Happy People Live Longer: Subjective Well-Being Contributes to Health and Longevity

Ed Diener*

University of Illinois and the Gallup Organization, USA

Micaela Y. Chan

University of Texas at Dallas, USA

Seven types of evidence are reviewed that indicate that high subjective well-being (such as life satisfaction, absence of negative emotions, optimism, and positive emotions) causes better health and longevity. For example, prospective longitudinal studies of normal populations provide evidence that various types of subjective well-being such as positive affect predict health and longevity, controlling for health and socioeconomic status at baseline. Combined with experimental human and animal research, as well as naturalistic studies of changes of subjective well-being and physiological processes over time, the case that subjective well-being influences health and longevity in healthy populations is compelling. However, the claim that subjective well-being lengthens the lives of those with certain diseases such as cancer remains controversial. Positive feelings predict longevity and health beyond negative feelings. However, intensely aroused or manic positive affect may be detrimental to health. Issues such as causality, effect size, types of subjective well-being, and statistical controls are discussed.

INTRODUCTION

When people list the key characteristics of a good life, they are likely to include happiness, health, and longevity. Similarly, scholars such as Edgerton (1992) define good cultures as those in which health and happiness flourish. In this paper we describe the evidence that subjective well-being (SWB) causally affects health and longevity. Interventions to raise SWB, as well as the theories that explain why SWB affects physiology, are beyond the page limitations and scope of this review.

We describe the evidence that indicates that SWB causally influences both health and longevity. Subjective well-being refers to people’s evaluations of

* Address for correspondence: Ed Diener, Department of Psychology, University of Illinois, 603 E. Daniel Street, Champaign, IL 61820, USA. Email: ediener@illinois.edu

© 2011 The Authors. Applied Psychology: Health and Well-Being © 2011 The International Association of Applied Psychology. Published by Blackwell Publishing Ltd., 9600 Garsington Road, Oxford OX4 2DQ, UK and 350 Main Street, Malden, MA 02148, USA.
their lives, which can be judgments such as life satisfaction, evaluations based on feelings, including moods and emotions. When people feel a sad mood or a joyful emotion it is because they feel their lives are going badly or well. Thus, SWB is a heterogeneous category that includes diverse phenomena ranging from optimism to low anger to work satisfaction. Through most of the paper we review measures of diverse SWB concepts together as though they have similar effects on health, and only occasionally mention when these effects diverge. The reason we combine the different types of SWB is that rarely have there been studies that differentiate and assess multiple types of SWB. Thus, we are not able to draw strong conclusions about which specific types of feelings are most related to health. Evidence has accumulated to show that positive and negative feelings have independent effects, but in most cases we have only a rudimentary understanding of how SWB concepts overlap or are independent in their effects on health. In a later section of the paper we describe the research that is needed to more finely dissect how various types of SWB influence health.

Early research on SWB and health established a correlation between the two. But because the studies were largely cross-sectional, often with small samples of convenience, it was impossible to determine the causal direction between SWB and health. However, there are now a number of converging lines of evidence based on diverse methodologies supporting the conclusion that SWB influences health and longevity:

1. Long-term prospective studies in which participants are followed over time, and initial levels of SWB are related to later health and longevity. These studies are most powerful when baseline levels of health are controlled, and socioeconomic status (SES) is often controlled as well. Survival in ill populations has been studied, as well as morbidity and mortality in initially healthy populations.
2. Studies in which natural levels of SWB are related to specific physiological processes that can affect health and longevity, as well as studies where changes in SWB are related to changes in physiological measures.
3. Studies in which moods and emotions are experimentally manipulated, and effects on physiological variables that could affect health are assessed.
4. Animal studies in which there is experimental control over the environment of the animals, and physiological and health measures are assessed in animals likely to differ in SWB, for example, in stress.
5. Quasi-experimental studies in natural settings, in which natural events can be examined for their effects on health outcomes.
6. Experimental intervention studies in which treatments are administered that can influence people’s long-term SWB. The treatment groups are
compared to control groups in terms of both SWB and physiological measures.

7. Studies on how quality of life factors such as pain and mobility are related to SWB.

We describe examples of each of the types of evidence, as well as discuss issues such as causality, effect size, methodological rigor, whether too much happiness can be detrimental to health, and whether there is a threshold effect for SWB. We focus on large-scale recent research, as well as studies that are diverse in the populations they sample and initial health-status. We describe a number of systematic reviews and meta-analyses that are available in specific areas, which provide more complete summaries of certain topics.

EMPIRICAL EVIDENCE BY METHODOLOGICAL CATEGORY

Longitudinal Studies of SWB, Health, and Longevity

A number of reviews and meta-analyses are available on the predictive power of SWB on health and longevity. Studies with large sample sizes have followed participants for a decade or more. In these studies SWB is usually predictive of mortality, controlling for initial health. Hemingway and Marmot (1999) found in a review of the literature that among studies that passed their “quality filter”, in 11 of 11 prospective studies depression and anxiety predicted coronary heart disease in healthy people, and in six of six studies they predicted disease progression in those with cardiovascular disease. The authors suggest that the causal role of the mental states is further supported by human and primate evidence on biological and behavioral pathways mediating these effects.

Lyubomirsky, King, and Diener (2005), in a meta-analysis of longitudinal studies, found an effect size of .18, indicating the standard deviation differences in health outcomes for low versus high SWB individuals. Similarly, Howell, Kern, and Lyubomirsky (2007) reviewed 49 prospective studies testing the predictive power of long-term well-being and ill-being, and found an overall effect size of .14 for longevity, comparing high and low SWB participants.

Chida and Steptoe (2008) conducted a meta-analysis of the prospective studies examining the association between positive well-being and mortality in both healthy and diseased populations. Positive psychological well-being was related to lower mortality in both healthy and diseased populations, independently of negative affect. Positive moods such as joy, happiness, and energy, as well as characteristics such as life satisfaction, hopefulness, optimism, and sense of humor were associated with reduced risk of mortality in healthy populations, and predicted longevity, controlling for negative states.
Positive affect (PA) was associated with reduced death rates in patients with HIV and renal failure. In the healthy population studies, higher quality studies yielded evidence of greater protective effects. In the diseased population studies the protective effects were greater when baseline disease and treatment were controlled.

Rugulies (2002) reported a meta-analysis of 11 studies examining whether depression predicts coronary heart disease. It was concluded that depression predicted cardiovascular disease in initially healthy people, with a greater risk for clinical depression than for depressed mood (risk ratios of 2.69 and 1.49, respectively). Studies that excluded participants with a suspicious EEG at baseline, and those with cardiac events early in the follow-up period showed a risk ratio of 1.51.

Williams and Schneiderman (2002) argued that there is now strong evidence that SWB is predictive of cardiovascular disease in healthy populations. They also concluded that SWB is predictive of cancer incidence and survival, although the evidence was limited. Pressman and Cohen (2005) reviewed evidence suggesting that positive affect is associated with physical health and longevity in normal populations, but concluded that the evidence is mixed for positive affect predicting survival in those with existing disease. Thus, a number of literature reviews and meta-analyses all conclude that SWB predicts health and longevity in healthy populations.

In Table 1 we present examples of prospective studies of SWB and longevity. The table shows the extent, range, and diversity of the findings. Several of the studies have overlapping samples, but different measures and time periods. As can be seen, SWB, especially in the form of positive affect, has been found to be associated with longevity in many samples (including very large ones), in a number of different nations, and controlling for potential confounds such as initial health and SES. The results leave little doubt that subjective well-being can predict longevity. In some studies SWB was associated with longevity only in a subset of the sample, such as only in men or for one type of SWB, and such differences provide leads for future research.

A current question without a definitive answer is whether SWB can improve people’s chances of surviving existing illnesses. The results on survival are mixed, with some studies showing that high SWB increases the likelihood of survival from certain illnesses, and other studies showing no effect. Pressman and Cohen (2005) suggested that positive states might be detrimental to the health of people with advanced diseases with a poor short-term prognosis, while being beneficial to those with diseases that have a better prospect of long-term survival. In addition, in a few cases such as asthma, highly aroused positive states might be detrimental, triggering attacks. In a review of prospective studies, Suls and Bunde (2005) concluded that negative emotions may play a stronger role in cardiovascular disease development than in progression once it is present. Veenhoven (2008) also
### TABLE 1
Longitudinal Studies of SWB and Mortality

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Sample and findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abel &amp; Kruger</td>
<td>2010</td>
<td>Photographs of 196 professional baseball players taken in 1952 were rated for smiling. Mortality occurring by 2009 was predicted by smiling.</td>
</tr>
<tr>
<td>Barefoot et al.</td>
<td>2000</td>
<td>1,250 coronary disease patients aged 46–58 were followed annually up to 19.4 years. Well-being and somatic symptoms significantly predicted survival.</td>
</tr>
<tr>
<td>Blazer &amp; Hybels</td>
<td>2004</td>
<td>4,162 participants in North Carolina, aged 65–105, with 10-year follow-up. Positive affect, but not negative affect, was related to longevity.</td>
</tr>
<tr>
<td>Brummett et al.</td>
<td>2005</td>
<td>866 coronary disease patients with an average age of 60.3 were followed for about 11.4 years, during which time 415 deaths occurred. The findings suggested that the relation between positive emotions and mortality may be partly mediated by lack of depressive emotion.</td>
</tr>
<tr>
<td>Brummett et al.</td>
<td>2006</td>
<td>4,989 students who filled out an optimism scale at entry into university in 1964–66 were followed for 40 years. Pessimistic individuals had lower rates of longevity compared with optimistic individuals.</td>
</tr>
<tr>
<td>Danner, Snowdon, &amp; Friesen</td>
<td>2001</td>
<td>180 Catholic nuns wrote autobiographies at an average age of 22. Relation between the emotional content and survival was assessed at age 75–94. Nuns writing more positive autobiographies when entering the convent in young adulthood lived longer than nuns writing less positive autobiographies.</td>
</tr>
<tr>
<td>Deeg &amp; van Zonneveld</td>
<td>1989</td>
<td>3,149 Dutch in a representative sample, aged 65–80 at baseline. Mortality was determined about 28 years later. Satisfaction with aging, income, and value of life were all related to longevity, even after controlling for symptoms and initial indicators of ill-health.</td>
</tr>
<tr>
<td>Friedman et al.</td>
<td>1995</td>
<td>The most cheerful of Terman’s gifted participants had more health problems (more likely to smoke and drink) and survival analysis showed them to die younger.</td>
</tr>
<tr>
<td>Giltay et al.</td>
<td>2004</td>
<td>Dutch elderly 65 to 85, N = 941, 9-year follow-up. Optimism predicted lower all-cause mortality, with a stronger effect for men in all-cause mortality but not cardiovascular mortality. Optimism predicted cardiovascular mortality controlling for chronic disease, smoking, hypertension, obesity, cardiovascular disease, and alcohol consumption. For both men and women there was a dose-response relation between optimism and mortality.</td>
</tr>
<tr>
<td>Authors</td>
<td>Year</td>
<td>Sample and findings</td>
</tr>
<tr>
<td>----------------------</td>
<td>------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Koopmans et al.</td>
<td>2010</td>
<td>861 Dutch elderly aged 65–85 in the Arnhem Elderly Study were followed for all-cause mortality after 15 years. Happiness was measured by reports of many happy moments and often laughing happily. Happy respondents had a .78 hazard ratio (controlled for age and sex) of mortality compared to unhappy respondents, and this persisted controlling for marital status and SES. In comparison, the hazard ratio for smoking was .72, and for number of diseases was .76. The relationship of happiness and longevity became nonsignificant when physical activity, smoking, and chronic disease at baseline were controlled (although the hazard ratio remained .92 for the happiest versus unhappiest tertiles).</td>
</tr>
<tr>
<td>Kubzansky et al.</td>
<td>2001</td>
<td>1,306 participants from the Greater Boston area, aged 21–80, were followed for 12 years. Optimism predicted lower rates of heart attack and fatal coronary heart disease. A dose-response relation was found between optimism and each of the cardiac outcomes.</td>
</tr>
<tr>
<td>Loberiza et al.</td>
<td>2002</td>
<td>Studied 193 patients receiving stem-cell transplants over a period of 2 years. Depressed patients had a threefold risk of dying compared to the nondepressed between 6 and 12 months after the operation, controlling for other prognostic factors. After 1 year, surviving depressed patients were more likely to be taking medications related to transplantation and less likely to be working.</td>
</tr>
<tr>
<td>Lyrra et al.</td>
<td>2006</td>
<td>Scandinavian twin study, 320 respondents 80 years and older. Low current “life satisfaction”, defined by zest and mood, almost doubled the risk for mortality in the low versus high quartiles. Controlling for depression, social functioning, and serious diseases did not reduce the life satisfaction effect.</td>
</tr>
<tr>
<td>McCarron et al.</td>
<td>2003</td>
<td>9,239 male students aged 16 to 30 were followed for an average of 20.5 years. Anxiety predicted all-cause mortality and cancer risk (Cox risk ratios of 1.36 and 1.51, respectively). Hypomaniac men had an increased risk of cardiovascular mortality (Cox 1.90).</td>
</tr>
<tr>
<td>Moskowitz et al.</td>
<td>2008</td>
<td>715 diabetics and 2,673 comparison control participants. Positive affect predicted all-cause mortality in diabetics, and enjoyment predicted lower risk of mortality beyond the effects of negative affect in a 20-year follow-up. Positive affect was not predictive of mortality in the entire comparison sample, but enjoyment and hope were predictive of lower mortality for those over age 65, and they predicted beyond negative affect. Positive affect remained predictive when other predictors were controlled.</td>
</tr>
<tr>
<td>Moskowitz</td>
<td>2003</td>
<td>407 HIV-positive people at baseline. Followed at 1, 2, and 3 years. Positive affect predicted mortality at 1 and 2 years, controlling for various biological factors and negative affect.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Sample and findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostir et al.</td>
<td>2000</td>
<td>2,282 Mexican Americans aged 65 to 99, followed for 2 years. Participants with high positive affect were half as likely to have died during the 2-year follow-up. Positive affect seemed to protect individuals against physical decline (e.g. becoming disabled, slow walking speed).</td>
</tr>
<tr>
<td>Scherer &amp; Herrmann-Lingen</td>
<td>2009</td>
<td>575 hospitalised patients, followed for 1 year after discharge. Single-item measure of positive affect (enjoyment) predicted survival, controlling for physician-rated prognosis, co-morbidity scores, and hemato-oncological disease.</td>
</tr>
<tr>
<td>Shirai et al.</td>
<td>2009</td>
<td>88,175 Japanese adults, aged 50 to 69, free of cardiovascular disease at baseline, were followed up on average after 12 years. Enjoyment of life was associated with lower risk of cardiovascular disease, stroke, and cardiovascular mortality for men only.</td>
</tr>
<tr>
<td>Tindle et al.</td>
<td>2009</td>
<td>Followed 97,253 women for about 8 years in the Women’s Health Initiative who were initially free of cancer and heart disease. Optimists had lower mortality from heart disease, fewer cardiovascular events, and black optimists also had lower rates of cancer-related deaths. Women high in cynical hostility had higher cancer mortality, cardiovascular problems, and overall mortality, with this effect being pronounced in blacks.</td>
</tr>
<tr>
<td>Whang et al.</td>
<td>2009</td>
<td>63,469 nurses aged 30–55 at entry in the Nurses’ Health Study cohort followed every 2 years for about 30 years. Depression predicted fatal cardiovascular disease.</td>
</tr>
<tr>
<td>Whooley &amp; Browner</td>
<td>1998</td>
<td>Prospective study of 7,518 white women 67 years and older, from several USA cities, were followed after 7 years, controlling for many diseases and cognitive functioning. Depression at T1 strongly predicted all-cause mortality, cardiovascular death, and cardiovascular disease, but not deaths from cancer.</td>
</tr>
<tr>
<td>Wilson et al.</td>
<td>2003</td>
<td>Catholic clergy (N = 851) were followed for a mean of 4.7 years. Depression and suppressed anger were predictive of mortality, but anger at others was not. Those high in internally directed negative affect were nearly twice as likely to die as those who were low in this characteristic.</td>
</tr>
<tr>
<td>Xu</td>
<td>2005</td>
<td>29-year Alameda County Study (USA) representative sample of 6,928 participants above the age of 20 at baseline. SWB was measured by combining scores on life satisfaction, positive affect, and a reverse score of negative affect. Subjective well-being reduced the risk of all-cause, natural-cause, and cardiovascular mortality. Positive feelings had an even stronger effect on these, and also predicted lower unnatural cause mortality (suicide, drug-dependency, alcohol-related liver disease, etc.). Effects continued after controlling for demographic variables, initial health and obesity, and health practices. The effects of negative feelings did not continue after the covariates were controlled.</td>
</tr>
</tbody>
</table>
concluded that “happiness” predicts longevity in healthy populations but may not cure illness in sick populations.

One complication in interpreting SWB effects is that in research controlling for baseline health the researchers might actually be studying whether SWB has a greater influence in later life than in earlier life because even at Time 1 SWB levels are likely to already have had an impact. However, there are studies in which high SWB clearly has been found to have positive effects on those with existing diseases. For example, Scheier et al. (1989) found that postsurgical physical recovery among coronary bypass patients was quicker for optimists, as was resumption of normal activities after hospital discharge.

Positive states are not likely to help people overcome any and all illnesses. Even if positive states boost people’s immune systems and have other desirable benefits, these might not be sufficient to vanquish certain very serious illnesses such as rabies or pancreatic cancer. Although a positive attitude can help a person’s quality of life when they have a fatal illness, it is likely that no amount of SWB can overcome some diseases. Thus, we must search for the conditions under which SWB can benefit the health of those with specific diseases.

In Table 2 we present prospective studies on SWB predicting later health and disease. The results are consistent in indicating that SWB predicts disease, although the findings are much clearer and complete for cardiovascular disease than other illnesses. These prospective studies indicate a payoff for healthy populations, and a weaker but positive effect in some diseased populations. The evidence that positive SWB helps those with diseases such as cancer appears to be mixed, with uncertain overall support at this time.

Even the impressively large and long-term prospective studies among healthy populations cannot definitively establish causality because initial...
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Sample and findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brummett et al.</td>
<td>2009</td>
<td>948 hospitalised coronary artery disease patients followed for 3 years. Lower positive emotions at Time 1 were associated with quicker decline in functional status, while lower positive feelings at follow-up were associated with decline only for men.</td>
</tr>
<tr>
<td>Collins et al.</td>
<td>2008</td>
<td>3,363 older Taiwanese were followed for 8 years. Mobility limitations were predicted by T1 life satisfaction and perceptions of future happiness only for those with no mobility limitations at T1, controlling for SES, health, social involvement, and depressive symptoms at baseline.</td>
</tr>
<tr>
<td>Davidson et al.</td>
<td>2010</td>
<td>1,739 Canadian adults in Nova Scotia, with 10-year follow-up. Positive affect predicted cardiovascular and ischemic heart disease. Increased positive affect was protective against 10-year incident CHD.</td>
</tr>
<tr>
<td>Davidson et al.</td>
<td>2010</td>
<td>1,739 Canadian adults in Nova Scotia, with 10-year follow-up. Positive affect predicted cardiovascular and ischemic heart disease. Increased positive affect was protective against 10-year incident CHD.</td>
</tr>
<tr>
<td>Fitzgerald et al.</td>
<td>2000</td>
<td>50 Caucasian CHD patients aged 38–77 followed 8 months after surgery. Dispositional optimism predicted decreased angina, positive affect, and risk-factor reduction.</td>
</tr>
<tr>
<td>Fredman et al.</td>
<td>2006</td>
<td>2-year study of 432 hip-fracture patients, aged 65 and older. High positive affect at Time 1 associated with faster walking and chair-stand speeds.</td>
</tr>
<tr>
<td>Freese et al.</td>
<td>2007</td>
<td>Failed to find self-reported health differences in the Wisconsin Longitudinal Study, with a 36-year follow-up, between those who smiled and did not smile in high school yearbook photos ((N = 3,007)).</td>
</tr>
<tr>
<td>Hamilton</td>
<td>1996</td>
<td>Cancer patients, (N = 213), were assessed 3 years after baseline. High positive mood predicted survival of lung cancer. Low levels of negative mood predicted survival of breast cancer.</td>
</tr>
<tr>
<td>Koivumaa-Honkanen et al.</td>
<td>2002</td>
<td>Finnish twins 18–54 years old, (N = 29,173). Life satisfaction predicted lower unintentional injury mortality after controls for demographic and health behavior variables for both men and women.</td>
</tr>
<tr>
<td>Koivumaa-Honkanen et al.</td>
<td>2004</td>
<td>Finnish twins aged 18–54 years old, (N = 22,136). Life satisfaction predicted lower disability pensions from psychiatric and nonpsychiatric causes, especially among the healthy, and after controls for demographics and health behaviors.</td>
</tr>
<tr>
<td>Nabi et al.</td>
<td>2008</td>
<td>10,308 civil servants aged 35 to 55 free of coronary heart disease at baseline, in London, with a 12-year follow-up. Positive affect and affect balance did not predict coronary heart disease. A weak positive association was found between negative affect and coronary events.</td>
</tr>
<tr>
<td>Ostir et al.</td>
<td>2004</td>
<td>1,558 nonfrail older Mexican Americans were followed over 7 years. Positive affect lowered risk of future frailty.</td>
</tr>
<tr>
<td>Ostir et al.</td>
<td>2001</td>
<td>2,478 older North Carolina, adults with no history of stroke at baseline followed over 6 years. Depression related to incidence of stroke, controlling for T1 demographics, smoking, BMI, blood pressure, and selected chronic diseases. Positive affect had a strong inverse incidence with stroke incidence.</td>
</tr>
</tbody>
</table>
unmeasured states of health and resources could produce the association between SWB and later health and longevity. Many of the plausible variables have been statistically controlled in the existing studies, but the possibility remains of other potential uncontrolled explanatory factors. Thus, we must consult other types of evidence as well.

**TABLE 2 Continued**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Sample and findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ringbäck et al.</td>
<td>2005</td>
<td>A representative sample of 34,511 Swedish persons aged 16 to 74 followed at 5 and 10 years. High baseline anxiety and nervousness predicted suicide attempts, psychiatric illness, hospital care, and ischemic heart disease, with stronger predictions for men.</td>
</tr>
<tr>
<td>Seeman et al.</td>
<td>2002</td>
<td>106 older adults aged 58–59 years old. Participants reporting more positive emotions with family and friends had fewer health symptoms and chronic conditions, and better subjective health. Those with fewer positive relationships had a higher allostatic load.</td>
</tr>
<tr>
<td>Shen et al.</td>
<td>2008</td>
<td>735 older men in the Normative Aging Study, with no history of heart disease or diabetes, were followed for 12.4 years. Controlling for SES and other biological factors, anxiety predicted a greater incidence of myocardial infarction (risk ratio of 1.43). The effects remained after controlling for health behaviors, depression, hostility, and negative emotion.</td>
</tr>
<tr>
<td>Siahpush et al.</td>
<td>2008</td>
<td>9,981 adult Australians were followed over 3 years. Happy and high life satisfaction participants had better physical health at 2-year follow-up, as well as a relative absence of long-term limiting health conditions, controlling for baseline health and other covariates.</td>
</tr>
<tr>
<td>Strik et al.</td>
<td>2003</td>
<td>Followed 318 male survivors of myocardial infarction for an average of 3.4 years. Anxiety and depression predicted cardiac events after adjusting for age and other factors. However, anxiety explained away the effects of depression on cardiac events. Anxiety was also a predictor of re-hospitalisation and frequent outpatient visits.</td>
</tr>
</tbody>
</table>

Human Studies of SWB, Physiology, and Health

Researchers have studied how both short- and long-term negative and positive affect are associated with physiological indicators in natural settings. Moods and emotions have been associated with cardiovascular indicators (Smyth et al., 1998; Steptoe, O’Donnell, Badrick, Kumari, & Marmot, 2007). Raikkonen, Matthews, Flory, Owens, and Gump (1999) found that pessimists have higher blood pressure levels. Steptoe, Wardle, and Marmot (2005)
found that positive affect in middle-aged men and women was associated with reduced neuroendocrine, cardiovascular, and inflammatory activity. The fibrinogen response to stress was smaller in happier individuals. Positive affect assessed periodically during the day was related inversely to heart rate assessed by ambulatory monitoring. Importantly, the effects were independent of distress. Blood pressure elevations during mental stress can be substantial, equaling those of exercise (Rozanski, Blumenthal, & Kaplan, 1999).

Fredrickson and Levenson (1998) found that films eliciting positive emotions speeded recovery from cardiovascular activation after participants had viewed a fear-eliciting film. Brummett, Boyle, Kuhn, Siegler, and Williams (2009) found that positive feelings were associated with lower blood pressure reactivity during sadness recall but not during anger recall, and were related to more epinephrine, as well as lower cortisol rise after waking. Ostir, Berges, Markides, and Ottenbacher (2006) found in a sample of Mexican-Americans aged 65 and older who were not on hypertensive medication that positive affect was associated with lower blood pressure. After adjusting for relevant risk factors, positive affect continued to be significantly associated with lower diastolic blood pressure.

The physiological changes resulting from moods are, in turn, related to changes in health. For instance, studies have shown that various forms of negative affect—from stress to anxiety to depression—are associated with deleterious changes in the cardiovascular system (Howell et al., 2007). Rozanski et al. (1999) described evidence showing that mental states such as stress and anger induced in the laboratory resulted in ischemia. Those experiencing ischemia in the laboratory are more likely to manifest it during the ECG monitoring of daily life events as well. Gullette et al. (1997) found that transitory negative emotions increased the relative risk of ischemia, as assessed with ambulatory ECG monitoring. Aboa-Éboulé et al. (2007) followed people after a myocardial infarction and found a higher incidence of future cardiovascular disease for people with high job strain.

Chida and Steptoe (2008) concluded that positive psychological states may influence inflammatory and coagulation factors, which are involved in cardiovascular disease. The lower levels of cortisol associated with positive states may reduce the risk of metabolic, cardiovascular, and immune diseases. Chida and Steptoe noted that the protective effects of SWB on mortality persisted even when the behavioral factors were controlled, suggesting that physiological mediators are involved.

Paterniti et al. (2001) followed participants for 4 years and found that those with initially high trait anxiety had greater thickening of carotid arteries over the period than those low in anxiety, and this occurred for both men and women. Sapolsky (2005) reviewed evidence indicating that chronic stress was related to hypertension and adult-onset diabetes. Smith, Glazer, Ruiz, and Gallo (2004) reviewed evidence indicating that anger and hostility were
related not only to the initial development of cardiovascular disease, but also to disease progression, as indicated by studies of ischemia and atherosclerosis. A similar conclusion was reached in a meta-analysis by Miller, Smith, Turner, Guijarro, and Hallet (1996). Marsland, Prather, Petersen, Cohen, and Manuck (2008) found that hostility and trait negative affect were predictive of inflammatory markers.

Kiecolt-Glaser, McGuire, Robles, and Glaser (2002) provided an excellent review of physiological pathways through which emotions can influence bodily reactions. Negative emotions enhance the production of proinflammatory cytokines, for example. Inflammation in turn has been linked to certain cancers, Alzheimer’s disease, arthritis, frailty, osteoporosis, and cardiovascular disease. Furthermore, negative feelings can contribute to delayed wound healing and infection.

SWB has not only been related to cardiovascular health, but also to immune functioning (Howell et al., 2007). Costanzo et al. (2004) found that angry individuals had a weaker immune response to a vaccine, whereas those high in optimism had a stronger response (see also Kohut, Cooper, Nickolaus, Russell, & Cunnick, 2002). Similarly, Byrnes et al. (1998) found immune decrements in pessimistic versus optimistic women with HIV. Herbert and Cohen (1993) in a meta-analysis found that stress predicted lower values of immune parameters. Interestingly, objective stress was a better predictor than self-reported stress, and this pattern was replicated by Segerstrom and Miller (2004). Rosenkranz et al. (2003), building on earlier work by Davidson, Coe, Dolski, and Donzella (1999), found that negative affect as indexed by both right prefrontal brain activation and startle-response predicted worse immune functioning.

Segerstrom and Sephton (2010) found among first-year law students that changes in both optimism and positive affect across time were associated with changes in immune responses. The effects of each persisted when controlled for the other, but were reduced to about half of their former strength. This dynamic relation over time suggests that increasing positive affect strengthens immunity, and that the relation between the two is not due simply to inborn temperament or stable differences in life circumstances.

Moods and emotions also can influence the reproductive system. For example, a recent study on fertility in women indicated that stress decreased the likelihood of pregnancy in those seeking to have children (Buck et al.,
The authors suggested that perhaps stress reduced fecundity through a sympathetic medullar pathway.

An intriguing recent finding is the effect of low SWB on telomere shortening. Shorter telomeres resulting from negative emotions could cause health issues in a variety of different bodily systems because of the greater probability that new cells will contain replication mistakes. Lung, Chen, and Shu (2007) found that major depressive disorder, as well as age, predicted shorter telomere length. Damjanovic et al. (2007) found that Alzheimer’s patient caregivers experienced both depressive symptoms and had shorter telomere length compared to controls. Tyrka et al. (2010) found that childhood maltreatment predicted shorter telomere length in adults, although Glass, Parts, Knowles, Aviv, and Spector (2010) failed to replicate this effect. Epel et al. (2004) found that both perceived stress and chronic stress were related to shorter telomere length. Cherkas et al. (2006) analyzed adult female twin pairs, and discovered that low SES predicted shorter telomere length beyond the effects of smoking, obesity, and lack of exercise. Thus, negative feelings could produce widespread premature aging in diverse bodily systems, resulting in a greater likelihood of health problems.

Positive affect is associated with protective psychosocial and behavioral factors such as greater social connectedness, perceived social support, optimism, and preference for adaptive coping responses, as well as a greater probability of performing health behaviors. Cross-cultural research has documented associations with exercising regularly, not smoking, and a prudent diet (Steptoe, Dockray, & Wardle, 2009). Grant, Wardle, and Steptoe (2009) studied a large sample of individuals in 21 nations and found that high life satisfaction was associated with not smoking, physical exercise, a healthier diet, and using sun protection. Patton et al. (in press) found in a prospective study of adolescents that optimism scores were strongly predictive of later depression, as well as predictive of less antisocial behavior and lower heavy drug use. An optimistic style was predictive of less onset of drug use for females but not males. Thus, positive affect, in addition to its physiological outcomes, also may be part of a broader profile of psychosocial resilience that reduces the risk of adverse physical health behaviors, which can influence multiple bodily systems.

It appears that short-term emotions, both negative and positive, can produce adaptive bodily responses, whereas long-term negative states often produce deleterious patterns (Segerstrom & Miller, 2004). Short-term changes in mood and physiology might reflect adaptive responses to challenges, and are not necessarily indicative of pathology, whereas chronic stress and depression can create physiological responses that are harmful. In the short run, diverting resources in response to threats makes evolutionary sense because animals then have more resources to devote to emergency behaviors, thus potentially saving their lives. However, in the long run such diversion of
bodily resources can lead to a failure to reproduce and repair bodily damage (Barnett & Hemsworth, 1990).

In sum, moods and emotions are consistently found to be associated with biological measures such as blood pressure, cortisol, and inflammation, as well as indicators of disease such as artery wall thickening. Importantly, the relation of positive feelings with physiology occurs in addition to the effects of negative feelings and depression, suggesting that positive affect may have distinctive biological correlates that can benefit health.

Experimental Manipulations of Emotions Combined with Physiological Outcome Measures

In experimental studies positive and negative moods are induced in some participants and contrasted with other mood conditions in terms of health-relevant physiological measures. For instance, Robles, Brooks, and Pressman (2009) conducted an experiment in which stress versus no stress was induced in two groups, and skin recovery time after tape-stripping was measured. Trait positive emotions predicted quicker skin barrier recovery in the stress-induced group, showing the buffering effect of positive feelings on the effects of stress on skin barrier recovery. Fredrickson, Mancuso, Branigan, and Tugade (2000) carried out an experiment in which participants who were exposed to a positive mood induction showed quicker cardiovascular recovery after a stressful task than subjects who were exposed to neutral or negative mood inductions.

In a controlled experiment (Kiecolt-Glaser et al., 2005) married couples were given blister wounds and assigned to a marital disagreement condition and to a social support interaction during two consecutive stays in a hospital setting. Following the marital conflict condition, participants had slower wound healing and lower cytokine production than they showed in the social support condition. In addition, couples who were generally higher in hostility showed slower wound healing than low hostile couples, as well as more tumor necrosis and a poorer immune response.

Several reviews and meta-analyses indicate that emotional states induced experimentally are associated with health-relevant physiological outcomes. Lyubomirsky et al. (2005) found an effect size of .38 between experimentally induced positive affect and physical outcomes such as immune function and cardiovascular reactivity. Pressman and Cohen (2005) reviewed both experimental and naturalistic ambulatory evidence showing that positive emotions are related in the preponderance of studies to immune, endocrine, and cardiovascular parameters. Howell et al. (2007) reviewed 139 experimental studies testing the impact of well-being on health-relevant physiological outcomes. Inductions of well-being and ill-being led to positive biological outcomes and negative biological outcomes, respectively. The impact of

well-being was much stronger for immune response and pain tolerance, and nonsignificant for cardiovascular reactivity, although positive emotions produced a significant drop in cortisol. The strongest effect size they reviewed was between transient positive emotions and sIgA antibody production.

Not all research has found physiological reactions in response to mood inductions (e.g. Kiecolt-Glaser et al., 2008), and therefore we need to explore in more depth what types of physiological responses occur in response to what levels and types of moods and emotions. In sum, a large number of experimental studies reveal that moods and emotions can influence health-relevant physiological responses with moderately strong effects, although in some cases no physiological effects are found for short-term mild moods.

**Animal Studies**

Animal studies reveal that conditions likely to cause stress have a negative impact on health. Manuck, Kaplan, and Clarkson (1983) found that socially stressed monkeys developed more extensive coronary artery atherosclerosis than unstressed controls. Capitanio and Lerche (1998) found that psychosocial experiences such as isolation are likely to produce a stressful state that is associated with shorter survival in SIV-infected monkeys. Salak-Johnson and McGlone (2007) reviewed animal studies on the relation of stress and immunity and found that chronic stress caused by psychosocial factors suppresses the immune system.

Rozanski et al. (1999) described animal research showing that the ventricular fibrillatory threshold is substantially reduced by a stressful environment. The authors concluded that “... these studies show that behavioral stress . . . significantly decreases the electrical stability of the heart” (p. 2206). They further conclude, based on both human and animal studies, that stress influences blood coagulation. Von Borell (1995) reviewed evidence showing that stress in pigs can cause elevated cortisol and suppress immune activity, and that social stress can decrease disease resistance in chickens.

Barnett and Hemsworth (1990) described studies indicating that the type of housing provided to pigs, which can influence levels of stress, influences plasma glucose, as well as decreased responsiveness of the immune system. Enteric bacteria may grow more rapidly in stressed animals (Freestone & Lyte, 2010). Tethered pigs show greater basal metabolism than group-housed pigs. Both housing systems and threatening human behavior can elevate plasma-free corticosteroids, with negative results for pregnancy, growth, and immune strength.

Boissy et al. (2007) reviewed methods for assessing positive emotions in animals, including observing certain behaviors such as play, affiliation, and vocalisations, and through certain environmental circumstances such as increasing or decreasing rewards. Although few studies have yet been
published on positive feelings in animals, several intriguing findings are reviewed by Boissy et al. They reviewed studies suggesting that both negative and positive psychosocial experience in pigs influences health. For example, pigs that learned a mastery task to obtain rewards, giving them some control over their environment, later showed quicker wound healing and carcass quality (Ernst, Tuchscherer, Kanitz, Puppe, & Manteuffel, 2006).

Social factors can have a positive effect on animal health. Cohen, Kaplan, Cunnick, Manuck, and Rabin (1992) found increased immune response in animals that were more affiliative, possibly due to the stress-buffering effect of affiliation. Detillion, Craft, Glasper, Prendergast, and DeVries (2004) showed that positive social interaction improved wound healing in hamsters. Craft (2006) found that social interaction among mice post-stroke helped decrease stroke-induced neuronal death.

Short-term stress can lead to adaptive changes in behavior and physiology that may not be detrimental to health.

**Quasi-Experiments of Natural Events and Health Outcomes**

Quasi-experimental studies suggest that emotional events and disasters are associated with cardiovascular and immune changes, and can trigger deaths in those who are psychologically affected by a disaster, probably in vulnerable populations. Rozanski et al. (1999) reviewed evidence showing that death spikes during the first month after bereavement, with greater than a twofold increase in mortality for men and a threefold increase for women, and then returns to normal levels. Similarly, they reported that there was a spike in deaths in Israel on the first day of missile strikes during the Gulf War of 1991, unrelated to direct deaths from the strikes. On the day of the 1994 earthquake in Los Angeles, deaths rose to five times the rate of the week before. Even observing exciting sports events seems to be able to trigger cardiac deaths (Carroll, Ebrahim, Tilling, Macleod, & Smith, 2002).

Evidence also connects major stressful events to physiological changes. Rozanski et al. (1999) described a quasi-experimental study in which blood samples were taken from hypertensive patients before and after an earthquake. The quake induced transient elevations in blood pressure and viscosity, and these parameters returned to baseline after 4 to 6 months. Marucha, Kiecolt-Glaser, and Favaghei (1998) assessed wound healing time in dental students during the summer vacation and again during the first examinations of the year. Students took on average three days longer to heal a small, standardised wound during the examinations, and interleukin messenger RNA was 68 per cent lower during the tests. The pattern of findings held for all 11 students in the study.

Work stress has been related to systematic differences in cortisol (Schlotz, Hellhammer, Schulz, & Stone, 2004). People with work overload and worry showed higher cortisol response at awakening and higher mean cortisol levels on weekdays but not weekends. Those reporting the most work stress showed the greatest weekend–weekday differences in waking cortisol response.

The effects of positive events and health appear to be mixed. Although Berthier and Boulay (2003) found deaths dropped in France when they won the World Cup, a study by Katz et al. (2005) found an increase in cardiac arrests in Switzerland during the World Cup. However, positive responses to sporting competitions can be confounded by behaviors such as alcohol consumption and smoking, failure to comply with medical regimens, a decrease in physical activity, and stress during the event. Thus, winning sporting events may not be a clear indicator of the effects of positive emotions. Furthermore, it is possible that the highly aroused positive emotions arising from exciting events can trigger cardiovascular problems in vulnerable individuals. It could be that single exciting discrete positive events are not as beneficial to health as are circumstances that produce long-term positive moods and emotions, which are usually of a less aroused type.

Interventions that Alter Long-Term SWB with Health Outcomes Assessed

A number of SWB interventions have led to changes in physiological functioning. Davidson et al. (2003) found increased positive affect and left-sided anterior brain activation in meditators compared to wait-list controls, and these were accompanied by increases in antibodies to flu vaccine. Gidron, Davidson, and Bata (1999) found that a hostility-reduction intervention in men with cardiovascular disease led to significantly lower diastolic blood pressure compared to control group participants, after a 2-month period. Reductions in hostility were correlated .47 with reductions in resting diastolic blood pressure. Schneider et al. (1995) found that transcendental meditation and progressive relaxation treatments both reduced blood pressure over a 3-month follow-up period, compared to a control group.

The physiological outcomes shown in the experimental intervention studies are capable of influencing health-relevant measures. Burton and King (2004) studied the health benefits of writing about intensely positive experiences versus a control topic. Those who wrote about positive topics had fewer health center visits for illness during the following 3 months. Holden-Lund (1988) assigned patients undergoing cholecystectomy to one of two treatments, either a control condition or a relaxation with guided imagery condition. Those in the treatment condition exhibited less wound inflammation and redness than the control participants.
Friedman et al. (1986) conducted an experimental intervention with patients who had suffered myocardial infarction, and who were observed for about 5 years after receiving counseling. Ninety-five per cent of patients exhibited Type A behavior at the beginning of the study, varying from moderate to very severe. There was a no-treatment control group, a cardiac counseling group, and a cardiac plus Type-A counseling group. The recurrence rate of MI was 12.9 per cent in the cardiac plus Type-A counseling group, 28.2 per cent in the control group, and 21.2 per cent in those receiving cardiac counseling only. Those who received Type-A counseling in addition to traditional cardiac counseling were less likely to die in the final years of the study.

An intervention that suggests the effects of psychosocial well-being on longevity occurred in a study of palliative care for patients with metastatic lung cancer. Temel et al. (2010) conducted an experiment in which one group of terminal cancer patients received palliative care earlier than typical, compared to the control group which received palliative care at the standard time. The early-care patients had fewer depressive symptoms and lived almost 3 months longer than the 9-month average survival time in the control group.

Schneiderman, Antoni, Saab, and Ironson (2001) concluded that the evidence that interventions have an impact on mortality and morbidity are not definitive, and depend on the particular disease state. Larger scale clinical trials on interventions with specific disease groups are needed to provide more certain conclusions. There are initially promising results for Type A interventions for health outcomes among cardiology patients, and psychosocial interventions for cancer patients. Psychosocial interventions can decrease distress and may improve immune function in HIV/AIDS patients. The intervention evidence is promising and large-scale treatment studies are needed.

Thus far, clear support that psychosocial interventions can alter survival in patients with metastatic cancer is mixed. Chow, Tsao, and Harth (2004) conducted a meta-analysis of experimental studies analyzing the effects of psychosocial interventions such as social support for the survival of patients with metastatic cancer over periods of 1 to 4 years. The authors found no effects of the interventions on survival time, although they did report that “contamination” of the control groups with natural social support is likely, and that most of the studies they reviewed had small samples and poor compliance. Thus, although there is promising evidence that efforts to raise well-being and lower negative states such as hostility can reduce heart disease and death, evidence that psychosocial interventions can help people with metastatic cancer is not yet convincing.

There are a number of hurdles for intervention studies. One is to actually reduce long-term negative affect and increase long-term positive affect. Rozanski et al. (1999) concluded that in some studies where psychosocial interventions have failed to produce health outcomes, in fact the interventions produced no reduction in distress. Furthermore, control group
participants may have substantial psychosocial resources, making it difficult to raise the SWB of the experimental group above the background condition of the control group. It might be that interventions are most likely to raise the SWB of individuals who are deficient in psychological and social resources. Existing studies indicate that interventions can in some cases affect physiology and health. The challenge is to determine which interventions will reliably influence SWB, and in turn affect which disease states.

**SWB’s Impact on Patients’ Quality of Life and Pain**

In a review of the pain and well-being literature, Pressman and Cohen (2005) found that in most studies they reviewed positive emotions were related to lower pain and greater tolerance for pain. Similarly, Howell et al. (2007) found in a meta-analysis a strong association between SWB and pain tolerance. For instance, Bruehl, Carlson, and McCubbin (1993) in an experimental paradigm found that positive mood induction participants reported less pain to finger pressure, and greater finger temperature recovery than controls. Willmarth (1999) hypnotically induced a positive mood and found decreases in self-reports of pain in chronic pain patients. Tang et al. (2008) found that an induction of depressed mood resulted in higher pain ratings at rest and lower pain tolerance, whereas induced happy mood resulted in the opposite pattern.

Fasman (2009) found that fibromyalgia patients had higher levels of pain thresholds for mild and moderate pain with higher levels of trait positive affect. Strand et al. (2006) studied rheumatoid arthritis patients over 8 weeks. High positive affect served to mitigate negative affect during periods of high pain. Master et al. (2009) found that women reported less pain to heat stimuli when looking at pictures of their partner. Thus, the effects of positive affect on pain are supported both in experimental laboratory studies and in research in natural settings, as well as with both self-report and pain tolerance as dependent measures.

Besides pain, high SWB can influence other aspects of the quality of life of patients. Positive emotions predicted recovery of greater functional status among stroke patients (Ostir, Berges, Ottenbacher, Clow, & Ottenbacher, 2008). Kung et al. (2006) found, however, that optimism was more strongly associated with quality of life in survivors of thyroid cancer than those with head and neck cancer. Thus, SWB helps not only health but quality of life when a person is sick.

**ISSUES**

**Causality**

How strong is the case that high SWB *causes* better health and longevity rather than simply predicts them? Prospective studies in which SWB precedes...
and predicts health and longevity, controlling for baseline health, make plausible the claim that SWB influences health. Despite the impressively large studies showing that SWB predicts health outcomes, the issue of unmeasured third variables remains. For instance, prenatal nutrition could conceivably influence both later SWB and health, and create an association between the two even in the absence of causality between them. Another third-variable explanation is that early home environment might influence both later SWB and health, and create the predictive association between the two. Miller and Chen (2010) found that a harsh family childhood environment was associated with a proinflammatory response style, and it is plausible that such a childhood also might predispose a person to lower SWB. Thus, third-variable explanations cannot be entirely ruled out by the longitudinal data, and additional potential explanatory variables should be assessed and analyzed in future studies.

Fortunately, additional methodological approaches provide corroborative and complementary evidence to suggest that SWB causally influences health. Experimental studies with animals, in which one condition is exposed to a negative or positive environment, indicate that environmental conditions, which are likely to induce negative or positive feelings, influence health. Quasi-experimental interventions with humans in which propinquity to emotional events is accompanied by physiological responses and higher death rates add to the evidence for causality.

Evidence that SWB can influence physiology and health also comes from human experimental studies, as well as from studies in which mood changes are tracked over time and physiological changes are monitored. There is substantial evidence that moods and emotions are associated with physiological responses, as well as with health outcomes. When people are followed over time, changes in their moods are usually tracked by changes in immune and cardiovascular measures. When moods are experimentally induced, physiological changes are often seen. These studies indicate that it is not simply long-term person factors such as SES, childhood nutrition, personality, or early family environment that cause the SWB and health link, because the health-relevant physiological changes track up and down with moods and emotions over time. For example, when couples argue they show physiological responses that can be detrimental to health in the long term, compared to the responses they show when they support each other. Finally, long-term chronic moods and emotions such as depression are related to physiological patterns that signal disease progression, such as thickening of artery walls. These studies indicate that people’s emotional responses are often accompanied by myriad physiological changes that over time are likely to cause health problems.

A final type of evidence for the causal role of SWB on health comes from randomised controlled intervention studies in which conditions designed to
enhance SWB are compared to control conditions. In a number of studies, activities that enhance SWB such as meditation have been shown to cause beneficial physiological responses. Although more intervention studies are needed, the initial findings are promising.

In sum, a strong case, but perhaps not an airtight case, can be made that SWB causally influences health and longevity. Although there are limitations in each type of evidence, studies converge from a number of complementary methodologies, including experiments and quasi-experiments, to form a compelling picture.

Ultimately causality is a theoretical issue that must be understood within a causal conceptual structure of a dynamic system. Single formal experiments shed some light on whether A causes B, but they are limited in terms of understanding the full causal system at work. For example, experiments tend to be focused on one or two independent variables, and therefore usually provide little insight into the full system that must be in place for the causal sequence to occur. Usually A is sufficient to cause B only if a set of additional circumstances is already in place. Furthermore, experiments usually demonstrate that a causal sequence can occur, but not whether it in fact does cause the outcome in the natural world. Experiments are an important method with which to explore causality, but other methods are essential to fully understand the causal system. In complex systems causality is not so much proven by a definitive experiment as it is developed over time as a theoretical model is developed, tested, and refined by a variety of complementary methodologies, which usually include randomised controlled trials. This is the type of evidence that has now been accumulated for the SWB and health connection. Furthermore, several promising conceptual models exist for understanding the effects of SWB on health (Davidson, 2004; Kiecolt-Glaser et al., 2002; Sapolsky, 2005).

Priorities for Future Research

There are several priorities for future research in order to fully understand the association of SWB and health.

1. Processes. What are the psychological processes that influence physiological changes related to health? How do feelings and thoughts lead to physiological changes in the immune, cardiovascular, and other bodily systems? How does SWB interact with social support to influence health? Social relationships have been found to have a strong association with mortality, and in fact show a larger effect on longevity than factors such as physical activity, body-mass index, air pollution, and drug treatment for hypertension (Holt-Lunstad, Smith, & Layton, 2010). Thus, an important
avenue for future research is to disentangle the effects of social support and SWB, recognising that each can influence the other.

2. Types of SWB. What types of SWB, for example, anger, affection, optimism, or life satisfaction, have effects on which physiological parameters? What is the structure of SWB that provides understanding of health outcomes? That is, which SWB variables are so highly related to one another that they provide no additional prediction of health beyond the others, and which SWB variables provide independent health predictions? How long-lasting do moods and emotions have to be in order to affect health?

3. Types of Health Outcomes and Subject Samples. What physiological systems and health outcomes does SWB most affect? When does SWB have little effect on health and longevity, and when does it have large effects? For example, which diseases are relatively impervious to the effects of SWB? At what ages can SWB have the largest effects on health outcomes?

A valuable addition to research on SWB and health would be to have measures of positive physical health, not simply measures of disease progression. Seligman et al. (2010) offer the following concepts that may reflect positive health:

- Rapid wound healing
- Low blood pressure
- High heart rate variability
- Parasympathetic tone
- High versus low density lipoprotein cholesterol
- Longer telomere length, age adjusted
- Maximal oxygen uptake (VO$_2$ Max)
- Low fibrinogen
- Renal and hepatic reserves

Much more research is required on the issue of what measures of positive health can reveal and whether the assessment of positive health can reveal the effects of SWB prior to noticeable illness.

We need more studies that follow people from young adulthood into old age, in order to assess the full impact of SWB on longevity, with less threat that initial health at baseline was already compromised by low SWB. In the case of older samples, controlling for baseline health could control away the earlier effects of SWB on health. We need research on more varied populations, for example, more studies of those living in very difficult or stressful situations. Finally, we need studies of natural situations that can cause large differences in SWB.
4. Interventions. At what levels of societal and individual SWB can interventions to raise SWB benefit health? At what levels is SWB high enough so that increases will not benefit health? Is the influence of SWB on health linear, convex, or concave? What types of SWB interventions, whether individual or societal, are most likely to benefit health?

Methodological Rigor

Studies in this field differ substantially in methodological rigor. One difference is in the measurement of SWB. Very few studies use measures of SWB besides self-report, such as reports by informants. Although survey self-report measures of SWB may be the best single method of assessment we currently have, the advantage of adding other types of measures is that they reduce concerns about overlapping method variance, for example when the health outcome itself depends to some degree on self-report. However, although the majority of work on SWB and health is based on self-report measures of SWB, not all is. For instance, Rosenkranz et al. (2003) found that negative affect as indexed by both right prefrontal brain activation and startle response predicted poorer immune system strength.

Smiling in photographs and ratings of autobiographies have been used to assess SWB. In addition, in studies of disasters such as earthquakes, and in experimental studies in which moods are induced, the research design does not primarily rely on self-report measures of SWB. Finally, moods such as stress are inferred in many studies based on environmental factors such as test-taking or having a child with a disease. Thus, there is multi-method evidence supporting the links of SWB to health. Furthermore, it is unlikely that biases in the self-report measures of SWB could produce spurious effects in research using outcomes such as mortality. Although personality biases might slant self-reports of SWB and illness in similar directions, the majority of outcome research does not depend on self-reports of health.

Early studies often suffered from small samples, low mortality, and brief follow-up periods (Kiecolt-Glaser et al., 2002). More experimental studies are being implemented, including intervention research. More studies that follow large numbers of people over many years are being conducted. The rigor of research has increased substantially since the early studies. There are high quality studies that show effects equal to or larger than studies of lesser quality (Cappelleri et al., 1996; Bausell, Lee, Soeken, Li, & Berman, 2004).

One important issue is whether the effects of SWB on health are due to inborn differences between individuals that will not be susceptible to interventions. It could be that factors such as a genetic predisposition and early nutrition can influence SWB and also longevity, but that levels of SWB resulting from changing causes of SWB such as circumstances or attitudes do
not influence health. Countering this possibility are the findings that changed levels of SWB are related to changes in physiology and health.

**Statistical Control**

The difficulties of interpreting findings after instituting statistical controls are underestimated by some researchers. Meehl (1970) and Kahneman (1965) explain the problems involved in statistical control. Kahneman described the undercontrol that usually occurs because most variables are measured imperfectly. Conversely, Meehl described several of the unintended types of over-control that can occur when statistical controls are employed. First, when statistical controls are introduced for one factor, the sample becomes less controlled on other factors. Meehl calls this problem “systematic unmatching” because when groups are statistically matched on one variable in the causal sequence, they must be systematically unmatched on another variable in the causal chain. For instance, if you control SES in the predictions of school outcomes, because SES predicts better school outcomes and you want to hold it constant, you will have made the participants less similar on other input variables. Various methods of control, including regressions approaches and partial correlations, matching of individual participants, and stratification, all suffer from similar shortcomings.

The second problem when controls are introduced is that greater weighting is given to certain less common participants. The problem is that statistical control makes the resulting groups less representative of the populations they are meant to represent. Finally, Meehl describes the issue of “causal arrow ambiguity”, an error based on the mistaken idea that we can cleanly sort variables in complex systems into dependent and independent variables. We might assume that we know the causal relation between variables such as income and health, or SWB and SES, when in fact we do not. Often our participants are to some degree self-selected into the very categories that many researchers want to control. Thus, we might be controlling away a substantial finding by statistical overcontrol. If SWB influences income, marital status, and whether a person smokes, as well as health, we will be controlling away true SWB effects if we control these other variables. Meehl’s concerns do not imply that statistical controls should never be undertaken, but they do mean that we must interpret the results carefully, and with knowledge of the pitfalls Meehl describes.

An example of statistical control reveals the complexities involved. If anger takes a progressive toll on cardiovascular health, and participants are 50 years old on entry into a study, controlling health at age 50 will answer a different question from that provided when initial health at age 50 is not controlled, or when controlling health at age 20. By controlling health at age 50, when anger might already have had a substantial detrimental impact, the
researcher is probably analyzing whether anger after age 50 has an incremen-
tal or greater impact than prior anger. Even if cardiovascular death is much
more likely after age 50, anger before age 50 might already have produced
substantial cardiovascular problems. Making matters even more challenging
is the fact that anger and health may differ in stability and in the reliability
with which they are measured. Thus, statistical controls must be introduced
in a conceptually and psychometrically sophisticated way to produce inter-
pretable results. A careful reading of Meehl is illuminating.

An example of the use of statistical controls comes from research reported
by Koivumaa-Honkanen et al. (2000). Following accepted practices in the
field, the authors controlled for factors such as marital status, social class,
smoking, alcohol use, and physical activity, which reduced the association
between life satisfaction and disease-related deaths, and made the association
inverse for women. However, these variables are not simple confounds. Past
research shows that the causal arrow can move from SWB to factors such as
marriage and income. Positive affect and life satisfaction in many circum-
stances increase people’s likelihood of marrying, having high income, not
smoking, and increasing their probability of exercising. Furthermore, these
factors probably in turn influence SWB. The control variables and SWB are
intricately intertwined in causal bidirectionality. Thus, controlling for these
factors might help illuminate the pathways mediating the connection going
from SWB to health, but post-control findings showing no further associa-
tion cannot be interpreted to suggest that SWB does not cause health out-
comes because SWB might have causally influenced the control variables.
Smoking, marriage, and other factors must not automatically be assumed to
be biases or confounds, because they might be mediators of the SWB and
health association.

It is essential to carefully consider what statistical controls show. In the
case of the Koivumaa-Honkanen et al. study, the statistical controls were not
inappropriate, but caution is needed in interpreting the results. For example,
Chida and Steptoe’s (2008) meta-analysis shows the study as one with a large
N in which SWB inversely predicted mortality. However, there were essen-
tially no effects of SWB for women in the study before statistical controls
were instituted. Further issues related to statistical controls, particularly in
mediation analyses, are discussed by Bullock, Green, and Ha (2010).

Variations in Outcomes across Types of SWB

Subjective well-being is a broad category that includes diverse phenomena
such as life satisfaction, positive affect, and low negative affect, such as
infrequent sadness, anger, and fear. Keyes (2007) reported data showing that
mental health is more than the absence of mental illness, suggesting that at
the very least we must consider two factors to reflect SWB—positive and
negative. Most reviewers now conclude that positive and negative states produce independent effects controlling for the other (e.g. Steptoe et al., 2009). For example, Richman et al. (2005) found that people with hope had a lesser chance of experiencing diabetes mellitus beyond the effects of negative emotions. Furthermore, in some instances positive states have produced effects when negative states do not. Ignoring positive emotions reflects a broad bias in the early days of this field. Pressman and Cohen (2005) suggested that some past findings on negative affect and health might have in fact resulted from differences in positive affect. In a meta-analysis of the literature, Howell et al. (2007) found that ill-being slightly more strongly predicted short-term health outcomes, whereas positive well-being slightly more strongly predicted long-term health outcomes, but in general the effects were of similar size.

Within the positive and negative categories, we can make finer differentiations. For instance, in the cardiovascular literature, some attempts have been made to differentiate the negative effects of hostility versus sadness versus anxiety. Thus far it seems that both anger/hostility and depressed mood, as well as severe depression, are detrimental to cardiovascular health. Suls and Bunde (2005) reviewed the literature on various forms of negative emotions and cardiovascular diseases. They suggested that although depression is consistently related to impaired cardiovascular health, there is still much uncertainty about how specific negative emotions such as depression, anxiety, and anger influence health in unison, in interaction, or independently.

Types of positive states such as optimism, joy, vigor, sociability, love, and contentment have not been clearly differentiated or measured in most research, and thus it is impossible to draw strong conclusions about what varieties of positive feelings are most beneficial to health, and at what levels. Marsland et al. (2007) discuss the fact that various states such as extraversion and optimism have not been clearly differentiated in terms of their health effects.

One division of SWB is into hedonic forms of happiness such as enjoyment of life versus what some have called, using Aristotle’s term, “eudaimonic” happiness (Vazquez, Hervas, Rahona, & Gomez, 2009). Eudaimonia refers to people developing their full potential, and therefore includes concepts such as mastery, meaning and purpose, and psychological growth. The distinction between hedonic and eudaimonic well-being is still being debated. Nonetheless, it will be useful to assess a wide range of states of psychological well-being in order to map their overlapping and independent contributions to health.

Seligman et al. (2010) list types of positive psychological well-being, including: curiosity, hardiness, engagement, internal locus of control, sense of coherence, purpose, marital satisfaction, vitality, meaning, and mastery. To the Seligman et al. list we might add enjoyment of life, low levels of anger and
depression, contentment, happiness, work satisfaction, work strain, and life satisfaction. The possible list is virtually limitless because new concepts can be created to describe nuanced differences in feelings and thoughts, as well as the situations that produce them. Clearly the proliferation of concepts requires pruning. Studies are needed that include a broad examination of many measures, based on large and diverse samples, to determine how the concepts are related to one another, and their independent ability to predict health outcomes beyond a general SWB factor score. Ideally, two or three different measures of each concept would be included so that latent trait scores might be created, and so that variance due to peculiarities of measures can be separated from the effects of the underlying constructs.

It might be that each of the myriad concepts of SWB can be reduced to several overarching concepts, and psychometric research is needed to accomplish this. In the meantime, new SWB concepts should be added cautiously until it can be demonstrated that they add prediction beyond highly studied concepts such as optimism, depression, life satisfaction, stress, and positive affect.

Variations across Populations and Diseases

It is likely that SWB has different effects depending on the types of diseases being considered, as well as the level of progression of the disease. Disease is a broad category covering many different physiological processes, many different causes, and many levels of severity. There is no reason to believe that SWB would affect all types of illness to the same extent.

It will not surprise anyone to learn that low SWB predicts mental problems and suicide. For instance, Bray and Gunnell (2006) found across 32 nations that happiness and life satisfaction were inversely associated with suicide rates. This is confirmed in studies of individuals, where SWB has been found to predict suicide (Koivumaa-Honkanen et al., 2001; Koivumaa-Honkanen, Honkanen, Koskenvuo, & Kaprio, 2003). In addition, SWB strongly and inversely predicts deaths due to nonintentional injuries (Koivumaa-Honkanen et al., 2000).

The case of optimism and health shows the intricate patterns that can emerge when analyzing particular disease states and outcomes. It is likely that optimism is a beneficial factor in normal populations, and predicts all-cause mortality. However, a recent study by Tomakowsky, Lumley, Markowitz, and Frank (2001) revealed that optimism among HIV infected men was associated with poorer immune status.

Segerstrom (2001, 2005) explains the mixed findings on optimism and health outcomes. Although this pattern has sometimes been explained by optimists being disappointed because their expectations are unrealistically high for their medical conditions, she explains the pattern in reference to goal
conflict. When optimistic people face goal conflict, they fare more poorly, but they fare better when not facing such conflicts. Because optimists are more likely to stay engaged with goals and not withdraw from them, they have more short-term stress in the face of goal conflict. Segerstrom found support in two studies for this explanation, using immune measures as outcomes.

Just as types of SWB and variations in disease states affect the SWB and health relation, so do the samples being considered. Among young adults health and resilience might be so strong that few SWB effects on disease-related deaths are found. Similarly, very old people might be so impaired and disease states so prevalent that SWB no longer predicts longevity. Similarly, levels of SWB vary across groups, thus affecting the degree to which SWB will predict health outcomes in them.

An example of sample-specific findings is reported in the meta-analysis of Howell et al. (2007) who found a strong and significant relationship between SWB and immune functioning in healthy samples. This effect was much weaker and nonsignificant in the ill. A number of such findings with differences in outcomes depending on the sample are reported in Tables 1 and 2. Such differences can give us greater insight into the dynamics of SWB and health, as well as the boundary conditions involved in the relations.

Dose-Response and Threshold Effects

There appears to be a dose-response relation between SWB and health outcomes, such that serious depression is very bad, dysphoria is bad but less bad than depression, and positive feelings are good (e.g. Giltay, Geleijnse, Zitman, Hoekstra, & Schouten, 2004; Kubzansky, Sparrow, Vokonas, & Kawachi, 2001), although there might be a ceiling effect of SWB beyond which increases are not helpful.

Several considerations lead us to inquire whether people can be too happy for it to benefit their health, or whether certain types of happiness such as hypomania or highly aroused positive affect might even be detrimental to health. Supporting the idea that people might sometimes be too happy for their health, McCarron, Gunnell, Harrison, Okasha, and Davey-Smith (2003) found that hypomanic young men had greater risk of cardiovascular mortality during the ensuing decades. Ritz and Steptoe (2000) found that extreme positive moods were associated with decreased pulmonary function.

Pressman and Cohen (2005) suggest that those “with diseases with high short-term mortality rates were harmed by high levels of PA” (p. 960), whereas patients with longer term expectations for survival may benefit or be unaffected by positive emotion. They write that, “High levels of PA in seriously ill populations could be harmful because they are associated with the underreporting of symptoms or overoptimistic expectations, both of which could result in failure to seek medical care or adhere to physical advice”
The authors conclude that in a few studies of the institutionalised elderly, higher rates of positive affect are related to higher rates of mortality.

One study that stands out in prospective studies of SWB and longevity is the Friedman et al. (1995) study of the “Termites”, the highly gifted children studied by Terman. They found that high “cheerfulness” was associated with greater mortality, running counter to the findings of most studies on positive feelings. However, the vast majority of the Terman sample were very happy, with few people at moderate or low levels of SWB. Thus, the correlation between cheerfulness and longevity was primarily a comparison of the very happy with the extremely happy.

Even if positive emotions have beneficial health effects, their benefits at high levels could be offset either by the physiological impact of high bodily arousal, or by the risks and activities undertaken by hypomanic and highly extraverted individuals. Such individuals might be more likely to smoke, drink excessively, drive fast, and participate in other risky behaviors. Thus, at very high levels positive feelings may lose their benefits.

Although intense positive emotions might in some cases be harmful, below these levels there might be a dose-response relation between SWB and health, in the range from clinical depression up through contentment and moderately high levels of happiness. A dose-response curve between depressive symptoms and cardiovascular disease in the absence of major depression (Rozanski et al., 1999) suggests that it is not just the lowest levels of SWB that are harmful.

**Effect Size**

Are the SWB effects of sufficient size to be of practical and policy significance? In a study of elderly Dutch over a 15-year period, unhappy seniors had a mortality risk of 1.28 compared to happy respondents. In a study of Finnish octogenarians (Lyra, Törmäkangas, Read, Rantanen, & Berg, 2006), the mortality risk for the quartile least satisfied with life in terms of zest and mood was 1.80 compared to the most satisfied quartile. Kiecolt-Glaser et al. (2002) reviewed studies on the size of effects on mortality for depression, anxiety, and anger. They concluded that the effects of depression on mortality are substantial, similar to the risk from smoking, hypertension, and diabetes. In patients suffering from acute coronary events, those with panic-like anxiety had three times the risk of a fatal heart attack over a 7-year follow-up compared to those without the anxiety.

Lett et al. (2004) found that depression in otherwise healthy populations was a risk factor for coronary artery disease of 1.5 to 2.0. In a meta-analysis of 40 studies, Chida and Steptoe (2008) found a psychological well-being risk ratio for mortality in healthy populations of .82, and a risk ratio in diseased population studies of .98. The risk ratio for mortality in healthy populations...
over age 60 was .74. Thus, SWB was beneficial in healthy populations, with an effect size that is of sufficient magnitude to be of importance to public health. However, the effect size found by Chida and Steptoe for mortality in diseased populations differed little from 1.0.

The effect sizes for SWB and specific causes of death can be lower or higher than the effect sizes for all-cause mortality. For example, Koivumaa-Honkanen, Honkanen, Koskenvuo, Viinamäki, and Kaprio (2002) reported that the risk ratio for dissatisfied compared to satisfied individuals for mortality due to injuries (both intentional and nonintentional) was 2.8. The risk ratio of fatal nonintentional death was 7.8 for dissatisfied women and 4.0 for dissatisfied men, compared to their satisfied counterparts.

How do the effect sizes compare with other lifestyle variables, which have been the focus of large public health campaigns? Smith et al. (2004) concluded that the effect sizes for hostility on cardiovascular disease “are as large as those associated with many traditional risks factors, and the associations are found even when a wide variety of potential confounding factors are controlled” (p. 1239). Kvaavik, Batty, Ursin, Huxley, and Gale (2010) reported the strength of the association between healthy lifestyle behaviors and mortality. For example, the mortality risk for current smokers versus current nonsmokers was 1.52 and that for those who infrequently eat fruit and vegetables compared to those who frequently eat them was 1.31. The risk for those doing none of the health behaviors was 3.49 compared to those who scored in a positive direction on all four of them. However, the prediction of specific diseases varied. For example, eating little fruit and vegetables predicted cancer risk of only 1.12. Kvaavik et al. estimated that those with all four positive health behaviors would live 12 years longer than those who were low on all four, an estimate similar to the 14-year estimate from Khaw, Wareham, Bingham, Welch, Luben, and Day (2008).

In terms of additional life-years, Veenhoven (2008) estimated that the effects of SWB on longevity might be 7.5 to 10.0 years, based on a small number of studies that reported effect size in life-year units. For example, the 10-year figure comes from Danner, Snowdon, and Friesen’s (2001) study of nuns—one of the largest longitudinal studies—and is a comparison of the happiest versus unhappiest quartiles. Pressman and Cohen (2010) found that famous psychologists who used positive emotion words in their autobiographies lived 4.2 years longer than those who did not, while the use of negative words did not predict longevity. Howell et al. (2007) estimated a 14 per cent longevity difference between happy and unhappy individuals based on a meta-analysis of 24 studies. Using the average correlation in the analysis and converting to standard deviation units, this could amount to 6 years’ difference in the USA between individuals who are two standard deviations apart on SWB, or 75 years versus 81 years life expectancy (Howell, 2010). Based on the age effects estimated from several reviews and studies, an unhappy person
in an economically developed nation might live 4–10 years less than a very happy person, recognising that such an estimate depends on many factors.

There is no underlying universal effect size for the association of SWB with health and longevity. Effect sizes depend on the amount of variability of SWB in a population, exposure to virulent pathogens, the length of the study, at what ages participants are observed, the reliability of the SWB measures, types of SWB assessed, and many additional factors. This variability is clearly demonstrated in a study on the effects of smoking (Doll, Peto, Wheatley, Gray, & Sutherland, 1994), in which British physicians were assessed over a period of 40 years. Death rates due to smoking were double in the second 20 years compared to the first 20 years. Had the investigators followed participants for 10 years and controlled for initial health at the start of the study, the effects would have been much smaller. Thus, the effects found in studies rarely give the full lifelong effects of lifestyle and personality factors.

Other Issues

An important issue is whether the benefits of SWB for health found in the research literature are in part due to publication bias in which primarily positive results are published. Several factors argue against this. Operating in the opposite direction is that for the majority of past studies in this field positive feelings were not assessed. Because positive feelings seem to have substantial effects, and sometimes have effects when negative emotions do not, a large number of studies may have failed to find effects due to not assessing a key form of SWB. Several of the meta-analyses (e.g. Segerstrom & Miller, 2004; Herbert & Cohen, 1993) have analyzed the distributions of research findings, and concluded that publication bias is unlikely to produce the full effects found, although it might have some effect. In some analyses no evidence of publication bias has been discovered, and in others researchers have found likely publication bias, but also that an extremely large number of unreported studies would be required to reverse the findings. Given the unsettled nature of this area, it seems unlikely that huge numbers of negative findings are unreported. Indeed, one could imagine situations in which methodologies that would be considered adequate in other areas of study would be considered inadequate in this area, resulting in a negative editorial bias. Nevertheless, careful attention to the file-drawer problem is warranted.

Originally skeptics criticised the idea that SWB and psychosocial processes could influence health and longevity. However, as evidence accumulated, much of the skepticism narrowed to more specific questions. Coyne and Tennen (2010; Coyne, Tennen, & Ranchor, 2010) concluded that evidence is lacking that a “fighting spirit” or “benefit finding” slow cancer progression. On the other hand, Spiegel and his colleagues (Spiegel, 1996; Spiegel et al., 2007) found that in some controlled trials psychological interventions do
extend the life of cancer patients, but this has not been replicated across all studies. A decade ago skepticism that hostility could increase the likelihood of heart disease was expressed (e.g. Myrtek, 2001; Petticrew, Gilbody, & Sheldon, 1999), but more recent reviews have concluded that the case for the link is compelling (Smith et al., 2004). Thus, over time skepticism has focused on the open questions that have not yet been answered in a clear and convincing way.

Bjornskov (2008) expressed new skepticism about the benefits of happiness for health. He suggested that society-wide happiness might decrease longevity because happy societies spend less on public health. In a sample of 15 economically developed European Union nations he found that the average life satisfaction in the societies negatively predicted their public health expenditures. Following up on this suggestion in 95 diverse nations included in the Gallup World Poll, we found the opposite of what Bjornskov found in his small and homogeneous sample of nations. We found that life satisfaction predicts longevity in nations after controlling per capita income, and we found that positive emotions predict a greater percentage of GDP spent on health, controlling for GDP. We will report these findings in detail in a later paper, but it appears to us that happy nations do not spend less on health or have shorter life expectancy.

TAKE-HOME MESSAGE

There now are sufficient studies on all-cause mortality and certain diseases to draw relatively strong conclusions. Our overall conclusion is that the evidence for the influence of SWB on health and all-cause mortality is clear and compelling, although there is much more uncertainty about how various types of SWB influence specific diseases, and about the role of the possible mediating processes. The effect sizes for SWB and health are not trivial; they are large when considered in a society-wide perspective. If high SWB adds 4 to 10 years to life compared to low SWB, this is an outcome worthy of national attention. When one considers that the years lived of a happy person are more enjoyable and experienced with better health, the importance of the SWB and health findings is even more compelling.

It is perhaps time to add interventions to improve subjective well-being to the list of public health measures, and alert policy makers to the relevance of SWB for health and longevity. Kobau et al. (in press) describe how interventions to enhance SWB are compatible with a public health perspective, not just with the medical intervention perspective. In public health society-wide and organisational interventions are used, and thus SWB might be raised by improving organisational and institutional factors in societies, not just through individual interventions. We need more research on what levels of
SWB are required to produce benefits, although current evidence suggests that individuals in the low range for SWB would likely experience better health if their SWB could be raised.

High subjective well-being is a state that many desire, some achieve, and a few despise as an unnecessary luxury or even a detriment. Given its clear and compelling relation to physical health and longevity, we need to begin thinking of societal SWB as something that is indeed desirable and beneficial.

ACKNOWLEDGEMENTS

Our thanks to the following for their helpful comments: Alex Zautra, Andrew Steptoe, Angus Deaton, Bert Uchino, Beverly Brummett, Carol Diener, Carmelo Vazquez, Charles Martin-Krumm, Chris Peterson, Ellen Langer, Glenn Ostir, Gregory A. Miller, H. Koivumaa-Honkanen, Howard Friedman, Howard Tennen, Janice Kiecolt-Glaser, John Helliwell, Sonja Lyubomirsky, Karen Matthews, Kyriakos Markides, Laura Kubzansky, Michael Frisch, Richard Eckersley, Robert Biswas-Diener, Robert Cummins, Ruut Veenhoven, Ryan Howell, Sarah Pressman, Suzanne Segerstrom, William Pavot, and Rosemarie Kobau. Our gratitude is also extended to Louis Tay, who conducted the national analyses for us on the relation of SWB, health expenditures, GDP, and life expectancy. Our thanks to the Robert Wood Johnson Foundation and the John Templeton Foundation for support that helped make the writing of this paper possible.

REFERENCES


patients after stem-cell transplantation for malignant diseases. *Journal of Clinical Oncology*, 20, 2118–2126.


