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Case 27-2021: A 16-Year-Old Boy Seeking Human Immunodeficiency Virus Prophylaxis

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PRESENTATION OF CASE

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Dr. Elizabeth A. Perzanowski (Pediatrics): A 16-year-old boy was seen in the infectious disease clinic at this hospital for consideration of preexposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection.

The patient identified as a cisgender male and reported having had more than 10 male sexual partners, many of whom he had met through online dating platforms. He had oral sex, as well as insertive and receptive anal intercourse. He used condoms intermittently. The patient had learned about HIV PrEP through websites linked to online dating platforms and expressed interest in initiation of HIV PrEP during a routine visit with his pediatrician. The patient reported that he might discuss this plan with one of his parents, but he had not yet chosen to disclose his sexual activity or his desire to initiate PrEP to either of them. He sought care at a sexual health clinic; because he was a minor seeking medication for HIV prevention rather than screening or treatment for other sexually transmitted infections, he was referred for an appointment on the same day with an internal medicine–pediatrics physician in the infectious disease clinic at this hospital for an evaluation for HIV PrEP.

The patient arrived at the clinic alone and requested that the content of the visit remain confidential. He reported feeling well, with no dysuria, penile discharge, genital lesions, or penile or testicular pain. He had a history of mild dyslexia, herpes labialis, and seasonal allergies. Two months earlier, he had been seen by his primary care physician because of intermittent rectal pain and slight hematochezia. A rectal examination performed during that visit had revealed mild irritation of the perianal skin and a healing fissure; the symptoms were attributed to constipation and resolved with the administration of polyethylene glycol and increased intake of dietary fiber. Current medications were oral penciclovir as needed and a lysine supplement. Immunizations were current, and the patient had no known allergies to medications. He was a sophomore in high school and was

physically active. He lived in an urban community in New England with his parents, younger sister, and pet cats; he had two older siblings who lived independently. He reported that he did not smoke cigarettes, drink alcohol, or use illicit drugs. His mother had a history of anemia, obesity, and nephrotic syndrome; a maternal aunt had leiomyosarcoma; a maternal uncle had epilepsy; and his maternal grandmother had hypertension, hyperlipidemia, and diabetes mellitus.

On examination, the patient was a well-appearing male adolescent. His race was recorded as Black in the electronic medical registration system. The vital signs were normal; the weight was 81.6 kg, the height 178 cm, and the body-mass index (the weight in kilograms divided by the square of the height in meters) 25.6. The mucous membranes were moist; there were no oropharyngeal exudates or ulcers. There was no rash or cervical, submandibular, supraclavicular, axillary, or inguinal lymphadenopathy. The abdomen was soft, without tenderness. The penis was uncircumcised; there were no genital ulcers, fissures, or other lesions of the perianal tissue. The remainder of the examination was normal. Blood levels of electrolytes were normal, as were results of kidney-function tests. Blood tests for hepatitis B surface antibody, hepatitis B surface antigen, hepatitis C antibody, and syphilis were negative, as were tests for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* nucleic acid performed on urine, an oropharyngeal swab, and a rectal swab. Screening tests for HIV types 1 and 2 were negative.

Management decisions were made.

DISCUSSION OF MANAGEMENT — CLINICAL PERSPECTIVE

Dr. Anne M. Neilan: This 16-year-old, sexually active male adolescent was referred for an evaluation for HIV PrEP. An estimated 1 in 2 Black men who have sex with men in the United States will become infected with HIV over a lifetime.¹ Among the nearly 50,000 adolescents and young adults (13 to 24 years of age) in the United States who are infected with HIV, 45% are unaware of the infection, as compared with just 12% of adults older than 24 years of age who are infected with HIV.² Those who are unaware of the infection miss opportunities for treatment and

improved health and contribute disproportionately to the infection of others. The highest rate of HIV transmission according to age group is among persons 13 to 24 years of age.³

PREEXPOSURE PROPHYLAXIS

PrEP is a preventive strategy aimed at decreasing the risk of HIV acquisition through the prophylactic administration of combination antiretroviral therapy in HIV-uninfected persons. PrEP is currently recommended for patients who are at high risk for HIV infection, such as this patient. At the time that this patient was seeking PrEP, only a fixed-dose combination pill of emtricitabine and tenofovir disoproxil fumarate (F/TDF) had been approved by the Food and Drug Administration for daily oral PrEP, and the indications had just been expanded to include use in persons weighing 35 kg or more.

PrEP is highly effective in preventing HIV infection in adults.⁴ Although data are limited in adolescents and young adults, particularly minors such as this patient, PrEP is considered to be feasible, acceptable, and safe in this group.^{5,6} However, questions remain about the long-term effect on bone mineral density, as well as how to support sustained adherence to the medication over time. The Centers for Disease Control and Prevention and the U.S. Preventive Services Task Force recommend that health care providers weigh the potential risks and benefits of administering PrEP to adolescents on an individual basis and in the context of local laws.^{7,8}

RISK ASSESSMENT

This patient had recommended indications for PrEP use; he was having anal sex without the use of condoms with male sexual partners whose HIV status was unknown.⁸ Although assessing an individual patient's specific risks can help to inform screening and counseling, the risk assessment performed during a single visit or with the use of electronic tools is limited.⁹ In a risk assessment of an adolescent, patient-provider dynamics and patient communication preferences are shaped by the emerging autonomy, maturity, and sexual experience of the patient.¹⁰ This patient's risk of HIV acquisition was clear; in other cases, the risk may be higher than either the patient or the provider estimates.¹¹ After I perform a medical evaluation and counseling,

I prescribe PrEP to patients who consider themselves to be at risk, an approach supported by the HIV Medicine Association.¹²

RISK COMPENSATION

In two U.S. studies of PrEP use in persons 15 to 22 years of age, 60 to 80% of the participants had had anal intercourse in the previous month and had not used a condom.^{5,6} Indeed, these study participants may not represent the highest-risk youth in the United States, given that 80% of the participants lived at home and were enrolled in school. During the study period, there was no evidence of risk compensation (i.e., an increase in risky behaviors with the use of prophylaxis). As when prescribing hormonal contraception, when I prescribe PrEP, I discuss the possibility of risk compensation with the patient and the plan to readdress this issue at future visits.¹³

INITIAL EVALUATION AND MONITORING

The initial evaluation of this patient for PrEP was focused on sexual risk factors, substance use, and signs or symptoms suggestive of acute HIV infection or other sexually transmitted diseases. He and I also discussed the rationale for laboratory monitoring and future visits.

Because the patient had not had a recent high-risk exposure and had no signs or symptoms consistent with acute HIV infection, a screening test for HIV was performed. We planned to repeat HIV testing in 1 month and then quarterly thereafter, in part due to the risk of developing drug resistance if HIV is acquired while the patient is taking F/TDF, a two-drug regimen that would not be appropriate for the treatment of HIV infection.

Vaccination status was obtained, including for human papillomavirus and hepatitis A,¹⁴ and screening tests were performed for other sexually transmitted diseases, including hepatitis B and C, gonorrhea, and chlamydia; the patient was offered collection swabs to obtain the specimens for gonorrhea and chlamydia testing. Chronic hepatitis B can flare if PrEP is discontinued. The level of hepatitis B surface antibody was not measurable (<10 mIU per milliliter), and the patient received a hepatitis B vaccine.¹⁵

When F/TDF for PrEP is provided, the serum creatinine clearance is measured and urinalysis is performed at baseline and biannually. These

tests monitor for signs of toxic effects in the kidneys, including a change in the estimated glomerular filtration rate and evidence of proximal tubular dysfunction or Fanconi's syndrome.

I counseled the patient that he would need to take PrEP for at least 7 days before he would be protected from HIV infection if he were to have receptive anal intercourse.

SIDE EFFECTS

I also counseled the patient regarding additional side effects of PrEP, including possible transient nausea and diarrhea, as well as the potential development of toxic effects in bone. In adults, F/TDF for PrEP is associated with a modest decrease in bone mineral density that appears to be most pronounced in the first 6 months of therapy¹⁶ and may be reversible.¹⁷ Data that emerged after this patient's evaluation show that, 48 weeks after discontinuation of PrEP in young men who have sex with men, bone loss was partially or fully reversed in those 18 to 22 years of age, but a bone mineral density lower than the baseline level often persisted in those 15 to 19 years of age.¹⁸ Bone changes appeared to increase with greater adherence (i.e., greater drug exposure).¹⁹ Adolescence is a critical time for attaining peak bone mass,²⁰ and the long-term implications of decreased bone mineral density due to F/TDF for PrEP are unclear. Emerging data suggest potentially important differential effects of PrEP on bone according to adherence, race, and sex.²¹⁻²³ The parathyroid hormone–fibroblast growth factor 23 axis is thought to be the primary contributor to TDF-associated changes in bone mineral density in adolescents and young adults, and the mechanism for such changes may be distinct from that in older adults. Vitamin D supplementation may mitigate these effects, although data from randomized, controlled trials are lacking.²⁴ With this physically active patient, I discussed these concerns, as well as general information on bone health, including sources of the recommended dietary requirement of calcium.

CONSENT FOR MINORS AND SAFETY

This patient was able to summarize the risks and benefits of PrEP that we discussed, and I considered him to be a mature minor. He expressed a desire to eventually disclose his decision to use PrEP to his parents, but he thought

that it was not in his best interest to do so immediately.

As a mandated reporter in the Commonwealth of Massachusetts, I assessed this adolescent for any potential neglect or abuse. In Massachusetts, the legal age of consent for sexual intercourse is 16 years. For anyone younger than 18 years of age, exchange sex in any form (e.g., the exchange of sex for money, food, or shelter) constitutes sexual exploitation, and reporting is mandated. To support providers in deciding when it is appropriate to report, many academic centers have consultative teams with expertise in child protection and advocacy, which are distinct from state-run child protective services. On the basis of my discussion with the patient during his initial visit, I did not have concerns about sexual exploitation or other safety issues related to my role as a mandated reporter.

CONFIDENTIALITY

For patients younger than 26 years of age, who may be a dependent on a parent's or guardian's health insurance plan, I discuss the risk of potential disclosure through summaries of payment or explanations of benefits. The Massachusetts Act to Protect Access to Confidential Healthcare, which took effect before this patient's evaluation, conceals sensitive diagnoses but not the provider's identity. This patient was advised to call his insurance company; he met with a clinic community navigator for assistance in contacting the insurance company. Payment for PrEP with the use of alternative sources of funding, outside health insurance coverage, is considered on a case-by-case basis. However, options are limited, and navigating payment for PrEP remains a barrier for patients and can result in intensive use of clinic staff resources. The annual cost of F/TDF for PrEP can be more than \$20,000 per year in the United States, as compared with \$60 per year in some other countries.²⁵

ADHERENCE

Long-term adherence to PrEP is a major concern in adolescents and young adults. In the two U.S. studies of PrEP use in persons 15 to 22 years of age, there were steep declines in medication adherence, even though the participants consistently attended clinic visits.^{5,6} The declines were most marked after 3 months of PrEP, when the interval between clinic visits (determined by the study

protocols) changed from 1 month to 3 months; Black males in particular were noted to be at risk for nonadherence. These and other data from the chronic disease literature suggest that adolescents require increased adherence support.

At the initial visit, the patient and I reviewed adherence strategies. He was given a pillbox with separate compartments for each day of the week and a keychain pill holder. A phone alarm was set in the office, and the patient identified where his medications would be stored, given his confidentiality concerns. A community navigator assisted the patient with completing a medication copayment card and accompanied him to pick up the medication. In addition, a community navigator checked in with him daily for several days after he started PrEP. Plans for visits, which were to take place monthly and eventually every third month, were tailored to his school schedule.

SAFE SEXUAL PRACTICES

Access to sex education is declining in U.S. schools,²⁶ and an important aspect of the initial visit was counseling on safe sexual practices. The patient and I discussed how to use condoms, including the single-use internal condom, and the role of lubricant. We discussed the differential risks conferred by participating in different sexual acts. For example, the per-act probability of acquiring HIV associated with receptive anal intercourse is more than 10 times as high as that associated with insertive anal intercourse.²⁷ We also discussed navigating sources of information on the Internet.

DISCUSSION OF MANAGEMENT — LEGAL PERSPECTIVE

Dr. Sheila Salvant Valentine: This case poses two legal issues: consent and confidentiality.

Patients need both the mental and the legal capacity to give informed consent for health services. Legal capacity means that a person has authority under the law to engage in certain activities. A person who has attained the age of majority is assumed to have the legal capacity to consent to health services. The age of majority, which varies according to state, is 18, 19, or 21 years. Parental consent for health services is needed for persons who have not yet attained the age of majority (minors), unless state laws allow

minors to access some health services without parental consent.

The age of consent can be waived on the basis of the disease for which the minor seeks health services. For services related to sexually transmitted diseases and HIV, some states have no minimum age of consent, whereas other states have an age of consent that is lower than the age of majority.²⁸

The age of consent can also be waived on the basis of the type of health services that the minor seeks. Some state laws permit minors to consent to services related to diagnosis, treatment, or prevention (which would include PrEP, although it is not specifically mentioned in the law). Only a few state laws specifically permit minors to consent to services related to the prevention of sexually transmitted diseases or HIV, such as PrEP.¹⁴ In states in which the law allows minors to access treatment but is silent regarding prevention, the ability of a minor to access PrEP may depend on whether “treatment” is defined narrowly or broadly.

In Massachusetts, the age of majority is 18 years; this patient was 16 years old at the time that he requested health services. However, in Massachusetts, the mature minor doctrine applies, stating that any minor with sufficient maturity can consent to some health services. This patient was deemed to be a mature minor, on the basis of the provider’s assessment.

However, the fact that minors can consent to PrEP does not mean that the service will not be disclosed to their parents. Laws vary from state to state regarding information that can be shared with parents. In Massachusetts, providers must keep services rendered to minors confidential unless the minor consents to the disclosure, a proper judicial order is issued, or there is an emergency.

In Massachusetts, there are also specific limitations regarding information that insurance carriers can disclose. For minors who gain access to HIV prevention services, such as this patient, the summary of payments must be addressed to the patient. For sensitive services, such as PrEP, only general information can be listed on the form. If there are no out-of-pocket costs, the minor can request that a summary of payments not be sent; if there are out-of-pocket costs, the minor can receive the summary of payments at any physical address of choice or online.²⁹ However, this statute applies to insur-

ance carriers and not to hospitals, and the hospital provided coverage in this case.

FOLLOW-UP

Dr. Perzanowski: At a follow-up visit 2 months after F/TDF for PrEP was initiated, the patient reported that he had been taking the medication as prescribed without adverse effects. Additional follow-up visits were scheduled.

One month later, the patient’s mother called the billing office at this hospital and reported that she had received a billing statement, addressed to her, referencing services rendered to the patient at his initial appointment at the infectious disease clinic. When the patient’s parents addressed the issue with the patient, he disclosed that he had sought confidential sexual health care and that he had started taking HIV PrEP.

MEDICAL ETHICS PERSPECTIVE

Dr. Amelia S. Knopf: This case highlights the ethical complexities of providing sexual and reproductive health services to minors. The foundational principles of biomedical ethics are respect for persons, for beneficence, and for justice.³⁰ These principles, which were originally proposed as a framework of norms for research, now extend beyond scientific studies to health care and public health.³¹

Respect for persons requires respect for autonomy, as well as protection of those with diminished or emerging autonomy.³⁰ Respect for autonomy is honored in the consent process and thus presents the most obvious form of ethical conflict in the clinical care of minors who seek sexual and reproductive health services. In the United States, children and adolescents are considered to have emerging autonomy until they reach the age of majority and therefore must receive protection from harm. Parents or guardians are traditionally the source of additional protection from responsibility for decision making, coercion, and harm. Thus, parents must provide permission for their minor child to receive treatment. In most health contexts, this model works reasonably well,^{32,33} but when the health problem is sensitive or associated with a stigma, it poses risks to the minor that must be considered.

In this case, the patient identified as a sexual

minority at risk of acquiring HIV, and he was not prepared to disclose this information to his parents. Inclusion of his parents in the decision-making process would have revealed to them this sensitive information, and he may have elected to forgo PrEP to maintain his privacy. Studies have shown that some adolescents who identify as a sexual or gender minority have concerns about such disclosures and the potential harms that could result from them and will avoid potentially beneficial clinical care when parental permission is required.³⁴⁻³⁷ Adolescents rely on their parents for support, and they risk losing this support — and also risk incurring physical or psychological harm — when sensitive information is disclosed in the context of health care.³⁸

Beneficence requires clinicians to weigh the risks of an intervention against its benefits. This case highlights the need to also weigh the risks of disclosure to parents against the potential benefits of parental engagement, which include supported decision making and mitigation of the risks of coercion and harm. In the United States and other contexts in which health literacy is high, adolescents reliably have the capacity to consent to medical interventions.³⁹⁻⁴¹ In this case, the physician assessed the patient's capacity and found that he understood the risks and benefits of PrEP and could apply this information to his own circumstances. The patient made the voluntary choice to seek PrEP and to fill the prescription he received; both actions indicate voluntary participation in care. The patient was faced with a high risk of acquiring HIV during his lifetime, with most of this risk incurred during adolescence and young adulthood. This led the clinician and the patient to determine that the risks associated with HIV infection outweighed those associated with PrEP use.

There is an emerging consensus that adolescents should have access to biomedical services for HIV prevention in clinical and research contexts.⁴²⁻⁴⁴ Studies have shown that many adolescents benefit from such participation and access and do not regret the decision to participate or encounter increased harms when they are allowed to give consent for themselves.^{45,46} Limiting adolescents' access to HIV prevention services is an issue of justice. Adolescents — especially young Black men who have sex with men — have a

disproportionate burden of HIV risk, and justice demands that clinicians and scientists respond by providing them with efficacious and safe methods of prevention.

ADDITIONAL FOLLOW-UP

Dr. Neilan: From our clinical practice manager, who had been contacted by the billing office, I learned that a billing statement had been sent to the patient's parents. In reviewing the case in detail, leadership overseeing the sexual health clinic, the infectious disease clinic, patient financial services, billing, patient privacy, and electronic medical records examined the multiple levels at which safeguards could be implemented to prevent the inadvertent disclosure of confidential services for minors in the future. Results included the development of protocols for the care of minors and handoffs between hospital practices, as well as scripts for staff and handouts for patients regarding bills and the explanation of benefits.

I spoke with the patient and his parents separately, both to apologize and to discuss the steps taken to address these issues. The patient reflected that he “felt outed” by the experience. He described the challenges that arose from him not being able to disclose his PrEP use on his own terms. He noted how fortunate he was to have a supportive family and that the consequences might have been quite different, even dangerous, in other families. Both the patient and his parents welcomed the opportunity to raise awareness about the issues discussed in this case. The patient continues to receive PrEP at a local clinic.

FINAL DIAGNOSIS

Risk of acquiring human immunodeficiency virus infection in an adolescent.

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, nor do they constitute legal advice.

This case was presented at Pediatrics Grand Rounds.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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REFERENCES

- Hess KL, Hu X, Lansky A, Mermin J, Hall HI. Lifetime risk of a diagnosis of HIV infection in the United States. *Ann Epidemiol* 2017;27:238-43.
- Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2014–2018. May 2020 (<https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-25-1.pdf>).
- Li Z, Purcell DW, Sansom SL, Hayes D, Hall HI. Vital signs: HIV transmission along the continuum of care — United States, 2016. *MMWR Morb Mortal Wkly Rep* 2019;68:267-72.
- Centers for Disease Control and Prevention. Pre-exposure prophylaxis (PrEP), 2021 (<https://www.cdc.gov/hiv/risk/prep/index.html#:~:text=Pre%2Dexposure%20prophylaxis%20>).
- Hosek S, Rudy B, Landovitz R, et al. An HIV preexposure prophylaxis (PrEP) demonstration project and safety study for young MSM. Johns Hopkins University. January 1, 2017.
- Hosek SG, Landovitz RJ, Kapogiannis B, et al. Safety and feasibility of antiretroviral preexposure prophylaxis for adolescent men who have sex with men aged 15 to 17 years in the United States. *JAMA Pediatr* 2017;171:1063-71.
- Centers for Disease Control and Prevention. Preexposure prophylaxis for the prevention of HIV infection in the United States — 2017 update: a clinical practice guideline, 2018 (<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>).
- U.S. Preventive Services Task Force. Final recommendation statement: prevention of human immunodeficiency virus (HIV) infection: preexposure prophylaxis. June 11, 2019 (<https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis>).
- Chou R, Evans C, Hoverman A, et al. Pre-exposure prophylaxis for the prevention of HIV infection: a systematic review for the U.S. Preventive Services Task Force. Rockville, MD: Agency for Healthcare Research and Quality, 2019 (<http://www.ncbi.nlm.nih.gov/books/NBK542888/>).
- Hoopes AJ, Benson SK, Howard HB, Morrison DM, Ko LK, Shafiq T. Adolescent perspectives on patient-provider sexual health communication: a qualitative study. *J Prim Care Community Health* 2017;8:332-7.
- Raspberry CN, Morris E, Lesesne CA, et al. Communicating with school nurses about sexual orientation and sexual health: perspectives of teen young men who have sex with men. *J Sch Nurs* 2015;31:334-44.
- Hardy WD, Person AK. HIVMA comments on the USPSTF recommendations for the use of PrEP. Arlington, VA: HIV Medicine Association. December 26, 2018 (<https://www.hivma.org/globalassets/hivma/news/uspstf-prep-recommendation-hivma-comments-12-26-18.pdf>).
- Marcus JL, Katz KA, Krakower DS, Calabrese SK. Risk compensation and clinical decision making — the case of HIV preexposure prophylaxis. *N Engl J Med* 2019;380:510-2.
- Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of hepatitis A virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices, 2020. *MMWR Recomm Rep* 2020;69:1-38.
- Weinbaum CM, Williams I, Mast EE, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm Rep* 2008;57:1-20.
- Mulligan K, Glidden DV, Anderson PL, et al. Effects of emtricitabine/tenofovir on bone mineral density in HIV-negative persons in a randomized, double-blind, placebo-controlled trial. *Clin Infect Dis* 2015;61:572-80.
- Glidden DV, Mulligan K, McMahan V, et al. Brief report: recovery of bone mineral density after discontinuation of tenofovir-based HIV pre-exposure prophylaxis. *J Acquir Immune Defic Syndr* 2017;76:177-82.
- Havens PL, Perumean-Chaney SE, Patki A, et al. Changes in bone mass after discontinuation of preexposure prophylaxis with tenofovir disoproxil fumarate/emtricitabine in young men who have sex with men: extension phase results of adolescent trials network protocols 110 and 113. *Clin Infect Dis* 2020;70:687-91.
- Havens PL, Stephensen CB, Van Loan MD, et al. Decline in bone mass with tenofovir disoproxil fumarate/emtricitabine is associated with hormonal changes in the absence of renal impairment when used by HIV-uninfected adolescent boys and young men for HIV preexposure prophylaxis. *Clin Infect Dis* 2017;64:317-25.
- Bonjour J-P, Chevalley T. Pubertal timing, bone acquisition, and risk of fracture throughout life. *Endocr Rev* 2014;35:820-47.
- Gabel L, Macdonald HM, McKay HA. Sex differences and growth-related adaptations in bone microarchitecture, geometry, density, and strength from childhood to early adulthood: a mixed longitudinal HR-pQCT study. *J Bone Miner Res* 2017;32:250-63.
- Weber DR, Moore RH, Leonard MB, Zemel BS. Fat and lean BMI reference curves in children and adolescents and their utility in identifying excess adiposity compared with BMI and percentage body fat. *Am J Clin Nutr* 2013;98:49-56.
- Spinelli MA, Glidden DV, Anderson PL, et al. Impact of estimated pre-exposure prophylaxis (PrEP) adherence patterns on bone mineral density in a large PrEP demonstration project. *AIDS Res Hum Retroviruses* 2019;35:788-93.
- Havens PL, Tamhane A, Stephensen CB, et al. Short communication: association of vitamin D insufficiency and protective tenofovir diphosphate concentrations with bone toxicity in adolescent boys and young men using tenofovir disoproxil fumarate/emtricitabine for HIV pre-exposure prophylaxis. *AIDS Res Hum Retroviruses* 2019;35:123-8.
- HIV prevention drug: billions in corporate profits after millions in taxpayer investments. House Committee on Oversight and Reform, 2019 (<https://oversight.house.gov/legislation/hearings/hiv-prevention-drug-billions-in-corporate-profits-after-millions-in-taxpayer>).
- Lindberg LD, Maddow-Zimet I, Boonstra H. Changes in adolescents' receipt of sex education, 2006–2013. *J Adolesc Health* 2016;58:621-7.
- Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. *AIDS* 2014;28:1509-19.
- Centers for Disease Control and Prevention. State laws that enable a minor to provide informed consent to receive HIV and STD services, 2021 (<https://www.cdc.gov/hiv/policies/law/states/minors.html>).
- The 192nd General Court of the Commonwealth of Massachusetts. Chapter 1760: health insurance consumer protections (<https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXXII/Chapter1760>).
- Department of Health and Human Services. The Belmont Report: ethical principles and guidelines for the protection of human subjects of research, 2016 (<https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html>).
- Beauchamp TL, Childress JF. Principles of biomedical ethics. 5th ed. New York: Oxford University Press, 2001.
- Brody JL, Annett RD, Scherer DG, Perryman ML, Cofrin KMW. Comparisons of adolescent and parent willingness to participate in minimal and above-minimal risk pediatric asthma research protocols. *J Adolesc Health* 2005;37:229-35.
- Brody JL, Scherer DG, Annett RD, Turner C, Dalen J. Family and physician influence on asthma research participation decisions for adolescents: the effects of adolescent gender and research risk. *Pediatrics* 2006;118(2):e356-e362.
- Macapagal K, Coventry R, Arbeit MR, Fisher CB, Mustanski B. "I won't out myself just to do a survey": sexual and gender minority adolescents' perspectives on the risks and benefits of sex research. *Arch Sex Behav* 2017;46:1393-409.

35. Reed JL, Huppert JS. Predictors of adolescent participation in sexually transmitted infection research: brief report. *J Adolesc Health* 2008;43:195-7.
36. Rojas NL, Sherrit L, Harris S, Knight JR. The role of parental consent in adolescent substance use research. *J Adolesc Health* 2008;42:192-7.
37. Wallace M, Middelkoop K, Smith P, et al. Feasibility and acceptability of conducting HIV vaccine trials in adolescents in South Africa: going beyond willingness to participate towards implementation. *S Afr Med J* 2018;108:291-8.
38. Morton MH, Dworsky A, Matjasko JL, et al. Prevalence and correlates of youth homelessness in the United States. *J Adolesc Health* 2018;62:14-21.
39. Hein IM, Troost PW, Lindeboom R, et al. Accuracy of the MacArthur competence assessment tool for clinical research (MacCAT-CR) for measuring children's competence to consent to clinical research. *JAMA Pediatr* 2014;168:1147-53.
40. Steinberg L. A social neuroscience perspective on adolescent risk-taking. *Dev Rev* 2008;28:78-106.
41. Weithorn LA, Campbell SB. The competency of children and adolescents to make informed treatment decisions. *Child Dev* 1982;53:1589-98.
42. Hoffman LF, Francis NK, Catalozzi M, Francis JKR, Stanberry LR, Rosenthal SL. Inclusion of adolescents in clinical trials for sexually transmitted infections: a review of existing registered studies. *J Adolesc Health* 2016;58:576-8.
43. Hume M, Lewis LL, Nelson RM. Meeting the goal of concurrent adolescent and adult licensure of HIV prevention and treatment strategies. *J Med Ethics* 2017;43:857-60.
44. Pace JE, Siberry GK, Hazra R, Kapogiannis BG. Preexposure prophylaxis for adolescents and young adults at risk for HIV infection: is an ounce of prevention worth a pound of cure? *Clin Infect Dis* 2013;56:1149-55.
45. Knopf AS, Ott MA, Liu N, et al. Minors' and young adults' experiences of the research consent process in a phase II safety study of pre-exposure prophylaxis for HIV. *J Adolesc Health* 2017;61:747-54.
46. Schenk KD, Friedland BA, Chau M, et al. Enrollment of adolescents aged 16-17 years old in microbicide trials: an evidence-based approach. *J Adolesc Health* 2014;54:654-62.

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