in all motor vehicles in public use (e.g., public and private buses, taxicabs, and any other vehicles carrying passengers).	Retain; still relevant.

		(Sub. Res. 2, A-84; Reaffirmed by CLRPD Rep. 3 - I-94; Reaffirmation A-04; Reaffirmed: BOT Rep. 29, A-04; Modified: CSAPH Rep. 1, A-14)	
H-150.931	Payment for Nutrition Support Services	Our AMA recognizes the value of nutrition support teams services and their role in positive patient outcomes and supports payment for the provision of their services. (Res. 705, A-14)	Retain; still relevant.
H-150.948	Increasing Awareness of Nutrition Information and Ingredient Lists	Our AMA supports ~~federal~~ legislation or rules requiring restaurants, retail food establishments, and vending machine operators that have menu items common to multiple locations, as well as all school and workplace cafeterias, especially those located in health care facilities, to have available for public viewing ingredient lists, nutritional information, and standard nutrition labels for all menu items. (Sub. Res. 411, A-04; Reaffirmation A-07; Reaffirmed in lieu of Res. 413, A-09, Res. 416, A-09 and Res. 418, A-09; Modified: BOT Rep. 1, A-14)	Retain as amended so as not limit legislation to the federal level.
H-155.988	Public Health and Safety Awareness	The AMA believes that attention to personal health and safety can dramatically improve well-being and reduce health care costs. (Res. 42, I-83; Reaffirmed: CLRPD Rep. 1, I-93; Reaffirmed: CMS Rep. 5, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-170.972	Role of Physicians in Improving Adolescent Health	The AMA supports programs that encourage teen health and supports the involvement of medical students, residents, and other physicians in educational efforts to enhance teen health. (Res. 431, A-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Modified: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-170.985	Science, Technology, Engineering and Mathematics Education	Our AMA is committed to working with other concerned organizations and agencies to improve science, technology, engineering and mathematics (STEM) education and literacy in the nation, and to increase interest in STEM on the part of the nation's youth, particularly underrepresented minorities. (Res. 2, A-88; Reaffirmed: Sunset Report, I-98; Modified and Reaffirmed: CSAPH Rep. 2, A-08; Reaffirmed in lieu of Res. 514, A-09; Reaffirmed in lieu of Res. 524, A-09; Modified: Res. 516, A-14)	Retain; still relevant.
H-175.995	Hair Analysis - A Potential for Medical Abuse	The AMA opposes chemical analysis of the hair as a determinant of the need for medical therapy and supports informing the American public and appropriate governmental agencies of this unproven practice and its potential for health care fraud. (Sub. Res. 67, I-84; Reaffirmed by CLRPD Rep. 3 - I-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-245.981	Vitamin K Prophylaxis in Newborn Infants	The AMA supports the intramuscular administration of a single dose of 0.5-1 mg of	Retain; still relevant.

		vitamin K1 in neonates at birth to prevent vitamin K deficiency bleeding. (Res. 514, A-94; Reaffirmed: CSA Rep. 6, A-04; Modified: CSAPH Rep. 1, A-14)	
H-25.994	Increased Liaison, Communication and Educational Efforts with the Elderly	The AMA supports (1) increasing communications and understanding between organized medicine and the elderly; (2) continuing contact with organizations such as the AARP, offering speakers for their meetings, and pursuing other steps to improve their understanding of physicians' problems and concerns; and (3) encouraging state and county medical societies to undertake similar efforts to increase liaison with the elderly. (Res. 133, A-84; Reaffirmed by CLRPD Rep. 3 - I-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-280.962	Dehydration	Evaluation and Management in Older Adults: The policy of the AMA is that undergraduate, graduate and continuing education programs for physicians and allied health professionals be encouraged to teach the science of dehydration in older adults; and that assessment of hydration status and potential for dehydration be incorporated when appropriate in hospital discharge planning, home health agency and nursing home assessments. The AMA: (1) encourages development of programs to increase physician awareness and skills in the evaluation of dehydration in long-term care residents and older adults living in the community setting; (2) encourages a leadership role for physicians as active team participants in long-term care facilities regarding quality assurance programs assessing the hydration status of residents and recommend appropriate reimbursement for those services; (3) encourages development of programs to increase awareness of the potential problem of dehydration in community residents; (4) encourages community nursing facilities that do not provide daily clinical laboratory services to make them available for residents so that necessary data on patient status can be provided promptly, even on a STAT basis. The ready availability of laboratory services could present unnecessary hospitalizations; and (5) encourages the expansion of research efforts in this area. (CSA Rep. 1, A-94; Reaffirmation A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-30.936	Prevention of Impaired Driving	Our AMA: (1) acknowledges that all alcohol consumption, even at low levels, has a negative impact on driver skills, perceptions, abilities, and performance and poses significant health and safety risks; (2) supports 0.04 percent blood-alcohol level as per se illegal for driving, and urges incorporation of that provision in all state drunk	Retain as amended as on-board devices or ignition interlock devices are now well supported by evidence and recommended the Community Preventive Services Task Force (CPSTF) for people who have been convicted of drunk driving.

		driving laws; and (3) supports 21 as the legal drinking age, strong penalties for providing alcohol to persons younger than 21, and stronger penalties for providing alcohol to drivers younger than 21. Education: Our AMA: (1) favors public information and education against any drinking by drivers; (2) supports efforts to educate physicians, the public, and policy makers about this issue and urges national, state, and local medical associations and societies, together with public health, transportation safety, insurance, and alcohol beverage industry professionals to renew and strengthen their commitment to preventing alcohol-impaired driving; (3) encourages physicians to participate in educating patients and the public about the hazards of chemically impaired driving; (4) urges public education messages that now use the phrase "drunk driving," or make reference to the amount one might drink without fear of arrest, be replaced with messages that indicate that "all alcohol use, even at low levels, impairs driving performance and poses significant health and safety risks;" (5) encourages state medical associations to participate in educational activities related to eliminating alcohol use by adolescents; and (6) supports and encourages programs in elementary, middle, and secondary schools, which provide information on the dangers of driving while under the influence of alcohol, and which emphasize that teenagers who drive should drink no alcoholic beverages whatsoever; and will continue to work with private and civic groups such as Mothers Against Drunk Driving (MADD) to achieve those goals. Legislation: Our AMA: (1) supports the development of model legislation which would provide for school education programs to teach adolescents about the dangers of drinking and driving and which would mandate the following penalties when a driver under age 21 drives with any blood alcohol level (except for minimal blood alcohol levels, such as less than .02 percent, only from medications or religious practices): (a) for the first offense - mandatory revocation of the driver's license for one year and (b) for the second offense - mandatory revocation of the driver's license for two years or until age 21, whichever is greater; (2) urges state medical associations to seek enactment of the legislation in their legislatures; (3) urges all states to pass legislation mandating all drivers convicted of first and multiple DUI offenses be screened for alcoholism and provided with referral and treatment when indicated; (4) urges adoption by all states of legislation calling for administrative suspension or revocation of driver licenses after conviction for driving under the influence, and mandatory revocation after a specified number of	

		repeat offenses; and (5) encourages passage of state traffic safety legislation that mandates screening for substance use disorder for all DUI offenders, with those who are identified with substance use disorder being strongly encouraged and assisted in obtaining treatment from qualified physicians and through state and medically certified facilities. Treatment: Our AMA: (1) encourages that treatment of all convicted DUI offenders, when medically indicated, be mandated and provided but in the case of first-time DUI convictions, should not replace other sanctions which courts may levy in such a way as to remove from the record the occurrence of that offense; and (2) encourages that treatment of repeat DUI offenders, when medically indicated, be mandated and provided but should not replace other sanctions which courts may levy. In all cases where treatment is provided to a DUI offender, it is also recommended that appropriate adjunct services should be provided to or encouraged among the family members actively involved in the offender's life; Repeat Offenders: Our AMA: (1) recommends the following measures be taken to reduce repeat DUI offenses: (a) aggressive measures be applied to first-time DUI offenders (e.g., license suspension and administrative license revocation), (b) stronger penalties be leveled against repeat offenders, including second-time offenders, (c) such legal sanctions must be linked, for all offenders, to substance abuse assessment and treatment services, to prevent future deaths in alcohol-related crashes and multiple DUI offenses; and (2) calls upon the states to coordinate law enforcement, court system, and motor vehicle departments to implement forceful and swift penalties for second-time DUI convictions to send the message that those who drink and drive might receive a second chance but not a third. On-board devices: Our AMA: (1) supports ~~further testing of~~ on-board devices or ignition interlock devices to prevent the use of motor vehicles by intoxicated drivers; ~~this testing should take place among the general population of drivers, as well as among drivers having alcohol-related problems;~~ (2) encourages motor vehicle manufacturers and the U.S. Department of Transportation to monitor the development of ignition interlock technology, and plan for use of such systems by the general population, when a consensus of informed persons and studies in the scientific literature indicate the systems are effective, acceptable, reasonable in cost, and safe; and (3) supports continued research and testing of devices which may incapacitate vehicles owned or operated by DUI offenders without needlessly penalizing the offender's family members.	

		(CCB/CLRPD Rep. 3, A-14)	
H-365.978	Adult Film Industry Worker Safety and Health	Our AMA: (1) supports legislation that would require the mandatory use of condoms in the production of adult films; (2) supports legislation that would improve the ability of local health departments and Occupational Safety and Health Administration (OSHA) to investigate and control occupational exposures to infectious diseases and enforce workplace regulations in a timely manner; and (3) urges that existing OSHA and other occupational standards be vigorously enforced to reduce exposure to infectious diseases within the adult film industry. (Res. 407, A-10; Reaffirmation A-14)	Retain; still relevant.
H-370.966	Amend Federal Law to Allow Clinical Research on the Safety and Effectiveness of HIV-Infected-to-HIV-Infected Organ Transplantation	Our AMA adopts a policy position in support of amending the Federal National Organ Transplant Act of 1984 (42 U.S.C. ? 274) to allow for clinical research to fully evaluate the clinical risks and benefits of HIV-infected organ donation to HIV-infected patients who elect to accept such organs and will work to support introduction and enactment of legislation to amend the Federal National Organ Transplant Act of 1984 (42 U.S.C. ? 274) to allow for clinical research to fully evaluate the clinical risks and benefits of HIV-infected organ donation to HIV-infected patients who elect to accept such organs. (Res. 2, I-11; Reaffirmed in lieu of Res. 5, I-14)	Rescind, accomplished. This was accomplished by the HOPE Act, which AMA supported.
H-370.974	Working Toward an Increased Number of Minorities Registered as Potential Bone Marrow Donors	The AMA supports efforts to increase the number of all potential bone marrow donors registered in national bone marrow registries, especially minority donors, to improve the odds of successful HLA matching and bone marrow transplantation. (Res. 501, I-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-440.836	Role of Pharmacists in Improving Immunization Rates	Our AMA believes that: 1. Physicians and medical professional organizations should support state and federal efforts to engage pharmacists in vaccinating target populations that have difficulty accessing immunizations in a medical home. Before administration of a vaccine, pharmacists should assess the immunization status of the patient, which includes checking an immunization registry when one exists. Pharmacists should ensure that a record of vaccine administration is transmitted to the patient's primary care physician and documented in the immunization registry, and that written or electronic documentation is provided to the patient. 2. Vaccination programs in pharmacies should promote the importance of having a medical home to ensure appropriate and comprehensive preventive care, early diagnosis, and optimal therapy. Physicians and pharmacists should work together in the community to: (a) establish referral systems to facilitate appropriate medical care if the	Retain; still relevant.

		patient's conditions or symptoms are beyond the scope of services provided by the pharmacies; and (b) encourage patients to contact a primary care physician to ensure continuity of care. 3. State educational requirements for pharmacists who administer vaccines should be based on ACIP recommendations and recognized standards and guidelines derived with input from physicians and pharmacists with demonstrated expertise in immunization practices. (CSAPH Rep. 4, I-14)	
H-440.837	Reducing Salmonella Outbreaks	Our AMA supports USDA and FDA efforts to improve standards for Salmonella testing and sampling in chicken slaughter facilities and other food processing plants to reduce human Salmonella infection. (Res. 506, A-14)	Retain; still relevant.
H-440.838	Genomic-Based Approaches to the Risk Assessment, Management and Prevention of Type 2 Diabetes	Our AMA encourages continued research into the potential of genomic information to improve risk assessment, management and prevention of type 2 diabetes, and will report back on important advances as appropriate. (CSAPH Rep. 2, A-14)	Retain; still relevant.
H-440.884	Food Allergic Reactions in Schools and Airplanes	Our AMA recommends that all: (1) schools provide increased student and teacher education on the danger of food allergies; (2) schools have a set of emergency food allergy guidelines and emergency anaphylaxis kits on the premises, and that at least one member of the school administration be trained and certified in the indications for and techniques of their use; and (3) commercial airlines have a set of emergency food allergy guidelines and emergency anaphylaxis kits on the premises, and that at least one member of the flight staff, such as the head flight attendant, be trained and certified in the indications for and techniques of their use. (Res. 415, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-440.899	Immunization Registries	Our AMA encourages: (1) physicians to participate in the development of immunization registries in their communities and use them in their practices for patients of all ages; (2) electronic health record (EHR) vendors to add features to automate the exchange of vaccination information in the patient EHR to state immunization registries to improve and help ensure completeness and accuracy of vaccination records. EHR vendors and registry administrators need to work with physicians and other health professionals to facilitate the exchange of needed vaccination information by establishing seamless, bidirectional communication capabilities for physicians, other vaccine providers, and immunization registries; and (3) all states to move rapidly to provide comprehensive lifespan	Retain; still relevant.

		immunization registries that are interfaced with other state registries. (Res. 415, A-99; Reaffirmed: 415, A-01; Reaffirmation A-09; Modified: CSAPH Rep. 4, I-14)	
H-440.919	Toward the Control of E. Coli Infection	The AMA: (1) urges physicians to: (a) familiarize themselves with infection due to E. coli 0157:H7; (b) regularly request culture for this organism in any study of infection associated with bloody diarrheal stools; and (c) expand efforts to educate consumers, food processors, and food handlers about the general importance of proper food handling and preparation; and (2) encourages and supports the continuing efforts of the FDA, and of the U.S. Department of Agriculture and its Food Safety and Inspection Service, to develop new and improved methods and technologies for reducing or eliminating bacterial contamination of meat and meat products for human consumption. (Sub. Res. 509, I-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-440.922	Gambling Disorder~~Can Become Compulsive Behavior~~	The AMA: (1) encourages physicians to advise their patients of the addictive potential of gambling; (2) encourages states which operate gambling programs to provide a fixed percentage of their revenue for education, prevention and treatment of gambling ~~compulsive behavior~~ disorder; and (3) requests that states which operate gambling programs affix to all lottery tickets and display at all lottery counters a sign which states that gambling may become a gambling disorder ~~compulsive behavior~~ and help is available through your local gambling hotline. (Res. 430, A-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain as amended to reflect updated language of the DSM-5-TR, which refers to “gambling disorder.”
H-440.938	Multiple-Drug Resistant Tuberculosis - A Multifaceted Problem	(1) ~~Testing~~ Screening for tuberculous infection should be performed routinely on all HIV-infected patients, according to current recommendations from the CDC ~~U.S. Public Health Service~~. (2) ~~Testing for HIV infection should be routinely performed on all~~ Routine HIV testing is recommended for persons with active tuberculosis. ~~(3) Reporting of HIV infection and tuberculosis should be linked to enhance appropriate medical management and epidemiologic surveillance.~~ (43) Aggressive contact tracing should be pursued for cases of active tuberculosis, especially if HIV-infected contacts or multiple-drug resistant tuberculosis strains have been involved. (~~5~~4) HIV-infected health care workers and their physicians must be aware of the high risk of clinical TB for persons whose immune systems are compromised, due to HIV or other causes. They should be carefully apprised of their risk, and the risks and benefits of their caring for persons with	Retain as amended. Updated terminology for accuracy, including reference of appropriate federal agency.

		active TB or suspected TB should be carefully considered. (~~6~~5) HIV-infected and other immunocompromised patients should be sufficiently separated from tuberculosis patients and the air they breathe so that transmission of infection is unlikely. (~~7~~6) All health care workers should have a tuberculin skin test upon employment, with the frequency of retesting ~~determined by the prevalence of the disease in the community~~ in accordance with CDC recommendations. Individuals with a positive skin test should be evaluated and managed according to current public health service recommendations. (~~8~~7) Health care facilities that treat patients with tuberculosis should rigorously adhere to ~~published public health service~~ CDC guidelines for preventing ~~the nosocomial~~ transmission of tuberculosis. (~~9~~8) Adequate and safe facilities must be available for the care of patients with tuberculosis; in some areas this may necessitate the establishment of ~~sanitariums or other~~ regional centers of excellence in tuberculosis treatment. (~~10~~ 9) Clinical ~~tuberculosis~~ laboratories should develop the capability of reliably performing or having reliably performed for them rapid identification and drug susceptibility tests for tuberculosis. (~~11~~ 10) Routinely, drug susceptibility tests should be performed on isolates from patients with active tuberculosis as soon as possible. (~~12~~ 11) A program of directly observed therapy for tuberculosis is a standard of care ~~should be implemented when patient compliance is a problem~~. (~~13~~ 12) The AMA should enlist the aid of the Pharmaceutical Research and Manufacturers of America (PhRMA) in encouraging manufacturers to develop new drugs and vaccines for tuberculosis. (~~14~~13) The federal government should increase funding significantly for tuberculosis control and research to curtail the further spread of tuberculosis and encourage development of new and effective diagnostics, drug therapies, and vaccines. (~~15~~14) The special attention of physicians, public health authorities, and funding sources should be directed toward high risk and high incidence populations such as the homeless, immigrants, minorities, health care workers in high risk environments, prisoners, children, adolescents, and pregnant people ~~women~~. (~~16~~15) The AMA will develop educational materials for physicians that will include but not be limited to the subtleties of testing for TB in HIV-infected individuals; potential risk to HIV-infected	

		individuals exposed to infectious diseases, including TB; and other issues identified in this report. (~~17~~16) The AMA encourages physicians to remain informed about advances in the treatment of tuberculosis, including the availability of combination forms of drugs, that may reduce the emergence of drug-resistant strains. (BOT Rep. OO, A-92; Sub. Res. 505, I-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-440.942	State Health Officer Report at Annual Meeting of State Medical Society Meetings	The AMA urges each state medical society to extend to their respective state health officer a standing invitation to participate in and report to the annual meeting of their house of delegates upon issues, accomplishments, problems, and needs of public health significance within the state. (Res. 429, I-91; Reaffirmed by Res. 417, I-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-45.976	Drug and Alcohol Use in Aviation	1. Our AMA urges the FAA to establish programs for personnel involved in all facets of aviation that reduce the impact of drug and alcohol use in order to further aviation safety. 2. Our AMA encourages continued studies by the Federal Aviation Administration of problems in the use of alcohol by pilots in general aviation and flight crews of commercial airlines. (CCB/CLRPD Rep. 3, A-14)	Retain; still relevant.
H-460.901	Genomics in Hypertension: Risk Prediction and Treatment	Our AMA encourages continued research on the genetic control of blood pressure, including in pediatric populations, and the development of genomic-based tools that may assist health professionals in better predicting risk and targeting therapy for hypertension, and supports the view that hypertension clinical trial designs should attempt to reduce phenotypic heterogeneity in order to improve the quality and interpretation of results. (CSAPH Rep. 1, I-14)	Retain; still relevant.
H-460.938	Effects of Electric and Magnetic Fields	The AMA: (1) will continue to monitor developments and issues related to the effects of electric and magnetic fields, even though no scientifically documented health risk has been associated with the usually occurring levels of electromagnetic fields; (2) encourages research efforts sponsored by agencies such as the National Institutes of Health, U.S. Department of Energy, and the National Science Foundation to continue on exposures to electromagnetic fields and their effects, average public exposures, occupational exposures, and the effects of field surges and harmonics; and (3) supports broad dissemination of findings and recommendations of authoritative, multidisciplinary committees, such as those convened under the auspices of the National Academy of Sciences, National Council on	Retain; still relevant.

		Radiation Protection, International Agency for Research on Cancer, and the National Institute for Environmental Health Sciences. (CSA Rep. 7 - I-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-460.940	Support for Federal Funding of Early-Stage Embryo Research	The AMA supports federal funding of biomedical research which promises significant human and scientific benefits. (Res. 242, I-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-460.988	Need for Continued Use of Animals in Research and Education	The AMA supports (1) the humane use of animals essential to research, education and the development of drugs and medical devices; and (2) efforts to assure the availability of animals for these purposes. (Res. 140, A-84; Reaffirmed by CLRPD Rep. 3 - I-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-480.949	Nanotechnology, Safety and Regulation	Our AMA: (1) recognizes the benefits and potential risks of nanotechnology; (2) supports responsible regulation of nanomaterial products and applications to protect the public's health and the environment; and (3) encourages continued study on the health and environmental effects of exposure to nanomaterials. (CSAPH Rep. 2, A-13; Reaffirmed in lieu of Res. 510, A-14)	Retain; still relevant.
H-480.975	Patents on Medical and Surgical Procedures	The AMA condemns the patenting of medical and surgical procedures and will work with Congress to outlaw this practice. (Sub. Res. 2, A-94; Reaffirmed: BOT Rep. 29, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-490.910	Secondhand Smoke	1. Our AMA urges the President of the United States to issue an Executive Order making all federal workplaces, including buildings and campuses, entirely smoke free and urges its federation members to do the same. 2. Our AMA supports legislation that prohibits smoking while operating or riding in a vehicle that contains children. (Res. 417, A-09; Appended: Res. 202, A-14)	Retain; still relevant.
H-490.912	Tobacco as an Incentive in Behavior Modification Programs	The AMA condemns the use of tobacco as an incentive in behavior modification programs. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-490.915	Tobacco Use in Prison Populations	It is the policy of our AMA to (1) recognize and promote the policy that all anti-smoking policies that apply to the general population should apply equally to persons who are incarcerated in local jails, state prisons, and federal prisons; (2) work actively to stop the manufacture of cigarettes by any prison or jail system in the United States; (3) work actively to stop the subsidy of cigarette sales in all jail and prison systems; (4) ensure that the prohibition of smoking by minors be enforced in	Retain; still relevant.

		the correctional system; (5) be committed to smoking cessation programs in correctional facilities and encourage physicians working in correctional systems to include smoking cessation counseling and programs for their patients who smoke; (6) work through its representative to the National Commission on Correctional Health Care to ensure that smoking cessation counseling be made a national standard for correctional medicine; (7) develop model legislation providing for smoke-free prison areas for all inmates, and particularly that common areas including cell blocks and recreation areas not be smoking areas; and (8) support legislation banning smoking in prisons and jails. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-495.979	Evaluation of the Health Hazards of Clove Cigarettes	AMA's existing policy vigorously opposing the use of any tobacco product is extended to include explicit opposition to the use of clove cigarettes. Further, AMA recognizes that clove cigarette smoking may present an additional hazard to susceptible individuals. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-495.980	Cigar Smoking	Our AMA will work to have federal and state governments take legal, regulatory, and educational action to protect the public from the ill effects of cigar smoking in a manner similar to those actions taken regarding cigarettes. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-495.982	Tax-Free Tobacco Products	Our AMA encourages Native American nations to stop selling tax-free tobacco products because of the profound public health implications of the sale of tax-free tobacco products. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-495.984	Tobacco Advertising and Media	Our AMA: (1) in keeping with its long-standing objective of protecting the health of the public, strongly supports a statutory ban on all advertising and promotion of tobacco products; (2) as an interim step toward a complete ban on tobacco advertising, supports the restriction of tobacco advertising to a "generic" style, which allows only black-and-white advertisements in a standard typeface without cartoons, logos, illustrations, photographs, graphics or other colors; (3) (a) recognizes and condemns the targeting of advertisements for cigarettes and other tobacco products toward children, minorities, and women as representing a serious health hazard; (b) calls for the curtailment of such marketing tactics; and (c) advocates comprehensive legislation to prevent tobacco companies or other companies promoting look-alike products designed to appeal to children	Retain; still relevant.

		from targeting the youth of America with their strategic marketing programs; (4) supports the concept of free advertising space for anti-tobacco public service advertisements and the use of counter-advertising approved by the health community on government-owned property where tobacco ads are posted; (5) (a) supports petitioning appropriate government agencies to exercise their regulatory authority to prohibit advertising that falsely promotes the alleged benefits and pleasures of smoking as well worth the risks to health and life; and (b) supports restrictions on the format and content of tobacco advertising substantially comparable to those that apply by law to prescription drug advertising; (6) publicly commends those publications that have refused to accept cigarette advertisements and supports publishing annually, via JAMA and other appropriate publications, a list of those magazines that have voluntarily chosen to decline tobacco ads, and circulation of a list of those publications to every AMA member; (7) urges physicians to mark the covers of magazines in the waiting area that contain tobacco advertising with a disclaimer saying that the physician does not support the use of any tobacco products and encourages physicians to substitute magazines without tobacco ads for those with tobacco ads in their office reception areas; (8) urges state, county, and specialty societies to discontinue selling or providing mailing lists of their members to magazine subscription companies that offer magazines containing tobacco advertising; (9) encourages state and county medical societies to recognize and express appreciation to any broadcasting company in their area that voluntarily declines to accept tobacco advertising of any kind; (10) urges the 100 most widely circulating newspapers and the 100 most widely circulating magazines in the country that have not already done so to refuse to accept tobacco product advertisements, and continues to support efforts by physicians and the public, including the use of written correspondence, to persuade those media that accept tobacco product advertising to refuse such advertising; (11) (a) supports efforts to ensure that sports promoters stop accepting tobacco companies as sponsors; (b) opposes the practice of using athletes to endorse tobacco products and encourages voluntary cessation of this practice; and (c) opposes the practice of tobacco companies using the names and distinctive hallmarks of well-known organizations and celebrities, such as fashion designers, in marketing their products;	

		(12) will communicate to the organizations that represent professional and amateur sports figures that the use of all tobacco products while performing or coaching in a public athletic event is unacceptable. Tobacco use by role models sabotages the work of physicians, educators, and public health experts who have striven to control the epidemic of tobacco-related disease; (13) (a) encourages the entertainment industry, including movies, videos, and professional sporting events, to stop portraying the use of tobacco products as glamorous and sophisticated and to continue to de-emphasize the role of smoking on television and in the movies; (b) will aggressively lobby appropriate entertainment, sports, and fashion industry executives, the media and related trade associations to cease the use of tobacco products, trademarks and logos in their activities, productions, advertisements, and media accessible to minors; and (c) advocates comprehensive legislation to prevent tobacco companies from targeting the youth of America with their strategic marketing programs; and (14) encourages the motion picture industry to apply an "R" rating to all new films depicting cigarette smoking and other tobacco use. (CSA Rep. 3, A-04; Appended: Res. 427, A-04; Reaffirmation A-05; Reaffirmation A-14)	
H-500.975	AMA Corporate Policies on Tobacco	(1) Our AMA: (a) continues to urge the federal government to reduce and control the use of tobacco and tobacco products; (b) supports developing an appropriate body for coordinating and centralizing the Association's efforts toward a tobacco-free society; and (c) will defend vigorously all attacks by the tobacco industry on the scientific integrity of AMA publications. (2) It is the policy of our AMA to continue to use appropriate lobbying resources to support programs of anti-tobacco health promotion and advertising. (3) Our AMA's House of Delegates endorses the April 24, 1996, statement by the AMA Secretary-Treasurer that all physicians, health professionals, medical schools, hospitals, public health advocates, and citizens interested in the health and welfare of our children should review their personal and institutional investments and divest of any tobacco holdings (including mutual funds that include tobacco holdings); and specifically calls on all life and health insurance companies and HMOs to divest of any tobacco holdings. (4) Our AMA defines the Tobacco Industry as companies or corporate divisions that directly produce or purchase tobacco for production or market tobacco products, along with their research and lobbying groups, including the Council for Tobacco Research and the Smokeless Tobacco Research Council. A company or corporate	Retain; still relevant.

		division that does not produce or market tobacco products but that has a tobacco producing company as or among its owners will not be considered a prohibited part of the tobacco industry as long as it does not promote or contribute to the promotion, sale and/or use of tobacco products. If such promotional practices begin, the company will be placed on an "unacceptable for support" list. (5) Accordingly, it is the policy of our AMA (a) not to invest in tobacco stocks or accept financial support from the tobacco industry; (b) to urge medical schools and their parent universities to eliminate their investments in corporations that produce or promote the use of tobacco and discourage them from accepting research funding from the tobacco industry; (c) to likewise urge all scientific publications to decline such funded research for publication; and (d) to encourage state and county medical societies and members to divest of any and all tobacco stocks. (6) Our AMA (a) encourages state and local medical societies to determine whether candidates for federal, state and local offices accept gifts or contributions of any kind from the tobacco industry, and publicize their findings to both their members and the public; and (b) urges state and county medical societies and local health professionals along with their allies to support efforts to strengthen state and local laws that require public disclosure of direct and indirect expenditures to influence legislation or ordinances, given recent allegations about tobacco industry strategies. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-505.962	Smoking on International Flights	The AMA (1) will join other concerned organizations to seek an FAA ban on smoking on all flights originating from or destined to the U.S.; and (2) in conjunction with the World Health Organization and the World Medical Association, will work with the medical department of the International Civil Aviation Organization to ban smoking on all international flights. (CSA Rep. 3, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Rescind, accomplished. Smoking is banned on international flights.
H-505.963	Federal Efforts Related to Smoking Cessation	Our AMA ~~endorses~~ supports the use of the federally-funded National Tobacco Quitline network and ongoing media campaigns to help Americans quit using tobacco. (CSA Rep. 3, A-04; Modified: CSAPH Rep. 1, A-14)	Retain as amended.
H-55.970	Uniform Cancer Staging	Our AMA (1) supports the tumor, node involvement, metastasis (TNM) system accepted by the American Joint Committee on Cancer and the Union for International Cancer Control for staging of cancer; (2) urges that this system be used in any published articles or information and be	Retain; still relevant.

		included as a requirement in Instructions to Authors; (3) encourages each state association to use this system in any educational forum or scientific meeting which it sponsors; and (4) supports general utilization of the Cancer Staging Manual developed by the American Joint Committee on Cancer. (CCB/CLRPD Rep. 3, A-14)	
H-55.972	Early Detection and Prevention of Skin Cancer	Our AMA: (1) encourages all physicians to (a) perform skin self-examinations and to examine themselves and their families on the first Monday of the month of May, which is designated by the American Academy of Dermatology as Melanoma Monday; (b) examine their patients' skins for the early detection of melanoma and nonmelanoma skin cancer; (c) urge their patients to perform regular self-examinations of their skin and assist their family members in examining areas that may be difficult to examine; and (d) educate their patients concerning the correct way to perform skin self-examination; (2) supports mechanisms for the education of lay professionals, such as hairdressers and barbers, on skin self-examination to encourage early skin cancer referrals to qualified health care professionals; and (3) supports and encourages prevention efforts to increase awareness of skin cancer risks and sun-protective behavior in communities of color. Our AMA will continue to work with the American Academy of Dermatology, National Medical Association and National Hispanic Medical Association and public health organizations to promote education on the importance of skin cancer screening and skin cancer screening in patients of color. (CCB/CLRPD Rep. 3, A-14)	Retain; still relevant.
H-60.923	Meningococcal Vaccination for School Children	Our AMA supports efforts to require that school children receive meningococcal vaccine ~~per~~ as recommended by the Advisory Committee on Immunization Practices guidelines. (Res. 414, A-14)	Retain as amended. The Advisory Committee on Immunization Practices recommends vaccines for use in the population but does not make decisions on school requirements.
H-60.938	Adolescent Sexual Activity	Our AMA (a) ~~endorses the joint position "Protecting Adolescents: Ensuring Access to Care and Reporting Sexual Activity and Abuse"; and (b)~~ supports the following principles for consideration in development of public policy: (i) Sexual activity and sexual abuse are not synonymous and that many adolescents have consensual sexual relationships; (ii) It is critical that adolescents who are sexually active receive appropriate confidential health care and screening; (iii) Open and confidential communication between the health professional and adolescent patient, together with careful clinical assessment, can identify the majority of sexual abuse cases; (iv) Physicians and other health care professionals must know their state laws and report cases of sexual abuse to the	Retain as amended to remove language endorsing a specific joint position statement, while retaining the principles.

		proper authority in accordance with those laws, after discussion with the adolescent and/or parent as appropriate; (v) Federal and state laws should support physicians and other health care professionals in their role in providing confidential health care to their adolescent patients; and (vi) Federal and state laws should affirm the authority of physicians and other health care professionals to exercise appropriate clinical judgment in reporting cases of sexual activity. (Res. 825, I-04; Modified: CSAPH Rep. 1, A-14)	
H-60.979	Physical Activity Guidelines	Our AMA supports the continued expert review and development of national guidelines regarding physical activity for all ages and the dissemination of such guidelines to physicians. (Res. 186, I-90; Reaffirmed: Sunset Report, I-00; Modified: BOT Rep. 10, A-14)	Retain; still relevant.
H-60.996	Missing Children Identification	The AMA supports (1) development of a means of identifying children; and (2) education of the public and parents on the fingerprinting and documentation of characteristic identifying marks as a matter of record, should it be necessary to assist officials in locating a missing child. (Res. 98, A-84; Reaffirmed by CLRPD Rep. 3 - I-94; Reaffirmed: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain; still relevant.
H-75.985	Access to Emergency Contraception	It is the policy of our AMA: (1) that physicians and other health care professionals should be encouraged to play a more active role in providing education about emergency contraception, including access and informed consent issues, by discussing it as part of routine family planning and contraceptive counseling; (2) to enhance efforts to expand access to emergency contraception, including making emergency contraception pills more readily available through pharmacies, hospitals, clinics, emergency rooms, acute care centers, and physicians' offices; (3) to recognize that information about emergency contraception is part of the comprehensive information to be provided as part of the emergency treatment of sexual assault victims and/or survivors; (4) to support educational programs for physicians and patients regarding treatment options for the emergency treatment of sexual assault victims and/or survivors, including information about emergency contraception; and (5) to encourage writing advance prescriptions for these pills as requested by their patients until the pills are available over-the-counter. (CMS Rep. 1, I-00; Appended: Res. 408, A-02; Modified: Res. 443, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	Retain as amended to reference updated terminology.
H-75.991	Requirements or Incentives by Government for the Use of Long-	(1) Involuntary use of long-acting contraceptives because of child abuse raises serious questions about a person's fundamental right to refuse medical treatment, to be free of cruel and unusual	Retain as amended to update terminology.

	Acting Contraceptives	punishment, and to procreate. The state's compelling interest in protecting children from abuse may be served by less intrusive means than imposing contraception on parents who have committed child abuse. The needs of children may be better met by providing close supervision of the parents, appropriate treatment and social services, and foster placement care when necessary. There is not sufficient evidence to demonstrate that long-acting contraceptives are an effective social response to the problem of child abuse. Before long-acting contraceptives could be considered as a response to individual cases of child abuse, the issue would need to be addressed by society broadly. Society must be careful about taking shortcuts to save resources when constitutional rights are involved. (2) Serious questions are raised by plea bargains, or negotiations with child welfare authorities, that result in the use of long-acting contraceptives. Such agreements are made in inherently coercive environments that lack procedural safeguards. In addition, cultural and other biases may influence decisions by the state to seek the use of a long-acting contraceptive. (3) If welfare or other government benefits were based on the use of long-acting contraceptive agents, individuals would be required to assume a potentially serious health risk before receiving their benefits. Government benefits should not be made contingent on the acceptance of a health risk. (4) Individuals should not be denied access to effective contraception because of their inability to pay ~~indigence~~. Use of long-acting contraceptives should be covered by Medicaid and other health insurance programs, both public and private. (5) Long-acting contraceptives may be medically contraindicated. Assessing the health risks of long-acting contraceptives is substantially outside the purview of courts and legislatures. (BOT Rep. EE, I-91; Reaffirmed: Sunset Report, I-01; Reaffirmation A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-80.996	Scientific Status of Refreshing Recollection by the Use of Hypnosis	The AMA believes that (1) With witnesses and victims concerning refreshing recollection, the use of hypnosis should be limited to the investigative process. Specific safeguards should be employed to protect the welfare of the subject and the public, and to provide the kind of record that is essential to evaluate the additional material obtained during and after hypnosis; (2) A psychological assessment of the subject's state of mind should be carried out prior to the induction of hypnosis in an investigative context, and informed consent should be obtained; (3) Hypnosis should be conducted by a skilled psychiatrist or psychologist, who is aware of the legal implications of the use of hypnosis for	Retain; still relevant.

		investigative purposes; a complete taped and/or precise written record of the clinician's prior knowledge of the case must be made; complete videotape recordings of the pre-hypnotic evaluation and history, the hypnotic session, and the post-hypnotic interview, showing both the subject and the hypnotist, should be obtained; (4) Ideally, only the subject and the psychiatrist or psychologist should be present; (5) Some test suggestions of known difficulty should be given to provide information about the subject's ability to respond to hypnosis; (6) The subject's response to the termination of hypnosis and the post-hypnotic discussion of the experience of hypnosis are of major importance in discussing the subject's response; (7) Medical responsibility for the health and welfare of the subject cannot be abrogated by the investigative intent of hypnosis; and (8) Continued research should be encouraged. (CSA Rep. K, I-84; Reaffirmed: CSA Rep. 5, A-94; Reaffirmed by CLRPD Rep. 3 - I-94; Reaffirmed and Modified: CSA Rep. 6, A-04; Reaffirmed: CSAPH Rep. 1, A-14)	
H-85.953	Improving Death Certification Accuracy and Completion	1. Our AMA: (a) acknowledges that the reporting of vital events is an integral part of patient care; (b) urges physicians to ensure completion of all state vital records carefully and thoroughly with special attention to the use of standard nomenclature, using legible writing and accurate diagnoses; and (c) supports notifying state medical societies and state departments of vital statistics of this policy and encouraging their assistance and cooperation in implementing it. 2. Our AMA also: (a) supports the position that efforts to improve cause of death statistics are indicated and necessary; (b) endorses the concept that educational efforts to improve death certificates should be focused on physicians, particularly those who take care of patients in facilities where patients are likely to die, namely in acute hospitals, nursing homes and hospices; and (c) supports the concept that training sessions in completion of death certificates should be (i) included in hospital house staff orientation sessions and clinical pathologic conferences; (ii) integrated into continuing medical education presentations; (iii) mandatory in mortality conferences; and (iv) included as part of in-service training programs for nursing homes, hospices and geriatric physicians. 3. Our AMA further: (a) promotes and encourages the use of ICD codes among physicians as they complete medical claims, hospital discharge summaries, death certificates, and other documents; (b) supports cooperating with the National Center for Health Statistics (NCHS) in monitoring the four existing models for collecting tobacco-use data; (c) urges the NCHS to identify	Retain; still relevant.

		appropriate definitions, categories, and methods of collecting risk-factor data, including quantification of exposure, for inclusion on the U.S. Standard Certificates, and that subsequent data be appropriately disseminated; and (d) continues to encourage all physicians to report tobacco use, exposure to environmental tobacco smoke, and other risk factors using the current standard death certificate format. (CCB/CLRPD Rep. 3, A-14; Modified: Speakers Rep., A-15)	
H-90.970	Disabled Parking	Our AMA: (1) encourages physicians to become familiar with laws in their states for certifying a patient's need for disabled parking privileges; and (2) supports efforts to educate the public on the appropriate use of parking spaces for the disabled. (CCB/CLRPD Rep. 3, A-14)	Retain; still relevant.

2. COMPARATIVE EFFECTIVENESS RESEARCH

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See Policies H-120.988, H-450.922 and H-460.909

INTRODUCTION

American Medical Association (AMA) Policy H-450.922, "Comparative Effectiveness Research," as adopted at A-23 asked that "our American Medical Association study the feasibility of including comparative effectiveness studies in various FDA drug regulatory processes, including comparisons with existing standard of care, available generics and biosimilars, and drugs commonly used off-label and over-the-counter." This report serves as the Council on Science and Public Health's response to this charge.

METHODS

English language articles were selected from searches of PubMed and Google Scholar using the search terms "comparative effectiveness research" and "comparative effectiveness research AND regulation." Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by government agencies and applicable organizations were also reviewed for relevant information.

BACKGROUND

Comparative effectiveness research (CER) is defined by the National Academy of Medicine as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care."[1] At the simplest level, CER shifts the clinical research question from "is this safe?" and "does this work?" to "is this better?". The question posed by the original resolution thus becomes whether the U.S. Food and Drug Administration (FDA) should ask sponsors to prove their new drug (or device) is superior to existing options on the market as a part of the regulatory process – either pre- or post-market approval.

The AMA has published several previous reports detailing the benefits of CER (including Council on Medical Service (CMS) Report 5-I-16 and CMS Report 4-I-19) and include a thorough list of principles the AMA holds for a federally funded CER entity. Briefly, these reports were focused on the incorporation of value into the pricing of

pharmaceuticals, which include utilizing CER to better understand the long-term cost of a treatment compared to its alternatives. As such, this report will focus solely on the use of CER in the regulatory context.

DISCUSSION

The Authority of the FDA

Under the Food, Drug and Cosmetics Act, the FDA assesses new drug applications for two criteria: safety and efficacy.[2] Within those criteria, however, the FDA commonly assesses new drug applications in the context of the disease state and the drug landscape.[3] Per the FDA's Guidance for Industry, the risk-benefit analysis for new drug applications includes the following criteria: (1) analysis of the condition, (2) current treatment options, (3) benefit, and (4) risk and risk management.[4] A new drug may be known to have serious side effects and toxicity, but if it is used to treat a terminal disease with no currently available treatment, the risk-benefit analysis by the FDA and its advisory committees may support approval. For example, the FDA advisory committee evaluating Trogarzo (ibalizumab-uiyk) for the treatment of multi-drug resistant HIV found that the underlying clinical trial design resulted in difficulty assessing the durability of the drug's effectiveness.[5] However, given the limited options for this high-need population, the advisory committee found this uncertainty to be tolerable, and ultimately recommended approval.

Under the current regulatory framework, the most common method to demonstrate efficacy and safety is through placebo-controlled studies. Using this model, researchers seek to prove that their new drug is efficacious by having beneficial outcomes compared to a placebo (passive control). By contrast, a CER approach for medications (or devices) may measure superiority, non-inferiority, or equivalence. CER requires an active control, in which outcomes of the agent are compared to a proven, efficacious treatment rather than being compared to placebo.[6,7] It should be noted that CER of active control superiority, non-inferiority, and equivalence studies are all routinely utilized by the FDA in approval decisions in the current regulatory framework, most commonly in instances where a placebo-controlled study may be unethical to perform.

Re-labeling Generic Drugs

CER is commonly used for evaluating the efficacy of off-label applications for drugs, as they may not have placebo-controlled clinical trials supporting off-label use.[8-10] One of the potential results of CER in this context is that non-inferiority trials may result in the re-labeling of drugs to expand approved indications. For example, lenvatinib (trade name Lenvima) was first granted orphan drug status in 2012 for treating thyroid cancer, but later had its approved indications revised by the FDA to include first-line treatment of unresectable hepatocellular carcinoma after a non-inferiority trial was performed comparing lenvatinib and sorafenib.[11]

The issue, however, comes down to which drugs are selected for evaluation and ultimately submitted for re-labeling. In the instance of lenvatinib, which is still under patent, the non-inferiority trial was sponsored by the patent holder and pharmaceutical company, Eisai.[12] Seeking labeling changes for off patent products, like generic medicines or medical devices, with no industry sponsor is much rarer due to the lack of financial incentive. One example of the difficulties in updating the labeling for a generic medicine is metformin, a first-line treatment for type 2 diabetes. In this instance, concerns over elevated rates of lactic acidosis resulted in the initial 1994 labeling having a contraindication of metformin in patients with elevated creatine levels.[13] By the mid-2000s, however, evidence suggested that this adverse event was rare, and lactic acidosis incidence rates in patients with diabetes receiving metformin were similar to those not receiving metformin.[14] Despite this evidence, it took four years and two citizen petitions by a group of physician experts and academic partners to get partial updates to the labeling of metformin.[13] Given the additional level of effort and advocacy required, using research (CER or otherwise) to inform updates in labeling of generic drugs is exceedingly rare and burdensome.
The AMA vigorously supports the physician's ability to exercise clinical judgement and prescribe medications off-label, yet the inclusion (or exclusion) of indications and contraindications in the FDA labeling can have significant ramifications on clinical uptake of medications and coverage by insurers.[15-18]

Novel Drug Submissions

Perhaps more nuanced is the potential role of CER in new drug applications and approvals, and whether the FDA should consider if a new drug is superior to what already exists on the market before granting approval. Proponents

argue that this approach has multiple benefits to the system, gives patients and physicians a better understanding of which medications to prioritize in treatment plans, incentivizes research into understudied diseases, disincentivizes advertising which conflates newness with effectiveness, and reduces the financial burden on government entities to fund post-market CER trials.[19]

A common example of how CER could have been used in the approvals process is the case of esketamine. Ketamine, which was originally approved by the FDA for as an anesthetic in 1970, has received attention for use in treatment-resistant depression (TRD).[20] Under normal chemical synthesis conditions, ketamine is made up of a 50:50 mixture of the enantiomers (R)-ketamine and (S)-ketamine (also known as esketamine). In 2019, Janssen received FDA approval for a nasal spray for TRD treatment that comprised of pure esketamine (i.e., no (R)-ketamine), under the trade name Spravato.[21] Esketamine was approved for TRD utilizing a placebo-controlled study, in which esketamine performance was found to be effective compared to placebo.[22,23]

Since its approval, however, esketamine has not been found to be superior to ketamine.[24] What is different, though, is their price. Esketamine is an on-patent medication, and as such was estimated by the Institute for Clinical and Economic Review to cost approximately $39,000/year compared to $5,300/year for generic ketamine.[25] However, due to other factors such as insurance reimbursement and manufacturer rebates, some studies found that patients may pay less out-of-pocket for esketamine, thus driving them towards the product which generates the most profit for the pharmaceutical company.[26]

However, this is ultimately not an issue for the FDA to adjudicate. Deviation from the FDA's role of evaluating "is it safe?" and "is it effective?" would be a radical expansion of scope and would likely endanger the ability for new medications to enter the market. As described above, the FDA already evaluates new drugs or devices within the context of available treatments and the severity of the disease.

Instead, the case of esketamine/ketamine further highlights the importance of AMA's advocacy efforts to make sure patients have access and insurance coverage to all medications that are deemed appropriate by their physician, whether they are prescribed for off-label indications or not. Esketamine and ketamine, while similar, have different administration routes and side effect profiles. As such, having both available in the physician's toolbox allows for the patient-physician relationship to be the guide to the treatment plan.

Additionally, "is it better?" may be a difficult bar to quantify, particularly for use cases with high levels of heterogeneity. For example, the addition of a zipper to a new medical device may not directly result in improved outcomes for patients, but a physician may appreciate the option. There are also questions as to for *whom* these new medications or devices need to be better. As noted above, esketamine may be more accessible for individuals who are averse to needles or otherwise unable to receive an infusion. Similarly, a new device may make modifications to allow for easier implantation by a physician with a dexterity impairment, but not impact patient care. It is unclear how CER could effectively capture these important use-cases in which innovation and choice is beneficial, but not measurable by clinical outcomes.

Finally, a requirement to prove that new medicines are better than current options may inadvertently isolate patient populations and make health inequities harder to overcome. For example, clopidogrel is an anti-platelet medicine commonly used for reducing the risk of stroke and heart attack. It is available as a generic medicine, taken orally, and is cheap, highly effective, and well-studied.[27] As such, it may be difficult for any new competing medication to become approved if it were required to prove superiority to clopidogrel, placing some patients at a disadvantage. Alternatives to clopidogrel are incredibly important to individuals with CYP2C19 genetic mutations, which can make them either hyper- or hypo-metabolizers of clopidogrel, leading to reduced efficacy or increased side effects, respectively.[28] CYP2C19 mutations are more prevalent in individuals of Asian and African ancestry.[29]

The pharmacogenomic response to clopidogrel is well-known and has resulted in an FDA black box warning on its label.[30] As such, one could imagine that CER for the purposes of a clopidogrel alternative could instead focus on its performance in relevant CYP2C19 genotypes. But this difference in response was not always known (the black box warning was added 13 years after approval), and there are likely an incalculable number of genetic mutations that influence drug interactions that are yet to be known and considered in prospective CER.

CURRENT AMA POLICY

As described above, the AMA has a long history of supporting off-label prescribing and reimbursement. Per Policy H-120.988, "Patient Access to Treatments Prescribed by Their Physicians," "[o]ur AMA confirms its strong support for the autonomous clinical decision-making authority of a physician and that a physician may lawfully use an FDA approved drug product or medical device for an off-label indication when such use is based upon sound scientific evidence or sound medical opinion; and affirms the position that, when the prescription of a drug or use of a device represents safe and effective therapy, third party payers, including Medicare, should consider the intervention as clinically appropriate medical care, irrespective of labeling, should fulfill their obligation to their beneficiaries by covering such therapy, and be required to cover appropriate 'off-label' uses of drugs on their formulary."

Additionally, per Policy H-460.909, "Comparative Effectiveness Research," the AMA broadly supports well-funded, scientifically rigorous CER entities, with two highlighted principles: "[t]he CER entity must not have a role in making or recommending coverage or payment decisions for payers," and "[p]hysician discretion in the treatment of individual patients remains central to the practice of medicine. CER evidence cannot adequately address the wide array of patients with their unique clinical characteristics, co-morbidities and certain genetic characteristics. In addition, patient autonomy and choice may play a significant role in both CER findings and diagnostic/treatment planning in the clinical setting."

CONCLUSION

Comparative effectiveness research is a critical tool for helping physicians give patients the highest quality, most affordable care possible. However, it may not be the most effective tool for determining what drugs should be available on the market. Instead of using CER as a regulatory requirement, it is likely better suited to be used as a tool for bringing affordable, effective medications to patients.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted and the remainder of the report be filed:

(1) That policy H-450.922, "Comparative Effectiveness Research" be amended by deletion to read as follows:
Our AMA will:
~~(1) study the feasibility of including comparative effectiveness studies in various FDA drug regulatory processes, including comparisons with existing standard of care, available generics and biosimilars, and drugs commonly used off-label and over-the-counter; and~~
~~(2)~~ (1) ask the National Institutes of Health to support and fund comparative effectiveness research for approved drugs, including comparisons with existing standard of care, available generics and biosimilars, and drugs commonly used off-label and over-the-counter.

(2) That policies H-120.988, "Patient Access to Treatments Prescribed by Their Physicians", and H-460.909, "Comparative Effectiveness Research" be reaffirmed.

(3) That our AMA support efforts to encourage and incentivize premarket comparative effectiveness research comparing emerging medications to existing treatment options to increase transparency about a treatment's efficacy once approved.

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APPENDIX - RELEVANT AMA POLICY

Patient Access to Treatments Prescribed by Their Physicians H-120.988
1. Our AMA confirms its strong support for the autonomous clinical decision-making authority of a physician and that a physician may lawfully use an FDA approved drug product or medical device for an off-label indication when such use is based upon sound scientific evidence or sound medical opinion; and affirms the position that, when the prescription of a drug or use of a device represents safe and effective therapy, third party payers, including Medicare, should consider the intervention as clinically appropriate medical care, irrespective of labeling, should fulfill their obligation to their beneficiaries by covering such therapy, and be required to cover appropriate 'off-label' uses of drugs on their formulary.
2. Our AMA strongly supports the important need for physicians to have access to accurate and unbiased information about off-label uses of drugs and devices, while ensuring that manufacturer-sponsored promotions remain under FDA regulation.
3. Our AMA supports the dissemination of generally available information about off-label uses by manufacturers to physicians. Such information should be independently derived, peer reviewed, scientifically sound, and truthful and not misleading. The information should be provided in its entirety, not be edited or altered by the manufacturer, and be clearly distinguished and not appended to manufacturer-sponsored materials. Such information may comprise journal articles, books, book chapters, or clinical practice guidelines. Books or book chapters should not focus on any particular drug. Dissemination of information by manufacturers to physicians about off-label uses should be accompanied by the approved product labeling and disclosures regarding the lack of FDA approval for such uses, and disclosure of the source of any financial support or author financial conflicts.
4. Physicians have the responsibility to interpret and put into context information received from any source, including pharmaceutical manufacturers, before making clinical decisions (e.g., prescribing a drug for an off-label use).
5. Our AMA strongly supports the addition to FDA-approved labeling those uses of drugs for which safety and efficacy have been demonstrated.
6. Our AMA supports the continued authorization, implementation, and coordination of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act.

Comparative Effectiveness Research D-460.973
Our AMA will solicit from our members and others articles or postings about current clinical topics where comparative effectiveness research should be conducted and will periodically invite AMA members to recommend topics where the need for comparative effectiveness research is most pressing, and the results will be forwarded to the Patient-Centered Outcomes Research Institute (PCORI) once it is established, or to another relevant federal agency.
Res. 221, A-11. Reaffirmed: BOT Rep. 7, A-21

Comparative Effectiveness Research H-460.909
The following Principles for Creating a Centralized Comparative Effectiveness Research Entity are the official policy of our AMA:
PRINCIPLES FOR CREATING A CENTRALIZED COMPARATIVE EFFECTIVENESS RESEARCH ENTITY:
A. Value. Value can be thought of as the best balance between benefits and costs, and better value as improved clinical outcomes, quality, and/or patient satisfaction per dollar spent. Improving value in the US health care system will require both clinical and cost information. Quality comparative clinical effectiveness research (CER) will improve health care value by enhancing physician clinical judgment and fostering the delivery of patient-centered care.
B. Independence. A federally sponsored CER entity should be an objective, independent authority that produces valid, scientifically rigorous research.
C. Stable Funding. The entity should have secure and sufficient funding in order to maintain the necessary infrastructure and resources to produce quality CER. Funding source(s) must safeguard the independence of a federally sponsored CER entity.

D. Rigorous Scientifically Sound Methodology. CER should be conducted using rigorous scientific methods to ensure that conclusions from such research are evidence-based and valid for the population studied. The primary responsibility for the conduct of CER and selection of CER methodologies must rest with physicians and researchers.
E. Transparent Process. The processes for setting research priorities, establishing accepted methodologies, selecting researchers or research organizations, and disseminating findings must be transparent and provide physicians and researchers a central and significant role.
F. Significant Patient and Physician Oversight Role. The oversight body of the CER entity must provide patients, physicians (MD, DO), including clinical practice physicians, and independent scientific researchers with substantial representation and a central decision-making role(s). Both physicians and patients are uniquely motivated to provide/receive quality care while maximizing value.
G. Conflicts of Interest Disclosed and Minimized. All conflicts of interest must be disclosed and safeguards developed to minimize actual, potential and perceived conflicts of interest to ensure that stakeholders with such conflicts of interest do not undermine the integrity and legitimacy of the research findings and conclusions.
H. Scope of Research. CER should include long term and short term assessments of diagnostic and treatment modalities for a given disease or condition in a defined population of patients. Diagnostic and treatment modalities should include drugs, biologics, imaging and laboratory tests, medical devices, health services, or combinations. It should not be limited to new treatments. In addition, the findings should be re-evaluated periodically, as needed, based on the development of new alternatives and the emergence of new safety or efficacy data. The priority areas of CER should be on high volume, high cost diagnosis, treatment, and health services for which there is significant variation in practice. Research priorities and methodology should factor in any systematic variations in disease prevalence or response across groups by race, ethnicity, gender, age, geography, and economic status.
I. Dissemination of Research. The CER entity must work with health care professionals and health care professional organizations to effectively disseminate the results in a timely manner by significantly expanding dissemination capacity and intensifying efforts to communicate to physicians utilizing a variety of strategies and methods. All research findings must be readily and easily accessible to physicians as well as the public without limits imposed by the federally supported CER entity. The highest priority should be placed on targeting health care professionals and their organizations to ensure rapid dissemination to those who develop diagnostic and treatment plans.
J. Coverage and Payment. The CER entity must not have a role in making or recommending coverage or payment decisions for payers.
K. Patient Variation and Physician Discretion. Physician discretion in the treatment of individual patients remains central to the practice of medicine. CER evidence cannot adequately address the wide array of patients with their unique clinical characteristics, co-morbidities and certain genetic characteristics. In addition, patient autonomy and choice may play a significant role in both CER findings and diagnostic/treatment planning in the clinical setting. As a result, sufficient information should be made available on the limitations and exceptions of CER studies so that physicians who are making individualized treatment plans will be able to differentiate patients to whom the study findings apply from those for whom the study is not representative.
CMS Rep. 5, I-08. Reaffirmed: Res. 203, I-09. Reaffirmation I-10. Reaffirmed: CMS Rep. 05, I-16. Reaffirmed: CMS Rep. 4, I-19.

3. SUPPORT FOR EVIDENCE-BASED USE OF BMI AS A MEASURE IN MEDICINE

Reference committee hearing: see report of Reference Committee D.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
TITLE CHANGED
REMAINDER OF REPORT FILED
See Policy H-440.797

INTRODUCTION

At the 2023 Annual Meeting of the American Medical Association (AMA) House of Delegates, Council on Science and Medicine (CSAPH) Report 7-A-23, "Support Removal of BMI as a Standard Measure in Medicine and Recognizing Culturally-Diverse and Varied Presentations of Eating Disorders," was adopted as amended, though the following recommendations were referred for study:

That our AMA recognizes:
(6) that in some clinical circumstances Body Mass Index (BMI) may have utility and that BMI > 35 should continue to be used for risk stratification.
(7) that BMI is a useful tool for population level surveillance of obesity trends due to its ease of use and low risk for application inconsistencies.
(8) that BMI is useful as an initial screener for metabolic health risks. (New HOD Policy)

BACKGROUND

CSAPH Report 7-A-232, which evaluated the problematic history of BMI and explored other alternatives to BMI, outlined the harms and benefits to using BMI and concluded that BMI is inaccurate in measuring body fat in multiple groups because it does not account for the heterogeneity across race/ethnic groups, sexes, and age-span. The report's recommendations recognized the issues with the use of BMI clinically and highlighted the need to use other methods. This report is a follow-up to that report which will focus on studying the recommendations noted above to assess if the evidence supports the inclusion of these recommendations into AMA policy.

METHODS

English language articles will be selected from searches of PubMed and Google Scholar using the search terms "Body Mass Index (BMI)", "BMI over 35 AND clinical utility", "BMI AND obesity trends", and "BMI AND metabolic health risks". Additional articles will be identified by manual review of the reference lists of pertinent publications. Web sites managed by government agencies and applicable organizations will also be reviewed for relevant information.

DISCUSSION

Ideally, an obesity classification system would be based on a practical measurement widely available to clinicians regardless of their setting, would accurately predict health risk (prognosis), and could be used to assign treatment strategies and goals.[1] The most accurate measures of body fat adiposity such as underwater weighing, dual-energy x-ray absorptiometry (DEXA) scanning, computed tomography (CT), and magnetic resonance imaging (MRI) are impractical for use in everyday clinical encounters.[1] Estimates of body fat, including body mass index (BMI, calculated by dividing the body weight in kilograms by height in meters squared) and waist circumference, have limitations compared to these imaging methods, but still provide relevant information and are easily obtained in a variety of practice settings.[1] Although BMI does not directly measure body fat, its utility as a risk estimate has been demonstrated in multiple population studies.[2–5] However, in some instances, the use of BMI as a surrogate measure of body fat may lead to an incorrect estimation of risk.[3,6] The inherent problems with using BMI alone to estimate risk is exemplified by the obesity paradox, the observed inverse correlation between BMI and mortality in patients with existing chronic heart failure, coronary heart disease, and chronic kidney disease.[3,7,8] However, it should be noted that the obesity paradox is not observed among people with very low BMI (<18.5) and very high (BMI >40.0). Although reasons for the obesity paradox remain uncertain, proposed confounding factors include the poor

sensitivity of BMI to detect excess adiposity versus lean muscle mass, body fat distribution, and the independent contribution of fitness.[3,9–11]

Further, the current BMI classification system is misleading regarding the effects of body fat mass on mortality rates.[1,12] Numerous comorbidities, lifestyle issues, gender, ethnicities, medically significant familial-determined mortality effectors, duration of time one spends in certain BMI categories, and the expected accumulation of fat with aging are likely to significantly affect interpretation of BMI data, particularly in regard to morbidity and mortality rates.[12] Such confounders as well as the known clustering of obesity in families, the strong role of genetic factors in the development of obesity, the location in which excessive fat accumulates, its role in the development of type 2 diabetes and hypertension, and so on, need to be considered when being applied to the general population.[12,13]

Should BMI >35.0 be used for risk stratification?

Currently, a BMI of 25.0 – 29.9 in the United States represents individuals who have "overweight" and a BMI of 30.0 and above represents people who have "obesity."[14] Simply put, obesity is a chronic, progressive, relapsing, and treatable multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences.[15] However, obesity is influenced by multiple factors. The environment influences the relationship between genetics and obesity risk.[13,14,16] Further, adverse workplace, school, social, and home environments, known as "obesogenic environments," affect physical and social structures and play a role in an individual's obesity risk.[14] For example, greater availability of fast-food restaurants, poor neighborhood walkability, and perceived safety risks can limit access to physical activity and healthy food options.[14,17] Additional risks for developing obesity include insufficient sleep and low socioeconomic status, in part mediated by chronic stress and food insecurity, which are commonly experienced by racial and ethnic minority populations.[14,18]

The literature about the use of BMI for risk stratification is mixed. For example, in many studies there is a clear empirical link between BMI and various health outcomes – especially in the case of high BMIs (BMI>40.0).[19] There is an observed relationship between obesity (BMI>35.0) and elevated mortality risk. In examining excess deaths in the U.S. associated with individuals with a BMI>35.0, some studies found that the highest number of deaths is associated with obesity, while other studies noted a 22 percent reduction in longevity among men who have obesity.[19–21] These results were consistent across diverse data sets, with multiple meta-analyses observing a 20–30 percent increased risk of mortality for obese individuals.[19,22,23]

However, in contrast to the above findings, studies have found that the association between BMI and all-cause mortality is a controversial topic. Multiple studies, including several systematic reviews and meta-analyses, have attempted to explain this association, and found different results.[22,24–27] The general association of BMI and all-cause mortality follows a U or J curve, with very high mortality among people with very low BMI (<18.5) and very high BMI (BMI >40.0).[24] The most common unexpected finding is that people defined as having a normal or ideal weight with BMI of 18.5 to 25.9 do not necessarily have the best survival.[24] In many cases, overweight people (BMI 25.0 to 30.0), and those who have mild to moderate obesity, (BMI of 30.0 to 35.0 and 35.0 to 40.0), show the best survival.[24] This phenomenon has been described as the "obesity paradox" and it is the subject of intense review due to the potential and very significant impact on many aspects of routine clinical practice and healthcare in general.[24,28–31] The obesity paradox has been described not only in the general population but also in multiple cohorts of people with highly prevalent medical conditions including diabetes, heart disease, kidney disease, cancer, stoke, and rheumatoid and osteo arthritis, among others.[22,24,32–37]

Further, it is worth pointing out two important caveats regarding current thresholds used to diagnose overweight and obesity and risk. The first is that although there is favor for the assignment of specific BMI cut-offs and increasing risk, relationships between body weight or fat distribution and conditions that impair health represent a continuum.[1] For example, studies have shown that increased risk for type 2 diabetes and premature mortality occurs well below a BMI of 30.0.[1,38] The second is there is a complex association between BMI and all-cause mortality when evaluated in the context of comorbidities and baseline mortality risk.[1] In general, comorbidities are better predictors of mortality risk except at extreme BMIs (BMI <15.0, 15.0 to 18.5, and ≥45.0). In patients with no or few comorbidities, BMI seems to better define mortality risk.[1] Aggressive management of comorbidities may provide better survival outcomes for patients with BMI between normal and moderate obesity (BMI of 18.5 to 25.0 and 35.0 to 40.0).[1,38]

Should BMI be used for population level surveillance of obesity trends?

BMI is by far the simplest and most cost-effective option for tracking obesity at the population level.[19,40] Its continued use by medical professionals, health researchers, and governmental agencies forms the basis of collective knowledge about the epidemiology of obesity in the U.S. and abroad.[19] The authority afforded by its use in science and medicine is further compounded by the public's ability to quickly interpret research using BMI.[19,41] Even at the individual level, the widespread availability of BMI equations and charts across numerous forms of media and communications – such as personal health-tracking applications/devices – encourages the self-evaluation of one's health relative to their weight, as the general population is empowered to freely calculate their own BMI. BMI, therefore, serves as a surveillance mechanism setting a standard by which changes in population health can be tracked.[19,41–44] However, as mentioned in the previous BMI report (CSAPH Report 7 A-23), the ease of calculating BMI only applies to the adult population and is inaccurate in children and adolescents because of growth. In the United States, obesity in children and adolescents are defined using threshold values from the 2000 CDC sex-specific body mass index-for-age growth charts.

In general, most existing obesity surveillance systems in the U.S. rely on BMI. Surveillance science has been slow to take advantage of research that identifies alternative anthropometric measures of obesity.[45] Combining two or more different anthropometric measures, such as waist-to-hip ratio and waist-circumference-to-height ratio, has been shown to work well and may be more sensitive to the accumulation of abdominal fat.[45–47] However, these measurements are more invasive and require additional considerations such as how to track trends using other measures and how to interpret those new measures on a population level. The biggest issue with current surveillance systems of obesity is that most surveillance does not include the measurement of policy or environmental factors that may influence obesity.[45,48] For example, there are still gaps in the availability of surveillance systems for areas such as community-level estimates of obesity-related environments, policies, programs, partnerships, and social norms; community-based physical activity programs; surveillance of local policies on nutrition standards for foods and beverages; community-level data on exposure to food marketing; national- and community-level data on worksite programs; and obesity-related policies on college campuses.[45,48] Further, high-risk populations, i.e., demographic or health status subgroups, are often not adequately represented in national or state-level surveys and longitudinal BMI measure analyses are uncommon, particularly among low-resource populations, which are at greater risk of having obesity.[45,48]

Should BMI be used as an initial screener for metabolic health risks?

The current use of BMI as an evaluative and predictive tool is controversial.[49] Originally conceived as a practical index of relative body weight, BMI is now wielded in medicine as a measure for disease and health risk, despite studies showing that BMI can be an inaccurate proxy for cardiometabolic markers of health (i.e., blood pressure, cholesterol levels) and imprecise in its prediction of health risks when applied to the diversity of human bodies.[49–52] The use of BMI as an initial screener for metabolic health risks is controversial. An example of why it is controversial can be examined in a subgroup of individuals that has been identified within the obese population, who do not display the typical metabolic disorders associated with higher BMI's and are hypothesized to have lower risk of obesity-related complications. Metabolically healthy obesity (MHO) has been previously defined as a subgroup of obese (which is measured by having a BMI ≥30) individuals who do not have insulin resistance, lipid disorders, or hypertension.[53,54] Multiple studies indicate 10-25 percent of individuals who have obesity, according to their BMI, can be categorized as MHO.[53–55] A study which used the National Health and Nutrition Examination Survey, a nationally representative sample of adults living in the U.S., to examine the MHO phenotype, found a prevalence of 32 percent among obese adults over the age of 20.[53,56] Further, studies examining cardiovascular disease (CVD) outcomes or all-cause mortality, were not able to demonstrate a significant association between MHO and increased risk of CVD and morbidity and mortality.[53]

Further, when thinking about screening tools, specificity should be factored in. Research has shown that BMI does not appropriately represent racial and ethnic minorities. For example, a longitudinal study of healthy women found that at the same BMI, Asians had more than double the risk of developing type 2 diabetes than Whites; Hispanics and Blacks also had higher risks of diabetes than Whites, but to a lesser degree.[57] Studies have found that Blacks have lower body fat and higher lean muscle mass than Whites at the same BMI, and therefore, at the same BMI, may be at lower risk of obesity-related diseases.[57,58] Finally, as mentioned in the previous BMI report (CSAPH Report 7 A-23) BMI has the following limitations: older adults tend to have more body fat than younger adults at an equivalent BMI; women have greater amounts of total body fat than men with an equivalent BMI; muscular

individuals, or highly-trained athletes, may have a high BMI because of increased muscle mass; and BMI also does not account for the life cycle and location of accumulated fat caused by hormones.[59–61] Given these limitations, certain groups of people are [?] more likely to be misclassified if BMI alone is used, and therefore these individuals may be subject to more unnecessary diagnostic testing/evaluation, unnecessary anxiety, and higher health care spending leading to inequities.

EXISTING AMA POLICY

Under existing AMA Policy H-440.866, "The Clinical Utility of Measuring Body Mass Index and Waist Circumference in the Diagnosis and Management of Adult Overweight and Obesity," the AMA supports: (1) greater emphasis in physician educational programs on the risk differences among ethnic and age groups at varying levels of BMI and the importance of monitoring waist circumference in individuals with BMIs below 35 kg/m2; (2) additional research on the efficacy of screening for overweight and obesity, using different indicators, in improving various clinical outcomes across populations, including morbidity, mortality, mental health, and prevention of further weight gain; and (3) more research on the efficacy of screening and interventions by physicians to promote healthy lifestyle behaviors, including healthy diets and regular physical activity, in all of their patients to improve health and minimize disease risks.

Further, under AMA Policy H-440.797, "Support Removal of BMI as a Standard Measure in Medicine and Recognizing Culturally-Diverse and Varied Presentations of Eating Disorders," the AMA recognizes: (1) the issues with using BMI as a measurement because: (a) of the historical harm of BMI, (b) of the use of BMI for racist exclusion, and (c) BMI cutoffs are based primarily on data collected from previous generations of non-Hispanic White populations and does not consider a person's gender or ethnicity; (2) the significant limitations associated with the widespread use of BMI in clinical settings and suggests its use be in a conjunction with other valid measures of risk such as, but not limited to, measurements of: (a) visceral fat, (b) body adiposity index, (c) body composition, (d) relative fat mass, (e) waist circumference and (f) genetic/metabolic factors; (3) that BMI is significantly correlated with the amount of fat mass in the general population but loses predictability when applied on the individual level; and (4) that relative body shape and composition heterogeneity across race/ethnic groups, sexes, genders, and age-span is essential to consider when applying BMI as a measure of adiposity.

CONCLUSION

BMI is an imperfect measure of body fat and may be influenced by many factors, including body composition of muscle mass, fat distribution, visceral vs. subcutaneous fat, and ectopic fat.[24] Physical fitness and nutritional status may play a more important role than BMI in predicting overall health and risk of mortality.[24,53] Current use of BMI as an evaluative and predictive tool is troubling. Originally conceived as a practical index of relative body weight, BMI is now wielded in medicine as a measure for disease and health risk, despite studies showing that BMI can be an inaccurate proxy for cardiometabolic markers of health (i.e., blood pressure, cholesterol levels) or lifestyle factors (i.e., physical activity, eating habits) and imprecise in its prediction of health risks when applied to the diversity of human bodies.[49–52] There is a complex association between BMI and all-cause mortality when evaluated in the context of comorbidities and baseline mortality risk.[24] Obesity is an important risk factor for many chronic and common clinical conditions. However, comorbidities are better predictors of mortality risk except at extreme BMIs.[24] In patients with no or few comorbidities, BMI seems to better define mortality risk.[24]

The U.S. currently conducts population level surveillance of obesity and individual obesity-related behaviors. However, to fully understand the etiology of obesity and the effects of prevention efforts, current surveillance systems must be expanded in terms of settings, measures, periodicity, and populations.[45] Increases in funding and infrastructure for local surveillance would assist in obtaining data on underserved populations to better understand health disparities in obesity and prevention efforts.[45] Also critical is the addition of environmental and policy measures to surveillance systems to allow for a better understanding of the global obesity epidemic and the effects of obesity prevention initiatives on the population.[45]
An accurate diagnosis of obesity prevents patients at risk due to excess adiposity from being erroneously labeled as "normal" and avoids labeling patients with no excess fat as overweight or obese.[14] As a result, this report supports the need to screen for secondary causes of obesity such as environmental factors, hormonal abnormalities (i.e., hypothyroidism, hypercortisolism), psychiatric diagnoses (i.e., binge eating disorder), iatrogenic obesity (i.e., medications), and genetic syndromes (i.e., proopiomelanocortin deficiency).[14,62] Further, assessment for weight-

related comorbidities such as nonalcoholic fatty liver disease or obstructive sleep apnea is important to understand the complexity of obesity in patients and guide treatment.[14,62]

RECOMMENDATION

The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed.

1. That AMA Policy H-440.797, "Support Removal of BMI as a Standard Measure in Medicine and Recognizing Culturally-Diverse and Varied Presentations of Eating Disorders," be amended by addition to read as follows:

1. Our AMA recognizes:
    1. the issues with using body mass index (BMI) as a measurement because: (a) of the historical harm of BMI, (b) the use of BMI for racist exclusion, and (c) BMI cutoffs are based primarily on data collected from previous generations of non-Hispanic White populations and does not consider a person's gender or ethnicity.
    2. the significant limitations associated with the widespread use of BMI in clinical settings and suggests its use be in a conjunction with other valid measures of risk such as, but not limited to, measurements of: (a) visceral fat, ~~(b) body adiposity index,~~ (e<u>b</u>) body composition, ~~(d) relative fat mass,~~ (~~e~~<u>c</u>) waist circumference and (~~f~~<u>d</u>) genetic/metabolic factors.
    3. that BMI is significantly correlated with the amount of fat mass in the general population but loses predictability when applied on the individual level.
    4. that relative body shape and composition heterogeneity across race/ethnic groups, sexes, and age-span is essential to consider when applying BMI as a measure of adiposity.
    5. that the use of BMI should not be used as a sole criterion to deny appropriate insurance reimbursement.<u>the use of BMI within the context of comorbidities, baseline mortality risk, and environmental factors such as chronic stressors, poor nutrition, and low physical activity may be used for risk stratification.</u>
    6. <u>BMI is a widely used tool for population level surveillance of obesity trends due to its ease of use and low risk for application inconstancies, but BMI does not fully capture the complexity of the obesity epidemic.</u>
    7. <u>that BMI, in combination with other anthropometric measures and environmental factors, may be useful as an initial screener to identify individuals for further investigation of health risks.</u>
    8. <u>that BMI, in combination with other anthropometric measures and environmental factors, may be useful as an initial screener to identify individuals for further investigation of health risks.</u>
2. Our AMA supports further research on the application of the extended BMI percentiles and z-scores and its association with other anthropometric measurements, risk factors, and health outcomes.
3. Our AMA supports efforts to educate physicians on the issues with BMI and alternative measures for diagnosing obesity.
4. Our AMA advocates for coverage of evidence-based alternative measures for diagnosing obesity.

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4. SEX AND GENDER DIFFERENCES IN MEDICAL RESEARCH

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See H-525.988

INTRODUCTION

At the 2023 Annual meeting of the American Medical Association (AMA's) House of Delegates, subclause 7 of Resolution 004 was referred. It stated that "[our AMA encourage] the [U.S. Food and Drug Administration (FDA)] to internally develop criteria for identifying medication and medical devices seeking FDA approval that were developed based on research that did not include adequate participation of women, and sexual and gender minorities [SGM]." Testimony at the meeting cited concern with this being too prescriptive of an approach for the AMA to take with the FDA on this topic. This report serves as the Council on Science and Public Health's response.

METHODS

English language articles were selected from searches of PubMed and Google Scholar using the search terms "gender bias AND clinical trials", "sex bias AND clinical trials", "gender differences AND adverse events", and "sex differences AND adverse events". Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by government agencies and applicable organizations were also reviewed for relevant information.

BACKGROUND

There has been a long and unfortunately exclusionary history for women, and sex and gender minorities (SGM) participating in clinical trials. Women participating in clinical trials became a topic of intense discussion in the United States and Europe after the tragic discovery of birth defects caused by thalidomide in the 1950s.[1] In response, Congress passed the Kefauver-Harris amendment to the Food, Drug, and Cosmetics Act in 1962 which dramatically expanded the role of the FDA beyond evaluating safety, but also effectiveness, resulting in the modern phased clinical trial model we know today.[2] By 1977, however, fears of another teratogen like thalidomide resulted in the FDA introducing regulations which functionally barred all women "of child-bearing age" from participating in clinical trials outside of life-saving drugs.[3]

After these regulations, the scientific community quickly recognized the impact that excluding women from clinical trials had on health equity, including a call from the U.S. Public Health Service Task Force on Women's Health to improve women's participation in clinical trials.[4] In 1993, the FDA repealed their 1977 rule, and Congress passed a mandate that all studies funded by the National Institute of Health (NIH) include women and assess differences amongst sexes.[5,6]

However, despite the changes in the regulatory environment, inequities in clinical trial participation and outcomes persist. These inequities have previously been studied in detail by the Council, and can be found in the 2016 report "An Expanded Definition of Women's Health."[7] This report outlined the ways in which health differences experienced by women are not just associated with reproductive health, and includes biological and socioeconomic factors that impact the risk and severity of conditions such as cardiovascular disease, autoimmune disease, Alzheimer's disease, and substance use disorders. Further, women's participation in research (both as participants and as investigators), was discussed, including the lack of female animals used in preclinical research impacting the ability to predict pharmacokinetic or pharmacodynamic differences using biologic sex as a variable.

Briefly, examination of clinical trials find that enrollment of women is still lower than expected – for example, in 740 clinical trials for cardiovascular disease (N = 862,652 adults), only 38 percent were women.[8] This trend is also observed across disease state, including psychiatric conditions and cancer.[9]

Reasons for this gap are multi-factorial, and include concerns related to side effects, impact on fertility, lack of women researchers, and the inability to take time for multiple site visits.[10] At the request of Congress, the National Academy of Sciences, Engineering, and Mathematics released a 2022 consensus study towards building equity in women and underrepresented groups in research.[11] In its recommendations, the report recommends a variety of strategies: starting with intention, establishing a foundation of trust, being proactive about removing barriers, being flexible, maintaining a strong network of interested groups, being cognizant of social and professional expectations, working in a representative team, and prioritizing resources for equity.

Participation of SGM in clinical trials is even less representative of the population. SGM, which may include individuals identifying as gay, lesbian, transgender, gender non-binary, or gender expansive, have historically been omitted entirely as a category for clinical research, even when they are a high-risk population. For example, surveys have found that individuals identifying as gay or lesbian have an approximately 61 percent prevalence of a substance use disorder compared to 24 percent for individuals identifying as heterosexual.[12] Yet despite the higher risk of substance use disorders, one analysis found that typically less than 5 percent of substance use disorder studies from 2007 to 2012 reported sexual orientation as a relevant participant demographic.[13] Similarly, a review of 764 cancer clinical trials from 1991 to 2017 (N = 462,449 patients) found that no trial reported sexual identity, and only two patients were reported as anything other than male or female – and in those instances, they were listed as the non-actionable categories "not reported" and "unknown."[14] Despite the lack of recognition in studies, SGM are at higher risk for developing cancers related to human immunodeficiency virus and human papillomavirus, or hormone-dependent cancers such as breast cancer in individuals receiving hormone therapy.[15,16]

The lack of participation of women and the lack of even tracking SGM in clinical trials has clear impacts on the care those populations subsequently receive. One commonly cited statistic is that women experience adverse drug reactions (ADRs) approximately twice as often as men, with the underlying reason being that lack of women's participation in clinical trials has led to poor understanding of the influence of sex on pharmacokinetics.[17] In an analysis of NIH-funded clinical trials performed in 2015, only 26 percent of studies explicitly used sex as a variable in their analysis, 72 percent made no mention of sex at all, and many studies with low enrollment of women still represented their data to suggest that it is generalizable across sexes.[18] For SGM, lack of interest by the research community contributes to the ongoing feelings of invisibility and mistrust of physicians.[19]

THE REGULATORY RESPONSE

The originally proposed resolution calls for the FDA to develop criteria for identifying medication and devices which did not adequately include women and SGM in clinical trials. In recent years, there have been several efforts at the FDA to improve diversity in clinical trials, in part driven by the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) and the Food and Drug Omnibus Reform Act of 2022 (FDORA).

Under Section 907 of FDASIA, FDA was tasked with evaluating clinical trial participation based on sex, age, race, and ethnicity. The "Section 907 report" included a 2014 action plan for enhanced collection, and included recommendations on more robust demographic information, training for reviewers to be more scrutinizing of demographic data, and tackling barriers for enrollment for certain subpopulations.[20]

Per FDORA, all drug and device sponsors are required to consider racial and ethnic diversity through the use of a Diversity Action Plan, to be submitted at the same time as their study protocol.[21] These plans require drug and

device sponsors to describe their rationale for enrollment, broken down by age, sex, racial, and ethnic characteristics, and a specific plan for how they intend on achieving these goals, including specific outreach. As of this writing (January 2024), the guidance has not been finalized, but it is expected to be public before the AMA 2024 Annual Meeting.

In August 2023, the FDA released an additional draft Guidance for Industry, "Postmarketing Approaches to Obtain Data on Populations Underrepresented in Clinical Trials for Drugs and Biological Products", which would allow the FDA to require post-market studies as a condition for approval for drugs or devices which did not have adequately diverse populations in the clinical trials.[22] Populations explicitly cited in the guidance include (but are not limited to): race, ethnicity, sex, age, gender identity, disability, pregnancy status, and lactation status. These post-market studies may include single-arm trials, randomized trials, real-world data collection, or pooled studies to assess pharmacokinetics and/or pharmacodynamics in populations understudied in the initial trials.

Finally, post-market studies do not always need to be conducted by the drug sponsor. While post-approval agreements may be strong incentives for drug sponsors with named drugs to maintain their approval while on-patent, many commonly used drugs that are currently off-patent and available as generics were developed without representative women or SGM participation in their clinical trials. As such, there is a distinct possibility that post-market trial requirements for generic drugs could result in lower cost medications simply leaving the marketplace. In those instances, targeted studies for medications at higher-risk for sex- and gender-specific adverse events may be well-suited for federal or academic entities.

EXISTING AMA POLICY

The AMA maintains a plethora of policies seeking to improve equity in both patient outcomes and workforce representation. Specific to this report, the AMA has policy recognizing the differences in health outcomes for women in cardiovascular disease (H-525.975, "Heart Disease in Women"), substance use (H-30.943, "Alcohol Use Disorder and Unhealthy Alcohol Use Among Women"), pharmacological response (D-525.993, "Education on Sex-Based Response to Opioids"), and even pharmaceutical advertising (D-105.996, "Impact of Pharmaceutical Advertising on Women's Health"). The AMA maintains policy specific to the health care needs of other gender identities, including a recognition of the higher risk for cancer in this population (H-160.991, "Health Care Needs of Lesbian, Gay, Bisexual, Transgender and Queer Populations"), and the need for improved gender identity and sexual orientation documentation in medical trials (H-315.967, "Promoting Inclusive Gender, Sex, and Sexual Orientation Options on Medical Documentation"). Additionally, it is the policy of the AMA that the FDA perform regular surveillance of research trial participants, and to adequately fund activities that increase participant diversity in trials (H-460.911, "Increasing Minority, Female, and other Underrepresented Group Participation in Clinical Research").

CONCLUSION

The lack of women and SGM participation in clinical trials has resulted in health inequities. Although it may have started as a well-intentioned response to teratogenic medication adverse events, legislative and regulatory actions have contributed to a drug and device development environment with limited inclusion and information on women and sex and gender minorities. Since the early 1990s, there have been changes to the regulatory landscape and efforts to improve the diversity of the research and development workforce, but progress is slow. The FDA has demonstrated a commitment to improving diversity in clinical trials which should be applauded, supported, and promptly strengthened.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted and the remainder of the report be filed:

That policy H-525.988, "Sex and Gender Differences in Medical Research" be amended by addition and deletion to read as follows:

> Our AMA:
> (1) reaffirms that gender and sex exclusion in broad medical studies questions the validity of the studies' impact on the health care of society at large;

(2) affirms the need to include people of all ~~genders~~ sexes and gender identities and expressions in studies that involve the health of society at large and publicize its policies;
(3) supports increased funding into areas of women's health and sexual and gender minority health research;
(4) supports increased research on women's health and sexual and gender minority health and the participation of women and sexual and gender ~~minorities~~ minority communities in clinical trials, the results of which will permit development of evidence-based prevention and treatment strategies for all women and sexual and gender ~~minorities~~ minority individuals from diverse cultural and ethnic groups, geographic locations, and socioeconomic status;
(5) recommends that all medical/scientific journal editors require, where appropriate, a sex-based and gender-based analysis of data, even if such
comparisons are negative; and
(6) recommends that medical and scientific journals diversify their review processes to better represent women and sexual and gender ~~minorities~~ minority individuals; and
(7) supports the FDA's requirement of actionable clinical trial diversity action plans from drug and device sponsors that include women, and sexual and gender minority populations; and
(8) supports the FDA's efforts in conditioning drug and device approvals on post-marketing studies which evaluate the efficacy and safety of those products in women and sexual and gender minority populations when those groups were not adequately represented in clinical trials; and
(9) supports and encourages the National Institutes of Health and other grant-making entities to fund post-market research investigating pharmacodynamics and pharmacokinetics for generic drugs that did not adequately enroll women and sexual and gender minority populations in their clinical trials, prioritizing instances when those populations represent a significant portion of patients or reported adverse drug events.

CITED AMA POLICY

Sex and Gender Differences in Medical Research H-525.988
Our AMA:
(1) reaffirms that gender exclusion in broad medical studies questions the validity of the studies' impact on the health care of society at large;
(2) affirms the need to include all genders in studies that involve the health of society at large and publicize its policies;
(3) supports increased funding into areas of women's health and sexual and gender minority health research;
(4) supports increased research on women's health and sexual and gender minority health and the participation of women and sexual and gender minorities in clinical trials, the results of which will permit development of evidence-based prevention and treatment strategies for all women and sexual and gender minorities from diverse cultural and ethnic groups, geographic locations, and socioeconomic status;
(5) recommends that all medical/scientific journal editors require, where appropriate, a sex-based and gender-based analysis of data, even if such
comparisons are negative; and
(6) recommends that medical and scientific journals diversify their review processes to better represent women and sexual and gender minorities.

An Expanded Definition of Women's Health H-525.976
Our AMA recognizes the term "women's health" as inclusive of all health conditions for which there is evidence that women's risks, presentations, and/or responses to treatments are different from those of men, and encourages that evidence-based information regarding the impact of sex and gender be incorporated into medical practice, research, and training.

Inclusion of Women in Clinical Trials H-525.991
Our AMA: (1) encourages the inclusion of women, including pregnant women when appropriate, in all research on human subjects, except in those cases for which it would be scientifically irrational, in numbers sufficient to ensure that results of such research will benefit both men and women alike; (2) supports the National Institutes of Health policy requiring investigators to account for the possible role of sex as a biological variable in vertebrate animal and human studies; and (3) encourages translation of important research results into practice.

Increasing Minority, Female, and other Underrepresented Group Participation in Clinical Research H-460.911
1. Our AMA advocates that:
a. The Food and Drug Administration (FDA) and National Institutes of Health (NIH) conduct annual surveillance of clinical trials by gender, race, and ethnicity, including consideration of pediatric and elderly populations, to determine if proportionate representation of women and minorities is maintained in terms of enrollment and retention. This surveillance effort should be modeled after National Institute of Health guidelines on the inclusion of women and minority populations. b. The FDA have a page on its web site that details the prevalence of minorities and women in its clinical trials and its efforts to increase their enrollment and participation in this research; and c. Resources be provided to community level agencies that work with those minorities, females, and other underrepresented groups who are not proportionately represented in clinical trials to address issues of lack of access, distrust, and lack of patient awareness of the benefits of trials in their health care. These minorities include Black Individuals/African Americans, Hispanics, Asians/Pacific Islanders/Native Hawaiians, and Native Americans.
2. Our AMA recommends the following activities to the FDA in order to ensure proportionate representation of minorities, females, and other underrepresented groups in clinical trials: a. Increased fiscal support for community outreach programs; e.g., culturally relevant community education, community leaders' support, and listening to community's needs; b. Increased outreach to all physicians to encourage recruitment of patients from underrepresented groups in clinical trials; c. Continued education for all physicians and physicians-in-training on clinical trials, subject recruitment, subject safety, and possible expense reimbursements, and that this education encompass discussion of barriers that currently constrain appropriate recruitment of underrepresented groups and methods for increasing trial accessibility for patients; d. Support for the involvement of minority physicians in the development of partnerships between minority communities and research institutions; and e. Fiscal support for minority, female, and other underrepresented groups recruitment efforts and increasing trial accessibility.
3. Our AMA advocates that specific results of outcomes in all clinical trials, both pre- and post-FDA approval, are to be determined for all subgroups of gender, race and ethnicity, including consideration of pediatric and elderly populations; and that these results are included in publication and/or freely distributed, whether or not subgroup differences exist.

Heart Disease in Women H-525.975
1. Our AMA supports increased awareness and education on preventive measures for heart disease in women and encourages comprehensive care of heart disease in women.
2. Our AMA urges research to address the gaps in knowledge related to coronary pathophysiology and diagnostic, treatment, and interventional strategies for heart disease in women; and to better understand the role of demographic, socioeconomic, and psychological factors in the onset of heart disease in women.

Alcohol Use Disorder and Unhealthy Alcohol Use Among Women H-30.943
The AMA recognizes the prevalence of unhealthy use of alcohol among women, as well as current barriers to diagnosis and treatment. The AMA urges physicians to be alert to the presence of alcohol-related problems among women and to screen all patients for alcohol us disorder and dependence. The AMA encourages physicians to educate women of all ages about their increased risk of damage to the nervous system, liver and heart disease from alcohol and about the effect of alcohol on the developing fetus. The AMA encourages adequate funding for research to explore the nature and extent of alcohol use disorder and unhealthy alcohol use among women, effective treatment modalities for women with alcohol use disorder and unhealthy alcohol use, and variations in alcohol use among ethnic and other subpopulations. The AMA encourages all medical education programs to provide greater coverage on alcohol as a significant source of morbidity and mortality in women.

Education on Sex-Based Response to Opioids D-525.993
Our AMA will include educational materials for physicians regarding sex-based differences in their resources related to the opioid epidemic. These sex-based differences include the perception of pain, the impact of co-morbid conditions, response to opioids, risks for opioid use disorder, issues with access, and outcomes of addiction treatment programs among women.

Impact of Pharmaceutical Advertising on Women's Health D-105.996
1. Our AMA urges the US Food and Drug Administration (FDA) to assure that all direct-to-consumer advertising of pharmaceuticals includes information regarding differing effects and risks between the sexes.

2. Our AMA urges the FDA to assure that advertising of pharmaceuticals to health care professionals includes specifics outlining whether testing of drugs prescribed to both sexes has included sufficient numbers of women to assure safe use in this population and whether such testing has identified needs to modify dosages based on sex.

Health Care Needs of Lesbian, Gay, Bisexual, Transgender and Queer Populations H-160.991
1. Our AMA: (a) believes that the physician's nonjudgmental recognition of patients' sexual orientations, sexual behaviors, and gender identities enhances the ability to render optimal patient care in health as well as in illness. In the case of lesbian, gay, bisexual, transgender, queer/questioning, and other (LGBTQ) patients, this recognition is especially important to address the specific health care needs of people who are or may be LGBTQ; (b) is committed to taking a leadership role in: (i) educating physicians on the current state of research in and knowledge of LGBTQ Health and the need to elicit relevant gender and sexuality information from our patients; these efforts should start in medical school, but must also be a part of continuing medical education; (ii) educating physicians to recognize the physical and psychological needs of LGBTQ patients; (iii) encouraging the development of educational programs in LGBTQ Health; (iv) encouraging physicians to seek out local or national experts in the health care needs of LGBTQ people so that all physicians will achieve a better understanding of the medical needs of these populations; and (v) working with LGBTQ communities to offer physicians the opportunity to better understand the medical needs of LGBTQ patients; and (c) opposes, the use of "reparative" or "conversion" therapy for sexual orientation or gender identity.
2. Our AMA will collaborate with our partner organizations to educate physicians regarding: (i) the need for sexual and gender minority individuals to undergo regular cancer and sexually transmitted infection screenings based on anatomy due to their comparable or elevated risk for these conditions; and (ii) the need for comprehensive screening for sexually transmitted diseases in men who have sex with men; (iii) appropriate safe sex techniques to avoid the risk for sexually transmitted diseases; and (iv) that individuals who identify as a sexual and/or gender minority (lesbian, gay, bisexual, transgender, queer/questioning individuals) experience intimate partner violence, and how sexual and gender minorities present with intimate partner violence differs from their cisgender, heterosexual peers and may have unique complicating factors.
3. Our AMA will continue to work alongside our partner organizations, including GLMA, to increase physician competency on LGBTQ health issues.
4. Our AMA will continue to explore opportunities to collaborate with other organizations, focusing on issues of mutual concern in order to provide the most comprehensive and up-to-date education and information to enable the provision of high quality and culturally competent care to LGBTQ people.

Promoting Inclusive Gender, Sex, and Sexual Orientation Options on Medical Documentation H-315.967
Our AMA: (1) supports the voluntary inclusion of a patient's biological sex, current gender identity, sexual orientation, preferred gender pronoun(s), preferred name, and clinically relevant, sex specific anatomy in medical documentation, and related forms, including in electronic health records, in a culturally-sensitive and voluntary manner; (2) will advocate for collection of patient data in medical documentation and in medical research studies, according to current best practices, that is inclusive of sexual orientation, gender identity, and other sexual and gender minority traits for the purposes of research into patient and population health; (3) will research the problems related to the handling of sex and gender within health information technology (HIT) products and how to best work with vendors so their HIT products treat patients equally and appropriately, regardless of sexual or gender identity; (4) will investigate the use of personal health records to reduce physician burden in maintaining accurate patient information instead of having to query each patient regarding sexual orientation and gender identity at each encounter; and (5) will advocate for the incorporation of recommended best practices into electronic health records and other HIT products at no additional cost to physicians.

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5. BIOSIMILAR/INTERCHANGEABLE TERMINOLOGY

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
IN LIEU OF RESOLUTION 504
REMAINDER OF REPORT FILED
See Policies D-125.987, D-125.989 and H-125.972

INTRODUCTION

Resolution 245-A-23, which was referred by the American Medical Association's (AMA) House of Delegates, stated as follows:

> That our American Medical Association repeal policy H-125.976, Biosimilar Interchangeability Pathway (Rescind HOD Policy);
>
> That our AMA advocate for state and federal laws and regulations that support patient and physician choice of biosimilars and remove the "interchangeable" designation from the FDA's regulatory framework. (Directive to Take Action)

This report serves as the Council on Science and Public Health's findings and recommendations after review of the evidence surrounding the "interchangeable" designation for biosimilar medications.

METHODS

English language articles were selected from searches of PubMed and Google Scholar using the search terms "biosimilar AND interchangeable." Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by government agencies and applicable organizations were also reviewed for relevant information.

BACKGROUND

This report deals with several technical terms, including discussion as to how they overlap and differ. As such, definitions are provided in Appendix 1 of this report for the following terms: biologic drug, small molecule drug, generic drug, biosimilar, and interchangeable.

Biosimilars are a classification of biologic medical products (such as recombinant proteins and gene therapies) which are nearly identical to an existing U.S. Food Drug and Administration (FDA) -approved biologic medicine (called the reference product or innovator product). In that sense, they are often thought of as the equivalent to the "generic" designation for small-molecule drugs, however they have several key differences which will be discussed later in this report.

Biosimilars are a relatively new class of large molecule medication, with the first follow-on (i.e., a new medication approved in an already established drug class) protein, Omnitrope (somatropin), not receiving FDA approval until 2005.[1] However, the FDA has not had a dedicated regulatory pathway for approving biosimilars until passage of the Patient Protection and Affordable Care Act of 2010, which resulted in the first true biosimilar being approved in 2015, when the leukocyte growth factor Zarxio (filgrastim-sndz) was deemed to be biosimilar to Neupogen (filgrastim).[2] As of December 2023, there have been 45 biosimilars approved by the FDA, including products such as biosimilars for Humira (adalimumab), Avastin (bevacizumab), and Lantus (insulin glargine).

Biosimilars have a unique naming convention compared to other classes of drugs. First, all biologic drugs are branded, even if they are a biosimilar. To distinguish between two biologic products, a 4-letter suffix is added to the non-proprietary name. For example, filgrastim is a recombinant form of granulocyte colony-stimulating factor. The first biologic drug product in this class was produced by Amgen under the trade name Neupogen (filgrastim). Once Neupogen lost its market exclusivity, biosimilars such as Zarxio (filgrastim-sndz), Nivestym (filgrastim-aafi), and

Releuko (filgrastim-ayow) were approved by the FDA. These were all found by the FDA to have similar efficacy and function to Neupogen but have their own brand name and suffix. This naming strategy is intended to convey that biosimilars such as Zarxio and Nivestym are *similar*, but not identical to Neupogen, and allows for easier pharmacovigilance in the event that those differences result in adverse event profile differences. For biologic drugs approved after March 23, 2020, the originator product also contains a 4-letter suffix.

Similar to the generic drug market, approvals of biosimilars are generally thought to lead to increased access and lower costs for expensive medications on the market. Per one analysis from 2016 (before nearly all biosimilars entered the market) biologic drugs comprised less than one percent of prescriptions in the United States, but accounted for over 28 percent of drug expenditures.[3] Since then, one study estimates that biosimilars saved patients $56 billion in medication spending, and account for approximately 60 percent of a given biologic drug's sales volume when biosimilar competition exists.[4] It should be noted, however, that the introduction of a biosimilar is not a guaranteed method for reducing cost and increasing access – somatropin, the first biologic drug to have a biosimilar approved, has actually had a nearly 20 percent increase in the reference product unit price since the introduction of follow-on competition, even though the follow-on product is markedly cheaper.[5]

Distinctions with Generic Drugs

As described above, many often think of biosimilars as the "generic drug" version of biologic medicines. However, there are several key differences, which are also summarized in Appendix 2.[6] The first major distinction between biosimilar large molecule drugs and generic small molecules drugs is the complexity of the underlying medicine. Small molecule drugs generally consist of relatively simple organic chemical structures with atom counts on the scale of 10s, and atomic weights on the scale of 100s of Daltons (Da). For example, acetylsalicylic acid (aspirin) has the chemical formula of $C_9H_8O_4$ (21 total atoms), and a molecular weight of 180 Da. Biologic drugs, by comparison, typically consist of thousands of atoms – adalimumab, a monoclonal antibody used for autoimmune disorders, has a molecular formula of $C_{6428}H_{9912}N_{1694}O_{1987}S_{46}$ (20,067 total atoms) and a molecular weight of 144,190 Da.

Biologic drug efficacy is very sensitive to the secondary, tertiary, and even quaternary structure, which describes how the molecule is folded and packed into shape.[7] For example, many biosimilars are antibody-based drugs, which require very specific folding patterns to generate the receptor binding affinity needed to provide the drugs action in the body. The "active" portion of the biosimilar may be a tiny fraction of the overall molecule while they also may contain several large components that do not contribute meaningfully to the efficacy of the medication. As such, biosimilars may have different chemical structures than their reference product, but if the difference only exists in non-active portions of the structure and does not impact other elements such as folding or polarity, then in theory they will retain similar efficacy.

To produce such complex moieties, biologic drugs are manufactured using unique strategies such as bioreactors. Rather than pursuing traditional chemical synthesis, manufacturers leverage living cells such as yeast or E. coli that are genetically modified to produce the desired product. Due to the relative lack of control over bioreactor manufacturing, there can be high levels of both inter- and intra-batch variability resulting in changes in protein sequence, higher order structure, aggregation, charge heterogenicity, oxidation, and any byproducts from the bioreactor organism that may impact drug function and immunogenicity.[8] Additionally, since the organisms responsible for producing the biologic drug are their own living system, they evolve and mutate over time, meaning that the output will slowly, irreversibly drift over time.[9] As such, there is significant effort, from industry and regulators, dedicated to monitoring and probing biologic drug manufacturing to ensure drug safety and efficacy are preserved in these manufacturing conditions.[8] Differences in manufacturing of biologics and small molecule drugs result in another key distinction – biosimilars are designed to have *similar* function and efficacy, but it is an impossible task to ever perfectly reproduce composition and structure.

Considering their unique composition, mechanism of action, and manufacturing, biosimilars and their approvals are regulated via their own distinct pathway by the FDA. Established by the Biologics Price Competition and Innovation Act of 2009 (BPCIA, passed within the broader Affordable Care Act), biosimilars are approved via an abbreviated 351(k) pathway compared to the 505(j) pathway for other small molecule generic drugs. Per the Hatch-Waxman Act, generic small molecule drug manufacturers are only required to establish bioequivalence for FDA approval.[10] Compared to small molecule generic drugs, biosimilar manufacturers are required to prove that their product utilizes the same mechanism of action, analytical studies proving similarity of the biologically active components, animal studies assessing toxicity, and clinical studies assessing efficacy, immunogenicity, pharmacokinetics, and

pharmacodynamics.[11] As a result, the cost associated with developing, testing, and seeking approval for a biosimilar is significantly higher than that of a generic drug – with some estimates as high as nine years and $300 million per biosimilar.[12,13]

Interchangeability

There is a continuing tension in how to best describe biosimilars. On the one hand, biosimilar naming and terminology needs to convey that they have been found to perform the same as the reference product. Yet on the other hand, it needs to convey that they are chemically *similar* – not identical. Due to the relative infancy of the field, the clinical implications have yet to be fully understood, especially when there can be significant molecule structural or compositional differences between biologic products that otherwise perform similarly.[14-18]

One of the primary sources of tension around communicating biosimilar drugs similarity and differences is the utilization of the term "interchangeable." As alluded to by the original Resolution 245-A-23, there are additional distinctions and implications between biosimilars and small molecule generic drugs when it comes to interchangeability and pharmacy-level substitutions. Per the BPCIA, "interchangeable" is an additional designation that can be given to biosimilars that allows for pharmacists to perform a substitution of two biologic drugs, if allowed by their state pharmacy laws, similar to generic small molecule drugs for their brand name product. Per the Public Health Service Act, "the [term interchangeable in] reference to a biological product […] means that the biological product may be substituted for the reference product without the intervention of the health care professional who prescribed the reference product."[19]

Beyond the baseline evidence that manufacturers provide for biosimilar approval, to be deemed "interchangeable" manufacturers must perform a switching study or interchangeable trial -- a two-arm clinical trial in which one arm receives the reference product continuously, and the other switches from the reference product to the biosimilar and back again. If there are no substantive differences in efficacy or immunogenicity upon switching back and forth between biosimilar and the reference product, the biosimilar may be deemed "interchangeable." It should be noted that to receive the initial FDA approval as a biosimilar, the drug must already have proven to have similar efficacy and immunogenicity to the reference product. Instead, interchangeable trials are meant to assess if there are any changes in efficacy and immunogenicity caused by the act of switching itself after a patient has already initiated treatment.

The "interchangeable" designation is therefore used primarily by pharmacists for performing medication substitutions. These medication substitutions are often required due to formulary restrictions by pharmacy benefits managers, cost-savings to the patient or available stock, among others. State laws vary greatly for how pharmacists may substitute biosimilars and other generic small molecule drugs.[20] For example, in Illinois, a pharmacist may substitute a biologic product with an approved interchangeable biosimilar after alerting the prescriber and the patient. In North Carolina, however, pharmacists may only substitute interchangeable biologics if it will result in cost savings for the patient, but they are not required to communicate this to the prescriber.

The international approach to biosimilar substitutions is mixed, which may be expected for a relatively new class of highly complex medicines.[21] The European Union's regulatory arm, the European Medicines Agency (EMA), does not have an additional category or testing requirements for substitutions and deems all biosimilars approved by the EMA to be interchangeable. However, individual member countries may have their own regulations.[22]

Beyond its role in state-level pharmacy laws, the interchangeable designation is often one of frustration for physicians, patients, and pharmacists. Due to their similarity to another drug, patients may expect that a biosimilar can be substituted at the pharmacy like other generic small molecule drugs, barring formulary restrictions. However, the interchangeability requirements leave patients confused, bring added work for physicians and pharmacists to communicate access challenges and mediate procurement of the appropriate agent to the patient. Further, educating patients on the regulatory nuance between biosimilar and interchangeability can leave everyone frustrated and confused with the process and potentially lead to treatment delays.

From a manufacturer's perspective, the interchangeable designation is a highly desirable one. The price of many biologic drugs is substantial, and being made available for pharmacy-level substitutions may be a significant competitive advantage in a growing marketplace. In one instance, the interchangeable designation of Semglee (insulin glargine-yfgn) resulted in the removal of the reference product, Lantus (insulin glargine), entirely from

major pharmacy benefit managers' drug formularies.[23] To further incentivize biosimilar developers to pursue interchangeable status, the FDA allows for the first interchangeable biosimilar of a drug to obtain market exclusivity status for a year.[24] However, given the high cost of bringing a biosimilar to market, performing an additional clinical trial to evaluate switching may be an additional barrier to entry for smaller biosimilar sponsors. Additionally, biologic drugs which have a biosimilar competitor available will be exempt from Medicare drug price negotiations with the newly founded Drug Price Negotiation Program.[25]
From a regulator's perspective, the interchangeable designation likely seems to be a cautious step towards regulating a new class of drugs where immunogenicity concerns are high. However, it is unclear if those concerns have been realized. Additionally, much of the interchangeable framework is directly outlined in the BPCIA, meaning it would require an act of Congress to significantly change it.

REGULATORY MOVEMENT

According to the FDA's Purple Book Database at the time of writing, there have been 45 biosimilar products approved in the United States, and seven have received the interchangeable designation.[26] Clinical trial data for failed studies is generally not published, but there have been no indications that any biosimilar which has pursued the interchangeable study has failed to achieve the interchangeable designation.

In late 2023, scientists from the FDA's Center for Drug Evaluation and Research published a meta-analysis evaluating the outcomes of 44 treatment switches across 21 different biosimilars, with a total of 5252 patients. In their review, they found that "no differences in terms of major safety parameters such as deaths, [non-fatal serious adverse events], and discontinuations were observed when patients are switched (to or from a biosimilar and its reference biologic) or not switched."[27] This supports the findings of European regulators, which stated "[the] EMA has approved 86 biosimilar medicines since 2006. These medicines have been thoroughly reviewed and monitored over the past 15 years and the experience from clinical practice has shown that in terms of efficacy, safety and immunogenicity they are comparable to their reference products and are therefore interchangeable."[28]

The above-mentioned FDA study appears to be part of a larger movement within the federal government more broadly to re-evaluate the role of interchangeable status. In September 2023, the FDA published a draft guidance to change the labeling for biosimilars.[29] Prior to this guidance, biologic medicine labeling had two distinct sections: a "biosimilarity statement" and an "interchangeability statement," where if not deemed interchangeable, the statement would be blank. Under the new guidance, the two are combined into a single statement to allow for those who are legally required to understand interchangeability status to be easily able to find it on product labeling, while prescribers or patients do not feel that their medication is of lower quality when seeing a blank interchangeability statement.

These movements by the FDA away from the interchangeable designation are matched by other federal entities. In a March 2022 report from the Office of the Inspector General (OIG), they found that Medicare was over-spending on biologic medicines by not fully incorporating biosimilars into their offerings, and instead focusing too heavily on reference products.[30] OIG estimated that Medicare Part D spending on biologics could be decreased by 18 percent ($84 million) annually, and out-of-pocket spending on these products for Medicare beneficiaries could decrease by 12 percent ($1.8 million) annually, if biosimilars were more broadly used.

Under current regulations, biosimilars may only be substituted with those deemed interchangeable, and only after explicit approval by the Centers for Medicare & Medicaid Service (CMS). In November 2023, CMS proposed rule changes to Medicare Advantage and Medicare Part D that would allow for plans to immediately substitute all biosimilars, including those not deemed interchangeable, for the reference product.[31] On January 4th, 2024, the AMA submitted comment to CMS on this proposed change, and cited concern that CMS movement was premature barring regulatory changes from the FDA, and that patients currently receiving the reference product should be exempt from substitutions without approval from their physician.
In March 2024, the Biden Administration released its draft budget for fiscal year 2025, which included a policy proposal to allow for all biosimilars, regardless of interchangeability status, be eligible for pharmacy level substitutions.[32] At the time of this report's writing (March 2024), it is unclear if this policy will be included in the final, approved budget for fiscal year 2025, but it is generally consistent with the direction federal regulations on biosimilar interchangeability has taken in recent years.

CURRENT AMA POLICY

The AMA currently has several policies regarding biosimilars, particularly around reimbursement and cost coverage. Of particular relevance to this report are two policies (full text of policies found at the end of this report): (1) H-125.976 "Biosimilar Interchangeability Pathway," states amongst other clauses, that "[the AMA] strongly support the pathway for demonstrating biosimilar interchangeability"; and (2) D-125.989 "Substitution of Biosimilar Medicines and Related Medical Products," which urges State Pharmacy Practice Acts to limit the authority of pharmacists to substitute biosimilars only when they have been deemed interchangeable by the FDA.

CONCLUSION

At the crux of this issue is balancing patient access to medications against the unknown risks of a newer class of highly complex medicines. Given the current state of the published evidence between the European Union and FDA reviews, it appears that the previous concerns over toxicity and immune response of switching biosimilars have not been realized. However, it is important to recognize that the evidence on interchangeability is still limited and that the field of biosimilars is in its infancy compared to our knowledge of generic small molecule drugs. Additionally, the term interchangeable, however flawed, is utilized by several entities beyond the FDA, including for Medicare reimbursement and state pharmacy laws. Therefore, the Council recommends that an approach be taken to retain the FDA's ability to assess and monitor potential risks of switching without placing an outsized importance and advantage in the marketplace on the completion of additional switching trials that have yet to yield value for patients and physicians.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted and the remainder of the report be filed:

1. That Policy H-125.976, "Biosimilar Interchangeability Pathway" be rescinded.
2. That our AMA encourage the FDA to continually collect data and critically evaluate biosimilar utilization including the appropriateness of the term "interchangeable" in regulatory activities.
3. That Policy D-125.989 "Substitution of Biosimilar Medicines and Related Medical Products" be amended by addition and deletion to read as follows:
   Our AMA urges that State Pharmacy Practice Acts and substitution practices for biosimilars in the outpatient arena: (1) preserve physician autonomy to designate which biologic or biosimilar product is dispensed to their patients; (2) allow substitution when physicians expressly authorize substitution of ~~an interchangeable~~ a biologic or biosimilar product; (3) ~~limit the authority of pharmacists to automatically substitute only those biosimilar products that are deemed interchangeable by the FDA.~~ in the absence of express physician authorization to the contrary, allow substitution of the biologic or biosimilar product when (a) the biologic product is highly similar to the reference product, notwithstanding minor differences in clinically inactive components; and (b) there are no data indicating clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product; and (c) the prescribing physician has been adequately notified by the pharmacist.
4. That Policy D-125.987, "Biosimilar Product Naming and Labeling" be reaffirmed.
5. That our AMA support evidence-based physician education on the clinical equivalence of biosimilars, the FDA approval process, and post-market surveillance requirements.

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CITED AMA POLICIES

Biosimilar Interchangeability Pathway H-125.976
Our AMA will: (1) strongly support the pathway for demonstrating biosimilar interchangeability that was proposed in draft guidance by the FDA in 2017, including requiring manufacturers to use studies to determine whether alternating between a reference product and the proposed interchangeable biosimilar multiple times impacts the safety or efficacy of the drug; and (2) issue a request to the FDA that the agency finalize the biosimilars interchangeability pathway outlined in its draft guidance "Considerations in Demonstrating Interchangeability With a Reference Product" with all due haste, so as to allow development and designation of interchangeable biosimilars to proceed, allowing transition to an era of less expensive biologics that provide safe, effective, and accessible treatment options for patients.
Res. 523, A-18

Substitution of Biosimilar Medicines and Related Medical Products D-125.989
Our AMA urges that State Pharmacy Practice Acts and substitution practices for biosimilars in the outpatient arena: (1) preserve physician autonomy to designate which biologic or biosimilar product is dispensed to their patients; (2) allow substitution when physicians expressly authorize substitution of an interchangeable product; (3) limit the authority of pharmacists to automatically substitute only those biosimilar products that are deemed interchangeable by the FDA.
Res. 918, I-08. Modified: CSAPH Rep. 1, I-11. Modified: CSAPH Rep. 4, A-14.

Biosimilar Product Naming and Labeling D-125.987
Our AMA urges the FDA to finalize Guidance on the naming and labeling conventions to be used for biosimilar products, including those that are deemed interchangeable. Any change in current nomenclature rules or standards should be informed by a better and more complete understanding of how such changes, including requiring a unique identifier for biologic USANs would impact prescriber attitudes and patient access, and affect post marketing surveillance. Actions that solely enhance product identification during surveillance but act as barriers to clinical uptake are counterproductive. However, because of unique product attributes, a relatively simple way to identify and track which biosimilar products have been dispensed to individual patients must be established. If unique identifiers for biosimilar USANs are required to support pharmacovigilance, they should be simple and the resulting names should reinforce similarities by using the same root name following standards for nonproprietary names established by the USAN Council. CSAPH Rep. 4, A-14

APPENDIX 1 - Definitions of key terms:

Biologic drug (or large molecule drugs): a classification of drugs which are produced by living organisms (such as human or animal cells, yeast, or bacteria), rather than by chemical synthesis. As such, this class of drug tends to replicate or mimic common biologic entities. For example, antibody- or protein-based drugs are common examples of biologic drugs.

Small molecule drug: A classification of drugs based on the number of atoms (typically <100) in their structure. Small molecule drugs are generally prepared using chemical synthesis techniques. Small molecule drugs are

estimated to represent over 90 percent of all pharmaceuticals used in the clinic today. Typically, small molecule drugs function by binding to a biological entity (protein, receptor, etc.) and altering its function.

Generic drug: A drug produced by a second manufacturer after the patent or other market protections have expired, allowing for manufacturers to be able to produce their own products with the same chemical substance as a branded drug. The term generic drug only applies to small molecule drugs, with few exceptions.

Biosimilar: A biologic drug that has a very similar structure and function to a branded biologic drug after its patent or market protections have expired. Unlike generic drugs, biosimilars are not required to be the same chemical compound, but they are required to have the same chemical structure to act on the body and efficacy.

Interchangeable: An additional designation provided for biosimilar drugs by the FDA. This designation is not required for market approval and indicates that a biosimilar has successfully demonstrated no changes in efficacy or immunogenicity when the biosimilar is substituted for the reference product after a patient has already initiated treatment with the reference product. This designation has implications for reimbursement, and state regulations around pharmacist practice.

APPENDIX 2

Table 1: Comparison of follow-on products for small molecule vs. biologic medicines.

Type of Medicine	***Small Molecule***	***Biologic***
Name of Follow-on Product	Generic	Biosimilar
Drug Molecule Complexity	Low	High
Size	Small (10s of Dalton)	Very Large (1000s of Dalton)
Manufacturing Process	Chemical synthesis	Bioreactor
Characterization	Simple	Complex
Batch-to-Batch Variability	Low	High, with potential for permanent formulation drift over time
Regulatory Pathway	Abbreviated New Drug Application	Abbreviated Biologics Licensing Agreement
Can Pharmacist Make Substitution?	Yes, if state pharmacy practice laws allow	Yes, if manufacturer successfully completes additional clinical trial where patients switch back and forth between reference and follow-on product AND state pharmacy practice laws allow
Nonproprietary Name	Same as reference product	Same as reference product with additional 4 letter suffix

6. GREENHOUSE GAS EMISSIONS FROM METERED DOSE INHALERS AND ANESTHETIC GASE

Reference committee hearing: see report of Reference Committee D.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See Policies H-135.907, H-135.913 and H-160.932

INTRODUCTION

American Medical Association (AMA) Policy H-135.913, "Metered Dose Inhalers and Greenhouse Gas Emissions," as adopted by the House of Delegates (HOD) at the 2023 Annual Meeting asked that our AMA study options for reducing hydrofluorocarbon use in the medical sector.

BACKGROUND

Asthma is a chronic respiratory disease that reversibly impacts the ability of air to move in and out of the lungs due, usually to inflammation of the airways, and requires ongoing medical mangement.[19,20] The potential factors that cause asthma are both environmental and genetic, including family history, allergies, viral respiratory infections, occupational exposures, smoking, air pollution, and/or obesity.[21] According to data from the National Health Interview Survey, during 2016 to 2018 approximately 8 percent of the U.S. population reported having asthma, with a higher prevalence among Black persons (10.7 percent) compared to White persons (8 percent).[20] Chronic obstructive pulmonary disease (COPD) refers to a group of respiratory diseases that cause airflow blockage and make breathing more difficult, including emphysema and chronic bronchitis.[22] About 16 million Americans have COPD and in 2018 it was the fourth leading cause of death in the U.S.[22,23] Exposure to tobacco smoke is a key contributor to the development and progression of COPD, but environmental exposures to air pollutants, genetic factors, and respiratory infections also play an important role.[23]

Metered-dose inhalers (MDIs) are medical devices used to deliver inhaled medication, typically for individuals with asthma and COPD. MDIs are pressurized and rely on liquefied-gas propellants to atomize medication for inhalation delivery. The pharmaceutical industry historically used chlorofluorocarbons (CFCs), specifically CFC-11, CFC-12, and CFC-114, as propellants. CFCs are synthetic, nontoxic, and nonflammable chemicals that contain atoms of carbon, chlorine, and fluorine. They were first developed in the late 1920s to replace toxic refrigerants that were being used at the time.[1] Following their initial development, CFCs were widely adopted and used in foam insulation, refrigeration, and aerosols (including MDIs).

While CFCs were found to be safe in their applications, they undergo significant chemical changes in the upper atmosphere and by the early 1970s, chemists from the University of California demonstrated that CFCs could be destroying the stratospheric ozone layer that helps shield the Earth from the sun's ultraviolet radiation.[1] By the 1980s, it was clear that stratospheric ozone loss was getting worse every year and CFCs were a major contributor. The global environmental response came in the late 1980s and resulted in the signing of the Montreal Protocol in 1987, which phased out the use of CFCs. MDIs and other medical uses of CFCs were exempted under the Montreal Protocol until safer alternatives could be identified. The pharmaceutical industry introduced hydrofluorocarbon (HFC) (also known as hydrofluoroalkanes - HFA) propellants for MDIs as replacements for CFCs in the mid-1990s, specifically HFC-134a in 1996 followed by HFC-227ea in 2006. However, it took over 20 years, until 2016, for all CFCs to be phased out of MDI applications.[2]

In addition to the use of HFCs in MDIs, modern anesthetic gases include the HFCs sevoflurane and desflurane, the CFC isoflurane, and nitrous oxide.[24] Anesthetic gases have been excluded from international protocols due to their medical necessity but measured concentrations of desflurane, the most damaging in terms of GHG warming potential, in the atmosphere have increased over the last few decades.[24] Therefore, exploring alternatives to the usage of these anesthetic gases is another way health care systems can reduce their carbon footprint and improve sustainability.

This report outlines the greenhouse gas (GHG) emissions and climate impacts of the use of CFCs and HFCs in the medical sector, with a focus primarily on MDIs and secondarily on anesthetic gases, followed by a discussion of potential alternatives and how they compare in terms of their carbon footprint, effectiveness, and cost.

METHODS

English language articles were selected from searches of PubMed and Google Scholar using the search terms "metered dose inhalers" AND "dry powder inhalers" AND "sustainability" as well as "anesthetics" AND "sustainability." Supplementary searches were performed on both effectiveness and cost differences between metered dose inhalers and dry powder inhalers. Additional articles were identified by manual review of the reference lists of relevant publications. Data regarding available asthma/COPD medications presented in Table 2 were extracted from FDA's approved drug website and individual medication prescribing sheets.[25]

DISCUSSION

Climate Impact of CFCs and HFCs

Despite improvements to the ozone layer after the Montreal Protocol, HFCs are powerful GHG that contribute to climate change. HFCs can be up to 3800 times more powerful of a GHG than carbon dioxide (see Table 1) and there is now increasing attention on the environmental impacts of HFCs.[26] Atmospheric concentrations of common HFCs used in medical sector have been found to be increasing since the early 1990s while CFCs previously used in MDIs have plateaued and decreased (see Figure 1).[27] Reducing the use of MDIs is consistently noted among the top high-priority and effective measures for reducing GHGs within the health care sector, as GHG emissions from the use of MDIs are substantial. MDIs are the most used inhalers in the world.[2,26] "In 2020, MDIs made up 75 percent of inhalers in use in the United States, with the equivalent emissions impact of driving half a million cars for a year."[3] Due to their wide usage, MDI prescriptions can account for about three percent of a health system's carbon footprint.[4]

As such, there is an unfortunate feedback loop between ongoing climate change impacts and treating asthma/COPD with MDI inhalers, as increased global warming will likely exacerbate existing asthma and respiratory issues, potentially requiring more acute treatment options which MDIs currently provide.[28] Recognizing the climate change impacts of HFCs, the Kigali Amendment to the Montreal Protocol calls for the phasing out of HFCs due to their climate warming potential, but medical uses for HFCs are currently exempted. Additionally, the American Innovation and Manufacturing Act of 2020, enacted by the U.S. Congress, directs the Environmental Protection Agency (EPA) to phase down the production and use of HFCs in consumer products, such as aerosols, refrigerants, etc., by 2036 but the rule also does not apply to MDIs.[29]

Additionally, direct emissions of anesthetic gases have been estimated to represent about three percent of the health care-related GHGs in high-income nations.[30] As noted in Table 1, desflurane has a GHG warming potential around 5-20 times higher than sevoflurane and isoflurane over a 100-year period and it is also generally more expensive.[31] While nitrous oxide is not a HFC, it also has deleterious climate impacts. Even though it has a lower global warming potential, it is also less potent than other inhalable anesthetics so is typically used in higher concentrations and has a long atmospheric lifetime, thus making it problematic from a sustainability perspective.

Metered Dose Inhalers - What are the alternatives?

Inhaled therapy is the primary pharmacological therapy for obstructive lung diseases such as COPD and asthma.[32] Obstructive lung disease management and control has two components, symptom control and risk reduction.[5] Inhalers are generally categorized as either reliever or preventer inhalers, with recent formulations combining these different types into one inhaler that is recommended for daily usage. Preventer inhalers contain an inhaled corticosteroid (ICS), and the Global Initiative for Asthma (GINA) and the Expert Panel Working Group of the National Asthma Education and Prevention Program Coordinating Committee (NAEPPCC) recommend most patients with asthma receive an ICS treatment.[5,33] Reliever inhalers include a short-acting β-agonist (SABA) which is intended to be utilized during asthma exacerbation events. GINA does not recommend treatment of asthma with SABA inhalers alone. Recent developments in asthma treatment recommend combined therapy, including anti-inflammatory reliever (AIR), which consists of ICS with a short-acting β-agonist reliever and maintenance and reliever therapy (MART) (ICS-formoterol), also called SMART in some places (single inhaler maintenance and reliever therapy), which combines ICS and long-acting beta-agonist (LABA) therapy together.[5]

In addition to different therapeutic approaches, there are different types of inhalers available: pressurized metered dose inhalers (pMDI), dry powder inhalers (DPI), and soft mist inhalers (SMIs). DPIs rely on delivering medication in the form of a fine powder that is activated by a person's breathing and SMIs use a spring action mechanism to deliver the medication in a fine mist. pMDIs and DPIs are the two most commonly prescribed and manufactured inhalers globally.[6] Table 2 provides a list of U.S. Food and Drug Administration (FDA) approved asthma/COPD medications, their therapy approach, and the type of inhalation device.

As shown in Table 2, SABA inhalers available in the U.S. are predominantly pMDIs while the ICS and combination therapy treatments are available as both DPI and pMDI inhalers. There is only one DPI reliever inhaler, the ProAir Respiclick/Digihaler, and only four inhalers are available as an SMI; these are only approved for the treatment of COPD. Currently, there is no DPI anti-inflammatory reliever (AIR) regimen, which combines ICS-SABA that is easy to use and affordable in the U.S., despite being more widely available in Europe (more on cost considerations below).[7]

Life cycle assessments comparing pMDIs to DPIs have overwhelmingly and consistently found that DPIs have a much lower carbon footprint due to their lack of an HFC propellant.[4,6] Estimates from the U.K. have projected a 96 percent reduction in the existing carbon footprint of asthma treatment if all pMDIs were switched to DPIs.[6] Similar life cycle assessments comparing SMI versus pMDIs in terms of overall carbon footprint found comparable reductions in GHG emissions.[6] Additionally, climate model estimates have demonstrated that the phasing out of HFCs, as proposed by the Kigali Amendment to the Montreal Protocol, could deliver 0.3 to 0.5°C degrees of climate benefit by 2100.[34] As the Kigali Amendment exempts HFCs for medical uses, it is possible that the elimination of HFCs in both medical uses and other commercial applications could deliver even greater climate benefit.

Safety and Effectiveness of MDIs

A barrier to switching from MDIs to DPIs has been the concern that DPIs are not as effective or are more difficult to use than MDIs. Except in circumstances where the patient cannot generate sufficient inspiratory airflow, such as with very young children (under the age of 5) or frail, older adults, research has demonstrated that DPIs are as effective and safe as MDIs for a majority of patients.[8–10] For example, a randomized controlled trial (RCT) of patients with COPD comparing the efficacy of a DPI versus a pMDI pharmaceutical formulation, found that the different inhaler types demonstrated similar efficacy and a similar proportion of patients in the different inhaler groups experienced any adverse effects from treatment.[9] In another study, researchers did a post-hoc analysis of patients from the Salford Lung Study in Asthma (a 12 month, multi-site RCT study conducted in the UK on patients with asthma and COPD) who switched from a pMDI to DPI during the study.[35] Patients that switched to DPIs halved their inhaler carbon footprint without loss of asthma control, and in fact, asthma control was consistently superior over the 12 months in the DPI group compared to the control group.[36]

Despite the popularity and widespread usage of MDIs, studies have shown that many patients use MDIs incorrectly, despite educational trainings on usage, resulting in improper inhalation techniques and poor asthma control and management.[11,12] DPIs have been found to be easier to correctly use compared to MDIs, which requires some level of coordination between inhaler actuation and patient inspiration to ensure correct inhalation and treatment.[11,13] Additionally, in a recent survey of asthma and COPD patients' inhaler preferences done in the U.K., "environmental sustainability" was found to be one of the more important characteristics, indicating that patients may be inclined to switch inhalers from an MDI to a DPI if the environmental impacts were discussed.[37]

While MDIs are the most used inhaler in the U.S., the U.K. has recently designated DPIs as the default treatment for patients 12 and older and removed two carbon-intensive inhalers from formularies.[38] Additionally, DPIs are the primary inhaler used in several other European countries.[3] For example, Sweden has a higher prevalence of asthma to the U.S. (11.6 percent of individuals in 2022 in Sweden compared to 7.7 percent in 2021 in the U.S.) and DPIs account for 90 percent of inhalers used.[39,40] Although there is no available evidence on the role of inhaler types to account for health outcome differences, Sweden has demonstrated better asthma-related mortality outcomes compared to the U.S.; in 2012 the age-standardized asthma mortality for the 5–34-year age group in Sweden was 0.00 compared to 0.37 in the U.S.[41]

Additionally, Finland in the early 1990s launched a national ten year program intended to improve asthma care and limit the projected increases in costs.[42] As part of this national program, the importance of preventative ICS versus

reliever medications was emphasized and a shift was promoted from MDIs to DPIs. As a result of this initiative, the number of patients using daily ICS went from around 33 percent in 1987 to over 85 percent in 2004 and while DPIs only accounted for 29 percent of inhalers sold in 1993, by 2003 they accounted for 84 percent.[42] These changes were concurrent with improved health outcomes, including a reduction in asthma related deaths and emergency room visits, and decreased direct annual costs associated with asthma.[42]

With the manufacturing of HFC propellent inhalers being an important component of their GHG emissions, several pharmaceutical companies have made promises to replace existing pMDIs with new HFC propellent that have a lower carbon footprint.[6] There are several new HFC inhaler formulations that have a much lower GHG warming potential (see Table 1), with at least one set to be released in 2025. This would help pharmaceutical companies meet their sustainability goals while also reducing GHG emissions from the overall healthcare sector, but these new HFC inhalers may be more costly than currently available low-GHG alternatives.

Cost considerations

Increased costs are another challenge of switching to DPIs from MDIs, which is partly driven by a lack of competitive DPIs/SMIs that have been approved and made available in the U.S. (as compared to Canada and European countries). At the start of 2019, there were no generic inhalers on the U.S. market. While there are multiple low-cost DPI inhalers available in Europe, there are few low-cost alternatives in the U.S.[7] Researchers estimate that a global inhaler transition where DPIs are the prevailing inhaler used could take a decade to implement and may lead to increased patient costs.[26,43] Currently, SABA relievers as DPIs compared to MDIs tend to be more expensive but the cost of HFC propellants is expected to rise due to global policy trends in phasing out the use of HFCs in products.[2]

One potential reason for the lack of competitive, low-cost alternatives to the prevailing MDIs on the market has been pharmaceutical companies' ability to maintain patent protections on their brand name products through secondary patents after the primary patent has expired.[14] Primary patents on pharmaceuticals cover the active ingredients within the medication while secondary patents can be claimed for peripheral aspects of the product, such as the propellants and delivery devices. Research on revenue earned on brand-name inhaler products in the U.S. found that manufacturers earned $67.2 billion while primary patents were active and $110.3 billion (62 precent) after primary patents had expired but when secondary patents were active, reflecting the importance of these secondary patents for maintaining high revenues while limiting potential competition.[14] The persistent high cost of inhalers in the U.S. has caught the attention of U.S. lawmakers. In January 2024, U.S. Senator Tammy Baldwin (D-WI) and colleagues launched an investigation into four pharmaceutical companies in regard to their high prices for inhalers.[44]

Despite the increased costs of switching to DPIs from MDIs, improved asthma management could help balance existing cost differentials. The overreliance on SABA (relief) inhalers alone in asthma treatment results in poor asthma management and health outcomes, which can lead to greater health care costs.[2] As one study notes, "[a]ny increase in low-cost salbutamol MDIs can potentially be offset by improving care to drive down their use … and by using more cost-effective controller medication. For patients with poor asthma control, escalating controller therapy is a cost-effective, but underused strategy."[2] Evidence from other countries demonstrate that a concerted effort to increase the use of ICS medication and reduce reliance on relief (SABA) medication, can improve asthma outcomes and lower costs.[42,45]

Policy recommendations to reduce the negative economic impacts of switching to lower carbon footprint inhalers are severalfold. Lawmakers could incentivize early entry of greener generic inhalers by extending the 180-day exclusivity period awarded to the first generic manufacturers to successfully challenge patents on a particular drug-device combination. The U.S Patent and Trademark Office could also pursue reforms to further examine drug-device combination patents and ensure the quality of patents issued on new inhalers. Lastly, the Centers for Medicare and Medicaid Services could determine a favorable reimbursement rate that is applicable for any greener inhalers when they gain approval, considering their overall environmental benefits, that would make them more favorable to include on insurance formularies.[15]

Other advantages to switching from MDIs to DPIs

There are a few other advantages to switching from pMDIs to non-propellent inhalers, like DPIs. First, because pMDIs can be challenging to use and less critical errors are made while using DPIs, overall asthma care could

improve.[45] Also, because not all pMDIs have a counter that shows how many doses are left, sometimes they are used when empty, also leading to poor disease control. Lastly, pMDIs are sometimes used with a spacer – which allows patients, particularly young children who may have difficulty using the inhaler, to deliver the medication in a slower, more controlled way – and these are supposed to be replaced every year.[46] However, a Dutch study found that only 60 percent of pMDI users received a new spacer annually, which may imply suboptimal quality of care. As DPIs do not require a spacer, their use eliminates these possible issues while also reducing the generation of non-reusable plastics.[45]

Equity considerations

There are important health equity considerations regarding asthma prevalence, management, and related health outcomes in the U.S. that make following current GINA and NAEPPCC care recommendations challenging.[47] Asthma disproportionality impacts Black, non-Hispanic, American Indian/Alaska Native, and Puerto Rican populations.[40,48,49] Additionally, individuals living below 100 percent of the poverty threshold have a higher asthma prevalence compared to other socio-economic groups (10.4 percent compared to 6.8 percent among individuals at 450 percent of poverty threshold or higher).[40] In terms of asthma management, racial and ethnic minority children are more likely to rely on SABA rather than ICS therapies, which, as noted above, can result in poorer asthma control and management.[49] Lastly, Black, non-Hispanics have a much higher asthma mortality rate compared to other racial and ethnic groups (24.4 per million for Black, non-Hispanics compared to 9.8 per million for white, non-Hispanic populations).[40] Financial barriers for those who lack insurance coverage for recommended combined therapies and working through authorizations and referrals for those with public health insurance also pose equity challenges.[47] Considering these existing health disparities and equity challenges, increased costs associated with new asthma medications could disproportionately impact low-income communities of color who are already burdened by asthma and has the potential to increase existing health disparities if asthma medication becomes more costly and inaccessible.

Prevention as a primary strategy and alternative

As noted above, two of the key risk factors for both asthma and COPD are tobacco smoke and air pollution.[21,23] Public health policy and educational campaigns over the last 50 years have been remarkably successful at lowering the prevalence of smoking and limiting indoor exposure to tobacco smoke, thus reducing this exposure pathway.[50–52] However, tobacco use still remains the leading cause of preventable disease and death in the U.S.[50] The introduction of e-cigarettes and vape pens in the past decade has led to an increase in e-cigarette usage, particularly among young adults, which may reverse the decades long downward trend in tobacco usage.[53] As such, there is still a critical need for continued public health efforts to reduce smoking and tobacco use, which would reduce the prevalence of asthma and COPD. Common outdoor air pollutants, including particulate matter, ozone, carbon monoxide, lead, sulfur dioxide, and nitrogen dioxide, are in part anthropogenic (human-caused) and result from the burning of fossil fuels for electricity generation, industrial uses, and motor vehicle use.[54,55] Federal and state policy to reduce air pollution has resulted in substantially better air quality over the last several decades, but high pollution levels are still a concern in many urban areas and for those living close to major sources of pollution, with low income communities of color experiencing disproportionately high exposure to air pollution.[56,57] Efforts to reduce fossil fuel emissions would thus have multiple co-benefits, including minimizing anthropogenic climate change by reducing GHG emissions, building more resilient communities, improving health equity, and reducing outdoor air pollutants resulting in improved respiratory outcomes.[55,58,59]

Anesthetic gases – Solutions and alternatives

Life cycle assessments of anesthetic gases have found that more than 95 percent of emissions occur in their waste phase, in that they are emitted freely to the outdoor atmosphere during use through medical gas evacuation systems or through unscavenged gas exhaled into the indoor environment that then flows outdoors.[18,30] To mitigate the negative environmental impact of anesthetic gases, clinical care recommendations, including those in the *Greening the Operating Room* report by the American Society of Anesthesiologists Committee on Environmental Sustainability, focus on delivery performance improvements, removing or avoiding the "worst" GHG offenders from hospital drug formularies, and substituting non-inhaled anesthetic gases when clinically appropriate.[18]

Delivery performance improvements are aimed at lowering the volume of anesthetic gases unnecessarily wasted or lost during usage. A simple way to minimize gas waste is to lower fresh gas flows during the maintenance phase of

the anesthetic, but continuous oxygen concentration monitoring is critical to prevent the possibility of hypoxemia.[16,18,31] Additional strategies to reduce gas flow and minimize environmental contamination of anesthetic gases have been outlined by the American Society of Anesthesiologists *Greening the Operating Room* report. Another strategy to reduce wasted gas is through improved delivery infrastructure. In older hospital buildings, nitrous oxide has been delivered through central piping systems, which over time have leaked nitrous oxide into the atmosphere. It is estimated that most nitrous oxide loss happens prior to its usage with the patient and it has been recommended that these piping systems should be decommissioned in existing infrastructure and avoided in new construction.[31] As an alternative, it is recommended that portable canisters should be substituted and should be closed between uses to avert continuous leaks.[31] Lastly, in terms of performance improvement, innovative methods for collecting and reusing anesthesia, thus preventing them from being released directly into the atmosphere, are currently being researched and evaluated.[18] However, these devices have not been widely used or evaluated on their efficacy, safety, benefit, or cost.[24]

When evaluating choice of inhaled anesthesia gases, two important considerations include GHG warming potential and the gas flowrate.[16,18] Desflurane has the highest GHG warming potential compared to other inhaled anesthetic gases and while nitrous oxide has a lower GHG warming potential, it requires greater quantities to meet similar clinical effectiveness. Nitrous oxide also persists in the atmosphere for more than 100 years, making its impacts felt over a much longer period of time compared to other anesthetic gases.[16] The larger quantities needed, and longer persistence in the atmosphere, makes nitrous oxide's environmental impact substantially greater than isoflurane or sevoflurane.[30] With these considerations, eliminating desflurane and nitrous oxide to the greatest extent possible in clinical practice, is recommended for improving the climate impact of anesthetic gases.[60] However, nitrous oxide continues to be useful for elimination of pain with no real alternative and therefore the use of portable cannisters with nitrous oxide is recommended versus using older building piping systems.[24,61] With desflurane, there is limited evidence of clinically meaningful differences over other anesthetic gases, except minor differences in faster mean wake up times following surgery.[31] However, desflurane is also more expensive than other anesthetic gases, therefore it's elimination or reduction in usage could result in cost savings for health care systems.[31]

A final practice consideration to improve sustainability and reduce GHG emissions is to use total intravenous anesthesia and/or regional anesthesia to eliminate volatile anesthetic emissions whenever possible. It is important to note that this recommendation is not a carbon-neutral strategy, as considerations must be made for minimizing single use plastics and unnecessary use of drugs and supplies, which also contribute to overall hospital waste streams that have their own carbon footprint. That being said, this alternative has been found to be associated with substantially less emissions, even considering their full life cycle.[17,31] To offset environmental impacts from intravenous anesthesia, there are several strategies to reduce anesthesia equipment waste generation overall, including: using prefilled syringes and appropriate sized vials for an individual patient, only opening equipment intended for immediate use, considering purchase of reusable or reprocessed equipment over disposable, reprocessing or recycling suitable disposable equipment, adjusting stock levels to minimize discarding expired items, reformulating prefabricated kits to eliminate unnecessary items, reformulating anesthesia supply carts to eliminate unnecessary items, and donating expired or unused open equipment.[16,62]

Challenges and barriers

Efforts to make anesthesia care more environmentally friendly have met several barriers. These include the need for more education among anesthesiologists on the environmental impacts of different anesthesia options as well as a lack of support from hospital leadership to implement sustainability efforts.[63] In a qualitative study of anesthesiologists, several participants reported a lack of knowledge and feedback as impediments to sustainable practices.[64] An educational intervention with this aim at the University of Wisconsin was found to be effective at reducing GHG emissions through changes in anesthetic practices and resulted in cost savings for the hospital.[65] Interestingly, the environmental impact of physician decisions was a greater motivational impact than monetary savings.[65] Thus, further advocacy and education is warranted to guide and encourage more sustainable anesthetic practices.[17]

Beyond increased education, efforts to bring practice changes to scale could include the integration of sustainability metrics into the Quality Payment Program established by the Medicare Access and Children's Health Insurance Program Reauthorization Act of 2015. If environmental costs, including GHG emissions associated with clinical practices, were to be incorporated into the cost component of the program, it could serve to reward waste reduction strategies and programs within healthcare systems.[66]

RELEVANT AMA POLICY

Current AMA policy recognizes that climate change is a public health crisis and supports action on reducing greenhouse gas emissions and reducing global warming.[67] AMA policy recognizes that minoritized and marginalized populations, children, pregnant people, the elderly, rural communities, and those who are economically disadvantaged will suffer disproportionate harm from climate change and the health care sector has an important role to play in reducing its greenhouse gas emissions.[67,68] Lastly, AMA policy on asthma control encourages physicians to make appropriate use of evidence-based guidelines, to provide self-management education tailored to the literacy level of the patient by teaching and reinforcing appropriate self-monitoring, the use of a written asthma action plan, taking medication correctly, and avoiding environmental factors that worsen asthma; and encourages physicians to incorporate the four components of care (assessment and monitoring; education; control of environmental factors and comorbid conditions; and appropriate medication selection and use).[69]

CONCLUSIONS

Asthma and chronic obstructive pulmonary disease (COPD) are two respiratory diseases with a large burden of disease in the U.S. and treatment options primarily consist of inhalation therapy, particularly using metered dose inhalers (MDIs).[20,22] MDIs rely on liquefied-gas propellants to atomize medication for inhalation delivery and represent the most used inhalers in the world.[2,3] Propellants in MDIs were historically chlorofluorocarbons (CFCs) but following evidence of their deleterious impact on the Earth's ozone layer, were switched to hydrofluorocarbons (HFCs). While HFCs do not negatively affect the ozone layer, they are potent greenhouse gases (GHG) and contribute a significant portion of overall emissions in the health care sector.[2]

Switching to low carbon footprint inhalers is an opportunity to not only reduce GHG emissions from the health care sector, but also to improve chronic asthma management and health outcomes through the broader usage of dry powder inhalers (DPI) or soft mist inhalers (SMI) containing an inhaled corticosteroid. Other countries, particularly in Europe, have either made commitments to switch primarily to using DPIs for asthma treatment or made the transition years ago and now an overwhelming majority of asthma patients use DPIs.[3,38,42] However, there are several barriers to switching to low carbon footprint inhalers in the U.S,, including a common perception among physicians that DPIs are more difficult to use as well as cost and access barriers to more affordable and environmentally friendly options available. While there are perceptions among physicians that DPIs are more difficult to use for some vulnerable populations, research has demonstrated that a relatively small proportion of asthma patients have insufficient respiratory capacity to use DPIs effectively and that DPIs are just as clinically effective as MDIs.[11–13] The cost and access barriers could be addressed through policy changes that incentivize the introduction of greener, generic inhalers on the U.S. market and the inclusion of more environmentally friendly options on insurance formularies.

In addition to the use of HFCs in MDIs, the other major source of HFC/CFC use in health care comes from anesthetic gases, which includes the HFCs sevoflurane and desflurane and the CFC isoflurane. With anesthetic gases, there are several well documented strategies to improve environmental sustainability, including the removal or avoidance of the "worst" GHG offender from hospital drug formularies (desflurane), substituting non-inhaled anesthetic gases when clinically appropriate, and minimizing gas waste by lowering fresh gas flows during the maintenance phase of the anesthesia.[18] The switch to more environmentally friendly anesthesia options presents an opportunity for health care systems to lower their carbon footprint and could result in cost savings.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed.

1. That Policy H-160.932, "Asthma Control" be amended by addition and deletion to read as follows:

   The AMA: (1) encourages physicians to make appropriate use of evidence-based guidelines, including those contained in ~~Expert Panel Report III: Guidelines for the Diagnosis and Management of Asthma released by the National Heart, Lung and Blood Institute and~~ the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group 2020 Focused Updates to the Asthma Management

Guidelines; (2) encourages physicians to provide self-management education tailored to the literacy level of the patient by teaching and reinforcing appropriate self-monitoring, the use of a written asthma action plan, taking medication correctly, and avoiding environmental factors that worsen asthma; ~~and~~ (3) encourages physicians to incorporate the four components of care (assessment and monitoring; education; control of environmental factors and comorbid conditions; and appropriate medication selection and use)~~.~~; and (4) will, in collaboration with interested parties and organizations, develop content to help physicians talk through the different asthma control options and their known economic costs and environmental impacts. (Modify Current AMA Policy)

2. That Policy H-135.913, "Metered Dose Inhalers and Greenhouse Gas Emissions" be amended by addition and deletion to read as follows:

    1. Our AMA will advocate to reduce the climate effects of hydrofluorocarbon propellants in metered-dose inhalers and encourage strategies ~~for encouraging~~ supporting the development and use of alternative inhalers and propellants with equal and or higher efficacy and less adverse effect on our climate.
    2. Our AMA ~~will advocate for~~ supports legislative and regulatory reforms~~,~~ that increase access to affordable ~~to keep~~ inhalers ~~medications affordable and accessible, will urge FDA to consider metered-dose inhaler propellant substitutions for the purposes of climate protection as drug reclassifications,~~ with lower greenhouse gas emissions that align with current recommended standards of care. Reforms should aim to ensure the quality of patents issued on new drug-device combinations, prevent new patents for minor changes made to delivery systems, and remove barriers to market entry for generic inhalers.
    3. Our AMA supports consideration of the environmental impacts of inhalers when creating prescription drug formularies and for the federal government to factor environmental impact into price negotiations with pharmaceutical manufacturers. ~~without new patent or exclusivity privileges, and not allow these substitutions to classify as new drug applications~~.
    4. Our AMA recognizes the unique role metered dose inhalers play, in combination with spacers and facemasks, in treating vulnerable patients who are unable to use other inhaler options due to age, physiologic limitation from weakness or neurocognitive limitations, including but not limited to children with asthma, patients with tracheostomies, patients with cerebrovascular injuries, and patients with neuromuscular diseases.

    ~~3. Our AMA will study options for reducing hydrofluorocarbon use in the medical sector.~~

3. That the following new policy be adopted.

    REDUCING ENVIRONMENTAL IMPACTS OF ANESTHETIC GASES
    The AMA, in collaboration with interested parties and organizations, will disseminate evidence-based content and recommended strategies to reduce the global warming impact of anesthetic gases and encourage the phasing out of desflurane as an anesthetic gas.

Table 1: Global warming potential of CFC/HFCs used in current and possibly future MDIs as well as common anesthetic gases[1]

	Name	Global Warming Potential
	Carbon dioxide – reference	1
MDI Propellants	HFO 1234ze (potential new propellant in future MDIs)	<1
	HFA152a (potential new propellant in future MDIs)	138
	HFA-134a (used in most current MDIs)	1300
	HFA-227ea (used in some current MDIs)	3350
	CFC-11 (previously used in MDIs)	4660
	CFC-12 (previously used in MDIs)	10200
Anesthetic Gase	Nitrous oxide[2] (N_2O)	273
	Isoflurane ($CF_3CHClOCHF_2$)	539

[1] Table adopted from Table 1 from this article: https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bcp.15135 and Table 1 from this article: https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196(23)00084-0/fulltext
[2] While nitrous oxide is not a hydrofluorocarbon, it is often discussed in tandem with hydrofluorocarbons in terms of climate impacts from anesthetic gases.

	Desflurane ($CF_3CHFOCHF_2$)	2590
	Sevoflurane ($(CF_3)_2CHOCH_2F$)	144
	Methoxyflurane ($CHCl_2CF_2OCH_3$)	4

Table 2: FDA Approved Asthma and COPD Medications[a]

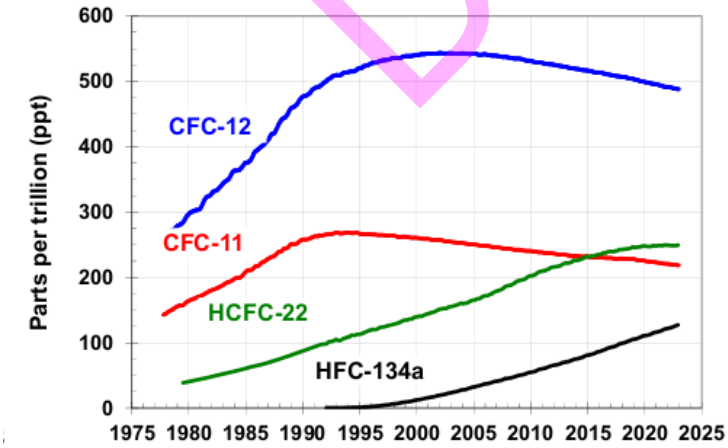
Drug name (active ingredient)	Company[b]	Method of Inhalation	Type of Treatment[c]	Target Disease
Aerospan (flunisolide)	Meda pharmaceuticals	pMDI	ICS	Asthma
Alvesco (ciclesonide)	Covis Pharma US	pMDI	ICS	Asthma
ArmonAir (fluticasone)	Teva	DPI	ICS	Asthma
Arnuity Ellipta (fluticasone furoate)	GlaxoSmithKline	DPI	ICS	Asthma
Asmanex (mometasone)	Organon	pMDI	ICS	Asthma
Asmanex Twisthaler (mometasone)	Organon	DPI	ICS	Asthma
Flovent HFA (fluticasone)[3]	GlaxoSmithKline	pMDI	ICS	Asthma
Flovent Diskus (fluticasone)	GlaxoSmithKline	DPI	ICS	Asthma
Pulmicort (budesonide)	AstraZeneca	DPI	ICS	Asthma
Qvar RediHaler (beclomethasone dipropionate)	Teva	pMDI	ICS	Asthma
Serevent Diskus (salmeterol xinafoate)	GlaxoSmithKline	DPI	ICS	Asthma/ COPD
Advair HFA (fluticasone propionate and salmeterol)	GlaxoSmithKline	pMDI	ICS/LABA	Asthma
Advair Diskus (fluticasone propionate and salmeterol)	GlaxoSmithKline	DPI	ICS/LABA	Asthma
Breo Ellipta (fluticasone furoate and vilanterol)	GlaxoSmithKline	DPI	ICS/LABA	Asthma/ COPD
Dulera (mometasone furoate and formoterol fumarate dihydrate)	Organon	pMDI	ICS/LABA	Asthma
Symbicort (budesonide and formoterol)	AstraZeneca	pMDI	ICS/LABA	Asthma/COPD
Trelegy Ellipta (fluticasone furoate, umeclidinium, and vilanterol)	GlaxoSmithKline	DPI	ICS/LAMA/ LABA	Asthma/COPD
Bretzi (budesonide, glycopyrrolate, and formoterol)	AstraZeneca	pMDI	ICS/LAMA/ LABA	COPD
Airsupra (albuterol and budesonide)	AstraZeneca	pMDI	ICS/SABA	Asthma
Arcapta (indacaterol)	Sunovion	DPI	LABA	Asthma
Foradil Aerolizer (formoterol fumarate)	Novartis	DPI	LABA	Asthma/COPD
Striverdi (olodaterol)	Boehringer Ingelheim	SMI	LABA	COPD
Incruse (umeclidinium)	GlaxoSmithKline	DPI	LAMA	COPD
Seebri (glycopyrrolate and formoterol)	Novartis	DPI	LAMA	COPD
Spiriva Respimat (tiotropium)	Boehringer Ingelheim	SMI	LAMA	Asthma/COPD
Spiriva HandiHaler (tiotropium)	Boehringer Ingelheim	DPI	LAMA	Asthma/COPD

[3] GlaxoSmithKline recently pulled Flovent HFA and Flovent Diskus from the market and it will now only be made available as a generic. https://www.cnn.com/2023/12/28/health/asthma-inhaler-generic-switch/index.html

Tudorza (aclidinium)	AstraZeneca	DPI	LAMA	COPD
Bevespi (glycopyrrolate and formoterol)	AstraZeneca	pMDI	LAMA/LABA	COPD
Anoro (umeclidinium and vilanterol)	GlaxoSmithKline	DPI	LAMA/LABA	COPD
Duaklir (aclidinium and formoterol)	AstraZeneca	DPI	LAMA/LABA	COPD
Stiolto Respimat (tiotropium and olodaterol)	Boehringer Ingelheim	SMI	LAMA/LABA	COPD
Utibron (glycopyrrolate and formoterol)	Sunovion	DPI	LAMA/LABA	COPD
ProAir (albuterol)	Teva	pMDI	SABA	Asthma
ProAir Respiclick/Digihaler (albuterol sulfate)	Teva	DPI	SABA	Asthma
Proventil HFA (albuterol sulfate)	Merck	pMDI	SABA	Asthma
Ventolin HFA (albuterol sulfate)	GlaxoSmithKline	pMDI	SABA	Asthma/COPD
Xopenex (levalbuterol)	Sunovion	pMDI	SABA	Asthma
Atrovent (ipratropium)	Boehringer Ingelheim	pMDI	SAMA	COPD
Combivent Respimat (ipratropium and albuterol)	Boehringer Ingelheim	SMI	SAMA/SABA	COPD

a: This list does not represent an exhaustive list of all FDA approved drugs for asthma and COPD but is intended to provide a snapshot of currently available inhalation therapies.
b: The company listed represents the pharmaceutical company that originally manufactured the drug. Several of these brand-name medications have been discontinued as generic formulations are available, while five have independent generics.
c: ICS: Inhaled corticosteroid; LAMA: long-acting muscarinic antagonist; LABA: Long-acting β-agonist; SABA: Short-acting β-agonist; SAMA: Short-acting muscarinic antagonist

Figure 1: Global average abundances of common CFCs and HFCs, from the NOAA global air sampling network since the beginning of 1979.[27] [To note: HCFC-22 is primarily used as a refrigerant in air conditioning units and is therefore not included in Table 1 as it is not healthcare related]



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7. ANDROGEN DEPRIVATION IN INCARCERATION

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See Policies D-430.997, H-345.981, H-430.975 and H-430.997

NOTE FROM THE COUNCIL: This report discusses sexual crimes, including against minors. The policy question posed in this report centers on the medical treatment and rehabilitation of those who have been convicted of sexual crimes, often against minors. Please use caution when reading, discussing, disseminating, and debating the contents of this report as they may be re-traumatizing or triggering.

INTRODUCTION

Resolution 501-A-23, "AMA Study of Chemical Castration in Incarceration" was adopted and states that "our AMA study the use of chemical castration in the treatment of incarcerated individuals with paraphilic disorders and for other individuals who commit sexual offenses, including ethical concerns over coercion in its use as an alternative to incarceration and in probation and parole proceedings."

This report serves as the Council on Science and Public Health's response to this charge. For the purposes of this report, the term "androgen deprivation" (AD) will be substituted for "chemical castration" to be more consistent with scientific literature, and to avoid the potential confusion of reversible AD with irreversible surgical castration, typically performed by surgical removal of the testes (orchiectomy).

METHODS

English language articles were selected from searches of PubMed and Google Scholar using the search terms "chemical castration", "androgen deprivation", "chemical castration AND incarceration", and "androgen deprivation AND incarceration". Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by government agencies and applicable organizations were also reviewed for relevant information.

BACKGROUND

Sexual crimes can cause significant trauma in their victims. Survivors can be subject to a lifetime of psychological trauma including self-blame, post-traumatic stress disorder, suicidal ideation, and structural changes in the brain.[1-4] This may be further challenging for those who experience this abuse at a younger age. However, incident rates of child sexual abuse may be difficult to properly assess due to the nature of the victims – e.g., victims may not understand they have been the victims of a crime, or they may rely on their assailant for their basic needs. One study estimates that up to 27 percent of girls and eight percent of boys experience childhood sexual assault in the United States.[5] Per the U.S. Sentencing Commission, approximately 1,000 cases per year in Federal courts involve sexual abuse, with 94 percent of offenders being men.[6]

The public perception of perpetrators of sexual crimes is extremely negative, resulting in the feeling that actions against these offenders should be more punitive and less rehabilitative compared to those who have committed non-sexual offenses.[7] Due to the prevalence and the severity of these crimes, along with the social outrage, public officials often seek non-traditional approaches for dissuading future sexual abuse, such as sexual offender registries, which are outside of the scope of this report.

One of the approaches, currently utilized in seven states (see Appendix 1), is the use of drugs to lower testosterone levels, with the belief that lower testosterone will reduce the likelihood of an individual committing a sexual crime. This report seeks to describe the current science in the diagnosis and management of paraphilic disorders, examine the utilization of AD in the criminal justice system, and discuss the ethical issues presented by legal mandates for AD in a carceral setting.

PARAPHILIC DISORDERS, STIGMA, AND THE CRIMINAL JUSTICE SYSTEM

It is important to distinguish the difference between paraphilias and paraphilic disorders. Per the Diagnostic and Statistical Manual of Mental Disorders (DSM), a paraphilia is "any intense and persistent sexual interest other than sexual interest in genital stimulation or preparatory fondling with phenotypically normal, physically mature, consenting human partners."[8] Examples of paraphilic disorders included in the DSM are exhibitionistic disorder, voyeuristic disorder, pedophilic disorder, and frotteuristic disorder. If the paraphilia is causing distress or impairment to either the individual or another person, it may be classified as a paraphilic disorder. The presence of a paraphilia itself does not necessarily warrant clinical intervention or a paraphilic disorder diagnosis. Additionally, it is critical to distinguish between paraphilic thoughts and paraphilic behaviors. This distinction is especially important when discussing criminal acts. Many individuals with paraphilic disorders do not act upon their desires, but they are still distressing and the individual would benefit from clinical support.[9]

Individuals with paraphilic disorders are subject to intense social stigma, which often results in feelings of guilt, shame, and self-loathing.[10] Clinically, this presents multiple issues, such as individuals being less likely to seek care, and making it more difficult to recruit patients for clinical trials of new treatments. This is particularly true in instances where individuals could be required to disclose that they are experiencing urges to perform criminal acts, even if they do not act upon them. As such, blanket approaches, particularly in the form of legal mandates, should be approached with skepticism as to whether they are truly informed by research and best practices, or a manifestation of the social stigma and bias towards punitive measures for those convicted of sexual offenses. Many of those with paraphilic disorders are themselves survivors of abuse, often experienced in childhood.[11]

Treatment for paraphilic disorders is difficult and nuanced. Paraphilic disorders are highly heterogeneous in their manifestation and presentation, ranging from urges to actions, which is further complicated by the social stigma preventing many from seeking care. AD seeks to reduce testosterone, and thus arousal. While this may be effective for some, many convicted of sexual crimes report that they were not seeking sexual gratification, but rather acted out of grievance, impulsivity, or a desire to exert control.[12] This highlights the intersection of many paraphilic disorders with other psychological conditions, emphasizing the importance of consistent, adjunctive psychotherapy, and why many pharmacotherapy approaches for paraphilic disorders go beyond just AD, often including antidepressants, anxiolytics, and mood stabilizers.[13-16]

ANDROGEN DEPRIVATION IN A CLINICAL SETTING

AD therapy is a commonly accepted medical treatment approach for managing prostate cancers, where hormones such as testosterone are required for cancer cell growth and proliferation.[17] Medications used for AD regimens vary and include leuprorelin, goserelin, and triptorelin, but generally the mechanism of AD action is either as an agonist or antagonist against luteinizing hormone-releasing hormone (LHRH), resulting in a reduction of testosterone production. Patients receiving AD for prostate cancer report loss of libido (up to 91 percent) and erectile dysfunction (up to 95 percent).[18] The high prevalence of sexual dysfunction, as well as the decrease in systemic testosterone levels (and thus presumed decrease in behaviors associated with testosterone, such as aggression) have led to the theoretical utility of AD for managing some types of paraphilic disorders.

As AD influences hormones, the level of side effects particularly in long-term use can be serious. In a long-term study of men with paraphilic disorders being administered triptorelin, 11 of 18 men saw decreases in bone density, with other reported side effects including persistent hot flashes, diffuse pain, and erectile dysfunction with age-appropriate sexual partners.[19] Depot medroxyprogesterone acetate (DMPA), which is the required medication for AD in the carceral context in California (described below), is contraindicated for people with adrenal disease, severe hypertension, risk of thromboembolic disease, diabetes mellitus, severe depressive disorder, pituitary disease, and meningioma. These side effects often result in high rates of discontinuation, which in the context of most state laws described later, would require the individual to return to prison.[20] Due to the side effect profile, the duration of treatment is a critical component. In the oncology setting, the duration of treatment is often on the scale of months, and there is some interest in an intermittent approach (where patients cycle on and off treatment) to better manage side effects.[21] Patients with paraphilic disorders may receive AD for years, thus subjecting them to more serious side effects.[22]

The evidence base for AD as a treatment for paraphilic disorders primarily comprises of case reports, small cohort, or uncontrolled studies. With those caveats, the current published works generally support that AD may be effective

for treating some people with paraphilic disorders. In one study, 29 men previously convicted of sexual crimes and presenting with paraphilic behaviors (child molestation, exhibitionism, or frottage) were treated with DMPA for six months.[23] In that period, one reported committing a sexual crime, while most described a near complete suppression of criminal sexual thoughts and activities. Another study of 46 male patients with paraphilic disorders undergoing group psychotherapy found that patients receiving DMPA in conjunction with psychotherapy had a lower relapse rate (15 percent) compared to those using psychotherapy alone (68 percent).[24] These findings are generally observed across the literature, with a meta-analysis (N = 22,181 persons across 69 total studies) finding that hormonal medication had an odds ratio of 3.08 for remission (thoughts, actions, or both) compared to an odds ratio of 1.45 for cognitive-behavioral therapy alone, with the caveat that most hormonal medication included in their analysis was administered in conjunction with cognitive-behavioral therapy.[25]

Finally, studies nearly universally focus on the impact of AD on men. While sexual crimes are disproportionately committed by men (97 percent of arrests for rape and 93 percent of arrests for other sexual crimes in 2019 were men), there is a noted lack of research available for treatment of women and people of other gender identities with paraphilic disorders, particularly those which may be utilizing hormone therapy for gender affirming care.[26]

ANDROGEN DEPRIVATION THERAPY IN THE CARCERAL SETTING

As of this writing, there are seven states (California, Florida, Iowa, Louisiana, Montana, Wisconsin, and Alabama) which use AD in some component of their judicial response to sexual crimes. A summary of state approaches is provided in Appendix 1 of this report. State approaches to AD generally vary over the level of discretion over who receives it, the duration, and whether it is tied to parole and/or probation.

In California, if an individual is convicted of a crime that is sexual in nature against a victim under the age of 13, a long-acting injection of DMPA may be a condition of their parole. If the individual has two convictions for sexual crimes against a minor, this injection is mandatory as a condition to receive parole.[27]

In Florida, all individuals convicted of sexual assault (regardless of age of victim) may be required, at the discretion of the presiding judge, to receive AD upon completion of their prison sentence after consulting a medical professional, not necessarily a physician.[28] The judge can decide the duration of AD, which can be lifelong. If an individual does not appear for their court-mandated AD administration, they are charged with an additional felony. Similar to California, AD in Florida becomes mandatory upon a second conviction.

Alabama, which adopted its AD statute in 2019, allows judges to decide if someone convicted of sexual crimes against a victim under 12 years old will receive AD after their first offense. Additionally, those convicted in Alabama are required to pay for their AD for an indeterminate period of time, but inability to pay may not be used as the basis to deny parole. It is unclear at this time if court-mandated AD would be reimbursed by insurance.

Interestingly, there does not appear to be a clear trend in the recent actions of states and AD laws. For example, Alabama enacted its statute in 2019, while a legislator in New Mexico introduced an AD bill in 2021 but it failed to pass. Meanwhile, Oregon (2001) and Georgia (2006) both had AD statutes that have since been repealed. In Oregon, the law was a time-limited pilot program that was not renewed upon its conclusion.[29] In Georgia, references to AD were removed from laws as an unspecified “policy decision,” with no other public justification provided.[30]

When trying to measure if AD laws are effective at reducing recidivism, it is critical to appreciate the difficulty in recruiting, retaining, and measuring behavioral outcomes in populations of those convicted of sexual crimes. This is a highly stigmatized population, and studies often require self-reporting of thoughts and actions and may involve confessing to a crime or thoughts that they feel deep shame towards. Efforts to measure recidivism as an endpoint are incredibly difficult to assess accurately due to the previously described factors which cause sexual violence to be underreported. This is especially true if AD is administered as a mandatory condition of parole. Individuals receiving parole are already a self-selecting population – they have indicated that they do not want to be incarcerated any more, meaning that incarceration is a deterrent for them. As such, individuals who receive AD as a condition of parole may already be a population less likely to re-offend, and the effect of AD on recidivism rates versus the fear of being incarcerated may be impossible to disentangle.

ETHICAL AND CONSTITUTIONAL CONCERNS

AD laws have been constitutionally challenged in state courts. For example, in 1984, a Michigan man convicted of rape was sentenced to one year in prison and five years of probation only if he received DMPA for AD.[31] The Michigan Court of Appeals found in *People v. Gauntlett*, this approach to be unconstitutional, with the rationale that DMPA was not FDA-approved for AD, and that the individual could not provide informed consent if this was court-mandated administration.[32]

While many AD laws in other states have not been challenged in courts, the outcome in Michigan highlights several of the criticisms against AD laws. Beyond concerns of drug efficacy, safety, and consent, there are additional concerns around the constitutionality of AD laws. For example, some have argued that AD violates the Eighth Amendment's protection against cruel and unusual punishment, or even that government intervention and mandating behavior-altering drugs may violate an individual's First Amendment rights to have freedom of thought or mental autonomy.[33]

Even in instances where an individual is provided a choice to receive AD, it is unlikely that this would truly be free from coercion. The social stigma of those with paraphilic disorders can be magnified in the carceral setting, and often results in those convicted of sexual crimes being targeted for violence. One study, for example, found that individuals convicted of sexual crimes made up 15 percent of an inmate population, but were the victims for over 30 percent of homicides in prison.[34]

Finally, while AD laws are intended to reduce the likelihood of committing additional sexual crimes, they do impact fertility and selective enforcement harkens back to America's dark history of eugenics. In the 1920s, dozens of states enacted eugenic sterilization laws, resulting in the forceful sterilization of populations deemed undesirable – often inmates, and disproportionately used against Black men and women.[35] Particularly in instances where the use of AD is at the discretion of the court, legal scholars worry that racist stereotypes of hyper-sexual Black men will result in disproportionately higher rates of AD administered to marginalized and minoritized groups, which could serve as a modern eugenics law.[36]

A review of the available literature was unable to identify analysis of the rate at which AD is used in the carceral setting, nor the demographics of those receiving it.

CURRENT AMA POLICY

The AMA, through both its policy and administration of the Code of Medical Ethics, has a strong history of opposing the use of medicine as punishment. Of particular relevance is Opinion 9.7.2, "Court-Initiated Medical Treatment in Criminal Cases" (full text available at end of report), which notes such treatments "raise important questions as to the rights of prisoners, the powers of judges, and the ethical obligations of physicians" and that "medical ethics do not require a physician to carry out civic duties [i.e., court-initiated medical treatments like AD] that contradict fundamental principles of medical ethics." The Code states that physicians who participate in court-initiated medical treatments should only do so "if the procedure being mandated is therapeutically efficacious" and is "not a form of punishment." Additionally, the Code explains that physicians should "[t]reat patients based on sound medical diagnoses, not court defined behaviors" and that they should "[d]ecline to provide treatment that is not scientifically validated."

As of this writing, it is likely that state laws imposing AD fail to meet the standards set forth by the Code of Medical Ethics. States either utilize automatic mandates or rely solely on the discretion of the courts for deciding who requires AD, removing physician discretion and clinical judgement, as well as eliminating the ability for the patient to provide consent. Additionally, some statutes specifically cite that AD must be performed using DMPA, which has not been FDA-approved for AD nor is it known to be included in any clinical guidelines for AD in the context of prostate cancer or paraphilic disorder treatment.[18] Finally, instances where AD may be optional as a condition for parole or probation likely violate patient voluntariness, in that a patient is forced to choose between extended incarceration or receiving a medicine, thus producing a highly coercive situation.

CONCLUSION

Sexual crimes can cause significant trauma in their victims and survivors may experience a lifetime of psychological trauma including self-blame, post-traumatic stress disorder, suicidal ideation, and structural changes in the brain. The public perception of perpetrators of sexual crimes is extremely negative, resulting in the feeling that actions against these offenders should be more punitive and less rehabilitative. While policymakers have sought non-traditional approaches to reduce the prevalence of sexual crimes in their communities, current state laws which remove physicians and instead mandate AD for convicted sex offenders are not supported by science and are contrary to the Code of Medical Ethics. AD should be viewed as a single tool in the physician's toolbox for treating some paraphilic disorders and should only be initiated using informed consent and a physician's best clinical judgement for a given patient and their circumstances, regardless of whether the examination occurs in a prison or a clinic.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted and the remainder of the report be filed:

1. That Policy H-430.977, "AMA Study of Chemical Castration in Incarceration" be rescinded.
2. That our AMA:
    a. Opposes laws, regulations, and actions of the court which remove physician autonomy and clinical judgement from treatment decisions regarding androgen deprivation (also known as chemical castration) for those convicted of sexual crimes.
    b. Opposes linkages of criminal sentencing, parole, or probation to court-mandated androgen deprivation.
    c. Encourages data collection on the utilization, court mandates, duration of therapy, and clinical outcomes of androgen deprivation in the carceral setting.
    d. Supports continued research for effective treatments for paraphilic disorders, including efforts to reduce stigma and recruit patients with paraphilic disorders into clinical trials.
3. That Policies D-430.997, "Support for Health Care Services to Incarcerated Persons," H-430.978 "Improving Care to Lower the Rate of Recidivism," and H-345.981 "Access to Mental Health Services" be reaffirmed.

APPENDIX 1

Table 1: Summary of state laws regarding androgen deprivation therapy (as of January 2024)

State	Code	Mandatory?	Age for victims and applications	Duration	Notes
Alabama	Section 15-22-27.4: Parole of persons convicted of sex offense involving person under 13 years of age	Discretion of court as a condition of parole	Sex crime with a victim under the age of 13	Can continue until the department of corrections deem no longer necessary	
California	CA Penal Code Section 645	First conviction: At court's discretion Second or subsequent conviction: Required	Any sex crimes against someone 13 years or younger	Continued until the Department of Corrections deems treatment no longer necessary	Specifically requires the use of medroxyprogesterone acetate.
Florida	Florida Statute 794.0235	First conviction: At court's discretion Second or subsequent conviction: Required	Applies to sexual battery convictions (adult or minors)	Duration will be determined by court and can be up to the life of the offender.	Requires a court appointed medical expert determination that defendant is appropriate candidate for treatment.

State	Code	Mandatory?	Age for victims and applications	Duration	Notes
Iowa	903B.10 Hormonal intervention therapy	First conviction: At court's discretion Second or subsequent conviction: Required unless court or board of parole determines the treatment would not be effective	For "serious sex offenses" with a minor under the age of 12 (sexual abuse of all degrees, assault, and sexual exploitation)	Treatment will continue until the agency in charge of supervision deems no longer necessary.	Offenders have to pay a "reasonable fee" to pay for the costs of treatment
Georgia	Formerly Ga. Code Ann. § 16–6-4 (2002) and Ga. Code Ann. § 42–9-44.2 (2002)	n/a	n/a	n/a	Repealed in 2006
Louisiana	RS 14:43:6	First conviction: At court's discretion Second or subsequent conviction: Required	All cases of first- or second-degree rape, OR sexual battery and molestation when the victim is under 13	Court will specify the duration of treatment, up to the life of the defendant.	Requires a court appointed medical expert determination that defendant is appropriate candidate for treatment
Montana	45-5-212 Assault on minor	First conviction: At court's discretion Second or subsequent conviction: Required	Applies to all convictions (adult or minors) of: -Sexual assault -Rape -Incest	Can continue until the department of corrections deem no longer necessary	
Oregon	Formerly Ore. Rev. Stat. § 144.625 (2001), Ore. Rev. Stat. § 144.627 (2001), Ore. Rev. Stat. § 144.629 (2001), Ore. Rev. Stat. § 144.631 (2001)	n/a	n/a	n/a	Repealed in 2001
Wisconsin	Wisconsin Statutes, Section 302.11(1)(b)2 Wisconsin Legislative Council IM-2021-07: Requirement for chemical castration	Discretion of Department of Corrections of Parole Commission	Sex crimes with a victim below the age of 13	Unspecified	

CITED AMA POLICY

Opinion 9.7.2, "Court-Initiated Medical Treatment in Criminal Cases"

Court-initiated medical treatments raise important questions as to the rights of prisoners, the powers of judges, and the ethical obligations of physicians. Although convicted criminals have fewer rights and protections than other citizens, being convicted of a crime does not deprive an offender of all protections under the law. Court-ordered medical treatments raise the question whether professional ethics permits physicians to cooperate in administering and overseeing such treatment. Physicians have civic duties, but medical ethics do not require a physician to carry out civic duties that contradict fundamental principles of medical ethics, such as the duty to avoid doing harm.

In limited circumstances physicians can ethically participate in court-initiated medical treatments. Individual physicians who provide care under court order should:

(1) Participate only if the procedure being mandated is therapeutically efficacious and is therefore undoubtedly not a form of punishment or solely a mechanism of social control.
(2) Treat patients based on sound medical diagnoses, not court-defined behaviors. While a court has the authority to identify criminal behavior, a court does not have the ability to make a medical diagnosis or to determine the type of treatment that will be administered. When the treatment involves in-patient therapy, surgical intervention, or pharmacological treatment, the physician's diagnosis must be confirmed by an independent physician or a panel of physicians not responsible to the state. A second opinion is not necessary in cases of court-ordered counseling or referrals for psychiatric evaluations.
(3) Decline to provide treatment that is not scientifically validated and consistent with nationally accepted guidelines for clinical practice.
(4) Be able to conclude, in good conscience and to the best of his or her professional judgment, that to the extent possible the patient voluntarily gave his or her informed consent, recognizing that an element of coercion that is inevitably present. When treatment involves in-patient therapy, surgical intervention, or pharmacological treatment, an independent physician or a panel of physicians not responsible to the state should confirm that voluntary consent was given.

Support for Health Care Services to Incarcerated Persons D-430.997

Our AMA will:
(1) express its support of the National Commission on Correctional Health Care Standards that improve the quality of health care services, including mental health services, delivered to the nation's correctional facilities;
(2) encourage all correctional systems to support NCCHC accreditation;
(3) encourage the NCCHC and its AMA representative to work with departments of corrections and public officials to find cost effective and efficient methods to increase correctional health services funding;
(4) continue support for the programs and goals of the NCCHC through continued support for the travel expenses of the AMA representative to the NCCHC, with this decision to be reconsidered every two years in light of other AMA financial commitments, organizational memberships, and programmatic priorities;
(5) work with an accrediting organization, such as National Commission on Correctional Health Care (NCCHC) in developing a strategy to accredit all correctional, detention and juvenile facilities and will advocate that all correctional, detention and juvenile facilities be accredited by the NCCHC no later than 2025 and will support funding for correctional facilities to assist in this effort; and
(6) support an incarcerated person's right to: (a) accessible, comprehensive, evidence-based contraception education; (b) access to reversible contraceptive methods; and (c) autonomy over the decision-making process without coercion.

Improving Care to Lower the Rate of Recidivism H-430.978

Our American Medical Association will advocate and encourage (1) federal, state, and local legislators and officials to increase access to community mental health facilities, community drug rehabilitation facilities, appropriate clinical care, and social support services (e.g., housing, transportation, employment, etc.) to meet the needs of indigent, homeless, and released previously incarcerated persons; and (2) federal, state, and local legislators and officials to advocate prompt reinstatement in governmental medical programs and insurance for those being released from incarceration facilities.

Access to Mental Health Services H-345.981

Our AMA advocates the following steps to remove barriers that keep Americans from seeking and obtaining treatment for mental illness:
(1) reducing the stigma of mental illness by dispelling myths and providing accurate knowledge to ensure a more informed public;
(2) improving public awareness of effective treatment for mental illness;
(3) ensuring the supply of psychiatrists and other well trained mental health professionals, especially in rural areas and those serving children and adolescents;
(4) tailoring diagnosis and treatment of mental illness to age, gender, race, culture and other characteristics that shape a person's identity;
(5) facilitating entry into treatment by first-line contacts recognizing mental illness, and making proper referrals and/or to addressing problems effectively themselves; and
(6) reducing financial barriers to treatment.

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8. DECREASING REGULATORY BARRIERS TO APPROPRIATE TESTOSTERONE PRESCRIBING

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See Policies D-185.981, D-270.983, D-480.964, H-65.976, H-95.946, H-140.824,H-160.991, H-185.927 and H-315.983

INTRODUCTION

Our American Medical Association (AMA) House of Delegates referred the second Resolve of Resolution 519-A-23, “Decreasing Regulatory Barriers to Appropriate Testosterone Prescribing.” The referred resolve asked that our AMA study the outcomes of expanding access to testosterone through decreasing state and health insurer regulatory requirements. In addition to the process limitations, other barriers to care for testosterone prescribing include prescription drug monitoring program (PDMP) state database reporting, telehealth, 30-day supply, and mail delivery limitations.

METHODS

English-language reports were selected from a PubMed and Google Scholar search through January 2024, using the text terms “testosterone,” “prescribing,” “barriers,” and “regulations.” Additional articles were identified by manual review of the references cited in these publications. Further information was obtained from the Internet sites of medical specialty societies, federal and state agencies, human rights organizations, legal organizations, among others to identify regulatory and legal barriers to testosterone treatments, prescribing, and access when medically indicated.

BACKGROUND

Testosterone is a hormone that is naturally produced in the body of all individuals. Testosterone replacement therapy (TRT) has been explored as a therapy for a variety of conditions, including low serum testosterone levels, hypogonadism, erectile dysfunction, osteoporosis, diabetes mellitus, and hypoactive sexual desire disorder.[1–7] Synthetic testosterone is classified as an anabolic-androgenic steroid designed to mimic natural testosterone.

Testosterone is also a vital component of gender affirming hormone therapy (GAHT) for transgender, non-binary, and/or gender diverse (TND) individuals, aiding in the development of secondary sex characteristics aligning with their gender identity including physical changes such as increased muscle mass and strength, fat redistribution, cessation of menstrual periods, heightened sex drive, facial and body hair growth, deepening of voice, and clitoral enlargement, among others.[8,9] These effects may begin within 1-6 months, while some may take up to 2-5 years after initiating therapy. The effects may significantly alleviate gender dysphoria, depression, psychological symptoms, and suicidality while enhancing overall quality of life, interpersonal functioning, psychological adjustment, sexual function, body satisfaction, and self-esteem among TND individuals.[8,10,11] GAHT is often maintained throughout life, and discontinuation of hormone therapy can lead to bone loss in TND individuals, particularly those who have undergone gonad removal, which highlights the importance for access to this therapy.[12]
Testosterone, when prescribed as part of medically monitored GAHT, is generally considered safe, with severe side effects being exceptionally rare.[13] Concerns regarding associations between testosterone and severe adverse effects, including mood alterations and cardiovascular disease, stem from administering multiple testosterone derivatives at doses ranging from 10 to 100 times higher than the normal physiologic levels. Individuals using high doses of testosterone have reported withdrawal symptoms, such as depression, fatigue, irritability, loss of appetite, decreased libido, and insomnia.[14] TRT, as compared to performance enhancing use, includes testosterone prescriptions within the physiological dosage range which is considered safe. Studies consistently demonstrate significant positive effects on various aspects of mental health and well-being among patients on TRT.[13,15] However, health care experts have called for further research into the long-term risks associated with testosterone products, including its potential impact on cardiovascular health and the occurrence of breast/chest and endometrial cancers.[16].[13,17–19]

DISCUSSION

Policy Affecting Appropriate Testosterone Prescribing in the United States

Recently, there has been a significant increase in state laws banning gender affirming care (GAC) including GAHT for TND people. Across the nation, state legislatures, governors, and administrative agencies are increasingly implementing measures to limit access to gender-affirming care, particularly targeting youth. GAC is supported by all major medical associations representing over 1.3 million U.S. physicians, including the AMA.[20]

Since 2021, 23 states have enacted laws that prohibit healthcare professionals from providing gender-affirming medical interventions, including hormone therapy and surgeries, to minor patients.[21] These legislative measures effectively ban evidence-based care for TND youth by imposing legal and professional penalties on health care professionals who provide GAC.[22] Some states have also taken steps to limit access to GAC for adults.[23] In addition to limiting access to medically necessary care, providers of GAC have also been threatened with violence, jeopardizing physician safety and practice.[24]

On a national level, in 2021, U.S. Department of Health and Human Services (HHS), Office for Civil Rights (OCR) expanded its interpretation and enforcement of Section 1557 of the Affordable Care Act (ACA) and Title IX of the Civil Rights Act, to include protection against discrimination based on sexual orientation and gender identity, ensuring access to GAC.[25] This was reiterated in 2022, when HHS issued a notice affirming its support for TND youths’ access to gender-affirming care.[26]

Regulatory Barriers to Appropriate Testosterone Prescribing

The primary regulatory obstacle to appropriate testosterone prescribing, in addition to state-based laws restricting care for TND patients, is its controlled substance scheduling status. Testosterone is currently categorized as a Schedule III drug under the Controlled Substances Act (CSA). Such classification indicates a potential for misuse, in addition to a potential to lead to physical dependence or psychological dependence.[27] Uniquely, testosterone was added to the Controlled Substances Act by the Anabolic Steroids Control Act of 1990, which classified all anabolic steroids as schedule III-controlled substances, with the aim to stop chemical performance enhancement in sports.[28] Congress effectively circumvented FDA's regulatory authority, by bypassing the typical scientific and evidence review to inform scheduling.[29] The act faced opposition from the AMA, the FDA, and the National Institute on Drug Abuse and despite this opposition was enacted by Congress.[29–31]
As a Schedule III controlled substance, testosterone is subject to more stringent regulations compared to other prescription medications. Regulations on controlled substances include shorter validity periods for prescriptions (physicians must rewrite prescriptions every 6 months), limitations on refill quantities (limited to 30-day supplies), and potential exclusions from telehealth and mail-order services of testosterone. Testosterone restrictions necessitate frequent communication between individuals using testosterone and their prescriber to maintain a continuous supply.[29] Amid the COVID-19 pandemic, temporary adjustments in regulations enabled individuals to acquire 100-day medication supplies via mail services, however testosterone remained exempt from these alterations due to its classification as a controlled substance.[29,32]

Prescription Drug Monitoring Programs

PDMPs are state-level electronic databases intended for public health surveillance, prescription monitoring, and to inform clinical decision-making. PDMPs track dispensed prescriptions based on the schedule level designated in the state controlled substances act (CSA). As of 2023, eight states monitor schedule II – IV via their PDMP, 45 states, territories, and districts monitor Schedules II through V, 32 states track "drugs of concern" (i.e., drugs not scheduled under their state CSA), and one state monitors all prescription medications.[33] Currently, testosterone is a monitored substance in all state PDMPs. Patients have raised concerns regarding the surveillance of medications, including fears of being outed by their health care professionals, pharmacists, law enforcement and others with access to their states' PDMP data.[34]

Almost all PDMPs can be used by court officials, probation and parole officers, and law enforcement agencies to prevent controlled substance diversion or monitor a patient's prescription use with a court order, search warrant, or subpoena.[35] Law enforcement permission to access PDMPs varies by state. As of 2022, 25 states require an active investigation or "official duties," 18 require a subpoena, 17 require a court order, and 11 require a search warrant to view PDMP records.[36,37] (See Table 1) Some states have multiple forms of law enforcement access requirements that are accepted.[55] As GAC becomes criminalized in some states, access to this data by law enforcement could be devastating for patients.

HIPAA's Privacy Rule regulates the use and disclosure of protected health information (PHI) by covered entities, but it does not specifically include PDMP data. In December 2023 members of Congress urged HHS to revise the Health Insurance Portability and Accountability Act (HIPAA) regulations to include PDMPs, after briefings with major pharmacies revealed that law enforcement agencies were secretly obtaining thousands of prescription records without a warrant.[38] All eight major pharmacy chains reported that "they do not require a warrant prior to sharing pharmacy records with law enforcement agents, unless there is a state law that dictates otherwise."[38] Gaps in federal privacy coverage of both medical, prescription, and PDMP data raises concerns to deter physician prescribing, pharmacist dispensing, and patients procuring medically indicated testosterone.[39] Ongoing research is essential to investigate the unintended consequences associated with granting law enforcement access to medical prescription histories, especially in the absence of a court order.

Insurer or Payer Barriers to Testosterone Prescribing and Access

Many transgender individuals do not have health insurance. Those with health insurance often encounter challenges with public and private insurers denying coverage for GAC, leaving patients with large out-of-pocket cost.[40–42] Findings from a 2022 nationally representative survey by the Center for American Progress show that over 25 percent of transgender participants faced denials for hormone therapy by health insurance providers.[43] According to the 2022 Employee Benefits Survey, among the 30 percent of U.S employer-provided health plans providing GAC,

only 25 percent cover GAC-related prescription drug therapy.[44] Moreover, only 26 percent include physician visits for GAC and only 21 percent cover GAC-related lab tests, both of which are typically necessary to be prescribed testosterone.[44]

Even though a large number of insurance companies now provide coverage to TND individuals because of federally mandated laws, many continue to deny coverage.[45] In 2021, 13 states reported that coverage of GAHT is not addressed in their states' statute or policy, and 2 states exclude coverage of GAHT.[46] The U.S. Transgender Survey reports that of adults utilizing GAHT, 21 percent (2,526 insured patients) of treatment claims have been denied.[47] Beyond these denials, TND individuals report various insurance-related hurdles, such as difficulties in obtaining coverage for GAC and other medical services, updating health insurance records, and issues related to network adequacy.[43] For example, individuals with insurance often need to obtain prior authorization before testosterone can be covered, delaying care up to 7 business days or more.[48] Among TND individuals, nonprescription hormone use is significantly higher among those whose claims were denied or were uninsured.[47]

Testosterone access is further complicated by insurance industry formulary drug tiers, in which "non-preferred" testosterone products are restricted via prior authorization or higher cost-sharing requirements.[46] In 2021, 34 out of 51 state Medicaid programs covered GAHT, while nine states and two territories did not provide coverage.[49] Confirmation regarding GAHT coverage could not be verified for eight states and three territories.[49]

There have been some successful initiatives to improve GAC accessibility through the expansion of state Medicaid essential health benefit plans and the explicit inclusion of GAC, including GAHT, in state Medicaid coverage laws.[50] For instance, in 2023 Colorado became the first state to explicitly integrate gender-affirming care to treat gender dysphoria, encompassing surgical procedures, hormone therapy, and mental and behavioral health services, into its benchmark health insurance plan for essential health benefits.[51] While further studies are needed to assess the impact of Colorado's expanded care, the coverage of GAC contributes to improved health outcomes while reducing gender dysphoria, depression, anxiety, and suicidality among TND Coloradans.[52,53]

AMA POLICY AND ADVOCACY

The AMA has robust policy regarding gender-affirming care, patient privacy, health equity, medical necessity, protecting the provider-patient relationship, telehealth, and prior authorization. Of particular relevance to this report is AMA Policy H-185.927, "Clarification of Evidence-Based Gender-Affirming Care," which emphasizes the importance of evidence-based gender-affirming care as determined through shared decision making between patients and physicians. This policy instructs our AMA to "oppose laws and policies that criminalize, prohibit or otherwise impede the provision of evidence-based, gender-affirming care" and to "advocate for federal, state, and local laws and policies to protect access to evidence-based care for gender dysphoria and gender incongruence." Additionally, our AMA advocates for equitable coverage of gender-affirming care by health insurance providers, both public and private, through Policy H-185.950, "Removing Financial Barriers to Care for Transgender Patients."

AMA policy H-315.983, "Patient Privacy and Confidentiality," affirms that HIPAA should be the minimal standard for protecting client-patient privilege, and that law enforcement agencies requesting private medical information should only be given access through a court order granted through clear and convincing evidence, with the records subject to stringent security measures.

Further, Policy G-605.009 directs the AMA to convene experts and stakeholders to "identify issues with physician payment and reimbursement for gender-affirming care and recommend solutions to address these barriers to care." The Task Force to Preserve the Patient-Physician Relationship When Evidence-Based, Appropriate Care Is Banned or Restricted has invited interested Federation partners to participate and is in the process of implementing this policy.

Protecting access to GAC has been a priority for the AMA for many years. Since the legislative attempts to ban GAC first emerged, the AMA has been working closely with state medical associations to oppose these inappropriate intrusions in the practice of medicine. The AMA has submitted testimony and sent letters to legislators in several states and has assisted behind-the-scenes in many more states. In 2021, the AMA also publicly urged governors across the country to reject state legislation aimed at prohibiting medically necessary gender affirming care for minor patients.[54] AMA advocacy has also supported state "shield laws" to protect physicians who provide GAC and their patients from interstate enforcement of GAC bans and promote telehealth access to GAC. The AMA

has also been very active in litigation and has submitted numerous amicus briefs urging courts to overturn laws that ban GAC.

Additionally, in 2019 the AMA published an issue brief with GLMA emphasizing the importance of health insurance coverage for transgender patients and asserting the medical community's duty to advocate for evidence-based care, reiterating that medical decisions should be made by patients, their relatives and health care professionals, not politicians.[55] Lastly, in response to policy that was adopted at the 2023 Annual Meeting Annual, D-270.983, "Decreasing Regulatory Barriers to Appropriate Testosterone Prescribing," the AMA asked the FDA to review the evidence on testosterone, with the possibility of updating recommendations to send to the DEA regarding its scheduling. In this letter the AMA conveyed concerns to the FDA Commissioner about the current scheduling of testosterone-containing drug products, suggesting that the existing schedule may unnecessarily restrict access to care for patients in critical need.[56]

CONCLUSION

Addressing regulatory obstacles to appropriate testosterone prescribing requires a multifaceted approach that encompasses both physician and patient perspectives. Initiatives such as rescheduling testosterone to expand access through telehealth and reducing regulation on dispensing are crucial steps toward ensuring equitable access to care. These measures not only enhance the availability of testosterone therapy but also promote patient-centered care by facilitating access to qualified health care professionals regardless of geographic location. Legislative and regulatory efforts must focus on addressing barriers such as the lack of confidentiality, privacy, and security of medical health data, which can undermine patient trust and deter individuals from seeking necessary care.

RECOMMENDATIONS

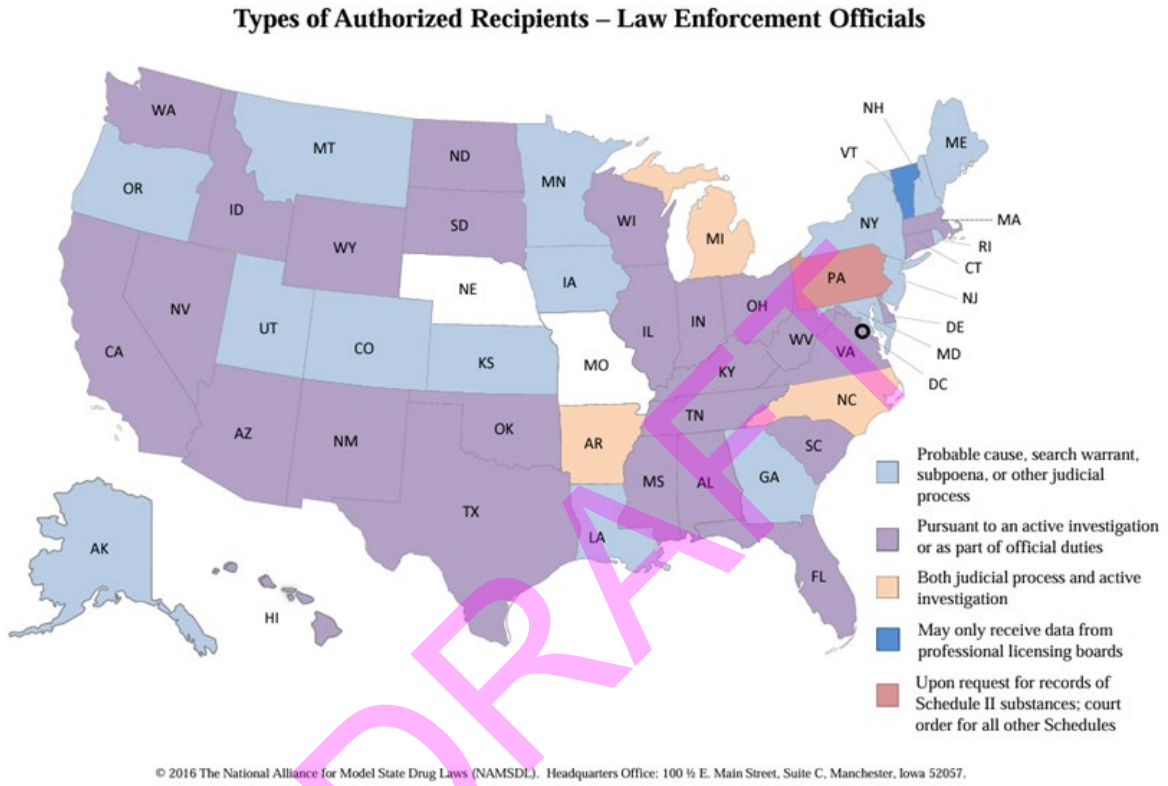
The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed:

1. That policy D-270.983, "Decreasing Regulatory Barriers to Appropriate Testosterone Prescribing," be amended by addition to read as follows:
   A. Our AMA will ask the FDA to review the available evidence and other data on testosterone and submit updated recommendations, if warranted, to the DEA, for its consideration of the scheduling of testosterone-containing drug products.
   B. Our AMA supports policies to remove barriers that delay or impede patient access to prescribed testosterone.
   C. Our AMA will continue to work alongside our partner organizations to promote advocacy and physician education on testosterone prescribing.

2. That Policies H-65.976, "Nondiscriminatory Policy for the Health Care Needs of LGBTQ Populations," H-140.824, "Healthcare Equity Through Informed Consent and a Collaborative Healthcare Model for the Gender Diverse Population," H-160.991, "Health Care Needs of Lesbian, Gay, Bisexual, Transgender and Queer Populations," H-185.927 "Clarification of Evidence-Based Gender-Affirming Care," H-95.946, "Prescription Drug Monitoring Program Confidentiality," H-315.983, "Patient Privacy and Confidentiality," D-185.981, "Addressing Discriminatory Health Plan Exclusions or Problematic Benefit Substitutions for Essential Health Benefits Under the Affordable Care Act," and D-480.964, "Established Patient Relationships and Telemedicine" be reaffirmed.

TABLE 1. The National Alliance for Model State Drug Laws Map of The Types of Authorized Recipients of PDMP Information – Law Enforcement Officials

The National Alliance for Model State Drug Laws. *Compilation of Prescription Monitoring Program Maps*. The National Alliance for Model State Drug Laws; 2016. Accessed January 31, 2024. https://namsdl.org/wp-content/uploads/Compilation-of-Prescription-Monitoring-Program-Maps.pdf



Note: As of 2019, Nebraska requires a subpoena, court order or approval, and a written request.[57] As of 2021, Missouri requires a subpoena, court order or approval for law enforcement to access their state PDMP.[58]

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9. PRESCRIBING GUIDED PHYSICAL ACTIVITY FOR DEPRESSION AND ANXIETY

Reference committee hearing: see report of Reference Committee D.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See Policy H-470.997

Resolution 421-A-23, as adopted by the American Medical Association's (AMA) House of Delegates. That policy (H-470.997, "Exercise and Physical Fitness") directs the AMA to:

> "study evidence of the efficacy of physical activity interventions (i.e., group fitness, personal training, or physical therapy) on behavioral activation and outcomes on depressive and anxiety symptoms."

BACKGROUND

In the U.S., five percent adults aged 18 and over experience regular feelings of depression and 12.5 percent have regular feelings of worry, nervousness, or anxiety.[8] Feelings of depression, in this case, is defined as feeling depressed daily and describing the level of depression as "somewhere in between a little and a lot" or "a lot" or feeling depressed weekly and describing the level of depression as "a lot." There are several different types of depressive disorders but, in general, depression is a mood disorder that affects how a person feels, thinks, and handles daily activities. Individuals may experience symptoms of persistent sadness or hopelessness, loss of motivation, low self-attitude, deceased energy, changes in sleep, appetite and concentration, anhedonia, and

sometimes suicidal ideation.[9] According to the National Institute of Mental Health, major depression is one of the most common mental health diagnoses in the U.S. and an estimated 21.0 million U.S. adults (a little over eight percent) have had at least one major depressive episode over their lifetime.[9] There are a variety of etiologies involved in depression, including genetic, environmental, psychological, and biochemical factors.[10] An individual has an increased risk of depression if they have a family history of depression, they have experienced trauma, major life changes, stress, chronic pain, certain physical illnesses (such as diabetes, cancer, or Parkinson's), or as a side effect to certain medication.[10]

Anxiety is a normal physiologic reaction and oftentimes can be positive. When anxiety is excessive, including somatic anxiety and impacts day-to-day functioning, it is considered an anxiety disorder.[11] Anxiety disorders are a spectrum of anxiety-related illnesses including but not limited to Obsessive Compulsive Disorder (OCD), Panic Disorder, Agoraphobia, and Generalized Anxiety Disorder (GAD).[11] Symptoms of generalized anxiety disorder may include feeling restless, on-edge, difficulty concentrating, increased irritability, and sleep disruption.[11] Anxiety comes from a complex interaction between biology and environment. Some factors may include genetics, brain function and chemistry, individual temperament, development, and one's perception of threats.[11] Anxiety disorders are often comorbid with other mental health conditions, including depressive disorders.
Interventions for treatment of depression and anxiety often include medication and/or psychotherapy, with the greatest evidence of effectiveness often including a combination of both medication and psychotherapy.[4] However, evidence has demonstrated a beneficial effect of exercise interventions on the prevention of depression. A recent meta-analysis found that people with high levels of exercise had lower odds of developing depression.[12] In other countries such as Australia, lifestyle management is recommended as the first-line treatment approach, though in practice, pharmacotherapy is often provided first.[13,14] While the many physical and mental health benefits of regular physical activity are well documented, as of 2019, only 23 percent of adults in the U.S. were meeting recommended levels of physical activity.[15,16,17] Many people in the U.S. could benefit from increased physical activity to help prevent, better manage, and improve mental health issues like depression and anxiety.

METHODS

English language reports were selected from searches of the PubMed and Google Scholar databases using the search terms: "physical activity prescribing" AND "depression", "physical activity prescribing", AND "anxiety", "park prescription programs", "prescribing physical activity", AND "insurance reimbursement," "minoritized communities" AND "prescribing physical activity," and "physical activity for mental health" AND "older (pregnant, minoritized, adolescent) individuals". Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by federal agencies and applicable professional and advocacy organizations, including the U.S. Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), the National Institute of Mental Health, and the American Council on Exercise were also reviewed for relevant information.

DISCUSSION

Physical activity is defined as bodily movement produced by movement of skeletal muscles that results in energy expenditure.[18,19] Exercise is a type of physical activity that involves planned, structured, and repetitive bodily movement, performed to maintain or improve one's physical fitness.[18] Numerous guidelines exist to promote recommended amounts of physical activity. HHS has developed general guidelines for physical activity for different age groups and populations with specific health concerns.[20] Specific recommendations for each group are summarized in Table 1, but for adults, the general recommendation is at least 150 minutes to 300 minutes of moderate-intensity physical activity each week (e.g., walking or biking at a leisurely to moderate-pace, and slow swimming) or 75 to 150 minutes of vigorous-intensity aerobic physical activity per week (e.g., fast-pace walking or biking, jogging, or sports play).

Physical activity intensity is based on the energy expenditure incurred during the activity, as expressed by multiples of 1 MET, which is the ratio of the metabolic rate for an activity divided by a standardized expression of the resting metabolic rate (RMR).[20] It has been noted that different populations, based on gender, age, etc., have different RMRs and correction factors have been applied to adjust for these individual differences.[20] However, in general, physical activity is categorized into three intensity levels, based on expended energy: light-intensity (1.6-2.9 METs), moderate-intensity (3-5.9 METs), and vigorous-intensity (≥6 METs).[20] It is important to note that energy expenditure is also determined by an individual's physical fitness. In other words, an individual who regularly

exercises may find fast-paced walking to be a moderate intensity exercise versus someone who has historically been physically inactive may find it to be of vigorous intensity. Lastly, different types of physical activity are based on the type of movement and the way in which different components of the body are engaged. Table 2 defines several common types of movement. To note, many physical activities combine more than one type of movement.

Biological Mechanisms Underlying the Role of Physical Activity on Depression and Anxiety

It has been demonstrated that exercise has beneficial effects in reducing symptoms of depression such as low mood, anhedonia, and loss of interest and on body functions such as cardiorespiratory system and cognitive function..[21] However, more research is needed into the mechanisms underlying the antidepressant effects of exercise. Most studies on the mechanisms of the antidepressant effect of exercise are mouse/rodent model studies, with some clinical studies in humans when feasible.[21,22] The biological pathways whereby regular physical activity might confer resilience include promoting an anti-inflammatory state, reducing the negative effects of oxidative stress, serving as a buffer against stress and stress-related disorders/chronic diseases, and enhancing neuroplasticity and neurogenesis.[21–25] In addition, exercise causes an increase in neurotransmitters associated with increased activity of dopamine, 5-hydroxytryptamine, and noradrenaline in the central nervous system.

Anti-inflammatory and Antioxidant Factors

A mechanism in which regular exercise and/or physical fitness may confer resilience is through minimizing inflammation. Psychological stress and physical inactivity/low aerobic fitness have all been associated with persistent, systemic, low-grade inflammation, and are associated with adverse effects on mental and physical health.[21,26,27] Systemic markers of inflammation include tumor necrosis factor alpha (TNFα), interleukin (IL)-1, IL-6, IL-8 and C-reactive protein (CRP), with elevated basal IL-6 and CRP levels being closely associated with persistent depressive symptomatology and cognitive dysfunction.[28] A randomized control trial (RCT) designed to assess the relative efficacy of aerobic exercise to augment selective serotonin reuptake inhibitor (SSRI) treatment of major depressive disorder (MDD) in treatment-resistant patients, found those who had high basal levels of serum TNFα were found to have a greater decrease in depressive symptoms over the 12-week aerobic exercise intervention.[28,29] These results suggest that high serum TNFα levels may differentially predict better outcomes with exercise and antidepressant medication as treatment as opposed to antidepressant medications alone, wherein high serum TNFα levels are linked to a poor treatment response.[28,29]

Oxidative Stress (OS)

Oxidative and nitrosative stress occurs when excess reactive oxygen species and reactive nitrogen species are produced as a byproduct of metabolic processing and have harmful effects on the body.[21] Organs such as the brain are particularly vulnerable to this damage because it has a high metabolic rate and lower antioxidant levels.[21,30] As a result, oxidative stress pathways may contribute towards the pathophysiology of psychiatric disorders, such as depression. Over time, the resulting damage may counteract neuroplasticity and contribute some of the structural abnormalities in people with depression.[21] Moderate aerobic exercise has been shown to reduce OS and inflammation.[21] It also reduces the concentration of several inflammatory biomarkers, such as IL-6, homocysteine, and TNF-α, and restrains the activity of nicotinamide adenine dinucleotide (NADH) oxidase, which results in metabolic oxidative stress.[21] One study illustrated that voluntary wheel running alleviated depression-like symptoms in male rats with prenatal ethanol exposure and that the positive effects of exercise were linked to increased levels of antioxidants.[21,31] In clinical studies, a 12-week aquatic exercise program in older adults with depression (n = 92) was shown to reduce depression and anxiety and decrease OS.[21,32]

Neurogenesis and Neuroplasticity

The beneficial effects of physical activity and increased cardiorespiratory fitness on brain health are well recognized. Chronic stress, exemplified by high level glucocorticoid exposure, decreases neurotrophic factor expression/signaling, neurogenesis and gliogenesis in the brain; this appears to be associated with reduced volumes of stress-sensitive brain regions as well as depression and cognitive dysfunction.[28,33,34] By contrast, regular exercise has been shown to enhance positive mood, decrease depression and anxiety, and increase cognitive function such as learning and memory in both animal and human studies.[28,29,35] Possible biological mechanisms mediating these effects include structural (i.e., increased neurogenesis, synaptogenesis, gliogenesis and angiogenesis) and

cellular/molecular changes in the brain.[28,35,36] Together, they can promote enhanced neuroplasticity and may be capable of blocking and/or reversing the detrimental effects of chronic stress on the brain.

One important growth factor that has received much attention is brain-derived neurotrophic factor (BDNF).[28,37] BDNF plays a critical role in integrating behavioral and metabolic responses to various challenging environments, including exercise.[28,37] Studies of outpatients with MDD and persistent depressive disorder demonstrated that both acute and regular exercise caused an increase in BDNF.[21] A study of elderly women with major depression showed that a single exercise session significantly increased serum BDNF levels; however, it showed a significant secondary decrease in BDNF serum levels after 30 min of rest. This suggests that acute exercise might be beneficial for MDD treatment, but further studies are needed.[21,38]

EFFICACY OF PHYSICAL ACTIVITY ON DEPRESSION AND ANXIETY IN DIFFERENT POPULATIONS

The sections below examine current evidence in the literature about the efficacy of physical activity on anxiety and depression in children and adolescents, older adults, adults with chronic health conditions and/or disability, pregnancy, and minoritized communities. There are many limitations in current literature surrounding the benefits of physical activity on anxiety and depression which includes, but are not limited to, the nature of the patient sample; the methods used to document anxiety and depression in the patient sample; the lack of inclusion of symptomology to describe anxiety disorders and depressive disorders in the patient sample; heterogeneity within the group of individuals who have similar depressive disorders or anxiety disorders; and the lack of objective measures of either functional or quality of life impairment. Further, it should be acknowledged that depression and anxiety are complex disorders that are influenced by many factors and are often comorbid with other mental health conditions.

Children and Adolescents

A systematic review and meta-analysis which included studies involving 2441 participants aged less than 19 years old, aimed to understand if physical activity interventions were associated with significant reductions in depressive symptoms compared with the control condition in children and adolescents.[39–44] This meta-analysis showed that physical activity interventions produced greater reductions in depressive symptoms compared with the control conditions.[39–44] However, these differences were not detected after a mean follow-up of 21 weeks, possibly due to the limited number of studies with follow-up outcomes.[39–44] Previous studies have shown that physical activity had greater benefits in participants aged 13 years or older than in younger participants.[45] It also has been demonstrated that three physical activity sessions per week and interventions that were shorter than 12 weeks induced greater benefits on depressive symptoms compared with other frequencies and durations.[45] These findings were reflected in the results of previous meta-analyses on the association between physical activity and depression, suggesting that increasing amounts of physical activity may not translate into greater reductions in depressive symptoms.[39,46,47] A recent cross-sectional study found a U-shaped association between physical activity frequency and mental health, such that 10 to 15 sessions per month induced the greatest mental health improvements.[39,48] In contrast, there is other evidence that greater than 10 to 15 sessions per month of physical activity have increasingly beneficial effects on mental health.[39,49] These discrepancies in the literature highlight the need for more comprehensive studies in this population to better understand the benefits of physical activity on depressive symptoms.

Older Adults

Regular physical activity can help older adults, aged 50 years and older, maintain and improve their mental health and cognitive ability, and reduce symptoms of depression and anxiety.[50–52] It can also improve other functional abilities, including physical function and balance, thereby preventing falls and fall-related injuries.[50,51,53] In addition to serving as an important pathway for improved mental health, physical activity brings social benefits, as being active offers the chance to build relationships and strengthen social networks around an older person.[50]

One study examined the minimal dose of moderate to vigorous physical activity (MVPA) associated with a reduced risk of depression and depressive symptoms in 4016 older adults, over a 10-year period.[50] Depression and depressive symptoms were measured using the short form of the Centre for Epidemiological Studies Depression scale along with the Composite International Diagnostic Interview for diagnosis of a major depressive episode during the past 12 months. Older adults performing between 400 to 600 MET minutes per week had a 16 percent lower rate of depressive symptoms and 43 percent lower odds of major depression.[50] These findings were consistent with meta-analytic data suggesting that mental health benefits among adults can be achieved with physical activity below

public health recommendations (600 MET-min/wk). Specifically, an activity volume equivalent to 2.5 hours per week of brisk walking was associated with a 25 percent lower risk of depression, and half that activity volume was associated with an 18 percent lower risk compared with no activity.[46,50] Minimally sufficient activity doses for depressive symptoms and major depressive disorder vary based on chronic disease status.[50] For depressive symptoms, older adults with chronic disease showed a significantly reduced risk (seven percent) at the WHO guideline threshold of 600 MET-min/wk, although the greatest decreases occurred with increasing physical activity dose, with a similar outcome observed for major depression.[50,54] Further, previous meta-analytic evidence that suggested significantly larger antidepressant effects of exercise training among adults with chronic illness who were meeting WHO guidelines for physical activity.[50,54–56]

Adults With Chronic Health Conditions and/or Disability

Regular physical activity is recommended for adults with chronic health conditions and/or a disability and can provide both physical and cognitive benefits.[20,54] For many chronic conditions, physical activity provides therapeutic benefits and is part of recommended treatment for the condition.[57] The benefits of physical activity for people with disabilities have been studied in diverse groups with disabilities related to traumatic events or to chronic health conditions. These groups include people with previous stroke, spinal cord injury, multiple sclerosis, Parkinson disease, muscular dystrophy, cerebral palsy, traumatic brain injury, limb amputations, mental illness, intellectual disability, and dementias including Alzheimer.[20,57] Studies have shown there was moderate-certainty to high-certainty evidence that physical activity decreased symptoms of anxiety and depression in people with chronic conditions.[20,57,58]
It should be noted that data assessing the benefits of physical activity in individuals with a disability is very limited. In individuals who are disabled and with schizophrenia or major depressive disorder, there is moderate-certainty evidence for the beneficial effects of physical activity on quality of life.[20,54,59] There is also moderate-certainty evidence that physical activity can have beneficial effects on cognition in people who are disabled with multiple sclerosis, Parkinson's disease, a history of stroke, ADHD and major clinical depression.[20,54,59]

Pregnancy

There is limited evidence on the efficacy of physical activity in reducing symptoms of anxiety and depression in people who are pregnant. Most studies focus on pregnant women, and this highlights a gap in current literature. Depression in pregnancy is a significant public health problem; both pregnancy and childbirth are some of the factors that contribute to the development of depression.[60,61] The incidence of depression in pregnancy ranges from 6–25 percent.[60,62–64] The incidence of depression during pregnancy, also varies depending on trimester.[60] It is estimated that the onset of depression occurs in 7.4 percent (2.2–12.6 percent) of pregnant women in the first trimester, in 12.8 percent (10.7–14.8 percent) of pregnant women in the second trimester, and in 12.0 percent (7.4–16.7 percent) of pregnant women in the third trimester.[60,65] In addition, according to WHO data, depression during pregnancy is a strong risk factor for the development of postpartum depression, which may affect 10–15 percent of pregnant women in the period of up to 12 months after delivery.[54,60] Moreover, prior studies have shown that a lack of proper treatment of depression in people who are pregnant and may have a negative impact on the fetus (i.e., premature delivery, reduced birth weight, as well as an increase in the concentration of stress hormones in the child).[60,66] Early and correct diagnosis can minimize the negative effects of depression on the birth parent's, fetus's, and child's health.[60,67]

Even a small amount of physical activity during pregnancy may reduce the severity of depressive symptoms, as well as the occurrence of depression.[60] The best forms of activity during pregnancy include walking, yoga, swimming and general exercises (i.e., breathing, posture, and Kegel exercises).[68] However, it should be noted that the physical capacity of pregnant women varies in terms of their baseline physical activity levels and individual trimesters.[68] Research on the influence of supervised training on depressive disorders shows that aerobic exercises performed three times a week for about 60 minutes can significantly reduce the symptoms of depression in pregnant women.[60,69–71] However, there are also reports indicating that physical activity already at the level of 1–2 sessions a week may also be beneficial in reducing the frequency and severity of depressive symptoms in pregnant women.[72] Being physically active in pregnancy not only has benefits of lowering the risk of developing depression in pregnancy, but also has the benefits of lowering the risk of developing depression in early and late postpartum.[60,70]

In addition, evidence suggests that women who do not exercise are more at risk of developing depressive disorders, both during pregnancy and postpartum compared to women who exercise.[60,70]

Minoritized Communities

Data on the benefits of physical activity on mental health in minoritized communities is limited, and many barriers exist for these communities. However, it has been noted that minority populations are more likely to seek care for mental health concerns from their primary care providers versus behavioral health professionals, underscoring an important opportunity for primary care physicians to engage with their patients on this issue.[73] Strategies to reduce depressive symptoms and improve emotional well-being in older Hispanic/Latinx adults are largely absent from the scientific literature. One study suggests that older Hispanic/Latinx adults displayed improvements in depressive symptoms at the 24-month follow up period following an exercise intervention that included four weekly one-hour group-based exercise classes targeting strength training, endurance, balance and flexibility.[74] The results of this study were consistent with previous research documenting the therapeutic health effects of structured exercise in older adults using Latin dance.[74,75] Culturally appropriate and cost-effective intervention modalities to reduce depression in Hispanics/Latinxs are both needed and critical given the stigma associated with mental health disorders in this population and reluctance in taking antidepressant medication.[74,76]

Multiple studies have found a significant inverse relationship between physical activity and depressive symptoms in Black adults.[77–80] In a mixed-methods study on aspects of depression among low-income black youth, life challenges faced by participants diminished the potential anti-depressant effects of exercise – highlighting the importance of the social determinants of health role as a moderator in the effectiveness of exercise as a therapy.[81] The available research has limitations and further studies are needed in this population to assess the benefits of physical activity on mental health.

Anxiety Studies

Studies assessing the impact of physical activity on anxiety disorders are limited. One study investigated cross-sectional and longitudinal associations between different amounts of moderate-to-vigorous physical activity and anxiety symptoms in older adults (50 years of age and older) in Ireland.[82] Compared with the inactive group, the minimally- and very-active groups were associated with an 8.4 percent and 18.8 percent lower odds of anxiety, respectively.[82] However, following adjustment, only high volumes of physical activity were significantly associated with lower prevalence of anxiety.[82]

Another study aimed to document the effect of add-on treatment with structured physical exercise in a clinical population of adolescents hospitalized for depression and anxiety in a psychiatric hospital in Belgium.[83] A group of 52 adolescent inpatients were randomly assigned to a physical exercise or control social relaxation program three to four times per week over a six-week period (20 hours in total).[83] The results showed a reduction in anxiety symptoms over time in both groups. Therefore, it was concluded that there was no benefit of sufficient effect size to attain significance.[83] To date, there is a significant lack of evidence for a reduction in symptoms of anxiety with exercise in young ambulatory patients.

Finally, a study in Sweden investigated the effects of an exercise intervention on symptoms of anxiety and to evaluate the benefit of moderate/high intensity exercise vs low intensity exercise, in primary care patients diagnosed with anxiety disorder.[84] Included in the study were patients aged 18 to 65 years of age and were diagnosed with anxiety disorders using Diagnostic and Statistical manual of Mental disorders (DSM-IV and V), including panic disorder (PD; DSM 300.01), generalized anxiety disorder (GAD; DSM 300.02) and anxiety not otherwise specified (NOS; DSM 300.00).[84] This study shows that both low- and moderate/high intensity exercise interventions improved anxiety symptoms at follow-up.[84] This was done using self-assessed severity of perceived anxiety symptoms using the clinically well-established psychiatric assessment scale Beck Anxiety Inventory.[84] These effects were independent of depressive symptoms, which is important to assess given the well-known benefits of exercise for patients with MDD.[84–86] Severity of ongoing symptoms of depression was self-assessed using the Montgomery Åsberg Depression Rating Scale (MADRS-S).[84] Although no clear dose-response effect of exercise intensity was observed, there was a significant trend in the proportion of patients with improved anxiety symptoms with increased exercise intensity.[84]

PHYSICAL ACTIVITY PRESCRIPTIONS

What is a Physical Activity Prescription?

Physicians may recognize the therapeutic benefit of physical activity and may have even counseled their patients to "exercise more," as part of their treatment. In fact, in a cross-sectional survey among faculty and staff from a large academic tertiary care medical center in the southeastern U.S. with nearly 200 respondents, more than half (58 percent) said they recommended exercise as part of treatment but roughly only a quarter offered specific exercise instructions (24 percent) or followed national guidelines (30 percent).[87] This type of general clinical advice to exercise is not what is referred to as a physical activity prescription.

A physical activity prescription is one that dictates a specific regimen of physical activity and, like any other medical prescription, includes details on the type, dose, frequency, duration, and therapeutic goal.[88] Another key component of the physical activity prescription is connecting patients with appropriate, supportive physical activity resources.[89] A critical component of counseling or prescribing physical activity to patients is understanding what different levels of physical activity intensity entail and what counts for the different types of activity (i.e., aerobic activities versus muscle strengthening).

It is also important to distinguish between physical therapy and a physical activity prescription. Physical therapy's universal aim is "to identify and maximize human movement potential within the spheres of promotion, prevention, treatment and rehabilitation," and has the potential to be an effective promotion of physical activity.[90] However, physical therapy has generally been employed as a means for restoration and maintenance of physical functioning in individuals who have experienced a disabling condition, loss of movement, or injury, as opposed to a method to improve physical activity in general.[90] Part of this is due to the insurance industry's payment system, which does not generally pay for physical activity programming.

Effectiveness of Physical Activity Prescriptions for Depression and Anxiety

While there have been numerous studies assessing the relationship (causal or otherwise) between physical activity and mental health disorders, there are fewer available studies evaluating the effectiveness of physical activity prescription-type interventions designed specifically for the treatment of depression and/or anxiety. A 2014 meta-analysis evaluating exercise as a treatment for depression identified five RCTs where exercise was found to be beneficial in the treatment of depression.[91] Specifically, treatment programs with exercise done at least three times a week, for a minimum of nine weeks, at moderate intensity were shown to be an effective for treatment of depression.[91]

A 2018 meta-analysis of RCTs evaluating the effects of Baduanjin (a traditional Chinese mind-body exercise) in adults diagnosed with any mental (depression, anxiety or mood) or physical illness (e.g., fatigue, diabetic mellitus, cancer, drug addiction, heart disease, stroke, and musculoskeletal disorder) found that despite wide heterogeneity among treatment interventions, in terms of frequency, length, intensity, etc., the Baduanjin intervention was effective in reducing both anxiety and depression among the patients.[92] A more recent RCT assessed the impact of Baduanjin on patients diagnosed with lung cancer who were experiencing depression and anxiety. After an eight-week intervention, the treatment group had statistically significant lower self-reported depression and anxiety scores compared to baseline.[93] Despite the positive and consistent findings on the impact of Baduanjin on depression and anxiety, the cultural context of these studies and focus on Baduanjin specifically may reduce the generalizability to the U.S. population.

There is also qualitative evidence from general practitioners in New Zealand on a physical activity prescription program, the Green Prescription, for treating depression. The Green Prescription program involved a prescription for physical activity provided by a general practitioner or nurse and lasted for a three-month period. Within those three months, individuals received monthly phone calls from patient support counselors to help set realistic physical activity goals and identify solutions for barriers encountered. All general practitioners interviewed in the study emphasized the importance of physical activity to improve mood and treat depression and noted its usefulness in helping lessen the need for pharmacotherapy.[94]

Making Physical Activity Assessment and Prescription a Medical Standard of Care

In April 2015, the American College of Sports Medicine and Kaiser Permanente convened a joint consensus meeting to discuss the development and implementation of a physical activity vital sign (PAVS) to be obtained and recorded regularly.[95,96] PAVS was documented based on the answers from two questions: 1. On average, how many days per week do you engage in moderate to vigorous physical activity (like a brisk walk) and 2. On average, how many minutes do you engage in physical activity at this level? It resulted in a "call to action" for current and future clinicians and the health care community to implement a PAVS in daily practice with every patient.[95,96] The health care team is uniquely positioned to address the importance of a healthy lifestyle, including physical activity, in the prevention and treatment of disease and disability.

As a result, Kaiser Permanente, Greenville Health System in South Carolina, and Intermountain Healthcare System in Utah successfully integrated the use of PAVS.[95,97] These organizations have been able to manage workflows and include the measure in their electronic health record alongside other vital signs. They have accomplished this goal working alongside different health record vendors, including Epic, HELP2, and iCentra.[95,97] Further, a study of 2.1 million adult patients from Kaiser Permanente in Southern California demonstrated that within the first year of implementation, they were able to capture a PAVS on 85 percent of eligible patients.[95,97] Importantly, the PAVS showed similar results to the reported number of minutes of exercise compared with other self-reported physical activity questionnaires, such as Behavioral Risk Factor Surveillance System (BRFSS) (50 percent) and the National Health and Nutrition Examination Survey (NHANES) (59.6 percent).[95,97]

Best practices to implement a uniform PAVS and physical activity prescription include increased education on benefits of physical activity on health, collaboration with large medical associations, alignment with current initiatives (i.e. Physical Activity Guidelines for Americans), and collaboration with local community groups, organizations, or facilities for counseling and assistance with culturally appropriate, basic physical activity information.[95] Due to its successful implementation, there are readily accessible resources (professionals, patient materials, and access to adequate facilities/equipment) to implement the recommendations for integrating PAVS and avenues to re-educate practicing clinicians and health care team members.[95] Further, at the level of the individual physician, medical practice, and health care system, there are a variety of incentives tied to quality measures or metrics. .[95,98]

When prescribing physical activity, what has been demonstrated to work well?

Treatment programs that incorporate aerobic activities at a moderate level of intensity either in a group or individual setting have been shown to be effective.[91] Programs that included some level of supervision by an individual trained in physical activity were recommended to achieve beneficial treatment.[91] Physicians should consider the following when developing a physical activity prescription for their patients. First and foremost, the prescription must be tailored to the individual and incorporate the following four steps: (1) take an exercise history, (2) identify any contraindications and refer those who require medical clearance to a sports/exercise specialist, (3) develop an effective but realistic program, and (4) provide advice on how to reduce sedentary behavior.[6] These considerations are critical, as developing an effective and specific physical activity program will depend on the patient's current level of activity and must be considerate of age and existing chronic conditions.[99] Another component of an effective physical activity prescription is considering exercise that integrates physical activity into an individual's daily life or habits, rather than making it an extra chore.[6,100]

A critical component of implementing physical activity prescriptions is the integration of PAVS in electronic health records.[97,100] Additionally, it has been recommended that a successful physical activity prescription intervention must engage the larger health care team, not just the clinician.[89,100] For the Green Prescription program in New Zealand, the health care team responsible for providing the physical activity prescription included patient support counsellors and nurses, who helped carry out more of the time-consuming tasks and administration of the program.[89] For additional guidance and resources on prescribing physical activity, the American College of Sports Medicine's Exercise site has a step-by-step guide for clinicians to utilize in their practice.[101]

CHALLENGES AND BARRIERS

A challenge for physicians in prescribing physical activity is the heterogenous nature of exercise activities and programs (as outlined above, there are many ways to exercise and at different levels of intensity, frequency, etc.) and knowing what is most appropriate for the patient. Another major barrier for physicians is the amount of need time to spend with patients to talk through a physical activity prescription, including, but not limited to, doing a baseline assessment, creating an individually tailored plan, and connecting the patient with appropriate resources.[94,100] Additionally, there is no standard of practice in the U.S. (like nutritional counseling) for physical activity counseling and prescription within a clinical setting.[89] However, the global health initiative, Exercise is Medicine®, is working to make physical activity assessment and promotion a standard within clinical care.[102]

Barriers that will be further discussed below also include inadequate provider reimbursement, training, and self-efficacy, insufficient health care system support, and scarcity of certified community resources to refer for evidence-based physical activity programming.[103–105] Poor care coordination and the inability to follow the progress of a referred patient are also important barriers to consider when establishing sustainable clinical-community linkages for physical activity-related care.[103,106]

Billing and Reimbursement for Prescribing Physical Activity

Billing rules set by the Centers for Medicare and Medicaid Services (CMS) and private insurers prohibit most allied health professionals from receiving reimbursement for providing exercise programming in mental health settings.[107–109] It should also be noted that some private insurance companies offer their members a variety of incentives to engage in exercise, such as reimbursement for gym memberships, cash rebates for selecting healthy food at the grocery store, and reduced premiums for people who engage in regular exercise.[107,113,114] A number of health insurance companies offer their members incentives for engagement in exercise.[107] Large corporations also offer incentives for engagement in exercise, such as on-site fitness equipment.[107,115] However, this creates an inequitable barrier for individuals who do not have access to private insurance companies or work for large corporations.

Logistical and Workflow Barriers for Physical Activity Assessment and Referrals

Despite the availability of evidence-based programs to improve physical health and wellness behaviors among people with mental health conditions, there are multiple policies and funding barriers that make it difficult for community mental health programs to offer these programs to consumers.[107,116] Health care policies typically “carve out” mental health funds from physical health funds, denying community mental health programs the financial ability to offer exercise programming.[107,116] Few funds are set aside for community mental health programs to train staff to deliver preventive health services like exercise programs.[107,108,116]

These barriers are perpetuated by fragmentation of preventive care in the U.S. and may explain the lack of standardized physical activity community-referral programs.[103] The national health promotion objectives have included a specific target to increase the proportion of primary care clinicians who routinely assess and counsel their patients on physical activity.[103] Occasional surveys of primary care practitioners and patients suggest that there has been little improvement over the last decade in physical activity assessment and promotion in clinical visits. The rates of clinician-initiated physical activity counseling continue to be low (<35 percent), particularly among women and racial minorities.[103,117] Rates for physical activity counseling among patients with CVD (41.2 percent), hypertension, (44.2 percent), obesity (46.9 percent), and diabetes mellitus (56.3 percent) are also suboptimal.[103,117]

Further, even though patients can be referred to either self-managed or community-based physical activity professionals/programs, health care systems are often unwilling to refer patients outside their system unless the professional/program referred to is part of a network where quality can be ensured and controlled.[95,103] The development of a database of local physical activity programming and other health resources (e.g., medical fitness centers, gyms with certified programming and personnel, parks, trails, community centers) classified by age, clinical conditions, insurance benefits, and other factors (such as cost, activities offered) can enable the provision of a robust, personalized list of potential places and programs when integrating into the clinical workflow, electronic health record (EHR), and patient portals.[103,118]

Education of the Health Care Workforce

To provide beneficial patient education, our nation's health care professionals must be educated in the vital role physical activity and/or structured exercise plays in preventing, treating, and managing disease and the need to screen, motivate, and educate patients about physical activity.[95,119] At the medical school level, there are innovative curricula, including those at the University of South Carolina School of Medicine Greenville and the University of Wisconsin, where exercise and lifestyle medicine are integrated into all four years of the students' undergraduate medical education.[95,120,121] The Accreditation Council for Graduate Medical Education sets the program requirements for residency and fellowship programs.[95,122] However, despite specific curricula to which a resident must be exposed during graduate medical training, in most specialties there are no current requirements that residents receive education and training in physical activity.

Electronic Health Record

A recommendation by the National Academies highlights the value of EHR to provide information to the health care team related to health and treatment.[103,123] Providing information pertaining to physical activity in the EHR creates an opportunity for the HCP to discuss patients' or clients' physical activity habits.[103,123] Discussion about physical activity will be easier if these measures are collected in a similar method across time and can be used between health record systems.

Two suggested methods for capturing physical activity for the EHR are self-reports and wearable devices such as pedometers or accelerometers.[103,124] An example of a self-report questionnaire that can ascertain compliance with the physical activity guidelines is called the Exercise Vital Sign (EVS), modified from the Behavioral Risk Factor Surveillance System.[97,103] The EVS consists of 2 questions that take approximately ≤1 minute to administer. Wearable activity monitoring (WAM) devices provide information on activity such as accelerometers counts, steps, and estimated minutes of physical activity at various intensity levels.[97,103] These devices can be worn on clothing or the waist, wrist, or ankle to measure physical activity. Comparisons of findings based on behavior questionnaires versus wearable devices find a remarkably similar relationship between physical activity and health outcomes, buttressing older data from questionnaire studies that underpin current physical activity guidelines.[125]

There are numerous devices available, with many wrist-based devices or smartwatches now also tracking heart rate to enhance physical activity intensity estimation. However, to date, there is no widespread integration of patient-generated data from wearable devices into the EHR.[103,126] No matter which method is used, self-report or wearable devices, linking physical activity data to the EHR provides a forum for health care professionals to initiate discussion and counseling on increasing physical activity. However, uniform access to wearable devices presents logistical and equity issues. There are also data privacy, integrity, provenance, and quality considerations that should be addressed. Integrating information into an EHR from external third-party sources can be a challenge and requires planning and preparation.

Environmental Equity Considerations

Another potential barrier for successful implementation of physical activity prescription programs is the community setting in which patients are expected to return and fulfill their physical activity regimen. For example, in a study assessing the level of physical activity among adolescent girls in relation to their proximity to parks, researchers found that girls who live near more parks, particularly near those with amenities conducive to walking and with active features (i.e., playgrounds, multipurpose fields, etc.), engaged in more physical activity compared to those who with access to fewer parks.[127] CDC's Active People, Healthy Nation campaign aims to get more Americans physically active using a number of evidence-based strategies to increase physical activity. As part of this campaign, CDC has noted "providing equitable and inclusive access to safe places for physical activity is foundational to each strategy."[128] However, inclusive and safe places to exercise are not equitably distributed among U.S. communities, with notable disparities in low income, minority communities.[128,129] Low income, minority communities face a number of societal, institutional, and environmental barriers to meeting physical activity recommendations, including lack of access to appropriate facilities (i.e., parks, recreation or fitness centers), perceived unattractiveness or cleanliness of one's neighborhood, and perceived safety and concerns of violence.[129] As such, the patient's neighborhood and socio-environmental conditions should be considered when developing a patient's physical activity prescription.

Evidence from other types of prescriptions for 'healthy behaviors'

The topic of physical activity prescriptions raises a larger question on whether physician prescriptions, which have historically been focused on pharmacological treatment, can be an effective intervention to motivate behavior changes that improve health. Similar prescription interventions include park prescription and healthy food prescription programs. Park Prescriptions are programs or interventions that include a health or social service provider, encourages patients/clients to spend time in nature, and have a goal of improving their health and well-being.[130] There are a few studies that have been conducted or are ongoing that aim to evaluate the effectiveness of park prescription interventions on physical activity and mental health outcomes.[131,132] In one RCT study evaluating a park prescription program intended to increase physical activity in parks, the intervention group demonstrated improved park use, physical activity in parks, recreational physical activity, and psychological quality of life.[132] However, one challenge in evaluating these types of programs is the ability to discern the independent effect of the 'physical activity' and 'park/nature' components of the program. Parks prescription interventions often have overlapping goals of improving access to nature and increasing physical activity. Thus, if one is trying to discern which component is helping with improved mental health outcomes, it is unclear which aspect of the program is "doing the work." This is a useful distinction to understand as there may be different biological mechanisms involved that connect access to nature/green space and mental health.

Similar to a lack of physical activity, a poor-quality diet is a leading risk factor for non-communicable diseases and has been implicated in the growing prevalence of chronic diseases, such as obesity and diabetes.[133] As a result, there has been a growing interest in incorporating "food as medicine" interventions within health care systems, one of which is the "produce prescription" program.[134] With this type of intervention, a physician or health care worker identifies patients who may be eligible to receive free or discounted healthy produce and patients are provided subsidized or free healthy foods, with options to redeem prescribed coupons at local food stores, farmers markets, or the direct provision of fresh produce at a community based organization, healthcare center, or delivered directly to their home.[134] A 2021 systematic review of literature evaluating the effectiveness of these types of interventions found there were statistically significant increases in fruit and vegetable consumption and decreases in body mass index and glycated hemoglobin (HbA1c) levels among program participants.[134] Whether either of these prescription-type programs demonstrate long-term improvements in health outcomes has yet to be studied, but the current evidence suggests they are effective at improving the adoption of healthy behaviors in the short term. Generally positive evidence from these other types of prescription programs provides credence to explore physician prescription programs as a worthwhile intervention to promote healthy behavior change in individual patients.

RELEVANT AMA POLICY

Under existing AMA Policy H-440.859 "American's Health" the AMA supports improving health through increased activity and proper diet a priority and calling on the federal government and state governments to develop new and innovative programs in partnership with the private sector that encourage personal responsibility for proper dietary habits and physical activity of individual Americans.

Policy H-150.965, "Awareness, Diagnosis and Treatment of Depression and other Mental Illnesses H-345.984" encourages medical schools, primary care residencies, and other training programs as appropriate to include the appropriate knowledge and skills to enable graduates to recognize, diagnose, and treat depression and other mental illnesses, either as the chief complaint or with another general medical condition, and supports additional research into the course and outcomes of patients with depression and other mental illnesses who are seen in general medical settings and into the development of clinical and systems approaches designed to improve patient outcomes. The policy also recognizes the impact of violence and social determinants on women's mental health. Further, the policy states that the AMA will work with the National Institute on Mental Health and appropriate medical specialty and mental health advocacy groups to increase public awareness about depression and other mental illnesses, to reduce the stigma associated with depression and other mental illnesses, and to increase patient access to quality care for depression and other mental illnesses.

CONCLUSIONS

Mental health disorders are among the leading causes of global health-related burden, with substantial individual and societal costs.[1,2] Depression is the leading cause of mental health-related disease burden, while anxiety is the most prevalent mental health disorder.[1] The role of lifestyle management approaches, such as exercise, sleep hygiene and a healthy diet, varies between clinical practice guidelines in different countries. In U.S. clinical guidelines, psychotherapy or pharmacotherapy is recommended as the initial treatment approaches, with lifestyle approaches considered as 'complementary alternative treatments' where psychotherapy and pharmacotherapy are 'ineffective or unacceptable.'[1,13]

One potential alternative to psychotherapy or pharmacotherapy to treat depression and anxiety is the prescription of physical activity. There have been hundreds of research trials examining the effects of physical activity on depression, with more limited studies examining the effects of physical activity on anxiety. Many of these studies suggest that physical activity may have similar effects to psychotherapy and pharmacotherapy (and with numerous advantages over psychotherapy and pharmacotherapy, in terms of cost, side-effects and ancillary health benefits).[1,135,136] Despite the evidence for the benefits of physical activity, it has not been widely adopted therapeutically as a prescribed alternate to psychotherapy or pharmacotherapy. The limited availability of evidence on the efficacy of physical activity prescriptions for various populations, patient resistance, the difficulty of prescribing and monitoring physical activity in clinical settings, as well as the huge volume of largely incommensurable studies, have impeded wider adoption.[5–7]

Further, a critical component of counseling or prescribing physical activity to patients is understanding what different levels of physical activity intensity entail and what counts for the different types of activity (i.e., aerobic activities versus muscle strengthening).[1] Physicians have expressed that insufficient knowledge or training is the most common potential barrier to prescribing exercise for patients with mental health conditions.[137] There are also many environmental equity considerations that need to be addressed before a physical activity prescription program can be applied broadly.

Despite these barriers, there are promising practices that can be implemented to begin incorporating physical activity prescriptions as a standard of care. One of these practices include the introduction of physical activity vital sign (PAVS).[95,96] PAVS is reliable and feasible and has been validated against established survey tools to quantify physical activity engagement. It has also been successfully implemented in large-scale demonstration projects.[97,103] Other practices include integrating the benefits of prescribing physical activity into undergraduate, graduate, and continuing medical education, establishing partnerships and community links to sustain and support equitable physical activity programs, and continued research into the efficacy of prescribing physical activity to treat depression and anxiety.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed.

1. That our AMA amend policy H-470.997, "Exercise and Physical Fitness" by addition and deletion to read as follows:

> Exercise and Physical Fitness H-470.997
> 1. Our AMA encourages all physicians to utilize the health potentialities of exercise for their patients as a most important part of health promotion and rehabilitation and urges state and local medical societies to emphasize through all available channels the need for physical activity ~~for all age groups and both sexes~~. The AMA encourages other organizations and agencies to join ~~with the Association~~ in promoting physical fitness through all appropriate means.
> ~~Our AMA will study evidence of the efficacy of physical activity interventions (i.e., group fitness, personal training, or physical therapy) on behavioral activation and outcomes on depressive and anxiety symptoms.~~

2. Our AMA advocates for continued research towards development of structured physical activity treatment plans for the specific diagnoses of anxiety and depression, as well as longitudinal studies to examine the effects of physical activity on health outcomes, particularly later in life.

3. Our AMA encourages:

1. The education of health care professionals on the role of physical activity and/or structured exercise in treating and managing anxiety and depression, the need to screen for levels of physical activity in patients, the need to motivate and educate patients of all ages about the benefits of physical activity, including positive mental health benefits.
2. The provision of coverage by health care payers and employers for fitness club memberships and access to other physical activity programs.
3. The implementation, trending, and utilization of evidence-based physical activity measures in the medical record for treatment prescription, counseling, coaching, and follow up of physical activity for therapeutic use.

Table 1 – Key Guidelines for Physical Activity, adopted from the U.S. Department of Health and Human Services Physical Activity Guidelines for Americans, 2nd edition.[20]

Age group/Population	Guidelines
Preschool-Aged Children (ages 3 through 5 years)	• Should be physically active throughout the day to enhance growth and development. • Active play that includes a variety of activity types is encourages.
Children and Adolescents (ages 6 through 17 years)	• Should do 60 minutes (1 hour) or more of moderate-to-vigorous physical activity daily. Most of the 60 minutes or more per day should be either moderate- or vigorous intensity aerobic physical activity and should include vigorous-intensity physical activity on at least 3 days a week. • Should include muscle-strengthening physical activity on at least 3 days a week. • Should include bone-strengthening physical activity on at least 3 days a week.
Adults (ages 18 through 64 years)	• Should do at least 150 minutes (2 hours and 30 minutes) to 300 minutes (5 hours) a week of moderate-intensity, or 75 minutes (1 hour and 15 minutes) to 150 minutes (2 hours and 30 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. • Should also do muscle-strengthening activities of moderate or greater intensity and that involve all major muscle groups on 2 or more days a week, as these activities provide additional health benefits.
Older Adults (aged 65+ years)	• For those who are able, recommended physical activity is the same as healthy adults. • As part of their weekly physical activity, should do multicomponent physical activity that includes balance training as well as aerobic and muscle-strengthening activities. • If unable to meet the above guidelines, they should be as physically active as their abilities and conditions allow.
Women During Pregnancy and the Postpartum Period	• Should do at least 150 minutes (2 hours and 30 minutes) of moderate-intensity aerobic activity a week during pregnancy and the postpartum period. • Should consult with their health care provider to monitor progress of pregnancy and whether or how to adjust their physical activity during pregnancy and after the baby is born.
Adults With Chronic Health Conditions and Adults with Disabilities	• For those who are able, recommended physical activity is the same as healthy adults. • If unable to meet the above guidelines, should engage in regular physical activity according to their abilities and should avoid inactivity.

	• Should be under the care of a health care provider and can consult with a health care professional or physical activity specialist about the types and amounts of activity appropriate for their abilities and chronic conditions.

Table 2 – Different forms of physical activity and bodily movements [20]

Activity Type	Definition and examples
Endurance (or aerobic) activities	Increases breathing and heart rate. Examples include brisk walking or jogging, biking, dancing, swimming.
Strength training or resistance training	Causes your muscles to contract against outside resistance. Examples include lifting weights or using resistance bands.
Bone-strengthening activity	Also referred to as weight-bearing or weight-loading activity, produces force on your bones that promotes bone growth and strength. Examples include jumping jacks, running, brisk walking, and weightlifting.
Balance activities	Activities aimed at improving postural control. They are particularly helpful for older adults as they help prevent falls. Examples include yoga, lower body strength training, and targeted exercises to improve balance.
Flexibility activities	Stretches muscles and helps individuals stay limber, improving range of motion and circulation. Examples include yoga and everyday stretching.

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10. TEENS AND SOCIAL MEDIA

Reference committee hearing: see report of Reference Committee D.

HOUSE ACTION: REFERRED

INTRODUCTION

At the 2023 Annual Meeting of the American Medical Association (AMA) House of Delegates (HOD), Resolution 430, "Teens and Social Media" was adopted. The policy (H-478.976, "Teens and Social Media,") as adopted, asked that our AMA "study and make recommendations for teenage use of social media, including proposing model state and federal legislation as needed, with a report back at the 2024 Annual Meeting."
At the 2023 Interim Meeting of the AMA HOD, Resolution 915, "Social Media Impact on Youth Mental Health," was referred. The resolution asked that our AMA:

(1) work with relevant parties to develop guidelines for age-appropriate content and access and to develop age-appropriate digital literacy training to precede social media engagement among children and adolescents;

(2) amend policy D-478.965 by insertion as follows: (4) advocates for and support media and social networking services addressing and developing safeguards for users, including protections for youth online privacy, effective controls allowing youth and caregivers to manage screentime content and access, and to develop age-appropriate digital literacy training; and

(3) advocate that the federal government requires social media companies to share relevant data for further independent research on social media's effect on youth mental health and fund future federal research on the potential benefits and harms of social media use on youth mental health.

METHODS

English language reports were selected from searches of the PubMed and Google Scholar databases using the search terms: "teens" AND "social media" as well as "adolescents" AND "social media." Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by federal agencies and applicable professional and advocacy organizations were also reviewed for relevant information.

BACKROUND

The co-occurrence of the growing ubiquity of social media use by adolescents and teens and the increase in poor mental health, among these same age groups, is alarming. These trends have prompted calls for action and research around adolescents and teens and their use of social media. A common theme in the research is that social media is not inherently beneficial or harmful. Instead, the effects of social media likely depend on what kids see, their pre-existing strengths and weaknesses, and their environment.[1–4] In particular, child-social media interactions may be bidirectional as users shape their experience which in turn shapes them and vice versa.[5,6] Further, many argue that it is important to move away from the false dichotomy of whether social media is hurting or helping adolescents -- instead researchers, parents, and policy makers should consider who is using social media, what are they using it for, when are they using it, and how are they using it.[7–9] The focus of this report will be on adolescents and teens aged 10-17.

Social Media Privacy, Transparency and Accountability

The American Psychological Association (APA) defines social media as, "interactive technologies that facilitate the creation and sharing of information, ideas, interests, and other forms of expression through virtual communities and networks."[10] This can include social networking, gaming, virtual worlds, video sharing sites, and blogs.[3] Social media, internet use, and screentime all fall under the umbrella of digital media - the parent category of all interactive media consumed through screens.[1] These terms are used interchangeably throughout the rest of the report, unless noted otherwise.

The different forms of social media have different possibilities for action and engagement, known as affordances. Affordances, include things like visibility, editability, persistence, replicability, searchability, scalability, and reachability and they manifest as the capacity for public posting, sharing functions, auto-scroll, gamified interaction, push notifications, private messaging, affiliations, and running counts of feedback on posts.[11–13]

Affordances can have meaningful influence on the actions of the user; therefore, many researchers advocate for an affordances approach to understanding and evaluating social media.[14] This is important because affordances are powered by and interact with computational algorithms. These algorithms moderate content by generating recommendations, ranking and removing content, and targeting ads.[3] A challenge with content moderation is that it is intrinsically subjective. The value and appropriateness of content depends on the context – the who, what, why, how, and when of the information being shared may determine if it is elevated, downplayed, or removed.

Most platforms use a mix of artificial intelligence and human editing to enforce content moderation.[3] This can create intentional manipulation of information on the part of individuals. For instance, Facebook allowed advertisers to choose to exclude whole racial, ethnic, and age groups from seeing their ads.[3,15,16] Similarly, TikTok issues separate content moderation approaches for different countries depending on the degree of social conservatism.[3,17] Many platforms can and do selectively reduce or increase the prominence of content from certain users without violating the terms of use.[3,18] There is also unintentional, or at a minimum unexplained, manipulation of information, caused by using machine learning algorithms for content modification. Machine learning algorithms are black box mechanisms that learn without explicitly being programmed. Companies know the inputs, outputs, and training data that go into their algorithms, but the internal processes by which most machine learning algorithms work are less clear. Additionally, algorithms are proprietary, so companies are reluctant to share the details they do have.[3,19,20] Consequently, the intrinsic subjectivity of content moderation is made more opaque by machine learning algorithms as well as the platforms' lack of transparency about them.[3,21]

Relying on machine learning for content modification is not inherently harmful, but it can create recursive feedback loops that exacerbate problems with harmful content and misinformation. The algorithms send users more of the content that they engage with, thereby creating the impression that theories and behaviors they are seeing are potentially more prominent than they are. Moreover, many users do not realize that social media platforms are designed to show them content that is most likely to keep them engaged and on the platform rather than providing a comprehensive view of the content of friends and family.[3,22] There is some evidence that recursive feedback loops and echo chambers exacerbate vaccine hesitancy.[3,23–25] Similarly, content modification, and the echo chambers it creates had a significant impact on behavior during the 2016 Election.[3,26–28]

Ultimately, the current processes for content moderation introduce bias on both the front end (e.g., the training data that informs the algorithms and intentional modification of information) and on the back end (e.g., recursive feedback loops and echo chambers). Content moderation also leverages user data, often in ways the user is unaware of, which raises ethical and privacy concerns.

Furthermore, there is concern among users that companies like Facebook (now Meta) both overlook the risks posed by their product and misrepresent their internal findings when necessary to benefit the company.[3,29,30] It is for these reasons that many criticize platforms and call for evaluation of algorithm bias, transparency, justice, and accountability.[3,20]

Adolescence as a sensitive period

One of the reasons parents, clinicians, researchers, and policy makers have raised alarm about social media use among adolescents is that adolescence is a developmentally sensitive period. There are three key features of adolescent brain development that may impact how youth engage with social media: (1) heightened sensitivity to rewards and dynamic changes in the dopaminergic system;[3,31–33] (2) protracted maturation of brain networks that support cognitive function;[34] and (3) neural sensitivity to specific types of social information.[3,35] As a result, adolescence is a time of tremendous cognitive, social, emotional, and physical change that involves both opportunity for maturation and vulnerability to environmental stressors.[3,36] Evidence from developmental neuroscience illustrates that adolescence is a time of heightened risk taking, impulsivity, and sensitivity to social stimuli.[4,37] Consequently, adolescents are particularly susceptible to environmental influences like drugs, social stress, cognitive training, and likely social media.[3,4,38–41] There is some concern that constant engagement in social media in early

adolescence may alter neural sensitivity to rewards and punishment.[3,42] Furthermore, changes in the reward circuit may be a factor in excessive and problematic internet and social media use.[3,43]

At the same time, self-presentation and identity exploration is an important part of adolescence that social media can support.[3,14,44,45] It is a critical time for building relationships and developing a social support system.[3] Adolescents demonstrate an increased ability to consider other perspectives, which drives empathetic and prosocial behaviors on the one hand, as well as increased social comparison on the other.[3,46] The strong desire for social connectedness demonstrated by adolescents suggests that they may be relaxed regarding privacy settings and connecting with strangers.[35,47] Online environments and social media interactions may also lower inhibitions and accelerate intimacy.[48] In this way, online environments create both benefits and risks to development of identity and social connectedness.[48] Adolescence is also a time of increased flexibility and plasticity so researchers and public health practitioners advocate leveraging the plasticity of adolescent brain for health promotion.[37]

Ultimately, the power of social media to influence well-being likely depends on developmental stage.[49] There is some evidence that the concept of adolescence should be expanded to include individuals aged 10 to 24.[40] An expanded definition of adolescence is essential for developmentally appropriate framing of laws, social policies, and service systems. There are ethical reasons to limit marketing to children and teens as they may struggle to resist advertising.[50]

YOUTH PREVALENCE, MOTIVATIONS, AND EXPERIENCES ON SOCIAL MEDIA

According to a 2022 Pew survey, 95 percent of teens in the U.S. have a smartphone and 97 percent use the internet daily, which represents a 22 percent increase over the last eight years.[51] The omnipresence of both internet and mobile devices in how youth engage in relationships, learn, and experience milestones reflects a massive cultural shift since the early 2000s.[52] Smartphone use starts in early adolescence, with 40 percent of children ages 8 to 12 owning a smartphone and 18 percent reporting social media use every day.[53]

The 2022 Pew survey also found that 35 percent of teens report using YouTube, Instagram, TikTok, Snapchat, and Facebook almost constantly.[51] Fifty-five percent of teens thought they used social media the right amount, 36 percent thought they use social media too much, and eight percent thought they used it too little.[51] Additionally, 54 percent thought it would be somewhat hard to give up social media.[51] Findings from the Pew study mirror older studies reporting that 50 percent of teens describe themselves as constantly connected and feel that they are addicted.[1,2] There are slight demographic differences as well. Black and Hispanic teens may use online media more than their White peers.[51] Girls use social media more than boys and also report that they would have a harder time giving up social media.[51] Finally, teens over 15 use social media more than teens under 15.[51]

The most popular platform is YouTube, used every day by 95 percent of teens.[51] YouTube is followed by TikTok at 67 percent, Instagram and Snapchat at 60 percent, Facebook at 32 percent, and then Twitter, Twitch, WhatsApp, Reddit, and Tumbler.[51]

Despite widespread use among children and adolescents, robust independent safety analyses on the impact of social media on youth have not yet been conducted.[4] Currently, we do not yet have enough evidence to determine if social media is sufficiently safe for children and adolescents. Yet, the body of research about potential harm evidences the importance of understanding the possible risks and proactively creating digital environments that safeguard children's and adolescents' mental health and well-being during critical stages of development.[4]

MOTIVATIONS FOR USE

Motivations for social media use among teens include social interaction, connection, curiosity-driven learning, information sharing, entertainment, relaxation, stress relief, escapism, novelty seeking, social capital, and appearance feedback.[3,54–56] Moreover, there is evidence that the ways in which youth engage with social media can improve and enrich their lives through social support, connection, community building, identity development, civic engagement, and exposure to new ideas.[57]

Friendship, social support, and connection

Social media plays a vital role in the development and maintenance of friendships and social connectedness.[54,57,58] Communication with friends and family is often reported as the most important function of social media,[59,60] particularly when family and friends are far away.[61] Fifty-seven percent of teens have met a new friend online.[60,62] There appear to be some gender differences in how boys and girls interact with friends on social media. Sixty-one percent of boys and 52 percent of girls made friends online, and video games play a critical role in boys' friendship development.[62] In contrast, one study found that on average, teen girls spend over two hours a day on TikTok, Snapchat, and YouTube and over 90 minutes a day on Instagram and messaging apps.[63] Roughly, 69 percent of teens feel better connected to their friends' feelings, 83 percent better connected to their friends' lives, and 68 percent receive social support during tough times from friends through social media.[62] In this way, social media may be helpful in combating social isolation and building social capital.[3,64]

There is some evidence that social media can both reduce stigma and be a venue for sharing coping strategies.[3] Social media provides a way for youth to connect with people in the same position, which can be particularly valuable to adolescents who feel excluded or otherwise lack offline support, including patients with rare diseases, individuals with disabilities, those who struggle with mental illness and/or obesity, and marginalized groups (e.g., LGTBQ+ youth).[1,4] For instance, through social media, teens who are neurodivergent can connect socially with others in a way that is manageable for them, thereby reducing loneliness.[3,65] Social media may also help teens and youth coping with grief,[66] navigating foster care,[67] dealing with cancer, diabetes, rare diseases,[68,69] and mental illness.[3,70] Sharing on social media about losses and stressors can provide a sense of connection, support, and understanding.[71] Similarly, social media can provide support and connection for young people who live in communities where sexual and gender diversity are not accepted, which may buffer them from stigma and loneliness.[3,72–74] This is particularly true for LGTBQ teens in rural areas that are able to find support they do not have offline by connecting with other queer youth.[3,72,75–77]

It is not clear if online and in-person relationships are equivalent; however, friendship and social connection facilitate a sense of belonging.[3,78] Moreover, friendship can reduce anxiety and improve life satisfaction in its own right.[3,79] Cross-sectional studies among undergrads provide some evidence that people who use social media to connect with a diverse friend group tend to have higher social self-efficacy.[3,80] Yet, the relative support provided by online social connection may be influenced by the individual and how they engage with social media.[3,81]

Self-expression, Identity exploration, and Independence

There is some evidence that social media can support self-expression, identity exploration, and independence.[3,14,44,45,57,60,82,83] Adolescents who communicated more with friends online had a greater self-concept clarity.[60] One systematic review found that LGBTQ youth negotiated and explored identity using social media to manage identities though anonymity, censoring locations and content, restricting audiences, and using multiple accounts.[72] This suggests social media may support the mental health and well-being of LGTBQ youth through identity management.[72] In particular, the online environment of social media creates a space to revel and express differences.[84] Similarly, many cis girls are meticulous about which platforms and accounts they use for specific tasks, because it allows them to experiment with different forms of expression and ways of presenting themselves to their peers.[3,85] Self-disclosure, a key process in asserting personal agency, may be facilitated through digital platforms.[3,81]

Self-directed learning, Creative expression, and Civic engagement

Social media can also facilitate exposure to new ideas, raise awareness about current events, increase community participation and civic engagement, and allow collaboration on schoolwork.[2] A study of teens in western countries found that social media use predicts greater ability for both reading and navigating information online.[3,86] There is also some evidence that when social media is used for classroom writing exercises, students demonstrate less writing anxiety and increased agency.[87] Similarly, online fanfiction communities facilitate informal learning by creating a space for youth to build literary skills and support the same skills in others.[87] The same can be said for other hobbies, interests, and activities that have a social media component and roughly 70 percent of teens use social media to express their creative side.[54] The informal learning environment of social media facilitates empowerment and agency among some young people.[3,88] It has also been associated with increases in self-motivation among adolescents.[3,88]

About two-thirds of teens ages 13-18 reported using social media to learn about different points of view or show support,[54] and 64 percent of teens look for news online.[3,89] Furthermore, evidence suggests youth who engage in online political discussions also engage in offline political discussions.[3,89,90] Therefore, social media may be a vehicle to engage and utilize the social and political power of young people through civic engagement.[3,90–92] Social media can facilitate political democracy, cultural democracy, and spread of knowledge.[93] Finally, there is some evidence that adolescents both seek out and share health information on social media.[53,54] Therefore, it may be an effective tool for health interventions and health promotion.[1,94,95] On the other hand, health misinformation can exacerbate adoption of harmful behaviors.[96]

ONLINE HARASSMENT AND EXPOSURE TO INAPPROPRIATE CONTENT

Cyberbullying and online harassment

There is evidence that social media increases risk of cyberbullying among youth.[1–3,60,83,97] According to a recent Pew survey, 46 percent of U.S. teens ages 13 to 17 report ever experiencing at least one of six cyberbullying behaviors.[51] Name-calling was most common, with 32 percent of teens reporting they have been called an offensive name online or on their cellphone.[51] False rumors (22 percent), receipt of explicit images (17 percent), pervasive questions about location (15 percent), physical threats (10 percent), and the sharing of explicit images of them without their consent (7 percent) were also reported.[51] There appear to be slight demographic differences in who experiences cyberbullying. Specifically, studies have shown that black teens experience more cyberbullying that their white peers,[51,98] LGBTQ youth experience more cyberbullying than their cisgender and heterosexual peers,[51,98] and adolescent girls experience more cyberbullying than adolescent boys.[51,63,99,100] Evidence also suggests that relationship issues (e.g., feeling left out and interpersonal drama) were the most common reason for cyberbullying among adolescent girls.[63,100]

Studies suggest that the size and type of the network as well as anonymity of those on the network impact the likelihood of harassment, but it is not easily predicted.[3,101,102] For instance, online harassment occurs often among video game users, particularly female gamers who commonly report sexual harassment.[3,103,104] One study found that indiscreet posting, time spent on social media, and personality traits were all predictors of cyberbullying.[105] There is some evidence of a relationship across studies between cyberbullying and depression among children and adolescents; however, the evidence of the effect of cyberbullying on other mental health conditions is inconsistent.[100] Adolescents' self-view and interpersonal relationships may be affected through social comparison and negative interactions, like cyberbullying and exposure to inappropriate content.[97]

Responses to cyberbullying are most often passive, with a pervasive lack of awareness or confidence that anything can be done.[100] Despite the prevalence of cyberbullying, some evidence suggests that in-person bullying is more common.[3,106]

Exposure to inappropriate content and misinformation

One major concern of parents, clinicians, researchers, and policy makers is that poorly regulated and moderated social media can result in youth exposure to inappropriate content (e.g., alcohol, tobacco, risky sexual behaviors, cyberflashing, porn, and self-harm).[1–3,107] A survey of more than 1,300 teens aged 13 to 17 found nearly three-fourths had seen pornography online, with social media being the point of access for about 18 percent.[3,108] Moreover, average first exposure was at 12 years old and accidental exposure accounted for 40 percent of cases.[3,108] Cyberflashing – the electronic transmission of sexually explicit photos without the recipients' consent – is a particularly troubling form of online harassment.[3,109] One survey found that 37 percent of girls and 20 percent of boys aged 12 to 18 had received sexual photos online, often from strangers,[3,110] and another study found more than 6 percent reporting the first flashing incident occurred between the ages of 12 and 14.[3,111] It is difficult to evaluate brief and limited exposures; however, there is evidence that repeated exposure to inappropriate content in childhood was associated with risky sexual behavior later in life.[107] Similarly, exposure to alcohol, tobacco, or risky sexual behaviors may be associated with initiation of those behaviors.[1]

Teens and adolescents may also be uniquely vulnerable to misinformation and disinformation because their maturity and cognitive capacities are still evolving.[3,112] Misinformation and disinformation can take a variety of forms including clickbait, hoax, rumor, satire, propaganda, and conspiracy theories.[113,114] Examples include things like foreign interference, political deceit, and claims for ineffective and unproven natural remedies and medical

advice.[112] Concerningly, many people lack the ability to identify misinformation and disinformation as evidenced by one study which found that the percentage of people who share fake news without the intention to mislead is five times higher than intentional spreaders.[115] A 2018–2019 survey of 3,446 U.S. high-school students demonstrated that 52 percent believed that a grainy video claiming to show ballot-stuffing in the 2016 Democratic primaries constituted 'strong evidence' of voter fraud in the US, and only 0.1 percent were able to track down the original video even though a quick search showed that it was actually shot in Russia.[112,116] Similarly, two-thirds could not tell the difference between news stories and 'sponsored content' (i.e. adverts) on a website.[112,116] Although teens and adolescents may be particularly vulnerable to misinformation and disinformation, there is currently very little data available to provide a clear picture of how misinformation and disinformation may affect their development, well-being, and rights.[112]

IMPACTS OF SOCIAL MEDIA ON ADOLESCENT HEALTH

To understand the impacts of social media on adolescent health, the conflicting and often reciprocal mechanisms through which online experience and health (physical and mental) influence each other must be disentangled.[3] However, there are several factors that make this extremely challenging, including:

(1) the direction of the relationship between social media and health is difficult to determine - social media use influences health and health influences social media use;
(2) the research lacks uniform, consistent, and comparable methodologies;
(3) social media is so ubiquitous it is difficult to separate the impact of exposure;
(4) different levels of analysis may reveal different dynamics – with large scale studies showing population level trends and psychological studies showing mixed, small, or no associations;
(5) social media is not a monolith, the affordances of different platforms and types of social media engender a wide variety of interactions, behaviors, and health impacts; and
(6) the heterogeneity of the literature and the primary reliance on cross-sectional studies (or meta-analysis of cross-sectional studies) make definitive conclusions and causal relationships limited. Most of the associations are qualified or limited to certain populations.[3]

Social Media and Physical Health: Sleep, Physical Activity, and Obesity.

There is evidence that social media use can disrupt sleep.[1–3,97,107,117,118] Specifically, increased duration of computer, internet, and social media exposure,[3,118] and the presence of a tv, computer, or mobile device in the bedroom in childhood were associated with fewer minutes of sleep, greater risk of sleep disturbances, longer sleep latency, worse sleep quality, and daytime dysfunction.[1,119] Gaming predicted delayed bedtimes and reduced attention the following day.[3,120] One study found that screen-based digital media use is closely associated with sleep duration and sleep quality in teens; however, they cautioned that more research was needed to determine the direction of the effect.[3,121] Another study found that smartphone use at night can delay sleep among adolescents.[3,122] In a nationally representative sample, one-third of parents of teens 12-17 had rules about smartphone use at bedtime and those kids had less daytime sleepiness.[3,123]

However, it is not clear if social media or devices more broadly are driving the relationship. There are three likely ways in which digital media use may disrupt sleep.[3,124] First, social media displaces sleep thereby delaying bedtime, disrupting sleep, and reducing sleep duration.[3,121,124] Second, devices can disrupt circadian rhythms though light emissions which heighten arousal and decrease sleepiness.[3,122,124] Third, social media may be psychologically stimulating in such a way that makes sleep difficult.[3,124,125] Determining which mechanism(s) are driving the association between digital media and poor sleep is necessary given that the cascading impacts of poor sleep and the potential harms of social media overlap significantly.

Observational studies suggest a significant association between poor sleep quality and excess social media use and negative mental health outcomes.[3,126] Therefore, the interplay between social media and sleep quality may impact mental health outcomes. Sleep loss is a risk factor for depression, mood disturbances, injuries, attention problems, and excessive weight gain.[3,127–129] Additionally, teens with restricted sleep have more problems with emotion regulation, anxiety, hostility, and fatigue.[3,130] One study also found that sleep-deprived participants showed worse mood, more social media use, and problems with concentration.[3,131] Moreover, findings from the Youth Risk Behavior Survey illustrated that teens who sleep four or fewer hours a night have 5.9 times higher odds of having a serious suicide attempt.[3,132] Some studies showed sleep quality mediating the relationship between social media use

and negative mental health outcomes in youth.[126] In particular, if social media displaces sleep and hobbies, it can be predictive of anxiety and depression.[3,133] Similarly, when screen time displaces sleep and exercise it is predictive of problematic use.[3,134,135] However, the current body of evidence on the directionality and relationships between social media use, mental health, and sleep is inconclusive.[3,126]

There is some evidence that social media use may correlate to non-adequate nutrition, non-physiologic postures, weight gain, and obesity.[1,2,107,117] Excessive TV viewing in early childhood is associated with an increased risk of obesity.[1] Social media could be displacing physical activity, sleep, studying, and other hobbies, resulting in a more sedentary lifestyle and an increased risk of obesity.[3,107,136] In support of this, another study found that increased digital media use was associated with a sedentary lifestyle.[3,137] Social media use is also associated with consumption of fast food, sugary drinks, snacks, and mindless eating.[3,138] One study theorizes that this may be occurring because social media is displacing regular meals.[3,138]

Social Media and Mental Health: Anxiety, Depression, and Loneliness

The findings on the association between social media and adolescent mental health are small, inconsistent, or non-existent. Moreover, the differences in findings appear to be explained by bidirectional interactions, methodological weaknesses and differences, and/or individual rather than population differences.

Several meta-analyses, systematic reviews, and other studies have found small negative associations between social media use and depression, anxiety, psychological distress,[139] loneliness, internalizing problems, and low offline social support.[3,139–147] At the same time, numerous other studies found the relationship between social media and adolescent mental health is non-existent, mixed, or inconsistent.[148–151] Specifically, there was no significant association between social media use and depression, anxiety, and life satisfaction.[148,150,152] Additionally, there is inconsistent evidence that social media makes social comparison, envy, and well-being worse.[149] Importantly, many of these studies note that predictive relationships between social media use and well-being are reciprocal, as well as present only in certain populations, developmental windows, or among certain patterns of use.[49,141–143,151–155]

For instance, one review found that early studies show comparison and envy are common on social media and linked to ill-being, whereas recent studies find positive, person-specific, conditional, and reciprocal effects.[149] Similarly, one study found that social media use in and of itself is not a predictor of life satisfaction; rather the relationship between self-reported estimates of social media use and life satisfaction is more nuanced, reciprocal over time, gender specific, and likely dependent on analytic methods.[152] Another study found that life satisfaction is most negatively associated with social media use in younger adolescents, but also noted possible developmental windows of sensitivity -- at ages 14-15 and 19 for boys and at ages 11-13 and 19 for girls.[49] A longitudinal study that characterized subgroups based on type of social media use found that the high social media use subgroup predicted higher depressive symptoms, panic disorder, delinquent behaviors, family conflict, and lower family and friend support than the high Instagram/Snapchat and low social media subgroup.[154] Similarly, in a study of U.S. undergrads, social media use was not predictive of impaired mental health; however, “vaguebooking” -- the practice of making a post on social media that is intentionally vague but highly personal and emotional -- was predictive of suicidal ideation.[151] This suggests how individuals use social media is more important than the amount of time they spend on social media, particularly considering that perceived parent-child conflict was a stronger predictor of mental health issues than social media use.[151]

There is also some evidence that young people who report symptoms of depression are using digital tools to learn about and help their mental health problems.[155] One study found that girls and LGBTQ teens were more likely to seek out online resources for mental health and showed interest in stories of others with similar experiences.[155] Those who benefit most from social media appear to be those who are marginalized as well as those with chaotic home lives, suggesting the benefits of online social support are most salient when offline social support is lacking.[51,54] These findings highlight the importance of researching patterns, quality, and type of use in addition to amount of use.

Additionally, there are methodological issues that further complicate definitive conclusions. Several studies note that wide variation in methods and rigor make it difficult to synthesize findings.[139,143,154,156,157] For instance, one systematic review found a small association between self-reported social media use and depressive symptoms, but noted that the studies had high heterogeneity, which suggests that other factors are likely moderating the relationship.[143] Another systematic review argued that small associations and inconsistent results may be influenced

by choice of mental health indication (e.g., presence of well-being is not necessarily the absence of ill-being and vice versa).[149] Furthermore, the research on social media and adolescent well-being primarily comes from cross-sectional studies, therefore causal associations may be unwarranted.[49,140,152,156–158] Finally, this research should consider a person-specific approach as individual differences may explain the mixed and inconsistent results.[156]

Ultimately, the presence of small associations as well as inconsistent and conflicting results highlights that the evidence is still too weak to promote a uniform interpretation or to support the conclusion that social media causes changes in adolescent mental health at the population level.[3,159] Moreover, the fact that social media use is linked in complex and ubiquitous ways with other aspects of life means it is unclear what such a small effect demonstrates.[159] Ultimately, more research is needed along with improved transparency and greater appreciation for individual differences.[4,159]

Problematic Internet Use and Internet Gaming Disorder

Internet gaming disorder is defined as persistent and recurrent use of the internet to engage in games, leading to clinically significant impairment or distress.[41] Problematic internet use is defined as internet use that creates psychological, social, school and/or work difficulties in a person's life.[160] This can include video gaming, social media use, web-streaming, and buying; however, those activities are characterized as excessive or poorly controlled preoccupations, urges, or behaviors regarding computer use and internet access that lead to impairment or distress. The key factor is that internet use becomes problematic when it causes dysfunction in daily life activities (e.g., school, sleep, exercise).[3,26,161] There appears to be significant overlap in internet gaming disorder, problematic social media use, and problematic internet use.[3,162,163] At this point it is unclear whether problematic social media use and gaming disorder are distinct or different manifestations of disordered tech use.[3]

There is some evidence that internet gaming disorder predicts depression, anxiety, social phobia, poor school performance, sleep disruption, and poor relationships with parents and peers.[3,164–167] There is also some evidence that problematic internet use is associated with depression, disturbances in sleep and mood, upward social comparisons, cybervictimization, and poor academic performance.[3,4,58,72,168–172] Problematic social media use is most common among older age groups and may be associated with irritability, nervousness, loneliness, and morning tiredness.[169] There are gender differences in internet gaming disorder, as it affects males 5 times more than females.[173] Moreover, there is some evidence that boys are more addicted to games whereas girls are more addicted to social media.[3,174]

Some researchers suggest that problematic internet use could explain the small negative associations between social media and youth mental health. For instance, problematic social media use mediated the association between depressive symptoms and cyberbullying.[142] Additionally, one study found that teens with problematic internet use reported more difficulty identifying and describing emotions, and there is some evidence that emotion regulation is a significant mediator in quality of parent-adolescent relationship.[175] Some researchers theorize that problematic internet use might be a coping strategy to compensate for emotion regulation deficits, which might explain why a good relationship with parents reduces problematic internet use.[175] However, problematic use is more complex than simply the amount of time spent on social media. It includes enduring preoccupation with social media, inability to stop, neglect of one's health and other areas of one's life.[156] Therefore, more research is needed to better understand the relationships between problematic internet use, social media, and adolescent mental health.

Attention and Learning

There is limited evidence that social media use negatively impacts attention and learning. One study found that time spent on social media predicts concentration problems in adolescent girls.[3,176] Additionally, there are small associations between both frequency of social media use and number of platforms and attention deficit hyperactivity disorder (ADHD).[3,177–179] However, it is not clear what is driving the association between social media use and decreased attention.[1]

There is some evidence that reading on screens is fundamentally distracting.[3,180] Others have suggested that multitasking is the root of the problem. High proportions of youth engage in heavy smartphone use and media multitasking.[97] Moreover, a recent meta-analysis found associations between multitasking and problems with attention, behavior regulation, impulsiveness, and memory.[3,181] Specifically, media multitasking is associated with negative effects on cognitive control, academic performance, and socioeconomic functioning.[3,97,181,182] One study

found that in three hours of studying, adolescents experienced an average of 35 social media distractions that diverted attention.[3,183] Additionally, another study found that the number of social media accounts correlated with parent reports of symptoms of inattention, hyperactivity, impulsivity, oppositional defiant disorder , anxiety, and depressive symptoms, and adolescent reports of fear of missing out and loneliness.[179] Therefore, it has been suggested that the amount of time spent online can have bidirectional effects on depressive symptoms and ADHD; this risk is particularly heightened in those with pre-existing poor mental health.[126]

Body Image and Eating Disorders

Significant research exists on the association between social media use and body image, but the findings are limited, and causal factors are difficult to differentiate. There is some evidence that social media use and consequent exposure to appearance-focused content may be weakly associated with poorer body image.[3,4,184,185] A cross-sectional study found that greater levels of self-objectifying social media use predicted greater body shame among youth, and the association was mediated by an associated increase in body surveillance.[3,186] Specifically, the role of body surveillance was stronger among girls and adolescents who are particularly focused on others for approval.[186] Body image concerns may be a key mechanism underlying the associations between adolescent girls' social media use and mental health.[187]

A scoping review found that social media use may have a variety of impacts on diet, exercise, and body image.[107] Similarly, another study found that the same platform that helped some patients find recovery support was also a source of body shaming and rumination for others.[3,188] Another review found that peer influences on social media span from healthy eating and exercise to disordered eating, and that dietary information shared on social media often misaligns with national dietary standards.[189] Similarly, one study found youth had an increased ability to recall unhealthy food, beverages, and brands particularly when celebrities and influencers are promoting them.[190]

PRIVACY

Researchers have found that the growing use of social networks has led to the emergence of ethical and privacy concerns regarding the management of user data and how social networks train algorithms for economic purposes to organize the content shown to users.[1,191] The new privacy paradox is that these sites have become so ubiquitous that users feel they must disclose information on them even though these sites do not provide adequate privacy controls.[3,192] Specifically, the privacy policies used by platforms either require or allow users to review and consent to their data collection and data use practices; however, most respondents agreed to the terms without reviewing them.[3,193,194] This could be because the policies themselves are long and technical, they do not provide consumers with meaningful choices, and people are skeptical of whether policies achieve their goals.[194] Concern over what platforms do with user data coupled with a sense of futility over having the agency to change anything may explain why a recent Pew survey found overall strong bipartisan support for more regulation of what companies can do with people's data, with 72 percent of Americans reporting that there should be more regulation than there is now.[194]

These issues may be even more salient for children. A recent Pew study found that Americans worry about kids' online privacy, with 89 percent of respondents reporting that they are very or somewhat concerned about social media platforms knowing personal information about kids.[194] Similar concern arises over how advertisers, online games, and gaming aps collect and use children's data.[194] However, respondent expectations regarding responsibility for protecting kids is placed primarily on parents at 85 percent, followed by technology companies at 59 percent and the government at 46 percent.[194]

The Children's Online Privacy Protection Act (COPPA), which was enacted in 1998, recognizes that young children cannot consent to the terms of use for data collection, and thus prohibits enticing personal disclosures through games and restricts advertising to children. Yet, COPPA only applies to kids under 13. Consequently, recent legislation has focused on age-appropriate design and proposed additional protections for adolescents.

There is mixed evidence on how adolescents and adults feel about online privacy. There is some evidence that older users are more concerned about privacy than youth.[195] Additionally, a strong desire among adolescents for social connectedness suggests that youth may be more inclined to have relaxed privacy settings and a show a greater willingness to connect with strangers.[3,35,196] However, a different study found a negative relationship between age and privacy; noting that young people are more likely to have taken action to protect their privacy than older

people.[192] Therefore, it is possible that the studies finding that young people are not concerned about their privacy may be because they are taking more precautions.

POTENTIAL APPROACHES TO PROTECT CHILDREN ON SOCIAL MEDIA

Despite widespread use among children and adolescents, the evidence on the potential harms and benefits is too weak to promote a uniform interpretation of the impact of social media on adolescent health at the population level. Nonetheless, the current body of research does highlight the importance of understanding the risks and benefits and proactively creating digital environments that protect and enrich children's and adolescents' health and well-being during critical stages of development.[1–4,41]

Recommendations for Industry

The most common recommendation for the social media industry is improved privacy protections, improved transparency, and a better system of reporting inappropriate content and ill-actors. Yet aside from internal efforts, like Facebook's Oversight Board, there has been little voluntary governance action on the part of industry.[197] Highlighting the success of the Global Internet Forum to Counterterrorism, the National Academy of Science, Engineering, and Medicine (NASEM) argues that the International Organization for Standardization (ISO) should convene an ongoing technical working group comprised of industry, academic, and civil stakeholders to develop standards for social media platform design, transparency, and data use.[3,198] Other researchers, professional organizations, and policy makers also advocate for development of industry standards.[4,197]

Specifically, the goals of the work group would be to develop standards that: (1) limit the personal information companies collect, the types of content available, and the prompts to extend time on a platform; and (2) develop easy to use, universal, transparent systems for reporting, follow-up, and adjudication for cases of online harassment and abuse.[3,4,197] Specifically, efforts should be made to move to a functional privacy system that emphasizes transparency of and access to inputs and outputs. On the front-end inputs would include: (1) a clear process for content moderation and use; (2) contents of privacy agreements; and (3) mandatory disclosures to users.[3] On the back-end, standard outputs might include: (1) platform health measures (e.g., content moderation and take down policies and data at the community, group level to evaluate platform toxicity); (2) algorithmic transparency standards and summaries at the user level; and (3) reports on efforts to remediate youth mental health problems on the platform.[3,4] This would improve privacy protections and transparency by making it clear what data is collected from minors, how it is collected and used, and what the consequences of use are. Furthermore, this would give companies and researchers more straightforward guidelines for measuring data collection risks that children encounter online, as well as technical standards to benchmark platform operations, transparency, and data use.[3] Arguably social media platforms would benefit from a standard guide of assessment to evaluate how their products influence youth well-being.

However, developing standards is insufficient unless social media companies adopt the standards both as their policy and as provisions in their terms of service.[3] There is a precedent of self-regulation in media (e.g., tv, movies, videogames, music) using industry standards, as well as early efforts at self-regulation evidenced by Facebook's Oversight Board.[3,197,199–201] However, given that the success of social media is contingent on engaging as many people for as long as possible, implementing standards aimed to reduce controversial, emotional, and inflammatory content might not be in their best interest. This is evidenced by the pending lawsuit to enjoin the California Age-Appropriate Design Code Act on first amendment violation claims.[202,203] Enacting a regulatory framework across jurisdictions on global companies is not always legally or logistically viable; however, voluntarily adopting standards now could reduce the likelihood of more sweeping regulatory action later.[3,197,204,205] Furthermore, evidence from political science literature on transnational governance shows that multistakeholder regulatory standards setting schemes can be a vital part of the corporate regulatory toolbox.[197] However, more research is needed to see how and if they can be implemented to protect adolescent social media users.[197]

A public statement of compliance with standards and a commitment to uphold those standards in the terms of service would be a meaningful step towards an enforceable legal structure.[3] Specifically, the Federal Trade Commission (FTC) can penalize firms that engage in unfair or deceptive business practices and has used this authority against companies that have failed to honor commitments made in their privacy policies and similar agreements.[206–208] Audit and systemic risk reports of compliance with the standards should be available to the FTC,

researchers, and the public. Social media companies should make a good faith effort to ensure access to data that facilitates research on the effects of social media on child and adolescent health possibly including removal of the prohibition on researchers' use of publicly available data.[3] More transparency would allow for comparisons across platforms and over time, which would provide a better insight for the companies, the public, and the FTC. Creation of a standard would also support and inform the FTC's use of consent decrees as a regulatory tool.[3,209] Once a company agrees to a consent decree – terms of the decree determine obligations to remediate regardless of whether the terms are within the FTC's authority.[3,210] Creation of an industry standard could support the FTC's governance by consent decree, even for providers who do not explicitly adopt the standard.[3]

Once standards have been created and adopted, it would be much easier to assess and remedy harms posed by social media. For instance, standards could be used to evaluate whether the platform has age-verification processes, data encryption, and privacy policies.[3] Similarly, they could be used to determine whether a platform's content is suitable for children by evaluating the likelihood of exposure to illegal and maladaptive behavior.[41] The first step towards benchmarking is transparency and more fair competition in an opaque market.[3] For instance, ethical artificial intelligence (AI) tool kits could help facilitate more open communication among technology developers, researchers, policy makers, and civil society.[3,211] Additionally, public documentation of the provenance of the dataset used to calibrate machine learning models is gaining traction as way to mitigate harms from biased models.[3,212]

NASEM makes a persuasive case that an ongoing technical workgroup to develop industry standards, ideally facilitated by ISO, as well as near uniform industry adoption of the standards in their policies and terms of service would improve privacy protections, improve algorithmic and other transparency, and facilitate a better system of reporting inappropriate content and ill-actors. However, this is new territory and despite the ISO's strong track record of developing complex technical international standards (e.g., information security management and data protection), it is difficult to fully assess if something similar would be an effective tool to regulate social media.[3,198]

Recommendations for the Federal Government

In addition to developing and adopting industry standards, another approach is to improve privacy protections and age-appropriate design at the federal and state level through legislation. This is further supported by the Surgeon General's Advisory on the effects of social media on youth mental health, which urges action to ensure social media environments are healthy and safe.[4] As noted earlier, COPPA recognizes that young children cannot consent to the terms of use for data collection, and thus prohibits enticing personal disclosures through games and restricts advertising to children.[213] Currently, when companies violate COPPA by collecting data for children under the age of 13, the FTC can and has issued fines. Specifically, in 2019, the FTC required Google to pay $170 million for data collection in violation of COPPA.[214] However, COPPA only protects children under the age of 13 so arguably one way to improve privacy protections for children would be to expand COPPA to include all minors. In 2021, legislation to extend COPPA protections to kids through age 16 was proposed with the Children and Teens' Online Privacy Protection Act, which would also require platforms and providers to report on foreseeable risks of harm.[215] However, there has been no action on the proposed legislation. The FTC also has authority over unfair and deceptive practices in commerce. Therefore, in response to concerns about the erosion of consumer privacy, in particular with data collection and use practices, the FTC has issued guidance documents on internet advertising.[3,216–218] Moreover, there is proposed rulemaking on commercial surveillance and data security.[3,219] Additional guidance and/or revisions from the FTC regarding how to make systems for reporting cases of online harassment and abuse that comply with COPPA would be benefical.[3]

In addition to improving children's privacy and better regulating social media providers through the FTC and COPPA, it may be beneficial to develop support programs for children and adolescents who experience digital abuse and evaluate the effectiveness of such programs, and the US Substance Abuse and Mental Health Services Administration is well positioned to do this.[3] Finally, assuming industry leaders do not voluntarily remove the prohibitions in their terms of service on the use of publicly available data for research, Congress could pass legislation to ensure researchers can access data to examine the effects of social media on child and adolescent health.[3]

Recommendations for State and Local Agencies

One potential way of making technology safer for kids is through age-appropriate design.[3,4] Some of the goals of age-appropriate design include: (1) centering the rights and developmental needs of children and (2) improving

privacy protections by addressing and modifying what data is collected from minors, how it is collected, and how it is used. In practice this might look like collecting the minimum information necessary and prohibiting the use of that information in commerce. It might also include shifting the burden to establish users' age to the producers of the technology as was done in the United Kingdom.[3,220] It would also likely discourage developmentally inappropriate persuasive design features (e.g., push notifications, like buttons, tones for new content, and endless scrolling).[41]

The increasing concerns about social media use and adolescent health has prompted federal, state, and local legislators to propose age-appropriate design measures to protect children while using the internet and internet-based forms of communication, including social media.[221,222] In 2023, 35 states and Puerto Rico introduced legislation around social media and youth, and 12 states enacted bills or adopted resolutions.[221] By and large, the goals of the legislation are to: (1) create study commissions and task forces to evaluate the relationship between social media and adolescent health; (2) require age verification and/or parental consent to open social media accounts; and (3) adding digital and media literacy to K-12 curriculums.

For instance, Utah enacted the Utah Social Media Regulation Act, which requires age verification of state residents and parental consent for those under the age of 18 to open an account.[223] It also limits the hours of access for certain users, subject to parental or guardian direction, and provides for a private right of action. Similarly, Arkansas created the Social Media Safety Act which requires age verification and parental consent for use of social media. It also establishes a mechanism for liability for failure to perform age verification for use of social media and for illegal retention of data.[224] In 2022, California passed the Age-Appropriate Design Code Act (AADC).[202] The law was modeled after the United Kingdom's Age-Appropriate Design Code which advocates for businesses to consider the best interests of children when designing, developing, and providing online services, products, or features likely to be accessed by children. Notable obligations under the Age-Appropriate Design Code Act include requiring providers to: (1) configure a high level of default privacy settings; (2) assess whether algorithms, data collection, or targeted advertising systems could harm children; and (3) use clear, age-appropriate language for user-facing information and documents.[222] In 2023 a lawsuit to invalidate the AADC on first amendment free speech grounds was filed in federal court by NetChoice, a coalition representing the country's tech companies.[203] The District for the Northern District of California granted a preliminary injunction against the AADC, the California Attorney General appealed, and a decision by the Ninth Circuit Court of Appeals is anticipated in Spring 2024.[202,203,225]

Efforts around age-appropriate design legislation are relatively new so the overall impacts are unclear. However, age verification, digital media literacy, and continued research appear beneficial and do not have obvious risks. Likewise, expansion of COPPA and provision of resources and support for those who experience online harassment have little formal evidence of effectiveness but are rationally grounded.

Recommendations for Parents and Kids

Parents and children are encouraged to use social media functions that facilitate social support, online companionship, emotional intimacy, and healthy socialization; particularly during periods of isolation, during stress, mental health crisis, and for marginalized groups.[41] To achieve this, it is recommended that families should collectively develop, review, and follow a family media use plan, which should outline developmentally appropriate types, times, methods, places for, and amounts of acceptable media us.[1,2,4,41] For instance, there is evidence of the impact of excessive digital technology use (e.g., screentime, tv, and social media) by adolescents on negative health impacts.[1,2,226] However, there has been a push among researchers to move away from focusing on screentime and instead to consider how, why, when, and with whom youth are engaging online. Despite this, the American Association of Pediatrics, American Psychological Association, and many other organizations and policy makers advocate for screen time limits and media-free time.[1,2] Specifically, it is recommended that adolescents abstain from using screens 1 hour before bed and that adolescents should not sleep with digital devices in their bedrooms.[7,52] Additionally, there is some evidence supporting open, non-judgmental communication between caregivers and children and some degree of parental monitoring of social media use.[1,2,41,97] Recent surveys suggest roughly 63 percent of adolescents and 70.8 percent of parents reported parental monitoring, and 74.3 percent of adolescents reporting being friends with their parents online.[179] Open communication is helpful for teaching digital literacy, which is necessary for children to understand the limits of "free digital products" that process access in exchange for data on user demographics, politics, mental health, and sexuality generated through engagement and viewing behavior.[50]

Recommendations for Clinicians

It is recommended that clinicians be aware of and talk with children and families about the risks and benefits of social media use.[1–3,107,227] Specifically, communication with adolescents is the most effective in the context of a therapeutic alliance that is open and non-judgmental.[97] Physicians should encourage: (1) setting boundaries for screentime and social media use; (2) discuss the risks and benefits of social media, including impact of smartphones on learning and the importance of digital media literacy; and (3) encourage communication between caregivers and children and advocate use of the Family Media Toolkit and Family Media Use Plan.[1,2,58,60,97]

Recommendations for Training and Education

One way to reduce potential harm to adolescents using social media is through improved digital media literacy. Specifically, it is important to train adolescents and those teaching and advising them skills for assessing and validating information on social media and the internet more broadly.[41,50,60,97,227] Moreover, the approach to digital media literacy needs to be multi-tiered and tailored to children, parents, educators, and clinicians. Specifically, comprehensive digital media literacy should be integrated into the standards set by state boards of education. Moreover, the U.S. Department of Education should draw national attention to the importance of comprehensive digital media literacy.[3] This is necessary to create both an online environment that protects youth and social media consumers who are empowered to protect themselves. Furthermore, educators and clinicians need to be trained in digital media literacy so they can adequately teach and advise adolescents on the risks and benefits of social media.[1–4] This could include incorporation of digital media literacy requirements for licensure as well as ongoing professional development training and resources for both educators and clinicians.[3] In addition to incorporating digital media literacy into training and licensure, additional efforts to improve dissemination of health-related digital media literacy is suggested.[227]

Recommendations for Research

Currently, the research on social media and adolescent health is limited.[3,4] Therefore, federal and non-profit research funders should support a research agenda that prioritizes: (1) the health consequences of social media use and the mechanisms of harm, (2) the epidemiology of problematic use, (3) interventions and other efforts to reduce and remediate harms arising from social media, (4) the role of parents and other adults in influencing positive use, and (5) algorithmic audits.[3,4] There is a need for validated tools to measure exposure to social media affordances, data sharing, and the establishment of long-term cohort studies. Special emphasis should be given to interdisciplinary approaches and study designs that attempt to understand causal directions.

RELEVANT AMA POLICY

The AMA has existing policy that addresses social media and mental health, gun violence, internet pornography, online streaming of sexual encounters, the effects of video game and internet overuse, disinformation, cannabis marketing, and online human subjects' research. In general, these policies advocate the use of education and legislation to: (1) increase awareness about potential risks associated with social media and internet use; and (2) reduce exposure to harmful content (e.g., gun violence, pornography, disinformation, etc.) particularly for children, adolescents, and young adults. Current policy also supports development and implementation of clinical tools for identification and treatment of harms that arise from exposure as well as continued research into potential harms and the effectiveness of screening and treatment. Detailed information on the current AMA policies can be found in the appendix.

CONCLUSION

Digital media, smartphones, and social media have a pervasive presence in nearly all aspects of youth and adolescent life. Despite substantial research efforts, the evidence is too weak to promote a uniform interpretation of the impact of social media on adolescent health at the population level. There are several factors contributing to the weak evidence including: (1) the reciprocal associations between social media use and health; (2) the lack of consistent and comparable methodologies; (3) entanglement of impact and exposure as a byproduct of social media's ubiquity; (4) different dynamics and trends depending on level of analysis; (5) the wide variety of interactions, behaviors, and health impacts engendered by social media; and (6) reliance on cross-sectional studies with high heterogeneity.

Although the evidence is too weak to provide a uniform interpretation, there are clear positive and negative trends. There is some evidence of potential benefit in the form of improved social support, identity development, civic engagement, and self-directed learning. There is also some evidence of potential harm including negative impacts on sleep, physical activity, and mental health, as well as exposure to inappropriate content, and data privacy issues. Furthermore, it is apparent that the relative risks and benefits of social media likely depend on individual differences in: (1) engagement with social media (e.g., what kids see and do online, who they talk to, when they use social media, and how they use social media); (2) pre-exiting strengths and weaknesses; and (3) the cultural, social, and physical environment.

Even though the evidence of harm is limited there is an urgent need for action for two reasons. First, the lack of algorithmic transparency, privacy protections, and accountability and redress for online harassment on most platforms is concerning given the power, reach, and ubiquity of social media. Second, the potential harms are serious, particularly during sensitive developmental periods; therefore, proactively creating digital environments that protect and enrich children's and adolescents' health and well-being is beneficial regardless of the evidence of harm. There are two key approaches that would likely facilitate the creation of safer, developmentally appropriate environments. First, federal and state legislative action (e.g., expansion of COPPA, implementation of age-appropriate design, and mechanisms to address online harassment), and second, development and widespread adoption of industry standards to benchmark platform operations, transparency, and data use. In addition to improving the digital environment, it is imperative that there are simultaneous efforts to address harms that still arise including: (1) education and training on digital media literacy and the potential harms posed by social media; (2) improved screening and support for those who experience harms (e.g., problematic internet use and online harassment); and (3) continued research of the health impacts of social media.

RECOMMENDATION

The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed:

1. That our AMA:

   (1) urges physicians to: (a) educate themselves about social media; (b) be prepared to counsel patients and/or their guardians about the potential risks and harms of social media; and (c) consider expanding clinical interviews to inquire about social media use.
   (2) encourages further clinical, epidemiological, and interdisciplinary research on the impact of social media on health.
   (3) supports education of clinicians, educators, and the public on digital media literacy and the health effects of social media.
   (4) recognizes that the relative risks and benefits of social media may depend on individual differences (e.g., social media engagement, pre-existing traits, and environment).
   (5) supports legislative, regulatory, and associated initiatives (e.g., development of industry standards, age-appropriate design, and funding programs that support those harmed by online harassment).
   (6) will collaborate with professional societies, industry, and other stakeholders to improve social media platform privacy protections, transparency (e.g., algorithmic, data, and process), data sharing processes, and systems for accountability and redress in response to online harassment.

2. That current AMA policy D-478.965, "Addressing Social Media and Social Networking Usage and its Impacts on Mental Health D-478.965" be amended by addition and deletion to read as follows:

   Our AMA: (1) will collaborate with relevant professional organizations to: (a) support the development of continuing education programs to enhance physicians' knowledge of the health impacts of social media and social networking usage; and (b) support the development of effective clinical tools and protocols for the identification, treatment, and referral of children, adolescents, and adults at risk for and experiencing health sequelae of social media and social networking usage; (2) advocates for schools to provide safe and effective educational programs ~~by which~~ so that (a) all students can learn to identify and mitigate the onset of mental health sequelae of social media and social networking usage, (b) all students develop skills in digital literacy to serve as an individual protective foundation for interaction with various types of digital media (including social media), and (c) at risk students' access to social media can be limited and/or closely monitored as individually

appropriate; (3) affirms that use of social media and social networking has the potential to positively or negatively impact the physical and mental health of individuals, especially adolescents and those with preexisting psychosocial conditions; (4) advocates for and support media and social networking services addressing and developing safeguards for users, including protections for youth online privacy, effective controls allowing youth and caregivers to manage screentime content and access, and development and dissemination of age-appropriate digital literacy training; and (5) advocates for the study of the positive and negative biological, psychological, and social effects of social media and social networking services use.

APPENDIX: Relevant AMA Policy

Addressing Social Media and Social Networking Usage and its Impacts on Mental Health D-478.965
Our AMA: (1) will collaborate with relevant professional organizations to: (a) support the development of continuing education programs to enhance physicians' knowledge of the health impacts of social media and social networking usage; and (b) support the development of effective clinical tools and protocols for the identification, treatment, and referral of children, adolescents, and adults at risk for and experiencing health sequelae of social media and social networking usage; (2) advocates for schools to provide safe and effective educational programs by which students can learn to identify and mitigate the onset of mental health sequelae of social media and social networking usage; (3) affirms that use of social media and social networking has the potential to positively or negatively impact the physical and mental health of individuals, especially adolescents and those with preexisting psychosocial conditions; (4) advocates for and support media and social networking services addressing and developing safeguards for users; and (5) advocates for the study of the positive and negative biological, psychological, and social effects of social media and social networking services use.

Minimizing the Influence of Social Media on Gun Violence H-478.977
1. Our American Medical Association calls upon all social media sites that allow posting of videos, photographs, and written online comments encouraging and glorifying the use of guns and gun violence to vigorously and aggressively remove such postings.
2. Our AMA strongly recommends social media sites continuously update and monitor their algorithms in order to detect and eliminate any information that discusses and displays guns and gun violence in a way that encourages viewers to act violently.
3. Our AMA will work with social media sites to provide educational content on the use of guns, inherent dangers, and gun safety in an effort to end the ongoing and devastating effects of gun violence in our communities.

Internet Pornography: Protecting Children and Youth Who Use the Internet and Social Media H-60.934
Our AMA:
(1) Recognizes the positive role of the Internet in providing health information to children and youth.
(2) Recognizes the negative role of the Internet in connecting children and youth to predators and exposing them to pornography.
(3) Supports federal legislation that restricts Internet access to pornographic materials in designated public institutions where children and youth may use the Internet.
(4) Encourages physicians to continue efforts to raise parent/guardian awareness about the importance of educating their children about safe Internet and social media use.
(5) Supports school-based media literacy programs that teach effective thinking, learning, and safety skills related to Internet and social media use.
(6) Actively support legislation that would strengthen child-centric content protection by internet service providers and/or search engines in order to limit the access of pornography to minors on the internet and mobile applications.

Addressing Public Health Disinformation Disseminated by Health Professionals D-440.914
Our AMA will collaborate with relevant health professional societies and other stakeholders:
(a) on efforts to combat public health disinformation disseminated by health professionals in all forms of media,
(b) address disinformation that undermines public health initiatives, and
(c) implement a comprehensive strategy to address health-related disinformation disseminated by health professionals that includes:
(1) Maintaining AMA as a trusted source of evidence-based information for physicians and patients.
(2) Ensuring that evidence-based medical and public health information is accessible by engaging with publishers, research institutions and media organizations to develop best practices around paywalls and preprints to improve access to evidence-based information and analysis.

(3) Addressing disinformation disseminated by health professionals via social media platforms and addressing the monetization of spreading disinformation on social media platforms.
(4) Educating health professionals and the public on how to recognize disinformation as well as how it spreads.
(5) Considering the role of health professional societies in serving as appropriate fact-checking entities for health-related information disseminated by various media platforms.
(6) Encouraging continuing education to be available for health professionals who serve as fact-checker to help prevent the dissemination of health-related disinformation.
(7) Ensuring licensing boards have the authority to take disciplinary action against health professionals for spreading health-related disinformation and affirms that all speech in which a health professional is utilizing their credentials is professional conduct and can be scrutinized by their licensing entity.
(8) Ensuring specialty boards have the authority to take action against board certification for health professionals spreading health-related disinformation.
(9) Encouraging state and local medical societies to engage in dispelling disinformation in their jurisdictions.

Television Broadcast and Online Streaming of Sexual Encounters and Public Health Awareness on Social Media Platforms H-485.994
Our AMA urges television broadcasters and online streaming services, producers, sponsors, and any associated social media outlets to encourage education about inclusive safe sexual practices, including but not limited to condom use and abstinence, in television or online programming of sexual encounters, and to accurately represent the consequences of unsafe sex.
Medical and Public Health Misinformation Online D-440.915
Our AMA:
(1) encourages social media companies and organizations, search engine companies, online retail companies, online healthcare companies, and other entities owning websites to further strengthen their content moderation policies related to medical and public health misinformation, including, but not limited to enhanced content monitoring, augmentation of recommendation engines focused on false information, and stronger integration of verified health information;
(2) encourages social media companies and organizations, search engine companies, online retail companies, online healthcare companies, and other entities owning websites to recognize the spread of medical and public health misinformation over dissemination networks and collaborate with relevant stakeholders to address this problem as appropriate, including but not limited to altering underlying network dynamics or redesigning platform algorithms;
(3) will continue to support the dissemination of accurate medical and public health information by public health organizations and health policy experts; and
(4) will work with public health agencies in an effort to establish relationships with journalists and news agencies to enhance the public reach in disseminating accurate medical and public health information.

Marketing Guardrails for the "Over-Medicalization" of Cannabis Use D-95.958
Our AMA will: (1) send a formal letter to the Food and Drug Administration and Federal Trade Commission requesting more direct oversight of the marketing of cannabis for medical use; (2) generate a formal letter for use by state medical societies requesting more direct oversight by state government of the marketing of cannabis; (3) support and encourage federal, state, and private sector research on the effects of cannabis marketing to identify best practices in protecting vulnerable populations, as well as the benefits of safety campaigns such as preventing impaired driving or dangerous use; (4) encourage state regulatory bodies to enforce cannabis-related marketing laws and to publicize and make publicly available the results of such enforcement activities; (5) encourage social media platforms to set a threshold age of 21 years for exposure to cannabis advertising and marketing and improve age verification practices on social media platforms; (6) encourage regulatory agencies to research how marketing best practices learned from tobacco and alcohol policies can be adopted or applied to cannabis marketing; and (7) support using existing AMA channels to educate physicians and the public on the health risks of cannabis to children and potential health risks of cannabis to people who are pregnant or lactating.

Principles of Human Subjects Research Shall Apply to Online Medical Research Projects H-460.898
Our American Medical Association declares social media sites' terms of service as an insufficient proxy for informed consent prior to being enrolled in any medical experiment and recommends that online social networks provide users with specific informed consent outlining the aims, risks and possible benefits of any medical experimental study prior to study enrollment.

Emotional and Behavioral Effects of Video Game and Internet Overuse H-60.915
Our AMA supports increased awareness of the need for parents to monitor and restrict use of video games and the Internet and encourage increased vigilance in monitoring the content of games purchased and played for children 17 years old and younger.

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11. STAND YOUR GROUND LAWS

Reference committee hearing: see report of Reference Committee D.

HOUSE ACTION: RECOMMENDATIONS ADOPTED
REMAINDER OF REPORT FILED
See Policies D-145.995, D-145.999, H-145.966, H-145.975 and H-145.997

INTRODUCTION

American Medical Association Policy H-145.966, "Stand Your Ground Laws" as adopted by the House of Delegates at the 2023 Annual Meeting (Resolution 435), asked that our AMA study the public health implications of "Stand Your Ground" laws and castle doctrine.

BACKGROUND

"Castle doctrine" refers to the legal right of a person to defend himself against an intruder in his home or other property, even if the use of deadly force is required. Stand Your Ground (SYG) laws expanded castle doctrine beyond one's home or property to public spaces where individuals have a legal right to be. Prior to the enactment of SYG laws, most states followed the common law self-defense rule, which imposed a duty to retreat before using force in self-defense, if safe retreat was possible. SYG laws generally removed the duty to retreat from a threat before using force in self-defense. Under SYG laws, individuals are allowed to use force, including lethal force, if they reasonably believe it is necessary to protect themselves or others from imminent harm.

In 2005, Florida passed the first SYG law in the United States.[1] According to the National Conference of State Legislatures, as of March 2023, laws in at least 28 states and Puerto Rico provide that there is no duty to retreat from an attacker in any place in which one is lawfully present.[2] At least ten states include language stating one may "stand his or her ground," while eight states permit the use of deadly force in self-defense through judicial decisions or jury instructions.[2]

Those who support the enactment of SYG laws generally believe that people have a fundamental right to "defend themselves from attack with proportionate force in every place they have a lawful right to be" which is thought to deter criminals by increasing their perceived risk of encountering an armed victim.[2] Critics are concerned these laws "unnecessarily encourage the use of deadly force as a low-cost license to kill instead of reserving it only as a protective measure."[3] SYG laws are commonly referred to as "shoot first" laws and are thought to encourage people to take the law into their own hands. There are also concerns that the laws exacerbate social inequities.

In this report, your Council on Science and Public Health reviews the available evidence regarding the public health impact of castle doctrine and SYG laws.

METHODS

English language articles were selected from searches of PubMed and Google Scholar using the search terms "stand your ground", "castle doctrine", "self-defense law". Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by government agencies and nonprofit organizations were also reviewed for relevant information.

DISCUSSION

There has been little research on the public health implications of castle doctrine. Researchers have sought to evaluate the effect of SYG and expanded self-defense laws on various factors including crime rates, homicide rates, and racial disparities in the application of the laws. It is worth noting at the outset that evaluating the effects of SYG laws is challenging, in part because the duty to retreat is a less distinct element of self-defense in practice.[4] Also because there are variations in the laws across jurisdictions and implementation of the law may also deviate from the original intent.[4]

Impact of SYG laws on homicide, firearm homicide, and violent crime

A retrospective analysis of data from 2000 to 2017 examined justifiable homicide (citizen-related justifiable homicide with a firearm) and homicide (non-justifiable citizen-related homicide) rates before and after enactment of SYG laws and in states with and without SYG laws. In states with SYG laws, the overall justifiable homicide rate was 0.126 per 100,000 population compared with 0.047 per 100,000 population in states without SYG laws. The homicide rate was 4.663 per 100,000 population in states with SYG laws compared to 3.301 per 100,000 population states without SYG laws.[5] In states with SYG laws, the rate of justifiable homicide increased with the enactment of SYG laws, from 0.091 pre-law to 0.141 per 100,000 population post-law, a 54.9 percent increase.[5] The homicide rate also increased with the enactment of SYG from 4.208 to 4.663 per 100,000 population, a 10.8 percent increase.[5] In states without SYG laws, the justifiable homicide rates increased 20 percent, from 0.044 to 0.053 per 100,000 population, but homicide rates decreased from 3.424 to 3.344 per 100,000 population, a 2.3 percent decrease.[5] The findings suggest that justifiable homicide and homicide were disproportionately higher in states with SYG laws and both the justifiable homicide rate by firearm and homicide rate had significant increases in states with SYG laws compared to states without such laws. While the intent of SYG laws was to deter violent crime, this analysis indicates the laws have had the opposite effect.[5]

Similarly, a cohort study evaluating the association of SYG laws with homicide and firearm homicide, nationally and by state, found that SYG laws were associated with an 8 – 11 percent national increase in monthly rates of homicide and firearm homicide.[6] Forty-one states were analyzed, including 23 states with SYG laws and 18 states without SYG laws. SYG laws were associated with a mean national increase of 7.8 percent in monthly homicide rates and 8.0 percent in monthly firearm homicide rates.[6] Increases in violent deaths varied across states, with the largest increases (16.2 to 33.5 percent) found in the South (e.g., Alabama, Florida, Georgia, Louisiana). The study found no differential associations by demographic group.[6]

A systematic review examining the available evidence on the impacts associated with SYG laws (or other expansions of self-defense laws) on violence, injury, crime, and firearm-related outcomes found the laws were associated with no change to small increases in violent crime (total and firearm homicide, aggravated assault, robbery) on average across states.[7] While Florida-based studies showed robust increases (24 percent to 45 percent) in firearm and total homicide.[7]

RAND's Gun Policy in America initiative examines the effects of firearm laws to improve public discussions and support the development of fair and effective firearm policies. Their review of the evidence on SYG laws concluded that there is moderate evidence that they may increase homicide rates, supportive evidence that they may increase firearm homicides, and limited evidence that they may increase the overall violent crime rates.[8]

Evaluating Florida's SYG law

Several studies have focused on evaluating Florida's SYG law specifically. In addition to this being the first jurisdiction with a SYG law, the high-profile and fatal shooting of Trayvon Martin, an unarmed Black teenager occurred in Sanford, Florida on February 26, 2012. Martin was killed by a White neighborhood watch volunteer who was later acquitted of second-degree murder and manslaughter on the basis of self-defense. The jury in the case was instructed about Florida's SYG law. The Governor of Florida created a Task Force on Citizen Safety and Protection to review the Florida statute to help "ensure the rights of all Floridians and visitors, including the right to feel safe and secure in our state."[9] The task force recommended keeping the SYG law in place, noting that all persons who are conducting themselves in a lawful manner have a fundamental right to stand their ground and defend themselves from attack with proportionate force in every place they have a lawful right to be.[9]

In evaluating the Florida law, several studies have found that it led to an increase in homicides and firearm homicides. A study evaluating whether Florida's SYG law had an impact on homicide and homicide by firearm between 2005 and 2014 found that the law was associated with a 24.4 percent increase in homicide and a 31.6 percent increase in firearm-related homicide.[10] Researchers found no change in rates of suicide or suicide by firearm.[10] A separate analysis of Florida's law found it was associated with a 44.6 percent increase in adolescent firearm homicide and may also exacerbate racial disparities.[11] A third analysis found that the impact of the law differed significantly by county urbanization, unemployment, and pre-law homicide rates.[12] The largest increases in homicide and firearm homicide occurred in proportionally safer, richer, and less ethnically diverse suburban

counties. These findings suggest that the law may have had the opposite effect than intended, and more strongly impacted counties considered safe, suburban and economically successful.[12]

Social inequities

It has been hypothesized that SYG laws will exacerbate social inequities in violent victimization as and that Black defendants accused of crimes will not have the same protections under these laws as similarly situated White defendants.[13] However, a systematic review that examined comparisons by race showed mixed findings, indicating there are not dramatic differences in increases in homicide rates among Black versus White people following the enactment of SYG laws.[7] Data suggests that at least in Florida, there appears to be racial bias in the criminal justice process in rulings on SYG cases.[7] In examining SYG cases in Florida from 2005 to 2013, it was found that race of the victim was a significant predictor of case outcome.[14] After controlling for other variables, the defendant is two times more likely to be convicted in a case that involves White victims compared to those involving non-White victims.[14]

A separate examination of FBI data from 2005-2010, examining more than 53,000 homicides, found large disparities in rulings justified based on the race of the defendant and the victim.[15] Nationally, the likelihood of a homicide being ruled justified is 281 percent greater when the defendant is White and the victim is Black compared to cases where both the defendant and victim are White.[15] White-on-Black homicides were the most likely to be ruled as justified (11.4 percent) while Black-on-White homicide was least likely to be ruled as justified (1.2 percent).[15]

There is very little evidence examining gender differences in the implementation of SYG laws and a lack of focus on the impacts of these laws on intimate partner violence or domestic violence, the most common forms of violence against women.[7]

POSITION OF OTHER NATIONAL ORGANIZATIONS

In 2013, the American Bar Association convened a National Task Force on SYG Laws to review and analyze the recently enacted Stand Your Ground laws in multiple states and their impact on public safety and the criminal justice system.[3] The Task Force has conducted a comprehensive legal and multidisciplinary analysis of the impact of the SYG laws. The national investigation revealed several important findings:

1. Based on recent empirical studies, SYG states experienced an increase in homicides.
2. Multiple states have attempted to repeal or amend SYG laws.
3. The application of SYG laws is unpredictable, uneven, and results in racial disparities.
4. An individual's right to self-defense was sufficiently protected prior to SYG laws.
5. Victims' rights are undermined in states with statutory immunity from criminal prosecution and civil suits related to SYG cases.

EXISTING AMA POLICY

Existing AMA policy does not address self-defense, castle doctrine, or SYG laws. Current policy does recognize that violence represents a public health crisis which requires a comprehensive public health response and solution (Policy D-145.995, "Gun Violence as a Public Health Crisis"). Policy also recognizes that uncontrolled ownership and use of firearms is a serious threat to the public's health inasmuch as the weapons are one of the main causes of intentional and unintentional injuries and deaths (Policy H-145.997, "Firearms as a Public Health Problem in the United States - Injuries and Death"). AMA policy also affirms that physical and verbal violence between law enforcement officers and public citizens, particularly within racial and ethnic minority populations, is a social determinant of health (Policy H-515.95, "Research the Effects of Physical or Verbal Violence Between Law Enforcement Officers and Public Citizens on Public Health Outcomes").

CONCLUSION

"Castle doctrine" refers to the legal right of a person to defend himself against an intruder in his home or other property, even if the use of deadly force is required. There is a lack of studies examining the impact of these laws. SYG laws, or expanded castle doctrine, generally removed the duty to retreat from a threat before using force in

self-defense. Under SYG laws, individuals are allowed to use force, including lethal force, if they reasonably believe it is necessary to protect themselves or others from imminent harm. While SYG laws can be challenging to evaluate, the best available evidence shows that these laws are associated with increased homicide and firearm homicide rates, resulting in preventable violent deaths. The application of SYG laws is unpredictable, uneven, and likely results in racial disparities.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted and the remainder of this report be filed.

1. That Policy H-145.966, "Stand Your Ground Laws" be adopted by addition and deletion to read as follows:

   Our AMA opposes stand your ground laws, which remove the duty to retreat before using lethal force if a person feels there is imminent risk of bodily harm, as these laws have been shown to increase homicide and homicide firearm rates and there is evidence of racial inequity in the implementation of the laws.

   Our AMA ~~will~~ supports continued study of the public health implications of "Stand Your Ground" laws and castle doctrine.

2. That Policies H-145.997, "Firearms as a Public Health Problem in the United States - Injuries and Death," D-145.995, "Gun Violence as a Public Health Crisis," H-145.975, "Firearm Safety and Research, Reduction in Firearm Violence, and Enhancing Access to Mental Health Care," and D-145.999 "Epidemiology of Firearm Injuries" be reaffirmed.

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12. UNIVERSAL SCREENING FOR SUBSTANCE USE AND SUBSTANCE USE DISORDERS DURING PREGNANCY

Reference committee hearing: see report of Reference Committee E.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
REMAINDER OF REPORT FILED
See Policies D-95.983, H-420.950 and H-420.969

INTRODUCTION

American Medical Association (AMA) Policy H-95.906, "De-Stigmatization and Management of Substance Use Disorders" as adopted at the 2023 Annual Meeting asks that our AMA study the feasibility, potential methodologies, and implications of early universal screening for substance use and substance use disorders during pregnancy.

At the meeting, robust testimony was heard regarding screening with concerns being raised regarding the complexity of screening when paired with mandatory reporting requirements. This report investigates the implications, feasibility, and methodology of universal screening for substance use and substance use disorders during pregnancy. This report serves as the Council on Science and Public Health's (CSAPH) findings and recommendations regarding universal screening for substance use and substance use disorders during pregnancy.

METHODS

English-language reports were selected from a PubMed and Google Scholar search through November 2023, using the text terms "screening", "universal screening", "pregnancy", and "substance use." Additional articles were identified by manual review of the references cited in these publications. Further information was obtained from the Internet sites of specialty physician societies, federal and state agencies, U.S. Department of Health and Human Services (HHS), and U.S. Preventive Services Task Force (USPSTF) to identify validated screening tools, recommendations, clinical guidelines, and position statements.

BACKGROUND

Nationally, one in five people use illicit substances during pregnancy.[1] Polysubstance use, which is defined as the use of two or more substances, is also common during pregnancy.[2] Data suggests that 38.2 percent of pregnant women who drink alcohol also report using one or more substance, the most common being tobacco and cannabis.[2] Overdose rates during pregnancy and the postpartum period increased 81 percent (from 6.56 to 11.85 per 100,000) from 2017 to 2020.[3] This trend has been exacerbated by the COVID-19 pandemic, leading to a surge in overdose-related deaths and intensifying concerns about pregnancy-associated substance use, primarily driven by synthetic opioids and psychostimulants (e.g., fentanyl, methamphetamine, cocaine).[3–5] In an analysis of data from 2017-2019 by the Centers of Disease Control, mental health conditions, including overdose and poisoning related to substance use disorder (SUD), were the leading causes of pregnancy-related death.[6]

Despite pregnancy offering a critical window for engaging individuals in medical care, pregnant individuals with SUD, particularly opioid use disorder (OUD), often avoid both prenatal and preventive health care due to stigma,

discrimination, inaccessibility of services, and prosecution or loss of infant custody.[7,8] Compounding these barriers, pregnant individuals with SUD face substantial complications linked to poorer obstetric and neonatal health outcomes including the pregnant persons' mortality, poor fetal growth, preterm birth, neonatal abstinence syndrome, and other conditions.[9] Even for those who are receiving treatment, returning to substance use in the postpartum period is prominent and can often result in fatal overdose due to decreased tolerance. In the postpartum period, overdose rates peak 7 to 12 months post-delivery for pregnant people who use substances.[10,11] During this critical period, treatment adherence is further complicated by the physical need of the infant for maternal bonding.[12]

Persistent racial disparities in perinatal OUD treatment contribute to significant challenges. Studies indicate that Black and Hispanic women are less likely to receive medications for opioid use disorder (MOUD) compared to their White counterparts.[13,14] Moreover, these challenges are compounded by further racial disparities, particularly affecting individuals of color, notably American Indian and Alaskan Native women, who encounter discrimination within both the health care system and the family regulation system.[15,16] Rural communities, despite experiencing higher rates of substance exposure in utero, encounter additional barriers in accessing essential care. [8,17] These disparities are indicative of broader social and economic inequities, including heightened obstacles to reproductive health care, underscoring the urgent need for targeted interventions and systemic changes.

DISCUSSION

Identification of substance use at any point during a pregnancy can support improved patient outcomes within the parent-infant dyad. AMA policy H-320.953, "Definitions of 'Screening' and 'Medical Necessity,'" defines screening as "health care services or products provided to an individual without apparent signs or symptoms of an illness, injury or disease for the purpose of identifying or excluding an undiagnosed illness, disease, or condition." Screening can be conducted using brief, in-depth, written, verbal, or computerized screening instruments and does not include biological specimens, such as urine or blood.[18] Universal screening, involving the screening of every pregnant individual, is designed to minimize clinician bias in individualized screening decisions and promote more standardized care while also destigmatizing substance use disorders.

Clinical screening tools recommended for prenatal substance use include the Prenatal Substance Abuse Screen for Alcohol and Drugs also known as the "4Ps" which stands for Parents, Partner, Past, and Present.[19] The 4Ps and the 4Ps Plus, which includes additional questions about depression and domestic violence are the only validated behavioral health screening instruments designed specifically for pregnant women.[20] The 4Ps Plus screener is one of the only validated tools for substance use during pregnancy demonstrating overall reliability of 0.62, relatively high sensitivity (87 percent), and specificity (76 percent).[21] Additionally, the CRAFFT instrument is recommended for screening substance use in adolescents and young adults, generally from ages 12 to 21.[22] The CRAFFT instrument has shown efficacy in detecting adolescent substance use, but it has not been thoroughly evaluated for use during pregnancy. Lastly, the National Institute on Drug Abuse (NIDA) Quick Screen is validated for screening for substance use in adults, but has not been validated for screening for pregnant individuals.[23] Despite screening instruments demonstrating strong performance on certain metrics, none exhibit consistently adequate performance across all studied measures. For example, in one study the NIDA Quick Screen exhibited notable specificity (0.99) across all substances but displayed very poor sensitivity (0.10–0.27). Often, screening instruments exhibit significant variations based on race, prenatal clinic, and economic status.[23] Future research endeavors should aim to identify the most effective screening instrument for substance use during pregnancy.[24]

Current clinical guidelines address screening for substance use. The American Society of Addiction Medicine (ASAM) and American College for Obstetricians and Gynecologists (ACOG) recommend early universal screening for substance use during the first prenatal visit using a validated screening to improve maternal and infant outcomes, advising early universal screening, brief intervention, and referral for treatment (SBIRT) model for the treatment of pregnant patients with OUD.[25] The SBIRT model has demonstrated effectiveness for reducing substance use.[26] Universal screening for opioid use is recommended instead of screening based factors such as "poor adherence to prenatal care or prior adverse pregnancy outcomes" to minimize missed cases of substance use as well as provider stereotyping and stigmatization of patients.[25] ASAM and ACOG committee opinion stresses the importance of a coordinated multidisciplinary approach without criminal sanctions for optimal support of the parent-infant dyad, discouraging health care professionals from separating the parent-infant dyad based solely on screening or SUD diagnosis, and emphasizing that screening should be done in partnership with pregnant people.[25] Further, the committee recommendations address clinical practices for chronic pain management, pharmacotherapy, monitoring infants for neonatal abstinence syndrome, opioid prescriptions during pregnancy, breastfeeding, postpartum

supportive services, and the integration of contraceptive counseling into SUD treatment for people of reproductive age.[25]

In 2020 the U.S Preventive Services Task Force (USPSTF) updated their 2008 recommendation on screening for unhealthy drug use for adults and adolescents, conducting two commissioned reviews of the evidence on screening (i.e., asking questions about unhealthy drug use). Unhealthy drug use is defined as "the use of illegal drugs and the nonmedical use of prescription psychoactive medications (i.e., use of medications for reasons, for duration, in amounts, or with frequency other than prescribed or use by persons other than the prescribed individual," this definition does not include alcohol or tobacco products.[27] The USPSTF concluded that there is insufficient evidence to assess the balance of benefits and harms of screening for unhealthy drug use in adolescents. However, for adults 18 years and older, the USPSTF denoted a B grade recommendation, concluding that screening has a moderate net benefit when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred.[27]

Of the 30 identified screening tools many had a sensitivity of 75 percent for detecting unhealthy drug use, misuse, dependence, or use disorders.[27] In this recommendation there are no tools suggested for screening during pregnancy, with the USPSTF only reviewing 12 studies that assessed the accuracy of 15 screening tools in nonpregnant people.[27] The majority of studies had varying definitions of the reference standard (i.e., drug use, misuse, abuse, dependence, and disorders) and no studies directly addressed the benefits or harms of screening on reducing drug use, drug-related health, social, or legal outcomes in adults or adolescents.[27] Lastly, the USPSTF noted several areas where further research is needed to develop recommendations. These include the effectiveness of screening in adolescents; optimal screening intervals; accuracy of screening tools; harms associated with punitive screening results; and strategies to improve access to pharmacotherapy and psychosocial interventions.[27]

The USPSTF commissioned two systematic reviews to evaluate the potential benefits and harms of substance use screening, psychosocial interventions, pharmacotherapy, and the accuracy of screening tools.[28] They found that despite the availability of validated screening tools, there are no direct studies on the benefits or harms of universal screening for adults or adolescents.[28] Psychosocial and pharmacotherapy interventions often do not show statistically significant improvement for screen-identified populations, except for those with OUD seeking treatment.[28] While physicians are crucial in addressing SUD, universal screening may not be justified without sufficient evidence for its benefits across all types of unhealthy drug use due to the lack of available treatment and local resources.[28] Physicians must carefully consider the consequences of screening in their clinical setting and the availability of treatment resources before implementing screening programs for SUDs. An examination conducted through a systematic review of research on involuntary substance use treatment revealed no evidence supporting the benefits of this practice and underscored a clear potential for harm.[29]

Overall, available medical society and health care organization statements regarding the efficacy of universal screening are mixed. While the Substance Abuse and Mental Health Services Administration recommends universal screening during pregnancy as a part of SBIRT in routine health care settings, the U.S. Department of Defense, Veterans Affairs, and the American Academy of Family Physicians indicate that evidence is insufficient to recommend routine screening for illicit drug use.[27,29–32]Additonally, the American Psychiatric Association position statement advocates for health care professionals to implement universal evidence-based screening methods for substance use and co-occurring mental health disorders among pregnant and lactating women, ensuring consistency and non-discrimination.[33] Screening during pregnancy should aim to enhance access to evidence-based treatment for substance use, as well as optimize medical, obstetric, and psychiatric care; emphasizing that screening should not be punitive in nature.[33] Thus, consensus regarding universal screening for substance use during pregnancy varies and depends on the patient subpopulation.

Substance Use in Pregnancy and Reporting Implications

The Child Abuse Prevention and Treatment Act initially enacted in 1974 and updated with the Comprehensive Addiction Recovery Act in 2016 (CAPTA/CARA), is a federal law that mandates the establishment of Plans of Safe Care to ensure the well-being and safety of newborns affected by substance use, as well as their families or caregivers.[34] While physicians must notify the state when a newborn has been exposed to substances per CAPTA/CARA, they are not required to file a report of suspected child abuse or neglect unless stipulated by state law.[35] The notification requirement necessitates the submission of deidentified, aggregate data on the number of children falling within relevant categories.[36] Research shows that over 80 percent of health care professionals are not

familiar with CAPTA/CARA.[37] Even though the notification requirement itself does not mandate the inclusion of patient-identifying information, there can still be adverse consequences for the parent-infant dyad.[36]

Beyond federal standards, many states have implemented additional notification and reporting requirements for substance use in pregnancy. Twenty-four states and the District of Columbia (DC) have passed laws classifying prenatal drug use as child abuse or neglect. Thirty-seven states and DC mandate reporting of "suspected" prenatal drug use to the state.[38] "Suspected" drug use involves assumptions or indications based on behavior or symptoms, whereas confirmatory laboratory results directly detect the presence of drugs in the body through analytical testing. Some states go further by requiring health care professionals to conduct prenatal substance use tests if they suspect substance use.[16] These measures compel health care professionals to report pregnant or postpartum individuals for alleged child abuse, in some states this includes receiving MOUD. Additionally, certain states have enacted legislation aimed at prosecuting pregnant individuals who use substances. This legislation usually involves labeling such behavior as fetal assault, chemical endangerment, and even murder.[39] The consequences of these laws and reports can be profound, including resulting in family separation, arrests, criminal charges, and incarceration, creating a cascade of adverse health outcomes that extend beyond the parent and infant. State-level policies concerning child abuse and mandatory reporting are associated with reduced utilization of prenatal and postpartum care among women who engage in substance use during pregnancy.[40] More information is needed regarding the health outcomes and equity implications related to these reporting laws. To alleviate potential adverse effects, including legal consequences tied to inquiring about substance use and documenting and reporting responses, clinicians should be well-versed in state requirements and adhere to best practices regarding informed consent for screening, recording screening results in medical records, reporting results to medico-legal authorities, and ensuring confidentiality protection.[41]

Challenges in Universal Screening

Physician confidence in conducting screening and brief interventions with pregnant patients varies. A survey of 1,500 U.S. adult medicine clinicians found that almost all (95 percent) of those who conducted screening and brief interventions in their practice reported implementing these measures with pregnant patients for alcohol use.[42] However, less than half (46.5 percent) of these clinicians felt confident in their screening practices.[42] In a study examining patient experiences and analyzing data from 103,608 people in the Pregnancy Risk Assessment Monitoring System between 2016 and 2018, around 95 percent of individuals reported being asked about cigarette or alcohol use during prenatal care, and 80 percent reported being asked about drug use.[43] The study reveals disparities in substance use screening during prenatal care appointments.[43] Further research is needed to understand the impact of screening approaches on outcomes in prenatal care settings.

A 1990 study in Pinellas County, Florida found profound racial disparities in child protective services (CPS) reporting during delivery against a background of universal screening for alcohol and illicit drug use in public and private prenatal care.[44] Around 15 percent of both Black and White mothers identified as using substances, with Black mothers exhibiting significantly higher rates of entering treatment compared to White mothers.[44] Despite higher treatment rates, Black mothers using substances were referred to CPS at much higher rates than their White counterparts using substances.[44] The researchers wrote, "we conclude that the use of illicit drugs is common among pregnant women regardless of race and socioeconomic status. If legally mandated reporting is to be free of racial or economic bias, it must be based on objective medical criteria."[44] A 2012 article that drew heavily on the Florida study showed that, despite nearly universal screening for prenatal drug use among Medicaid patients in one California county, and similar results among racial groups enrolled in Medicaid, overall CPS referrals for Black mothers occurred at nearly four times the rate of White mothers.[15] The authors caution that we cannot count on universal screening to promote equity, either through making referrals more objective or through improved treatment participation rates.[15]

Lastly, in a study examining primary care physicians' implementation of screening, several barriers were identified.[45] Time constraints, challenges related to parental involvement (for adolescents), perceived ineffectiveness of brief intervention services, and a lack of training in providing brief intervention were among the obstacles to screening and brief intervention.[45] Physicians recommended boosting screening rates through increased reimbursement and the allocation of dedicated resources.[45]

AMA POLICY AND ADVOCACY

Our AMA maintains comprehensive policies addressing substance use during pregnancy. AMA Policy H-420.969, "Legal Interventions During Pregnancy," states that criminal sanctions or civil liability for harmful behavior by the pregnant woman toward her fetus are inappropriate; that pregnant [people who use substances or have a substance use disorder] should be provided with rehabilitative treatment appropriate to their specific physiological and psychological needs; and that in order to minimize the risk of legal action by a pregnant patient or an injured fetus, the physician should document medical recommendations made including the consequences of failure to comply with the physician's recommendation. Policy H-420.962, "Perinatal Addiction - Issues in Care and Prevention," encourages the federal government to expand funding allocated to drug treatment, prevention, and education to establish and make broadly available specialized treatment programs for [pregnant people with substance use disorder] and breastfeeding people wherever possible.

AMA Policy H-420.950, "Substance Use Disorders During Pregnancy," reiterates our AMA's support of brief interventions and referral for early comprehensive treatment using a coordinated multidisciplinary approach without criminal sanctions. Additionally, this policy opposes any efforts to imply that a positive verbal substance use screen, a positive toxicology test, or the diagnosis of substance use disorder during pregnancy automatically represents child abuse and opposes the filing of a child protective services report or the removal of infants from their mothers solely based on a single positive prenatal drug screen without appropriate evaluation. Our AMA further advocates for appropriate medical evaluation prior to the removal of a child and advocates that state and federal child protection laws be amended so that pregnant people who use substances and/or have a SUD are only reported to child welfare agencies when protective concerns are identified by the clinical team, rather than through automatic or mandated reporting of all pregnant people with a positive toxicology test, positive verbal substance use screen, or diagnosis of a SUD. This policy position is reiterated in D-95.983, "Mandatory Drug Screening Reporting," which states that our AMA will work with appropriate state and specialty medical societies and with state legislative bodies to ensure that physicians not be required to report patients with [positive] urine drug test results to the police; and continue to promote education of physicians regarding the importance of referring patients found to have [positive] urine drug tests for appropriate medical treatment.

Additionally, in 2022 our AMA and several other medical societies jointly formulated model state legislation to facilitate the "enhancement of access to evidence-based, non-judgmental, and non-punitive maternal treatment."[46] The proposed legislation, titled "An Act to Create and Implement Family Care Plans for Infants, Children, and Families," underscores the significance of establishing and defining "plans of family care."[46] These plans aim to provide "supportive care and fulfillment of needs for pregnant, postpartum, and parenting individuals, newborns, children, and families."[46]

CONCLUSION

In theory, universal screening for substance use in pregnancy presents a potential avenue for enhancing health outcomes for pregnant individuals who use substances and their infants as well as preserving the parent-infant dyad. However, amidst the backdrop of stringent state policies, mandatory reporting, and obstacles in accessing evidence-based care, universal screening may have unintended consequences. Additional research on the impacts of mandatory reporting laws of substance use in pregnant people needs to be addressed to reduce bias, inequities in care, and fear of pregnant people to access the care they need.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed:

1. That our AMA:
   A. Encourage ongoing research on the benefits and risks of universal screening for substance use during pregnancy including the impact of mandatory reporting laws, evaluation of patient outcomes, effectiveness across different age groups, optimal screening intervals, equity considerations, and efficacy of different screening tools.

B. Support the development and dissemination of physician education and training on federal and state laws governing mandatory notification and reporting of substance use during pregnancy, and the benefits and consequences of screening implementation in health care settings on a state-by-state basis.

2. That AMA policy H-420.950, "Substance Use Disorders During Pregnancy," be amended by addition and deletion to read as follows:
Our AMA will:
(1) support brief interventions (such as engaging a patient in a short conversation, providing feedback and advice) and referral for early comprehensive treatment of pregnant individuals with opioid use and opioid use disorder (including naloxone or other overdose reversal medication education and distribution) using a coordinated multidisciplinary approach without criminal sanctions;
(2) acknowledges the health benefits of identifying substance use during pregnancy and opposes any efforts, including mandatory reporting laws, that ~~to~~ imply ~~that~~ a positive verbal substance use screen, a positive toxicology test, or the diagnosis of substance use disorder during pregnancy automatically represents child abuse or neglect;
(3) support legislative and other appropriate efforts for the expansion and improved access to evidence-based treatment for substance use disorders during pregnancy;
(4) oppose the filing of a child protective services report or the removal of infants from their ~~mothers~~ parent(s) solely based on a ~~single positive~~ prenatal drug screen and/or biological test(s) for substance use without appropriate evaluation;
(5) advocate for appropriate medical evaluation prior to the removal of a child, which takes into account (a) the desire to preserve the individual's family structure, (b) the patient's treatment status, and (c) current impairment status when substance use is suspected or confirmed; and
(6) advocate that state and federal child protection laws be amended so that pregnant people with substance use and substance use disorders are only reported to child welfare agencies when protective concerns are identified by the clinical team, rather than through automatic or mandated reporting of all pregnant people with a positive toxicology test, positive verbal substance use screen, ~~or~~ diagnosis of a substance use disorder, or use of evidence-based treatments for substance use disorder.

3. That current AMA policies H-420.969, "Legal Interventions During Pregnancy," and D-95.983, "Mandatory Drug Screening Reporting" be reaffirmed.

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13. DECREASING YOUTH ACCESS TO E-CIGARETTES

Reference committee hearing: see report of Reference Committee D.

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See Policies H-495. 969, H-495.970, H-495.971, H-495.971, H-495.976 and H-495.986

INTRODUCTION

The American Medical Association (AMA) House of Delegates (HOD) referred Resolution 919, "Decreasing Youth Access to E-cigarettes" for study. This resolution asked that our AMA support the inclusion of disposable and tank-based e-cigarettes in the language and implementation of any restrictions that are applied by the Food and Drug Administration (FDA) or other bodies to cartridge-based e-cigarettes. It also proposed amendments to policy H-495.986, "Tobacco Product Sales and Distribution," to (1) support measures that prevent retailers from opening new tobacco specialty stores in proximity to elementary schools, middle schools, and high schools and (2) support measures that decrease the overall density of tobacco specialty stores, including but not limited to, preventing retailers from opening new tobacco specialty stores in proximity to existing tobacco specialty stores.

The Reference Committee recommended adoption of the policy as amended, with amendment by deletion of number 2 above due to concerns that the density recommendations represented the restriction of free commerce capabilities.

The resolution was ultimately referred for study due to the introduction of significant amendments on the HOD floor seeking to clarify multiple points in existing policy unrelated to the amendments proposed by the resolution.

The Council has previously presented several reports to the HOD on e-cigarettes, these include CSAPH Report 6-A-10, "Use of Electronic Cigarettes in Smoking Cessation Programs,"; CSAPH 2-I-14, "Electronic Cigarettes, Vaping, and Health: 2014 Update"; and CSAPH 5-A-18, "Tobacco Harm Reduction: A Comprehensive Nicotine Policy to Reduce Death and Disease Caused by Smoking," The AMA Board of Trustees also provides the HOD with an annual update on tobacco, which includes updates on e-cigarettes. This report will not repeat information included in those reports, but rather will provide an update on the narrow ask of the resolution, which focuses on youth access.

METHODS

English language reports were selected from searches of the PubMed, Google Scholar, and Cochrane Library databases using the search terms: "e-cigarettes", "ENDS", "electronic cigarette", AND "youth access." Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by federal agencies and applicable professional and advocacy organizations were also reviewed for relevant information.

BACKGROUND

Tobacco use is the leading cause of preventable disease, disability, and death in the United States (U.S.). Moreover, tobacco product use, including the use of e-cigarettes, during adolescence increases the risk for lifelong nicotine addiction and adverse health consequences. This is an extremely important issue considering that in 2023, roughly 2.80 million U.S. middle and high school students used at least one tobacco product, including e-cigarettes.[1]

Current Prevalence and Recent Trends Among Youth

Youth e-cigarette use remains a critical public health concern in the U.S. For the 10th year, e-cigarettes have been the most commonly used tobacco product among both middle and high school students. According to the most recent data from the National Youth Tobacco Survey (NYTS), 2.13 million students use e-cigarettes with 4.6 percent of middle school and 10.0 percent of high school students reporting current use.[1,2] From 2022 to 2023, a significant decline in current e-cigarette use occurred among high school students (from 14.1 percent to 10.0 percent); this decline did not reflect a switch to cigarettes, whose use remained stable at 1.6 percent. While e-cigarette use increased among middle school students from 3.3 percent in 2022 to 4.6 percent in 2023, this increase was not statistically significant. Among students who had ever used an e-cigarette, 46.7 percent reported current use, 25.2 percent used e-cigarettes daily, and 89.4 percent used flavored e-cigarettes with fruit (63.4 percent) and candy (35.0 percent) being the most common flavors.[1]

Disposables were the most used device type among students who reported current e-cigarette use, with over 60 percent of students using disposable e-cigarettes. Prefilled and refillable pods or cartridges and open tank and mod systems were less frequently used at 16.1 percent and 5.9 percent respectively.[1] Disposable e-cigarettes have changed dramatically in recent years. Between 2017 and 2022, e-cigarettes quintupled in volume capacity, nearly tripled in average nicotine strength, and fell in average per ml price of e-liquid by nearly 70 percent.[3] The increased popularity of disposable e-cigarettes may be because they are relatively inexpensive, have a high nicotine content, and they are exempt from the 2020 FDA enforcement prioritization of prefilled and closed-cartridge e-cigarettes for flavors other than tobacco and menthol.[4]

Perceptions of harm and motivations for use

Several systematic reviews and studies have evaluated motivations for e-cigarette use and perceptions of harm. Commonly reported motivations include curiosity, appealing flavors, family and peer influence, and stress reduction.[5–8] One systematic review found that social acceptability, convenient and customizable features, a variety of flavors, and a lack of awareness about the presence of nicotine as common reasons for e-cigarette use.[9] Another found that youth report flavor variety, device modifiability, the ability to perform tricks, and concealment from authority figures among the primary appeals of e-cigarettes.[10] Findings suggest that prevalence of both e-cigarette and cigarette use among parents, siblings, and close friends was higher in adolescents who have ever used an e-cigarette.[7]

Adolescent e-cigarette users also exhibit lower perceptions of harm and more positive attitudes towards e-cigarettes when compared with non-users.[7,8,11] Specifically, in comparison to non-users, young people who were e-cigarette users were more likely to perceive e-cigarettes as healthier and less addictive than tobacco cigarettes.[8,12–14] One study found most e-cigarette users view flavored e-cigarettes as less harmful with 55.5 percent believing they were not addictive.[13] Other reviews echo this concerning finding that many individuals were unaware that e-cigarettes contained nicotine.[9,11] Still others found youth perceived gradations in harm relating to the frequency and intensity of use and by type of product.[15] In contrast, nonusers were more prone to consider e-cigarettes harmful to children.[7]

HEALTH EFFECTS OF E-CIGARETTE USE

The health effects of e-cigarette use have been reviewed in previous CSAPH reports. The evidence on the health impacts of e-cigarettes is mixed. There are clear short term adverse effects that could result from using e-cigarettes including sore throat, headache, cough, elevated heart rate, nausea, and vomiting.[11,16] Additionally, there are severe acute adverse effects including nicotine poisoning from accidental ingestion, e-cigarette or vaping product associated lung injury, and trauma from exploding devices that has been reported.[17] However, the evidence on long term impacts of e-cigarettes is more attenuated, not as strong, and often based on small cross-sectional or relatively short longitudinal epidemiological studies.

Despite the limited evidence on the long-term effects of e-cigarettes on health, there are potentially concerning trends regarding the association between both e-cigarette use and exposure to the ingredients found in e-cigarette vapor and negative cardiovascular, pulmonary, immune, and developmental health impacts that warrant continued study and evaluation.

Safety of Aerosolized e-liquid

Propylene glycol, glycerol, nicotine, flavoring agents, and their degradation byproducts (e.g., formaldehyde, acetaldehyde, acrolein, glycidol) have all been shown to have deleterious effects on respiratory tissues and function.[18,19] An analysis of 30 products on the U.S. market revealed that 13 were more than one percent by weight flavor chemicals identified as reactive aldehydes.[19] Reactive aldehydes are also thought to be the primary contributors to combustible cigarette–induced cardiovascular disease and chronic obstructive pulmonary disease (COPD).[20,21] Multiple analyses of e-cigarette vapor's cytotoxicity have demonstrated that while it varies, some flavors are cytotoxic or contain flavoring chemicals at concentrations high enough to be cytotoxic when vaped.[19,22]

E-cigarette vapor also contains heavy metals, likely from the heating element metals that are released into the aerosols.[20,23,24] A lifetime of chromium and nickel exposure from daily inhalation of two mL e-liquid was used to estimate the risk of cancer and noncancer health effects, with chromium and nickel estimated to be the primary contributors. Notably, nickel is one of the few carcinogens found to be higher in e-cigarettes than in combustible cigarettes.[20,25] E-cigarette vapor contains copious fine and ultra fine particles.[22] There is strong evidence that frequent low or short-term levels of exposure to fine and ultrafine particles can contribute to pulmonary and systemic inflammatory processes as well as potentially increasing the risk of cardiovascular and respiratory disease.[22,26–28] Moreover, higher e-liquid nicotine concentration is associated with higher particle numbers.[22]

Finally, most e-cigarettes contain nicotine, which activates the sympathetic nervous system, thereby directly effecting the cardiovascular system.[20,29] Nicotine-stimulated catecholamine release by the sympathetic nervous system activates β-adrenergic receptors in the heart, resulting in increased heart rate, cardiac contractility, and workload.[20,30] Long-term overstimulation of the sympathetic nervous system can result in cardiac remodeling, which promotes the development of heart failure and increases arrhythmogenesis.[20,29] Nicotine also affects the vasculature by inducing vasoconstriction, resulting in elevated blood pressure.[20,29,30] In a randomized study of healthy younger smokers, acute use of nicotine-containing e-cigarettes had vascular hemodynamic effects suggestive of vascular remodeling and increased sympathetic activation of the cardiovascular system.[20,31] The findings suggest cardiovascular changes consistent with the development of cardiovascular disease with nicotine inhalation from e-cigarettes.[20]

Cardiovascular, Pulmonary, and Immunological Impacts of e-cigarette use

There is some evidence that using e-cigarettes may negatively affect cardiovascular function. One review found that cardio-respiratory function in e-cigarette users was more impaired than in never smokers.[16,32] Reviews have also

found that chronic e-cigarette users had elevated heart rate and blood pressure.[16,20] Other studies found that e-cigarettes may be associated with inflammation, oxidative stress, and hemodynamic imbalance, leading to increased risk of cardiovascular disease.[20,33–35] E-cigarette use might be linked to pre-symptomatic cardiovascular dysfunction, which could have a significant health impact during adulthood.[33] Research has also found that e-cigarette use was associated with sympathetic activation, vascular stiffening, and endothelial dysfunction.[20,36] There is also evidence of higher incidence tissue damage and compromised vascular function among e-cigarette users compared to non-users.[36]

The aerosol condensate generated from different e-cigarette devices, products, and e-liquids results in different effects on endothelial and pulmonary epithelial cell toxicity, likely a result of the extreme variability in product characteristics.[20] There is some evidence that e-cigarette users' airways are more friable than non-users.[16,37] The same review found changes in lung function over 3.5 years of use and speculated that long-term exposure could lead to emphysema, loss of pulmonary capillaries, and reduced airway function.[16,38] Another review found increased biomarkers of pulmonary disease among observational epidemiological studies associated with vaping as well as a higher incidence of pulmonary disease.[36] Several large population-based studies in adolescents have noted increased asthma diagnoses, school absences due to asthma, and respiratory symptoms for youth who currently use or have used e-cigarettes.[20,33]

There is some evidence suggesting e-cigarette use is associated with increased oxidative stress which can cause the release of pro-inflammatory cytokines.[16,39,40] Therefore, it is possible that e-cigarette use may impair ability to fight infection.[16] Similarly, research has found that e-cigarette use might be associated with reduced pulmonary immune function.[11]

FEDERAL ACTIONS

Legislative actions

Since 2018, federal legislative activity has included the 2019 amendment of the Federal Food, Drug, and Cosmetic Act to raise the federal minimum age for sale of tobacco products from 18 to 21 years. In 2020, the Preventing All Cigarette Trafficking (PACT) act was amended to prevent online sales of e-cigarettes to children.[41] Specifically, it requires remote sellers of tobacco products to pay all applicable federal, state, and local taxes, and comply with all applicable state and local laws including age verification. PACT also prohibits delivery vendors from using the U.S. postal service to ship e-cigarettes. These federal legislative actions arose in conjunction with administrative and judicial actions.

Administrative actions

In January of 2020, the FDA finalized enforcement policy on unauthorized flavored open-system tank- and cartridge-based e-cigarettes that appeal to children, including fruit and mint ingredients, but excluded menthol and tobacco-flavored products.[42] Importantly, disposable e-cigarettes were exempt from the policy and as a result there was a market shift to disposables. More recently, federal legislation expanded the definition of tobacco products to include synthetic nicotine in March 2022, in response to the emergence and market proliferation of disposable e-cigarettes with e-liquids advertising synthetic nicotine -- thereby granting FDA regulatory authority over these products. To date, the FDA has authorized marketing of 23 tobacco-flavored e-cigarette products and devices from three companies with the FDA citing potential smoking cessation benefits to adults and low risks posed to youth.[43,44] Meanwhile, all other disposable e-cigarette brands are being sold without marketing authorization.[3]

STATE AND LOCAL ACTIONS

Considering the success of tobacco control policies to reduce traditional cigarette smoking among youth, there is reason to believe extending similar policies like online sales restrictions, limits on marketing and promotion, package and labeling requirements, retailer licensing requirements, retailer zoning and location restrictions, taxes, and flavor restrictions could reduce e-cigarette initiation and use among youth.[45]

Online Sales Restrictions

In 2020, PACT was amended to include e-cigarettes, thus prohibiting online sales of e-cigarettes to children. Yet, there are serious enforcement challenges posed by online sales and delivery services. A study that reviewed FDA e-

cigarette warning letters issued by the Center for Tobacco Products to online retailers in 2018 showed that 98.2 percent of violations pertained to the sales of an e-cigarette product to a minor and/or use of marketing that appeals to children.[46]

In response, state and local governments have begun enacting legislation to further prohibit and regulate online sales. In June 2019, San Francisco, California, became the first city in the U.S. to ban the retail and online sale of e-cigarettes.[47,48] As of May 2022, the Public Health Law Center also found that at least fourteen states have laws prohibiting direct-to-consumer shipments of some tobacco products. Five of these states have enacted more comprehensive laws, including extending these prohibitions to e-cigarettes.[49] Additionally, an evaluation of e-cigarette delivery laws found extensive heterogeneity. There were 34 states with e-cigarette delivery sales laws in place, and of those states, 27 required at least one form of age verification, 12 required mandatory packaging labels, seven required permits for online vendors, seven required government ID for release, four did not specify, and 11 had no specific requirements.[50]

Limits on marketing and promotion

While the FDA has broad authority to restrict the advertising and marketing of all tobacco products, the FDA and FTC only currently require e-cigarette ads to be factually accurate and avoid targeting youth.[10,45]

A recent study of online e-cigarette vendors in California found that 50 percent of the websites included marketing themes related to physical health benefits of e-cigarette use, 57.7 percent had sales, discounts, and other promotions, 65.4 percent had fruit-flavored disposable e-cigarettes, 69.2 percent had promotional email newsletters, and 88.9 percent did not require users to create an age-verified account to receive email newsletters.[51] This is concerning considering that the lessons learned from traditional cigarette control demonstrate that the retail environment is a key driver of cigarette use.[52,53] Furthermore, a longitudinal cohort study using PATH data found that past 12-month and past 30-day e-cigarette use was significantly associated with recalled exposure to e-cigarette advertisement on social media, websites, and at gas stations and convenience stores.[54] Similarly, research demonstrates that e-cigarette use was associated with advertising and media exposure.[53]

Presently, there is little to no evidence that limits on marketing and promotion reduce e-cigarette use among youth, but there is a growing body of evidence that suggests marketing and promotion to youth are common and that exposure to e-cigarette advertising is associated with e-cigarette use. Therefore, continued efforts to regulate youth exposure to e-cigarettes in media, advertising, and other promotion is warranted.

Retailer licensing

Requiring retailers to obtain a license to sell e-cigarettes is another traditional cigarette control measure that might be helpful at reducing e-cigarette initiation and use. One cross-sectional study suggests that strong local tobacco retailer license ordinances, particularly those that also provide adequate resources to fund regular compliance checks and enforcement, may lower rates of cigarette and e-cigarette use among youth and young adults.[55] For instance, participants in jurisdictions with more restrictive ordinances had lower odds of ever cigarette use and of past 30-day use.[55] Additionally, compliance checks of vendors have been shown to reduce sales to minors; however, the actual impact on smoking rates is less clear as youth obtain e-cigarettes from means other than legal purchase.[55]

Currently, 40 states and territories require retailers to obtain a license to sell e-cigarettes over the counter.[56] Furthermore, when retailer licensing was implemented in Pennsylvania, it resulted in a significant decline in past 30-day e-cigarette use by adolescents.[45] A review of e-cigarette tobacco retail licensing law, identified 23 laws that clearly defined a license term, 23 laws required a license fee, and 19 laws identified penalties for violations that included both license suspension and revocation.[57] The evidence of effectiveness of retailer licensing regulations on e-cigarette initiation and use is limited, but promising.

E-cigarette tax and other price strategies

There is strong evidence that increasing traditional cigarette taxes decreases cigarette consumption and increases quit rates among both adults and adolescents.[58–60] Additionally, increasing the price of tobacco reduces tobacco initiation among youth.[59] Therefore, e-cigarette taxes and price strategies have been proposed as a potential tool to reduce e-cigarette use. However, the effectiveness of e-cigarette taxes and price strategies may depend on whether e-

cigarettes and traditional cigarettes are used concurrently or as substitutes. If either e-cigarettes or traditional cigarettes are substitutes, then increased taxes on one would drive users to the other and vice versa.[58]

As of February 2024, 36 states and Washington DC have enacted an e-cigarette tax.[56] There is some evidence that e-cigarette taxes increased e-cigarette prices and reduced sales of e-cigarettes, but they also increase sales of traditional cigarettes, suggesting the two may be substitutes.[3,61–63] In contrast, one study found that higher cigarette excise taxes decrease both cigarette and e-cigarette purchases, suggesting that cigarettes and e-cigarettes are used in tandem.[64] as Additionally, one prospective cohort study of young adults in the U.S. found that increased prices of rechargeable e-cigarette products did not significantly change past 30-day e-cigarette use or cigarette use.[65]

While there is some evidence e-cigarette taxes curb e-cigarette use among youth, more evidence is needed to assess their effectiveness and better understand their impact on traditional cigarette use.

Flavor restrictions

In 2009 the FDA banned flavored cigarettes, but it was not until 2020 that similar federal bans were extended to e-cigarettes -- banning all non-tobacco and non-menthol flavored cartridge-based e-cigarettes.[10] Although the FDA flavor ban is a step in the right direction, disposable e-cigarettes were exempt, and the market shifted accordingly. A longitudinal cohort survey of adults aged 18-24 from Atlanta, Boston, Minneapolis, Oklahoma City, San Diego, Seattle found that only 8.4 percent of participants reduced their e-cigarette use after the FDA ban was implemented.[66] Instead, while 35.8 percent used available flavors like tobacco and menthol, 30.4 percent continued to use tank-based e-cigarettes, and 10.1 percent switched to tank-based e-cigarettes.[66]

This highlights the need for additional action at the state and local level. In 2018, San Francisco was the first city to ban all flavored tobacco products, including menthol, in conventional cigarettes.[47] After more than 200 localities imposed a variety of restrictions, Michigan became the first state to ban all flavored e-cigarettes under a temporary emergency order that is renewable.[47] Currently, over 360 localities have passed flavor restrictions.[67] Evidence is limited, but there are some promising findings from New York City and Massachusetts suggesting that sales for flavored tobacco products decreased overall following a ban.[45] Additionally, a cross-sectional study found that statewide restrictions on the sale of flavored e-cigarettes in Massachusetts, New York, Rhode Island, and Washington were associated with a reduction in total e-cigarette sales.[68]

E-cigarette retailer zoning and location restrictions

Current evidence indicates that e-cigarette retailers are frequently located near schools. In a study of two counties in Kentucky, an estimated 67.5 percent of sampled schools had at least one tobacco retailer that also sold e-cigarettes within one mile (1.61 km) of the school.[69] Another study from Orange County, California found that over half of public middle and high schools had at least one e-cigarette specialty retailer within one mile of the school.[70]

One study identified a significant positive association between e-cigarette retailer density within a half-mile of a high school and the likelihood that a student ever and currently used e-cigarettes.[71] Another study identified a significant positive association between the presence of e-cigarette specialty retailers within one-quarter mile of a middle school and the likelihood of e-cigarette lifetime use. However, a significant positive association was not present among high school students.[72] While site-based studies have found varying results, a study based on geospatial data found an association between the presence of tobacco retailers near certain schools and e-cigarette use among students, but this association was not consistent across all the studied counties.[73] Other research suggests a positive association between higher retailer density in egocentric residential neighborhoods around homes and current smoking in adults and adolescents; however, the density of retailers and their proximity to schools showed either no association or an inverse association with adolescent smoking.[74] Likewise, another study found that e-cigarette retailer proximity and density surrounding a school were not significantly associated with the likelihood of ever or currently using e-cigarettes.[75]
Many states and localities have tried to reduce exposure, initiation, and use of e-cigarettes through retailer zoning and location restrictions and these efforts are rationally grounded; however more research is needed to conclusively determine the impact of retailer proximity and youth initiation.

Product packaging

Under the Deeming Rule, e-cigarettes are required to include warning labels about the addictiveness of nicotine. Additionally, 33 states have implemented their own packaging laws.[45] There is some evidence that text-based warning messages influenced young non-smokers' perceptions in a way that may dissuade e-cigarette use, but warnings appearing on advertisements had little impact.[76] One study found that the perceived warning effectiveness for discouraging youth initiation was higher for warnings that focused on negative impacts to the brain and harmful chemicals compared to warnings focusing on nicotine dependency or use disorder.[77] In conclusion, there is limited evidence of the effectiveness of warning labels on e-cigarettes; however, there is evidence that many adolescents are unaware that e-cigarettes contain nicotine. Ultimately, more research is needed on nicotine warnings for e-cigarettes, including on the message content, placement, and the impact on consumers' product knowledge, risk perceptions, and use intentions.[78]

State and local regulatory efforts and pre-emption issues

State and local efforts to enact e-cigarette regulations often come across preemption barriers. Although many states have made efforts to enhance e-cigarette regulations through limits on promotions and advertising, requiring licensing for over-the-counter sales, including e-cigarettes in smoke free air policies, and implementing face-to-face sales mandates, state level preemption is prohibiting many cities and municipalities from implementing stricter local policies. In the U.S., 25 states preempt stricter local e-cigarette regulations in 55 laws. Specifically, 19 laws preempt advertising regulations, 11 laws preempt licensure requirements, four laws preempt ordinances for indoor clean air, and 21 laws preempt youth access. States without preemption laws should be encouraged to adopt language that expressly preserves local authority.[79]

EXISTING AMA POLICY

Existing AMA policy recognizes that the use of products containing nicotine in any form among youth, including e-cigarettes, is unsafe and can cause addiction. Furthermore, the AMA supports legislation and associated initiatives to prevent e-cigarettes from reaching youth and young adults through various means, including, but not limited to, CDC research, education, and a campaign for preventing and reducing use by youth, young adults and others of e-cigarettes, and combustible and emerging tobacco products (Policy H-495.972, "Electronic Cigarettes, Vaping, and Health"). The AMA also supports applying the same marketing and sales restrictions that are applied to tobacco cigarettes, including prohibitions on television advertising, product placement in television and films, and the use of celebrity spokespeople; requires the use of secure, child- and tamper-proof packaging and design, and safety labeling on containers of replacement fluids (e-liquids) used in e-cigarettes (Policy H-495.973, "FDA to Extend Regulatory Jurisdiction Over All Non-Pharmaceutical Nicotine and Tobacco Products").

AMA policy supports the development of model legislation regarding enforcement of laws restricting children's access to tobacco, including but not limited to attention to the following issues: (a) provision for licensure to sell tobacco and for the revocation thereof; (b) appropriate civil or criminal penalties (e.g., fines, prison terms, license revocation) to deter violation of laws restricting children's access to and possession of tobacco; (c) requirements for merchants to post notices warning minors against attempting to purchase tobacco and to obtain proof of age for would-be purchasers; (d) measures to facilitate enforcement; (e) banning out-of-package cigarette sales ("loosies"); and (f) requiring tobacco purchasers and vendors to be of legal smoking age (Policy H-495.986, "Tobacco Product Sales and Distribution").

CONCLUSION

Despite the recent decline in e-cigarette use among high school students and ongoing efforts at the national, state, and local levels to implement tobacco control strategies, including FDA regulatory actions, e-cigarette use among adolescents remains unacceptably high. According to the NYTS, 2.13 million students use e-cigarettes, with 4.6 percent of middle school and ten percent of high school students reporting current use.[1] There is clear evidence of adverse health effects due to e-cigarette use, but the evidence on the long-term impacts is more attenuated, not as strong, and often based on small cross-sectional or relatively short longitudinal epidemiological studies. Additionally, there is limited evidence of the effectiveness of state-level efforts like face-to-face sales mandates, marketing and promotion limits, retailer licensing, price policies and taxes, and flavor restrictions on reducing e-cigarette initiation and use. Despite the limited evidence, many polices enacted to address youth access are rooted in

evidence-based nicotine control strategies that worked well with traditional cigarettes. Therefore, it seems likely that they have the potential to reduce e-cigarette initiation and use. Continued research is needed to better understand effective interventions and policies, including how they influence traditional cigarette smoking, e-cigarette vaping, and other tobacco use.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted, and the remainder of the report be filed:

1. That our AMA supports the inclusion of all forms of e-cigarettes (e.g., disposable, refillable cartridge, and tank-based e-cigarettes) in the language and implementation of relevant nicotine-based policies and regulations by the Food and Drug Administration or other regulatory agencies.

2. That current AMA Policy H-495.986, "Tobacco Product Sales and Distribution," be amended by addition to read as follows:

   Tobacco Product Sales and Distribution, H-495.986
   (1) recognizes the use of e-cigarettes and vaping as an urgent public health epidemic and will actively work with the Food and Drug Administration and other relevant stakeholders to counteract the marketing and use of addictive e-cigarette and vaping devices, including but not limited to bans and strict restrictions on marketing to minors under the age of 21;
   (2) encourages the passage of laws, ordinances and regulations that would set the minimum age for purchasing tobacco products, including electronic nicotine delivery systems (ENDS) and e-cigarettes, at 21 years, and urges strict enforcement of laws prohibiting the sale of tobacco products to minors;
   (3) supports the development of model legislation regarding enforcement of laws restricting children's access to tobacco, including but not limited to attention to the following issues: (a) provision for licensure to sell tobacco and for the revocation thereof; (b) appropriate civil or criminal penalties (e.g., fines, prison terms, license revocation) to deter violation of laws restricting children's access to and possession of tobacco; (c) requirements for merchants to post notices warning minors against attempting to purchase tobacco and to obtain proof of age for would-be purchasers; (d) measures to facilitate enforcement; (e) banning out of-package cigarette sales ("loosies"); and (f) requiring tobacco purchasers and vendors to be of legal smoking age;
   (4) requests that states adequately fund the enforcement of the laws related to tobacco sales to minors;
   (5) opposes the use of vending machines to distribute tobacco products and supports ordinances and legislation to ban the use of vending machines for distribution of tobacco products;
   (6) seeks a ban on the production, distribution, and sale of candy products that depict or resemble tobacco products;
   (7) opposes the distribution of free tobacco products by any means and supports the enactment of legislation prohibiting the disbursement of samples of tobacco and tobacco products by mail;
   (8) (a) publicly commends (and so urges local medical societies) pharmacies and pharmacy owners who have chosen not to sell tobacco products, and asks its members to encourage patients to seek out and patronize pharmacies that do not sell tobacco products; (b) encourages other pharmacists and pharmacy owners individually and through their professional associations to remove such products from their stores; (c) urges the American Pharmacists Association, the National Association of Retail Druggists, and other pharmaceutical associations to adopt a position calling for their members to remove tobacco products from their stores; and (d) encourages state medical associations to develop lists of pharmacies that have voluntarily banned the sale of tobacco for distribution to their members; and
   (9) opposes the sale of tobacco at any facility where health services are provided; and
   <u>(10) supports measures that decrease the geographic density of tobacco retail stores, including but not limited to, preventing retailers from selling tobacco products in stores in close proximity to schools.</u>

3. That our AMA reaffirm Policies H-495.970, "Regulation of "Cool/Non-Menthol" Tobacco Products, H-495.971 "Opposition to Addition of Flavors to Tobacco Products," and H-495.976, "Opposition to Exempting the Addition of Menthol to Cigarettes."

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