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“When Will it Help?” Incorporating Lagtime to Benefit into Prevention Decisions for Older Adults

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Prevention holds the promise of maintaining good health by testing, diagnosing and treating conditions before they cause symptoms. However, prevention can harm as well as help when tests or treatments for asymptomatic conditions cause immediate complications. “Lagtime to benefit” (LtB) is defined as the time between the preventive intervention (when complications and harms are most likely) to the time when improved health outcomes are seen.⁽⁵⁾ Just as different interventions have different magnitudes of benefit, different preventive interventions have different LtB, ranging from 6 months for statin therapy for secondary prevention to >10 years for prostate cancer screening.⁽⁶⁾ Many standardized measures such as relative risk, odds ratio and absolute risk reduction quantify the magnitude of benefit (“How much will it help?”). However, the measures and methodologies to calculate a LtB (“When will it help?”) are underdeveloped and often not reported.

For older adults, the question “When will it help?” is just as important as “How much will it help?” If an older adult's life expectancy (LE) is substantially shorter than the LtB for a preventive intervention, performing that intervention exposes them to the immediate risks of the intervention with little likelihood of surviving long enough to benefit.⁽⁷⁾ In addition, the factors associated with limited LE, such as increased age, comorbidities and functional limitations are strong risk factors for complications and side effects of interventions, further increasing the chances that prevention would harm rather than help these patients. Many guidelines now recommend targeting preventive interventions such as colorectal and prostate cancer screening to those patients whose LE is greater than the LtB.⁽¹⁰⁾

Further, treatment for many chronic asymptomatic conditions in older adults also has immediate risks and delayed benefits. For example, treatment for hypertension can quickly lead to orthostatic hypotension and falls but decreased cardiovascular outcomes occur many

months or years later. Glycemic treatment for diabetes can cause immediate hypoglycemia, with the hope of preventing vascular complications in the future. Given immediate risks and delayed benefits, treatments of asymptomatic conditions should also be targeted to older patients whose LE is greater than the LtB.

Juxtaposing an older patient's LE and the LtB may help clinicians identify which patients are more likely to be helped by a preventive intervention and which patients are more likely to be harmed

1. Estimate the patient's life expectancy (LE)
2. Estimate the preventive intervention's lagtime to benefit (LtB)
- 3a If $LE \gg LtB$, the intervention may help and should generally be recommended.
- 3b If $LE \ll LtB$, the intervention is more likely to harm and generally should not be recommended.
- 3c If $LE \sim LtB$, the benefits versus harms of the preventive intervention are a “close call” and patient preferences (e.g., the degree of importance placed on the potential benefits and harms) should play the dominant role in decision making.

This article will describe how guidelines are already using age as a crude marker for LE and show how explicitly accounting for LE could improve prevention decisions. To help clinicians apply our framework, this article will outline ways to determine LtB and LE, highlighting how online LE calculators (i.e. eprognosis.com) may facilitate LE prediction. Finally, this article will demonstrate how this framework could be applied for a hypothetical patient during a Medicare Annual Wellness visit.

Moving Beyond Age as a Crude Marker for Life Expectancy

Many guidelines use age as the main criterion for recommending preventive interventions, with the specific age threshold determined by the average LE for the selected age group. For example, US Preventive Services Task Force (USPSTF) recommends routine colorectal cancer screening for older adults age 50-75.(10) One reason for the 75 year old threshold is that the *average* LE for 75 year old Americans (11.1 years in 200014) is similar to the LtB for colorectal cancer screening (10.3 years4).

However, older adults at the same age display tremendous heterogeneity in their LE. For example, although the average LE for a 75 year old is 11.1 years, the healthiest quartile of 75 year olds will live 15.7 years while the sickest quartile of 75 year olds will only live 5.9 years.(7) Featuring age cut-offs prominently in guidelines while burying the LE rationale focuses attention on age rather than the other key components of LE such as comorbidities or functional limitations.

Focusing on age rather than LE can lead to poor prevention decisions. For example, a 70 year old gentleman with oxygen-dependent lung disease and restricted mobility falls within the age range where routine colorectal cancer screening is recommended, but he has a limited LE and is unlikely to benefit from colorectal cancer screening. Conversely, an 80 year gentleman who walks 9 holes for golf weekly does not fall within the age range where

colorectal cancer screening is recommended, but has a good chance of surviving to benefit from screening.

Mortality indexes that incorporate comorbid conditions and functional status along with age are more accurate than age alone and could help clinicians improve LE prediction, resulting in improved prevention decisions.⁽⁶⁾ For example, mortality indexes that account for severe lung-disease and functional limitations would accurately identify the 70 year old gentleman as having a LE <10 years, while predicting that the 80 year old gentleman would have a LE >10 years. Thus, moving beyond age and explicitly accounting for LE by using mortality indexes (or otherwise accounting for key predictors of LE) would allow for more individualized decision-making.

How to Determine LtB for Preventive Interventions

Unlike magnitude of benefit, measures of LtB are rarely reported. Given the importance of LtB in determining whether a preventive intervention is appropriate for an older adult, all future research on preventive interventions should report the LtB (“when will it help?”) along with the magnitude of benefit (“how much?”). Further, for currently accepted preventive interventions where further studies are unlikely, original trial data should be re-analyzed using quantitative methods to determine the LtB.⁽⁴⁾

If quantitative meta-analyzed estimates are unavailable, the LtB can be estimated by reviewing Kaplan-Meier survival curves of the intervention and control groups. The time-point at which the curves last separate provides a qualitative estimate of the LtB for a given intervention.

Applying the Framework During An Annual Medicare Wellness Visit

Mr. A is a 75 year old gentleman who has hypertension (blood pressure 135/75), diabetes, chronic obstructive lung disease and difficulty walking several blocks. He is wondering whether he should be screened for colorectal cancer.

1) Determine the patient's life expectancy

Using published general mortality indexes for older adults from a systematic review, the Lee index is identified as appropriate for this patient. Using the web calculator at www.ePrognosis.com, the Lee index estimates that the patient has a 4 year mortality risk of 45%, suggesting a LE of approximately 5 years.

2) Determine the LtB for colorectal cancer screening and blood pressure control

Our recent study quantified the LtB for screening fecal occult blood testing to be 10.3 years for an absolute risk reduction of 1 death prevented for 1000 persons screened.⁽⁴⁾ Since the LtB exceeds the patient's LE, it is unlikely that he would benefit from screening; thus, screening would not be recommended.

The ADVANCE study suggests benefits of more intensive blood pressure control in older patients with diabetes appear at 12-18 months.⁽¹⁶⁾ Given Mr A's LE of 5 years, continuing more intensive blood pressure control would be recommended.

Conclusion

Preventing illness through early detection and treatment is a central component of care for older adults. However, nearly all prevention exposes patients to immediate risks for the hope of improved future health outcomes. Thus, it is critical to the answer to the question, “When will it help?” when individualizing preventive decisions in older adults. While research will continue to improve the accuracy of LE prediction and LtB, guidelines should move beyond age and explicitly encourage clinicians to juxtapose these 2 elements to improve the targeting of prevention.

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