Death of a partner ranks first among the major life stressors.\(^1\) Centuries of literature and extensive quantitative research document the link between grief and adverse changes in physical and mental health.\(^2-4\) All-cause mortality risk and cause-specific mortality from accidents, cancer, heart disease, and suicide increase after spousal bereavement.\(^1,6\) Although it was long thought that perhaps the widowhood effect was a reflection of shared lifestyle and risk factors for spouses, increasingly rigorous controls for shared risk factors make this explanation unlikely. There is also growing recognition that in the period leading up to spousal death, there are often profound emotional and physical stressors that may affect the health of the surviving spouse. These stressors include caregiving and grief related to the illness and impending loss of a loved one, as well as financial worries for many spouses. Indeed, a major challenge in research on caregiving is distinguishing the mental and physical health effects of providing care from the effects of having a loved one who needs care, for example, a spouse with severe illness.

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Although the association between bereavement and mortality, sometimes dubbed “the widowhood effect,” has long been recognized, it has not been clear how to translate this empirical association into better health for the surviving spouse. As with many findings on social or psychosocial determinants of health, it is easy to dismiss the widowhood effect as unfortunate but inevitable. The article by Shah et al\(^7\) in this issue of *Circulation* upends this perspective by providing compelling evidence on modifiable mechanisms that elevate the cardiovascular risk of surviving spouses. This work fits within the social epidemiology translation framework, which notes that evidence on social risk factors for disease can be used to guide interventions to reduce the incidence of disease, to improve diagnoses so that patients receive timely treatment, and to improve disease management (Figure). Effective interventions may target the physical system or individuals and the contexts in which they live. The findings of Shah et al are most relevant for guiding interventions to improve the management of chronic conditions. Their results show that even in a patient population receiving an overall high quality of care, small differences in routine medical care and medication coverage emerge in the period before and immediately after bereavement. These differences likely contribute to worsened cardiovascular outcomes in the bereaved. This finding is good news because it suggests that the excess mortality in widows could be mitigated by improvements in healthcare delivery systems. The authors identified 12 722 bereaved subjects ≥60 years of age with preexisting cardiovascular disease (coronary heart disease, stroke, diabetes mellitus, or hypertension) and matched these individuals to married, nonbereaved control subjects in The Health Improvement Network, a representative primary care database from the United Kingdom. They examined routine annual care: doctor visits, blood pressure and cholesterol measurements, depression screening, influenza vaccine, and prescription coverage for lipid-lowering, antiplatelet, and renin-angiotensin system drugs.

In a clever design intended to rule out the possibility that bereaved individuals were intrinsically different from their nonbereaved counterparts, Shah et al used both within-subjects and between-subjects comparisons. Bereaved subjects served as their own controls for the within-person analyses. Most indicators of care, including primary care physician contacts, increased in the year after bereavement compared with care received by the same individual in the year before bereavement. For blood pressure and cholesterol screening, it was even possible to show that care 2 years before bereavement was better than in the year immediately before bereavement. In other words, these were not simply individuals unlikely to receive care but rather patients with established and successful care routines who fell through the cracks in the year before bereavement. Shah et al strengthen their within-person findings by adding a between-person comparison using a matched group of patients who were married at the time of the index patients’ bereavement. For most of the process-of-care measures, the proportion of the soon-to-be-bereaved subjects who received care in the year before their spouse’s death was lower than in the comparison group, but these differences were reduced or eliminated the year after bereavement. One interesting exception relates to primary care contacts. Frequency of primary care contacts in the year before bereavement was similar to contact frequency among the nonbereaved; however, in the year after bereavement, primary care contacts increased among surviving spouses.

Figure 2 of Shah et al reveals a powerful, and modifiable, picture: For all cardiovascular medications examined
(antiplatelet, lipid-lowering, and renin-angiotensin system drugs), coverage falls transiently in the peribereavement period beginning weeks before bereavement and lasting until ≈3 months after bereavement. Prior work has shown an immediate increased risk of myocardial infarction in the days after the death of a significant loved one. Data from the multicenter Determinants of Myocardial Infarction Onset Study showed a 21.1-fold increase in acute myocardial infarction within 24 hours of the death of a significant other in a case-crossover analysis of 1985 subjects. Risk declined over the ensuing week, with overall individual risk ranging from 1 excess myocardial infarction per 1394 exposed individuals at low baseline cardiovascular risk to 1 excess myocardial infarction per 320 exposed individuals at high risk. Case-crossover studies have been influential in widowhood effects research, but findings of short-term spikes in mortality in the immediate postbereavement period are consistent with the possibility that substantial risk accumulates in the prebereavement period, as the results of Shah et al suggest.

Other types of emotional stressors have also been linked to incident cardiovascular events. Episodes of anger, mental stress, natural disasters, and physical exertion are associated with a temporally related increased risk of myocardial infarction. In The Health Improvement Network subjects, the adverse physiological effects of stress—catecholamine release, increased myocardial oxygen demand, increased platelet adherence, and increased coronary vascular resistance—may be destructively exacerbated by a reduction in antiplatelet, lipid-lowering, and renin-angiotensin system medications. In patients at risk for myocardial infarction triggered by anger, aspirin has been shown to be protective, supporting the authors’ contention that a decline in essential cardioprotective medications in the setting of acute grief mediates adverse health outcomes.

Empirical evidence on the importance of social connections for health suggests that the overall effects of social isolation and loneliness are very general and influence many health outcomes; indeed, Elwert and Christakis showed that mortality risk in an individual was elevated after the death of his/her spouse for nearly every category of cause of death for either spouse, with the exception of Alzheimer or Parkinson disease mortality. However, there is also evidence that cardiac processes are especially responsive to psychological experiences and therefore to social contacts. In the late 1990s, intriguing accounts of a “broken heart” syndrome, Takotsubo syndrome, or stress-induced cardiomyopathy were described, reflecting a novel cardiac pathology linked specifically to psychological stress. This syndrome is characterized by ECG ST-segment elevation and left ventricular apical ballooning in the absence of causative coronary obstruction, triggered by emotional stress. First noted in a widow and in postmenopausal Japanese women, Takotsubo syndrome is likely mediated by the toxic effects of high catecholamine levels.

Previous studies evaluating the use of health care in the bereaved have shown contradictory results. In 1 study of bereaved spouses, the risk of a new illness and self-reported medication use were higher, but the number of doctor visits did not change. However, a study of widows showed reduced use of healthcare services by subjects with high levels of grief despite higher rates of hypertension and functional impairment. A study of Medicare claims data in a very large cohort of elderly couples showed a consistent decline in the delivery of preventive healthcare measures before and at the time of spousal death, with a particularly high mortality risk for the surviving partner in the first month of bereavement. In the present study of subjects with cardiovascular disease, a reduction in annual measures of blood pressure, cholesterol measurements, and cardiovascular drug therapy was noted in the year before bereavement.

The results of Shah et al suggest that the effect of widowhood on mortality could be mitigated by improving continuity of care systems. Translating these results into improved care will be easier in systems with an excellent
data infrastructure to provide timely information to clinical teams. To the extent that the patient must coordinate receipt of his or her own care, including tasks such as scheduling appointments or refilling prescriptions, interruptions in care during anguish personal episodes are more likely. Even care processes that are successful during “normal” periods may fail to provide effective care for the recently widowed. Identifying vulnerable surviving spouses cannot wait until after bereavement has already occurred; the Shah et al. results suggest the most important period may actually precede the spouse’s death or follow in the immediate wake of the bereavement. Although an alert primary care physician may notice and respond to the death of a patient’s spouse, in most care systems, the primary care physician would not learn of this death until the critical period of vulnerability for the survivor had already passed. The most effective remediation strategies are likely to be specific to the care delivery system and may require experimenting with alternative quality improvement strategies. For example, accountable care organizations may often provide care for both spouses and have the technological capacity to link health records of family members, thereby identifying spouses of gravely ill patients for targeted outreach. In many cases, the individual will already have frequent contacts with the health care system in the course of seeking care for his or her spouse. Such contacts may offer opportunities to improve care at the time when it is most likely to have a beneficial effect: before bereavement.

Acting on the findings of Shah et al could have important population health impacts. In the United States, the majority of older adults are married, and the vast majority of those marriages will end in widowhood. Although Shah et al focused on patients with a diagnosed cardiovascular condition, these diagnoses are extremely common and include a large fraction of older adults in the developed world. A key next question is the extent to which similar patterns emerge for other major life stressors such as the death or illness of parents or friends or even apparently smaller stressors such as moving home or retiring. Although these events may be associated with less grief, they similarly may transiently compromise the capacity of individual patients to effectively manage their healthcare needs. Furthermore, we need to understand whether similar breakdowns in care affect individuals without diagnosed cardiovascular conditions. The Shah et al. example was well chosen because it is possible to evaluate the importance of continued medication adherence for this population, but similar lapses in care may be relevant for others without these diagnoses. Regardless, it seems likely that structuring healthcare delivery systems to function well even when the patient has other major emotional and time demands is likely to improve care for all patients.

Research such as that by Shah et al provides an example of an emerging genre of translational social epidemiology, moving beyond documenting social determinants of health to identifying effective strategies to improve the health of vulnerable populations. Much research in social epidemiology has focused on determinants of disease incidence, but the social epidemiology translation framework highlights many additional avenues to translate evidence on social determinants of health to reduce morbidity and mortality (Figure). Many of the most promising new directions are likely to follow the strategies suggested by the research of Shah et al and focus on opportunities to improve the delivery of clinical care. As optimism about personalized and precision medicine becomes increasingly prominent, the Shah et al. findings remind us that health is not exclusively, or perhaps even primarily, a consequence of innate individual characteristics. Health is shaped by each person’s family, community, and social context. Indeed, the next generation of health care may be most effective if we move toward “contextualized” medicine in which we consider how the effects of genetic or clinical characteristics are modified by social networks, economic circumstances, environmental conditions, and other factors outside the traditional purview of clinical care. Currently, there is a remarkable evidence gap at the intersection of the personal and contextual. The work by Shah et al represents a step toward filling this gap.

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References


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Kristen K. Patton and M. Maria Glymour

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