



Review article

A review of the literature on wellbeing and modifiable dementia risk factors



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ABSTRACT

Wellbeing—defined broadly as experiencing one's life as enjoyable and fulfilling—has been associated with lower risk for Alzheimer's disease and related dementias. The mechanisms underlying this association are largely unknown. However, prior research and theory suggest that wellbeing impacts health behaviors and biological systems that are relevant to cognitive and brain health. Several of these factors have also been identified by the 2020 Lancet Commission on Dementia Prevention, Intervention, and Care as modifiable dementia risk factors. In the current review, we summarize and evaluate the evidence for associations between wellbeing and each of the 12 Lancet Commission risk factors. We found relatively consistent evidence for associations between higher wellbeing and lower levels of most of the risk factors: physical inactivity, social isolation, smoking, depression, hypertension, diabetes, hearing loss, traumatic brain injury, and air pollution. By contrast, we found evidence for only modest associations between wellbeing and education and mixed evidence for associations of wellbeing with alcohol use and body weight. Although most of the reviewed evidence was observational, longitudinal and experimental evidence suggests that many of the observed associations are likely bidirectional. These findings suggest that modifiable dementia risk factors may be mediators (i.e., intermediate steps in the causal chain) and/or confounders (i.e., variables that impact both wellbeing and dementia, and thus could induce a spurious association) of the association between wellbeing and dementia. We conclude by discussing next steps to test mediation hypotheses and to account for potential confounding in the relation between wellbeing and dementia.

Wellbeing has been robustly associated with lower dementia risk (see Willroth et al., 2023 for a review). Wellbeing is a multidimensional construct that includes positive affect (the general tendency to experience positive emotions such as joy, excitement, and contentment) (Watson et al., 1988), life satisfaction (a global assessment of a person's quality of life according to their chosen criteria) (Diener et al., 1985), sense of purpose (i.e., the extent to which one feels that they have personally meaningful goals and directions guiding them through life) (Hill et al., 2016; Ryff, 1989; Scheier et al., 2006), and dispositional optimism (i.e., the generalized, relatively stable tendency to expect good outcomes across important life domains) (Scheier and Carver, 2018), among other components (Willroth, 2022). Each of these components of wellbeing has been prospectively associated with better cognitive

function or lower dementia risk (see Willroth et al., 2023), highlighting the potential promise of targeting wellbeing in dementia prevention efforts. However, the mechanisms linking higher wellbeing to lower dementia risk remain largely unknown.

The 2020 Lancet Commission on Dementia Intervention, Prevention, and Care identified 12 modifiable dementia risk factors that together account for approximately 40 % of the population variability in risk for developing dementia: physical inactivity, social isolation, smoking, depression, hypertension, diabetes, hearing loss, higher body weight, alcohol use, education, traumatic brain injury, and air pollution (Livingston et al., 2020). Prior research has shown that wellbeing may impact several of these risk factors, suggesting that these factors may be key mechanisms through which wellbeing transmits its protective

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effects (see Fig. 1 Panel A). At the same time, several of these risk factors have been shown to impact wellbeing, suggesting that they may be potential confounders (i.e., variables that impact both wellbeing and dementia, and thus could induce a spurious association) to consider in the relation between wellbeing and dementia (see Fig. 1 Panel B).

In the present review, we summarize the evidence for associations between wellbeing and each of the Lancet Commission's modifiable dementia risk factors. When available, we highlight research methods that support causal inference, such as experiments and randomized controlled trials, as well as observational methods that may support causal inference under certain conditions. This information will inform future research on mechanisms that link higher wellbeing to lower dementia risk and will point to potential confounders that should be accounted for in future work on wellbeing and dementia.

1. Wellbeing and dementia

Previous research has found that multiple aspects of wellbeing are associated with better cognitive function (Bell et al., 2022; Dewitte et al., 2021; Gerstorff et al., 2007; Hittner et al., 2020; G. Kim et al., 2019; Windsor et al., 2015; Wingo et al., 2020), lower incident cognitive impairment and dementia (Bell et al., 2022; Boyle et al., 2010; Peitsch et al., 2016; Rawtaer et al., 2017; Sutin et al., 2018), and greater cognitive resilience to dementia-related neuropathology (Boyle et al., 2012; Willroth et al., 2022). These effects have been observed at the between- and within-person levels, in cross-sectional and longitudinal studies, and when adjusting for potential confounders such as socio-demographic characteristics and apolipoprotein E (APOE) genotype. Additionally, evidence from a Mendelian randomization study, a statistical technique that combines genetic and epidemiological data to estimate causal effects, is consistent with a causal effect of wellbeing on Alzheimer's disease risk (Ma et al., 2021).

Theoretical models and empirical evidence suggest that wellbeing may impact dementia through behavioral, social, and biological pathways. For example, research suggests that people with higher wellbeing are more likely to engage in health-protective behaviors such as physical exercise (e.g., Baumann et al., 2017; Pfund et al., 2022), are less likely to engage in health-detrimental behaviors such as smoking (e.g., Kim et al., 2020; Morimoto et al., 2018), and are more likely to have positive social experiences that are beneficial for health (e.g., Pfund et al., 2022; Weston et al., 2021). In addition, wellbeing is associated with physiological systems implicated in cognitive and brain health including better immune, endocrine, and cardiovascular function (see Cross and Grimm,

2018; Pressman and Cohen, 2005; Ryff et al., 2004). Research is needed to directly test these and other plausible mechanisms of associations between wellbeing and dementia. Identifying mechanisms underlying the association between wellbeing and dementia will improve our understanding of why wellbeing is associated with dementia risk and would directly inform psychosocial prevention and intervention efforts (see Discussion for more details).

2. Wellbeing and modifiable dementia risk factors

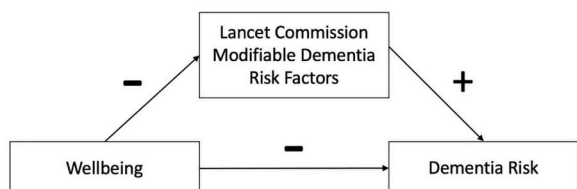
In the following sections, we review evidence for associations between wellbeing and each of the 2020 Lancet Commission modifiable dementia risk factors (see Table 1 for summary). Our goal is to provide a high-level overview of research on associations between wellbeing and all 12 risk factors rather than an in-depth or systematic review of any specific component of wellbeing or any individual risk factor. Given this broad scope, we did not conduct a formal systematic review. One author was assigned to each risk factor and that author used Google Scholar and/or PubMed to identify relevant studies published in the English language. In many cases, search engine results were combined with the authors' own knowledge of the published literature. Research designs that support causal inference were prioritized as well as systematic reviews and meta-analyses. Search terms were selected based on the following working definition of wellbeing. Specifically, we focused on positive aspects of wellbeing such as trait positive affect, life satisfaction, sense of purpose, Ryff's six-factor model of psychological wellbeing (Ryff, 1989), and dispositional optimism. Our working definition of wellbeing excluded aspects of psychological functioning that conceptually overlap with the Lancet Commission risk factors, such as depression, health-related quality of life, and social wellbeing. Finally, when relevant, we also included search terms and reviewed research on the inverse of the risk factors, such as physical activity in addition to physical inactivity and social activity and social support in addition to social isolation.

3. Physical inactivity

Significant research has considered associations between wellbeing and physical (in)activity. This accumulation of work has been motivated by the common public interest in whether exercise makes people feel better, which could then help motivate them to continue being physically active. Numerous studies have pointed to positive associations between wellbeing and physical activity across multiple different samples (for reviews, see Martin Ginis et al., 2010; Netz et al., 2005; Wiese et al., 2018; Zhang and Chen, 2019). A meta-analytic review of more than 150 observational and experimental studies found that, on average, physical activity held a small-to-moderate positive association with wellbeing (Buecker et al., 2021). Given the large number of studies reviewed, the authors were able to consider multiple moderators of these effect sizes. For instance, the effect size did not systematically differ across studies employing different measures of wellbeing (e.g., quality of life, affect, happiness, or life satisfaction). Moreover, associations did not seem to differ based on physical activity type or intensity. A review of studies on sedentary behavior came to a similar conclusion: higher wellbeing was associated with less sedentary behavior, though effect sizes depended on the measurement of sedentary behavior (Sui et al., 2021).

A handful of studies have found evidence for prospective effects of higher wellbeing on later increases in physical activity and decreases in inactivity across multiple measures of wellbeing (Kekäläinen et al., 2020; Kim et al., 2020; Yemiscigil and Vlaev, 2021; Zhang and Chen, 2021). One study applied a random intercept cross-lagged panel model to five waves of monthly data and found bidirectional within-person associations between changes in moderate (but not vigorous) physical activity and later sense of purpose, and vice versa (Pfund et al., 2022). Random intercept cross-lagged panel models afford several benefits for

A. Lancet Commission Modifiable Dementia Risk Factors may Mediate the Relation between Wellbeing and Dementia Risk



B. Lancet Commission Modifiable Dementia Risk Factors may Confound the Relation between Wellbeing and Dementia Risk

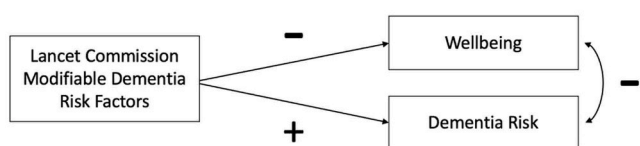


Fig. 1. Schematic depiction of potential causal relations among wellbeing, modifiable dementia risk factors identified by the Lancet Commission, and dementia.

Table 1
Summary of evidence for associations between wellbeing and modifiable dementia risk factors.

Risk Factor	Evidence for an Association between Wellbeing and the Risk Factor	Evidence for Potentially Causal Effects of Wellbeing on the Risk Factor	Evidence for Potentially Causal Effects of the Risk Factor on Wellbeing
	Research in this column was either cross-sectional or employed longitudinal methods that provide limited information on potential causal relations (e.g., concurrent associations, correlated change, prospective effects across only two time points, or longitudinal studies that did not account for prior levels of the outcome variable).	Research in this column experimentally manipulated wellbeing, or used observational methods that may support causal inference under certain conditions (e.g., cross-lagged effects of wellbeing in random intercept cross-lagged panel models; prospective effects of wellbeing on subsequent disease incidence in initially healthy samples). Threats to causal inference are discussed.	Research in this column experimentally manipulated the risk factor, or used observational methods that may support causal inference under certain conditions (e.g., cross-lagged effects of the risk factor in random intercept cross-lagged panel models). Threats to causal inference are discussed.
Physical Inactivity	Evidence for negative association between wellbeing and physical inactivity (Kekäläinen et al., 2020; Kim et al., 2020; Martin Ginis et al., 2010*; Pfund et al., 2022; Sui et al., 2021*; Wiese et al., 2018*; Yemiscigil and Vlaev, 2021; Zhang and Chen, 2019*; Zhang and Chen, 2021).	Month-to-month increases in sense of purpose predict subsequent increases in moderate (but not vigorous) intensity physical activity, even when accounting for the between-person association and autoregressive effects in a random intercept cross-lagged panel model (Pfund et al., 2022). Unmodeled time-varying confounders could also account for the observed cross-lagged effect.	Meta-analytic evidence for experimental and prospective effects of physical activity interventions and physical activity levels on higher subsequent wellbeing (Buecker et al., 2021*; Marquez et al., 2020*; Netz et al., 2005*). However, limited preregistered and high-powered experimental research on this topic (Folk and Dunn, 2023*). Among high-powered experimental research, consistent evidence for short-term effects of physical activity interventions on wellbeing, but evidence for long-term effects are more limited (Folk and Dunn, 2023*). Month-to-month increases in moderate (but not vigorous) intensity physical activity predict subsequent

Table 1 (continued)

Risk Factor	Evidence for an Association between Wellbeing and the Risk Factor	Evidence for Potentially Causal Effects of Wellbeing on the Risk Factor	Evidence for Potentially Causal Effects of the Risk Factor on Wellbeing
Social Isolation	Evidence for a negative association between wellbeing and social isolation (Kelly et al., 1987*; Macdonald & Hülür, 2021; Mei et al., 2021*; Pinquart, 2002*; Pinquart and Sörensen, 2000*; Pfund et al., 2020*; Pfund et al., 2022; Rafnsson et al., 2015; Weston et al., 2021).	More experimental or prospective longitudinal research is needed to test the effects of changes in wellbeing on later changes in social isolation and related factors.	increases in sense of purpose, even when accounting for the between-person association and autoregressive effects in a random intercept cross-lagged panel model (Pfund et al., 2022). Unmodeled time-varying confounders could also account for the observed cross-lagged effect. Experimental research provides evidence for causal effects of social activity on increased in-the-moment wellbeing (Kardas et al., 2022; Schroeder et al., 2022); however, it remains an open empirical question whether social isolation and related factors have a causal effect on long-term changes in wellbeing. Limited research.
Smoking	Evidence for a negative association between wellbeing and smoking behavior (Carvajal et al., 2000*; Kim et al., 2020; Morimoto et al., 2018*; Yang and Ma, 2021*; Zullig et al., 2001*).	Individuals who received smoking cessation treatment that targeted positive affect had higher odds of smoking abstinence across follow-up time points relative to individuals who received a standard smoking cessation treatment (Kahler et al., 2015). Replication is needed.	
Depression	Evidence for a negative association between wellbeing and depression (Burns et al., 2022; Grant et al., 2013; Green et al., 1992; Keyes et al., 2010; Koivumaa-Honkanen et al., 2004; Koivumaa-Honkanen et al., 2001; Li et al., 2022*; Liu et al.,	People with low wellbeing were twice as likely to experience high levels of depression 10 years later when accounting for prior levels of depression and other potential confounders such as sociodemographic	Increases in depression predict subsequent decreases in wellbeing, even when accounting for the between-person association and autoregressive effects in random intercept cross-

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Table 1 (continued)

Risk Factor	Evidence for an Association between Wellbeing and the Risk Factor	Evidence for Potentially Causal Effects of Wellbeing on the Risk Factor	Evidence for Potentially Causal Effects of the Risk Factor on Wellbeing
	2009*; Samaranayake and Fernando, 2011*).	characteristics and personality traits (Wood and Joseph, 2010). Unmodeled confounders could also account for the observed findings. People with low wellbeing at baseline were significantly more likely to use mental health services in the subsequent five years, even when adjusting for use of mental health services in the prior three years (Michalski et al., 2022). However, this study did not control for prior levels of depression. Increases in wellbeing predict subsequent decreases in depression, even when accounting for the between-person association and autoregressive effects in random intercept cross-lagged panel models (Gudmundsdottir et al., 2023 ; Joshnloo and Blasco-Belled, 2023). Unmodeled time-varying confounders could also account for the observed cross-lagged effects.	lagged panel models (Gudmundsdottir et al., 2023 ; Joshnloo and Blasco-Belled, 2023). Unmodeled time-varying confounders could also account for the observed cross-lagged effects.
Hypertension	Evidence for a negative association between wellbeing and hypertension (Blanchflower and Oswald, 2008* ; Kubzansky et al., 2020 ; McLeish et al., 2022* ; Mojon-Azzi and Sousa-Poza, 2011* ; Ostir et al., 2006* ; Szabo et al., 2020*). However, null findings have also been observed for some types of wellbeing (Coelho et al., 2000* ; Szabo et al., 2020*).	Higher wellbeing has been prospectively associated with reduced risk for subsequently developing hypertension among adults without hypertension at baseline (Richman et al., 2005, 2009 ; Steptoe and Wardle, 2005 ; Trudel-Fitzgerald et al., 2014). However, null findings have also been observed for some types of wellbeing (Limited research with some longitudinal evidence that hypertension onset does not impact longitudinal trajectories of sense of purpose (Hill et al., 2021).

Table 1 (continued)

Risk Factor	Evidence for an Association between Wellbeing and the Risk Factor	Evidence for Potentially Causal Effects of Wellbeing on the Risk Factor	Evidence for Potentially Causal Effects of the Risk Factor on Wellbeing
		Guimond et al., 2021 ; Trudel-Fitzgerald et al., 2014). Moreover, although these studies excluded people with hypertension at baseline, unmodeled time-varying or time-invariant confounders could also account for the observed findings.	
Diabetes	Wellbeing is negatively associated with diabetes and positively associated with glucoregulation in adults with and without diabetes (Boylan et al., 2017* ; Celano et al., 2013* ; Papanas et al., 2010*).	Higher wellbeing has been prospectively associated with reduced risk for subsequently developing diabetes (Boehm et al., 2015 ; Okely and Gale, 2016 ; Shirom et al., 2012) and better glucoregulation (Hafez et al., 2018) among adults without diabetes at baseline. Although these studies excluded people with diabetes at baseline, unmodeled confounders could also account for the observed findings.	Limited research with some longitudinal evidence that diabetes onset does not impact longitudinal trajectories of sense of purpose (Hill et al., 2021).
Hearing Loss	Wellbeing is positively associated with hearing loss (Cao et al., 2023 ; Merten et al., 2021* ; Sutin et al., 2022).	Among adults who reported good to excellent hearing at study baseline, higher sense of purpose has been associated with lower risk of developing subsequent self-reported or objective hearing loss (Sutin et al., 2022). Although this study excluded people with self-reported hearing loss at baseline, unmodeled confounders could also account for the observed findings.	Limited research.
Higher Body Weight	Evidence is mixed with some support for a positive relation between wellbeing and higher body weight (e.g., Archangelidi and Mentzakis, 2018* ;	Evidence is mixed. Among individuals with a body mass index between 23 and 28 at study baseline, higher sense of purpose has been associated	Longitudinal increases in wellbeing have been shown to predict subsequent increases in body weight, even

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Table 1 (continued)

Risk Factor	Evidence for an Association between Wellbeing and the Risk Factor	Evidence for Potentially Causal Effects of Wellbeing on the Risk Factor	Evidence for Potentially Causal Effects of the Risk Factor on Wellbeing
	Fang et al., 2022 ; Morris et al., 2010*) and some support for a negative association (e.g., Jackson et al., 2015 ; Kuroki, 2016*).	with lower risk of subsequently developing a body mass index outside of this range (Kim et al., 2020). Although this study focused on people with a body mass index between 23 and 28 at study baseline, it did not control for prior body weight and other unmodeled confounders could also account for the observed findings. Longitudinal increases in wellbeing have been shown to predict subsequent increases in body weight, even when accounting for the between-person association and autoregressive effects in random intercept cross-lagged panel models (Fang et al., 2022). Unmodeled time-varying confounders could also account for this finding. A positive psychological intervention designed to increase wellbeing demonstrated statistically non-significant effects on changes in body mass index (Kushlev et al., 2020).	when accounting for the between-person association and autoregressive effects in random intercept cross-lagged panel models (Fang et al., 2022). Unmodeled time-varying confounders could also account for this finding.
Alcohol Use	Evidence is mixed with some support for a negative association (Koivumaa-Honkanen et al., 2012 ; Zullig et al., 2001*); some support for a positive association (Patrick et al., 2016) particularly in the moment of alcohol use (Dora et al., 2023 ; Geiger and MacKerron, 2016); and some null findings (Burriss et al., 2009* ; Grant et al., 2009* ; Sin et al., 2015). Other research suggests that it might depend on the type of use (Geiger and	Limited research.	Limited research.

Table 1 (continued)

Risk Factor	Evidence for an Association between Wellbeing and the Risk Factor	Evidence for Potentially Causal Effects of Wellbeing on the Risk Factor	Evidence for Potentially Causal Effects of the Risk Factor on Wellbeing
Education	MacKerron, 2016 ; Parackal and Parackal, 2017*). Most correlational studies of educational attainment and wellbeing have found either no association or a modest positive association (see Helliwell et al., 2012^ for brief review). The relation may also be nonlinear such that individuals with secondary education have higher wellbeing than individuals with either primary or tertiary education (Hartog and Oosterbeek, 1998).	Limited research.	Policies that increase educational attainment have demonstrated small positive effects on wellbeing, largely through their effects on income (e.g., Oreopoulos and Salvanes, (2011)).
Traumatic Brain Injury	Traumatic brain injury survivors report lower wellbeing than individuals without traumatic brain injury (Dijkers, 2004*).	Limited research.	Traumatic brain injury survivors report lower wellbeing after injury compared to before injury (Dijkers, 2004*).
Air Pollution	Wellbeing tends to be lower in countries (Luechinger, 2010* ; Welsch, 2007*) and regions (Brown et al., 2003* ; Dijkers, 2004* ; Faul and Coronado, 2015* ; Jehu et al., 2022* ; Kirkcaldy and Furnham, 2000* ; Ravert et al., 2013*) with more air pollution (for review see (Li et al., 2018*)). In addition, self-reported air pollution exposure has been associated with lower wellbeing (Li et al., 2014* ; Rehdanz and Maddison, 2008*). Research using air pollution modeling systems to model exposure in specific locations at particular times provides additional support for an association between individual-level air pollution exposure and wellbeing (Ambrey et al., 2014 ; MacKerron and Mourato, 2009 ; Orru et al., 2016 ; Zhang et al., 2017).	Limited research.	Limited research.

Note. *Cross-sectional. ^Review or meta-analysis.

causal inference because they disentangle between-person variance from within-person variance and account for autoregressive effects of both variables in the model. Thus, these effects can be interpreted as potentially causal. However, unmodeled time-varying confounders could lead to spurious cross-lagged effects.

There is somewhat more evidence for effects in the opposite causal direction, such that engagement in physical activity promotes greater wellbeing (Buecker et al., 2021). Experimental studies that included a physical activity intervention evidenced stronger effect sizes compared to correlational studies (Buecker et al., 2021), suggesting that the effects of physical activity on higher wellbeing may be causal. Further support for the beneficial effects of physical activity comes from the quality of life literature, where a systematic review of randomized controlled trials and longitudinal studies suggested “strong” evidence for the positive effects of physical activity on later wellbeing (Marquez et al., 2020). It is noteworthy that the strength of evidence differed across groups; for instance, there was limited support for the benefits of physical activity on wellbeing among youth, and the researchers called for further work among individuals with dementia given limited evidence in this population. In contrast to the total body of experimental evidence, a recent systematic review and meta-analysis found few experimental studies of the effects of physical activity interventions on later wellbeing when focusing only on studies that were well-powered and preregistered (Folk and Dunn, 2023). Among high-powered experimental research, this review found consistent evidence for short-term effects of physical activity interventions on increased wellbeing, but evidence for long-term effects was more limited.

Taken together, the current literature suggests that wellbeing is positively associated with physical activity. The effect appears to be bidirectional, with experimental evidence for the effects of physical activity on higher wellbeing, and strong observational evidence for the effects of at least some types of wellbeing on higher subsequent levels of at least some types of physical activity.

4. Social isolation

In this section, we review evidence for associations between wellbeing and a range of constructs related to social isolation, including quantity and quality of social interactions, social network size, relationship quality, and social support. Having few social interactions or a small social network are measures of social isolation, and each of these other social constructs may impact the degree to which individuals *feel* socially isolated. Social factors are so consistently tied to wellbeing that certain theoretical models of wellbeing have included social components in their definitions of wellbeing (e.g., (Disabato et al., 2019; Keyes, 1998; Ryff, 1989; Willroth, 2022)). Theoretical accounts of the association between wellbeing and social factors generally suggests a reciprocal relationship: positive social interactions and strong and supportive social relationships support wellbeing, and in turn, wellbeing promotes positive social interactions and supports the formation and maintenance of strong and supportive social bonds.

Consistent with these theoretical accounts, positive social interactions have been associated with a higher sense of purpose at both the between- and within-person levels (Pfund et al., 2022). In other words, people who generally have more positive social interactions report having a higher sense of purpose, and, on days in which people have more positive social interactions than usual, they report a higher sense of purpose than usual (Pfund et al., 2022). These patterns align with findings prior to and following the start of COVID-19, where older adults reported more experiences of positive affect when feeling satisfied with their social interactions (Macdonald & Hülür, 2021). More frequent social interactions and larger social networks have also been associated with higher wellbeing among older adults (Kelly et al., 1987; Mei et al., 2021; Rafnsson et al., 2015). Above and beyond the *quantity* of social interactions, meta-analytic work has found that the *quality* of social contact may be even more important for wellbeing (Pinquart,

2002; Pinquart and Sörensen, 2000). High quality social relationships may improve wellbeing, and at the same time, people with higher wellbeing may be more likely to perceive their social interactions and relationships positively.

Social support, or the extent to which people perceive that their emotional and practical needs are being met by their social networks, may be a key mechanism linking social interactions to wellbeing. For example, people who experienced increases in perceived social support and decreases in social strain over time also increased in sense of purpose over time (Weston et al., 2021). Higher social contact frequency was also associated with a higher sense of purpose, though perceived increases in social support and perceived decreases in social strain were still associated with increases in sense of purpose above and beyond social contact frequency. Associations between social factors and wellbeing can also be found in specific relationships. For example, people with a higher sense of purpose generally have more satisfying and stable friendships and parental relationships (Pfund et al., 2022) and people with higher quality romantic relationships (e.g., relationship satisfaction, commitment) generally report having a higher sense of purpose and experiencing more positive emotions (Pfund et al., 2020). Moreover, work has highlighted that better romantic relationship quality is associated with subsequent increases in sense of purpose across three months (Pfund and Hill, 2022). By contrast, sense of purpose was not associated with subsequent changes in romantic relationship quality; however, this may have been because romantic relationship quality was highly stable across this relatively short time interval making it difficult to predict changes in romantic relationship quality.

Taken together, theoretical models suggest that wellbeing shapes individuals' social experiences, and, in turn, these social experiences shape later wellbeing. Longitudinal evidence is generally consistent with these theoretical models, such that changes in social factors tend to coincide with changes in wellbeing. However, most longitudinal research on this topic has focused on correlated change, rather than disentangling prospective effects of changes in social factors on later changes in wellbeing and vice versa. Experimental research provides evidence for causal effects of social activity on increased in-the-moment wellbeing (Kardas et al., 2022; Schroeder et al., 2022); however, it remains an open empirical question whether social activity has causal effects on long-term changes in wellbeing. More experimental or prospective longitudinal research is needed to test the effects of changes in wellbeing on later changes in social factors.

5. Smoking

Cross-sectional research has found that people higher in wellbeing are less likely to smoke cigarettes (Morimoto et al., 2018; Zullig et al., 2001). Moreover, prospective longitudinal research has found that among people who did not smoke at study baseline, individuals with higher sense of purpose were less likely to subsequently start smoking (Kim et al., 2020). However, all of the people who started smoking during the study period were former smokers at the start of the study period; thus, reverse causality is also plausible such that individuals' former smoking status could have contributed to their lower sense of purpose at study baseline. Among middle school students, multiple aspects of wellbeing have been cross-sectionally associated with lower likelihood of smoking and prospectively associated with less smoking escalation across two time points (Carvajal et al., 2000).

Studies examining the role of positive affect in smoking cessation treatment have found mixed evidence for a link between positive affect and smoking behavior. For example, one study found that individuals who received smoking cessation treatment that targeted positive affect had higher odds of smoking abstinence across follow-up time points relative to individuals who received a standard smoking cessation treatment (Kahler et al., 2015). These results were stronger among individuals who used more positive affect strategies and who experienced higher positive affect. In contrast to these findings, another study did not

find an association between baseline positive affect and odds of smoking abstinence among individuals receiving smoking cessation treatment (Heffner et al., 2018). These divergent results could be because the Kahler et al. (2015) study specifically targeted positive affect in the intervention, whereas the Heffner et al. (2018) study simply assessed positive affect at study baseline. There is also some evidence that recently stopping smoking is associated with higher emotional well-being (Yang and Ma, 2021). However this study was cross-sectional and thus it is unclear whether stopping smoking increased emotional well-being, people with higher wellbeing were more likely to stop smoking, or if a third variable influenced both wellbeing and smoking behavior.

A few mechanisms have been proposed to explain the association between higher wellbeing and less smoking. First, people with higher wellbeing may be more proactive in protecting their health. Specifically, higher optimism and a higher sense of purpose have each been associated with more persistence in engaging with health-adaptive behaviors, greater avoidance of unhealthy habits, and the ability to persist in goal-directed behaviors (Carvajal et al., 2000; Kelloniemi et al., 2005; Kim et al., 2020; Morimoto et al., 2018; Steptoe, 2019). Therefore, individuals with higher wellbeing may be motivated to avoid smoking due to the potential negative health consequences. Second, wellbeing may reduce stress reactivity (Hill et al., 2018) and encourage healthier coping mechanisms. Since stressful events are associated with smoking relapse events (Schultz et al., 2022) and the onset of smoking (Carvajal et al., 2000), individuals with higher wellbeing may be more likely to adopt healthier coping habits.

In sum, people with higher wellbeing are less likely to smoke, less likely to escalate their smoking behaviors, more likely to stop smoking, and more likely to remain abstinent from smoking. There is also some evidence that smoking cessation interventions targeting positive affect may promote smoking abstinence. However, the majority of reviewed findings could be explained by multiple underlying causal relations, and thus more research is needed.

6. Depression

Depression is characterized by persistent low mood and loss of interest or pleasure. Although wellbeing and depression are related, prior theory and research indicates that they are distinct constructs rather than simply two ends of the same continuum (Agteren and Iasiello, 2020; Westerhof and Keyes, 2010). Regarding their associations, research has shown that higher wellbeing is significantly associated with lower depression both cross-sectionally (Samaranayake and Fernando, 2011; Liu et al., 2009; Koivumaa-Honkanen et al., 2004; Koivumaa-Honkanen et al., 2001; Li et al., 2022) and prospectively (Burns et al., 2022; Grant et al., 2013; Green et al., 1992; Keyes et al., 2010; Koivumaa-Honkanen et al., 2004; Wood and Joseph, 2010).

The majority of prospective longitudinal research on the relation between wellbeing and later depression did not control for prior levels of depression or autoregressive effects. Thus, reverse causality or confounding may be alternative explanations for many of the observed prospective effects of wellbeing on later depression. However, a handful of longitudinal studies took steps to rule out these possibilities. For example, one study found that people with low wellbeing at baseline were significantly more likely to use mental health services in the subsequent five years, even when adjusting for use of mental health services in the prior three years (Michalski et al., 2022). Although this study statistically controlled for prior mental health service use, it did not control for prior levels of depression or other mental health symptoms. In another large cohort of more than 5000 participants, people with low wellbeing were twice as likely to experience high levels of depression 10 years later when accounting for prior levels of depression and other potential confounders such as sociodemographic characteristics and personality traits (Wood and Joseph, 2010).

The relation between wellbeing and depression may also be bidirectional. For example, one study applied random intercept cross-lagged

panel models to eight waves of data across 16 years and found significant bidirectional associations between wellbeing and depressive symptoms (Joshani and Blasco-Belled, 2023). Similarly, another study applied random intercept cross-lagged panel models to three waves of data across eight years and observed bidirectional associations between sense of purpose and depression, with stronger prospective effects of sense of purpose on later depression relative to the prospective effects of depression on later sense of purpose (Gudmundsdottir et al., 2023). As noted previously, random intercept cross-lagged panel models afford several benefits for causal inference, at least in the absence of unmodeled time-varying confounders, and as such these findings provide strong observational evidence for effects of wellbeing on later depression and vice versa.

There are several potential explanations for the association between wellbeing and depression. People with higher wellbeing are more likely to seek help for mental health problems from their friends and family members (Goodwin et al., 2016), and therefore may be more likely to receive informal support to reduce depressive symptoms. In addition, people with higher wellbeing are more likely to engage in a range of healthy lifestyle behaviors which may reduce risk of depression (Alvaro et al., 2013; Heponiemi et al., 2006; Pearce et al., 2022). The majority of the research reviewed here was conducted in samples that were not selected for depression, suggesting that the association between wellbeing and depression is likely present in the general population. However, similar effects have also been observed in individuals receiving outpatient psychiatric treatment for depression (e.g., Koivumaa-Honkanen et al., 2001). Overall, the current literature suggests that there is a clear association between higher wellbeing and lower depression and the association is likely bidirectional.

7. Hypertension

Higher wellbeing has been cross-sectionally and prospectively associated with lower incidence of hypertension and high blood pressure across a range of wellbeing constructs, including overall wellbeing (McLeish et al., 2022), happiness (Steptoe and Wardle, 2005), positive emotion (Ostir et al., 2006), hope (Richman et al., 2005), and emotional vitality (Richman et al., 2009; Trudel-Fitzgerald et al., 2014). Longitudinal research has found that higher initial happiness and emotional vitality levels are connected to lower likelihood of currently having hypertension, as well as lower risk of subsequently developing hypertension among individuals without hypertension at baseline (Richman et al., 2009; Steptoe and Wardle, 2005; Trudel-Fitzgerald et al., 2014). Evidence for life satisfaction and optimism is mixed, and as such it is difficult to draw direct conclusions about these components of wellbeing. Specifically, some research has indicated that lower life satisfaction is cross-sectionally associated with hypertension (Mojon-Azzi and Sousa-Poza, 2011; Szabo et al., 2020; Blanchflower and Oswald, 2008) and higher optimism is associated with lower likelihood of subsequently developing hypertension among individuals initially without hypertension (Kubzansky et al., 2020). However, this is in contrast with other studies which did not observe significant associations for either life satisfaction (Guimond et al., 2021), optimism (Szabo et al., 2020; Trudel-Fitzgerald et al., 2014), or general wellbeing (Coelho et al., 2000). The heterogeneity in findings between studies may be due to methodological differences, such as use of different methods to assess presence of hypertension (e.g., objective versus subjective measurements) or inclusion of different covariates across studies. Additional rigorous investigations are needed to compare the associations between a broad range of wellbeing constructs and risk of hypertension, ideally using longitudinal methods that account for blood pressure levels prior to wellbeing measurement.

To this point, research on wellbeing and hypertension has mainly focused on cross-sectional associations between wellbeing and hypertension, or on how higher wellbeing may reduce risk for subsequently developing hypertension among adults without hypertension at baseline

(e.g., Richman et al., 2005, 2009; Steptoe and Wardle, 2005). This unidirectional focus is, in part, due to the proposed mechanisms put forth for why higher levels of wellbeing may promote lower incidence of hypertension. For example, researchers have proposed that higher wellbeing promotes lower risk for hypertension through both psychosocial and physiological mechanisms, such as better social relationships, lower levels of cortisol, better immune function, being more in tune with health information and health risks, and being better at coping with emotions and stress (Ostir et al., 2006; Richman et al., 2005; 2009). Research has rarely considered the alternative pathway such that hypertension might lower wellbeing. However, one longitudinal study found that there were no meaningful differences in sense of purpose trajectories across eight-years between individuals diagnosed with hypertension during the study period and those who were not when using propensity score matching based on sociodemographic characteristics, work status, and initial sense of purpose (Hill et al., 2021). Thus, observational evidence suggests that higher wellbeing may help people avoid the onset of hypertension, though there is no evidence that receiving a hypertension diagnosis impacts wellbeing.

In summary, previous research suggests that there are consistent prospective effects of a range of wellbeing constructs on the likelihood of developing hypertension, though the evidence is mixed for some wellbeing constructs, such as life satisfaction and optimism. This research was conducted in general population samples or in individuals who did not have hypertension at baseline. Thus, it is unclear how wellbeing may affect blood pressure management among patients diagnosed with hypertension. Further research is needed to understand the underlying mechanisms of the association between wellbeing and hypertension, and to test for potentially causal effects of hypertension on wellbeing and vice versa.

8. Diabetes

Researchers have suggested that positive wellbeing characteristics may prove critical for promoting glucose control in people diagnosed with diabetes (Celano et al., 2013; Papanas et al., 2010). In support, research finds associations between sense of purpose and better glucose regulation in adult samples (Boylan et al., 2017; Hafez et al., 2018). Moreover, research shows that sense of purpose is associated similarly with positive health outcomes for adults with and without diabetes (Weston et al., 2023). As such, researchers have called for increased attention to wellbeing interventions for promoting preventive medicine among those with diabetes (e.g., Massey et al., 2017).

Prospective longitudinal research has also examined whether wellbeing predicts future onset of Type 2 diabetes in people without diabetes diagnosis at baseline. Life satisfaction has been shown to prospectively predict lower incidence of diabetes (Shirom et al., 2012). Another study found modest associations between life satisfaction, emotional vitality, and lower subsequent risk for physician-diagnosed diabetes (Boehm et al., 2015), even when accounting for demographic covariates. However, this same study did not observe associations between wellbeing and later risk for diabetes as assessed by glucose screening test. Additional work also found that a general quality of life composite (including control, autonomy, self-realization, and pleasure) predicted reduced future risk of physician-diagnosed diabetes (Okely and Gale, 2016).

Less work has focused on the effects of diabetes on later wellbeing, in part because it is difficult to tease out whether diabetes onset yields changes in wellbeing given the numerous third variables common to both diabetes onset and wellbeing. However, work with propensity score matching did not find evidence that the onset of diabetes in older adulthood impacts sense of purpose (Hill et al., 2021). In sum, there is consistent evidence for prospective effects of wellbeing on physician-diagnosed and self-reported diabetes. These effects are potentially causal; however, unobserved third variable confounders that have more immediate effects on wellbeing but more delayed effects on diabetes could also explain the observed patterns. By contrast, relatively

little research has examined effects of diabetes on later wellbeing.

9. Hearing loss

Recent research has shown that aging adults with a higher sense of purpose had better subjective hearing (Sutin et al., 2022) and better hearing acuity as measured by audiometric tests (Merten et al., 2021). Among adults who reported good to excellent hearing at study baseline, higher sense of purpose has been associated with lower risk of developing subsequent self-reported or objective hearing loss (Sutin et al., 2022). While no research has directly examined *why* sense of purpose or other aspects of wellbeing may be associated with reduced risk for hearing loss, a few mechanisms have been proposed (see Sutin et al., 2022 for discussion). First, wellbeing may protect against hearing loss by lowering the risk of cardiovascular disease, which can contribute to hearing loss by decreasing blood flow to the cochlea and auditory nerve (Oron et al., 2014). Research suggests that individuals with a higher sense of purpose are at lower risk for cardiovascular disease (Kim et al., 2019), and thus may also be at lower risk for hearing loss. Second, people with a higher sense of purpose are more likely to utilize preventative health care (Kim et al., 2014). Therefore, they may be more likely to receive early treatment for health conditions that cause secondary hearing loss, reducing their risk for decreased hearing acuity. Third, people with higher wellbeing may be more motivated to seek treatment for their hearing loss for social reasons. For example, concerned family and friends may encourage their loved one with hearing loss to seek treatment, or individuals with hearing loss may be more motivated to seek treatment to participate more fully in social activities (Kochkin, 2007).

In addition to acting as a protective factor against hearing loss, prior research has suggested that wellbeing may be negatively impacted by hearing loss, potentially due to increased difficulty participating in social interactions (Cao et al., 2023). However, this research was cross-sectional and thus more research is needed to determine whether this effect is causal. Taken together, initial evidence suggests that wellbeing may protect against hearing loss, and hearing loss may lead to lower wellbeing. However, more research is needed to determine whether these effects are causal. In addition, more research is needed to determine whether wellbeing protects against progressive hearing loss in individuals with hearing impairment.

10. Higher body weight

We refer to the Lancet Commission risk factor of a body mass index greater than 29.9 as “higher body weight” because studies have found the traditional medical classification term “obese” can be stigmatizing (Logel et al., 2015; Meadows and Daníelsdóttir, 2016; Puhl, 2020) and can have potentially detrimental health effects (Puhl, 2020). We focus on higher body weight for consistency with the Lancet Commission risk factor; however, it is notable that very low body weight in older adulthood has been associated with lower quality of life (Selvamani and Singh, 2018) and significant weight loss may occur in individuals with dementia (Singh-Manoux et al., 2018). In addition, while body mass index is often utilized as an indicator of health, many researchers have questioned the validity of this measure due to inconsistent findings and a variety of third variables that may influence associations between body mass index and health outcomes (Bacon and Aphramor, 2011; Rothman, 2008; Tomiyama et al., 2016).

Research on the relation between wellbeing and higher body weight is mixed. Some studies have observed a positive relation between wellbeing and higher body weight (e.g., Archangelidi and Mentzakis, 2018; Fang et al., 2022; Morris et al., 2010), whereas other research has observed a negative association (e.g., Jackson et al., 2015; Kuroki, 2016). Some research suggests that wellbeing may protect against higher body weight. For example, among participants with a body mass index between 23 and 28 at study baseline, higher sense of purpose has

been associated with lower risk of subsequently developing a body mass index outside of this range (Kim et al., 2020). Conversely, a longitudinal study found that wellbeing and body mass index share a positive reciprocal relationship (Fang et al., 2022). In addition to these directionally mixed results, null results have also been observed. For example, a positive psychological intervention designed to increase wellbeing demonstrated statistically non-significant effects on changes in body mass index (Kushlev et al., 2020).

Despite these mixed findings, several mechanisms have been proposed to explain why wellbeing may be associated with body weight. For example, a negative association between wellbeing and higher body weight may be explained by health behaviors or stress processes. Higher wellbeing may increase engagement in sustainable health-promoting behaviors, such as consumption of nutrient-dense foods, engagement in regular physical activity, and better sleep quality (Hill et al., 2019; Markwald et al., 2013), all of which may prevent weight gain. Higher wellbeing may also help individuals cope with stress (Burrow et al., 2016; Hill et al., 2018; Kim et al., 2019; Pfund et al., 2023), preventing behavioral and physiological changes that may contribute to poor metabolic health and weight gain (e.g., Foss and Dyrstad, 2011; George et al., 2010; Vicenati et al., 2009). Considering the opposite causal direction, higher body weight may negatively impact wellbeing through increased body weight stigma and discrimination (Carr and Friedman, 2005; Friedman et al., 2005; Myers and Rosen, 1999; Sutin and Terracciano, 2013).

Taken together, evidence for associations between wellbeing and higher body weight is mixed, and causal evidence is limited.

11. Alcohol use

Evidence for associations between wellbeing and alcohol use is mixed. Some studies have found a negative association (Zullig et al., 2001) particularly at higher levels of alcohol use (Koivumaa-Honkanen et al., 2012), and others have found no association (Burriss et al., 2009; Grant et al., 2009; Sin et al., 2015). Still other studies have found that alcohol is associated with higher levels of in-the-moment wellbeing. For example, an ecological momentary assessment study found that alcohol use was associated with higher wellbeing in the moment, but the association was much smaller when considering later wellbeing (Geiger and MacKerron, 2016). Another daily diary study found that higher average levels of positive affect were associated with greater average alcohol use, but higher levels of daily positive affect compared to one's personal average was only associated with greater alcohol use for college students (Patrick et al., 2016). A meta-analysis of daily diary and ecological momentary assessment data found that individuals are more likely to drink when experiencing higher levels of positive affect (Dora et al., 2023).

The relation between alcohol use and wellbeing may also depend on the type of alcohol use or the timescale. For example, "low-risk alcohol use" has been positively associated with wellbeing whereas "high-risk alcohol use" has been negatively associated with wellbeing (Parackal and Parackal, 2017). Similarly, when considering long-term shifts in alcohol use behaviors across 12 years, one study found that increases in alcohol use problems were associated with decreases in wellbeing, but changes in levels of alcohol use were not associated with changes in wellbeing (Geiger and MacKerron, 2016). Taken together, additional research is needed to further clarify the factors that impact the association between wellbeing and alcohol use, and whether observed effects are causal.

12. Education

Most correlational studies of educational attainment and wellbeing have found either no association or a modest positive association (see Helliwell et al., 2012 for brief review). The relation may also be nonlinear such that individuals with secondary education have higher

wellbeing than individuals with either primary or tertiary education (Hartog and Oosterbeek, 1998).

Policies that raise the minimum age that individuals can leave compulsory education provide natural experiments to evaluate the causal effects of education on wellbeing. Research has found that these policies have small positive effects on wellbeing, largely through their effects on income (e.g., Oreopoulos and Salvanes, 2011), a known correlate of wellbeing (Diener and Biswas-Diener, 2002; Kudrna and Kushlev, 2022; Pfund et al., 2023). Research on the prospective or causal effects of wellbeing on educational attainment is more limited. In contrast to the other risk factors, education is typically attained in childhood and young adulthood. Thus, examining prospective effects of wellbeing on educational attainment would require assessments of early life wellbeing. The limited existing research suggests that poor mental health, which is related to low wellbeing, is prospectively associated with less persistence in education and lower educational attainment (e.g., Cornaglia et al., 2012).

In sum, there is evidence that higher educational attainment may modestly improve wellbeing through related variables such as income, and initial but limited evidence that low wellbeing may be prospectively associated with lower educational attainment.

13. Traumatic brain injury

Wellbeing has not been directly linked to the prevention of traumatic brain injury. However, indirect evidence suggests that wellbeing may protect against traumatic brain injuries through a reduction in accidents. For example, prior studies have found that people with higher wellbeing have a lower risk of vehicle collisions and falls, two of the leading causes of traumatic brain injuries (Faul and Coronado, 2015; Jehu et al., 2022; Kirkcaldy and Furnham, 2000). This may be due to engagement in less risk-taking behaviors and more health-promoting behaviors that can reduce fall risk among people with higher wellbeing (Hill et al., 2019; Kim et al., 2014; Ravert et al., 2013).

In addition, research suggests that traumatic brain injury survivors report lower wellbeing after injury compared to before injury and compared to individuals without traumatic brain injury (Dijkers, 2004). Among traumatic brain injury survivors, injury severity was not a consistent predictor of wellbeing (Dijkers, 2004). Instead, studies suggest that social disengagement and employment loss are fairly common among traumatic brain injury survivors (Brown et al., 2003; Kersel et al., 2001) and have been linked to lower wellbeing (Cicerone and Azulay, 2007; Corrigan et al., 2001). Therefore, it is plausible that traumatic brain injury may negatively impact wellbeing at least partially through these psychosocial pathways.

Taken together, indirect evidence suggests that wellbeing may protect against traumatic brain injury by reducing the risk of vehicle collisions and other accidents that are common causes of traumatic brain injury such as falls, however research is needed to test this possibility. Conversely, there is evidence that traumatic brain injury negatively impacts wellbeing.

14. Air pollution

Previous research has shown that wellbeing tends to be lower in countries (Luechinger, 2010; Welsch, 2007) and regions (Brown et al., 2003; Dijkers, 2004; Faul and Coronado, 2015; Jehu et al., 2022; Kirkcaldy and Furnham, 2000; Ravert et al., 2013) with more air pollution (for review see Li et al., 2018). In addition, self-reported air pollution exposure has been associated with lower wellbeing (Li et al., 2014; Rehdanz and Maddison, 2008). Research using air pollution modeling systems to model exposure in specific locations at particular times provides additional support for an association between individual-level air pollution exposure and lower wellbeing (Ambrey et al., 2014; MacKerron and Mourato, 2009; Orru et al., 2016; Zhang et al., 2017).

Although the methods employed in most of these prior studies cannot

establish causal effects, it seems most likely that exposure to air pollution negatively impacts wellbeing or that unmeasured confounders account for the observed associations. However, there is the potential for wellbeing to influence experiences of air pollution as well, based on research linking wellbeing to selective migration. Specifically, research conducted in the United Kingdom found that people with lower wellbeing are more likely to move to urban areas (Hoogerbrugge and Burger, 2022) where exposure to certain types of air pollution is more common.

In sum, there is consistent evidence for a negative association between wellbeing and air pollution exposure; however, causal evidence is limited.

15. Discussion

The current review synthesized evidence for associations between wellbeing and each of the 2020 Lancet Commission modifiable dementia risk factors. We found relatively consistent evidence for associations between higher wellbeing and lower levels of at least nine of the 12 risk factors: physical inactivity, social isolation, smoking, depression, hypertension, diabetes, hearing loss, traumatic brain injury, and air pollution. We found evidence for only modest associations between wellbeing and education and mixed evidence for associations of wellbeing with alcohol use and body weight. In many cases, past research supports bidirectional relations between wellbeing and several of the risk factors. This suggests that modifiable dementia risk factors may be either mediators or confounders of the association between wellbeing and dementia. We discuss both possibilities below and make recommendations for future research on wellbeing, modifiable dementia risk factors, and dementia.

15.1. Modifiable dementia risk factors as mediators

The current review demonstrated that several of the Lancet Commission risk factors may be plausible mechanisms linking wellbeing to dementia risk. This is consistent with theoretical accounts that suggest that wellbeing improves health through behavioral, social, and biological pathways (see Cross and Grimm, 2018 for review). Given the relatively small and potentially cumulative effects of each individual risk factor on dementia risk (Livingston et al., 2020), it is plausible that the protective effects of wellbeing are transmitted through multiple modifiable dementia risk factors either simultaneously or in a serial manner. For example, increases in wellbeing may cause an individual to engage in more physical and social activity while also lowering their likelihood of developing Type 2 diabetes and motivating them to seek treatment for hearing loss. In turn, changes in each of these risk factors may accumulate to reduce overall dementia risk. This suggests that targeting wellbeing in dementia prevention efforts may be a highly effective way to reduce multiple risk factors simultaneously.

Despite conceptual support for several of the Lancet Commission's modifiable dementia risk factors as potential mediators of the association between higher wellbeing and lower dementia risk, this question still needs to be formally tested. Future research should directly test modifiable dementia risk factors as potential mechanisms linking wellbeing to dementia while taking special care to account for potential reverse causality and confounding. Reverse causality between wellbeing and plausible mediators poses a threat to causal inference, given evidence for bidirectional relations between wellbeing and many of the modifiable dementia risk factors. When testing mediation models using observational data, researchers should use data and statistical models that can disentangle between-person associations from prospective within-person effects of wellbeing on later levels of the risk factor(s) and vice versa. For example, random intercept cross-lagged panel models (Hamaker et al., 2015) are well-suited to test whether wellbeing change predicts subsequent changes to risk factors, and in turn whether changes to risk factors predict subsequent changes to cognition. This approach has several advantages for handling potential reverse causality and

confounding. First, through the inclusion of random intercepts, the model adjusts for stable between-person differences in wellbeing, the risk factor(s), and cognition. In doing so, the model isolates within-person effects from between-person effects and accounts for unobserved time-invariant confounders in the estimates of the within-person effects. Second, this model controls for prior levels of all variables in the model, such that the cross-lagged paths estimate the effect of change in one variable on change in the other variables. Third, this model is flexible enough to accommodate mediation tests and can be used to estimate potentially bidirectional relations between all variables in the model. Although useful for ruling out some common threats to causal inference, like most observational methods, random intercept cross-lagged panel models on their own cannot establish causality because unmodeled time-varying confounders can still cause spurious cross-lagged effects.

Identifying mediators of the association between wellbeing and dementia would improve our understanding of *why* higher wellbeing is associated with lower dementia. In addition to improving our theoretical and conceptual models, identifying mechanisms linking wellbeing to dementia may benefit intervention development and evaluation. One challenge of interventions with prevention as the goal is that it would likely take years or even decades to detect an effect of a wellbeing-enhancing intervention on lower incident dementia in an initially healthy sample. However, identifying mechanisms that occur earlier in the causal chain would enable interventionists to first test the effects of wellbeing-enhancing interventions on mechanisms that may be impacted over a shorter time frame. This would allow researchers and funders to invest resources into longer follow-up periods for only the most promising interventions. For example, if social activity and hypertension mediate the effects of wellbeing on dementia, wellbeing-enhancing interventions that increase social activity and decrease hypertension in the short-term may be the most likely to lower dementia risk in the long-term. Prevention efforts may also benefit from coupling wellbeing interventions with interventions designed to target specific behavioral risk factors such as physical inactivity given that increases in wellbeing and increases in physical activity may mutually reinforce on another. Thus, such interventions may be more effective than targeting just wellbeing or targeting just the risk factor(s). Finally, it is also possible that wellbeing impacts dementia risk *directly*, independent from its effects on other modifiable dementia risk factors. Estimating this direct effect after accounting for indirect effects through known modifiable dementia risk factors is an important step to test this possibility.

15.2. Modifiable dementia risk factors as confounders

In addition to investigating mechanisms of the association between wellbeing and dementia risk, it is also important to consider potential confounders, or variables that may causally impact both wellbeing and dementia, and therefore lead to observations of a spurious association (or spurious lack of association) between wellbeing and dementia. The current review found relatively consistent evidence for potentially causal effects of many of the Lancet Commission risk factors on wellbeing, suggesting that it may be important to account for these variables when isolating the effect of wellbeing on dementia risk. For example, experimental evidence suggests that physical and social activity may increase wellbeing and lower dementia risk. To address this possibility, research on wellbeing and dementia should utilize tools of causal inference that account for modifiable dementia risk factors as potential confounders. Models that disentangle between- and within-person associations, like the random intercept cross-lagged panel model described in the previous section, are useful for accounting for relatively time-invariant confounders (e.g., prior traumatic brain injury, early life educational attainment) regardless of whether they are included in the model and can be used to model time-varying confounders (e.g., within-person changes in physical inactivity and social isolation).

In addition to longitudinal modeling and statistical adjustment, other

tools of causal inference may be useful to account for the potential confounding effects of modifiable dementia risk factors. For example, randomized controlled trials of positive psychological interventions can be used to test the effects of experimentally manipulated wellbeing on later modifiable dementia risk factors, cognitive function, and dementia. Moreover, experimental manipulations of some of the risk factors (e.g., physical activity) can also be used to isolate the effects of the risk factors on later wellbeing, cognitive function, and dementia. Overall, there is a clear need for future research on causal linkages between wellbeing and other modifiable dementia risk factors, and for such work to consider the impact on later cognitive outcomes as well.

As such, randomized controlled trials are a promising and important future direction particularly as the field moves towards developing and testing dementia prevention strategies that target wellbeing. However, as noted above, this approach will require longer follow-up periods than most previous randomized controlled trials of positive psychological interventions (Kubzansky et al., 2023) to observe effects on cognitive function and incident dementia, which take time to manifest. An alternative or complement to randomized controlled trials is Mendelian randomization. Mendelian randomization is a statistical technique that combines genetic and epidemiological data to address confounding and reverse causality when estimating causal effects. One such Mendelian randomization study found suggestive evidence for causal effects of wellbeing on Alzheimer's disease (Ma et al., 2021). As with the other analytic approaches, Mendelian randomization relies on a set of strong assumptions: In this case, that the genotype is associated with wellbeing, that the pathway between the genotype and dementia operates through wellbeing only, and that the genotype is independent of other variables associated with dementia. If these assumptions are met, then the observed relation can be considered causal.

15.3. Limitations and future directions

The current review provided an overview of research on associations between wellbeing and the Lancet Commission modifiable dementia risk factors. We prioritized coverage of a broad range of wellbeing constructs and all 12 risk factors. Future research will benefit from more focused reviews of specific wellbeing constructs and individual risk factors, including systematic search processes, quantitative meta-analysis, coordinated data analysis, and evaluation of the evidentiary strength of individual studies. In addition to reviewing the existing literature, it will also be important for future research to replicate and extend research on associations among wellbeing, modifiable dementia risk factors, and dementia. For some of the risk factors, such as alcohol use and body weight, findings were mixed and research designs that support causal inference were limited. Moreover, as noted earlier, even relations that are considered well-established in the literature may need to be explored further to help establish causality. As such research accrues, it is important for wellbeing scientists and dementia prevention researchers to continuously update their theoretical and conceptual models, research questions, and methods based on the best-available evidence.

16. Conclusion

We found consistent evidence in the published literature for associations between higher levels of wellbeing and lower levels of most of the Lancet Commission's modifiable dementia risk factors. Theory and existing empirical evidence suggest that many of these relations are potentially bidirectional such that higher wellbeing mitigates risk factors and in turn, lower levels of the risk factors support later wellbeing. This suggests that modifiable dementia risk factors may be both mediators (i.e., intermediate steps in the causal chain) and confounders (i.e., variables that impact both wellbeing and dementia, and thus could induce a spurious association) of the relation between wellbeing and dementia. This finding points to important next steps for isolating causal effects of wellbeing on dementia and for determining how wellbeing

may transmit its protective effects.

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Declaration of Competing Interest

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