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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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In Reply: The call by Drs Leese and Orkin for more robust research on community-based naloxone access bolsters our appeal for urgent scale-up in resources to support the study of overdose fatality prevention. A long-standing problem among nonmedical drug users, opioid overdose began reaching epidemic proportions in the United States by 2004. Yet it took until 2009 for the US government to issue its first research grants to evaluate overdose fatality prevention interventions. This funding is just starting to bear fruit: an epidemiological study recently concluded that locales that implemented community-based overdose prevention with naloxone rescue kits experienced reduced opioid overdose mortality compared with those that did not.[1]

Extensive evidence of the positive effect of community-based—as well as health care–based—opioid overdose fatality prevention programs already exists.[2-5] Although it is true that many of the earlier evaluations use surrogate end points (eg, ability to respond to an overdose, rescue self-report), surrogate end points are generally appropriate in research involving life-threatening conditions. Leese and Orkin cite one study that found that 16% fewer program participants reported calling 911 at the scene of an overdose after training compared with before[6]; it is not clear, however, if the training stressed the importance of calling for help even if individuals completely recovered. Since the study was conducted in 2004-2005, this has become a core element of overdose response training and numerous evaluations have failed to identify any significant reduction in help seeking (or other adverse effects).[2]

Leese and Orkin appear to suggest that randomized controlled trial evidence must come before any public health response to the opioid overdose epidemic, but there is currently no overdose prevention modality that meets this standard. Many lifesaving public health interventions have emerged without randomized controlled trials because the preponderance of observational and epidemiological research had been sufficient in the face of mounting harm, calling the ethics of experimental randomization into question. Examples include seat belts to prevent traffic fatalities and syringe access to curb human immunodeficiency virus transmission. We believe that, in view of the rapidly mounting overdose death toll, there is an imperative for intervention based on best-available evidence while advocating for additional research.

The principal purpose of our Viewpoint was to highlight a range of opportunities to prevent opioid overdose fatalities. The public health and cost-effectiveness evidence is now sufficient to scale-up prehospital naloxone use, but only as a part of a comprehensive approach that integrates safe opioid prescribing education, raising of public awareness, increased access to opioid agonist treatment, and a number of other underused tools. There is no question that opioid users deserve the same quality of research, care, and concern as other patients; this is precisely what motivated our call for a multipronged approach to prevent deaths attributable to opioid overdose. Urgent action to address this burgeoning epidemic is needed.

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. All authors reported receiving grants from the National Institute on Drug Abuse. Mr Beletsky reported being a consultant to the US Centers for Disease Control and Prevention and the Open Society Foundations. Dr Walley reported being a consultant for Social Sciences Innovations Corp and the Massachusetts Department of Public Health; being employed by the Boston Public Health Commission as the medical director of the opioid treatment program; and receiving a grant from the National Institute on Alcohol Abuse and Alcoholism. Dr Rich reported receiving funding from the National Institute of Allergy and Infectious Diseases.

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RESEARCH LETTER

Predicting 10-Year Mortality for Older Adults

To The Editor: Preventive interventions, such as cancer screening, expose patients to immediate risks with delayed benefits, suggesting that risks outweigh benefits in patients with limited life expectancy. Recent guidelines recommend considering patients' life expectancy when deciding whether to pursue preventive interventions with long

lag times to benefit (≥7 years) such as colorectal cancer screening and intensive glycemic control for diabetes.[1,2] However, most mortality indices have focused on short-term risk (≤5 years).[3,4] We examined whether our previously developed 4-year mortality index[5] accurately predicted 10-year mortality.

Methods. Like our previous analysis, this analysis uses the 1998 wave of the Health and Retirement Study (HRS), a nationally representative cohort of community-dwelling US adults older than 50 years. The HRS cohort was divided geographically into development (East, Central, and West; n=11 701) and validation (South; n=8009) cohorts. Self-report data were collected primarily through telephone interviews (response rate 81%).

The primary predictor was a 12-item mortality index (ages 60-64 years: 1 point, ages 65-69 years: 2 points, ages 70-74 years: 3 points, ages 75-79 years: 4 points, ages 80-84 years: 5 points, ages ≥85 years: 7 points; male sex: 2 points; current tobacco use: 2 points; body mass index <25: 1 point; diabetes: 1 point; nonskin cancers: 2 points; chronic lung disease: 2 points; heart failure: 2 points; difficulty bathing: 2 points; difficulty managing finances: 2 points; difficulty walking several blocks: 2 points; and difficulty pushing/pulling large objects: 1 point). Our outcome was death through 2008 (10-year mortality), confirmed with the National Death Index.

A risk score was calculated for each participant by summing the points for each risk factor present. We calculated the 10-year mortality rates across point scores. Kaplan-Meier methods were used to display the validation cohort survival experience, and logistic regression with bootstrapping was used to determine the C statistic, 95% confidence intervals, and 2-sided *P* values. A *P* value of less than .05 was considered statistically significant. Cox proportional hazards analyses yielded similar results.

The committee on human research of the University of California, San Francisco, approved this study with a waiver for informed consent. The statistical software used was STATA version 12.0 (StataCorp).

Results. Baseline characteristics of the cohort were described in detail previously.[5] Briefly, in the validation cohort, the mean (SD) age of participants was 67 (10) years; 56% (n=4516) were women, 11% (n=826) reported a history of cancer, 16% (n=1246) reported diabetes mellitus, 18% (n=1414) reported difficulty in at least 1 activity of daily living, and 32% (n=2527) died during the 10 years of follow-up. The development cohort had similar characteristics.[5]

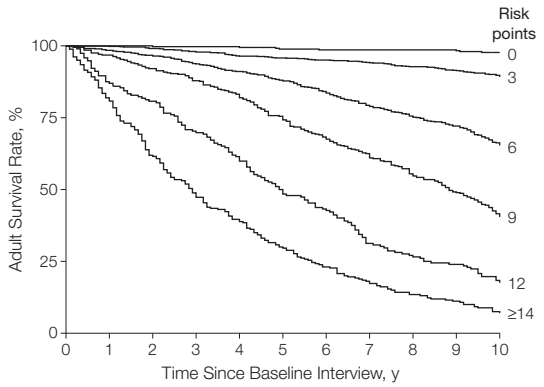
In the development cohort, 10-year mortality rates ranged from 2.5% (95% CI, 1.1%-3.9%; n=12/486) for participants with 0 points to 96% (95% CI: 94%-98%; n=298/310) for participants with 14 or more points. In the validation cohort, 10-year mortality rates ranged from 2.3% (95% CI, 0.7%-3.8%; n=8/354) to 93% (95% CI, 90%-96%; n=239/257) (TABLE). The C statistic for the index was 0.838 (95% CI, 0.830-0.846) in the development cohort and 0.834 (95% CI, 0.824-0.843) in the validation cohort. There was no evidence of poor calibration (validation cohort, Hosmer-Lemeshow *P*=.38).

Table. Validation of the Lee Index for 10-Year Mortality

		Observed[b]			
		Development Cohort (n = 11 701)		Validation Cohort (n = 8009)	
	Predicted Mortality (95% CI), %[a]	No. Died/ No. at Risk	Mortality (95% CI), %	No. Died/ No. at Risk	Mortality (95% CI), %
Point score					
0	2.8 (1.3-4.2)	12/486	2.5 (1.1-3.9)	8/354	2.3 (0.7-3.8)
1	4.0 (2.6-5.4)	22/739	3.0 (1.8-4.2)	25/489	5.1 (3.2-7.1)
2	6.0 (4.8-7.3)	67/1366	4.9 (3.8-6.1)	62/889	7.0 (5.3-8.6)
3	9.1 (7.6-11)	151/1474	10 (8.7-12)	100/971	10 (8.4-12)
4	14 (12-16)	214/1445	15 (13-17)	147/986	15 (13-17)
5	21 (19-23)	275/1330	21 (19-23)	195/842	23 (20-26)
6	30 (27-33)	368/1162	32 (29-34)	258/758	34 (31-37)
7	40 (36-43)	346/886	39 (36-42)	272/637	43 (39-47)
8	52 (48-55)	387/758	51 (48-55)	260/498	52 (48-57)
9	62 (58-66)	334/551	61 (57-65)	234/401	58 (54-63)
10	71 (67-76)	286/407	70 (66-75)	216/308	70 (65-75)
11	81 (76-85)	268/320	84 (80-88)	189/232	82 (77-87)
12	85 (81-90)	206/244	84 (80-89)	159/192	83 (78-88)
13	89 (85-94)	150/174	86 (81-91)	144/159	91 (86-95)
≥14	95 (93-98)	298/310	96 (94-98)	239/257	93 (90-96)
C statistic	0.847 (0.839-0.854)		0.838 (0.830-0.846)		0.834 (0.824-0.843)

[a] Calculated from the model with 12 risk factors.
[b] Calculated from a model with only risk points, with the 12 risk factors contributing to the risk point total.

Figure. Kaplan-Meier Survival in Validation Cohort by Selected Risk Points



No. at risk

Risk points							
	0	355	355	354	349	345	180
	3	973	964	939	919	884	476
	6	762	737	694	640	566	295
	9	404	372	336	275	221	113
	12	192	155	118	83	52	23
	≥14	260	161	103	60	35	14

The Kaplan-Meier survival curves showed that the differences in survival by point score seen at 4 years were magnified at 10 years (FIGURE).

Comment. We validated a mortality index that accurately stratified older adults into groups at varying risk for 10-year mortality. Extending the index from 4 to 10 years did not diminish the model discrimination (validation cohort, C statistics 0.817 vs 0.834; $P = .35$), suggesting that the risk factors important for 4-year mortality prediction are also important for 10-year mortality prediction. The model compares favorably with other mortality indexes that predict mortality beyond 7 years.[3]

One limitation of the index is that it was developed and validated in a single, large, national study and should be validated on a separate population to assess generalizability.

Patients identified by this index as having a high risk of 10-year mortality may be more likely to be harmed by preventive interventions with long lag times to benefit, whereas patients identified as having a low risk of 10-year mortality may be good candidates for such interventions.

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Author Contributions: Dr Lee had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Acquisition of data: Stijacic-Cenzer, Lee.
Analysis and interpretation of data: Cruz, Covinsky, Widera, Stijacic-Cenzer, Lee.
Drafting of the manuscript: Cruz, Stijacic-Cenzer, Lee.
Critical revision of the manuscript for important intellectual content: Covinsky, Widera, Lee.
Statistical analysis: Stijacic-Cenzer, Lee.
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CORRECTION

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