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Positive health: connecting well-being with biology

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Two key types of well-being, eudaimonic and hedonic, are reviewed. The first addresses ideas of self-development, personal growth and purposeful engagement, while the second is concerned with positive feelings such as happiness and contentment. How well-being varies by age and socio-economic standing is briefly summarized, followed by examination of its biological correlates (neuroendocrine, immune, cardiovascular, rapid eye movement (REM) sleep). Preliminary findings on a sample of ageing women showed that those with higher levels of eudaimonic well-being had lower levels of daily salivary cortisol, pro-inflammatory cytokines, cardiovascular risk, and longer duration REM sleep compared with those showing lower levels of eudaimonic well-being. Hedonic well-being, however, showed minimal linkage to biomarker assessments. Future research directions building on these initial findings are discussed.

Keywords: eudaimonic well-being; hedonic well-being; neuroendocrine; immune; cardiovascular; sleep

1. INTRODUCTION

Defining human health as more than the absence of illness has been a long-standing though elusive objective (World Health Organization 1948). One route to advancing health, construed as the presence of wellness, is to focus on what it means to flourish, such as having a sense of purpose and direction in life, good-quality relationships with others, and opportunities to realize one's potential (Ryff & Singer 1998). Of critical importance in this view is mapping the physiological substrates of human flourishing. The core hypothesis of positive health, in fact, is that the experience of well-being contributes to the effective functioning of multiple biological systems, which may help keep the organism from succumbing to disease, or, when illness or adversity occurs, may help promote rapid recovery. Numerous layers of empirical evidence must be assembled to test these ideas (see Ryff & Singer 2000; Singer & Ryff 2001). We contribute preliminary evidence to support this theory by examining biological correlates of two distinctive types of well-being: eudaimonic and hedonic.

We first review the meaning of these two types of well-being and summarize what is known about their socio-demographic correlates. We then summarize findings from a sample of ageing women on links between these two types of well-being and multiple biomarkers (neuroendocrine, immune, cardiovascular). Links to objective sleep assessments are also included. Because of the preliminary nature of the study (i.e. small sample, cross-sectional design), additional factors that need to be considered in multivariate, longitudinal designs are considered. We conclude with observations about the general pattern of findings and the subsequent steps needed to advance understanding of the processes whereby psychological well-being may be protective of good health.

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2. VARIETIES OF WELL-BEING: WHAT IS IT AND WHO HAS IT?

Articulating the components of human flourishing has engaged scholars across the centuries (Coan 1977). Indeed, philosophers have offered multiple meanings of what constitutes the good life (Becker 1992), such as the pursuit of human perfection, or the satisfying of human needs and desires. Empirical research on well-being was launched in the 1960s via an interest in depicting the quality of life in America (Campbell *et al.* 1976). Since that time, the scientific study of well-being has proliferated (Diener *et al.* 1999), with distinctions increasingly drawn between eudaimonic and hedonic aspects of well-being (Waterman 1993; Kahneman *et al.* 1999; Keyes *et al.* 2002; Ryan & Deci 2001). These terms are defined in the following two sections, and what is known about how the two types of well-being vary as a function of age, socio-economic status, and race/ethnicity is briefly summarized.

(a) *Eudaimonic well-being: the realization of personal potential*

Aristotle first wrote about eudaimonia as the realization of one's true potential (see Ryff 1989). According to this view, each individual comes into life with unique capacities, known as one's 'daimon'. The central task of life is to recognize and realize these talents. Variants of such ideas filtered into subsequent formulations of the human condition, such as existential philosophy (Sartre 1965), which underscored the responsibility of the individual to find meaning in his or her existence, even in the face of harsh or absurd realities. In psychology, numerous accounts of well-being such as the formulation of self-actualization by

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Maslow (1968), or the view of the fully functioning person by Rogers (1961), drew on these portrayals of the organism striving to make the most of his or her own potential. Other accounts, such as the model of psychosocial development by Erikson (1959), the formulation of maturity by Allport (1961) or the characterization of the individuation process by Jung (1933), offered positive alternatives to the Freudian depiction of the human psyche anchored in conflict and anxiety. Theirs was a benign and hopeful vision that construed the individual as forever engaging in new life challenges that contributed to greater self-knowledge, maturity and effectiveness.

Translating these ideas to the empirical level required developing operational measures of well-being. One such framework focused on the primary points of convergence in the above characterizations (Ryff 1989), which translated to six key dimensions of well-being. These were operationally defined with structured self-report scales designed to measure *self-acceptance*, the capacity to see and accept one's strengths and weaknesses; *purpose in life*, having goals and objectives that give life meaning and direction; *personal growth*, feeling that personal talents and potential are being realized over time; *positive relations with others*, having close, valued connections with significant others; *environmental mastery*, being able to manage the demands of everyday life; and *autonomy*, having the strength to follow personal convictions, even if they go against conventional wisdom. Complete definitions and details of the scale construction and validation process are summarized in Ryff (1989).

A large body of empirical research has examined how eudaimonic well-being varies by socio-demographic factors such as one's age, gender, socio-economic status, race/ethnicity or culture (e.g. Ryff & Singer 2002*a*; Ryff *et al.* 2003). A further line of inquiry has focused on how well-being is affected by various challenges in life, such as parenthood, including having a child with disabilities, growing up with an alcoholic parent, giving care to an ill or disabled significant other, or experiencing relocation (e.g. Kling *et al.* 1997; Ryff *et al.* 2002). These diverse studies have been conducted with both national and local samples, using cross-sectional as well as longitudinal designs.

Patterns of age variation in eudaimonic well-being have been replicated across multiple samples. Aspects of well-being, such as self-acceptance, show little variation by age from young adulthood through midlife to old age, while environmental mastery shows increments with age. Purpose in life and personal growth, however, show dramatic age decrements across these age periods. Cross-sectional findings leave unanswered whether such patterns are due to cohort differences or maturational processes. However, longitudinal queries have demonstrated that eudaimonic well-being is not trait-like, but rather is dynamic, showing cross-time change as individuals negotiate particular life transitions (e.g. Kwan *et al.* 2003).

With regard to socio-economic standing, eudaimonic well-being is positively correlated with both educational attainment and occupational status (e.g. Marmot *et al.* 1997; Ryff *et al.* 1999). However, we have also found that variability in eudaimonic well-being increases as one moves down the educational hierarchy (figure 1; Ryff *et al.* 2004). The figure, using data from the MIDUS (Midlife in the US) national survey, arrays the maximum, minimum, 25th, 50th and 75th centile values for individuals with a college education, some college, high school degree or less than high school education. These varying distributions also show that substantial numbers of individuals with limited educational attainment nonetheless have high eudaimonic well-being (Markus *et al.* 2004). Similarly, we have also found that ethnic minority status is a *positive* predictor of well-being: i.e. American minorities, on average, are more likely to have high eudaimonic well-being than their white majority counterparts (Ryff *et al.* 2003). A key question from the positive health perspective is whether high eudaimonic well-being in contexts of inequality, or discrimination, confers protection at biological levels. Probing correlates of well-being across multiple physiological systems is a first step in this inquiry.

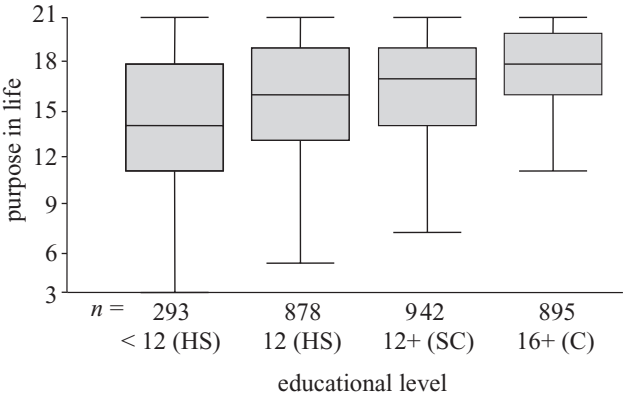

Figure 1. Five-number summaries (maximum, minimum, 25th, 50th and 75th centile values) of purpose in life for individuals with differing years of education. 16+(C), 4-year college degree; 12+ (SC), some college; 12 (HS), high school diploma; < 12 (HS), less than high school diploma. Source: MIDUS: Midlife in the US National Survey.

(b) *Hedonic well-being: experiences of happiness and satisfaction*

Research on hedonic well-being also has a long tradition, but one rooted in ideas of pleasure, happiness and the satisfaction of human appetites. The ancient Greeks (e.g. Epicurus), as well as subsequent philosophies of Hobbes and Bentham, elaborated the essentials of hedonism (Ryan & Deci 2001). In the present era, the field of hedonic psychology is defined as the scientific study of what makes experiences and life pleasant and unpleasant (Kahneman *et al.* 1999). Most prior empirical research in this realm falls under the umbrella of 'subjective well-being' (Diener & Lucas 1999), which has typically been defined in terms of three components: life satisfaction, the presence of positive affect, and the absence of negative affect.

Early scientific studies of subjective well-being were conducted by social scientists interested in evaluating the quality of life in America, beyond what was discernible from economic indicators (e.g. Gurin *et al.* 1960; Cantril 1965; Bradburn 1969). This work was largely sociological in nature, probing socio-demographic correlates of well-being (i.e. how it varied as a function of age, marital status, income, occupational status, religion or geographical region). Subsequent work became more psychologically oriented and broadened the scientific agenda to include studies of how personality characteristics, goals and coping

strategies may affect happiness as well as how these factors interact with external life circumstances to influence subjective well-being (see Diener *et al.* 1999).

What is known about ageing and subjective well-being? Initial research challenged the expectation that later life would be accompanied by decrements in well-being. Several studies have converged to show increases in life satisfaction with age (Shmotkin 1990; Diener & Suh 1998). Research on positive affect (cross-sectional and longitudinal) has shown evidence of both decline and gains with age, whereas negative affect seems to remain stable for some and decline for others (Shmotkin 1990; Diener & Suh 1998; Mroczek & Kolarz 1998; Charles *et al.* 2001). Overall, the average older age profile of hedonic well-being is mostly positive, a finding that has led many to focus on the adaptation processes that older persons employ to maintain their levels of happiness and life satisfaction (Diener *et al.* 1999).

With regard to socio-economic standing and hedonic well-being, wealthy people are consistently found to be happier than poorer people, but the effects are small (Diener *et al.* 1999). In addition, the relation between wealth of a nation and average levels of subjective well-being is positive and strong (Diener *et al.* 1995*a*). Nonetheless, research both within and between countries has clarified that increases in income are not associated with increases in well-being (Diener *et al.* 1993; Diener & Suh 1997), suggesting that expectations, goals and comparison processes influence subjective well-being. It has also been found that people who strongly desire money and wealth (defined as extrinsic goals) are more unhappy than those who do not (Kasser & Ryan 1993, 1996), with the effect replicated in less economically developed nations (Ryan *et al.* 1999). Progress toward intrinsic goals, such as positive relationships, personal growth and community generativity, has been shown to enhance well-being (Sheldon & Kasser 1998).

(c) *Toward integration: related but distinct constructs*

Recent findings from the MIDUS national sample of Americans ($n = 3032$, aged 25–74 years) in which both eudaimonic and hedonic well-being were assessed demonstrates that they are related, but distinct, constructs (Keyes *et al.* 2002). That is, the best-fitting model is one that posits two correlated latent constructs rather than one general factor, or two orthogonal factors. Thus, although highly correlated, each construct retains its uniqueness as a separate component of overall well-being. Not surprisingly, it is the strongly existential aspects of eudaimonic well-being (i.e. purpose in life, personal growth) that are most sharply differentiated from the affective and life satisfaction assessments of hedonic well-being.

The study also identified socio-demographic and personality predictors of well-being. The probability of optimal well-being, defined as being high on both eudaimonic and hedonic well-being, increased as age, education, extraversion and conscientiousness increased and as neuroticism decreased. Alternatively, those with higher eudaimonic than hedonic well-being (*ca*. 23% of the sample) tended to be younger, have more education and have higher levels of openness to experience. Those with higher hedonic than eudaimonic well-being (*ca*. 22% of the sample) had less education, were more likely to be midlife and older adults, and had lower levels of openness to experience.

The above investigation provides a useful starting point for assessing biological correlates of well-being. That is, because the research confirms their status as related but distinct constructs, it is useful to investigate whether eudaimonic and hedonic well-being have distinct biological signatures.

3. EUDAIMONIC AND HEDONIC WELL-BEING: LINKS TO BIOLOGY

The key hypothesis of positive health is that well-being will be accompanied by optimal functioning of multiple physiological systems (Ryff & Singer 1998; Singer & Ryff 2001). Over the long term, this biopsychosocial interplay is proposed to comprise part of the mechanistic processes that delay the onset of morbidity, help the organism maintain functional capacities, and thereby extend periods of quality living. An initial step toward testing these broad claims is to investigate whether those with high well-being, indeed, have lower profiles of biological risk across multiple physiological systems, as well as higher profiles of 'good' biomarkers (e.g., HDL cholesterol). Although psychological factors have long been studied as influences on cardiovascular, neuroendocrine and immune function, such inquiry has been overwhelmingly focused on the negative, probing how psychosocial adversity (e.g. child abuse, stress in the workplace, caregiving, loneliness, neuroticism, depression) elevates biological risk (e.g. Cacioppo *et al.* 1998, 2002; Lundberg & Frankenhauser 1999; Heim *et al.* 2000; Feldman & Steptoe 2003). Our aim is to probe the counterpoint question—namely, whether well-being is associated with reduced biological risk.

Because little is known about well-being and biology, it is unclear whether eudaimonic and hedonic well-being would have similar or different biological correlates. Both involve positive psychological functioning and thus might be expected to show similar links to biology. Alternatively, purposeful life engagement (eudaimonic well-being) evokes an active, striving organism, sometimes in the face of adversity. As such, eudaimonic well-being may prompt greater biological activation of the organism than states of happiness or contentment (hedonic well-being). Such activation may not be of the kind that contributes to pathogenesis. For example, Dienstbier (1989) describes a pattern of arousal in contexts of stress that contributes to physiological toughening, defined to include resistance to brain catecholamine depletion and suppression of pituitary adrenal–cortical responses.

(a) *Sample and measures*

We investigate these questions with a sample of ageing women ($n = 135$) on whom comprehensive assessments of well-being and biomarkers were available. The sample does not provide gender comparisons in links between well-being and biology, nor does it offer insight into the dynamic, cross-time associations between well-being and biology. However, ageing has been a key forum within which well-being has been studied, and the sample does afford comparisons between those just entering the later years and those who are 75 and older. The biomarker data were collected as part of a comprehensive biomedical assessment obtained during an overnight stay at the

General Clinical Research Center on the University of Wisconsin-Madison campus.

The women in the study ranged in age from 61 to 91 years and, on average, had moderate retirement incomes and slightly more than a high school education. Over half were widowed. All had been participants in a prior four-wave longitudinal study involving the later life transition of community relocation. Approximately half of the original sample was targeted for recruitment for a fifth wave of data in which psychosocial assessments were repeated and comprehensive biomarkers were collected. Comparison with the larger sample showed that the biomarker sub-sample was not significantly different in reported health (chronic conditions, health symptoms), income or marital status. However, the biomarker sample was significantly younger, had more education, and higher scores on four out of six aspects of eudaimonic well-being (environmental mastery, personal growth, purpose in life, self-acceptance) compared with the original sample. No comparisons on hedonic well-being were available as those measures were added to the study at Time 5.

Eudaimonic well-being was measured with 14-item scales of the six dimensions of well-being (Ryff 1989) described previously. Hedonic well-being was assessed in terms of positive affect, as measures of life satisfaction were not available. Two versions of positive affect were included: (i) 10 items from the Positive and Negative Affect Schedule (PANAS). Inventory (Watson *et al.* 1988) that asked how the respondent felt (e.g. excited, enthusiastic, proud, alert, determined) on an average day; and (ii) 14 items from the short-form MASQ (Watson *et al.* 1995) that asked respondents how much they had felt various positive emotions (e.g. happy, cheerful, optimistic, having fun, looking forward to things) in the past week.

We included biomarkers from diverse physiological systems: neuroendocrine, immune and cardiovascular. Because little prior knowledge exists on the physiological substrates of flourishing, the objective was to be broad and inclusive. Increasing scientific focus is on the interplay among these systems; that is, how they are mechanistically linked to each other (e.g. Miller *et al.* 2002; Kunz-Ebrecht *et al.* 2003). In addition, we included assessments of sleep, which allowed us to probe whether well-being is positively linked with restorative processes. Details regarding specific markers in each of these areas are provided in the following summary of findings.

With regard to statistical analyses, distributions for all measures were examined, trimmed for outliers and symmetrized (normalized) as needed. Transformations are noted in tables 1–3 of reported results. To probe differences by age, all analyses were first examined for the full sample, then for those aged 65+, and finally for those aged 75+. Because of the large number of coefficients examined, significant effects are reported only if they met one of two conditions: (i) the magnitude of the association was significantly different from zero at $p < 0.01$; or (ii) among $p < 0.05$ findings, there had to be at least *two* significant effects for any scale of well-being or any biomarker for results to be reported.

Table 1. Pearson correlations between eudaimonic well-being and neuroendocrine and immune measures.
(Full sample $n = 135$.)

	eudaimonic[a]		
	personal growth	purpose in life	autonomy
neuroendocrine measures			
salivary cortisol (slope)			
age 65+ ($n = 92$)	0.21*		
age 75+ ($n = 52$)	0.29*	0.29*	
noradrenaline[b]			0.21**
immune measures			
sIL-6r			
age 65+ ($n = 92$)		−0.27**	

[a] Well-being scales are cubed to symmetrize distributions.
[b] Square root taken to symmetrize distributions.
* $p < 0.05$, ** $p < 0.01$.

4. RESULTS

(a) *Neuroendocrine correlates*

Psychological and social factors have been previously linked with neuroendocrine factors, although most inquiry has focused on the negative, such as elevated levels of cortisol, adrenaline or noradrenaline among caregivers (Cacioppo 1994; Uchino *et al.* 1996; Cacioppo *et al.* 1998) and those exposed to early childhood abuse (Heim *et al.* 2000). Flatter slopes of daily salivary cortisol have also been associated with repression of emotion (Giese-Davis *et al.* 2000) and have predicted early death among breast cancer patients (Sephton *et al.* 2000).

In our investigation, measures of neuroendocrine function included daily salivary cortisol, overnight urinary adrenaline and noradrenaline, and, from fasting blood samples, dihydroepiandrosterone-sulphate (DHEA-S). Saliva samples were obtained three times a day over a period of 4 days. The first sample was collected in the morning after the respondent had been awake for 30 min, but before brushing teeth, drinking coffee or eating breakfast. The second sample was collected at midday before eating lunch, and the third sample in the evening before brushing teeth and going to bed. Analyses focused on the slope of salivary cortisol, averaged across the four days of assessment.

Table 1 presents bivariate correlations between three scales of eudaimonic well-being and two neuroendocrine measures. No significant effects were evident for hedonic well-being. Significant positive associations were found between average daily slope of salivary cortisol and personal growth for the aged 65+ sample. For the age 75+ sample, significant effects were obtained for both personal growth and purpose in life (despite the notable reduction in sample size). The direction of these effects is illustrated in figures 2 and 3. It should be noted that the figures do not display the actual slope of salivary cortisol, but rather the *association* between obtained slopes, averaged across 4 days, and the given scale of well-being. Average slope values range from those that were strongly negative, which corresponds to steeply downward slopes in cortisol from early morning through midday to evening, to values that were close to zero, which corresponds to nearly flat diurnal

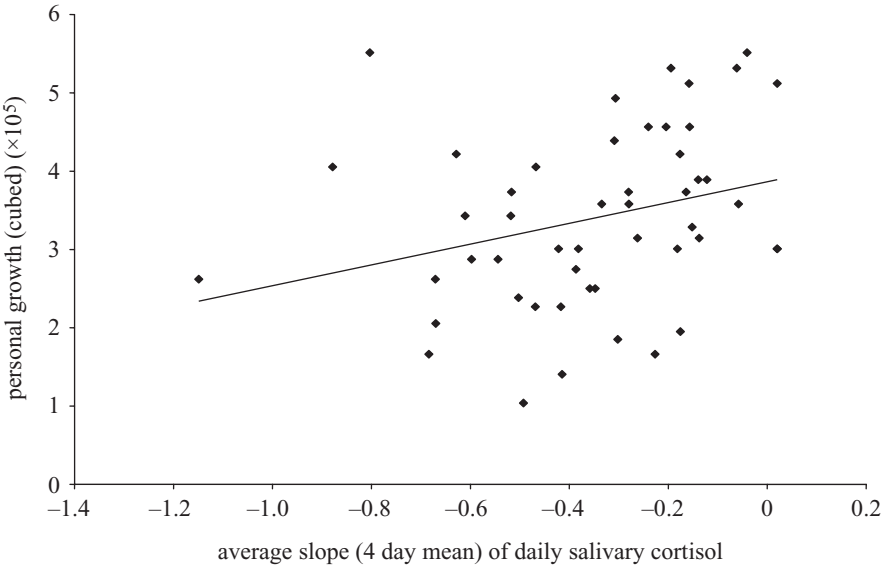

Figure 2. Relationship between average slope of daily salivary cortisol and personal growth (older women 75+, $n = 52$). Scores on well-being were cubed to obtain a symmetric distribution.

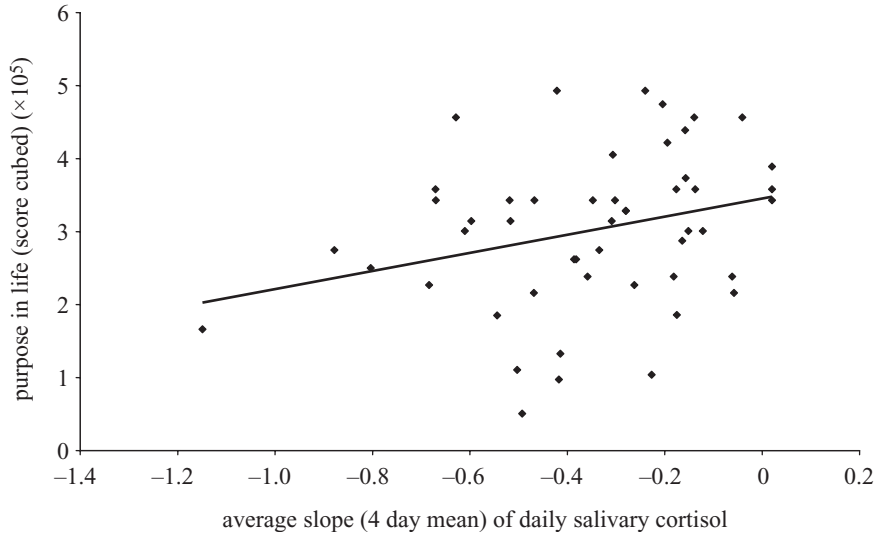

Figure 3. Relationship between average slope of daily salivary cortisol and purpose in life (older women 75+, $n = 52$). Scores on well-being were cubed to obtain a symmetric distribution.

slopes throughout the day. Well-being scores on the vertical axis were cubed to symmetrize the distributions. These patterns were examined with robust regression using least-trimmed squares (Rousseuw & Hubert 1996; Chau 2002), which detects outliers and performs least-squares regression on the remaining observations.

What both figures show is that older women with higher levels of personal growth and purpose in life had *flatter* daily slopes of salivary cortisol. That is, as values on well-being increased, average values on the slope of salivary cortisol moved from negative to near zero. Subsequent examination of means at the three diurnal points clarified that individuals with higher scores on purpose and growth started the day with *lower* levels of salivary cortisol and *stayed lower* through the day than individuals with lower scores on these two dimensions of eudaimonic well-being.

The only other significant outcome for neuroendocrine markers was the finding that women with higher scores on autonomy, which assessed the capacity to follow one's own convictions (even if they go against conventional wisdom), had significantly higher levels of noradrenaline than women reporting lower levels of autonomy.

(b) *Immune correlates*

Inflammatory response has increasingly been targeted as an integral part of the stress response (Black 2003). In addition, chronic inflammatory processes, characterized by the presence of certain cytokines, particularly IL-6, are implicated in diverse health outcomes (atherosclerosis, insulin resistance, type II diabetes, metabolic syndrome X) (Black 2003). The interplay between stress and hormonal signals (glucocorticoids) that terminate inflammation has also received attention (Miller *et al.* 2002). Our question was whether high well-being would be linked with *lower* levels of inflammatory cytokines. Table 1 also shows the significant bivariate association between reported levels of purpose in life and sIL-6r, measured from plasma. This effect, as predicted, is negative, showing that those with

Table 2. Pearson correlations between well-being and cardiovascular measures.
(Full sample $n = 135$.)

	eudaimonic[a]					hedonic
	positive relations	personal growth	purpose in life	environmental mastery	self-acceptance	MASQ positive
cardiovascular measures						
weight	-0.26^{**}	—	—	—	—	—
age 65 + ($n = 119$)	-0.21^{*}	—	—	—	—	—
waist–hip ratio[b]	-0.32^{***}	—	-0.17^{*}	—	—	—
age 65 + ($n = 119$)	-0.30^{***}	—	—	—	—	—
age 75 + ($n = 66$)	-0.29^{*}	—	—	—	—	—
HDL cholesterol	—	0.17^{*}	0.22^{**}	—	—	0.18^{*}
age 65 + ($n = 119$)	—	—	0.21^{*}	—	—	—
total/HDL cholesterol[c]	—	-0.16^{*}	—	—	—	—
age 65 + ($n = 119$)	—	-0.20^{*}	—	—	—	—
glycosylated HG	-0.21^{**}	—	—	—	—	—
age 65 + ($n = 119$)	-0.21^{*}	—	—	-0.20^{*}	-0.19^{*}	—

[a] Well-being scales are cubed to symmetrize distributions.
[b] Square root taken to symmetrize distributions.
[c] Natural log taken to symmetrize distributions.
$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

higher levels of life purpose had significantly lower levels of sIL-6r. When compared with the corresponding coefficients for hedonic well-being and sIL-6r, no significant differences were obtained.

(c) *Cardiovascular correlates*

Both neuroendocrine and inflammation markers have been studied as primary mediators of cardiovascular risk (Sapolsky *et al.* 2000). Table 2 presents bivariate correlations between scales of eudaimonic and hedonic well-being with cardiovascular measures. Numerous significant effects are evident for eudaimonic dimensions of well-being, with all effects being in the predicted direction: i.e. those with higher well-being had lower cardiovascular risk. One biomarker, HDL cholesterol, is considered good for health, and the associations with this measure were positive.

Specifically, scores on positive relations with others were negatively linked with weight, waist–hip ratio and glycosylated haemoglobin (a marker for diabetes). These effects were evident for the full sample and the 65+ sample. Among women aged 75+, those with good-quality relationships had significantly lower waist–hip ratios, even though the sample was reduced by nearly half. Personal growth was positively correlated with HDL, the good cholesterol, and negatively with the total to HDL cholesterol ratio (for the full sample and those aged 65+). Purpose in life was also positively correlated with HDL cholesterol (full sample and those aged 65+) and negatively with waist–hip ratio. Those with higher levels of environmental mastery and self-acceptance had significantly lower levels of glycosylated haemoglobin. Finally, the only effect obtained for positive affect was a positive association between HDL cholesterol and the MASQ version of positive affect.

(d) *Sleep correlates*

An important part of healthy functioning is to experience good quality sleep, which provides numerous restorative functions (e.g. Sejnowski & Destexhe 2000). Emerging data in both humans and animals suggest that circadian regulation may be an important prerequisite for the maintenance of host defences against cancer (Sephton & Spiegel 2003). Sleep has also been shown to play a mediating role in the link between socio-economic status and health (Moore *et al.* 2002), and among healthy older adults, those with longer sleep latencies and poorer sleep efficiency were at greater risk of death than those with shorter latencies and better sleep efficiency (Drew *et al.* 2003). In light of these findings, our question was whether high profiles of eudaimonic or hedonic well-being are conducive to good sleep patterns.

We investigated these associations using the Nightcap, which assesses basic parameters of sleep (Mamelak & Hobson 1989). The system consists of an eye sensor that monitors eyelid motion with a small strip taped to the eyelid. It is battery powered and relatively unobtrusive (it involves tying a kerchief around the head). Respondents were trained in the use of the Nightcap at the General Clinical Research Center and took it home to wear for four consecutive nights. The Nightcap provides indices of time awake, time in REM and non-REM sleep, body movements and sleep duration.

Table 3 presents bivariate correlations between measures of well-being and the scales derived from the Nightcap. Those with higher levels of environmental mastery (age 65+) had longer periods of time in bed, longer sleep duration, and longer REM sleep than those with lower levels of environmental mastery. For respondents aged 75+, those with higher environmental mastery also had earlier onset of REM sleep than those with lower levels of mastery. Also among the oldest women, those with higher levels of positive relations with others had longer REM sleep and lower duration of body moving during sleep.

(e) *Caveats: relationships with health status and depression*

The modest nature of effects described above, combined with the small sample size and cross-sectional design, do

Table 3. Pearson correlations between eudaimonic well-being and sleep.
(Full sample $n = 135$. Well-being scales cubed to symmetrize distributions.)

	eudaimonic		
	positive relationships	purpose in life	environmental mastery
sleep cap: mean total time in bed			
age 65 + ($n = 82$)	—	—	0.25*
sleep duration			
age 65 + ($n = 82$)	—	—	0.22*
body moving (min)			
age 75 + ($n = 43$)	−0.35*	−0.30*	—
1st REM onset			
age 75 + ($n = 43$)	—	—	−0.28*
REM sleep (min)			
age 65 + ($n = 82$)	—	—	0.19*
age 75 + ($n = 43$)	0.32*	—	—

* $p < 0.05$.

not warrant multivariate analyses. However, because other factors may bear on the findings, we include preliminary probes in two areas: health status and depression. Measured in terms of reported number of chronic conditions, health status revealed no significant links to eudaimonic or hedonic well-being. However, women with higher numbers of chronic conditions did have significantly higher weights ($r = 0.25$, $p < 0.01$), waist–hip ratios ($r = 0.30$, $p < 0.001$) and levels of glycosylated haemoglobin ($r = 0.31$, $p < 0.001$) and lower levels of DHEA-S ($r = -0.20$, $p < 0.05$). These findings underscore the need to build health into the formulation. Our implicit model construes health problems as the downstream *outcome* of biomarkers that are in zones of elevated risk, and in other longitudinal studies of ageing we have shown that higher allostatic load (which combines risk across multiple physiological systems) is a significant predictor of incident cardiovascular disease, decline in cognitive and physical function, and mortality (Seeman *et al.* 2001). Whether higher well-being might reduce the likelihood of these effects by helping keep diverse biomarkers in healthy zones is a key question for future research. Pursuing it, however, will require longitudinal investigations that simultaneously track well-being, biomarkers and health status in large samples.

Although our focus is on psychological well-being, mental maladjustment may also be implicated in the above associations with biomarkers. For example, depression has been linked with diverse medical conditions, and there is growing interest in the role of cortisol in understanding these effects (Brown *et al.* 2004). Major depression had been measured (using DSM-IV criteria) in prior waves of our longitudinal study. On the basis of such prior data, we identified 22 women in the biomarker sample ($n = 135$) who met criteria for major depression in one or more prior waves of longitudinal assessment. Although such data do not address current depressive status, they are nonetheless relevant given previously documented long-term relationships, both between prior life challenges (e.g. abuse) and subsequent pathophysiology of depression and anxiety, as well as between major depression and its distal consequences for the stress system (Meyer *et al.* 2001; Penza *et al.* 2002).

To probe whether the above cases showing a history of major depression might be responsible for 'carrying' the associations reported above, we partitioned the sample into those who had experienced depression and those who had not, and then re-ran all analyses. For women with no history of depression ($n = 113$), the majority of previous effects (75%) remained statistically significant; if significant trends were included, 89% of the previous effects were still evident. Alternatively, among women with prior episode(s) of major depression ($n = 22$), there were, with two exceptions, no significant associations between well-being and biomarkers. The small size of the depression sample could, of course, account for the lack of effects. However, the two significant associations that did occur pertained to a single eudaimonic measure (personal growth), which was correlated with two neuroendocrine factors. Among women with depression in their past, those with higher levels of personal growth had significantly lower levels of adrenaline ($r = -0.43$, $p < 0.05$) and significantly higher slopes of salivary cortisol ($r = 0.60$, $p < 0.01$). Because of the ongoing interest in links between depression and cortisol, we plotted the latter effect and found that the direction of the association was the same as that reported for the full sample (see figure 2): namely, those with higher levels of personal growth had *flatter* slopes of daily salivary cortisol. Investigation of means at each of the three timepoints (early morning, midday, evening) also paralleled the main sample findings (i.e. those with higher well-being started lower and stayed lower on salivary cortisol throughout the day). Viewed collectively, these preliminary probes offer little support that depression is a third variable accounting for the prior findings.

A related probe pertained to whether well-being and depression are best construed as opposite ends of a bipolar continuum, or are more appropriately seen as independent (orthogonal) domains of mental health assessment. We therefore conducted individual-level analyses of well-being profiles of the 22 women with a history of major depression. These analyses revealed three subtypes. The first ($n = 4$) fitted the bipolar conception—that is, their history of depression was accompanied by very low profiles of well-being, operationalized as being 1 or 2 standard deviations below the mean for the full sample, on the majority of

well-being scales. Another subtype ($n = 5$) consisted of women who could be characterized as resilient—that is, although they had previously experienced major depression, their current well-being scores were close to the mean for the full sample, or 1 standard deviation above it, on *all* scales. The largest subtype ($n = 12$), however, consisted of women whose scores on the majority of well-being scales were within 1 standard deviation of the mean for the full sample on the majority of well-being scales. Overall, such preliminary probes offer limited support for mental health conceived as a single continuum with depression at one pole and well-being at the other.

5. DISCUSSION AND FUTURE DIRECTIONS

Although the findings presented above have numerous limitations (small sample, cross-sectional design, bivariate analyses), they offer a first look at linkages between two prominent aspects of psychological well-being, eudaimonic and hedonic, and diverse biomarkers. The overall pattern of effects is clearly modest, but there are nonetheless consistencies in the data that call for further investigation.

With regard to neuroendocrine markers, older women with higher levels of purpose in life and personal growth showed flatter diurnal slopes of daily salivary cortisol than those with lower levels of such well-being. Specifically, those who were purposefully engaged in life and continued to experience self-development started the day with lower cortisol levels and stayed lower throughout the day than those with lower profiles of purpose and growth. Such findings converge with the work of Lindfors & Lundberg (2002), who used the same measures of eudaimonic well-being in a mixed age sample of men and women and found that those with high well-being had significantly lower salivary cortisol output than those with low well-being.

With regard to catecholamines, one positive association survived our screening criteria: higher levels of autonomy were associated with higher levels of noradrenaline. Because stress has been previously linked with increased levels of adrenaline and noradrenaline (e.g. Cacioppo *et al.* 1998), our finding underscores the need for future research to clarify distinctions between elevated levels of catecholamines that signify disregulation from those that may reflect normal healthy functioning. Population-level studies, particularly those that establish *normative distributions* on such biomarkers by age and gender, as well as that provide links to downstream health outcomes, are imperative to distinguish between healthy and unhealthy neuroendocrine activation.

Eudaimonic well-being (purpose in life) was also linked to pro-inflammatory cytokines, specifically, the soluble receptor for IL-6. Although there is growing interest in pro-inflammatory cytokines, emphasis to date has been exclusively focused on the negative—the role of psychological stress in activating the inflammatory response (e.g. Miller *et al.* 2002; Kunz-Ebrecht *et al.* 2003), with downstream consequences for multiple health outcomes, such as atherosclerosis, insulin resistance, type II diabetes and metabolic syndrome X (Black 2003). The present findings are the first, to our knowledge, to document that high purposeful engagement among older women is associated with lower levels of inflammation response. Such preliminary results call for further investigation with larger, more diverse samples as well as linkage to related processes, such as the glucocorticoid response, so as to elaborate possible protective mechanisms.

Eudaimonic well-being, particularly the dimensions of positive relations with others, personal growth and purpose in life, also revealed extensive links to cardiovascular markers, with all effects occurring in the predicted direction. Thus, older women with higher levels of eudaimonic well-being had lower levels of glycosylated haemoglobin, lower waist–hip ratios and lower total/HDL cholesterol ratios, and they weighed less than those with lower levels of eudaimonic well-being. Those with higher levels of personal growth and life purpose also had significantly higher levels of HDL, the good cholesterol, than those who reported less purposeful engagement and continued growth. Again, these findings extend prior literatures, which have documented not only that such cardiovascular markers are predictive of downstream coronary heart disease, diabetes and atherosclerosis (e.g. Badimon *et al.* 1992; Seeman *et al.* 1993; Corti *et al.* 1995; Feldman & Steptoe 2003), but also that psychosocial and socio-demographic factors (e.g. sense of control, coping, social support, socio-economic status) are linked with such biomarkers (e.g. Feldman & Steptoe 2003).

Sleep was a further area of assessment showing significant associations to multiple aspects of eudaimonic well-being. Women who reported higher levels of environmental mastery showed longer periods of sleep duration and time in bed as well as well as faster onset of REM sleep and longer duration REM sleep. Those with good-quality relationships and higher profiles of purpose also showed, but, only in women age 75+, less body movement during sleep. Such findings augment the literature documenting links between sleep and morbidity and mortality (Moore *et al.* 2002; Drew *et al.* 2003; Sephton & Spiegel 2003) but, importantly, point to possible psychosocial antecedents to good sleep. Of course, benefiting from the restorative functions of sleep (Sejnowski & Destexhe 2000) probably contributes to good-quality relationships, purposeful engagement and continued growth. Through time, such reciprocal relationships between well-being and sleep may be integral features of what helps keep the organism free from illness, disease and disability.

Had our study focused exclusively on the biology of hedonic well-being, only one significant effect would have been reported: HDL (the good) cholesterol was positively associated with positive affect as measured by the MASQ, which assesses happiness and the enjoyment of life. Why did hedonic well-being show so few connections to biology? One possibility is that most people report themselves to be happy (Diener & Diener 1996). Thus, there may be less variation in reports of positive affect, which in turn restricts the linkage that can be shown with biology. Another possibility is that positive affect may require different biomarkers, such as dopamine (Depue & Collins 1999*a*,*b*) or serotonin (Katz 1999), to show effects. The age of the sample may also be involved—some contend that there is a reduction in the basic processes of arousal and activation with ageing (Panksepp & Miller 1996), which may translate to more modulated profiles of affect intensity. All possibilities point to valuable directions for future research.

That eudaimonic and hedonic well-being may not have equivalent neurobiological correlates is further evident in

studies of well-being and neural circuitry. Substantial EEG studies indicate that the prefrontal cortex has asymmetric involvement in the experience of affect (Davidson 2000). Individuals with high and stable levels of left-sided greater than right-sided frontal activation report greater positive and lower negative affect compared with individuals showing a pattern of relative right-sided frontal activation. When such studies have included assessments of eudaimonic and hedonic well-being, both have been found to be linked with greater left than right superior frontal activity, but it is only for eudaimonic well-being that electroencepalogram asymmetry explains variance beyond that accounted for by approach-oriented positive affect (Urry *et al.* 2004). Going from the brain to immune function, higher left-sided relative to right-sided activation has also been associated with higher antibody response to an influenza vaccination challenge (Rosenkranz *et al.* 2003).

Several remaining issues merit consideration in building on these preliminary findings. An important question is whether well-being is merely the flip side of distress, depression and maladjustment. If so, probing the biological correlates of well-being may not be distinctive from large prior literatures documenting how negative psychological factors contribute to elevated risk across numerous systems (cardiovascular, neuroendocrine, immune). Our limited look at depressive profiles among the present respondents does not suggest this is the case. In other work, we have documented that there are substantial numbers of people who do not suffer from major depression, but who nonetheless lack high well-being (Singer *et al.* 1998). Those who study positive and negative affect have also invested extensive effort on the question of bipolarity (e.g. Bradburn 1969; Diener *et al.* 1995*b*; Russell & Carroll 1999), with considerable evidence confirming the functional separation of the two. Links to biomarkers will probably constitute critical evidence for establishing the independence or bipolarity of psychological well-being and ill-being. Flourishing and its attendant biology may, however, require an enriched array of biomarkers (e.g. endorphins, dopamine, opioid peptides, oxytocin (Ryff & Singer 1998; Taylor *et al.* 2003)).

A second issue pertains to the dimension of time and its role in understanding the biology of well-being. Broadly speaking, extant research on psychosocial factors and health adopts one of two temporal perspectives. There are longitudinal studies, in which time is long-term, and the emphasis is on cumulative, naturally unfolding processes. Our prior work has, for example, probed the connections between long-term social relational profiles and allostatic load, a measure of wear and tear on multiple physiological systems (Singer & Ryff 1999), showing that men and women with more positive relationship profiles from childhood to adulthood had a lower likelihood of having high allostatic load in adulthood. Alternatively, by contrast, there are short-term, mechanistic studies, in which variables (e.g. stress) are manipulated and the consequences for neuroendocrine or immune response, or both, are tracked with the goal of understanding how these systems communicate with each other (Sapolsky *et al.* 2000; Miller *et al.* 2002; Kunz-Ebrecht *et al.* 2003; Maier 2003; Maier & Watkins 2003).

These two levels of inquiry each contribute important advances, but the connections between them are frequently missing, such that mechanistic studies ignore naturally occurring trajectories of change in psychosocial and biological profiles with consequences for health, while longitudinal, epidemiological inquiries fail to clarify mechanistic processes. Both levels of inquiry are fundamental for advancing the positive health agenda, and ideal designs for bridging these levels of inquiry are those that *blend* both types of research.

A third issue pertains to research on resilience, which takes well-being into interesting territory where the focus is on those who maintain high well-being *in the face of adversity*. Defining resilience and how it arises (i.e. identifying relevant protective factors) is of increasing interest in the study of children and adults (Ryff & Singer 2002*b*). We have examined resilience in multiple life contexts: those who have maintained (or regained) high eudaimonic well-being in the face of major life challenges (e.g. relocation, caregiving) as well as those who sustain high eudaimonic well-being despite socio-economic disadvantage (Singer & Ryff 1999; Ryff *et al.* 2004) or ethnic/minority status (Ryff *et al.* 2003). What remains untested as yet is whether such high well-being vis-à-vis adversity is consequential for health. That is, does it confer protection against illness, disease and disability and, if so, what are the intervening mechanisms? These questions call for inquiries that connect profiles of well-being to biomarkers, but do so in contexts of high life challenge.

Finally, there is a pressing need to have measures of both eudaimonic and hedonic well-being incorporated in national-level health statistics across multiple countries. This practice would facilitate comparisons of statistics such as active life expectancy and expected number of disability-free life years between those with higher versus lower levels of well-being. We anticipate that the protective effects of high levels of well-being should be reflected in longer active life expectancy and disability-free life years. A movement in this direction was initiated by Statistics Canada 10 years ago (Stephens *et al.* 2000), but much more needs to be done if we are to have an international comparative picture of the protective effects of high well-being.

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GLOSSARY

HDL: high-density lipoprotein
IL: interleukin
MASQ: Mood and Anxiety Symptom Questionnaire
REM: rapid eye movement
sIL-6r: soluble receptor for interleukin 6