

Title

A review of psychological well-being and mortality risk:
Are all dimensions of psychological well-being equal?

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Abstract

Increasing evidence suggests that psychological well-being (PWB) is associated with lower chronic disease and mortality risk and may be enhanced with relatively low-cost interventions. While many interventions are targeted at specific dimensions of PWB (e.g., optimism, purpose in life), limited research has evaluated rigorously whether distinct PWB dimensions may differentially impact physical health outcomes. Without clear understanding of which dimensions of PWB are most relevant for physical health, effectiveness of PWB interventions to improve physical health will be limited and difficult to assess. A growing body of research has considered multiple PWB dimensions in relation to mortality risk, but a comparison of findings across studies has not been done. This chapter summarizes the empirical evidence regarding specific relationships between all-cause mortality and multiple dimensions of PWB (e.g., life purpose, mastery, positive affect, life satisfaction, optimism). It also reviews possible biological (e.g., inflammation, antioxidants) and behavioral (e.g., smoking, physical activity) mechanistic pathways that could explain these associations. Methodological considerations for epidemiological studies targeting the potential protective role of psychological well-being in risk of mortality (and other health-related outcomes) are discussed, and recommendations for future directions in this field are provided.

Introduction

Over the past decades, evidence for the physical health benefits of enhanced psychological well-being (PWB) has expanded dramatically (Boehm & Kubzansky, 2012; Pressman, Jenkins, & Moskowitz, 2019). Notably, research in the fields of behavioral and psychosomatic medicine, as well as health psychology have substantially contributed to this body of work (Boehm & Kubzansky, 2012; Folkman & Moskowitz, 2000; Kobau et al., 2011; Pressman et al., 2019; Seligman & Csikszentmihalyi, 2000; Steptoe, 2019; Van Cappellen, Rice, Catalino, & Fredrickson, 2018). Yet, such work is still neglected by the public health community. For instance, the discipline of epidemiology maintains a primary focus on risk, deficits, and problems rather than identifying and promoting factors that might serve as assets to enhance health and longevity (VanderWeele et al., in press). Similarly, although it is well accepted that PWB represents more than the absence of psychological distress (e.g., depressive and anxiety symptoms; Boehm & Kubzansky, 2012; Ryff et al., 2006), in medicine, PWB assessment is not part of usual care (VanderWeele, McNeely, & Koh, 2019). Nonetheless, associations of PWB with subsequent physical health outcomes have been well-documented, with findings generally suggesting that higher PWB is associated with reduced risk of chronic diseases like cardiovascular disease and diabetes, as well as increased likelihood of healthy aging and longevity (Boehm & Kubzansky, 2012; Pressman et al., 2019; Steptoe, 2019). However, there are some conflicting results in this literature, which may explain, at least in part, ongoing skepticism among the broader scientific community as to the importance of PWB as a health asset (Miller, Sherman, & Christensen, 2010).

Until recently, most investigators have not carefully distinguished between dimensions of PWB regarding their impact on physical health, or considered whether all dimensions have

similar effects (Diener, Lucas, & Oishi, 2018), even though PWB is clearly comprised of distinct dimensions (e.g., positive affect, optimism, life satisfaction). While distinct dimensions of PWB may share common variance, they could differentially impact physical health, thereby explaining certain conflicting findings (Pressman et al., 2019). If PWB is to be embraced by the public health community as a health asset and incorporated into decision-making and policies, along with efforts targeting other established social determinants of physical health like poverty, education, discrimination, and social capital (Berkman, Kawachi, & Glymour, 2014; Marmot & Wilkinson, 2005), these distinctions need to be made clear.

In this chapter, we review the empirical evidence from the most rigorous methods available on associations of multiple PWB dimensions with all-cause mortality, an objective endpoint and the aftermath of various chronic diseases. We consider those dimensions that have received some attention in the literature and have been captured by leading theoretical perspectives in PWB research (described below); these dimensions include life purpose, personal growth, mastery, autonomy, *ikigai*, life satisfaction, positive affect, sense of coherence, optimism, and emotional vitality. We further consider potential behavioral and biological mechanisms that could underlie these associations and whether such mechanisms are likely to be similar across different dimensions of PWB. Finally, we discuss future avenues for research in this field.

Defining Well-Being

Well-being is a complex and multifactorial construct. Measures of well-being are sometimes divided into objective measures, which mostly seek to capture “standard of living” as reflected by levels of education or income, physical health, and subjective measures, which seek

to capture psychological, social, and spiritual experiences based on an individual's perceptions (Lee Kum Sheung Center for Health and Happiness, 2017; National Research Council, 2013). When these measures concern psychological aspects (e.g., happiness) and are derived from cognitive and affective judgements a person makes about his/her life, they are often referred to as measures of psychological well-being (PWB). PWB has been a central area of research in psychology for decades (Kobau et al., 2011; Seligman & Csikszentmihalyi, 2000), most commonly used in studies as an outcome in its own right. It is also increasingly taken up in epidemiologic research, to understand its contribution to health outcomes, and more broadly, to public health, notably to implement country-level monitoring and policies promoting overall health (Diener & Seligman, 2018; Kobau et al., 2011).

Distinct theoretical perspectives have been proposed to characterize PWB research thus far (for more details, see Boehm & Kubzansky, 2012; Hernandez et al., 2018; National Research Council, 2013; Ryff, 2017; Steptoe, 2019): hedonic well-being (e.g., feeling happy), evaluative well-being (e.g. being satisfied with life, although life satisfaction is also sometimes categorized as an hedonic dimension), eudaimonic well-being (e.g., finding purpose in life, having a sense of mastery and autonomy in one's own decisions), and other constructs that contribute to feeling whole or well (e.g., optimism). While some of these dimensions may be conceptualized as more stable over time, like psychological attributes (e.g., optimism, life satisfaction), others may be more variable or transient states (e.g., positive affect, happiness).

Research has documented statistically significant associations between PWB constructs themselves. For instance, pioneering work showed magnitude of estimates varying from small (e.g., $r = .13$ between purpose in life and autonomy) to moderate (e.g., $r = .46$ between self-acceptance and mastery) when evaluated among a nationally-representative sample of 1,108 U.S.

adults, aged 46 years on average (Ryff & Keyes, 1995). Since then, various studies have aimed to replicate these results using the same scales. Stronger correlations have been observed in both larger U.S. samples and non-U.S. representative samples: for example, $r = 0.60$ between self-acceptance and mastery in a nationally-representative sample of 3,487 midlife adults in the U.S. (Hsu, Hsu, Lee, & Wolff, 2017), whereas $r = 0.57$ between purpose in life and autonomy among 1,179 midlife women in the U.K. (Abbott et al., 2006). However, in some cases estimates were somewhat weaker: for example, $r = .39$ between self-acceptance and mastery among 4,960 older adults in Canada (Clarke, Marshall, Ryff, & Wheaton, 2001). Research conducted in younger adults, such as colleges students, also revealed significant but moderate correlations between various measures of life satisfaction and positive affect (i.e., r values from 0.43 to 0.52; Lucas, Diener, & Suh, 1996). Overall, these findings suggest that although some variation may exist across samples, PWB dimensions may both share a latent factor and yet also represent distinct constructs.

Psychological Well-Being and All-Cause Mortality

Psychological Well-Being as a Determinant of Physical Health

Given various PWB dimensions, measured with self-reported scales in most cases, have been linked with myriad health-related outcomes, it is plausible that PWB would be reliably associated with all-cause mortality. In prior research conducted in the general population (i.e., non-medical samples), greater PWB levels have been related to lower risk of various chronic conditions (e.g., cardiometabolic diseases, infectious illness, arthritis), and of physical and cognitive decline, though results with cancer are less clear (Boehm & Kubzansky, 2012; Kim et al., 2017; Okely, Cooper, & Gale, 2016; Okely & Gale, 2016; Pressman et al., 2019; Ryff,

Heller, Schaefer, van Reekum, & Davidson, 2016). Emerging evidence also suggests that various PWB dimensions, particularly higher levels of optimism, positive affect, and life satisfaction, are associated with lifespan (i.e., life duration) and exceptional longevity (Lee et al., 2019; Liu et al., 2014), which is typically defined as survival to 85 years or beyond (Newman & Murabito, 2013; Revelas et al., 2018). Life extension in individuals who experience greater levels of PWB could be explained, at least in part, by compressed morbidity and aging in health. This hypothesis is in fact supported by recent prospective study results showing that midlife adults with higher levels of optimism and mastery, respectively, are more likely to be healthy agers compared to their counterparts with lower PWB levels (James et al., 2019; Kim et al., 2019; Latham-Mintus, Vowels, & Huskins, 2018).

Existing Methodological Concerns

Although the PWB-health relationship is likely to be bidirectional, whereby PWB influences physical health outcomes and vice versa, the primary interest of this body of research is to determine whether PWB is causally related to health outcomes. Such examination is crucial from a primary or primordial prevention perspective; in fact, if such effects exist, subsequent efforts should develop and implement specific policy and interventions that target PWB to improve physical health and longevity. However, even when studies use longitudinal data to examine relationships, whereby PWB precedes subsequent health outcomes, due to methodological limitations it is not always clear whether observed associations 1) would remain after more rigorous confounder control (i.e., a third factor influencing both PWB and health); and 2) do not capture reverse causation (i.e., health status driving PWB levels). Considering

mortality risk, an objective endpoint, offers some methodological strengths such as virtually no misclassification, and research that requires a longitudinal design by nature of the outcome.

Overview of Meta-Analyses Targeting Mortality

Recent meta-analyses have suggested that distinct PWB dimensions are protective against mortality (Cohen, Bavishi, & Rozanski, 2016; Martin-Maria et al., 2017; Rozanski, Bavishi, Kubzansky, & Cohen, 2019; Zhang & Han, 2016). For instance, after pooling 10 studies (total N=136,265), higher versus lower levels of purpose in life were associated with a multivariate-adjusted 17% reduced mortality risk (relative risk, RR=0.83, 95% confidence intervals [CI]=0.75-0.91) over a mean follow-up of seven years (Cohen et al., 2016). Results from 9 pooled studies comprising 188,599 participants further suggested a 14% decreased risk in all-cause mortality (RR=0.86, CI=0.80-0.92) over 8 to 40 years for individuals with highest versus lowest levels of optimism (Rozanski et al., 2019). Another meta-analysis combined 22 studies with sample sizes ranging from 101 to 97,253 participants (Zhang & Han, 2016); each included study assessed the risk of mortality for higher versus lower levels of either a PWB dimension (i.e., optimism, life satisfaction, happiness, and positive affect) or a related well-being construct (i.e., attitude towards aging) as the exposure. The authors evaluated first the association of mortality risk with overall well-being (all exposures pooled) and then examined mortality risk with each exposure separately. Results from unadjusted models indicated a 25% decreased risk of mortality for elevated levels of overall well-being, as well as 46%, 28%, 29%, and 16% decreased risk of mortality for elevated levels of life satisfaction, happiness, optimism, and positive affect, respectively, over 17 years on average. Interestingly, effect estimates from individual exposures evaluated independently were statistically significantly different from one

another ($p < .05$), but after adjustment for covariates, the differences in the magnitude of associations was attenuated and non-significant. However, it was unclear whether each individual exposure remained associated with mortality after such statistical control since the multivariate estimates were reported for overall well-being only (showing a 15% reduced risk of mortality; Zhang & Han, 2016). Findings from another meta-analysis of 90 studies ($N=1,309,527$; 50% of studies with at least 10 years of follow-up) examining life satisfaction, positive affect, and purpose in life also suggested that estimates of mortality associations across these three PWB dimensions did not significantly differ (Martin-Maria et al., 2017). Moreover, in this meta-analysis, the associations with mortality remained statistically significant after covariate control: compared to participants with lower levels, those with higher levels of life satisfaction, positive affect, and purpose in life had a 12%, 8%, 7% decreased risk of mortality over the follow-up periods across studies.

However, in all of these meta-analyses the quality of statistical adjustment for potential confounders in the included studies was variable and the cause of death was heterogeneous (e.g., all-cause and some cause-specific deaths pooled), which prevent more precise conclusions. Moreover, certain PWB dimensions have received more attention than others, probably due to data availability across selected samples. Notably, numerous individual studies have considered life satisfaction (Martin-Maria et al., 2017; Zhang & Han, 2016). There have also been sufficient studies on purpose in life and optimism to conduct meta-analyses on these PWB dimensions (Cohen et al., 2016; Rozanski et al., 2019); of note, in the purpose in life meta-analysis the inclusion criteria was fairly large and comprised studies on closely-related construct such as *ikigai*, which conceptually captures more than life purpose (as detailed below). Conversely, fewer focused on positive affect (Martin-Maria et al., 2017) or, when they did, some of the

included studies used lower levels of negative affect (e.g., sadness, depressive symptoms) as an indicator of higher levels of positive affect (Zhang & Han, 2016). This is problematic because the absence of psychological distress does not necessarily denote the presence of PWB (Boehm & Kubzansky, 2012; Ryff et al., 2006) and depression scales were not developed to measure positive affect per se (Ryff et al., 2006; Ryff & Singer, 2007).

Criteria for Selecting Studies Included in this Chapter

Here, we provide an overview of the evidence as to whether and how various PWB dimensions are associated with reduced risk of all-cause mortality in follow-up. Literature searches within PubMed and PsycInfo databases targeted individual prospective and longitudinal studies evaluating the role of at least one PWB dimension with all-cause mortality risk, written in English or French. Dimensions needed to be evaluated with a PWB scale rather than one aimed at measuring psychological distress. Additional studies were obtained through bibliographies of eligible articles. Individual studies included in this narrative review were selected for their methodological rigor, with some of them being included in the meta-analyses cited above, whereas others were published subsequently. In considering rigorous studies, we retained studies that adjusted for all the following categories of potential covariates at baseline (i.e., when PWB was measured): sociodemographic factors (e.g., age, sex, education), medical status (e.g., blood pressure, body mass index, chronic conditions), and health behaviors (e.g., smoking, physical activity). Therefore, all reported estimates (e.g., hazard ratios, relative risk) in this chapter are multivariate estimates from studies that statistically adjusted for at least one indicator of each of these three categories of covariates in their analytic models¹. Some studies further adjusted for

¹ In two cases – autonomy and emotional vitality – cited studies included some but not all of the mentioned covariates at baseline. The selection of studies was less strict for these two PWB dimensions because of the scarcity

psychological distress, to account for its potentially confounding role between PWB and mortality, as well as to determine PWB's role on mortality beyond any effects of ill-being (e.g., anxiety and depression symptoms; as depicted in Figure 1). Some studies also additionally controlled for self-rated health, which is one of the strongest predictors of future morbidity and mortality risk and is usually assessed via one item asking whether individuals perceive their health as excellent, very good, good, fair or poor (Jylha, 2009; Picard, Juster, & Sabiston, 2013). We explicitly mention in the following sections when studies performed further statistical adjustment for psychological distress and/or self-rated health, beyond the sociodemographics, medical, and behavioral covariates mentioned above.

Results of the Narrative Review

Dimensions related to eudaimonic well-being.

Purpose in life. Experiencing a sense of purpose and direction in one's life has been studied substantially, with results indicating a consistent association with reduced mortality over each study's follow-up period. The three studies described below have all used the purpose in life subscale from the Scales of Psychological Well-Being (Ryff, 1989). In one of the most rigorous studies included in the meta-analysis cited above (Cohen et al., 2016), every standard deviation (SD) increase in life purpose was associated with 40% decreased hazard of 5-year mortality (hazard ratio, HR=0.60; CI=0.42-0.87) among 1,236 older U.S. adults from the Rush Memory and Aging Project, and Minority Aging Research Study (mean age=78 years; Boyle, Barnes, Buchman, & Bennett, 2009). In the Women's Health Initiative cohort, after additional statistical control for psychological distress in multivariable models, greater life purpose was

of mortality studies available in the literature. We make note of which covariates were considered when describing the studies.

also associated with lower likelihood of death over a 2-year period in 7,675 U.S. women aged 65 years and older (Zaslavsky et al., 2014). Interestingly, in a recent study of 6,985 older adults from the nationally-representative Health and Retirement Study (hereafter referred to as HRS), conducted after publication of the meta-analysis, the association was maintained not only after adjustment for traditional covariates and psychological distress, but also after further controlling for other PWB dimensions including optimism, positive affect, and social participation (lowest versus highest quintiles of life purpose: HR=2.43, CI=1.57-3.75; Alimujiang et al., 2019).

Some research has examined the role of *meaning* in life but the results are less convincing than those assessing purpose. Purpose in life and meaning in life are two terms that some studies have treated interchangeably as referring to the same underlying construct. However, emerging theoretical and empirical work has led to greater distinction between the terms and the recent development of a tripartite model of meaning in life, which consists of three subconstructs: (1) *purpose* in life; (2) coherence/comprehension (the degree to which people perceive that their lives as making sense); and (3) significance/mattering (the degree to which people feel their existence is of significance, importance, and value in the world; George & Park, 2017; Hanson & VanderWeele, this volume [2020]; Martela & Steger, 2016). These constructs may be differentially associated with mortality. A study of 1,361 older U.S. adults (mean age=79 years) over five years evaluated meaning in life with a shortened version of Krause's scale (Krause, 2004), which captures four domains (i.e., values, purpose, goals, and reconciliation with the past) that can be related to the three subconstructs reported above. No relationship of meaning in life with all-cause mortality (OR=0.97; CI=0.93-1.01) was found in multivariable models adjusting for self-rated health, although it is worth noting that in the sociodemographics-adjusted model, the association was small but statistically significant (OR=0.92; CI=0.89-0.96;

Krause, 2009). These results could also raise the question of whether “meaning” and “purpose”, often used interchangeably, might indeed capture constructs that relate differently to mortality.

Personal growth. To our knowledge, personal growth—that is, whether individuals seek to realize their full potential and recognize that the self is constantly developing (Boehm & Kubzansky, 2012; Ryff & Keyes, 1995)—has been explored in relation to mortality risk in only one study. In the Women’s Health Initiative investigation described above, using items from the Scales of Psychological Well-Being (Ryff, 1989), personal growth levels were associated with lower 2-year mortality rates, when personal growth was considered as a continuous (per 1-unit increase: HR=0.95; CI=0.93-0.98) or categorical variable (lower versus higher [reference group] quartile: OR=2.10, CI=1.42-3.08; Zaslavsky et al., 2014). As mentioned earlier, this study also evaluated life purpose, and a comparison of multivariable-adjusted estimates for life purpose versus personal growth (ORs=3.55 versus 2.10) suggested stronger associations of purpose with mortality in these women aged 65 years and older.

Mastery. Mastery—whether individuals effectively manage their environments or perceive life as being under their control (Boehm & Kubzansky, 2012; Ryff & Keyes, 1995)—has been well-studied in relation to mortality, although not all investigations have rigorously taken into account key potential confounders (e.g., sociodemographics, medical status). Among those who did, an early investigation followed 2,829 Dutch adults (aged 55-85) from the Longitudinal Aging Study Amsterdam (LASA) for up to three years (Penninx et al., 1997). In this study, each 1-unit rise in mastery as captured by an abbreviated 5-item version of the Pearlin Mastery Scale (Pearlin & Schooler, 1978) was associated with 6% lower mortality odds (odds ratio, OR=0.94, CI=0.89-0.99), even after extensive adjustment of covariates including PWB correlates such as self-rated health, social support, self-efficacy, and self-esteem. Likewise,

among English adults from the EPIC-Norfolk Study (N=20,495; aged 41-80), every 1-SD increase in mastery based on a modified 7-item version of the Pearlin Mastery Scale was associated with a 18% lower rate of death (RR=0.82, CI=0.76-0.89) over five years, after further controlling for psychological distress (Surtees, Wainwright, Luben, Khaw, & Day, 2006). Similar results have also been obtained in U.S. samples and with alternative measures of mastery. For example, in the Midlife in the United States study (MIDUS), authors developed several additional items and combined them with some items from the Pearlin Mastery Scale (Turiano, Chapman, Agrigoroaei, Infurna, & Lachman, 2014).

Autonomy. Although research is sparse, available evidence to date has not found consistent associations of mortality risk with autonomy, characterized as the extent to which individuals act independently without concern for external pressures (Boehm & Kubzansky, 2012; Ryff & Keyes, 1995). For example, in a relatively large study of 9,420 midlife British adults (mean age=58 years), the autonomy subscale from the Control, Autonomy, Self-Realization, and Pleasure (CASP) scale (Hyde, Wiggins, Higgs, & Blane, 2003) was considered in relation to mortality risk over a 5-year period (Netuveli, Pikhart, Bobak, & Blane, 2012). Autonomy scores were modestly but significantly related to the hazard of death in the unadjusted model (per 1-SD increase: HR=1.07, CI=1.00-1.13) but were attenuated and no longer statistically significant in multivariate models that further controlled for self-rated health and psychological distress (per 1-unit increase: HR=1.02; CI=0.96-1.09; although health behaviors were not assessed in this study; Netuveli et al., 2012). While these results may reflect a true null association, different findings may be obtained with the use of a different autonomy scale. In fact, the 19-item CASP scale (Hyde et al., 2003) includes general statements such as “*I can do the things that I want to do*”, which could be conflated with a sense of physical autonomy. By

contrast, the autonomy subscale from the Scales of Psychological Well-Being (Ryff, 1989) refers more to the psychological facet of autonomy (e.g., “*My decisions are not usually influenced by what everyone else is doing*”), which may relate differently to mortality. To our knowledge, no studies have examined a measure that solely captures psychological autonomy in relation to mortality risk among non-medical samples.

Ikigai. This term is uniquely Japanese and does not directly translate to a single English term that has been examined in non-Japanese samples. *Ikigai* has been defined as having a sense of happiness, worth, and benefit of being alive (Sone et al., 2008; Tanno et al., 2009). While it largely captures eudaimonic well-being (e.g., life purpose), it also encompasses aspects of hedonic well-being (e.g., pleasure), though usually assessed with only one item (Sone et al., 2008; Tanno et al., 2009). Findings, obtained from a handful of published studies, are generally positive. For example, using data from the nationwide Japan Collaborative Cohort Study for Evaluation of Cancer Risk (N=73,272; aged 40-79), adults with versus without *ikigai* had a reduced hazard of mortality over five years (HR_{men}=0.80; CI=0.72-0.89; HR_{women}=0.80; CI=0.69-0.92; Tanno et al., 2009). In another Japanese cohort, the Ohsaki National Health Insurance Cohort Study (N=43,391; aged 40-79), lower and moderate *ikigai* levels (versus higher) were related to an increased 7-year hazard of death (HR_{moderate}=1.1; CI=1.0-1.2; HR_{lower}=1.5; CI=1.3-1.7), with further adjustment for self-rated health not altering these results (Sone et al., 2008).

Dimensions related to hedonic well-being.

Positive affect. Feeling happy, joyful, cheerful, excited and proud are often included in the construct of positive affect. As mentioned earlier, there has been a substantial number of studies conducted on positive affect’s role in mortality risk, although the number is somewhat

reduced after excluding studies that measured (the absence of) negative affect, because it does not truly capture positive affect. In one study using data from the German Aging Survey (N=3,124; aged 40-85), every unit increase in positive affect, as assessed with 10 items from the Positive and Negative Affect Schedule (PANAS) measure (Watson, Clark, & Tellegen, 1988), was associated with a 19% lower 14-year mortality risk, after adjusting for sociodemographics, medical status, psychological distress, and also life satisfaction (HR=0.81, CI=0.70-0.93); further controlling for self-rated health and physical activity attenuated the association (HR=0.88, CI=0.76-1.02; Wiest, Schuz, Webster, & Wurm, 2011). However, in a recent study of adults from Norway (N=5,554; aged 47 to 74) that also used the 10 PANAS items, even after adjusting for sociodemographics, medical status, health behaviors (smoking, alcohol use, and physical activity), and psychological distress, positive affect remained significantly associated with mortality risk (Petrie et al., 2018). Specifically, individuals categorized in the lower versus higher tertile of positive affect scores had a 38% increased risk of death (HR=1.38; CI=1.12-1.71) over an average of 16.5 years of follow-up. No significant association was obtained for participants in the moderate tertile and results were robust to further adjustment for psychological distress (Petrie et al., 2018).

Happiness. Although happiness is a pleasurable feeling that is sometimes included in positive affect, it has also been studied as a separate construct in prior PWB-mortality research. In a subset of the Million Women Study (N=719,617; aged 53-72), English women who said they were “unhappy” or “usually happy” on a 1-item measure did not differ in mortality risk in 10-year follow-up compared to those who said they were “happy most of the time” (RR=0.98, CI=0.94-1.01; RR=0.99, CI=0.96-1.01, respectively; Liu et al., 2016). While this study has drawn media attention because of its methodological strengths (e.g., large sample size, statistical

control for multiple covariates), its conclusions obtained from the use of a single happiness item have also has generated some controversy within the scientific community based on this and other methodological limitations and concerns (e.g., Diener, Pressman, & Lyubomirsky, 2015; Kubzansky, Kim, Salinas, Huffman, & Kawachi, 2016). Moreover, the thin distinction between some levels of exposure (i.e., “happy most of the time” [reference group] versus “usually happy”) could also have contributed to the null results. Likewise, another rigorous study of 861 older adults from the Arnhem Elderly Study found no association between happiness assessed with two items (i.e., “*I have many moments of happiness*” and “*I often laugh happily*”) and mortality over a 15-year follow-up period (Koopmans, Geleijnse, Zitman, & Giltay, 2010). Taken together, findings from studies on positive affect and happiness as a unitary construct may suggest that the comprehensive experience of various types of positive affect, rather than the sole experience of feeling happy as captured by single items, matters more in terms of longevity.

Dimensions related to evaluative well-being.

Life satisfaction. Life satisfaction can be measured either globally, capturing the extent to which individuals judge their life as a whole to be satisfactory, or specifically, by individual life domains (e.g., work, family). Although a handful of studies have investigated the role of specific life domains in mortality risk, they were not included in the current narrative review either because they considered mortality from coronary heart disease solely (Boehm, Peterson, Kivimaki, & Kubzansky, 2011), or did not adjust for health behaviors (St John, Mackenzie, & Menec, 2015). Yet, these preliminary results suggest that some, but not all dimensions of life satisfaction could relate to mortality risk, supporting the need for further research in this area. Global life satisfaction is frequently measured with a single item. As a result, it has been included in various epidemiological cohorts and other long-standing population-based studies,

which has provided follow-up periods long enough to ascertain death cases in multiple studies on this topic. Unlike happiness, the use of single life satisfaction items has been validated in three large studies and has shown substantial degree of criterion validity with multi-item, validated scales of life satisfaction (Cheung & Lucas, 2014).

A Canadian population-based study (N=73,904; aged 18 to >80) revealed that “very dissatisfied” versus “very satisfied or satisfied” individuals had an increased mortality risk over six years (HR=1.70, CI=1.16-2.51), after controlling for numerous relevant covariates (Rosella, Fu, Buajitti, & Goel, 2018). These results were consistent with other studies conducted amongst different samples using single life satisfaction items, including among 4,458 Australian adults over nine years (Boehm, Winning, Segerstrom, & Kubzansky, 2015) and 10,957 German adults over 20 years (Hulur et al., 2017). In the German Aging Survey described earlier, mortality risk was reduced by 11% for each unit increase in life satisfaction, as measured with the 5-item Satisfaction With Life Scale (Pavot, Diener, Colvin, & Sandvik, 1991), after further adjusting for sociodemographics, medical status, psychological distress and also positive affect (HR=0.89, CI=0.79-1.00), but the association was substantially attenuated and became not statistically significant after additional control for self-rated health and physical activity (Wiest et al., 2011). Although the estimate appears stronger with positive affect than life satisfaction in this study (even when both were included simultaneously in the statistical models), these dimensions were assessed with distinct scales and scores were not standardized, which precludes formal comparison. Other authors have reported an elevated 12-year risk of mortality with lower life satisfaction (assessed using the 20-item Life Satisfaction Index A [LSI-A]) among 1,939 Korean men and women from the Kangwha Cohort (Kimm, Sull, Gombojav, Yi, & Ohrr, 2012). However, a closer look at the 20 items composing the LSI-A revealed that, while most captured

life satisfaction, some queried other PWB dimensions (e.g., *“I expect some interesting and pleasant things to happen to me in the future”*), as well as physical states (e.g., *“I feel old and somewhat tired”*; Neugarten, Havighurst, & Tobin, 1961), which raises the question as to whether the association obtained in this study was truly driven by life satisfaction per se.

Other psychological well-being dimensions.

Sense of coherence. Sense of coherence is a fairly stable personality disposition that encompasses three constructs: the belief that what happens in individuals’ lives is rational, predictable, structured, and understandable (comprehensibility); that adequate and sufficient resources are perceived to be available to help resolve difficulties as they arise (manageability); and that the demands created by exposure to adversity are seen as challenges and are worthy of engagement (meaningfulness; Antonovsky, 1987). It may be worth mentioning that, when looking more closely at the items usually used to measure these constructs, the meaningfulness items (e.g., *“Do you usually feel that your daily life is a source of personal satisfaction?”*; *“How often do you have a feeling that there’s little meaning in the things you do in your daily life?”*) seem to overlap with other PWB dimensions, such as life satisfaction and meaning in life. For this reason, future studies about sense of coherence should consider associations by constructs separately, to disentangle whether any protective effects on mortality risk might instead be attributed to other PWB constructs captured by this construct. Models that include other PWB dimensions, in addition to sense of coherence as the exposure, would also speak to whether sense of coherence may uniquely contribute to mortality risk.

That said, sense of coherence when taken as a whole appears to be related to reduced mortality risk over time in several studies that have been conducted on the topic. One of the most rigorous early studies evaluating its role in mortality risk was conducted in the EPIC-Norfolk

Study among 16,668 men and women aged 41-80 at baseline (Surtees, Wainwright, Luben, Khaw, & Day, 2003). Sense of coherence was captured by the sum of three items each measuring one of the three primary constructs in the theory (i.e., manageability, comprehensibility, and meaningfulness; Lundberg & Peck, 1995). Adults with higher (versus lower) sense of coherence had a 24% reduced risk of 6-year mortality (RR=0.76, CI=0.64-0.90), after control for multiple covariates including psychological distress. These results were replicated among 10,863 Dutch adults aged 20-65 from the Monitoring Project on Chronic Risk Factors (MORGEN project) who completed the same three items in a subsequent study with an average follow-up of 14 years (Super, Verschuren, Zantinge, Wagemakers, & Picavet, 2014). Findings with this longer follow-up period showed that compared to participants with moderate levels of sense of coherence, those with lower levels had a 27% increased risk of mortality (HR=1.27; CI=1.01-1.59), even after further adjustment for self-rated health (Super et al., 2014). Somewhat surprisingly, no significant differences were observed between moderate and higher levels, perhaps hinting at a threshold effect at which lower sense of coherence levels can be harmful for longevity. Alternatively, some authors have reported poorer psychometric properties, including lack of discrimination across higher scores, for this 3-item version of the Antonovsky's scale compared to the longer 13- and 29-item versions (Olsson, Gassne, & Hansson, 2009).

When researchers did use these more comprehensive assessments of the three sense of coherence constructs, results were generally consistent, albeit more nuanced. For instance, one study of 585 men from The Israel Study of Glucose Intolerance, Obesity, and Hypertension Study followed for 22 years used the original Antonovsky 29-item scale (Antonovsky, 1993); results showed that men with the highest versus lowest tertile of scores had a 34% reduced risk of mortality (HR=0.66, CI=0.46-0.94; Geulayov, Drory, Novikov, & Dankner, 2015). Although

the association was not statistically significant among men with an intermediate versus lower level of sense of coherence, every 1-unit increase in sense of coherence was modestly but significantly associated with reduced mortality risk (HR=0.99, CI=0.99-1.00; Geulayov et al., 2015). In another investigation using an abbreviated 13-item version of Antonosky's scale among 7,933 adults from the National FINRISK Study, every 1-SD increase was related to 10% lower risk of death (HR=0.90; CI=0.84-0.97) over 14 years follow-up on average (Haukkala, Kontinen, Laatikainen, Kawachi, & Uutela, 2010). These findings might suggest that a smaller, monotonic increase in sense of coherence also matters for reducing mortality risk. However, because further adjustment in this study for depressive symptoms attenuated associations whereby they were no longer statistically significant, it remains unclear whether sense of coherence has an independent effect or is distinct from the lack of psychological distress (Haukkala et al., 2010).

Optimism. Optimism has been conceptualized either as a dispositional trait—a person's general expectation that the future will turn out well or that good things will happen in the future—or an explanatory style, in this case a person's tendency to make internal, stable, and global attributions for good events (Scheier & Carver, 2018; Tennen & Affleck, 1987). Prior work suggests these forms of optimism are moderately to highly correlated (Kubzansky et al., 2002; Scheier, Carver, & Bridges, 2001). While dispositional optimism has been considered in multiple investigations of both chronic disease and mortality risk, explanatory style optimism has not been assessed in relation to mortality risk specifically thus far. Evidence indicates that higher dispositional optimism is associated with lower mortality risk. A study of 97,253 women aged 50-79 participating in the Women's Health Initiative showed that scoring in the highest versus lowest quartile of optimism, as defined by the 6-item Life Orientation Test-Revised (LOT-R)

scale (Scheier, Carver, & Bridges, 1994), was related to a 14% reduced hazard of mortality over eight years ($HR=0.86$, $CI=0.79-0.93$), even after adding psychological distress to multivariable models (Tindle et al., 2009). Analyses conducted in another cohort of midlife U.S. women, the Nurses' Health Study, replicated these results using the same research design (Kim et al., 2017). Additionally, a Netherlands-based study among men and women aged 65-85 ($N=941$; from the Arnhem Elderly Study) found a similar pattern over a 9-year period ($HR_{\text{highest versus lowest quartiles}}=0.71$; $CI=0.52-0.97$), despite using a different optimism measure (seven items derived from the Dutch Scale of Subjective Well-Being for Older Persons scale). However, these results were not adjusted for psychological distress (Giltay, Geleijnse, Zitman, Hoekstra, & Schouten, 2004).

Because of the lack of studies considering explanatory style optimism in relation to mortality, we cannot directly compare mortality findings across the two forms of optimism. However, in a very recent investigation, researchers used the Revised Optimism-Pessimism (PSM-R) index derived from the Minnesota Multiphasic Personality Inventory (Malinchoc, Offord, & Colligan, 1995) to measure explanatory style optimism among 1,429 U.S. men from the VA Normative Aging Study and assess its association with longevity (Lee et al., 2019). Results suggested that those in the highest versus lowest quartile of optimism scores were significantly more likely to reach the age of 85 over a 30-year period ($OR=1.5$, $CI=1.0-2.3$), after adjustment for sociodemographics, medical status, health behaviors, and further control for psychological distress (Lee et al., 2019). Such findings provide promising preliminary evidence that the explanatory style of optimism is also related to mortality risk.

Emotional vitality. Emotional vitality is a positive state characterized by feelings of enthusiasm, energy, and interest, combined with an ability to effectively regulate emotions,

thoughts, and behavior (Kubzansky & Thurston, 2007; Ryan & Frederick, 1997). Although no studies to date have evaluated its association with all-cause mortality risk while adjusting for sociodemographics, medical status, and health behaviors, secondary results reported in a study of emotional vitality and risk of coronary heart disease provide some preliminary evidence (Kubzansky & Thurston, 2007). Using data from the National Health and Nutrition Examination Survey (NHANES) cohort with 6,265 adults, researchers created an emotional vitality index using six items from the General Well-Being Schedule (Fazio, 1977). Findings suggested that moderate and higher versus lower levels of emotional vitality were associated with a 19% and 24% reduced risk of mortality, respectively, over a mean of 15 years of follow-up ($HR=0.81$, $CI=0.72-0.91$; $HR=0.76$; $CI=0.68-0.85$) when controlling for sociodemographics (Kubzansky & Thurston, 2007).

Overall psychological well-being. A few other studies have investigated effects of global measures of psychological well-being in relation to mortality risk. For instance, in a subset of the MIDUS cohort ($N=3,032$; aged 25-74), scores on items assessing positive affect, life satisfaction, eudaimonic well-being and social well-being were combined to capture positive mental health—also labeled *flourishing* by the authors (Keyes & Simoes, 2012). Multivariable results indicated that those who were not versus were flourishing according to this composite had significantly greater odds of 10-year mortality ($OR=1.62$; $CI=1.00-2.62$). Similar results were obtained from a recent 10-year study conducted as part of a larger cohort grouping 12 European countries (the Survey of Health Ageing and Retirement in Europe [SHARE]), in which the 19-item CASP scale capturing a sense of control, autonomy, pleasure and self-realization (Hyde et al., 2003) was administered to 13,596 adults aged 50 years and over (Okely, Weiss, & Gale, 2018). Specifically, for every 1-SD increase on the index score, mortality risk was reduced by 8%

(HR=0.92; CI=0.86-0.97) after additional control for psychological distress and country-level health care (Okely et al., 2018).

Summary

Consistency of associations. Overall, this narrative review of the existing literature indicates that several PWB dimensions are associated with a reduced risk of all-cause mortality among the general population, with small to medium effects. These relationships were observed in studies with large sample sizes and over a range of follow-up period durations. Associations were robust to adjustment for numerous covariates, including potential mechanisms that could explain associations (e.g., health behaviors); for some dimensions, associations were consistently evident regardless of which scale was used to assess the same PWB construct (e.g., optimism). Among the dimensions reviewed for which at least a few studies were available, purpose in life, optimism, and life satisfaction most consistently showed a significant association with reduced mortality risk, independent of covariates, followed by *ikigai*, positive affect, mastery, and sense of coherence. Available results with happiness, personal growth, and autonomy suggested no effect or were too limited to draw firm conclusions.

Other potentially important PWB dimensions, including self-acceptance, joy, and awe, have not been investigated with all-cause mortality risk using prospective research designs and rigorous control for traditional medical and behavioral risk factors. Whether studies of PWB and mortality will benefit from using a combined (e.g., flourishing) versus specific (e.g., life purpose) measure of PWB has not been sufficiently evaluated in prior work. Based on findings reported throughout this chapter, we suggest that retaining an understanding of how individual components of PWB relate to mortality (and other physical health outcomes) remains a valuable

endeavor. Nonetheless, some research questions will clearly benefit from combining various components of PWB. For example, if investigators are considering PWB as an outcome and trying to assess ways to optimize individuals' overall sense of well-being, a combined measure may be highly valuable (VanderWeele, 2017). However, when trying to understand whether some dimensions may play a stronger/independent role in longevity, these composite scores also limit our understanding of the specific dimensions that matter and further constrain our ability to make appropriate recommendations for future interventions (Scheier & Carver, 2018; VanderWeele, 2017).

Quality of statistical adjustment for covariates. Nearly all studies described in our review carefully controlled for baseline sociodemographics, medical status, and health behaviors, and even after further adjustment for psychological distress, associations were generally evident. When adjusting for self-rated health, some of these studies of certain domains (i.e., purpose in life, autonomy, positive affect, life satisfaction), though not all (i.e., mastery, *ikigai*), indicated null estimates. However, controlling for self-rated health may sometimes be an overadjustment (Diener et al., 2018; Kubzansky et al., 2016), because this rating is both defined and influenced by functional health, physical conditions, and most importantly, psychological distress and well-being (Jylha, 2009; Picard et al., 2013). Nevertheless, those PWB dimensions that are associated with lower mortality even after adjustment for self-rated health arguably manifest even stronger evidence for an independent relationship.

Comparison of effect estimates across dimensions. Only a handful of the cited studies above have considered more than one PWB dimensions permitting direct comparisons within study. For instance, the British study of 9,420 adults followed over five years (Netuveli et al., 2012) evaluated four domains of PWB (sense of control, self-realization, autonomy, pleasure)

and results suggested that only a sense of control and self-realization were significantly associated with mortality risk in separate models. However, in most studies even when more than one PWB dimension was investigated, few authors evaluated their independent roles by including dimensions simultaneously in the analytic models. One exception is the German Aging Survey study in which independent effects of life satisfaction and positive affect with all-cause mortality were reported (Wiest et al., 2011). Yet, PWB scores came from different scales and were not standardized, which precludes comparing their respective estimates vis-à-vis magnitude since they are not on the same scale. In Alimujiang and colleagues' study, the fully-adjusted estimate of the relationship between purpose in life and all-cause mortality remained statistically significant beyond adjustment for optimism and positive affect; however, estimates for these two other PWB dimensions were not reported (Alimujiang et al., 2019). Thus, while these PWB factors appear conceptually distinct, it remains uncertain whether they independently reduce all-cause mortality and if so, what is the relative magnitude of their effects.

Potential Mechanistic Pathways

There are various theoretical models explaining how PWB can potentially influence health outcomes, including mortality. We will focus on biological and behavioral processes here, as depicted in Figure 1. Also shown in this figure are the potential effects of PWB on stress-related processes. Briefly, it is postulated that another way by which PWB influences physical health is by reducing the frequency/severity of stress-related factors, such as perceived stress and negative emotions, and their harmful impact on health outcomes. For more details on this stress-buffering effect, we refer the readers to a recent article on the topic (Pressman et al., 2019).

Both observational and interventions studies targeting PWB's role on biobehavioral processes are reported below. Examples of observational studies were selected for their rigorous research design, analogous to those used in the mortality studies described above. Interventions studies cited in the current section are primarily at the individual level, derived from research in positive psychology, which generally shows modest but positive changes in PWB levels following interventions aiming to enhance one or multiple PWB dimensions (Bolier et al., 2013; Chakhssi, Kraiss, Sommers-Spijkerman, & Bohlmeijer, 2018; Sin & Lyubomirsky, 2009; Trudel-Fitzgerald et al., in press). While the contribution of biological and societal factors in one's PWB has been widely documented (Bartels, 2015; Kobau et al., 2011; Kubzansky et al., 2018; Patel et al., 2018; Steptoe, 2019), individual choices and behaviors, such as self-regulation and lifestyle habits, are also important determinants of PWB (Kubzansky et al., 2018; Van Cappellen et al., 2018). Readers interested in examples of institution-level interventions and policies to increase dimensions of well-being are referred to a recent narrative review by Trudel-Fitzgerald and colleagues (in press).

Behavioral Factors

Observational studies. Results obtained in the general population have shown that individuals experiencing greater levels of PWB are more likely to engage in favorable health behaviors and less likely to adopt detrimental ones (Boehm, Chen, et al., 2018; Boehm & Kubzansky, 2012; Hernandez et al., 2018; Kubzansky et al., 2018; Pressman et al., 2019; Scheier & Carver, 2018) that are important for extending lifespan (Loef & Walach, 2012; Song & Giovannucci, 2016). Yet, almost all prospective studies have investigated only one behavior or have focused on only one PWB dimension, optimism being the most frequent (Baruth et al.,

2011; Boehm, Chen, et al., 2018; Boehm, Soo, et al., 2018; Giltay, Geleijnse, Zitman, Buijsse, & Kromhout, 2007; Haller, 2016; Hernandez et al., 2019; Hingle et al., 2014; Kim, Kubzansky, Soo, & Boehm, 2016; Progovac, Chang, et al., 2017; Progovac, Donohue, et al., 2017).

Nonetheless, a recent prospective study considered both happiness and optimism in relation to the adoption of multiple health behaviors in over 35,000 midlife women from the Nurses' Health Study cohort who were free of chronic disease at baseline (Trudel-Fitzgerald et al., 2019).

Results indicated that women with moderate and higher levels of dispositional optimism compared to those with lower levels, were 22% and 40% more likely to report sustaining a healthy lifestyle, respectively, over a 10-year period and after adjusting for demographics and psychological distress. This dose-response relationship was also obtained when evaluating associations with each single health-related behavior included in the lifestyle index separately (i.e., physical activity, diet, smoking, alcohol consumption, and body mass index). Highly comparable findings were observed with happiness levels, captured with a 1-item measure, over a 22-year period (Trudel-Fitzgerald et al., 2019). Importantly, although bidirectional associations were found between PWB and lifestyle levels, estimates were larger when happiness and optimism were considered as the exposures/predictors rather than the outcomes (Trudel-Fitzgerald et al., 2019). Aside from conventional lifestyle factors, medical adherence could also mediate the association of PWB with mortality and chronic disease risk. For instance, a prospective study among 7,168 midlife adults from the HRS cohort suggested that higher levels of purpose in life were related to a greater likelihood of using preventive health care services, such as obtaining a cholesterol test or colonoscopy over six years (Kim, Strecher, & Ryff, 2014). Associations were maintained even after adjusting for psychological distress and positive affect (Kim et al., 2014).

Intervention studies. Several studies have evaluated whether interventions to modify PWB will affect subsequent lifestyle habits to test more directly whether PWB causally contributes to health behaviors, with most of them conducted in medical patient samples. Even fewer investigations have targeted multiple PWB dimensions, but available results suggest specificity, whereby either i) some but not all PWB dimensions (targets of intervention) impacted the outcome, or ii) some but not all health behaviors (outcomes) were effectively altered by the intervention. For example, a recent clinical trial evaluated changes in positive affect and in dispositional optimism across the 4-month window following a positive psychology intervention generally targeting gratitude, personal strengths, and meaning in life among 128 patients with an acute coronary syndrome (Duque, Brown, Celano, Healy, & Huffman, 2019). Results indicated that increases in positive affect but not optimism led to greater adherence to multiple health behaviors (e.g., diet, physical activity). Although these findings hint at a distinct influence by separate PWB dimensions, replication of this study is needed as these findings could be a methodological artifact, influenced by the small sample size and related limited statistical power. Moreover, a recent randomized-controlled trial (N=159) showed that HIV patients who received a positive psychology intervention aimed at increasing positive affect specifically, were more likely to adhere to their antiretroviral therapy in the following 15-month period compared to the control group, whereas no differences between groups over time were observed on the adoption of risky sexual behaviors (Moskowitz et al., 2017). However, the intervention was composed of eight strategies targeting multiple PWB dimensions, leaving it unclear whether some dimensions might be more potent with regard to improving medical adherence. Overall, evidence that health behaviors substantially change after an intervention to enhance specific components of PWB (or PWB more generally) is still limited and mixed.

Whether such changes are maintained over time is also uncertain, even though few studies to date have sought to examine this directly. The field will benefit from additional randomized-controlled trials with longer follow-up periods (Hernandez et al., 2018; Pressman et al., 2019).

Biological Factors

Although biological factors are often considered as potential mechanistic pathways, relative to studies of behavioral pathways, fewer biological factors have been investigated in prospective longitudinal studies despite their direct association with age-related processes (Castagne et al., 2018; Sebastiani et al., 2017). Because collection of biospecimens and biomarker data is resource-intensive, most studies to date are based on cross-sectional data. While such findings can provide preliminary information, they also generally preclude interpretation about directionality/causality. Most studies that do include elements of time ordering are conducted within short-term experimental settings, and as a result, they cannot inform understanding of natural, secular trends over time.

Observational studies. Several prospective studies of PWB and health-relevant biological processes that controlled for sociodemographics, medical status, and health behaviors have been conducted and findings are suggestive. Notably, higher levels of PWB were associated with reduced future risk of dysregulated levels of blood pressure (Richman et al., 2005; Trudel-Fitzgerald, Boehm, Kivimaki, & Kubzansky, 2014) and glucose control (Hafez et al., 2018; Okely & Gale, 2016; Tsenkova, Karlamangla, & Ryff, 2016), and slower progression of carotid intima medial thickness (Matthews, Raikonen, Sutton-Tyrrell, & Kuller, 2004), as well as with healthier levels of lipids (Radler, Rigotti, & Ryff, 2018; Soo, Kubzansky, Chen, Zevon, & Boehm, 2018) over time. Interestingly, several of these studies have considered more than one

PWB dimension. In some cases, methodological artifacts, such as the use of a limited 1-item measure of the exposure (Trudel-Fitzgerald et al., 2014) or a very small number of outcomes (Richman et al., 2005), constrains more definite conclusions as to whether distinct PWB dimensions impact subsequent biological processes differently. A recent MIDUS study in which *trajectories* of six distinct PWB dimensions, all measured with the Scales of Psychological Well-Being (Ryff, 1989), were investigated in relation to lipids over up to 10 years among 1,054 midlife adults is worth mentioning (Radler et al., 2018). Results indicated that adults with persistently high (versus low) levels of mastery and self-acceptance had significantly healthier levels of HDL-cholesterol and triglycerides, whereas no association was found when evaluating trajectories of the other PWB dimensions as exposures (e.g., autonomy, personal growth, purpose in life), nor when considering LDL-cholesterol as the outcome.

PWB has been examined in relation to several markers of other health-related biological processes in prospective studies. For instance, higher PWB levels based on the CASP scores were associated with lower levels of c-reactive protein (CRP) but not fibrinogen, two inflammation markers that were assessed two years after PWB amongst 5,622 British adults 50 years and older from the English Longitudinal Study of Ageing (ELSA; Okely, Weiss, & Gale, 2017). Evidence also indicates that both hedonic and eudaimonic dimensions of PWB are significantly associated with greater likelihood of maintaining healthy functioning in these biological processes (Boylan & Ryff, 2015; Zilioli, Slatcher, Ong, & Gruenewald, 2015). More specifically, in a sample of 1,205 midlife U.S. adults followed for 10 years in MIDUS, for every 1-SD increase in life satisfaction there was an 18% lower odds ($OR=0.82$; $CI=0.69-0.97$) of developing metabolic syndrome (e.g., unhealthy levels of triglycerides, cholesterol, blood pressure, glucose, and central obesity). The effect estimate was even larger (per 1-SD increase,

OR=0.77; CI=0.65-0.93) for a eudaimonic well-being measure—a composite of autonomy, environmental mastery, personal growth, positive relationships, purpose in life, and self-acceptance—(Boylan & Ryff, 2015). However, the authors did not report whether these two PWB indicators were associated with the outcome independent of one another. In this study, authors also observed comparable estimates between overall life satisfaction and eudaimonic well-being, respectively, in relation to the number of dysregulated metabolic components exhibited by the participants 10 years later, but did not assess the likelihood of developing each component separately (Boylan & Ryff, 2015). Another longitudinal investigation within MIDUS and using the same PWB measure examined a different index of biological function, allostatic load, which captures biological wear-and-tear (Zilioli et al., 2015). In this study allostatic load was measured by dysregulated functioning in cardiometabolic parameters, inflammatory processes, sympathetic nervous system [SNS], parasympathetic nervous system [PNS], and hypothalamic pituitary adrenal [HPA] axis. Results obtained in 985 midlife adults suggested that higher levels of purpose in life were significantly related to lower levels of allostatic load 10 years later, even after adjusting for sociodemographics, psychological distress, and positive affect (Zilioli et al., 2015).

Preliminary research on several other potential biological pathways are worth mentioning as well, although few studies compared multiple PWB dimensions and, most importantly, nearly all were cross-sectional. First, investigators are increasingly conducting research using genetic markers. For instance, authors evaluated the association of optimism with telomere length in several samples of European men with n's varying from 101 to 178, and reported null findings (Rius-Ottenheim et al., 2012). However, these studies used a 4-item optimism measure that was not previously validated. Another line of work has reported more positive findings considering

dispositional optimism in relation to gene expression among 114 Japanese men (Uchida, Kitayama, Akutsu, Park, & Cole, 2018). Using a genomic approach, other investigators reported separate gene regulation profiles associated with hedonic versus eudaimonic PWB dimensions among 84 U.S. adults (Fredrickson et al., 2013). While these findings seem to hint at critical biological variations underlying PWB dimensions, they have been somewhat controversial, notably because of the substantial overlap between the scores obtained from psychological scales used, and the numerous covariates included in the statistical models (Coyne, 2013), suggesting the need for future replication. Second, one study has considered PWB in relation to antioxidants, posited to serve as a marker of a restorative health promoting process. Results obtained in 982 midlife men and women from MIDUS suggested that dispositional optimism was associated with some (e.g., α -carotene and lycopene [carotenoids]) but not all (e.g., α -tocopherol [vitamin E], lutein [carotenoid]) antioxidant indicators on average two years later (Boehm, Williams, Rimm, Ryff, & Kubzansky, 2013). Longitudinal studies targeting these biological processes are clearly needed.

Intervention studies. From a clinical trial perspective, only a handful of studies have investigated whether changes in various PWB dimensions induced by an intervention translate into changes in biomarkers levels. Most of this work has been done in patient populations. In the randomized-controlled trial among 159 HIV patients described earlier (Moskowitz et al., 2017), substantial improvement on viral load levels were obtained from pre- to post-assessment in the intervention group (versus the control group), but no effects were observed on changes in CD4 cells. While these results may hint at the possibility of outcome-specificity, exposure-specificity cannot be disentangled due to the multi-component nature of the intervention during which multiple dimensions of PWB were manipulated.

Interestingly, another randomized-controlled trial among 69 cardiac patients compared levels of biomarkers obtained from blood sample before and after three positive psychology interventions to the levels obtained in a wait-list condition (Nikrahan et al., 2016). The interventions were each informed by one of three different frameworks and consisted of six weekly 90-minute in-person group manualized sessions. Specifically, as reported by the study authors (Nikrahan et al., 2016), the first strategy aimed to increased optimism, positive affect, identifying and using personal strengths, and finding meaning in life; a second strategy targeted the improvement of optimism, gratitude, as well as religion/forgiveness, social relationships, physical activity, and adaptive coping skills; the third strategy focused on optimism, in addition to becoming more present-oriented, reducing negative cognitions/affect, increasing organizational/productivity skills, setting realistic goals, and focusing on positive personality traits like being genuine. While there was moderate overlap between the three interventions, notably with the inclusion of optimism strategies, each had some unique elements. Inflammatory markers were collected at pre- (baseline) and post-intervention (week 7), and at the follow-up assessment (week 15), while markers of the HPA-axis activity were assessed pre- and post-intervention only.

Results for inflammatory markers indicated greater decline in CRP levels, but not IL-1 or IL-6, from pre- to post-intervention among participants in the first or third program versus those in the control group, after adjustment for clinical variables and psychological distress ($p=.04$). No significant changes were noted from baseline to 15-week follow-up in these two intervention groups. Conversely, compared to the control group, the second program led to no changes from pre- to post-intervention in inflammation markers, but to a marginally significant decline in IL-1 from baseline to follow-up ($p=.07$). Results with HPA-axis activity marker similarly

distinguished the three programs, as only the second one was related to an alteration of the cortisol awakening response ($p=.03$), beyond control for clinical variables, psychological distress, and awakening time. The authors postulated that changes in eudaimonic PWB dimensions (e.g., meaning in life), rather than in hedonic ones (e.g., positive affect), might have driven these results (Nikrahan et al., 2016). Of course, caution is warranted when interpreting these exploratory results as they are based on small sample sizes; with groups varying from 13 to 15 participants, significant results may indeed be due to chance rather than true effects. However, we describe this study in detail because of its rigorous design and implementation, and its novelty in considering multiples biomarkers and distinct positive psychology interventions in relation to various PWB dimensions, in hopes that work like this will encourage future investigations with larger sample sizes to replicate these results.

Summary

Altogether, prospective observational and intervention research on biological and behavioral processes offer sufficient positive results to suggest that further research is warranted. However, important to note is that most results are small to modest, and it is sometimes unclear whether positive findings from intervention studies are due to strategies that aim to increase overall versus specific dimensions of PWB (e.g., multicomponent interventions to increase overall well-being versus the “best possible self” exercise to increase optimism). Nonetheless, because even changes of small magnitude at the individual level may translate into large changes at the population level, the potential benefits of such interventions on mental and physical health, including mortality risk and related biobehavioral pathways, may be substantial.

In the future, researchers should prioritize methodologically rigorous studies (either observational or experimental) that are i) based on larger sample sizes, to obtain more stable (and perhaps larger) estimates, and ii) longitudinal, to lower potential for reverse causation. Explicitly comparing PWB dimensions is also warranted. Specifically, in observational studies, considering multiple PWB dimensions will help clarify whether some relate more strongly than others to these potential biobehavioral mechanistic pathways over time; in intervention studies, clarifying whether strategies *a priori target* and ultimately, *impact* one or more PWB dimensions will bring a more nuanced understanding of the mechanisms of change. Intervention studies among non-medical populations are also needed.

Other biological processes that are restorative by nature, such as antioxidant, should also be investigated in future longitudinal studies. Moreover, given the dynamic nature of these processes, subsequent research should take a deeper look into bidirectional associations (Ryff, 2017; Trudel-Fitzgerald et al., 2019) to determine whether and when PWB truly acts as either a determinant or outcome of these processes. Additionally, consideration of the interrelations between biological and behavioral factors, as depicted in Figure 1, will likely lead to a more complex, but also more realistic, understanding of the extent to which these potential mechanistic pathways influence each other when relating PWB to mortality risk. Preliminary exploration of this issue has been done, notably in the MIDUS study on antioxidants described above (Boehm et al., 2013). Findings revealed that health behaviors accounted for nearly half (46%) of the association between optimism and total carotenoid concentrations in particular. Because health behaviors and antioxidant levels were assessed at the same time point in this study, the direction of effects remain unclear. Further examination of the intertwined longitudinal relationships between behavioral and biological processes with optimal temporality is warranted.

Methodological Considerations

Findings from existing epidemiological studies may inform future research. In addition to conducting studies using the most rigorous designs possible (e.g., longitudinal, rigorous control for potential confounders), future work will benefit from considering a number of key issues highlighted here. We consider these issues according to their relation with PWB, mortality or other physical health related outcomes, or covariates including potential confounders, pathways (mediators), or effect modifiers (moderators). We end by considering potential biases and related issues.

Challenges Related to Studying Psychological Well-Being as an Exposure

Comparison of PWB dimensions. Firstly, as argued throughout this chapter, a critical task for future studies is to shed light on how various PWB dimensions relate to health, both separately and synergistically (Diener et al., 2018; Pressman et al., 2019; Steptoe, 2019). As of today, it remains difficult to compare the magnitude of the effects because, among the few studies that compared several PWB dimensions in relation to mortality, most did not use standardized and comparable scores of the PWB exposures. Although numerous large-scale studies have administered at least one PWB measure to their participants (e.g., Women's Health Initiative cohort, Nurses' Health Study, Midlife in the United States Study, Health and Retirement Study, Longitudinal Aging Study Amsterdam, EPIC-Norfolk Study, Japan Collaborative Cohort Study), the various indicators are often queried years apart, which limit direct comparison. Including a richer set of PWB measures simultaneously in these studies to permit comparison across constructs and expanding PWB assessments to other large national

cohorts may be a challenge given that questionnaire space is limited, but remains highly warranted.

To disentangle the unique versus shared contribution of PWB dimensions more optimally, some authors have suggested setting up studies allowing the contrast of PWB dimensions that rely on the same time frame (e.g., past few days versus over a lifetime; Pressman et al., 2019). In fact, prior work has demonstrated that using the same time frame for distinct PWB measures, notably positive affect and life satisfaction, increased the strength of the correlation between scores but did not fully account for their conceptual differences (Luhmann, Hawkley, Eid, & Cacioppo, 2012); however, these authors have not explored whether such nuances are associated with health-related outcomes. Comparing how items within the same scale are associated with health outcomes may also help to capture active ingredients (e.g., across facets of positive affect; Petrie et al., 2018). A related research question of importance is whether prediction of mortality risk is enhanced by assessing two or more PWB dimensions and combining their scores to identify participants who report, for instance, higher levels on all, some, or none of the PWB dimensions.

Temporality. Other methodological concerns pertain to temporal aspects of the exposure, notably how often PWB is measured, what is the time frame used to capture PWB, and to what extent PWB dimensions are stable constructs over time.

Frequency of assessment. First, the vast majority of longitudinal studies presented in this chapter have relied on a single assessment of PWB mean levels in relation to mortality risk. However, multiple assessments of PWB over time may provide complementary information via the characterization of PWB dynamics. For instance, *variability* in the experience of PWB may matter for physical health as well. As an example, in a study of 4,458 Australian adults (Boehm

et al., 2015), life satisfaction was assessed annually over nine years and results suggested that the risk of mortality was elevated in those with lower mean life satisfaction level, averaging all available PWB assessments, and increased even more strongly if participants exhibited high variability in their PWB scores over time (p -value for mean \times standard deviation interaction $\leq .001$). Similarly, studies examining *(in)stability* of PWB levels over time could shed additional light on this question. For instance, German adults who reported less versus more decline in their trajectory of life satisfaction scores had a reduced risk of mortality over a 20-year follow-up period (Hulur et al., 2017). Other markers of PWB dynamics, such as *inertia*, the resistance to affective change (Ong & Ram, 2017), have not been studied yet in relation to mortality to our knowledge.

Time frame and cognitive orientation to PWB constructs. A related, albeit distinct, issue is that some PWB dimensions rely on individuals' assessment of their past experiences (e.g., life satisfaction), while others capture their present (e.g., positive affect), or future/predicted experiences (e.g., optimism)². Whether different dimensions of PWB differentially predict mortality or other health-related outcomes may relate in part to what individuals are assessing when they self-report PWB. In a 3-year study conducted in nationally-representative Spanish sample of adults aged 18 and older (Martin-Maria et al., 2016), positive and negative affect was assessed with the Day Reconstruction Method (DRM; Kahneman, Krueger, Schkade, Schwarz, & Stone, 2004), which restricts evaluation of affect to the prior day during various activities. In the same study, the Cantril Self-Anchoring Striving Scale (Cantril, 1965) was also used to determine the extent to which individuals thought they were living the worst versus best possible

² Other authors have referred to these various timeframes by distinguishing “experiential” from “evaluative” measures, where the former captures in situ reports of emotional experiences whereas the latter captures global retrospective evaluations (Diener et al., 2018).

life (on a 11-point Likert scale); this measure is highly correlated with life satisfaction (Helliwell, Barrington-Leigh, Harris, & Huang, 2010). Results indicated that 1-unit increase in positive affect based on an individual's experience of 1 day was related to an 18% decreased risk (HR=0.82, CI=0.68-0.99) of mortality over the follow-up, but life evaluation based on an individual's assessment of their current and past experiences more generally was not associated with mortality risk (Martin-Maria et al., 2016). These findings were evident after including both PWB indicators in the analytic model as well as adjusting for conventional covariates and negative affect. Such results may suggest that assessment of current PWB levels predict mortality risk more strongly than retrospective levels, but replication is warranted. In fact, effects of positive affect and life evaluation might also differ between, for instance, Spanish versus American participants, as well as individuals in early versus late adulthood.

Stability of PWB constructs. Furthermore, some PWB dimensions may be conceptualized as more stable (trait-like; e.g., optimism, life satisfaction) than others (state-like; e.g., positive affect, happiness) over days or weeks. The magnitude of changes as a response to external events, called *affective reactivity* (Ong & Ram, 2017), could vary across PWB dimensions depending on whether they are more trait-like or state-like. For instance, 181 men from the VA Normative Aging Study included in an 8-day daily diary study reported every evening various information like daily stressors along with positive and negative affect (Mroczek et al., 2015). While daily average positive affect was not related to mortality risk over the 10-year follow-up, every 1-unit *decrease* in positive affect *following the experience of a daily stressor* was related to 132% increased risk of mortality (HR=2.32, CI=1.32-4.00), after adjusting for sociodemographics, medical status, and psychological distress. Whether changes in PWB dimensions that are believed to be more stable (e.g., optimism) following a minor or major

stressor (e.g., argument with a loved one, accident/illness) is related to mortality has not been well studied.

Altogether, considering temporal aspects of PWB suggests the potential importance of studies that include not only repeated measures of PWB levels over many years, but also intensive measurement of PWB levels over consecutive days or weeks. Such measures can be obtained via methods such as Experience Sampling Methods (ESM) and Emotional Momentary Assessment (EMA; Diener et al., 2018; Steptoe, 2019); novel metrics, including recurrence quantification analysis (Jenkins, Hunter, Richardson, Conner, & Pressman, 2019), could also help characterize PWB dynamics in future health-related research (Pressman et al., 2019). However, according to some authors, it remains unclear whether these strategies provide significantly greater advantages over more traditional approaches, such as using the average and standard deviation calculated from scores obtained on self-reported scales and EMA metrics (Dejonckheere et al., 2019; Diener et al., 2018). Regardless, considering these temporal aspects of how PWB is experienced might provide additional information about aspects that distinguish PWB dimensions. Further research needs to determine whether and to what extent the use of dynamic measures can add to our understanding of PWB's role in health outcomes and mortality.

Potential detrimental effects. Another methodological issue of note is whether extreme PWB levels might have a detrimental influence on subsequent health-related outcomes (Diener et al., 2018). For example, it is possible that unrealistic optimism (e.g., “I am convinced I won’t get lung cancer”) or extreme positive affect (e.g., being overly excited) may be followed by adverse health consequences such as smoking habits or increased blood pressure, respectively. Few authors have examined this question empirically, especially within longitudinal research designs, mostly investigating the question with optimism as a predictor of future health behaviors. For

instance, a study on unrealistic optimism reported that overly optimistic expectations led to greater alcohol consumption one year later in college freshmen (Dillard, Midboe, & Klein, 2009). Conversely, in the study of over 35,000 midlife women described previously (Trudel-Fitzgerald et al., 2019), those who had the highest score on the optimism scale (19% of the sample) were still significantly *more likely* to sustain an healthy lifestyle over the 10-year follow-up period compared to their least optimism counterparts. This discrepancy could be due, at least partly, to the age group under examination, with younger individuals more prone to extreme levels of PWB that can lead to being unrealistic.

Some detrimental effects of PWB on biological factors have been documented. Much of this work was conducted among college students in a series of naturalistic studies of short duration (under a year; Segerstrom, 2005). While greater optimism levels generally had a protective association with markers of cellular immunity (e.g., number of CD4+ T cells in peripheral blood), a detrimental effect was observed when optimistic individuals persisted in rather than disengaged from a challenge, such as trying to balance extramural commitments with school requirements (Segerstrom, 2005). These findings suggest that not only *extreme levels* of some PWB dimensions could potentially have a detrimental impact on health-related outcomes for certain populations, but also potentially the *context* in which PWB dimensions are experienced, and their *duration*, even when levels are not extreme. To our knowledge, no mortality studies have specifically tackled this issue of potential detrimental effects by distinct dimensions of PWB. Additionally, less much is known about extreme levels of other PWB exposures and other health-related outcomes in various populations.

Challenges Related to Studying Mortality or Other Physical Health Endpoints as Outcomes

Objective data. While the methodological issues identified above are largely related to methods for assessing, conceptualizing, and evaluating the exposure (PWB), another key element for the PWB-health research pertains to the importance of using objective outcomes. This may seem obvious for mortality, which cannot be self-reported and is usually obtained from medical registers; yet, favoring objectively defined chronic disease diagnoses (e.g., as validated by a physician blinded to the study hypotheses or hospital records) whenever possible will lower risk of bias whereby individuals with higher PWB levels may report their physical health more favorably.

Reverse causation. Along the same lines, reverse causation—whereby participants' declining physical health preceding mortality might impact the assessment or report of PWB levels—is a critical concern that should be addressed in all studies. Increasingly, researchers conduct sensitivity analyses among individuals who survived for at least 1-2 years post-baseline to address this issue. In the few studies cited above that included such lagged models, associations were robust and yielded similar results (e.g., Boyle et al., 2009; Rosella et al., 2018; Sone et al., 2008), which strengthens the evidence for that PWB may causally contribute to health outcomes.

Causes of death. Differences in associations of PWB with varying causes of death have been noted in the handful of studies that had sufficient statistical power to explore this research question. In distinct studies that all controlled for sociodemographics, medical status, and health behaviors and considered either life purpose (Alimujiang et al., 2019), mastery (Surtees et al., 2006), sense of coherence (Surtees et al., 2003), *ikigai* (Tanno et al., 2009), optimism (Tindle et al., 2009) or overall PWB (Okely et al., 2018) in relation to cause-specific mortality, all obtained

estimates suggesting stronger associations of PWB with cardiometabolic-related mortality compared to cancer-related mortality, over follow-up periods of less than 10 years (except Tanno et al., 2009). As for cancer incidence, the smaller, often null estimates may truly reflect the absence of an association. However, methodological artifacts might also contribute to these findings. First, if the magnitude of the linkages is smaller for PWB with cancer than with cardiovascular outcomes, a larger sample size will be required to detect an effect with cancer. Second, because many cancers are relatively rare resulting in small case counts, studies often combine cases across cancer sites to increase power. Yet, it is well documented that different cancer sites represent different disease processes, with some being potentially more sensitive to psychosocial and behavioral factors than other (e.g., lung versus pancreas; Poirier et al., 2019; Trudel-Fitzgerald, Chen, Singh, Okereke, & Kubzansky, 2016). Third, unlike cardiometabolic outcomes, carcinogenesis development and progression are long-term processes, sometimes occurring over more than a decade (Conner et al., 2014; Labidi-Galy et al., 2017), which may not be captured adequately over shorter follow-up periods.

Challenges Related to Covariates

Confounding and mediation. Another concern is the adequate adjustment for potential confounders, especially with regard to third variables that influence both the exposure and the outcome. Although most recent studies have carefully controlled for conventional potential confounders (e.g., sociodemographics, medical status), it is not always the case. Failure to do so not only overlooks possible confounding effects, but also limits comparisons of effect estimates across studies, even when they are obtained from the same PWB scales.

The issue of confounding is particularly important when considering the role of behavioral factors in the relationship of PWB with mortality or other physical health outcomes. Health behaviors can either act as confounders in the association or as mechanisms linking PWB to mortality risk (Hernandez et al., 2018). Most studies to date have treated health behaviors as potential confounders, adjusting for baseline health behaviors. However, such studies cannot evaluate the possibility that health behaviors are one mechanism by which PWB may influence subsequent physical health outcomes, as baseline behavioral factors do not provide optimal temporality for evaluating mediation. Because few studies have explicitly examined such mediation patterns (see Okely et al., 2017 as one of the exceptions), it remains unclear the extent to which such behavioral factors may lie on the pathway between PWB and mortality risk. Such distinction remains important when trying to understand processes of change, to inform intervention strategies (Czajkowski et al., 2015; Nielsen et al., 2018). With multiple waves of data, such issues can, however, be addressed by controlling for health behaviors that are measured *prior* to PWB assessment, and by treating as mediator those health behaviors that are measured *subsequent* to the PWB assessment (VanderWeele, 2015). Due to developments within the causal inference framework, there is also growing awareness among scholars that exposure*mediator interactions may exist (Valeri & Vanderweele, 2013) and should be considered in future research investigating PWB's role in mortality risk.

Moderation by sociodemographic factors. Moreover, associations have been rarely investigated across sociodemographic groups and most studies were conducted in Western countries, which may not be generalizable to other subgroups.

Race and culture. Differences in the experience, value, and understanding of PWB dimensions across various countries, races, and cultures have been documented (Choi &

Chentsova-Dutton, 2017; Diener et al., 2018; Ma, Tamir, & Miyamoto, 2018; Ryff, 2017; Weziak-Bialowolska, McNeely, & VanderWeele, 2019; Wirtz, Chiu, Diener, & Oishi, 2009). In fact, preliminary observational findings obtained in the studies described previously hint that various sociodemographic factors may modify the PWB-mortality relationship. For instance, in the Women's Health Initiative study of optimism and mortality (Tindle et al., 2009), race/ethnicity modified the association, whereby the estimates were larger in Blacks versus White participants ($HR_{Blacks}=0.67$; $CI=0.50-0.90$ versus $HR_{Whites}=0.87$; $CI=0.80-0.96$; interaction test, $p\text{-value}=0.02$). However, the vast majority of studies cited above were conducted in high-income countries, circumscribed to certain races and cultures, which may not be generalizable to other populations. Hence, it remains unclear as of now whether findings obtained from existing rigorous studies assessing the PWB-mortality association would translate into similar results across race and cultures worldwide, given documented differences in the experience, value, and understanding of PWB. Although a relationship between PWB and reduced mortality risk is likely evident across many different populations (Pressman, Gallagher, & Lopez, 2013), some PWB dimensions may not translate or be relevant in certain cultures or population settings. Thus, careful assessment of which PWB dimensions are appropriate for study in different populations will be critical.

In an attempt to tackle potential cultural differences, the recent multi-country study described earlier (Okely et al., 2018) evaluated the interaction of overall PWB with levels of individualism within each European country, hypothesizing that the association of PWB with mortality would be stronger in more individualistic countries because of the emphasis they place on well-being. The authors relied on Hofstede's definition of individualism, which applies to a society *"in which the ties between individuals are loose: everyone is expected to look after him-*

or herself and his or her immediate family,” and on his related Individualism Index³ (Hofstede et al., 2010). The 11 European countries including 13,596 adults 50 years and over from the SHARE cohort were categorized in tertiles based on their score on the Individual Index (e.g., Netherlands were in the highest and Greece was in the lowest tertile). Multivariable models further controlled for psychological distress and, importantly, country-level health care to rule out influences other than individualism that might be due to country differences.

Although the PWB*individualism interaction term was not statistically significantly related to all-cause mortality within the whole sample (p -value=.15), when considering cardiovascular mortality specifically PWB remained significantly associated with mortality only amongst adults with the highest level of individualism (HR=0.64, CI=0.50-0.84). As reported by the authors (Okely et al., 2018), it is unclear whether these findings reflect greater value placed on PWB in individualistic versus collectivistic cultures, or instead, a failure to measure PWB accurately in collectivistic cultures. Nonetheless, such results remain intriguing, especially when contrasted with the large body of evidence showing that stronger and larger social networks, which are more closely related to collectivism than individualism, are consistently related to lower risk of death (Holt-Lunstad, Robles, & Sbarra, 2017; Holt-Lunstad, Smith, & Layton, 2010).

Sex, education, and age. Other sociodemographic factors beyond race and culture may also impact PWB’s association with mortality. Sex may be an important consideration as some studies have noted sex differences in these associations while others have not. For example, in one of studies considering *ikigai* (Tanno et al., 2009), although men and women with higher

³ This index provides a score for each country that captures its relative position against other countries. As examples, the U.S. is ranked first position with a score of 91, The Netherlands is found a few positions after with a score of 80, whereas Greece is ranked 45th with a score of 35 and Guatemala is in the last position (76th) with a score of 6 (Hofstede, Hofstede, & Minkov, 2010).

(versus lower) levels of *ikigai* had reduced mortality risk within five years of follow-up ($HR_{men}=0.80$; $CI=0.72-0.89$ versus $HR_{women}=0.80$; $CI=0.69-0.72$) of similar magnitude, beyond five years the estimates became stronger for men compared to women ($HR_{men}=0.85$; $CI=0.80-0.90$ versus $HR_{women}=0.93$; $CI=0.86-1.00$; interaction test, $p\text{-value}<.05$). Socioeconomic status may also modify associations of PWB with mortality. For instance, in a study evaluating mastery levels in relation to mortality risk, positive associations were evident in those with low, but not high, educational attainment; while stratified HRs were not reported, the interaction test was statistically significant with $p\text{-value}<.01$ (Turiano et al., 2014). Age may also be relevant. When considered in stratified analyses, estimates are generally similar among younger and older individuals, regardless of the PWB dimension studied in relation to mortality (e.g., Petrie et al., 2018; Sone et al., 2008; Tanno et al., 2009; Wiest et al., 2011). That said, few studies systematically considered this factor as a potential effect modifier, often because studies from epidemiological cohorts are based in midlife and older adults and given that health-related outcomes investigated are more often evident in older populations. In fact, participants in the “young” group of these stratified analyses are generally 40 years and older. Yet, evidence suggests that levels of certain PWB dimensions, as well as cognitive processes involved in these psychological factors (e.g., emotion regulation), vary by life stages (Lockenhoff & Carstensen, 2004; Scheibe & Carstensen, 2010). As proposed in Figure 1, considering PWB early in the life course, as well as its interaction with biobehavioral processes during that period, may be an important time window for investigating these associations to facilitate developing and evaluating primary prevention strategies likely to impact lifelong physical health and mortality risk. Thus, we strongly recommend future research considers age as a modifier, as well as other sociodemographic factors, more comprehensively.

Potential Biases and Related Issues

Survivor bias. In epidemiological cohorts where PWB measures were queried later in the life course, it is possible that individuals included in PWB-mortality studies because they did complete the exposure measure are in fact different than those who did not survive to this assessment, also known as “survivor bias” or left truncation (Banack, Kaufman, Wactawski-Wende, Troen, & Stovitz, 2019). Participants from a larger cohort who are excluded from a specific analytic sample because they chose to not complete a specific scale (here, the one used to measure the PWB exposure) may be different than participants who did complete the scale and in turn were included in the analytic sample. Reporting descriptive statistics of eligible and ineligible participants can hint to the presence or not of such bias; yet, other more precise methods, including inverse probability weights (IPW) whereby individuals included in the analytic sample are up-weighted to account for themselves as well as those with similar characteristics who unable to make it to the exposure assessment, could be included in future studies to help reduce concerns about this potential selection bias (Banack et al., 2019). Besides, it is worth briefly mentioning the potential influence of attrition over the follow-up period. For instance, while survival is the outcome of interest in mortality studies, it is not the case in investigations that focus on chronic disease incidence or potential biobehavioral pathways. When death occurs during follow-up, this can lead to “**selection bias** due to loss to follow-up” or right truncation (Banack et al., 2019), which may impact a study results and conclusions. Besides mortality, someone may no longer participate in a study because of major psychological distress, cognitive decline, or health-related problems, for example. Such reasons for dropout remain conceptually challenging because they likely relate to either the exposure or outcome of interest. Here again, various strategies can be implemented to assess the presence of such bias, ranging

from descriptive statistics to identify potential differences, to IPW to be included in the models, or sensitivity analyses that are conducted among non-dropouts only (Banack et al., 2019).

Internal versus external validity. Another concern relates to who participates in studies of PWB and mortality or other physical health outcomes. As noted previously, most studies have been conducted in Western population and midlife to older individuals. Although the homogeneity of a population can enhance a study's internal validity, results cannot necessarily be generalized to other populations, including Eastern and younger individuals. This field of research will benefit highly from future work on the association of PWB with risk of mortality and other health-related outcomes among more diverse or understudied populations.

Summary

In brief, prioritizing methodological rigor in future studies will help to provide more compelling evidence regarding whether PWB is a causal contributor of health-related outcomes, and will facilitate more accurate comparison across PWB dimensions as well as replication of studies in this field. Systematically incorporating well-being scales in large national cohort studies that provide follow-up periods long enough to tackle outcomes such as chronic diseases and mortality risk will be required. Such inclusion in recurring surveys would also permit investigation of more complex research questions, such as exploring the association between temporal dynamics of PWB with mortality risk. Including psychosocial measures in these multi-use samples has never been a simple task, given that most of these scales comprehensively capture constructs with numerous items and such studies are often highly sensitive to participant burden. Yet, taking into consideration constraints commonly encountered in such specific

contexts (e.g., space limitations), certain items have recently been recommended to guide selection of measures and stimulate work in this area (VanderWeele et al., this volume [2020]).

Conclusion

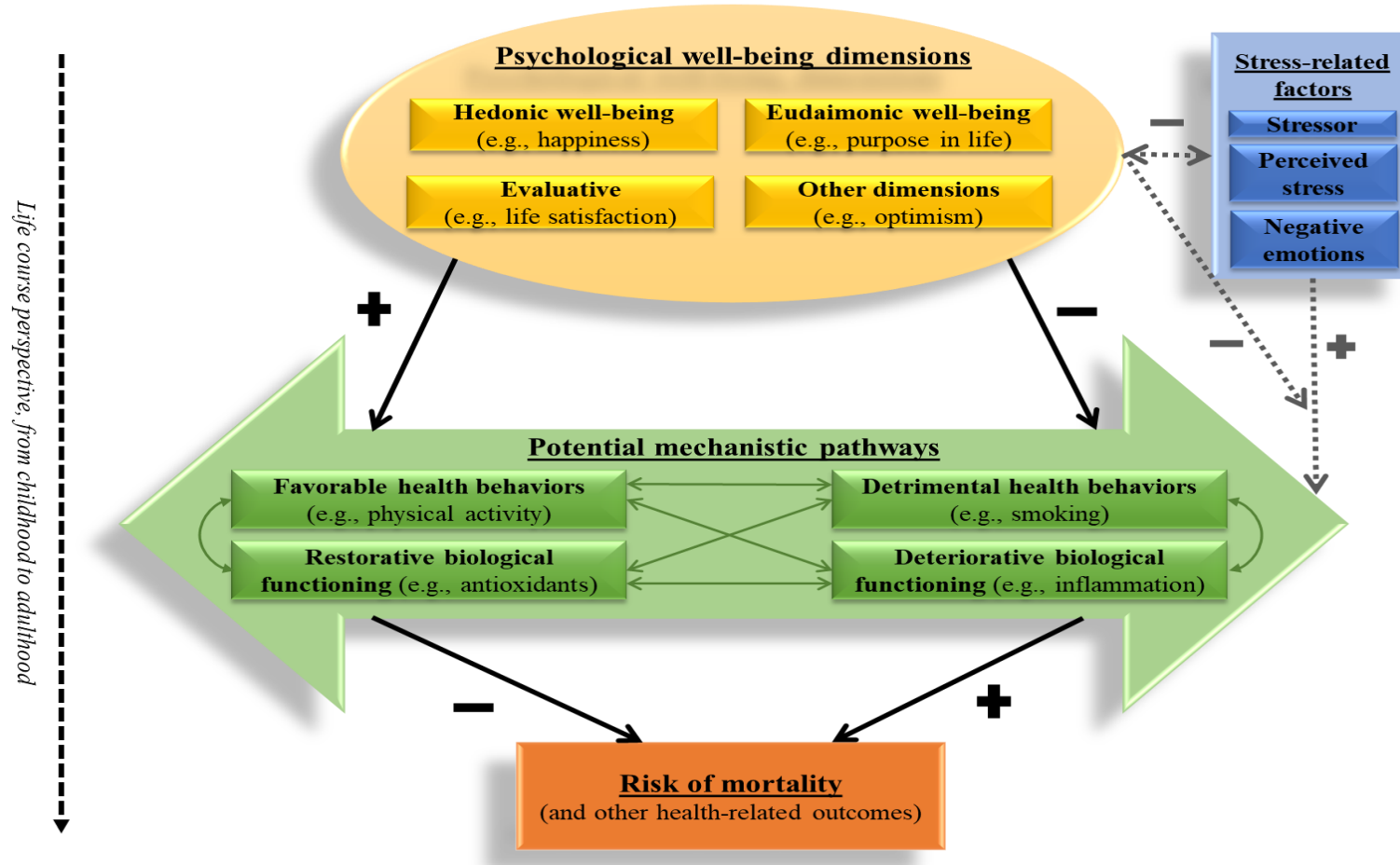
In this chapter, we summarized studies that have rigorously investigated the association between various dimensions of psychological well-being (PWB) and mortality risk. The most consistent evidence was obtained for purpose in life, optimism, and life satisfaction, further supporting their systematic inclusion in large national cohorts; followed by *ikigai*, positive affect, mastery, and sense of coherence. In these prospective studies, small to moderate associations were observed even beyond rigorous control for traditional sociodemographic, medical and behavioral risk factors. Available multivariable results with other PWB dimensions suggested no effect (e.g., happiness) or were too limited (e.g., personal growth, autonomy, emotional vitality) to draw firm conclusions. We also reviewed biological and behavioral mechanistic pathways that could explain the PWB-mortality linkage. Current findings from both epidemiological studies and clinical trials suggest PWB dimensions are associated with health behaviors (e.g., smoking, diet, physical activity) with the strength of the associations varying depending on the behavior; analogous results were noted for biomarkers (e.g., inflammation, HPA-axis activity). We concluded with various methodological considerations that we suggest may guide subsequent research that can most effectively inform the field.

Recommendations for Future Studies

Based on these considerations, we conclude with 12 recommendations for future work in this area. From a study design perspective, when feasible, researchers should consider 1)

including an understudied population; 2) including more than one PWB dimension per study; 3) administering repeated measures of distinct PWB dimensions, and 4) combining traditional self-reported scales with intensive longitudinal assessment (e.g., EMA). From an analytic perspective, whenever possible we suggest 1) standardizing scores if obtained from different PWB scales; 2) exploring the potential detrimental effect of extreme PWB levels in health-related outcomes; 3) considering the role of relevant covariates as potential confounders (i.e., sociodemographics, medical status, health behaviors, psychological distress); 4) implementing strategies to overcome potential selection bias; 5) evaluating PWB-mortality associations by cause of death; 6) examining the potential mediating role of biobehavioral pathways with accurate analytic techniques and optimal temporality in the sequence of construct assessments; 7) using stratified analyses to verify the PWB-mortality association by sociodemographic characteristics; 8) determining the robustness of the association by excluding early deaths (or disease cases). Building evidence in this way would generate stronger evidence for a causal association and could guide the selection of PWB dimensions for randomized-controlled trials conducted in specific populations and for specific outcomes. It would also contribute to the development of more targeted interventions that could be broadly disseminated at the population level. Such interventions could improve not only PWB, but may have the potential to promote and maintain physical health as well (Kobau et al., 2011; VanderWeele et al., in press).

FIGURE 1. Potential biobehavioral pathways relating psychological well-being to risk of mortality



Notes. Model adapted from Boehm & Kubzansky, 2012; Kubzansky et al., 2018; Trudel-Fitzgerald, Qureshi, Appleton, & Kubzansky, 2017. For the purpose of this chapter, other psychosocial assets (e.g., social integration, emotional support) are omitted from this figure. Likewise, while bidirectional effects between psychological well-being and biobehavioral processes are likely, in keeping with the focus of the chapter, only single-direction arrows are shown. For a more in-depth explanation of the role of stress-related factors in the PWB-health associations above, we refer readers to Pressman et al., 2019.

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