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Ann Intern Med 2018 Jul 24

Finding Ways for Older Patients to Lower Their Drug Costs

Medicare prescription drug plans imposed higher out-of-pocket costs for many common cardiac medications than a generic-drug discount program.

Insured patients often pay out of pocket for prescription drugs, although some patients opt to use generic-drug discount programs that typically sell 30-day generic medications for US$4. To see whether these discount programs save money for Medicare beneficiaries with any of seven common cardiovascular conditions, researchers examined copayment charges in 2155 Medicare prescription drug plans (PDPs) for

27 generic cardiovascular medications that were available for a $4 charge at a single discount program (Walmart).

In 2017, a median of 21% of plans (interquartile range [IQR], 16%–38%) required patients to pay more than $4 for covered medications. Medicare Advantage plans, which also cover other medical expenses, generally had higher out-of-pocket costs than standalone PDPs; the median out-of-pocket monthly cost for a lower-tier drug (e.g., a preferred generic) was $2 (IQR, $0–$5) versus $1 (IQR, $0–$2). These differences were even more pronounced in the higher tiers (median drug cost, $10 vs. $3).

COMMENT: Affordable medications are essential to ensure patient adherence, reduce healthcare costs, and improve patient outcomes. In this brief report, out-of-pocket costs for common cardiovascular medications were lower in a generic-drug discount program than in PDPs. Although the differences in absolute costs may seem small, many of the cardiac patients we care for are on multiple medications — these out-of-pocket expenses quickly add up. We clinicians should encourage our patients to shop around for their generic drugs or to enroll in standalone PDPs.

CITATION(S): Liu P et al. Medicare beneficiary out-of-pocket costs for generic cardiovascular medications available through $4 generic drug discount programs. Ann Intern Med 2018 Jul 24; [e-pub]. (https://doi.org/10.7326/M18-0965)

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AJR Am J Roentgenol 2018 Jul; 211:217

Should I Order Imaging to Evaluate Breast Pain?

In a retrospective study, almost all diagnostic imaging for breast pain was negative.

Breast pain is common but the cause is not always clear, producing anxiety over the possibility of underlying malignancy. Although breast cancer is not associated with breast pain, many patients are referred for diagnostic imaging (usually with negative results). Researchers at MD Anderson Cancer Center reported imaging findings for 799 patients who presented with breast pain at three community-based breast imaging centers in 2014.

The initial imaging modality was breast ultrasound for women younger than 30 and digital mammography (sometimes with tomosynthesis) for those aged ≥30 who had not had a mammogram within the last 6 months. Breast MRI was performed only when ordered by the referring physician. Most patients presented for diagnostic imaging; of these, 95% had negative findings and 5% had positive (but benign) findings. Only one patient had an incidental breast cancer, which was contralateral and detected with tomosynthesis. The cost of breast imaging was $87,322 in women 40 or younger and $152,732 in older women.

COMMENT: Given the lack of association between breast pain and breast cancer, the costs reported here represent an excessive utilization of healthcare resources. Evaluation and counseling should take place in a primary care setting. Most patients need reassurance and medical explanations of their symptoms; usually, breast pain is not caused by an underlying malignancy but rather by hormonal and fibrocystic changes that can be managed conservatively. If the clinical breast examination and recent screening mammogram (in women older than 40) are negative, conservative measures include wearing and sleeping in a supporting bra, keeping a symptom calendar to determine any cyclic changes, and avoiding nicotine, caffeine, and salty or fatty foods. Topical creams with diclofenac and evening primrose oil can be effective. As breast pain is not a surgical disease, diagnostic imaging and referral to a surgical specialist may well be unnecessary.

CITATION(S): Kushwaha AC et al. Overutilization of health care resources for breast pain. AJR Am J Roentgenol 2018 Jul; 211:217. (https://doi.org/10.2214/AJR.17.18879)

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JAMA Intern Med 2018 Aug 6

How Common Is Endometrial Cancer in Women with Postmenopausal Bleeding?

A systematic review and meta-analysis suggest 9% of women presenting with this symptom will be found to harbor endometrial malignancy.

Endometrial cancer characteristically presents with postmenopausal bleeding (PMB), yet we still have insufficient data to help counsel women with PMB regarding their likelihood of having this malignancy. Likewise, we lack precise estimates of the proportion of women with endometrial cancer who will present with PMB. To address these issues, investigators performed a systematic review and meta-analysis of 129 studies including 34,432 women with PMB and 6358 with endometrial cancer.

Pooled risk for endometrial cancer among women with PMB was 9% (95% confidence interval, 8%–11%); risk was higher among women not using hormone therapy (HT) than among HT users (12% vs. 7%; $P<0.001$ for heterogeneity). Prevalence of PMB among women with endometrial cancer was 91% (95% CI, 87%–93%).

COMMENT: Although endometrial cancer is the most common gynecologic cancer among U.S. women, population-based screening for this malignancy is not recommended. However, as the incidence of and mortality from endometrial cancer continue to rise, early detection is ever more important. As an editorialist notes, risk for endometrial cancer in women with PMB is similar to that of colorectal cancer in individuals with rectal bleeding (8%) and breast cancer in women with a palpable mass (10%), supporting current guidance that recommends evaluation of women with PMB (NEJM JW Womens Health Jun 2018 and *Obstet Gynecol* 2018 May; 131:e124). The present findings will enhance our counselling of patients while also facilitating future efforts to augment detection of endometrial cancer.

CITATION(S): Clarke MA et al. Association of endometrial cancer risk with postmenopausal bleeding in women: A systematic review and meta-analysis. JAMA Intern Med 2018 Aug 6; [e-pub]. (https://doi.org/10.1001/jamainternmed.2018.2820)

Matteson KA et al. Opportunities for early detection of endometrial cancer in women with postmenopausal bleeding. JAMA Intern Med 2018 Aug 6; [e-pub]. (https://doi.org/10.1001/jamainternmed.2018.2819)

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Ann Intern Med 2018 Jul 3; 169:36.

Understanding Overdiagnosis as a Consequence of Cancer Screening

Helping clinicians, patients, insurers, and policymakers better understand and communicate about this screening outcome.

Overdiagnosis represents a central concern regarding the potential harms of cancer screening. In a Special Article funded by the Agency for Healthcare Research and Quality, the authors focus on defining, estimating, and communicating with patients about this important but elusive concept. Overdiagnosis — defined as detection of histologically confirmed cancer through screening that would not otherwise have been diagnosed during a person's lifetime had screening not happened — is not the only harm that can result from cancer screening. False-positive results, which occur when a screening test erroneously suggests cancer is present (e.g., positive breast imaging results leading to a negative biopsy) may be confused with overdiagnosis.

Because overdiagnosis cannot be directly measured (and cancer incidence varies widely with geographic region, race/ethnicity of the study population, and research methodology), estimates vary widely. Accordingly, reports estimating overdiagnosis should also note relevance to U.S. populations. Patients may best comprehend the concept of overdiagnosis when it is expressed as the number of overdiagnosed cancer cases per total number of persons screened. In the “excess-incidence” strategy, the number of cancers observed in a screened population is compared with that expected without screening; the difference represents the number of overdiagnosed cancers. Population-based randomized trials with long follow-up and minimal screening in the comparison groups provide the most reliable estimates of overdiagnosis.

COMMENT: The U.S. public often finds it difficult to understand how cancer screening can generate harms; thus, it's challenging for clinicians to effectively communicate this concept to patients. Enthusiastic media-based support for screening, fears about cancer, low levels of health literacy, and financial incentives associated with fee-for-service healthcare combine to create formidable barriers to understanding and addressing overdiagnosis. For example, when national guidelines recently changed to advocate cervical cancer screening every 3 to 5 years instead of annually, I encountered numerous confused, angry patients. When discussing overdiagnosis, clinicians should consider their patients' values and priorities, keep the message simple, and discuss both the benefits and harms of screening.

CITATION(S): Davies L et al. Defining, estimating, and communicating overdiagnosis in cancer screening. Ann Intern Med 2018 Jul 3; 169:36. (https://doi.org/10.7326/M18-0694)

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Making Informed Decisions About Cancer Screening

Screening tests for early cancer detection have both risks and benefits; knowing them can help you make informed decisions.

Screening for cancer seems like a good idea — after all, who wouldn't want to find any type of cancer (for example, cervical, breast, or colon cancer) when it can be most effectively treated and cured? Screening means looking for cancer before any symptoms appear.

Examples of screening tests are mammograms for breast cancer, Pap smears and human papillomavirus (HPV) tests for cervical cancer, and colonoscopies for colon cancer. Screening works best during the period of precancerous changes (abnormal cells or tissue that are not cancer but could become cancer) or very early cancer that has not yet caused serious damage or spread to other body organs. Screening also works best if there's a treatment that's most effective when used early. However, screening has some drawbacks, so consider the following benefits and possible harms.

Benefits of Cancer Screening:

Reassurance: If your screening test shows no signs of cancer, you can breathe a sigh of relief and get on with your life.

Early detection and more-successful treatment: If the screening test shows signs of precancer or early cancer, you can be treated for it. This may mean shorter or simpler treatment, longer life, and better quality of life.

Harms That Might Result from Cancer Screening: False positive: Some results might show findings suggesting you could have an early cancer when you really don't. Since you and your clinician (doctor, nurse practitioner, nurse midwife, physician assistant) don't want to ignore a possible cancer, you'll probably have further testing. After a mammogram, for example, you may be called back for more breast images or a biopsy (when a small amount of tissue is removed for close examination). If this turns out to be a false-positive result, you will have been through the anxiety, inconvenience, discomfort, and expense of extra testing even though you don't have cancer. This happens more often with certain tests (for example, yearly mammograms).

False negative: Screening tests might miss a cancer that is actually present. In this case, you will be falsely reassured.

Unpleasant test effects: Examples include possible discomfort with a mammogram, exposure to radiation from a CT scan for lung cancer, or bleeding from a colonoscopy.

Overdiagnosis: Some cancers never cause any serious illness or death and in fact would never have been found during your lifetime if you hadn't had the screening test. These “indolent” cancers (as well as cancers that *are* a threat to health) may be found with screening tests. Unfortunately, even cancer experts cannot tell the difference between an indolent cancer and one that will progress, so the cancer will probably be treated. Cancer treatments (surgery, radiation, medication) can be unpleasant and expensive and can interfere with quality of life. The difference between a false-positive result and overdiagnosis is that a false-positive, after further testing, turns out not to be cancer. With overdiagnosis, a cancer is present — but it is one that doesn't interfere with the length or quality of your life.

The issue of overdiagnosis is confusing for both women and clinicians. It complicates deciding whether or not to have a screening test (like mammography). Consider the example of a woman who chooses to have a mammogram at age 50. The mammogram finds a cancer. If this cancer represents overdiagnosis, the surgery and radiation therapy she receives is unnecessary — and this woman would have been better off had she not had the mammogram in the first place.

On the other hand, if the cancer found in this 50-year-old woman is a “real” cancer (one that would grow and perhaps spread), then early diagnosis with the mammogram allowed her to avoid more extensive treatment (such as chemotherapy); it might even have prevented her from dying from breast cancer.

Making an Informed Decision: So how do you decide whether to choose screening for cancers such as cervical, breast, colon, and lung cancer? Check out the decision-making aids under the Resources below. Consider (and discuss with your clinician) these issues:

- Is this cancer preventable (or easier to treat successfully) if it's found by screening? The Pap smear and HPV test is a success story. By detecting precancerous changes, these tests have made most cervical cancers almost entirely preventable. The screening downsides (discomfort of a pelvic exam, false positives and negatives) seem small compared to the upside.
- Do I have a higher than average chance of developing this type of cancer? For instance, women who have close family members with breast or ovarian cancer or who have genetic mutations (changes) that make these cancers more likely, have good reasons to be screened for breast cancer. For women with risk factors for developing certain types of cancer, it may make sense to screen for these cancers — and to do so on a different schedule than for women at “average” risk.
- How many people who get this test will have false-positive or false-negative results?
- What harms might result from the test itself? How common are they?
- Will finding this type of cancer early make a difference in how well treatment works?
- How do I personally feel about being screened?

Don't Forget Prevention: There are some things you can do to lower your risk for some cancers:

- Don't smoke; and if you do smoke, it's never too late to stop.
- Eat healthful foods, exercise, and maintain a healthy weight.
- If you are having children, breast-feed your babies to lower your risk for breast cancer.
- Get immunized against HPV (if you qualify) to lower your risk for cervical cancer. If you have children, be sure they also get immunized against HPV at the appropriate age to decrease their risk (and their future partners' risks).

In Conclusion: Understanding the possible benefits and possible harms of cancer screening — while considering your own thoughts and feelings — will help you make personal decisions about getting screened.

Resources

- National Cancer Institute
- Agency for Healthcare Research and Quality

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Neurology 2018 Aug 7; 91:e517

How Might Late-Life Blood Pressure Be Related to Cerebrovascular and Alzheimer Disease Pathology?

Analyses of studies with both longitudinal and autopsy data reveal that high blood pressure levels and declines contribute to cerebral pathology.

Blood pressure can contribute to cognitive decline. To investigate whether blood pressure is associated with cerebral pathology, researchers combined longitudinal and postmortem data from three similarly designed, prospective studies of aging in late life involving 1288 individuals.

The mean and change in systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined annually. Mean follow-up was 8 years, and mean age at death was 88.6. Postmortem neuropathologic outcomes included chronic macro- and microinfarcts, vessel disease, and Alzheimer disease (AD) pathology. Mean SBP was 136 mm Hg at baseline, with an average annual decline of 0.8 mm Hg. Mean DBP was 72 mm Hg at baseline, with an average annual decline of 0.1 mm Hg.

A higher mean SBD and a faster decline in SBD were associated with increased odds of having ≥1 infarct. Greater change in the SBD slope was associated with cortical infarcts, whereas higher mean SBD was associated with subcortical infarcts. Higher mean SBD also was associated with more-severe vessel disease and with more AD tangle pathology. DBP had a weaker and less-reliable association with the number of infarcts; however, both a higher DBP mean and a faster decline in DBP were associated with greater severity of atherosclerosis.

COMMENT: The strength of this study was the inclusion of autopsy data. Both higher means of blood pressure and faster declines contributed to pathological findings. Correlation of the results with cognitive and other clinical data is needed to provide guidance on an optimal blood pressure range for older adults.

CITATION(S): Arvanitakis Z et al. Late-life blood pressure association with cerebrovascular and Alzheimer disease pathology. Neurology 2018 Aug 7; 91:e517. (https://doi.org/10.1212/WNL.0000000000005951)

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Neurology 2018 Jul 31; 91:e455

Organic Solvents Contribute to Risk for Developing Multiple Sclerosis

Risk was highest in smokers who carried certain HLA alleles and were exposed to organic solvents.

Previous studies have suggested a possible link between organic solvent exposure and development of autoimmune disease. Investigators conducted a population-based, case-control study using the Swedish multiple sclerosis (MS) registry to assess the roles of organic solvents, human leukocyte antigen (HLA) alleles, and cigarette smoking in determining risk for MS. Participants included 2325 patients with recently diagnosed MS who completed a standardized questionnaire on environmental exposures and lifestyle factors and who were matched with 4948 controls from the national population register.

Organic solvent exposure was reported by 465 participants, and risk for MS increased with this exposure (odds ratio, 1.5); in addition, dose effects were demonstrated. Evaluation of HLA allele carriage showed that

individuals who carried HLA-DRB1*15 (which raises risk for MS) but not HLA-A*02 (which is protective), had higher MS risk than those who were HLA-DRB1*15–negative and HLA-A*02–positive (OR, 7.9). Smokers had higher risk than nonsmokers (OR, 1.5). Participants who carried the susceptibility HLA, smoked, and were exposed to organic solvents had the highest risk compared with those who had no risk factors (OR, 30.3).

COMMENT: This interesting study may provide important clues regarding pulmonary irritation, activation of the immune system, and MS risk. Organic solvent exposure, smoking, and HLA carriage (i.e., genetic and environmental factors) all seem to interact in conferring likelihood of developing MS; thus, risk was compounded 30-fold in those who were positive for all three factors. Although organic solvent exposure is a risk factor, its effect is less marked when acting alone. As with any case-control study, recall bias can be a concern; moreover, the number of patients in the highest-risk group was relatively small. Still, these findings suggest that organic solvent exposure confers modest risk for developing MS.

CITATION(S): Hedström AK et al. Organic solvents and MS susceptibility: Interaction with MS risk HLA genes. Neurology 2018 Jul 31; 91:e455. (https://doi.org/10.1212/WNL.0000000000005906)

Bell JS and DeLuca GC. Genes, smoking, and organic solvent exposure: An alarming cocktail for MS risk. Neurology 2018 Jul 31; 91:199. (https://doi.org/10.1212/WNL.0000000000005896)

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Obstet Gynecol 2018 Aug; 132:453

Gauging the Efficacy of Pharmacologic Agents for Female Sexual Dysfunction

A meta-analysis finds that much of the benefit seen in trials may represent a placebo effect.

Clinical trials of pharmacologic agents to treat female sexual dysfunction (FSD), which encompasses hypoactive sexual desire, arousal, orgasmic, and sexual pain disorders, have often observed a substantial placebo effect. To assess the extent of this effect, investigators conducted a systematic review and meta-analysis of randomized, controlled trials that used the Female Sexual Function Index (FSI; scored from 0 to 36, with scores below 26.6 indicating dysfunction) as an outcome. The placebo effect on the FSI was compared with each study's treatment effect.

Eight eligible trials included 3,959 women who received placebo or one of the following agents: flibanserin, bupropion, onabotulinum toxin A, intravaginal prasterone, intranasal oxytocin, ospemifene, or bremelanotide. The FSI score improved by 3.62 among women assigned to placebo and 5.35 among women assigned to active treatment, indicating that about two thirds of the improvement noted in these trials represented a placebo effect.

COMMENT: Although female sexual dysfunction is widely prevalent, few pharmacologic treatments are available. The observation that most of the improvement noted in clinical trials is due to a placebo effect may be frustrating for women, clinicians, and researchers looking for effective pharmacologic treatments; it may also illustrate the shortcomings of attempting to treat a multifactorial entity with a single approach. On a more positive note, nonpharmacologic measures — including education, self-monitoring, and counseling — are available and may be of therapeutic value in addressing FSD.

CITATION(S): Weinberger JM et al. Female sexual dysfunction and the placebo effect: A meta-analysis. Obstet Gynecol 2018 Aug; 132:453. (https://doi.org/10.1097/AOG.0000000000002733)

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Pediatr Res 2018 Jun 13

Parents' Screen Time Linked to Children's Behavior Problems

Interruptions in parent–child interactions due to parents' technology device use predicted worse child behavior and vice versa.

Electronic device use by parents that interferes with parent–child communication or activities has been associated with childhood behavior in cross-sectional studies, but longitudinal studies exploring how they relate are lacking.

Researchers analyzed survey data collected at four time points over 6 months from 172 couples (337 individuals) having at least one child aged 1 to 5 years. Ninety-one percent of parents were white and 72% had at least a bachelor's degree. Surveys included parents' self-reported measures of: 1) frequency of technology device use interrupting parent–child interactions; 2) externalizing and internalizing child behaviors, and; 3) parent stress. Responses were tested for associations between the three variables.

As hypothesized by the researchers, the relationship between parent device use interruptions and child behavior was bidirectional and was mediated by parent stress. More device use interruptions predicted child externalizing behavior, more child externalizing behavior predicted parent stress, and more parent stress predicted more device interruptions. There was more-limited evidence of the same relationships for child internalizing behavior.

COMMENT: When discussing child screen time with parents, clinicians can include parent device use as well. This study supports a balanced approach, acknowledging that parents' devices allow them some relief from the stresses of parenting young children, but cautioning that when they interfere with parent–child interactions and activities, child behavior can worsen, creating a vicious cycle. Future studies need to focus on more-diverse parent populations.

Note: Jenny Radesky, MD, is an author of this study and an associate editor for NEJM Journal Watch Pediatrics and Adolescent Medicine but had no role in selecting or summarizing this article.

CITATION(S): McDaniel BT and Radesky JS. Technoference: Longitudinal associations between parent technology use, parenting stress, and child behavior problems. Pediatr Res 2018 Jun 13; [e-pub]. (https://doi.org/10.1038/s41390-018-0052-6)

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https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(18)30269-4/fulltext

Analysis of ADHD Drugs: Use Methylphenidate in Kids, Amphetamines in Adults

By Joe Elia, Edited by David G. Fairchild, MD, MPH, and Lorenzo Di Francesco, MD, FACP, FHM

A meta-analysis of the drugs used to treat attention-deficit/hyperactivity disorder in the short term finds the best choices to be methylphenidate in children and adolescents, and amphetamines in adults, according to a *Lancet Psychiatry* report.

Researchers examined efficacy and tolerability data from published and unpublished double-blind, randomized, controlled trials. The 133 trials included some 14,000 children and 10,000 adults. Other drugs evaluated in the "network meta-analysis," which allows indirect comparisons of drugs not directly tested head-to-head, included atomoxetine, bupropion, clonidine, guanfacine, and modafinil.

Overall, results favored using methylphenidate in children and adolescents, and amphetamines in adults as first-line, short-term (12 weeks or under) treatment.

Asked to comment, Dr. Barbara Geller of *NEJM Journal Watch Psychiatry* wrote: "The two most effective drugs (methylphenidate for children, amphetamine for adults) should be prescribed first because they have good safety records after decades on the market."

LINK(S): Lancet Psychiatry article (Free)
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JAMA Pediatr 2018 Aug; 172:e180739

New Evidence That Early Solids May Lead to Better Infant Sleep

Introducing solids at 3 months was linked to longer sleep and fewer serious sleep problems in infants and toddlers.

Although official infant feeding recommendations in the U.S. and other countries include waiting until 6 months to introduce solids, parents often introduce them earlier to help their infants sleep.

Researchers performed a secondary analysis of data from a randomized controlled trial of early infant food introduction and food allergies. In the original trial, 1303 exclusively breast-fed infants from England and Wales were randomized to start solids at 3 months (early introduction) or 6 months (standard introduction). Data on infant sleep were collected by parent self-report 15 times from ages 3 months to 3 years; 94% completed the final survey. In this secondary analysis, researchers compared child sleep duration, nighttime waking, and sleep problems between groups.

Infants in the early-introduction group slept longer and woke less frequently in the night. In an adjusted intention-to-treat analysis, they slept a mean of 8 minutes more and had 9% fewer wakings per night over the course of the study. The effect of early solids peaked at 6 months, with an average of 17 minutes more sleep

per night. Parents of infants in the standard-introduction group were significantly more likely to consider their child's sleep a very serious problem (odds ratio, 1.8). Effects were stronger in a per-protocol analysis.

COMMENT: Although delaying solids has been associated with health benefits, this study supports the common belief among parents that their children will sleep better if fed earlier. While clinicians may focus on healthy weight and maximizing breast-feeding when making recommendations, we should recognize the high value parents place on better sleep and be prepared to acknowledge evidence that supports their beliefs. While doing so, we can offer other suggestions for improved infant sleep and continue to recommend delaying solids until about 6 months.

CITATION(S): Perkin MR et al. Association of early introduction of solids with infant sleep: A secondary analysis of a randomized clinical trial. JAMA Pediatr 2018 Aug; 172:e180739. (https://doi.org/10.1001/jamapediatrics.2018.0739)

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N Engl J Med 2018 Aug 9; 379:535.

Vitamin D Disappoints in a Perinatal Setting

Large trial finds no benefit of maternal vitamin D supplementation regarding infant growth.

Small-for-gestational-age infants face greater risk for adverse health outcomes. Observational studies (and a few small trials) indicated that vitamin D levels were associated with fetal and infant growth; thus, the Gates Foundation funded a randomized, double-blind, placebo-controlled trial involving 1300 mothers in Bangladesh (where vitamin D deficiency is common) to examine the effects of maternal vitamin D supplementation on infant growth. Participants were enrolled during the third trimester and randomized to receive placebo or vitamin D supplementation. The first intervention group received a weekly dose of 28,000 IU of vitamin D through 26 weeks postpartum; the other three groups received prenatal-only supplementation (in weekly doses of 4200 IU, 16,800 IU, or 28,000 IU) and postpartum placebo. Mothers were followed up weekly from enrollment until 26 weeks postpartum; infants were further assessed at 9 and 12 months of age.

Although vitamin D supplementation had the expected effects on serum 25-hydroxyvitamin D, calcium, and parathyroid hormone concentrations, no benefit was seen for the primary outcome (infant length for age at 1 year) or multiple secondary outcomes (e.g., other infant anthropometric measurements, preterm birth, stillbirth, gestational hypertension, congenital anomalies, infant neurologic disabilities, infant rickets).

COMMENT: It's disappointing that this rigorous trial does not lend support to routine vitamin D supplementation during late pregnancy or postpartum. Whether preconception vitamin D levels affect pregnancy outcomes remains an open question, especially given a recent observational study showing that vitamin D levels before conception (but not during early pregnancy) were associated with risk for pregnancy loss (Lancet Diabetes Endocrinol 2018 May 30). While we await further studies, efforts to improve pregnancy outcomes should focus on the myriad aspects of preconception care that are known to improve pregnancy outcomes (NEJM JW Womens Health Jun 2018 and *Lancet*, multiple citations).

CITATION(S): Roth DE et al. Vitamin D supplementation in pregnancy and lactation and infant growth. N Engl J Med 2018 Aug 9; 379:535. (https://doi.org/10.1056/NEJMoa1800927)

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J Pediatr 2018 Jun 26

Ambulatory Care Visits for Otitis Media Are Reduced Since PCV-7 and PCV-13 Introductions

In the U.S., there were 6 million fewer visits for ear infections in young children each year between 2000 and 2014.

Otitis media (OM) can be caused by *Streptococcus pneumoniae* and both the 7-valent pneumococcal conjugate vaccine (PCV-7) and newer PCV-13 have been found to reduce the incidence of OM in children (NEJM JW Pediatr Adolesc Med Aug 2018 and *Lancet Child Adolesc Health* 2018; 2:561).

Using nationally representative survey data on ambulatory care visits in the U.S., researchers analyzed trends in visits for OM in children aged <18 years from before the introduction of PCV-7 in 2000 until after the introduction of PCV-13 in 2010. Results were as follows:

- In children aged <2 years, OM-related visits to physician offices decreased from 826 to 387 visits per 1000 children between the pre–PCV-7 period (1997–1999) and post–PCV-13 period (2012–2014).
- In the post–PCV-13 period, OM-related office visits declined an additional 37% from the post–PCV-7 period (2002–2009) in children aged 2 to 4 years.
- Between the pre–PCV-7 and post–PCV-13 periods, OM-related emergency department visits declined from 187 to 114 visits per 1000 children aged <2 years.
- Between 2000 and 2014, there was an estimated annual reduction of 6 million ambulatory visits for OM in children aged <5 years. The decline was similar regardless of sex, race/ethnicity, or insurance status.

COMMENT: The decline in visits for OM to provider offices and emergency departments after the introductions of PCV-7 and especially PCV-13 indicate a great benefit to children's health and potential healthcare cost savings. This retrospective study does not provide any new insights into the microbiology of the infections in children who continue to seek ambulatory care for OM, which future studies should characterize.

CITATION(S): Kawai K et al. Ambulatory visits for otitis media before and after the introduction of pneumococcal conjugate vaccination. J Pediatr 2018 Jun 26; [e-pub]. (https://doi.org/10.1016/j.jpeds.2018.05.047)

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