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Issues and Questions Surrounding Screening for Cognitive Impairment in Older Patients

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The importance of addressing age-associated cognitive impairment cannot be overstated. The rising prevalence of cognitive impairment such as mild cognitive impairment (MCI) and dementia, including Alzheimer disease, is becoming a world-wide concern.¹ In this issue of *JAMA*, the US Preventive Services Task Force (USPSTF) concludes that “the current evidence is insufficient to assess the balance of benefits and harms of screening for cognitive impairment in older adults (I statement).”² This recommendation is based on an evidence report and systematic review of the literature that assessed the accuracy of cognitive screening instruments and the benefits and harms of interventions to treat cognitive impairment.³ That report represents an update of the previous report on this topic published in 2014.⁴

The report addresses 5 key questions and assimilates data from the previous report with new evidence. The conclusions of the updated report are quite similar to those presented in 2014. While screening instruments can detect cognitive impairment fairly well, there was no convincing evidence that screening for cognitive impairment improves patient or caregiver outcomes, nor does it cause harm. The implications of these conclusions for clinical practice and research are substantial. The first key question addressed the utility of screening for cognitive impairment in community-dwelling older adults in a primary care setting. Only 1 randomized clinical trial (RCT) had focused on addressing this issue, and it failed to demonstrate any benefit or harm from screening for cognitive impairment.⁵ The conclusion of the updated report relies in part on findings from this 1 study. The trial compared random assignment of cognitive screening with no screening among 4004 older primary care patients with no indication of cognitive impairment, and those who screened positive on the instruments were referred for a voluntary diagnostic assessment. Of those who screened positive (n = 134), only 46 (34%) underwent subsequent evaluation. Accordingly, the

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findings most likely have limited statistical power to detect differences in outcomes and may reflect other underlying differences in pursuing an evaluation, such as degree of impairment. Furthermore, when the topic of diagnostic assessment was mentioned to potential trial participants, only a minority of participants agreed to participate in the trial, most likely introducing bias. In addition, because the participants were followed up for up to 12 months, it might be difficult to interpret any effect on decision-making, patient-family/caregiver, or societal outcomes in relatively few participants over a brief period. Therefore, while this RCT was the only study found for key question 1, it is clear that the trial could not resolve many of the questions it was designed to address.

The second key question pertained to the accuracy of screening instruments to detect cognitive impairment. Many of these instruments are brief, which is necessitated by the time pressures of a primary care practice and, as such, the instruments lack some sensitivity. Nevertheless, the standard instruments that have been in place for many years appear to be adequate for assessing some degree of cognitive impairment. The most frequently used instrument, the Mini-Mental State Examination, has good sensitivity and specificity to detect dementia.⁶ It likely performs less well in detecting MCI because the instrument is not sufficiently sensitive to detect subtle impairment and was designed prior to development of the construct of MCI. A 2018 evidence-based review of the literature on MCI by the American Academy of Neurology documented the prevalence and outcome of MCI in a large database and supported its utility as a clinical construct.⁷ Newer screening instruments have focused on the more subtle degrees of cognitive impairment and may be more useful in that setting. Nevertheless, the standard brief screening instruments appear to perform reasonably well.

The third key question pertained to the harms of screening for cognitive impairment and basically concluded that there was no evidence of harm, which is an important finding. However, the relatively short follow-up period of many studies may be insufficient to yield any meaningful results.

The fourth key question evaluated interventions for mild to moderate dementia or MCI in the community setting. The data on this issue were consistent with many other reviews of this topic, such as the 2017 report by the National Academies of Sciences, Engineering, and Medicine.⁸ In general, most of the pharmacologic interventions for cognitive impairment produce statistically significant but modest benefits. In the absence of any other useful pharmacological treatments, many patients and clinicians prefer to use the medications. There is no doubt, however, that additional therapeutic interventions are needed. Similarly, nonpharmacologic interventions (such as physical exercise and cognitive activities) have shown small clinical effects. There was also modest evidence that education and case management interventions may benefit caregiver burden and depression outcomes. A meta-analysis of the data did not support an advantage suggesting that one type of intervention (psychoeducation vs care of case management vs other caregiver or caregiver-patient dyad interventions) was associated with better outcomes relative to another.²

The fifth key question examined the harms of interventions in individuals with some degree of cognitive impairment. There are well-documented adverse effects of pharmacologic

interventions, but they are generally manageable and tolerated. However, these necessitate judgment on the part of the clinician, patient, and family with respect to relative risk of adverse effects compared with the modest treatment benefits that might be expected. There was no evidence of significant serious adverse events with the medications. The nonpharmacologic interventions basically did not produce any harm.

These data collectively do not provide strong support for the role of screening for cognitive impairment or treatment of cognitive deficits. However, the lack of evidence in the literature does not necessarily mean that screening has no benefits. There are important challenges in designing and executing RCTs to answer many of the important questions surrounding screening and treatment of cognitive impairment, including recruiting adequate samples of representative participants. Attention should be given to funding and assisting in the education of potential participants for these types of studies. There is a concern that the outcomes of this report could have a negative influence on future participation, although the USPSTF has carefully delineated research needs and gaps.

Patients and clinicians might be concerned that an implication of this report is that screening is of no value and therefore the widespread underdiagnosis of MCI and dementia is of no consequence.⁹ That would be unfortunate. A negative interpretation of the value of cognitive screening in the primary care setting would ignore the potential value to patients and families of the knowledge of the patient's cognitive function. It is important for patients to appreciate whether their or others' concerns over their cognitive function portend an implication for cognitive dysfunction over time. Similarly, a report of no clinically relevant cognitive impairment might be useful and reassuring to the patient.

This issue will become even more salient with the inevitable availability of biomarkers for Alzheimer disease and other dementias such as amyloid and tau detected with positron emission tomography scans and blood biomarkers. Results from the IDEAS study suggested that both positive and negative results of biomarkers may lead to changes in clinician's behavior with respect to the use of medications to treat Alzheimer disease.¹⁰ Whether primary care screening will be useful in prioritizing biomarker use will require careful investigation.

As of 2011, the Medicare Annual Wellness Visit now includes reimbursement for cognitive screening.¹¹ Although the results of the updated report from the USPSTF would question the utility of screening, clinicians should carefully consider including this component in primary care assessment. There are several reasons that identification of cognitive impairment in primary care may be important and were not addressed with the USPSTF report. One report suggested that an estimated 10% of cognitive impairment may be due to "reversible" or partially reversible causes such as depression, medication adverse effects, and metabolic disorders.¹² Screening for cognitive impairment could lead to earlier identification and resolution of these conditions. In addition, screening may be useful for improving care for a variety of medical problems exacerbated by cognitive impairment. For example, if an older patient is having difficulty managing diabetes mellitus, it would be helpful for the clinician to have information about the patient's cognitive status and offer treatment modifications or additional support or oversight for medical care. In addition, serial cognitive assessments

most likely would be more valuable than a single cross-sectional assessment. While any individual assessment may be difficult to interpret, serial assessments of a patient over time may provide valuable information for the patient's care and planning for needed support.

The focus on cognitive impairment and the scholarly approach taken by the USPSTF has resulted in an important summary of the available evidence. However, the implications of these results in primary care settings are of some concern. The absence of evidence for benefit may lead to inaction. Primary care physicians are challenged with regard to the time allotted to assess patients, and this report might give them a rationale to discontinue or not undertake this component of the assessment. It would be a mistake if clinicians did not consider the value of screening for cognitive impairment on a case-by-case basis. With the development of disease-modifying therapies for some of the underlying neurodegenerative diseases that contribute to cognitive impairment, the importance of screening will become increasingly apparent.

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