

## Age-related Differences in the Consequences of Obesity on Cardiovascular Disease, Type 2 Diabetes, Osteoarthritis, Cancer, Physical Function, Osteoporosis, Cognitive Function, and Mortality Risk in the Elderly

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**ABSTRACT:** The purpose of this review was to describe the health consequences of obesity in older adults. Although obesity is associated with risk of cardiovascular disease, type 2 diabetes, hypertension, and dyslipidemia in the elderly, the association appears to be weaker in older compared to younger adults. Obesity in older adults is also associated with significantly higher risk of osteoarthritis, postmenopausal breast cancer, and impairments in physical function. However, the influence of obesity on mortality risk, osteoporosis, fracture risk, and cognitive function in older adults is not well understood. Intentional weight loss in obese older adults may be beneficial for metabolic health and physical function, but more long-term studies are needed. When examining the influence of obesity on different health parameters, future studies should consider using alternative measures of obesity beyond body mass index (BMI), such as waist circumference, and also investigate how body weight changes across the lifespan may influence health. The association between obesity and different health parameters in older adults appears to be more complex than in younger adults, and thus requires further investigation.

**KEYWORDS:** obesity, older adults, mortality risk, physical function, weight loss

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### Introduction

Older adults are a rapidly growing population, representing 13% of the United States population in 2010, and it is projected that they will represent 20% of the population by the year 2030.<sup>1</sup> Not only is the number of older adults increasing, but so is the prevalence of obesity in the elderly population. Over the past 30 years, the number of obese older adults has doubled<sup>2</sup> to 35.4% in 2012.<sup>3</sup> The growing prevalence of obesity is a public health concern worldwide. Obesity is now estimated to be responsible for 5% of all deaths globally<sup>4</sup> and is associated with an increased risk for many cardiometabolic risk factors, such as type 2 diabetes, dyslipidemia, hypertension, gall bladder disease, certain cancers, and coronary heart disease.<sup>5</sup> However, the negative effects of obesity on health are not as clear in older as in younger adults.<sup>6–8</sup> In fact, obesity has

been associated with beneficial effects in older adults, such as increased bone mineral density, decreased osteoporosis,<sup>9</sup> and most notably lower mortality risk.<sup>10</sup> Whether weight loss is safe for the obese elderly is also controversial.<sup>11</sup> However, there are many aspects of obesity that are detrimental in adults of all ages, and may be particularly relevant for elderly individuals, such as decreased physical function,<sup>12</sup> increased prevalence of type 2 diabetes,<sup>13</sup> and lower cognitive function.<sup>14</sup> Thus, the purpose of this review is to describe the health consequences of obesity in the older adult population. Specifically, this review will address the effects of obesity on metabolic health, mortality risk, physical function, osteoarthritis, osteoporosis, breast cancer, cognitive function, and the effects of weight loss in the obese older adult population. A summary of the findings is provided in Table 1.



## Metabolic Health Risk Associated with Obesity in the Elderly

Obesity is associated with negative health outcomes in both younger<sup>5</sup> and older adults.<sup>2</sup> The combination of older age and obesity may augment the risk for certain negative health risk factors, such as fasting glucose, type 2 diabetes, and hypertension.<sup>15</sup> However, others have reported that the relationship between obesity and metabolic health risk may differ by age. The association between obesity and metabolic health risk has been reported to be weaker in older adults compared to younger adults for prevalent cardiovascular disease,<sup>6</sup> hypertension, dyslipidemia, and type 2 diabetes.<sup>5,6,16</sup> Similarly, unlike in middle-aged and old adults, body mass index (BMI) was not associated with risk of future cardiovascular events in very old adults.<sup>17</sup> Thus, the association between obesity and metabolic health risk may not be consistent across the life span.

The increased obesity-related health risk that is observed in older adults may be partially because of the age-associated changes in body composition. Aging is associated with decreases in subcutaneous fat, increases in visceral adiposity, and redistribution of fat to ectopic sites such as skeletal muscle, liver, and heart.<sup>18–21</sup> These fat depots are associated with insulin resistance independent of overall body fat.<sup>22</sup> Further, these age-related differences in body composition can be observed independent of differences in body weight.<sup>23</sup> Waist circumference has also been reported to continuously increase throughout the life span, even when there is no change or a decrease in body weight.<sup>24,25</sup> A high waist circumference has been associated with increased risk of incident heart failure in old men and women independent of BMI.<sup>26</sup> Thus, BMI may mask the redistribution of fat to the abdominal area during aging, which is a potential explanation for why the association between BMI and health in older adults is augmented. Conversely, the association between obesity and aging may be weakened over time because of a “survival bias,” whereby obese middle-aged adults who have obesity-related conditions are more likely to die prematurely,<sup>9</sup> and may be less likely to be recruited or ineligible to participate in studies.<sup>27</sup> Further, obese adults who do survive into older age may be more resistant to the negative effects of obesity.<sup>9</sup> Finally, the decrease in height that is associated with aging may artificially elevate BMI.<sup>23</sup>

## Mortality Risk

As with morbidity, the association between obesity and mortality in the elderly population is less clear. Whereas obesity was associated with higher mortality risk in young and middle-aged adults, it was associated with similar or lower mortality risk than normal weight in older adults.<sup>7,8,28,29</sup> In fact, most studies that have assessed the obesity–mortality risk relationship in older adults using BMI report either lower mortality risk<sup>10,30,31</sup> or a similar mortality risk in obese compared to normal weight older adults.<sup>32–36</sup> However, some studies do report that obesity is associated with higher mortality risk in older adults.<sup>37,38</sup> Masters et al recently suggested

**Table 1.** Summary of the influence of obesity on health parameters in older adults.

CONDITION	ASSOCIATION WITH OBESITY	EFFECT OF AGE
Metabolic health risk	<ul style="list-style-type: none"> <li>Obese older adults are still at an increased risk for type 2 diabetes, hypertension, dyslipidemia, and cardiovascular disease</li> </ul>	<ul style="list-style-type: none"> <li>Weaker association compared to younger adults</li> </ul>
Mortality risk	<ul style="list-style-type: none"> <li>Waist circumference may be a better indicator of mortality risk than BMI in the elderly</li> <li>Important to consider patterns of body weight change across the lifespan</li> </ul>	<ul style="list-style-type: none"> <li>Much weaker association than younger adults</li> </ul>
Physical function	<ul style="list-style-type: none"> <li>Obesity is associated with greater risk of disability and impairments in mobility and activities of daily living</li> </ul>	<ul style="list-style-type: none"> <li>Stronger than in younger adults</li> </ul>
Osteoarthritis	<ul style="list-style-type: none"> <li>Most prevalent form of arthritis and exacerbated by obesity</li> <li>May reduce number of quality adjusted life years</li> </ul>	<ul style="list-style-type: none"> <li>Stronger than in younger adults</li> </ul>
Osteoporosis	<ul style="list-style-type: none"> <li>Obesity generally associated with increased bone mineral density</li> <li>Some evidence that a high waist circumference is positively associated with osteoporosis independent of body mass</li> <li>Association between obesity and osteoporotic fracture risk is not clear</li> </ul>	<ul style="list-style-type: none"> <li>Stronger than in younger adults</li> </ul>
Cognitive function	<ul style="list-style-type: none"> <li>Obesity may be associated with poorer executive functioning and global cognition</li> <li>Association between obesity and dementia is not well understood</li> </ul>	<ul style="list-style-type: none"> <li>Not well understood at any age</li> </ul>
Breast cancer	<ul style="list-style-type: none"> <li>Increased risk of breast cancer in obese postmenopausal women</li> <li>Obesity is associated with poor prognosis of breast cancer regardless of menopausal status</li> </ul>	<ul style="list-style-type: none"> <li>Risk of breast cancer grows stronger with age</li> <li>Prognosis of breast cancer worse at any age</li> </ul>
Weight loss	<ul style="list-style-type: none"> <li>Imperative to include an exercise component to a weight loss intervention to preserve lean mass</li> <li>Association between weight loss and mortality risk is not well understood</li> <li>Evidence for improved osteoarthritis-related pain, physical function, and metabolic health</li> </ul>	<ul style="list-style-type: none"> <li>Less clear than in young adults</li> </ul>



that survey-based estimates of the relationship between obesity and mortality risk in different age groups is confounded because of disparate cohort mortality and age-related survey selection bias.<sup>39</sup> In contrast to population-based studies that report that the association between obesity and mortality risk is weakened in older adults,<sup>7</sup> the association between obesity and mortality risk has been reported to actually grow stronger with age after accounting for age-related survey selection bias and cohort differences in mortality risk.<sup>39,40</sup>

As with morbidity, the attenuated association between obesity and mortality risk in elderly adults may also be explained by several factors, such as “survival bias” or the “obesity paradox”. The obesity paradox has been observed in patients with heart failure, hypertension, and coronary artery disease, and in those who have undergone cardiac revascularization,<sup>41</sup> wherein obese adults who experience cardiovascular events have a better prognosis than normal weight individuals. This may be because many diseases are associated with a catabolic state, and thus, obese individuals with heart failure may have more metabolic reserve than lean individuals.<sup>42</sup> Further, normal weight or lean persons who experience a cardiovascular event may have a greater genetic predisposition for cardiovascular disease or may be resistant to medical interventions.<sup>43</sup> Therefore, obesity in individuals with established cardiovascular disease or heart failure may have a survival advantage over normal weight patients, which could be an explanation for the lower mortality risk observed in obese older adults.

Limitations of BMI in older adults, such as decrease in height and redistribution of fat mass associated with aging,<sup>23</sup> may also obscure the true association between obesity and mortality risk. Waist circumference provides a better indicator of body fat distribution than BMI and thus may be a more useful measure to predict mortality in the elderly.<sup>30</sup> Waist circumference is associated with morbidity and mortality independent of BMI in young and old,<sup>44–47</sup> likely because of the strong association between waist circumference and visceral fat.<sup>48</sup> Older adults have more visceral fat than younger adults for a given BMI,<sup>49</sup> which may in part explain why older adults are at an elevated health risk for certain negative metabolic health outcomes.<sup>6</sup> Waist-to-hip ratio has also been demonstrated to be a better predictor of higher mortality risk in older adults than BMI.<sup>50,51</sup> Thus, because of the significant changes in body composition that may be masked by BMI in older adults, measures of body fat distribution, such as waist circumference or waist-to-hip ratio, may be more valuable than BMI when assessing mortality risk in older populations. However, Kuk and Ardern reported that the association between obesity and mortality risk remained negative when obesity was assessed using BMI or waist circumference.<sup>7</sup> Nevertheless, the association between obesity and mortality risk in older adults remains controversial.

This controversy may also be in part because of changes in obesity over the lifespan. In particular, body weight

fluctuations during middle age and between middle and old age may also be important to consider when assessing mortality risk in older adults. Several studies have reported that weight loss between middle age and old age<sup>52,53</sup> may be associated with higher mortality risk,<sup>53,54</sup> as weight loss is often associated with underlying disease in older adults.<sup>55</sup> Further, only weight gain during young and middle adulthood, and not weight gain later in life, is associated with higher mortality risk.<sup>53,54</sup> Conversely, other studies report that adults who are obese during middle age and continue to gain weight as an older adult<sup>56,57</sup> may have a significantly higher mortality risk compared to those who remain non-obese during both age periods. Further, even an obese stable body weight during both middle age and old age<sup>52</sup> may be associated with higher mortality risk compared to those who remain non-obese during both age periods. Therefore, it may be important to consider patterns of body weight across the lifespan and not just during older age when assessing mortality risk.

### Physical Function

Although underweight is associated with poorer physical function outcomes in older adults,<sup>58,59</sup> obesity also puts older adults at a higher risk for disability and physical function impairments, such as sit-to-stand dependence and difficulty walking short distances,<sup>60–66</sup> as well as impairments in activities of daily living.<sup>58,62,65</sup> Aging is associated with body compositional changes that may exacerbate the detrimental effects of a high body weight. Among older adults, both older age and obesity were associated with greater risk of falls and greater impairments in activities of daily living after a fall, while obesity was also associated with a lower probability of serious injury from a fall.<sup>67</sup> Sarcopenic obesity is an increase in fat mass that is masked by concomitant reductions in lean mass.<sup>68</sup> Sarcopenic obesity is associated with higher risk for chronic health conditions than having either condition alone, and it has recently been suggested that sarcopenic obesity is a strong risk factor for frailty,<sup>69</sup> leading to falls, worsening disability, co-morbid conditions, hospitalizations, and premature mortality.<sup>70</sup>

Older obese adults are at a higher risk for physical disability and lower quality of life, even when they are not at an increased risk for premature mortality. Several longitudinal studies have reported that obese older adults were at a significantly higher risk for developing arthritis and type 2 diabetes,<sup>44</sup> self-reported and measured functional limitations,<sup>35</sup> physical disability,<sup>10,44</sup> and recovering from a disability<sup>31</sup> despite having a similar or lower mortality risk as normal weight older adults. This may result in a large proportion of obese older adults living the last years of their life with functional disability and co-morbid health conditions.

### Osteoarthritis

Osteoarthritis is the most prevalent form of arthritis and one of the most common sources of pain and disability among



elderly adults.<sup>71</sup> There is evidence that osteoarthritis is more common in women than men.<sup>72</sup> Osteoarthritis is most common in older adults and is exacerbated by obesity, particularly in the knee and wrist.<sup>73,74</sup> Older women have been reported to have a higher prevalence of osteoarthritis than younger women with comparable obesity levels.<sup>75</sup> Further, a combination of older age and obesity has been reported to be associated with greater risk of knee osteoarthritis, increased prevalence of knee osteoarthritis-related pain, stiffness, disease severity, and decreased physical function,<sup>76</sup> as well as risk of total hip replacement because of osteoarthritis.<sup>77</sup> There is evidence that among older adults, obesity is associated with a greater risk of progressive knee osteoarthritis compared to non-obese;<sup>78</sup> however, this is not supported by all studies.<sup>79</sup> In older Americans, the number of quality-adjusted life years lost was greater in those with both obesity and knee osteoarthritis (3.5 years) compared to those with obesity (2.5 years) or knee arthritis (1.9 years) alone.<sup>80</sup> The time course of obesity may also be important in the development of osteoarthritis, as a sustained high BMI throughout adulthood was associated with the highest risk of osteoarthritis.<sup>81</sup> Therefore, there is unequivocal evidence that obesity is associated with risk and burden of osteoarthritis, particularly in older women.

### Osteoporosis

Osteoporosis is the age-related microarchitectural deterioration of bone leading to skeletal fragility and fractures.<sup>82</sup> Traditionally, obesity has been considered to be associated with increased bone mineral density and protective against osteoporosis,<sup>83–86</sup> likely because of a greater mechanical loading on the bone as a result of larger body mass.<sup>87</sup> One study reported that obese postmenopausal women developed osteopenia 3–5 years after post-menopause compared to normal weight women. However, this was mainly because of a higher bone mineral content at baseline as rate of bone loss was similar between lean and obese women.<sup>88</sup>

Whether obesity is indeed protective for risk of osteoporosis has recently been questioned. Zhao et al demonstrate that fat mass is negatively associated with bone mass after adjusting for the mechanical loading effect of body weight on bone mass.<sup>87</sup> Furthermore, young adult females who gained weight over five years had higher bone mineral density but lower bone strength when normalized for body weight compared to stable weight females.<sup>89</sup> Similarly, waist circumference has been positively associated with risk of osteoporosis<sup>90</sup> and inversely associated with bone mineral density<sup>90–93</sup> independent of body mass. Conversely, others have also reported that in older postmenopausal women, a high waist circumference may be beneficial for bone mineral density and osteoporosis<sup>94</sup> independent of BMI.<sup>86</sup>

The association between obesity and fracture risk is more controversial. A meta-analysis reported that low BMI was associated with an increased risk of osteoporotic fracture, whereas a high BMI was associated with a lower risk.<sup>95</sup> Age is

associated with increased risk of osteoporotic fracture, while higher body fat percentage is associated with lower osteoporotic fracture risk in women.<sup>96</sup> Conversely, another study reported that increasing age and BMI were associated with a higher risk of vertebral fracture, despite obese adults having a higher bone mineral density.<sup>97</sup> Furthermore, in postmenopausal Japanese women, obesity is associated with higher risk of vertebral fracture, and similar risk of femoral neck and long-bone fracture, independent of bone mineral density.<sup>98</sup> Finally, another study reported that obese women were more likely to experience incident ankle or upper leg fracture, but not wrist fracture, compared to non-obese women.<sup>99</sup> The complex association between obesity and fracture risk may be because of the differential effects of obesity on fall risk and bone strength. Although obesity may be associated with higher bone mineral density, it is also associated with increased fall risk.<sup>67</sup> Further, the increased subcutaneous adipose tissue thickness is also hypothesized to act as a cushion, protecting against bone fractures.<sup>100</sup> Nevertheless, whether or not obesity, as determined by BMI, body fat percentage or waist circumference is indeed beneficial for osteoporosis, or fracture risk is still not established and requires further investigation.

### Cognitive Function

Obesity may also have detrimental effects on the brain and is associated with increased risk of cognitive decline.<sup>14</sup> BMI has been reported to be independently associated with decreased attention, processing speed, and fine motor speed across the life span, and obesity-related deficits in executive function may be exacerbated with increasing age.<sup>101</sup> Furthermore, studies have demonstrated that obese older adults perform poorer on tests of memory<sup>14,102</sup> as well as tests that measure global cognitive function and psychomotor speed<sup>102</sup> than their leaner counterparts.

Obesity has also been associated with increased risk of specific types of dementia, such as Alzheimer's disease.<sup>103,104</sup> A higher BMI is also associated with lower brain volume in older patients who have already been diagnosed with mild cognitive impairment or Alzheimer's disease.<sup>105</sup> Some studies suggest that obesity is associated with risk of dementia in middle-aged adults but may be protective for dementia risk in older adults.<sup>106,107</sup> However, this paradoxical relationship may be partly explained by the fact that unintentional weight loss is positively associated with increasing severity of dementia, and may even be a symptom before diagnosis.<sup>108</sup> Clearly, more studies are needed to clarify the complex association between body weight, age, and dementia.

### Breast Cancer

Although there is evidence that obesity increases the risk for some types of cancer,<sup>109</sup> whether there is an interaction between obesity and age on cancer risk is less established. Most evidence supporting an interaction between age and obesity is for breast cancer. The proportion of women



diagnosed with breast cancer aged 65 and older has increased 3% over the past several decades, with an increase in obesity likely being a contributing factor.<sup>110</sup> Although both older age and obesity are associated with breast cancer risk,<sup>111,112</sup> the association between obesity and breast cancer risk may also depend on menopausal status.<sup>113,114</sup> While obesity is positively associated with breast cancer risk in postmenopausal women,<sup>115–118</sup> there is evidence that obesity has no association or an inverse association with breast cancer risk in premenopausal women.<sup>115,116,118</sup> In contrast, obesity was reported to be associated with a higher breast cancer risk for premenopausal women but not postmenopausal women in a population at high risk for breast cancer.<sup>119</sup>

Obesity is associated with worse prognosis for breast cancer regardless of menopausal status.<sup>120</sup> In both premenopausal and postmenopausal women, obesity has been associated with large tumor size and high histological grade.<sup>113,120</sup> This is because obese women are more likely to have their breast cancer detected via imaging techniques rather than clinical or self-examination, and have a higher proportion of large tumors and lymph node metastases at diagnosis compared to non-obese women.<sup>121</sup> Several studies have shown that obesity is associated with increased mortality risk in women with breast cancer independent of age.<sup>122–124</sup> Furthermore, in pre- and postmenopausal women, both adult obesity and significant weight gain after diagnosis have been associated with a higher mortality risk in women with breast cancer compared to those with normal weight and stable weight, respectively.<sup>125–127</sup> However, the negative effects of weight gain may be stronger among premenopausal women compared to postmenopausal women.<sup>120,128</sup> Therefore, there is strong evidence for an increased risk of breast cancer in obese postmenopausal women, but the prognosis for breast cancer seems to be worse for obese women regardless of menopausal status.

### Weight Loss in Older Adults

Whether obese older adults should attempt weight loss is a controversial issue.<sup>11</sup> Weight loss in the elderly has been associated with loss of bone mass,<sup>129–131</sup> increased risk of fractures,<sup>132</sup> higher mortality risk,<sup>57,133</sup> and is often accompanied by a loss of lean mass.<sup>131,134–136</sup> Moreover, a regain in body weight does not fully restore lean mass.<sup>137</sup> Therefore, preservation of lean mass may be critical when older adults undergo a weight loss intervention. Many studies have demonstrated that including exercise as part of the weight loss intervention is associated with positive health outcomes, and may allow older adults to lose a significant amount of fat mass with no or little loss in lean mass,<sup>130,134,138,139</sup> have increases in muscle strength,<sup>130,134,138,139</sup> lose less bone mineral density and bone mass,<sup>131,135</sup> have improvements in walking speed and physical function status,<sup>138</sup> have mobility-related self-efficacy and improvements in pain related to knee osteoarthritis,<sup>140</sup> as well as have improvements in insulin resistance, metabolic risk factors, and disabilities.<sup>141</sup>

When examining weight loss and health outcomes, it is important to distinguish between intentional and unintentional weight loss. Unintentional weight loss in the elderly is often associated with poor health and disease process leading to increased mortality risk.<sup>55</sup> However, even when weight loss is intentional the association with mortality risk in older adults is equivocal. Two recent randomized controlled trials reported that weight loss as a result of diet or a combination of diet and exercise in overweight and obese older adults was associated with no excess mortality risk compared to the control groups.<sup>142,143</sup> However, other observational studies have reported that intentional weight loss over the long term may be associated with higher mortality risk in overweight or obese middle-aged and older adults,<sup>144</sup> even when there is a lack of co-morbid conditions at baseline.<sup>144,145</sup>

A recent systematic review and meta-analysis of weight loss interventions in the elderly concluded that there is a lack of high-quality evidence to support weight loss in the elderly for metabolic health, physical function, or quality of life.<sup>146</sup> However, individual studies of weight loss interventions in the elderly have demonstrated improvements in osteoarthritis-related knee pain,<sup>147,148</sup> measures of physical functioning,<sup>138,149,150</sup> glucose tolerance,<sup>151</sup> inflammation,<sup>147,150</sup> HbA1c and muscle strength,<sup>152</sup> as well as decreased blood pressure and cardiovascular events.<sup>153</sup> Intentional and clinically significant weight loss in obese adults has also been associated with improvements in attention/executive functioning and memory.<sup>154–156</sup> However, only two studies have included older adults,<sup>155,156</sup> and more research is needed to confirm the association between weight loss and cognitive function in the obese elderly. In addition, to our knowledge there have been no studies that have attempted to determine the effects of intentional weight loss on cognitive function in obese adults with dementia. Although more randomized controlled trials are needed to further elucidate the association between weight loss and health outcomes in older adults, it seems that intentional weight loss, particularly when achieved partly through exercise, may be beneficial for metabolic health, physical function, and cognitive function in older obese adults.

In summary, the increased prevalence of obesity in the growing aging population is a major public health concern, and poses a huge threat to health care systems. Although obesity is associated with negative metabolic risk factors in the elderly, this association may be attenuated for certain risk factors in older compared to younger adults. There is much evidence to support that obesity in older adults is associated with significantly high risk of osteoarthritis, postmenopausal breast cancer, and poor breast cancer prognosis as well as impairments in mobility, activities of daily living, and physical functioning. However, the influence of obesity on mortality risk, osteoporosis, and fracture risk in the older adult population is still not well understood. Future studies should consider additional measures of obesity beyond BMI when assessing these relationships, such as waist circumference or waist-to-hip



ratio, as they are better measures of body fat distribution. In addition, considering how body weight changes across the lifespan may be equally important when examining risk for mortality, cognitive decline, and dementia. Although some studies have shown that weight loss interventions in obese older adults that include an exercise component are beneficial for metabolic health and physical function, more long-term studies are needed. In conclusion, the association between obesity, weight loss, and health in older adults is more complex than in younger adults, and thus the consequences of obesity in older adults require further investigation.

### Author Contributions

Wrote the first draft of the manuscript: REB. Contributed to the writing of the manuscript: JLK. Agree with manuscript results and conclusions: REB, JLK. Made critical revisions: JLK. All authors reviewed and approved of the final manuscript.

### DISCLOSURES AND ETHICS

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests. Provenance: the authors were invited to submit this paper.

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