February 2016 intended to improve delivery systems for AIANs. The guidance is designed to encourage new care coordination agreements between IHS and Tribal facilities and other health care providers that would provide AIANs access to a wider array of services and clinicians.[6]

Looking ahead, targeted outreach and enrollment efforts will be key for continued coverage gains and overcoming enrollment barriers faced by AIANs, including mistrust of governments, certain cultural beliefs, and a preference for using IHS services and the belief among some AIANs that the federal government should fund all AIAN care through IHS.[7] The Department of Health and Human Services provided grants for AIAN communities to develop strategies to enroll eligible children in Medicaid and the Children's Health Insurance Program; additional funds will be awarded to continue this effort.[8] In the face of substantial health needs, Medicaid can provide immediate benefits to AIANs and leverage federal dollars to improve capacity at IHS and Tribal facilities, enhancing access to a broader set of services to meet their needs.

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COMMENT & RESPONSE

In Defense of Off-label Prescribing

To the Editor The study by Eguale and colleagues[1] demonstrates that off-label use of prescription drugs is associated with increased ADEs (adverse drug events) only when such use lacks strong scientific evidence. Specifically, off-label uses of drugs with strong scientific evidence had the same risk of ADEs as on-label use. This finding implies that the extreme expense and delay caused by the process of US Food and Drug Administration (FDA) approval of an already-approved drug for a new indication may not be necessary if strong scientific evidence supports such use. The take-home message of this study is not that we need to crack down on off-label prescribing but that we need to crack down on unscientific prescribing.[2] Electronic health records should be programmed to discourage unscientific prescribing, not off-label prescribing. Because off-label prescriptions backed by strong evidence are just as safe as prescriptions for FDA-approved indications, the FDA ban on promotion of the former denies patients the benefits of safe and scientifically proven medications. The focus should shift to suppression of off-label prescribing only when it is not backed by strong evidence.

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In Reply Unscientific prescribing constitutes 4 of 5 off-label uses,[1-3] and this unscientific prescribing has resulted in a 54% increased risk of adverse drug events compared with on-label uses.[2] To crack down on unscientific prescribing, drug regulatory bodies need to demand strong scientific evidence from pharmaceutical companies to safeguard the public.

Scientific evidence for off-label use takes years to develop. Older drugs have more off-label use compared with recently introduced drugs,[1] and these same drugs have more off-label use backed with strong scientific evidence. Drugs approved before 1996 have more off-label use compared with drugs approved after 1996, and as many as 25% of these off-label uses of older drugs (before 1996) have strong scientific evidence compared with only 7.5% of drugs approved after 1996. We need to be cautious in the use of recently introduced drugs for off-label uses owing to a lack of strong scientific evidence.

We[1] have also shown that, with the aid of electronic health records, accurate documentation of treatment indications is possible and can answer important patient safety questions. Documentation of treatment indication is 1 value-added feature for physicians and facilitated the creation of a problem list of active and current diagnoses, as

well as allowing an automated check for drug-disease interactions.[4] Electronic health record implementation would be greatly aided if clinically relevant features are added to electronic systems.

Physicians have broad discretion in drug prescribing, but this broad discretion comes with great responsibility. Physician education needs to incorporate a principle of conservative prescribing with high index of suspicion for adverse effects, especially for unscientific off-label uses, vigilance about indication creep, and use of unbiased drug-knowledge bases.[5] The lack of knowledge about drugs and their approved indication and the difficulty of keeping up with the ever-changing drug information are affecting how well patients are treated. Using computerized decision support systems, we could fill the knowledge gap by supplying drug approval status and the degree of scientific evidence at the point-of-care.

When physicians prescribe medications for unscientific, off-label uses, their patients suffer adverse drug events. Patients expect that physicians base their prescriptions on scientific evidence, but 4 out of 5 drugs that are prescribed off-label are prescribed for unscientific use. Keeping current on ever-changing drug information is difficult, and it is difficult to understand why, in such an environment, we allow drug companies to promote unscientific, off-label uses of medications to physicians.

The expensive and long approval process required by the US Food and Drug Administration (FDA) is exactly what produces the scientific evidence that physicians need to prescribe appropriately. Instead of weakening these institutions, we should also give them the mandate to monitor off-label use,[6] as part of Risk Evaluation and Mitigation Strategies[7] that would require physicians to document treatment indication as a means of monitoring off-label use; an approach that we have shown is feasible with the aid of electronic health records and computerized prescribing. We owe it to our patients to strengthen the FDA, Health Canada, and other drug regulatory bodies to protect our patients from the effects of (and promotion of) unscientific, off-label uses of medications.

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Hypertension, the Swedish Patient Register, and Selection Bias

To the Editor It is with interest that I read the article by Crump et al[1] in a recent issue of *JAMA Internal Medicine* concerning physical fitness and body mass index (BMI) at military conscription and its association with future hypertension.[1] However, I do have some concerns about the use of a hypertension diagnosis in the Swedish Patient Register as an outcome.

The Swedish Patient Register is based on specialized care, whereas hypertension in Sweden is almost exclusively managed in primary care. According to the study by Crump et al,[1] 6% of participants had hypertension at the age of 46 years. In a Swedish epidemiological study, where all inhabitants in Västerbotten County at age 40 and 50 years were invited, the frequency of hypertension was 17.7% and 35.2%, respectively.[2] Thus, hypertension in the study by Crump et al is heavily underreported, detecting one-third to one-sixth of people with hypertension. The authors recognize that underreporting might be a problem but do not report the magnitude of this problem. Also, they state that detection of people with hypertension is likely nondifferential with respect to physical fitness and BMI and hence dilute the results rather than introduce bias. With that underreporting is nondifferential, I must disagree.

Patients end up in the Swedish Patient Register because they are in need of specialized care, and hypertension is registered *en passant* during these visits. Both physical fitness and BMI at conscription has previously been associated with coronary heart disease and stroke,[3,4] 2 significant reasons to end up in the register. The association between coronary heart disease, stroke, and hypertension is well established. Hence, the results reported by Crump et al[1] suffer from selection bias, compromising their validity.

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