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The Interpersonally Sensitive Disposition and Health: An Integrative Review

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This article reviews studies that have examined the association between constructs related to interpersonal sensitivity (IS) and morbidity and mortality from major medical illnesses. We define IS as a stable trait characterized by ongoing concerns about negative social evaluation. This disposition makes people vigilant for as well as sensitive to others' evaluations of them. To avoid negative social evaluation, they adopt defensive behaviors such as submission and inhibition. Aspects of IS are captured by various constructs, including introversion, rejection sensitivity, social inhibition, social anxiety, and submissiveness. The review includes 76 long-term prospective studies across 4 outcome categories, namely, infectious disease, cancer, cardiovascular disease (CVD), and all-cause mortality. Three general conclusions are established. First, IS individuals are at increased risk of infectious diseases and possibly CVD, but not cancer and not all-cause mortality. Second, the positive studies provide evidence that IS temporally precedes disease, and go a long way toward ruling out the most plausible alternative explanations based on confounders, supporting a tentative causal interpretation of the data. However, unmeasured potential confounders make it impossible to be certain about whether IS drives the effects on mortality and morbidity. Third, the effects of introversion are accentuated and may only become apparent in contexts that activate social-evaluative concerns (e.g., exposure to early life residential mobility, living with the stigma of human immunodeficiency virus). Findings are discussed in regard to potential psychosocial and psychobiological mechanisms as well as implications for future work concerning IS and health.

Keywords: personality, interpersonal sensitivity, introversion, morbidity, mortality

Decades ago, the interpersonal theorist Karen Horney referred to social stress as “basic anxiety,” or the threat of being alone and isolated in a world conceived as potentially hostile (Horney, 1937). She viewed this anxiety as underlying a profound sensitivity to “any rejection or rebuff, however slight” (p. 135). These types of concerns have long been thought to compromise the subjective and interpersonal wellbeing of those who experience them persistently (Bowlby, 1969; Erikson, 1950; Horney, 1937; Sullivan, 1953; also see Downey & Feldman, 1996; Downey, Freitas, Michealis, & Khouri, 1998). But in recent studies it has become clear that such concerns, particularly when they are dispositional, may have even further consequences, and play a role in compromising certain aspects of physical health. In this regard a handful of studies have converged upon the provocative finding that individuals high in what we call interpersonal sensitivity (IS) are at increased risk for

acquiring major diseases and dying from them more rapidly than would be expected. For instance, one study showed that introverts developed significantly worse symptoms compared to extraverts following exposure to a virus that causes a common cold (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997). Another study showed that sensitivity to rejection was associated with accelerated progression of human immunodeficiency virus (HIV) infection (Cole, Kemeny, & Taylor, 1997). In fact, men at the 75th percentile on rejection sensitivity experienced HIV-related mortality approximately 2 years earlier than their counterparts at the 25th percentile. In another study, social avoidance emerged as a risk factor for long-term death from cardiovascular disease (CVD; Berry, Lloyd-Jones, Garside, Wang, & Greenland, 2007), and in yet another, concealing one's sexual identity from others was associated with a higher incidence of cancer over a 5-year period (Cole, Kemeny, Taylor, & Visscher, 1996).

Of course, not all studies have found links between IS and health outcomes, and even for the ones that have there is uncertainty about interpretation. Specifically, while the results of these studies are consistent with the hypothesis that IS is causing disease to develop or progress more quickly, it is equally plausible that in some cases emerging disease is driving changes in social behavior, or that both are being influenced by a common underlying process, like genetic liabilities or prenatal complications. In addition, the question remains of whether we should be treating studies on introversion, rejection sensitivity, and social avoidance as evidence of the same phenomenon, as these constructs tap somewhat unique aspects of interpersonal behavior. Finally, even if there is a

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—SPH

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link between IS and health, it is unclear whether there are plausible mechanistic explanations for how it could arise.

The goal of this review is to deal with these issues by addressing three specific questions: (a) Are IS individuals at risk for adverse health outcomes? (b) If so, what's the nature of this association—is IS causing disease, is disease causing IS, or do both arise out some common underlying process? (c) Do the various measures that tap elements of IS capture the same underlying construct, or is there a health-relevant core that's common to each of them? As a secondary goal, we also speculate about biobehavioral mechanisms that might underlie any connection of IS to health.

Conceptualization of Dispositional IS

We define IS as a stable trait characterized by ongoing concerns about negative social evaluation. This disposition makes people vigilant for as well as sensitive to others' evaluations of them. To avoid negative social evaluation, they adopt defensive behaviors like submission and inhibition. This conceptualization follows closely the suite of motivational, cognitive, and behavioral changes that Dickerson and Kemeny (2004) hypothesized occur when people encounter social-evaluative threats. Whereas their analysis focused on how these responses play out in acutely threatening situations, we suggest that some individuals have a dispositional tendency to experience the same kinds of evaluative concerns and ensuing cognitions, emotions, and behaviors. Elements of this disposition overlap with a number of other individual difference variables that have been studied in relation to physical health, including introversion, submissiveness, social inhibition, rejection sensitivity, social avoidance, social anxiety, and Type D personality. A number of these elements are also considered in research guided by the interpersonal approach to health (Newton, 2009; T. W. Smith, Glazer, Ruiz, & Gallo, 2004). Thus, our goal here is not to introduce a new personality construct. It's simply to ask whether a large amount of previously disparate research might be parsimoniously synthesized under the common rubric of IS.

Table 1 provides a summary of the concepts that we believe capture elements of IS. We argue that each of these concepts taps a part of the IS construct, though a somewhat unique one and often in an imperfect manner. This is most clear when IS is broken into cognitive/affective (vigilance for and sensitivity to negative social evaluations) and behavioral components (defensive postures like submission and inhibition that are intended to minimize such evaluations). When viewed in this light the cognitive/affective component of IS reflects the rejection sensitivity inherent in Downey's conceptualization. According to her definition, people who are sensitive to social rejection tend to anxiously expect, readily perceive, and overreact to it (Downey, Feldman, Khuri, & Friedman, 1994; Feldman & Downey, 1994). In contrast, the behavioral component of IS reflects submission, inhibition, and avoidance, concepts that are captured by other indicators we reviewed above. See Figure 1 for an illustration of how the various concepts considered in the health literature map onto our thinking about IS.

The distinction between cognitive/affective and behavioral components of IS is conceptually important for at least two reasons. First, it may help elucidate whether certain aspects of IS are especially influential for health, and second, it can potentially shed light on underlying mechanisms. Thus, in the review we differentiate studies according to the elements of IS that their instruments focus upon. We also differentiate studies along motivational lines, emphasizing how different goals may underlie the interpersonal tendencies captured by various constructs. For example, introversion is characterized by low thresholds for arousal, and as a result, the avoidance of situations and activities that involve strong stimulation (Strelau & Eysenck, 1987). Thus, introversion can be thought of as a preferred way of negotiating the social world—sometimes it is motivated by social evaluative concern and other times it is not. In contrast, the avoidant behavior associated with shyness, social avoidance, and social anxiety is driven mainly by fear (e.g., of strangers, of negative evaluation). Accordingly, both an introverted person and a socially anxious person are likely to endorse the item "I prefer to do things alone" (Costa &

Table 1
IS Constructs and Core Features

| IS constructs | Core features |
|-------------------------------------|---|
| Rejection sensitivity | The tendency to anxiously expect, readily perceive, and overreact to social rejection (Downey et al., 1994; Feldman & Downey, 1994). |
| Social anxiety and avoidance | A condition characterized by extreme discomfort upon exposure of possible scrutiny of unfamiliar people. This can lead to avoidance of anxiety-provoking situations. |
| Social and psychological inhibition | A failure to publicly express any subjectively significant private experience, including, but not limited to, emotional, social, and behavioral impulses (Cole, Kemeny, Taylor, & Visscher, 1996). |
| Behavioral inhibition | A quiet, vigilant, and affectively subdued response to unfamiliar situations, especially unfamiliar people. |
| Shyness | The behaviorally inhibited temperament is usually described in young children (G. A. Kaplan et al., 1994). An emotional-behavioral syndrome characterized by social anxiety and interpersonal inhibition and avoidance (M. R. Leary, 1986). |
| Submissiveness | The tendency to stay in the background and to let others lead and dominate. |
| Introversion–extraversion | One of the "Big Five" characteristics thought to represent the basic structure of personality. Reflects a person's preferences for social situations (McCrae & Costa, 1997). |
| Type D | The interaction of negative affectivity and social inhibition. Negative affectivity denotes the tendency to experience increased negative distress across time and situations. Social inhibition refers to the tendency to inhibit the expression of these negative emotions in social interactions (Denollet, 1998, 2005). |

Note. IS = interpersonal sensitivity.

| Overarching Construct | Interpersonal Sensitivity | | | |
|--|---------------------------|--------------|---------------------------|---|
| IS Components | Motivational | | Cognitive/Affective | Behavioral |
| | Fear | Preference | | |
| Constructs that Reflect Elements of IS | Social anxiety Shyness | Introversion | Rejection sensitivity | Inhibition Submissiveness Avoidance |
| | | | Shyness Social Anxiety | |

Figure 1. This figure illustrates that interpersonal sensitivity (IS) is a multidimensional construct, with motivational, cognitive/affective, and behavioral components. The lower order constructs that we examine in the review (e.g., rejection sensitivity and avoidance) each capture one or more component(s) of IS. For example, rejection sensitivity captures IS cognitions and affective states, whereas inhibition captures IS behaviors. Moreover, shyness and social anxiety capture all of the IS components, including the motivational state of fear.

McCrae, 1992b), yet the introvert is not necessarily motivated by social fear. Thus, there are important motivational distinctions between these constructs, which may have implications for their relationship to health.

Constructs That Capture Elements of IS Concepts

As noted, the literature on health has considered a number of constructs that capture elements of IS (see Tables 2, 3, 4, and 5 for details of how these constructs were measured in various studies). Probably the closest approximation to our conceptualization is Downey’s construct of *rejection sensitivity*, which is defined as the extent to which people perceive negative social evaluations as either likely or important (Cole et al., 1997). Also relevant here are studies of *social anxiety and social avoidance*. Social anxiety is a condition characterized by extreme discomfort upon exposure to possible scrutiny by unfamiliar people. When this discomfort leads to avoidance of the anxiety-provoking situations and interferes with role fulfillment, it can merit a psychiatric diagnosis of social anxiety or social phobia (American Psychiatric Association, 2000). However, in all of the studies we review, these traits are conceived of and measured in a dimension manner. As noted, IS has behavioral manifestations, which can include *social and psychological inhibition*, defined as the failure to publicly express a subjectively significant experience, including, but not limited to, emotional, social, and behavioral impulses (Cole, Kemeny, Taylor, & Visser, 1996). A related phenomenon at the trait level is *shyness*, conceived of as an emotional-behavioral syndrome characterized by social anxiety and interpersonal inhibition and avoidance (M. R. Leary, 1986). In children, a syndrome called *behavioral inhibition* is characterized by a quiet, vigilant, and affectively subdued response to unfamiliar situations, especially unfamiliar people (Kagan, Reznick, & Snidman, 1988). By our conceptualization, people high in IS also tend to be characterized by *submissiveness*, a tendency to stay in the background and to let others lead and dominate. They do so to avoid conflict, rejection, and other forms of negative social encounters.

Another concept in the health literature with potential relevance to IS is *introversion-extraversion*, a broad domain included in the

Five-Factor Model of personality advocated by Costa and McCrae, which reflects a person’s preference for social situations (Costa & McCrae, 1992a; McCrae & Costa, 1997). As noted, introverts have low arousal thresholds, which motivates them to avoid highly stimulating situations, which in most cases are social in nature (Strelau & Eysenck, 1987). For some introverts, these socially avoidant behaviors are also motivated by the kinds of evaluative concerns that form the core of IS. However, these concerns don’t underlie all, or probably even most, instances of behavior that would be characterized as introversion. As we will see, this ambiguity about motivation makes it challenging to interpret the literature on introversion with respect to IS.

A final concept in the health literature with relevance to IS is the *Type D personality*. Type D personality is defined by the interaction between social inhibition (the tendency to inhibit the expression of emotion and behavior in social situations) and negative affectivity (depression, anxiety, irritability; Pedersen & Denollet, 2003), but we included it in the review because of the social inhibition component. The fact that Type D captures both distress and social inhibition distinguishes it from the other constructs we review and also complicates interpretation of the literature vis a vis IS.

Evidence for Validity of the IS Construct

There is preliminary evidence for the construct validity of IS. Much of it derives from research on the Interpersonal Circumplex,

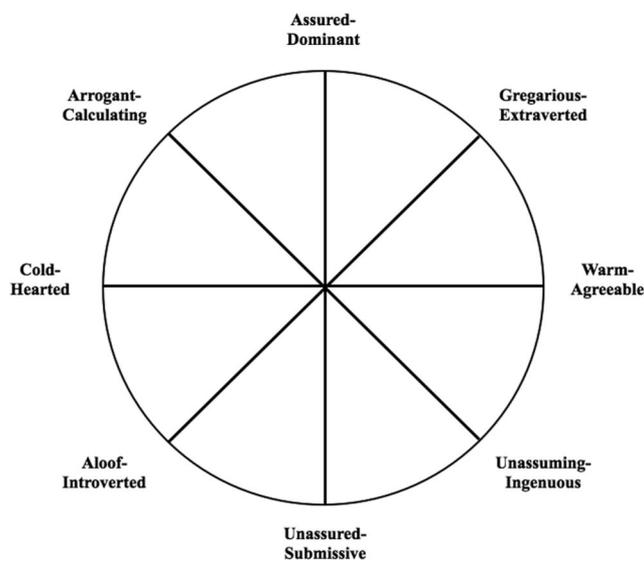


Figure 2. This figure shows the circumplex structure of the Revised Interpersonal Adjective Scale (Wiggins, Trapnell, & Phillips, 1988). According to interpersonal theory, two primary dimensions underlie most aspects of interpersonal behavior—status, agency, or instrumentality (i.e., the vertical dimension) and love, warmth, or communion (i.e., the horizontal dimension). Research evidence indicates that constructs that capture elements of interpersonal sensitivity are placed between the scales Unassured-Submissive and Aloof-Introverted (Brookings et al., 2003). Adapted from “Psychometric and Geometric Characteristics of the Revised Interpersonal Adjective Scales (IAS-R),” by J. S. Wiggins, P. Trapnell, and N. Phillips, 1988, *Multivariate Behavioral Research*, 23, Figure 1, p. 518. Copyright 1988 by Psychology Press.

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Table 2
IS and Infectious Disease

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|---|---|--|
| 1 | (Cole et al., 2003) Social inhibition Composite measure of introversion, social avoidance, and emotional inexpression | $N = 54$ 26–55 years | Morbidity HIV-positive gay men with no history of AIDS Time since seroconversion ranged from 7 to 158 months Median CD4 level of 558 cells/mm ³ | Baseline viral load set points (+) Plasma viral load suppression following initiation of highly active antiretroviral therapy (HAART) (+) Recovery of CD4+ T cell level following HAART (–) | Follow-up of 12–18 months. Social inhibition was a risk factor for enhanced viral pathogenesis. Covariates for viral load set point and viral load suppression analyses: Results remained statistically significant after controlling for depression, anxiety, and generalized negative affectivity. Similar findings emerged in analyses controlling for demographic characteristics, duration of infection, prior antiretroviral treatment, health-relevant behaviors, and high-risk sexual activity. Covariates for recovery of CD4+ T cell level: Results remained significant after controlling for baseline CD4+ T cell level, prior reverse transcriptase inhibitor monotherapy, and duration of HAART. |
| 2 | (Ironson et al., 2008) Introversion NEO-PI–R | $N = 104$ 38 ± 8.5 years | Morbidity HIV-positive patients with no history of AIDS (68% male) Participants had CD4 counts between 150 and 500 at study entry ($M = 291 \pm 99$) | Viral load slope (+) CD4 cell slope (+) | 4-year follow-up. Introversion was associated with faster disease progression. Findings were independent of antiretroviral medication, initial disease status (CD4 or viral load), race, gender, age, and education level. |
| 3 | (Thornton et al., 2000) Introversion Eysenck Personality Questionnaire | $N = 143$ 40 ± 8 years | Morbidity Long-term HIV-positive homosexual or bisexual men with no history of AIDS or AIDS-related complex (ARC) Median of 8.6 years of infection, mean CD4 count of 455 ± 285 cells/mm ³ | Time to CD4 count < $200 \times 10^6/l$ (0) Time to AIDS-related complex diagnosis (0) AIDS diagnosis (0) | Follow-up of 5–30 months, 45 participants diagnosed with ARC or AIDS. Introversion was unrelated to HIV progression. |
| 4 | (Cole, Kemeny, Taylor, Visscher, & Fahey, 1996) Psychological inhibition Participants rated the extent to which they were “in the closet” | $N = 80$ 23–50 years | Survival/morbidity Initially healthy HIV-positive gay men Participants had normal CD4 levels at study entry (median = 686 cells/mm ³), indicating that they were in the earliest stage of infection | Time to 15% CD4 T lymphocyte level (+) Time to AIDS diagnosis (+) Time to HIV-related mortality (+) | Over the course of the 9-year follow-up, 34% of the sample received an AIDS-related diagnosis, and 26% died of an AIDS-related disorder. HIV progression advanced more rapidly to the degree participants concealed their homosexual identity. <i>(table continues)</i> |

Table 2 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|--|--|--|
| 5 | (Cole et al., 1997) Rejection sensitivity (stranger-public) The focus was on rejection sensitivity in the context of homosexual identity management | $N = 72$ Over 18 years | Survival/morbidity Initially healthy HIV-positive gay men | Main effects Time to 15% CD4 T lymphocyte level (+) Time to AIDS diagnosis (+) Time to HIV-related mortality (+) Interaction with concealment Time to 15% CD4 T lymphocyte level (+) Time to AIDS diagnosis (+) Time to HIV-related mortality (+) | Findings controlled for age, CD4 level at study entry, antiretroviral use, sexual practices, and health behaviors. An analysis of potential mediators indicated that the accelerated course of HIV infection in closeted participants could not be attributed to differences in anxiety, depression, social support, repressive coping style, primary partner status, or anonymous sexual contact. 9-year follow-up. Increased rejection sensitivity associated with increased accelerations in HIV progression. The interaction revealed that the effect of rejection sensitivity was evident among gay men who were "out of the closet," but not among those who concealed their homosexual identity. Coefficients adjusted for age, CD4T lymphocyte level at study entry, rates of unprotected anal-receptive intercourse, aerobic and anaerobic exercise, sleep disruption, smoking, heavy alcohol consumption, and use of drugs. |
| 6 | (Cole, Kemeny, Taylor, & Visscher, 1996) Psychological inhibition Participants rated the extent to which they were "in the closet" | $N = 222$ Over 18 years | Prospective Homosexual and bisexual males | Incidence of infectious diseases (pneumonia, bronchitis, sinusitis, tuberculosis) (+) | There were 39 cases of infectious disease over the course of the 5-year follow-up. Concealment of homosexual identity associated with a higher incidence of infectious disease. Results remain significant after controlling for demographic characteristics, health-relevant behavioral patterns, depression, anxiety, NA, repressive coping, and social desirability response bias. <i>(table continues)</i> |

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Table 2 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|--|--|--|
| 7 | (Totman et al., 1980) Introversion Eysenck Personality Inventory | $N = 52$ 18–49 years | Quasi-experimental Inoculation with 2 rhinoviruses Healthy adults (33% male) | Clinician symptom ratings of upper respiratory tract infection (+) Virus shedding (+) | Introverts developed worse symptoms and infections compared to extroverts. Analyses control for the effect of pre-experimental antibody level. And, the findings were independent of Totman et al.'s Change Index (which measures life events that involve change in a person's general level of activity). |
| 8 | (Broadbent et al., 1984) Introversion Eysenck Personality Questionnaire | $N = 173$ Not reported | Quasi-experimental Inoculation with rhinovirus or influenza virus Unspecified sample | Clinician symptom ratings of upper respiratory tract infection (0) Virus shedding (rhinovirus) (+) | Higher degree of rhinovirus in introverts compared to extroverts, but only among participants with high existing antibodies. No effects among participants who received influenza virus. No effect of introversion on clinical score. Covariates are unclear. |
| 9 | (Cohen et al., 1997) Introversion Goldberg's Adjective Scale | $N = 276$ 18–55 years | Quasi-experimental Inoculation with 1 of 2 rhinoviruses Healthy adults (45% male) | Incidence of colds (infected and met illness criteria) (+) | Participants higher on introversion showed increased susceptibility to colds. Findings adjusted for prechallenge antibody titer, age, body mass index, time of year, race, sex, viral type, and education level. |

Note. Studies 4 and 5 were based on the same sample. The results from Study 6 are presented in both the infectious disease and cancer tables. IS = interpersonal sensitivity; ID = identification; CD4 = cluster of differentiation 4; NEO-PI-R = NEO Personality Inventory—Revised; (+) = positive association; (–) = negative association; (0) = no association; NA = negative affectivity.

a well-validated model of interpersonal behavior (Kiesler, 1991). The circumplex is defined by two orthogonal axes (status, agency or instrumentality (i.e., the vertical dimension) and love, warmth, or communion (i.e., the horizontal dimension)), and the space in the circumplex reflects various blends of the two axial dimensions (see Figure 2). These dimensions are thought to underlie most aspects of interpersonal behavior (e.g., T. F. Leary, 1957; Wiggins, 1979). Thus, the circumplex provides a framework (or nomological net; Cronbach & Meehl, 1955) for comparing, contrasting, and integrating personality traits (Gurtman, 1992), and it can reveal subtle nuances in the content of interpersonal scales (Brookings, Zembar, & Hochstetler, 2003). The utility of this framework for understanding how social behavior relates to health outcomes has been demonstrated in studies of heart disease risk (see T. W. Smith et al., 2004; T. W. Smith, Traupman, Uchino, & Berg, 2010).

The Circumplex has been used to examine the psychometric properties of concepts that capture elements of IS. For example, in a recent study, the Circumplex was used to map scores on the Rejection Sensitivity Questionnaire (RSQ; Downey & Feldman, 1996) in relation to other interpersonal constructs and measures (Brookings et al., 2003). The RSQ presents hypothetical situations

(e.g., You ask your parents to come to an occasion important to you) and asks respondents to rate (a) degree of anxiety and concern about the outcome, and (b) expectations of acceptance or rejection. Results indicated that the RSQ is placed between the octant scales Unassured-Submissive and Aloof-Introverted, and it is located closer interpersonally to Autonomy compared to Sociotropy, indicating that rejection sensitive persons are more likely to avoid rejection by “keeping a safe distance” from others (autonomy) rather than by seeking intimacy with them (sociotropy). Other personality constructs with similar angular placements include measures of social avoidance and distress, trait anxiety, generalized discomfort, emotionality/fear and nonassertion (Wiggins & Broughton, 1991). Taken together, these findings suggest that the constructs we review here as reflections of dispositional IS cluster in the same region of the Interpersonal Circumplex and are characterized by introversion, submissiveness, and social avoidance.

Further evidence for treating the concepts reviewed here as reflections of an underlying IS disposition comes from dozens of studies showing associations among them (e.g., Bienvenu et al., 2004; Brookings et al., 2003; Cole, Kemeny, Fahey, Zack, & Naliboff, 2003; Collins, Westra, Dozois, & Stewart, 2005;

Table 3
IS and Cancer

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/ sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|--|---|--|
| 10 | (Kavan et al., 1995) Social anxiety Social introversion MMPI basic scale The factors were based on a 21-factor solution developed and validated by Johnson et al. (1984) | Cancer patients: $n = 61$ (diagnosed between 1977 and 1988) Noncancer: $n = 61$ (matched on age and education) Age not reported | Prospective (nested case-control) Male veterans who completed the MMPI between 1947 and 1975 | Incident colon cancer (0) | Average follow-up of 20 years. Social anxiety did not discriminate the colon cancer group from controls. |
| 11 | (Dattore et al., 1980) Social anxiety Social introversion MMPI basic scale | Cancer patients: $n = 75$, mean age of 64 years Noncancer patients: $n = 125$, mean age of 53 years | Prospective (nested case-control) Male veterans who had entered the Leavenworth, Kansas, Veterans Affairs Hospital Premorbid MMPI scores for persons with and without cancer | Incident cancer (0) | Median of 4.6 years between administration of MMPI and first noted diagnosis in cancer group. Social anxiety did not discriminate cancer patients from controls. |
| 6 | (Cole, Kemeny, Taylor, & Visscher, 1996) Psychological inhibition Participants rated the extent to which they were "in the closet" | $N = 222$ Over 18 years | Prospective Homosexual and bisexual males | Cancer onset (+) | 20 events were observed over the 5-year follow-up. Concealment of homosexual identity was associated with a higher incidence of cancer. Results remain significant after controlling for demographic characteristics, health-relevant behavioral patterns, depression, anxiety, NA, repressive coping, and social desirability response bias. |
| 12 | (Persky et al., 1987) Submission and shyness Cattell's 16 personality factors Social anxiety Social introversion MMPI basic scale | $N = 2,018$ 40–55 years | Prospective Initially healthy men employed at the Western Electric Company's Hawthorne Works | Cancer incidence (0) Cancer death (0) | There were 212 cancer diagnoses and 123 cancer deaths over the 20-year follow-up. Submission, shyness, and social anxiety were unrelated to cancer morbidity and mortality. |
| 13 | (Schapiro et al., 2001) Introversion Eysenck Personality Inventory | $N = 1,031$ Population representative of the age group 40 years in Copenhagen County | Prospective Danish citizens born in 1936 Population-based | Cancer incidence (0) | Over the 20-year follow-up, 113 malignancies were observed. There was no association between introversion and cancer incidence. |
| 14 | (Nakaya et al., 2006) Introversion Eysenck Personality Inventory | $N = 1,020$ Population representative of the age group 40 years in Copenhagen County | Prospective Population-based Danish citizens born in 1936 189 cancer cases identified in Danish Cancer Registry (34% male) | All-cause mortality (0) Cancer-related death (0) | Participants were followed for an average of 6 years from cancer diagnosis. There were 82 deaths from all causes, 84% cancer related. Introversion was unrelated to cancer survival. |

(table continues)

Table 3 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/ sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|--|---|--|
| 15 | (Nakaya et al., 2003) Introversion Japanese version of the Eysenck Personality Inventory-Revised | $N = 30,277$ 40–64 years | Prospective Population-based, residents of rural northern Japan | Incident cancer (0) | There were 986 incident cases of cancer over the 7-year follow-up. Introversion was unrelated to cancer incidence. |
| 16 | (Nakaya, Tsubono, Nishino, et al., 2005) Introversion Japanese version of the Eysenck Personality Inventory-Revised | $N = 41,442$ 40–64 years | Prospective Population-based, residents of Japan 890 cases of cancer identified in first 7 years (57% male) Exclusion of subjects with cancer in first 3 years of follow-up | Mortality among cancer patients (0) | Participants were followed for an average of 3.7 years from cancer diagnosis. There were 356 deaths. Introversion was unrelated to mortality. |
| 17 | (Nakaya et al., 2010) Introversion Eysenck Personality Inventory | $N = 59,548$ | Prospective, population-based cohort study involving Swedish and Finnish participants 51% female in Finnish cohort, and 52% female in Swedish cohort | Cancer risk (0) Cancer survival (0) | Over a maximum of 30 years follow-up there were 4,631 cancer cases identified in Sweden and Finland. For cancer survival analysis, only the Finnish data were used (2,733 cancer cases and then 1,548 deaths). Introversion was not associated with cancer risk at all sites; however, introversion emerged as a protective factor for risk of lung cancer. Introversion was not associated with death after cancers at all sites or at specific cancer sites. |
| 18 | (Lillberg et al., 2002) Introversion Eysenck Personality Inventory | $N = 12,009$ Over 18 years | Prospective Women in the Finnish Twin Cohort Study Population-based | Development of breast cancer (0) | 253 cases of breast cancer were identified over 20-year follow-up. Introversion was not a significant predictor of breast cancer risk. |
| 19 | (Hansen et al., 2005) Introversion Eysenck Personality Inventory | $N = 29,595$ 15–48 years | Prospective Population-based Swedish Twin Registry | Cancer onset (0) | There were 1,898 incidents of cancer over the mean follow-up of 25 years. Introversion was unrelated to cancer onset. |
| 20 | (Hislop et al., 1987) Introversion Eysenck Personality Inventory | $N = 133$ <55 years | Survival/morbidity Women who had been recently diagnosed with breast cancer (90% of the baseline questionnaires were completed within 3 months of diagnosis) | Risk of death from all causes (+) Disease recurrence (0) | There were 26 deaths (25 attributed to breast cancer) and 38 disease recurrences over the 4-year follow-up. Introversion was associated with increased risk of death over the course of the follow-up. Results controlled for age, clinical stage, pathologic nodal status, histologic grade of tumor, and estrogen receptor status. Findings were independent of expressive activities, anger, and cognitive disturbances. |

(table continues)

Table 3 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/ sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|---|--|---|
| 21 | (Ratcliffe et al., 1995) Introversion Eysenck Personality Inventory | $N = 63$ 19–73 years | Survival Patients with Hodgkin's disease and non-Hodgkin's lymphoma (56% male) | All-cause mortality (0) | There were 27 deaths over the 5-year follow-up. Introversion was unrelated to mortality. |
| 22 | (Greer et al., 1979) Introversion Eysenck Personality Inventory | $N = 69$ <70 years | Survival/morbidity Women who had been diagnosed with breast cancer 3 months earlier | Metastatic disease alive or dead (0) | Over the course of the 5-year follow-up, there were 16 patients with metastases, and 18 had died. Introversion was unrelated to metastatic disease. |
| 23 | (Aarstad et al., 2002) Introversion Eysenck Personality Inventory | $N = 78$ 59.4 ± 1.3 years | Survival Male patients with newly diagnosed head and neck squamous cell carcinoma (HNCSS) and controls with benign head and neck disease | HNCSS survival (0) | There were 24 HNCSS deaths over the average follow-up time of 5.6 years. Introversion was unrelated to survival. |
| 24 | (Dean & Surtees, 1989) Introversion Eysenck Personality Inventory | $N = 121$ 20–60 years | Survival/morbidity Women with early primary operable breast cancer Personality inventory administered 3 months after operation | Death from all causes (0) Recurrence (0) | Over the 6–8 year follow-up, there were 37 recurrences and 22 deaths from all causes (21 from breast cancer). Introversion was unrelated to cancer morbidity and mortality. |
| 25 | (Canada et al., 2005) Introversion Eysenck Personality Questionnaire | $N = 60$ 21–70 years | Survival/morbidity Patients with Stage 1 malignant melanoma assessed shortly after surgery | Rate of cancer death (0) Rate of recurrence (0) | Over the 10-year follow-up, there were 19 recurrences and 15 deaths. Introversion unrelated to cancer mortality and recurrence. |
| 26 | (Denollet, 1998) Type D The Trait Anxiety Scale and the Social Inhibition Scale of the HPPQ | $N = 246$ 31–79 years | Survival/morbidity Men who had been diagnosed with coronary heart disease | Rate of cancer diagnosis (+) Rate of cancer death (+) | Over the 6–10 year follow-up, 12 patients were diagnosed with cancer (9 cancer deaths and 3 cancer cases who were still alive). Type D personality was a significant prognostic factor for cancer morbidity and mortality in men with established CHD. Age ≥ 56 years, poor exercise tolerance, and pessimism were identified as independent predictors of cancer development. When Type D was added to the model, the final variables included Type D and age ≥ 56 . |
| 27 | (Stavraky et al., 1988) Submission Cattell's 16 personality factors | $N = 224$ (75% male) 44% > 60 years | Survival Newly diagnosed lung cancer patients | Lung cancer mortality (0) | There were 137 deaths over the 1-year follow-up. Submissiveness was unrelated to lung cancer mortality, yet the "reserved" factor emerged as a significant predictor. |

Note. There was sample overlap between Studies 13 and 14 and between Studies 15 and 16. The participants in Study 26 represent a subsample from the cohort described in Study 40 (see Table 4). The results from Study 6 are presented in both the infectious disease and cancer tables. IS = interpersonal sensitivity; ID = identification; (+) = positive association; (–) = negative association; (0) = no association; MMPI = Minnesota Multiphasic Personality Inventory; NA = negative affectivity; HPPQ = Heart Patients Psychological Questionnaire; CHD = coronary heart disease.

Table 4
IS and Cardiovascular Disease

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|--|---|--|
| 28 | (Räikkönen et al., 2001) Social anxiety The Social Anxiety subscale of the Self-Consciousness Scale | $N = 541$ 42–50 years | Prospective Healthy normotensive middle-aged women | Incident hypertension (+) | Average of 9.2 years of follow-up, during which time 75 women became hypertensive. The effect remained significant after controlling for BMI, but became nonsignificant after adjustments for SBP and family history of hypertension. |
| 29 | (Shen et al., 2008) Social anxiety Social introversion MMPI basic scale | $N = 735$ ≈45–75 years | Prospective Older men without a history of coronary disease or diabetes from the Normative Aging Study | MI (+) | There were 75 MIs (fatal and non-fatal) over the average follow-up of 12.4 years. Increased social anxiety associated with increased risk of MI. Association remained significant after controlling for age, education, marital status, fasting glucose, body mass index, high-density lipoprotein cholesterol, and systolic blood pressure. The relationships remained significant after further adjustment for health behaviors, medications for hypertension, high cholesterol, and diabetes during follow-up and psychological variables, including depression, Type A behavior, hostility, anger, and negative emotion. |
| 30 | (Berry et al., 2007) Social avoidance Subscale of the Cook–Medley Hostility Scale | $N = 2,107$ 40–55 years | Prospective Males free of baseline CVD in the Western Electric Study | CHD mortality (+) CVD mortality (+) Non-CVD mortality (0) | There were 404 CHD deaths, 541 CVD deaths, and 412 non-CVD deaths over the 30-year follow-up. Social avoidance was associated with CHD and CVD. Findings remained significant after controlling for traditional risk factors and other Cook–Medley scales (hostile affect, aggressive responding, and cynicism). |
| 31 | (Whiteman et al., 1997) Submissiveness Bedford–Foulds Personality Deviance Scales | $N = 1,592$ 55–74 years | Prospective Population based Edinburgh artery study (51% male) Those with history of angina or MI at baseline were excluded | Non-fatal MI (–) Fatal MI (0) Total MI (–) (only among women) Angina (0) | Over the 5-year follow-up, there were 85 non-fatal MIs, 33 fatal MIs, and 89 developed angina pectoris. Higher levels of submissiveness were significantly associated with reduced odds of a non-fatal MI and, among women only, total MI (combined fatal and non-fatal). In the adjusted models, the association remained significant for women only. |

(table continues)

Table 4 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|---|--|--|
| 32 | (Nakaya, Tsubono, Hosokawa, et al., 2005) Introversion Eysenck Personality Questionnaire– Revised | $N = 29,767$ Early 50s | Prospective Population-based, residents of rural northern Japan (48% male) | Mortality from ischemic heart disease (0) Mortality from stroke (0) | Covariates included baseline CV disease (ankle-brachial pressure index) and baseline risk factors (social class, blood pressure, serum cholesterol, serum triglycerides, body mass index, smoking, and alcohol consumption). Over the 11-year follow-up, there were 90 deaths from ischemic heart disease and 131 deaths from stroke. Introversion was unrelated to mortality. |
| 33 | (Carpeggiani et al., 2005) Submission and shyness Cattell's 16 personality factors | $N = 246$ <65 years | Survival Patients with acute myocardial infarction (89% male) | MI (fatal and nonfatal) Submission (0) Shyness (0) Cardiac deaths Submission (0) Shyness (0) | Over maximum follow-up of 8 years, there were 30 cardiac deaths and 19 non-fatal acute MIs. Submission and shyness were unrelated to CV outcomes. |
| 34 | (Denollet et al., 2007) Type D DS14 | $N = 51$ 54 ± 10 years | Survival/morbidity Patients suffering from end stage heart disease (75% male) Type D measured in pre-transplant period | Out-of-hospital death (+) Rate of moderate to severe allograft rejection among surviving transplant recipients (0) Total unfavorable outcomes (+) | Over the course of the 5.4 year follow-up, there were 6 deaths after successful transplants, and 25 participants had unfavorable outcomes (combination of death, rejection episode grade $\geq 3A$, or number of days from transplant to the incidence of the first rejection post-transplant ≤ 2 weeks). Type D patients were at increased risk for out-of- hospital death (adjusted for recipient age at time of transplant and gender) and total unfavorable outcomes (adjusted for recipient age, donor age, and female-to- male mismatch). Findings for unfavorable outcomes remained significant after adjusting for other clinical risk factors like donor brain death, urgent transplantation, and recipient diabetes, body mass index, and hypertension. <i>(table continues)</i> |

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Table 4 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|---|---|---|
| 35 | Pedersen et al., 2004) Type D DS14 | $N = 875$ Type D (61 ± 12 years) Non-Type D (63 ± 11 years) | Survival/morbidity Patients with ischemic heart disease following percutaneous coronary intervention with sirolimus-eluting stents or bare stents (72% male) Type D measured 6 months after implantation | Death and non-fatal MI (+) | 9-month follow-up, 20 events (total of deaths from all-cause and non-fatal MI). Findings controlled for gender, age, stent type, and previous coronary artery bypass graft surgery (no other clinical risk factors were related to death or MI). |
| 36 | (Pedersen et al., 2007) Type D DS14 | $N = 358$ 62 years | Survival/morbidity Patients with ischemic heart disease following percutaneous coronary intervention with sirolimus-eluting stents (71% male) Type D measured 6 months after implantation | Clinical events (death or MI) (+) | 2-year follow-up, 22 events (composite of death and MI). Type D emerged as a significant prognostic factor, independent of age, sex, CAD history, multi-vessel disease, diabetes, hypercholesterolemia, hypertension, renal impairment, and smoking. |
| 37 | (Denollet et al., 1995) Type D Combination of the State Trait Anxiety Inventory and the Social Inhibition Scale of the HPPQ | $N = 105$ 45–60 years | Survival Male patients who had survived a recent MI | Cardiac mortality (+) Total mortality (+) | There were 15 deaths over the course of the 2–5 year follow-up. Type D significantly improved the predictive value of a model based on biomedical risk factors (i.e., low exercise tolerance, previous or anterior MI, smoking, and age). |
| 38 | (Denollet & Brutsaert, 1998) Type D Combination of the State-Trait Anxiety Inventory and the Social Inhibition Scale of the Heart Patients Psychological Questionnaire | $N = 87$ 41–69 years | Survival/morbidity Patients who had experienced an MI within the 2 months before study entry Global left ventricular ejection fraction (LVEF) of 50% or less (93% male) | LVEF after MI (0) Long-term incidence of cardiac events (+) Long-term cardiac death (+) | Over the 6–10 year follow-up, there were 21 cardiac events, 13 of which were fatal. Type D personality was associated with long-term cardiac events in patients with reduced ejection fraction after MI. Type D was retained in a Cox proportional hazards model, which included a range of potential confounders (i.e., LVEF of 30% or less, three-vessel disease, poor exercise tolerance, history of previous MI, smoking after MI, and negative emotions [anxiety, anger, and depression]). |

(table continues)

Table 4 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|--|---|---|---|
| 39 | (Cserép et al., 2010) Type D 14-item Type D scale | $N = 180$ Mean age at baseline MACCE negative: 56.8 ± 11.2 MACCE positive: 59.1 ± 8.2 | Survival/morbidity Cardiac surgery patients (68 and 64% male in the MACCE negative and positive groups, respectively) | Major adverse cardiac and cerebrovascular event including death (+) | By the end of the 5th year of follow-up, 81 patients had had a major adverse cardiac or cerebrovascular event including death. Type D predicted risk for cerebrovascular events 5 years after surgery. These findings were significant for social inhibition, negative affectivity, and their sum. A propensity score analysis was used to adjust for a comprehensive set of pre-operative and operative characteristics, including previous MI, previous CABG, history of arrhythmia, CHF, diabetes mellitus, hypercholesterolemia, cerebrovascular disease, chronic renal insufficiency, hypertension, and previous psychiatric hospitalisation, additive EuroSCORE, number of grafted vessels, CPB, aortic cross-clamp time, permanent stroke, reoperation for any reason, serious infection, prolonged mechanical ventilation, renal failure requiring dialysis, duration of ICU and hospital stay. |
| 40 | (Denollet et al., 1996) Type D Combination of the Trait-Anxiety Scale and the Social Inhibition Scale of the HPPQ | $N = 303$ 31–79 years | Survival Patients with angiographically documented CHD (88% male) | Cardiac death (+) Non-cardiac death (+) | 38 patients had died (24 were cardiac-related) over the course of the 6–10 year follow-up. Type D personality was significantly associated with mortality, independent of biomedical prognostic factors. The results were significant for cardiac and non-cardiac death. Biomedical and psychosocial factors, including impaired left ventricular function, three-vessel disease, low exercise tolerance, the lack of thrombolytic therapy after MI, hyperlipidaemia, and depressive symptoms emerged as independent predictors of mortality in a stepwise logistic regression model. When Type D was added to the model, it was retained, but depression was not. <i>(table continues)</i> |

Table 4 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|---|--|--|
| 41 | (Denollet et al., 2000) Type D 16-item Type D Scale | $N = 319$ 35–70 years | Survival/morbidity Patients with coronary heart disease (had experienced a myocardial infarction or coronary bypass/angioplasty within 2 months before entering the program) (92% male) | Cardiac events and revascularization (+) Non-fatal myocardial infarction or cardiac death (+) | There were 48 cardiac events, including non-fatal MI, cardiac death, and revascularization procedures. This includes 22 fatal and non-fatal cardiac events. Type D personality was associated with an increased risk of cardiac events over 5-year follow-up. Type D and disease severity were entered into a stepwise logistic regression model predicting adverse cardiac events. The model included LVEF of 50% or less, Type D, and age ≤ 55 years, but not poor exercise tolerance or symptoms of depression/anxiety. |
| 42 | (Denollet, Pedersen, Vrints, & Conraads, 2006) Type D 16-item Type D Scale | $N = 337$ 35–75 years | Survival/morbidity Patients with CHD (88% male) | Major adverse cardiac events (+) Death/infarction (+) | Over the course of the 5-year follow-up, there were 46 major adverse cardiac events (defined as composite of cardiac death, MI, CABG, and percutaneous coronary intervention). This includes 4 deaths and 8 MIs. Type D patients were at increased risk for cardiac events and death/infarction over the course of 5-year follow-up. This finding remains significant after controlling for psychological stress as measured by the 12-item GHQ. Medical treatment variables and cardiac risk factors were unrelated to clinical end points. However, acute MI at baseline, left ventricular ejection fraction $\leq 40\%$ and no invasive treatment with CABG were significant predictors of total cardiac events at follow-up. However, Type D personality remained an independent predictor over and above these factors. |
| 43 | (Denollet, Pedersen, Ong, et al., 2006) Type D 14-item Type D scale | $N = 875$ 62 ± 11 years | Survival/morbidity Patients with ischemic heart disease following PCI with bare or sirolimus-eluting stents (72% male) | Major cardiac event (+) Death and non-fatal MI (+) | There were 100 adverse cardiac events (death, MI, coronary artery bypass, or PCI) over the course of the 9-month follow-up. This includes 20 deaths and MIs. Patients who were high on both negativity and inhibition were at increased cardiac risk. <i>(table continues)</i> |

Table 4 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|--|---|--|
| | | | Type D measured 6 months after implantation | | Demographics, stent type, clinical factors and high negativity/low inhibition and high negativity/high inhibition were entered into a multi-variable Cox regression model predicting cardiac events. The final model retained high negativity/high inhibition and history of CABG. Similar findings emerged for the more specific end of death/MI. |
| 44 | (Martens et al., 2010) Type D 14-item Type D scale | $N = 466$ >30 years | Survival Acute MI patients (78% male) | Total cardiac events (+) | 16 cases of cardiac death and 28 recurrent MIs over average follow-up of 1.8 years. Potential confounders were identified in univariate analysis. The final model adjusted for age, cardiac history, statins, SSRIs, LVEF, and depression. |
| 45 | (Schiffer et al., 2010) Type D 14-item Type D scale | $N = 232$ Mean age of 65.5 years | Survival Chronic heart failure outpatients with LVEF $\leq 40\%$ (75% male) | Total cardiac mortality (+) Late cardiac mortality (>6 months) (+) | 47 patients died due to cardiac causes over an average follow-up of 30.7 months. Sex, age, and LVEF were also associated with mortality. When entered into the model together, the effect of Type D was reduced to a trend ($p = .08$). However, Type D emerged as an independent predictor of late cardiac mortality. |
| 46 | (Pelle et al., 2010) Type D 14-item Type D scale | $N = 641$ Mean age at baseline = 66.6 ± 10 years | Survival/morbidity Outpatients with chronic heart failure (74.3% male) | Cardiac mortality (0) All-cause mortality (0) | 123 deaths, 76 due to cardiac cause. Mean follow-up of 37.6 months (3.13 years). Type D was associated with neither all-cause mortality nor cardiac mortality. In analyses with continuous scores, neither social inhibition, negative affectivity, nor the interaction between the two were independently associated with all-cause mortality or cardiac mortality. |

Note. There was overlap between the samples in Studies 35, 36, and 43, and Studies 37, 38, and 40. Study 32 is based on the same cohort that was presented in Studies 15 and 16 (see Table 3). IS = interpersonal sensitivity; ID = identification; BMI = body mass index; SBP = systolic blood pressure; MI = myocardial infarction; CVD = cardiovascular disease; (+) = positive association; (-) = negative association; (0) = no association; CHD = coronary heart disease; CAD = coronary artery disease; HPPQ = Heart Patients Psychological Questionnaire; MACCE = major adverse cardiovascular and cerebrovascular event; CABG = coronary artery bypass grafting; CHF = congestive heart failure; EuroSCORE = European system for cardiac operative risk evaluation; CPB = cardio-diopulmonary bypass; ICU = intensive care unit; GHQ = General Health Questionnaire; SSRI = selective serotonin reuptake inhibitor.

Table 5
IS and All-Cause Morbidity and Mortality

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|--|---|--|--|
| 47 | (G. A. Kaplan et al., 1994) Shyness 17 selected items from various scales | $N = 2,503$ 42–60 years | Prospective Men in the Kuopio Ischemic Heart Disease Risk Factor Study (random selection of men from Kuopio region in eastern Finland) | All-cause mortality (0) | There were 167 deaths over 5.9 years. Shyness was unrelated to risk of death. |
| 48 | (Barefoot et al., 1989) Social avoidance Subscale of the MMPI-based Cook–Medley Hostility scale | $N = 118$ 20–45 years | Prospective Lawyers completed Hostility scale in 1956 and 1957 (sex break-down not reported) | All-cause mortality (0) | There were 13 deaths over the course of 29 years. Social avoidance was unrelated to mortality. However, other subscales of the Cook–Medley (Cynicism, Hostile Affect, and Aggressive Responding) emerged as significant predictors. Data on traditional risk factors were not available. |
| 49 | (Hearn et al., 1989) Social avoidance Items from MMPI Hostility subscale | $N = 1,313$ Mean age at follow-up was 52.3 ± 2.0 years | Prospective Male college freshmen at the University of Minnesota | CHD mortality (0) Total mortality (0) | Over the 33-year follow-up, there were 69 deaths (13 attributable to CHD, 13 to cancer, and 27 to other causes). Social avoidance was unrelated to mortality. |
| 50 | (Kubzansky et al., 2009) Childhood behavioral inhibition Behavioral assessments by trained psychologist | $N = 569$ Personality assessments at age 7 years Second assessment at age 35 years | Prospective Subsample of the Providence cohort of the National Collaborative Perinatal Project (60% male) | Number of medical conditions (0) | 94 participants reported a medical condition over the 28-year follow-up. Childhood behavioral inhibition was unrelated to medical conditions in adulthood. |
| 51 | (Trumbetta et al., 2010) Social anxiety MMPI Social Introversion scale | $N = 1,812$ The majority were 14–15 years of age | Prospective Adolescent boys from Hathaway's normative Minnesota Multiphasic Personality Inventory (MMPI) sample | All-cause mortality (–) | There were 418 deaths over the course of the 60-year follow-up. Social anxiety was protective among men <75 years, but not among men who died before the age of 55 years. Findings were independent of other MMPI scales, IQ, SES, age, and adolescent health status. |
| 52 | (Fry & Debats, 2009) Introversion NEO Five-Factor Inventory | $N = 450$ 65–80+ years | Prospective Elderly men and women living in Canada 42% male | All-cause mortality (+) | There were 138 deaths over an average follow-up of 6.5 years. Introversion was associated with increased risk of mortality, controlling for number of medical visits at baseline; global index score for disability at baseline, and global satisfaction with family support at baseline. <i>(table continues)</i> |

Table 5 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|--|---|---|-----------------------------------|---|
| 53 | (Maier & Smith, 1999) Introversion Items selected from the NEO Five-Factor Inventory | $N = 516$ 70–103 years | Prospective Participants in the Berlin Aging Study (~50% male) | All-cause mortality (+) | Over the course of the 3–6 year follow-up, 50% of participants had died. Introversion was significantly associated with increased mortality risk. However, the results were no longer significant after controlling for age. |
| 54 | (Wilson et al., 2004) Introversion NEO Five-Factor Inventory | $N = 883$ ≈61–89 years | Prospective Catholic clergy members (31% male) | All-cause mortality (+) | Average follow-up of 5.1 years, 182 events. Introversion was associated with increased mortality risk (controlling for age, gender, and education). The association was not strongly affected by the number of medical conditions at baseline or health-related behaviors. However, the effect was no longer significant after adjusting for other personality traits, or for level of cognitive and motor functioning. |
| 55 | (Korten et al., 1999) Introversion Eysenck Personality Questionnaire–Revised | $N = 897$ 70 years and older | Prospective Australian community dwelling elderly (50% male) | All-cause mortality (0) | Over the course of the 3–4 year follow-up, 110 men and 62 women died. Introversion was unrelated to mortality. |
| 56 | (Weiss & Costa, 2005) Introversion NEO Five-Factor Inventory | $N = 1,076$ 65–100 years | Prospective Medicare patients (27% male) | All-cause mortality (0) | There were 424 deaths over the 5-year follow-up. No evidence for a relationship between introversion and mortality. |
| 57 | (Iwasa et al., 2008) Introversion Japanese version of the NEO-PI–R | $N = 1,228$ 65 years and older | Prospective Japanese community-dwelling elderly (40% male) | All-cause mortality (+) | There were 127 deaths over the 5-year follow-up. Findings controlled for age, number of years of education, living alone, presence of psychiatric problems, presence of chronic diseases. |
| 58 | (Chapman et al., 2010) Introversion The Midlife Development Inventory | $N = 2,998$ 25–74 years | Prospective cohort study in the United States (52% male) | All-cause mortality (0) | There were 179 deaths over the 10-year follow-up. Introversion was unrelated to survival. |

(table continues)

Table 5 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|--|--|---|--|
| 59 | (Martin et al., 2007) Introversion Sociability scale—items from Terman's (1947) study that reflect fondness of large groups This study is an expansion of earlier work based on the same data (Friedman et al., 1993; Schwartz et al., 1995) | $N = 1,253$ Children were 11 years of age at baseline Mean age of 30 years at adult assessment | Prospective Gifted children assessed in the 1920s as part of the Terman Life-Cycle Study (56% male) | Childhood measure All-cause mortality (0) Adult measure All-cause mortality (0) | Over the 7 decades of follow-up, 492 men had died, and 297 women had died. Childhood and adulthood introversion were unrelated to mortality. A recent study analyzed follow-up data collected when Terman's participants were in their 70s, and there was still no evidence of an association between introversion and mortality (Friedman, Kern, & Reynolds, 2010). |
| 60 | (Mroczek & Spiro, 2007) Introversion (baseline and slope) Eysenck Personality Inventory | $N = 1,663$ 43–91 years | Prospective Older men in the Department of Veterans Affairs' Normative Aging Study | All-cause mortality Baseline introversion (0) Slope (0) | There were 503 deaths over the 18-year follow-up. Baseline introversion and change in introversion were unrelated to mortality. |
| 61 | (Taylor et al., 2009) Introversion NEO Five-Factor Inventory | $N = 1,322$ Mean age of approximately 70 years at baseline | Prospective Population-based Edinburgh Artery Study | All-cause mortality (0) | There were 407 deaths over the 10-year follow-up. Introversion was unrelated to mortality. |
| 62 | (Huppert & Whittington, 1995) Introversion Eysenck Personality Inventory | $N = 6,096$ 18 years and over | Prospective Population based Residents living in England, Scotland, and Wales (Health and Lifestyle Survey) | All-cause mortality (0) | There were 474 deaths over a follow-up of 7 years. Introversion was unrelated to mortality. |
| 63 | (Oishi & Schimmack, 2010) Introversion and interaction between introversion and residential mobility | $N = 7,115$ 20–75 years | Prospective Population based Adults in the Midlife in the United States Study (48% male) | Main effect All-cause mortality (0) Interaction with residential mobility All-cause mortality (+) | There were 421 deaths over the 10-year follow-up. There was no main effect of introversion on mortality. Yet, there was a significant interaction between introversion and residential mobility in the prediction of mortality. Specifically, introverts who moved homes more often in childhood were at increased risk. |
| 64 | (Shipley et al., 2007) Introversion Eysenck Personality Inventory | $N = 5,424$ 18–99 years | Prospective Population based Residents living in England, Scotland, and Wales (Health and Lifestyle Survey) (55% male) | All-cause mortality (0) Disease categories: CVD (–) CHD (0) Stroke (0) Respiratory disease (+) Lung cancer (0) All non-lung cancer (0) | There were 1,335 deaths over the 21-year follow-up. There was no clear relationship between introversion and mortality. Introversion was protective for CVD death in those between 40 and 59 years (adjusting for age and (table continues) |

Table 5 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|---|-----------------------------------|---|
| | | | | | gender), but not after adjusting for SES, health behaviors, forced expiratory volume, blood pressure, and body mass index. Introversion was significantly associated with risk for respiratory diseases, independent of demographic and health-related variables. The covariates were age, gender, occupational social status, education, smoking status, alcohol consumption, physical activity, forced expiratory volume, blood pressure, and BMI. |
| 65 | (Wilson et al., 2005) Introversion NEO Five-Factor Inventory | $N = 6,158$ $\approx 61-89$ years | Prospective Older adults drawn from neighborhoods in Chicago (39% male) | All-cause mortality (+) | There were 2,430 deaths over an average of 6.2 years. High introversion associated with an increased risk of death after 6 years of observation. Analyses controlled for age, sex, race, and education, and findings remained significant after controlling for chronic cardiac related conditions, current and past use of tobacco, alcohol consumption, and BMI. The association between introversion and mortality was reduced after controlling for cognitive, physical, and social activity. |
| 66 | (Ploubidis & Grundy, 2009) Introversion Eysenck Personality Inventory | $N = 5,755$ Mean age = $45.16 \pm$ $SD 16.53$ | Prospective Nationally representative sample of adults living in private households in Great Britain | All-cause mortality (-) | 20-year follow-up, 2,431 deaths. Introversion had a negative indirect association with mortality risk, with most of the effect being mediated by smoking, psychological distress, and somatic health. The role of mediators in the association between extraversion and mortality risk was stronger in women compared to men. Models are independent of age at baseline and social class. |

(table continues)

Table 5 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|---|--------------------------------|---|
| 67 | (Morris et al., 1993) Introversion Eysenck Personality Inventory | $N = 84$ Survivors (71 ± 10 years) Non-survivors (75 ± 7 years) | Survival Stroke inpatients assessed 2 months post-stroke (54% male) | All-cause mortality (+) | 7 subjects died over the 15-month follow-up. Extroversion was associated with mortality, such that the non-survivors were more introverted than the survivors. Results controlled for depressive symptoms and cognitive impairment (the two other variables that predicted mortality). Survivors and non-survivors were compared on demographics and clinical risk factors. Only cognitive impairment differed significantly between the groups. |
| 68 | (Carinci et al., 1997) Introversion Eysenck Personality Inventory | $N = 2,449$ $96.3\% \leq 70$ years | Survival Patients who had survived an acute myocardial infarction (88% male) | All-cause mortality (+) | There were 63 deaths over the course of the 6-month follow-up. Introversion was associated with increased risk for mortality. Results adjusted for clinically relevant risk factors. Clinical prognostic factors were forced into the model, and a backward selection strategy was applied to the psychological variables. Clinical prognostic factors included exercise test positive, exercise test ineligibility, electrical instability, recovery phase left ventricular dysfunction, previous acute myocardial infarction, age > 70 years, hypertension, sex, early ventricular failure, and late ventricular failure. |
| 69 | (Christensen et al., 2002) Introversion NEO Five-Factor Inventory | $N = 174$ Surviving 52 ± 16 years Deceased 61 ± 17 years | Survival Patients with chronic renal insufficiency (57% male) | All-cause mortality (0) | There were 49 deaths over the average follow-up of 49 months. Introversion was unrelated to survival. |
| 70 | (Aquarius et al., 2009) Type D 14-item Type D scale | $N = 184$ 65 ± 10 years | Survival Patients recently diagnosed with symptomatic peripheral arterial disease (64% male) | All-cause mortality (+) | There were 16 deaths over the course of the 4-year follow-up. Age, diabetes, and renal disease were independent predictors of mortality. Yet, Type D predicted over and above these risk factors. Analyses controlled for age and sex. |

(table continues)

Table 5 (continued)

| Study ID | Citation/personality variable | Sample size and baseline age (range or $M \pm SD$) | Type of study/sampling strategy | Outcomes and direction of finding | Follow-up, number of adverse events, and covariates |
|----------|---|---|---|-----------------------------------|--|
| 71 | (Pedersen et al., 2010) Type D 14-item Type D scale | $N = 371$ Mean age of 57.7 + 12.0 | Survival Consecutively implanted ICD (implantable cardioverter defibrillator) patients (79.5% men) | All-cause mortality (+) | There were 25 deaths a median of 2 years post-implantation. Type D emerged as an independent predictor of mortality, adjusted for gender, age, ICD indication, coronary artery disease, and shocks (appropriate or inappropriate) during the follow-up. |
| 72 | (Coyne et al., 2011) 14-item Type D scale | $N = 706$ Mean age of 70.7 ± 11.5 | Survival Patients with heart failure (61.8% male) | All-cause mortality (0) | There were 192 deaths over the 18-month follow-up. Type D classification was not significantly associated with mortality. These findings held up in analyses of continuous scores. There were no effects of social inhibition, negative affectivity, or the interaction between the two. |
| 73 | (de Voogd et al., 2009) Type D 16-item Type D scale | $N = 112$ Mean age of 60.8 ± 10.3 years | Survival Patients with chronic obstructive pulmonary disease (48% male) | All-cause mortality (0) | There were 48 deaths over the 7-year follow-up. Type D was unrelated to survival among patients with chronic obstructive pulmonary disease. Moreover, there was no main effect of social inhibition. |
| 74 | (Grande et al., 2011) Type D 16-item Type D scale | $N = 1,040$ Mean age of 63 ± 11 | Survival German cardiac patients (76% male) | All-cause mortality (0) | There were 172 deaths over course of the 6-year follow-up. Type D classification was not significantly associated with mortality. These findings held up in analyses of continuous scores. There were no effects of social inhibition, negative affectivity, or the interaction between the two. Of note, results indicated that mortality in patients with high social inhibition was higher early in the follow-up period and lower in later periods. |
| 75 | (Volz et al., 2011) Type D 14-item Type D scale | $N = 111$ Mean age of 57 ± 14 | Survival Patients with chronic heart failure (82% male) | All-cause mortality (0) | There were 11 deaths over the average follow-up of 2.8 years. Type D was unrelated to survival among patients with chronic heart failure. |

Note. There was overlap between the samples used in Studies 62 and 64. Studies 61 and 31 (see Table 4) were based on the same cohort. IS = interpersonal sensitivity; ID = identification; (+) = positive association; (−) = negative association; (0) = no association; MMPI = Minnesota Multiphasic Personality Inventory; CVD = cardiovascular disease; CHD = coronary heart disease; SES = socioeconomic status; NEO-PI-R = NEO Personality Inventory—Revised; BMI = body mass index.

Downey & Feldman, 1996; Heiser, Turner, & Beidel, 2003; J. R. Kaplan et al., 1996; Kocovski & Endler, 2000; M. R. Leary, Atherton, Hill, & Hur, 1986; Pachankis, Goldfried, & Ramrattan, 2008; Pilkonis, 1977; Stavray, Donner, Kincade, & Stewart, 1988; Whiteman, Deary, Lee, & Fowkes, 1997). The most compelling evidence derives from studies that have examined associations among multiple concepts we have discussed. For instance, a composite measure of social inhibition created by Cole et al. (2003) included three key features of IS - the broad introversion-extraversion dimension, social avoidance, and emotional inhibition. The mean correlation between measures was .62, which represents almost 40% overlap in variance. In addition, Downey and Feldman (1996) showed that their rejection sensitivity measure correlated positively and significantly with a number of dispositional variables that we argue tap features of IS. These concepts include introversion, social avoidance, social distress, and a measure of interpersonal sensitivity, all of which correlate with the RSQ in the .40 to .49 range. Studies like these provide initial evidence that the concepts reviewed here capture an overlapping phenomenon, which we argue is IS. Of course each of them also captures some unique features of interpersonal behavior, which we have discussed above.

With all that said, there is insufficient evidence at present to render judgments about the validity of the IS construct. Thus, additional research is needed to evaluate the claims we are making about the structure of IS. Of particular importance would be studies of discriminant validity, which examine whether IS relates to health in a manner that is independent of other constructs with which it has some conceptual overlap (e.g., hostility, negative affect, dominance; see below for more discussion of these issues). Also important would be additional studies of convergent validity that make use of behavioral and physiological criterion variables, so as to minimize the impact of common method variance. For example, laboratory studies have shown that socially inhibited individuals show higher cardiac output and increased SBP and DBP responses during socially threatening tasks (Habra, Linden, Anderson, & Weinberg, 2003; Williams, O'Carroll, & O'Connor, 2009), providing initial evidence of an association between IS and physiological criterion variables.

The Conceptualization and Measurement of Health

The review focuses on studies that relate IS to the objective clinical endpoints of morbidity (the onset of a disease, usually marked by a formal diagnosis) and mortality (death, either from a specific disease, or from any cause). Studies that relied upon self-reports of symptoms or quality of life were omitted because of the potential biases they introduce (e.g., social desirability, exaggeration). This is especially important given that personality is almost always measured via self-reports and, as a result, any linkage between IS and health outcomes measured in this way could be driven by common method variance and generic response styles. For example, a person who is likely to exaggerate the extent of his or her social anxiety is also likely to exaggerate the number or severity of physical symptoms, which could lead to a spurious association between the two. Without objective verification we can't know whether these reported symptoms reflect underlying

disease versus benign sensations. Thus, by limiting the review to studies that make use of objective outcomes, we maximize the chances that any observed linkages reflect direct effects of IS on disease pathophysiology, as opposed to associations driven by perceptual and/or reporting tendencies related to personality.

Why Would Dispositional IS Be Linked to Health?

There are three plausible scenarios to explain any association between IS and health. First, IS may cause disease to develop or to progress more quickly by modifying underlying pathogenic mechanisms. There are behaviorally and biologically plausible mechanisms by which this could occur. As we have noted, IS reflects ongoing concerns about negative social evaluation. IS makes people vigilant for and sensitive to others' evaluations of them; in order to avoid such evaluations they adopt defensive behaviors like submission and inhibition. Paradoxically, these behaviors often bring about the very social difficulties IS individuals are trying to avoid. In particular, inappropriate submissive behaviors can detract from the quality of social interactions (Keltner, Young, & Buswell, 1997), and in the case of negative interactions, IS can motivate defensive behaviors that escalate conflict. IS can also give rise to self-fulfilling prophecies wherein concerns about rejection actually increase a person's likelihood of being rejected (Downey et al., 1998). Thus, IS individuals are more likely to experience social interactions characterized by dissatisfaction, conflict, and rejection.

We know from laboratory research that both social-evaluative concerns and abrasive social interactions have biological consequences. Those consequences often entail activation of the hypothalamic-pituitary-adrenocortical (HPA) axis and the sympathetic nervous system (SNS) and reductions in parasympathetic nervous system regulation of target organs like the heart (Bosch et al., 2009; Dickerson & Kemeny, 2004; Dickerson, Gruenewald, & Kemeny, 2004; Kiecolt-Glaser, Gouin, & Hantsoo, 2010; Repetti, Robles, & Reynolds, 2011). These responses are characterized by increased circulating concentrations of hormones like cortisol, epinephrine, and norepinephrine, as well as alterations in the magnitude of local autonomic drive on target organs. Assuming this physiologic milieu is evoked with some regularity, it could have implications for the many bodily tissues regulated by the HPA axis and the branches of the ANS. Receptors for the hormonal products of these circuits are widespread in bodily tissues, including those that comprise the cardiac, vascular, metabolic, skeletal, immune, and nervous systems. With prolonged exposure to elevated levels of these hormones, or durable changes in the extent of local autonomic drive, various functions of these tissues are thought to become dysregulated (McEwen & Stellar, 1993). For example, with lasting stress the immune system's antiviral response becomes impaired, and mild, chronic inflammation develops. In the metabolic system, visceral adiposity increases, glucose control diminishes, and lipid profiles become unfavorable. In the cardiovascular system, signs of preclinical disease emerge, like endothelial dysfunction, arterial stiffness, and elevated blood pressure (Bailey, Engler, Hunzeker, & Sheridan, 2003; Harris & Matthews, 2004; Irwin & Cole, 2011; Manuck, Marsland, Kaplan, & Williams, 1995; Marques, Silverman, & Sternberg, 2009; Thayer & Sternberg, 2006). In concert with genetic liabilities and relevant exposures—e.g., to pathogens in the case of infectious disease,

and to carcinogens in the case of cancer—these dysregulations are thought to heighten susceptibility to various conditions, and accelerate their progression (Antoni et al., 2006; Kop & Cohen, 2007; Sloan & Collado-Hidalgo, 2007).

Of course, this scenario assumes that the association between IS and disease outcomes is causal in nature. However, there are at least two alternative interpretations of this association that are equally plausible. The first is a model in which disease causes changes in social behavior. For example, advanced infections like HIV can enter the central nervous system and change social behavior (Barak et al., 2002). In addition, inflammation resulting from many infectious, neoplastic, vascular, and autoimmune diseases can lead to sickness behaviors, one of the cardinal features of which is social withdrawal (Dantzer, 2004). Thus, according to these explanations, people get withdrawn when they are sick because the agents that cause disease (viruses) or the body's response to them (inflammation) have effects on the central nervous system that manifest in reclusive social behavior.

To effectively rule out this alternative explanation, studies would need to measure IS when people are young and healthy, and then follow them over long timeframes to see who gets sick. This can establish temporal precedence. However, this approach is often infeasible when the researcher's aim is to study the role of IS in clinical populations. Thus, in such studies, it is important that participants are enrolled and personality is measured in the very early stages of disease before there are central nervous system consequences and that factors like disease stage and medication use are carefully measured and controlled for.

Another alternative interpretation for any association (whether temporal precedence is established or not) is that there is some common underlying process that affects both the tendency to be interpersonally sensitive *and* biological processes that contribute to disease, and as a result, gives rise to a spurious or inflated linkage. To the extent that such a process can be identified up front and measured well, it can be dealt with thorough statistical controls. For instance, most studies consider possible third factors like SES, demographics, and other theoretically derived confounders. However, not all potential third factors are easy to identify, much less measure. For example, there could be specific genetic variants or groups of such variants that give rise to both IS and disease outcomes. And, unless we could identify them up front, it would be impossible to control for them. Other possible confounders include intrauterine complications, low birth weight, and early life exposures to toxins like lead or radiation.

Unfortunately, these alternatives are very difficult to evaluate. Animal studies can help because aspects of IS can be manipulated through breeding (e.g., Cavigelli, 2005; Cavigelli & McClintock, 2003), and potentially confounding environmental exposures can be controlled in the laboratory. This substantially reduces (and in some cases eliminates) the chances that factors like intrauterine complications, low birth weight, and pollutant exposures are driving associations. However, even in these circumstances the possibility remains that some disease-causing genetic variants assort with IS during breeding, which creates a confound that even tightly controlled animal studies cannot disentangle.

Some clarity on the issue of causality can be gained through studies that examine whether the health costs of IS vary across contexts. For instance, Oishi and Schimmack (2010) showed that introverts have an elevated mortality risk relative to extroverts, but

only when they had experienced a good deal of early life residential mobility. This type of interaction provides some indirect evidence that introversion may be acting causally, if only because the confounding scenarios get more complicated and more difficult to imagine. For example, it could be argued that intrauterine nutritional deprivation, which manifests in low birth weight, predisposes kids to both introversion and health problems later in life. But it is not clear why this scenario would only play out in people whose families moved around a good deal while they were children. (Unless the moves contributed to a particularly detrimental kind of deprivation that didn't generally arise under other circumstances.) Although this explanation is plausible, the causal model is more attractive because it fits conceptually, and it is more parsimonious. That being said, in an observational literature like this one, we can never completely eliminate the possibility that some underlying confounder is driving the association.

A related issue concerns the role of other psychological characteristics in the IS-health association. Of particular relevance here are constructs like hostility, negative emotions, dominance, and social relationships that have conceptual overlap with IS and have known relations with health outcomes. Specifically, hostility is an established risk factor for CVD, and it is significantly correlated with IS constructs, including social inhibition and rejection sensitivity (Barefoot, Dodge, Peterson, Dahlstrom, & Williams, 1989; Cole et al., 2003; Romero-Canyas, Downey, Berenson, Ayduk, & Kang, 2010). However, hostility can be distinguished from the IS constructs by increased amounts of dominance and disagreeableness. Hostility is characterized by cynicism and mistrust, and it is closely related to angry and aggressive dispositions (T. W. Smith et al., 2004). Moreover, London, Downey, Bonica, and Paltin (2007) found that anxious expectations of rejection uniquely predicted social anxiety and withdrawal, whereas angry expectations uniquely predict aggression and feelings of victimization. Thus, the authors suggest that "angry expectations fuel 'fight' responses to social threat, whereas anxious expectations fuel 'flight' responses (social anxiety and withdrawal)" (p. 498). Thus, hostility and IS may also be distinguished in terms of cognitions and both behavioral and affective responses to rejection. Nonetheless, given the overlap between hostility and IS, we take note of studies that measure and control for hostility.

Similarly, constructs reflecting IS reliably covary with negative mood states like anxiety and depression (Ayduk, Downey, & Kim, 2001; Cole et al., 1997; Heiser et al., 2003). These mood states have also been linked to health outcomes, including CVD, infectious disease, and premature mortality (Carney & Freedland, 2003; Cohen et al., 1995; Suls & Bunde, 2005). IS also relates to the more dispositional tendency to experience negative emotions, termed neuroticism. However, the latter constructs' links with health seem to be principally mediated through symptom perception and reporting, rather than changes in underlying disease processes (Cohen et al., 1995; Costa & McCrae, 1987; Watson & Pennebaker, 1989). That said, the role of negative affectivity in the IS-health relationship is important to consider, particularly in the Type D literature, because this construct is defined in terms of high levels of both social inhibition and negative affectivity, an issue we return to later in the review.

Finally, elements of IS covary with trait dominance. This overlap is especially apparent for the submissiveness element of IS because submissiveness and dominance are often viewed as oppo-

site ends of a continuum. As would be expected, submissiveness and dominance are negatively correlated (Moskowitz & Coté, 1995), yet other IS elements are also associated with dominance, including rejection sensitivity and social anxiety (Brookings et al., 2003; Watson & Friend, 1969). Given that trait dominance has been linked to coronary heart disease (Houston, Chesney, Black, Cates, & Hecker, 1992; Siegman et al., 2000; T. W. Smith et al., 2008), it is important to be mindful of the potential role of dominance in the relationship between IS and health. Finally, elements of IS overlap with the kinds of social niches that people inhabit, as well as their subjective experiences of those environments. This is important because constructs like social isolation, perceived support, and loneliness are reliably associated with health outcomes (Cohen et al., 1997; Cohen & Wills, 1985; Hawley & Cacioppo, 2010), and it is likely that they play some role in the IS-health relationship. Thus, we take note of studies that measure and control for aspects of the social environment.

Method

Literature Search

We attempted to locate all articles that had ever been published on this topic. Articles were identified through searches of PubMed and Psych Info. Each search crossed key words reflecting indicators of IS, introversion, submissiveness, inhibition (including psychological, social, and behavioral inhibition), shyness, social avoidance, rejection sensitivity, social anxiety, and Type D, with key words reflecting health endpoints (morbidity and mortality). Additional articles were found by combing the reference sections of pertinent articles in the area. To guarantee that the articles have passed a first check of quality control via peer-review, we excluded book chapters, dissertations, and conference abstracts. One potential drawback of this approach is that the pool of studies reviewed may be biased toward those with positive findings.

Inclusion Criteria

Articles were included in the review if they appeared in an English-language journal, measured an individual difference construct that reflected IS, and related it to morbidity or mortality from infectious disease, cancers, and CVD. We also included studies with all-cause mortality as an endpoint. Because of the article's focus on physical illness, we excluded studies of suicide, accidents, and psychiatric conditions. We also excluded articles that focused on morbidity and mortality from physical illness but did so in conditions where there was too little research to merit a formal review—for example, one survival study of patients with chronic renal failure (Burton, Kline, Lindsay, & Heidenheim, 1986) and two studies of incident asthma in adults (Huovinen, Kaprio, & Koskenvuo, 2001; Loerbroks, Apfelbacher, Thayer, Debling, & Stürmer, 2009).

Besides these criteria, studies were excluded if they used a cross-sectional or limited prospective design. This criterion maximized the rigor of the reviewed evidence and helped us to distinguish between the various interpretations of the relationship between IS and health (i.e., reverse causality and potential third variables). In particular, we focused on long-term prospective studies because they are the only ones that can realistically tell us

about temporal precedence. We excluded one type of prospective design (the limited one) because it does not lend itself to clear interpretation. In limited prospective studies, personality is measured in a high-risk group (e.g., women with suspicious mammograms) only weeks or days before the diagnosis is finalized. This approach raises concerns that any subsequent associations reflect the influence of the impending diagnosis (or the disease process itself) on the way that subjects report their level of IS. Using these criteria we located a total of 76 articles that formed the basis of the review. They were based on 63 independent samples and were published between 1979 and 2011.

Findings

Tables 2–5 present summaries of the studies included in the review. Each table focuses on a specific health outcome (infectious disease, cancer, CVD, or all-cause mortality) and includes information about study design, sample population, covariates, and the direction of effects. Table 6 summarizes the number of positive and negative studies within each outcome and across the various IS concepts. Before reviewing the results for each health outcome, we discuss the methodological features of the studies under review, and highlight some limitations of them that complicate interpretation of the findings.

Methodological Characteristics

The mean sample size across the studies in the review was 3,698 (range of 51 to 59,548), while the mean number of adverse events (e.g., diagnosis, myocardial infarction, death) was 385 (range of 7 to 4,631). The mean follow-up length was 10 years (range of .5 to 60). The review included nine studies on infectious disease, 19 studies on cancer, 19 studies on CVD, and 29 studies on mortality from all causes. The number of studies focusing on each IS-relevant construct was 37 for introversion, 20 for Type D, nine for social anxiety and avoidance, seven for shyness and inhibition, four for submissiveness, and one for rejection sensitivity. Constructs reflecting IS were generally assessed with standardized questionnaires. In most cases psychometric evidence of their reliability and validity was presented and it was satisfactory. Three studies measured multiple IS constructs and one used a composite measure. In regard to study design, 37 studies used prospective designs in which initially healthy participants were followed until they experienced an adverse medical outcome, 36 enrolled samples of patients who had already been diagnosed with a disease, and followed them to determine how quickly it progressed or led to death, and three used quasiexperimental designs in which individuals at varying levels of IS were exposed to a virus that causes an upper respiratory tract infection, and then monitored to determine the presence and severity of infection.

As a whole this literature has a number of methodological features that complicate interpretation of the findings. First, the majority of studies in this review relied on single-point personality assessments. This is problematic because some aspects of personality have been shown to change over time (Roberts & Mroczek, 2008), thus baseline measures may not be valid indicators of interpersonal behavior 10 or 20 years later. However, the primary consequence of this approach would be to undermine the reliability of the IS measure, which would have the effect of making links

Table 6
Tally of Positive Studies by Health Outcome and IS Construct

| Construct/outcome | All studies | | Experimental and truly prospective studies only | |
|-------------------------------------|-------------------------------|-----------------------|---|-----------------------|
| | No. of positive studies/total | % of positive studies | No. of positive studies/total | % of positive studies |
| IS construct | | | | |
| Introversion–extraversion | 13/37 | 32 | 9/23 | 35 |
| Submissiveness | 0/4 | 0 | 0/2 | 0 |
| Shyness and behavioral inhibition | 0/4 | 0 | 0/2 | 0 |
| Social avoidance | 1/3 | 33 | 1/3 | 33 |
| Social and psychological inhibition | 4/4 | 100 | 2/2 | 100 |
| Type D | 15/20 | 75 | | |
| Rejection sensitivity | 1/1 | 100 | | |
| Social anxiety | 2/6 | 33 | 2/5 | 40 |
| Health outcome | | | | |
| Infectious disease ^a | 8/9 | 89 | 5/5 | 100 |
| Cancer ^b | 3/19 | 16 | 1/11 | 9 |
| Cardiovascular disease ^c | 15/19 | 79 | 3/5 | 60 |
| All-cause mortality ^d | 10/29 | 34 | 6/20 | 30 |

Note. IS = interpersonal sensitivity.

^a IS constructs examined: 5/9 introversion, 3/9 social or psychological inhibition, 1/9 rejection sensitivity. ^b IS constructs examined: 13/19 introversion, 3/19 social anxiety, 2/19 submissiveness, 1/19 psychological inhibition, 1/19 shyness, 1/19 Type D (some studies measured more than one IS construct). ^c IS constructs examined: 13 Type D, 3 social anxiety and avoidance, 2 submissiveness, 1 introversion, 1 shyness. ^d IS constructs examined: 18/29 introversion, 6/29 Type D, 3/29 social anxiety and avoidance, 2/29 shyness and behavioral inhibition.

between IS and health more difficult to detect. Thus, one-time measures of IS might account for some of the null effects in the literature, but they are unlikely to systematically bias the evidence in a way that leads to spurious findings. Second, a number of studies used personality measures that do not have well-established psychometric properties (Cole et al., 1997; G. A. Kaplan et al., 1994; Kubzansky, Martin, & Buka, 2009; Martin & Friedman, 2000). Again, the primary consequence of this limitation would be to attenuate links between IS and health, because poor reliability and validity will constrain the magnitude of the association that can emerge. Uncertainty about psychometrics also makes it difficult to interpret null findings, because it is unclear whether they represent the true state of affairs (the variables are unrelated), or are just an artifact of unreliable or invalid measures. Third, many of the studies in the review used relatively short follow-up times, with 43% following participants for 5 years or under. Reverse causality is a more plausible alternative explanation in these studies because disease-related variables may influence personality well before diagnosis. Finally, the findings presented in this review were often based on small samples and relatively few events. For instance, 46% of the studies used sample sizes under 400, and in the smallest studies, the analyses were based on fewer than 50 adverse events. Studies with small samples (and more important, small numbers of adverse events) have less statistical power to detect associations, and more perniciously, they can produce biased parameter estimates (Babyak, 2004). For these reasons, the review will give more weight to studies with large sample sizes, well-validated measures, and relatively long follow-ups to delineate the nature of the relationship between IS and health.

We initially attempted to perform a meta-analysis of this literature, because it would provide a more transparent and quantitative synthesis than a narrative review. However, in the early stages of this process it became evident that we would not be able to

accurately combine the effect sizes across studies. The problem was that studies varied in terms of whether they reported aggregate outcomes over the length of follow-up (e.g., odds ratios and relative risks) vs. time-to-event statistics like Kaplan–Meier or Cox regression models. There is no established algorithm for pooling these metrics accurately, unless one has access to data at the level of the individual patient (see Michiels et al., 2005). Because many of the studies in the review were published decades ago, it is unlikely that we could retrieve such data from authors. Thus, we chose to synthesize this literature narratively.

Infectious Disease

Nine studies examined the relations of IS to infectious disease, including progression of HIV, incidence of infections like pneumonia and bronchitis, and incidence of colds following inoculation with a virus (see Table 2). With one exception, results indicated that IS individuals were more vulnerable to infectious disease or its complications than their less sensitive counterparts. This was true despite significant variability in the element of IS measured.

Five studies examined the prospective relationship between IS and the progression of HIV/AIDS. Two of these focused on introversion, while three examined social/psychological inhibition and rejection sensitivity. In these studies the IS construct was measured at a fairly early stage of HIV infection, and then follow-up assessments were used to gauge whether disease progression varied by IS. For example, Ironson, O’Cleirigh, Weiss, Schneiderman, and Costa (2008) measured introversion among HIV seropositive patients with no history of AIDS, and then tracked their viral load and CD4 cell counts for 4 years. Results indicated that introversion was associated with more rapid increases in viral load and more rapid declines in CD4 cell number. However, an earlier study with a similar design (albeit a shorter

follow-up time) showed that introversion was unrelated to markers of disease progression (Thornton et al., 2000).

Cole and colleagues conducted three studies relating IS elements to HIV progression among gay men with no history of AIDS. One focused on social inhibition (a composite measure of introversion, social avoidance, and emotional inexpression; Cole et al., 2003), and another on concealment of homosexual identity (Cole, Kemeny, Taylor, Visscher, & Fahey, 1996). (In the case of the latter, there's some ambiguity regarding the motivation for concealment, and in some cases it may have more to do with a person's social context rather than underlying concerns about negative social evaluation.) In both studies the more inhibited participants showed faster HIV progression on multiple dimensions compared to their less inhibited counterparts. However, model overfitting is a potential problem in the earlier study (Cole, Kemeny, Taylor, Visscher, & Fahey, 1996), as there was a large set of potential confounds and mediators (see Table 2). While this kind of rigor bolsters confidence in the validity of the conclusions, estimates drawn from statistical simulations indicate that models need at least five, and probably 10 or more, events for each predictor modeled to avoid the problems associated with model overfitting, which can include biased parameter estimates and an overly optimistic fit (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996). In Cole et al.'s (1996) study, the ratio was 27:10, which means that there were less than three adverse events (i.e., AIDS-related diagnosis and death) for each predictor modeled.

Finally, Cole et al. (1997) examined the interaction between psychological inhibition and rejection sensitivity in a reanalysis of the 1996 data. In particular, being out of the closet was associated with worse HIV outcomes for those high in rejection sensitivity, but better ones for those who were low in rejection sensitivity. Thus, the combination of high rejection sensitivity and being out of the closet (and thereby exposed to the threat of homophobic social rejection) was most detrimental to these patients' health. This finding suggests that social context is likely to be an important moderator in the IS-health relationship; in other words, that the health-damaging effects of IS may be most pronounced in milieus where concerns about negative social evaluation are most regularly activated.

While these findings are consistent with the hypothesis that IS influences the rate of HIV progression, the short follow-up in some cases—that is, 12–18 months in Cole et al.'s (2003) most recent study and the clinical nature of the population raises concerns about temporal ordering and potential confounds. In particular, inflammation resulting from HIV migration into the central nervous system could have brought about behavioral changes including social withdrawal, which may have influenced reports of social inhibition. This is not especially likely given that subjects entered the study at a fairly early stage of HIV infection. Moreover, a similar pattern of findings was indicated in a lengthy prospective study linking concealment of homosexual identity to the 5-year incidence of common infectious diseases, like pneumonia, bronchitis, sinusitis, and tuberculosis (Cole, Kemeny, Taylor, & Visscher, 1996). Given that the participants were healthy at the outset, the findings provide stronger evidence of temporal precedence.

Finally, three studies used viral challenges to examine the association between IS and susceptibility to upper respiratory infections. Each of these studies involved recruiting a group of healthy volunteers, measuring personality, and then inoculating the partic-

ipants with rhinovirus and/or influenza virus. These quasiexperimental designs are powerful because they involve controlled exposure to the pathogen. By doing so they ensure that characteristics like introversion are not simply affecting a person's chances of being exposed to the virus in the first place. Because personality is measured before inoculation, they also eliminate the possibility of reverse-directionality problems, such as disease triggering reports of IS.

Two early studies showed that introverts more frequently developed infections and symptoms following viral challenge compared to extraverts (Broadbent, Broadbent, Phillpotts, & Wallace, 1984; Totman, Kiff, Reed, & Craig, 1980). Cohen's group has since replicated this finding (Cohen et al., 1997) in a large viral-challenge study, showing that introverts are significantly more likely to develop colds upon viral exposure than extraverts. Thus, the common cold studies provide convincing evidence that introversion is associated with increased vulnerability to infection.

Infectious disease summary. The studies on IS and infectious disease were all based on relatively small sample sizes (Ns ranged from 54 to 276). However, the positive findings across all three viral challenge studies (100%) and five of the six longitudinal studies (83%) provide consistent evidence of an association between IS dispositions and vulnerability to infection. Moreover, the viral challenge studies in particular allow us to rule out the alternative explanation that infection precedes IS. That said, we can still not exclude the possibility of unmeasured confounds playing a role in these associations.

It should be noted that in both the viral challenge studies and the longitudinal studies on HIV progression, IS participants are likely to be experiencing a disproportionate amount of psychosocial stress due to the social context they inhabit. In the viral challenge studies, the participants are quarantined with strangers in a novel environment for five to 7 days. This situation would be uncomfortable for most people, but especially so for IS individuals because they are anxious about novel people and situations. To the extent that this is true, one plausible interpretation of the findings above is that the heightened infectious susceptibility among high IS persons derives from their reactivity to the quarantine, rather than their personality per se. This would not imply that personality is unimportant in infectious risk but that its influence is accentuated, and perhaps only becomes apparent, when people high in IS are placed in social contexts that activate their concerns about negative evaluation. A parallel argument could be made for the HIV studies. Patients with this condition are highly stigmatized in most societies, and they often come from social and ethnic groups that are socially and economically marginalized. And as Cole has shown in his research on closeting, the adverse health effects of IS only become apparent when gay men are public about their sexuality, a stance that presumably increases the frequency with which they perceive and experience interpersonal slights, rejection, and hostility.

In summary, these findings suggest that social context may play a large role in shaping whether IS comes to exert adverse influences on health. This may be especially true for characteristics like introversion. In particular, it may be that introverts are generally able to construct nonthreatening social worlds, a phenomenon referred to as niche-picking (Scarr & McCartney, 1983). However, if they are forced into a particular setting they lose this control and become vulnerable to adverse health outcomes.

Incidentally, a similar pattern has been seen in an animal model of HIV infection. Research by Capitanio and colleagues has shown that sociability (a trait that has been compared to extraversion in humans; Gosling & John, 1999) explains variability in outcomes related to SIV, a simian model of HIV infection. One study rated rhesus macaques on sociability and later inoculated them with SIV. Animals lower in sociability had great viral loads four and 6 weeks later, compared to their more sociable peers. (Capitanio, Mendoza, & Baroncelli, 1999). In a more recent study, macaques rated as high or low on sociability were assigned to stable and unstable social conditions. Unstable social conditions induce a highly stressful state in adult male monkeys (Capitanio, Mendoza, Lerche, & Mason, 1998). In the stable condition, animals met daily in groups of three, whereas in the unstable condition, group size and membership varied daily. Animals were formed into the social groups for 100 min per day, three to 5 days per week. Following 3 days of exposure to the social groups, animals were inoculated with SIV. Results indicated that within the first 2 weeks post inoculation, low-sociable animals displayed more submissive behavior and higher interferon-stimulated gene activity, but only in the unstable group. In addition, the association between low sociability and interferon-stimulated gene expression was mediated by submissive behavior (Capitanio et al., 2008). The expression of interferon-stimulated genes was associated with viral set point. Thus, much like what we see in the human studies, Capitanio et al.'s work suggests that the social context amplifies the association between IS and infectious disease.

Cancer

Nineteen studies examined the relations of IS to cancer morbidity and mortality, although only three (16%) revealed positive findings (see Table 3). The majority of the studies (68%) focus on introversion, while the others look at social anxiety, submissiveness, psychological inhibition, shyness, and Type D personality.

First, two nested case-control studies were used to examine the association between social anxiety and incident cancer in men (Dattore, Shontz, & Coyne, 1980; Kavan, Engdahl, & Kay, 1995). In both cases results indicated that social anxiety did not discriminate the cancer group from the controls. However, both studies also used an automated stepwise regression with the full set of MMPI factors, leading to the problem of model overfitting. This increases the risk that unimportant variables are retained in the model and/or important ones are left out (Babyak, 2004).

In addition, two prospective studies examined the association between a range of IS constructs (inhibition, submission, shyness, and social anxiety) and cancer outcomes. First, Cole, Kemeny, Taylor, and Visscher (1996) measured concealment of homosexual identity among 222 homosexual and bisexual males and then followed them over 5 years (this study is also included in the section on infectious disease). Over the course of the follow-up, 20 participants were diagnosed with neoplastic diseases, which were mostly cancers of the skin or face. Results indicated that gay men who concealed their homosexual identity experienced a significantly higher incidence of cancer. Given the 5-year follow-up period and the fact that participants were healthy at study entry, it seems likely that IS preceded the development of cancer in this cohort, but we cannot be certain because some neoplastic conditions emerge over long periods of time. However, the small num-

ber of events raises concerns about overfit models. Second, Persky, Kempthorne-Rawson, and Shekelle (1987) examined the relationship between personality and cancer incidence and death among 2018 healthy men. Three IS constructs were measured, including Cattell's submission and shyness factors and MMPI social introversion (a measure of social anxiety). Given the relatively large number of events (212 cancer diagnoses) and long follow-up (20 years), this is the strongest study testing the relations of submission, shyness, and social anxiety to cancer outcomes. Even so, none of the IS constructs was significantly associated with cancer morbidity or mortality.

Seven population-based prospective studies followed healthy individuals over time to examine the role of introversion in cancer incidence (Hansen, Floderus, Frederiksen, & Johansen, 2005; Lillberg, Verkasalo, Kaprio, Helenius, & Koskenvuo, 2002; Nakaya et al., 2010, 2006, 2003; Nakaya, Tsubono, Nishino, et al., 2005; Schapiro et al., 2001). All of them yielded nonsignificant findings despite the use of well-validated personality measures and large sample sizes. For example, in a study by Nakaya, Tsubono, Nishino, et al. (2005), 890 cases of cancer were identified in years four through seven of follow-up. As the authors note, the exclusion of participants diagnosed in the first 3 years of follow-up is a major strength of the study because subclinical symptoms caused by as-yet diagnosed cancers may have influenced responses to the personality questionnaire.

Six additional studies examined the association between EPI/EPQ introversion and morbidity and mortality among patients already diagnosed with cancer. Five of these studies yield nonsignificant findings (Aarstad, Heimdal, Aarstad, & Olofsson, 2002; Canada, Fawzy, & Fawzy, 2005; Dean & Surtees, 1989; Greer, Morris, & Pettingale, 1979; Ratcliffe, Dawson, & Walker, 1995), while one suggested that introversion is associated with mortality among breast cancer patients (Hislop, Waxler, Coldman, Elwood, & Kan, 1987). Each study was based on a small sample ($Ns < 140$) with relatively few events (< 40). In fact, the findings for each of these studies should be interpreted with caution given problems associated with model overfitting and statistical procedures (including the use of univariate screening of potential confounds and automated stepwise procedures to identify significant predictors).

Denollet (1998) examined Type D personality (see page 34 for more information on this construct) and rate of cancer diagnosis and death among 246 men who had been diagnosed with coronary heart disease. At the 6–10-year follow-up, 12 patients had been diagnosed with cancer (nine cancer-related deaths and three cancer cases who were still alive). Type D personality emerged as a significant predictor of both cancer incidence and mortality. However, given the small number of adverse events ($n = 12$) and the large number of potential covariates, this study is vulnerable to the problem of model overfitting. Even if there is a statistically genuine association between Type D and cancer incidence among CHD patients, reverse causality is a plausible alternative explanation. CHD gives rise to inflammation, which promotes social withdrawal and contributes to some cancers (Coussens & Werb, 2002; Mantovani, Allavena, Sica, & Balkwill, 2008). Thus, a comprehensive set of controls is needed to control for this scenario and other related baseline differences in disease characteristics.

Finally, submissiveness was measured among 224 newly diagnosed lung cancer patients via Cattell's 16 Personality Factors

(Stavraky et al., 1988), yet Cattell's submission factor was unrelated to risk.

Cancer summary. These data do not provide convincing evidence for an association between IS and cancer. Positive findings did emerge in a handful of fairly weak studies, but in the large, population-based work, there was no consistent evidence for an association. Null findings were also reported in 5/6 studies of patients with existing cancers. It is worth noting that all seven of the large studies and all of the patient studies measured introversion. This raises questions about how to interpret the negative findings because, as we noted above, people can endorse traits of introversion for variety of reasons, some of which don't involve social-evaluative concerns. Also, none of the cancer studies occurred in a socially threatening context (as was case the case for the infectious disease research) that would be expected to trigger evaluative concerns or unmask the introverts who have them. Thus, on the basis of these studies, we cannot be certain whether the null results arose from imprecise measurement of IS, or reflect a negligible influence of IS on cancer development and progression.

The studies of IS that did report associations with cancer focused on inhibition. This was the case in the studies of Type D (Denollet, 1998) and the concealment measure used by Cole's group (Cole, Kemeny, Taylor, & Visscher, 1996). Thus, it could be that cancer progression is affected by one component of IS, the tendency for inhibited behavior, but not others. However, it is worth keeping in mind that all of the positive findings with inhibition were based on small samples and relatively few events, so it is difficult to draw any definitive conclusions about their meaning, much less whether they reflect differential influences of various IS components. Indeed, a large prospective study with measures of these components would be needed to test this hypothesis directly.

Cardiovascular Disease

Nineteen studies in this review examined the relationship between IS and CV morbidity and mortality (see Table 4). Overall these studies yielded consistent evidence of a link between IS and CV risk, with all but four studies reporting significant associations, after controlling for a number of potentially important confounders. However, as discussed below, the majority of studies with positive findings have methodological features that complicate their interpretation.

Five prospective studies examined whether variables reflecting IS predict CVD morbidity and mortality among initially healthy adults. All three studies on social avoidance/anxiety yielded significant findings, such that increased anxiety/avoidance was associated with increased hypertension incidence (in the unadjusted model; Rääkkönen, Matthews, & Kuller, 2001), greater risk of myocardial infarction (MI; Shen et al., 2008) and increased risk for CHD and CVD mortality (Berry et al., 2007). It should be noted that the Berry study is the best powered of the studies (404 CHD deaths, 541 CVD deaths, and 412 non-CVD deaths), and that could be why it finds the most robust effects. Moreover, the studies by Berry and colleagues and Shen and colleagues statistically controlled for a comprehensive set of traditional risk factors, as well as psychosocial risk factors such as hostility.

Whiteman et al. (1997) examined the association between submissiveness and CV risk in a cohort from the Edinburgh Artery Study ($N = 1,592$). Results indicated that, among both men and women, increased submissiveness was associated with decreased risk of nonfatal MI, whereas among women only, increased submissiveness was associated with decreased risk of total MI (combined fatal and nonfatal). However, in the adjusted models, submissiveness remained independently associated with risk of MI among women only. These findings suggest that submissiveness is a protective factor, which is opposite to what we would expect. (We discuss this counterintuitive finding later in the article.) Finally, in the only CVD study looking at introversion, the EPI was administered to 29 767 residents of Miyagi Prefecture in northern Japan (Nakaya, Tsubono, Hosokawa, et al., 2005). Over an 11-year follow-up, there were 90 deaths from ischemic heart disease and 131 deaths from stroke, yet introversion was unrelated to risk for these outcomes.

Fourteen studies examined the association between IS and clinical outcomes in patient populations. One administered Cattell's Sixteen Personality Factors Questionnaire to 246 patients at discharge from acute MI (Carpeggiani et al., 2005). Results indicated that neither Cattell's submission nor shyness factors were independently associated with cardiac risk. However, the results of this study should be interpreted with caution because of problems associated with stepwise variable selection and model overfitting.

The other 13 studies examined the association between Type D personality and cardiac outcomes among CHD patients. These studies yielded fairly consistent associations, though some important conceptual and methodological features complicate interpretation of their results. In particular, most of the studies had quite low ratios of events to predictors, which raises concerns about spurious results due to model overfitting. Moreover, patients were often categorized as Type D when they scored above established cutoffs on both general distress (depression, anxiety, irritability) and social inhibition, yet the rationale and procedures for looking at this combination of traits was inconsistent across articles (see Denollet, Pedersen, Ong, et al., 2006; Denollet, Sys, & Brutsaert, 1995; Denollet et al., 1996). In one article, Denollet and colleagues argue that the inhibition of the expression of substantial emotional distress may be damaging to health (Denollet et al., 1995). In another article, they argue that these personality traits may promote social alienation and depression, which have also been linked to poor outcomes in cardiac patients (Denollet et al., 1996). And, in a more recent publication, the authors argue that the social isolation resulting from inhibited personality may potentiate the adverse effect of negative emotions (Denollet, Pedersen, Ong, et al., 2006). These are all plausible hypotheses, which could be tested using statistical moderation or mediation. However, most of these studies group patients into Type D and non-Type D categories, without separately examining the main effects of social inhibition and negative affect, or the interaction between the two (T. W. Smith, 2011). Finally, many researchers have expressed concerns about the approach of categorizing patients as Type D or not based on whether their scores exceed the scale cutoff. This approach makes the somewhat questionable assumption that Type D traits are best conceived as categorical rather than dimensional. In fact, a recent study used taxometric procedures to address this question in a sample of 1012 healthy young adults (Ferguson et al., 2009). Graphical representations and fit indices indicated that

Type D is more accurately represented as dimensional rather than categorical. Apart from the conceptual problems with the cutoff approach, there are methodological concerns as well. In particular, dichotomizing continuous variables increases the probability that spurious associations with an outcome will emerge (MacCallum, Zhang, Preacher, & Rucker, 2002). See T. W. Smith (2011) for additional commentary on Type D personality. Readers should keep these concerns in mind as we summarize the Type D findings below.

Five of the Type D studies with positive findings had too few adverse events (range from 6–22) given the number of predictors and covariates entered into the statistical models (Denollet & Brutsaert, 1998; Denollet, Holmes, Vrints, & Conraads, 2007; Denollet et al., 1995; Pedersen et al., 2007, 2004). However, Type D studies based on larger samples and/or longer follow-up times (Cserép et al., 2010; Denollet, Pedersen, Ong, et al., 2006; Denollet, Pedersen, Vrints, & Conraads, 2006; Denollet et al., 1996; Denollet, Vaes, & Brutsaert, 2000; Martens, Mols, Burg, & Denollet, 2010; Schiffer, Smith, Pedersen, Widdershoven, & Denollet, 2010) to some degree bolster confidence in the findings above. For example, two studies followed relatively large samples over 5 years. The first followed 319 patients with CHD, 48 of whom experienced a cardiac event or revascularization over the course of the study (Denollet et al., 2000). The second study followed 337 patients with CHD, and 46 cardiac events occurred over the course of the study (Denollet, Pedersen, Vrints, & Conraads, 2006). In both cases, results indicated that Type D was significantly associated with cardiac risk, independent of biomedical factors and psychological factors like anxiety, depression, and perceived stress. Moreover, in a study with a follow-up period of six to 10 years, Denollet et al. (1996) showed that Type D patients had a four-fold risk of mortality compared with non-Type D patients over a six to 10 year follow-up. In particular, 27% of Type D patients died, whereas only 7% of non-Type D patients died. However, based on these findings it's unclear whether the action is with negative affectivity or social inhibition, so it's difficult to know what this means for IS. However, a recent study by Cserép et al. (2010) examined this question directly. The authors reported 81 adverse events (i.e., major adverse cardiac or cerebrovascular event including death) over a 5-year follow-up. Type D emerged as a significant predictor of CV risk, even after controlling for a comprehensive set of preoperative and operative characteristics. Importantly, this study also examined the main effects of social inhibition and negative affectivity, and both were significantly associated with risk, providing some support for the IS argument we're making here.

Only one study examining the impact of Type D on cardiovascular risk reported null findings (Pelle et al., 2010). In this study Type D was measured in 641 outpatients with chronic heart failure. There were 123 deaths over a mean follow-up of 3.13 years, yet Type D was unrelated to both cardiac mortality and all-cause mortality. Moreover, in analyses with continuous scores neither social inhibition, negative affectivity, or the interaction between the two were independently associated with mortality (both cardiac and all-cause).

Taken together, the Type D studies provide consistent evidence that Type D adds to the prognostic information available from biomedical risk factors. However, many of these studies identify a small number of events relative to the number of predictors, which

raises serious concerns about the validity of the parameter estimates reported. That said, the effect that overfitting has on regression coefficients is not uniformly positive. An overfit model may yield estimates that are overly optimistic, which would favor rejecting the null, but it can also cause estimates to be overly pessimistic (Babyak, 2004). The fact that Type D emerges as predictor of CHD outcomes across nine different samples, and always does so in the same direction, makes it seem quite unlikely that this is all reducible to statistical artifact. Moreover, two recent meta-analyses of Type D studies suggest that the effect is quite large (Denollet, Schiffer, & Spek, 2010; Reich & Schatzberg, 2010). For example, in their meta-analysis of nine prospective studies (6121 cardiac patients), Denollet and colleagues showed that Type D was associated with a more than 3-fold increased risk of poor prognosis.

However, we continue to have conceptual and methodological concerns about this literature that make us reluctant to offer strong conclusions about it. First, all of the Type D studies focus on patient populations, and this makes it very difficult to disentangle the temporal ordering of events, i.e., whether IS precedes disease or vice versa. Second, though a handful of studies have suggested that the combination of social inhibition and negative affect is particularly detrimental to CVD patients (see Denollet, Pedersen, Ong, et al., 2006; Denollet et al., 1996), it remains unclear conceptually and mechanistically why this disposition would pose any greater health risk than being elevated on either trait in isolation (T. W. Smith, 2011).

Finally, distress forms a major part of the Type D construct, and itself is a well-established risk factor for CVD (Suls & Bunde, 2005). Because most of the studies reviewed here do not examine the Type D components separately, it is entirely possible that the morbidity and mortality findings are driven by the influence of distress. If so, these studies would have limited relevance to our discussion of IS. A handful of recent studies have addressed this issue directly. As noted, the study of cardiac surgery patients, by Cserép et al. (2010), found that social inhibition was uniquely predictive of adverse outcomes. In other studies, authors have made strides methodologically, analyzing Type D components dimensionally and considering main effects of social inhibition, negative affectivity, and the interaction between the two (i.e., Coyne et al., 2011; Grande et al., 2011; Pelle et al., 2010; the Coyne and Grande studies are reported in more detail in the All-Cause Morbidity and Mortality section). Although none of these studies showed a main effect of social inhibition, Grande and colleagues found an interaction between social inhibition and time such that mortality in patients with high social inhibition was higher early in the follow-up period and lower in later periods. Thus, the evidence for a main effect of social inhibition is inconsistent across the Type D studies, an issue that should be taken seriously moving forward.

CVD summary. The findings for CVD are mixed. The most persuasive evidence for IS comes from large prospective studies that have linked social anxiety/insecurity to hypertension (Räikkönen et al., 2001) and susceptibility to MI (Shen et al., 2008), and a 30-year study that linked social avoidance to CHD morbidity and CVD mortality (Berry et al., 2007). The latter findings are methodologically compelling because of the long follow-up and large sample size (i.e., $N = 2,107$, with greater than 400 events in each analysis).

However, the CVD literature contains some null findings, which raise concerns to be taken seriously. In particular, introversion was unrelated to mortality from ischemic heart disease and stroke (Nakaya, Tsubono, Hosokawa, et al., 2005), and submissiveness was associated with reduced risk of nonfatal MI in men and women and total MI in women only (Whiteman et al., 1997). The null findings for introversion are consistent with those in the cancer studies. Although it is unclear what to make of the submissiveness findings, the authors suggest that the Personality Deviance Scale submissiveness items emphasize contentment with personal role. Example items include “When in a group, I have been quite content to be led” and “I have been happy to play second fiddle.” To better understand this pattern of findings, it may be important to distinguish “voluntary” from “involuntary” submissive. For instance, a person may choose to behave submissively to increase belongingness in a particular group or family. In contrast, involuntary submissive responses are more likely to occur in the context of social threat, and they may be more taxing to the body (Gilbert & McGuire, 1998; Newton, 2009). That issue aside, the meaning of these items is difficult to ascertain, because their wording conflates submissive tendencies and feelings of contentment. Either of these constructs, or their interaction, could underlie the reported associations.

Interpretation of the submissiveness findings are further complicated by research on the role of dominance in CVD. For example, a recent cross-sectional study of healthy older couples showed that spouse ratings of dominance were associated with coronary artery calcification in both men and women (T. W. Smith et al., 2008), and in a prospective study of older men, self-reported dominance was significantly associated with increased risk of combined nonfatal MI and fatal CHD over the course of the 8-year follow-up (Siegman et al., 2000). Finally, in an early study of males between 39 and 59 years of age, socially dominant interview behaviors were positively related to CHD incidence over an 8.5-year follow-up period (Houston et al., 1992). Given these data, we cannot be sure if the submissiveness findings discussed above are about dominance or submissiveness.

Finally, the positive findings across the Type D studies are suggestive of an association between IS and morbidity/mortality in cardiac patients. It's impressive that significant associations have emerged in nine independent samples, and done so above and beyond the effects of such a variety of traditional biomedical predictors. However, as we have noted, these studies have conceptual and methodological features that dampen confidence in their findings and make it unclear just how much they are tapping the inhibition element of IS in the way that we conceptualize it.

All-Cause Morbidity and Mortality

Twenty-nine studies examined the association between dispositional IS and all-cause morbidity and mortality. As shown in Table 5, the findings were inconsistent across studies. Twenty prospective studies assessed the relationship between IS and all-cause morbidity and mortality in samples of initially healthy individuals. The majority of these focused on introversion, but there was also a handful of studies looked at various IS constructs including shyness (G. A. Kaplan et al., 1994), social avoidance (Barefoot et al., 1989; Hearn, Murray, & Luepker, 1989), behavioral inhibition (Kubzansky et al., 2009), and social anxiety (Trumbetta, Seltzer,

Gottesman, & McIntyre, 2010). However, all of these studies yielded null findings, with the exception of the findings reported by Trumbetta and colleagues indicating that social anxiety was protective among men who died between the age of 55 and 75. This association is in the opposite direction to what our IS conceptualization would predict.

Of the 15 prospective studies looking at introversion, five were relatively small, with samples that ranged from 450 to just over 1,000, adverse event frequencies that ranged from 138 to 424, and follow-up times that ranged from three to 7 years. Three of these studies showed a positive relationship between introversion and all-cause mortality (Fry & Debats, 2009; Maier & Smith, 1999; Wilson, Mendes de Leon, Bienias, Evans, & Bennett, 2004), while two reported null findings (Korten et al., 1999; Weiss & Costa, 2005). However, among the five studies with samples ranging from 1200 and 3000 and adverse event frequency ranging from 127 to 503, one showed a positive association between introversion and mortality (Iwasa et al., 2008), while the other four studies yielded null findings (Chapman, Fiscella, Kawachi, & Duberstein, 2010; Martin, Friedman, & Schwartz, 2007; Mroczek & Spiro, 2007; Taylor, Whiteman, Fowkes, & Lee, 2009). Thus, as the studies get larger, the proportion of positive results decreases.

This trend continues among the largest introversion studies. In particular, there were five studies with sample sizes greater than 5,000, well-validated measures (the NEO and the EPI), and relatively long follow-ups (6–21 years). Three reported null findings (Huppert & Whittington, 1995; Oishi & Schimmack, 2010; Shipley, Weiss, Der, Taylor, & Deary, 2007), one reported significant findings in the expected direction (Wilson et al., 2005), and one reported significant findings in the unexpected direction (with introversion emerging as a protective factor; Ploubidis & Grundy, 2009). Thus, even among the most highly powered studies, the findings for introversion are inconsistent at best. However, it's difficult to interpret these results given that individuals can score high on introversion without experiencing social evaluative threat.

Consistent with this reasoning, Oishi and Schimmack (2010) found no evidence of a main effect of introversion on mortality but did report a significant interaction between introversion and residential mobility. Specifically, findings indicated that introverts who had moved frequently as children were more likely to have died during the 10-year follow-up than other subjects. Among extraverts, childhood residential mobility was unrelated to mortality risk as adults. This suggests that the impact of introversion on mortality depends on contextual factors like the early life social environment. These findings resemble those that emerged in the viral challenge and HIV progression studies, in that they suggest the effects of IS on health are accentuated, and maybe only become apparent, when sensitive individuals find themselves in social contexts where their fears get activated and they are more likely to perceive and experience slights, rejection, conflict, etc. Moreover, this type of interaction is suggestive of a causal association, although potential third variables cannot be ruled out definitively.

Nine studies examined the relationship between IS constructs and mortality in populations of medical patients. Two of the three studies focusing on introversion yielded significant findings, although in one case the findings were based on only seven deaths (Morris, Robinson, & Samuels, 1993), and in the other, the follow-up period was only 6 months (Carinci et al., 1997). The third study followed patients with chronic renal insufficiency

(Christensen et al., 2002). There were 49 deaths over an average follow-up period of 49 months, yet introversion was unrelated to all-cause mortality risk.

Six studies examined the impact of Type D personality on all-cause mortality among cardiac patients, with two reporting positive findings (Aquarius et al., 2009; Pedersen, van den Broek, Erdman, Jordaens, & Theuns, 2010) and four reporting null findings (Coyne et al., 2011; de Voogd et al., 2009; Grande et al., 2011; Volz et al., 2011). Importantly, the studies that yielded significant effects were based on a small number of adverse events (<30), while the studies that did not show an effect tended to be larger (48 events in one and greater than 150 events in two). Moreover, Coyne and colleagues and Grande and colleagues tested the statistical interaction on continuous social inhibition and negative affectivity scores, which is the established approach for testing synergistic effects (T. W. Smith, 2011). There was no evidence of interaction or main effects in either of the studies, although Grande et al. (2011) found a significant social inhibition by time interaction due to a decreasing hazard ratio for social inhibition over time. This means that mortality in patients with high social inhibition was higher early in the follow-up period and lower in later periods.

All-cause morbidity and mortality summary. Findings across studies suggest that risk of all-cause mortality is unrelated, or at best weakly related, to the extent of IS. In regard to the prospective studies, only four of the 20 (20%) yielded positive findings, and one of these effects became nonsignificant after controlling for other personality traits and level of cognitive and motor functioning. That said, all but four of these studies focused on the introversion-extraversion dimension of personality. Thus, it's difficult to say whether IS *per se* is unrelated to all-cause morbidity/mortality, or the null findings reflect the imprecise measurement of IS by means of introversion. The latter interpretation is suggested by Oishi and Schimmack's (2010) findings on the interaction between introversion and residential mobility in the prediction of mortality. This work suggests that introversion is only detrimental to health when people are forced into socially evaluative or difficult environments, like having to make new friends each year at school. If this is true, it may explain why most of the studies that examined main effects of introversion on health in free-living community populations failed to document associations. Finally, the effects of IS on mortality were weak in the survival studies, with only four of the nine studies (44%) yielding significant findings.

Discussion

This review yielded three major findings. First, the evidence strongly suggests that an interpersonally sensitive disposition heightens risk for morbidity and mortality from infectious diseases. There is also some evidence suggestive of an influence for IS in the context of CVD, though we have lower confidence in these results because of design and analysis features that often make these data difficult to interpret. There is minimal evidence for a role of IS in cancer outcomes and overall mortality. Second, the positive studies in this review provide reasonably persuasive evidence that IS precedes disease. In particular, many studies used long follow-up periods and the viral-challenge designs measured personality prior to the inoculation. Moreover, studies have ruled

out some of the most plausible alternative explanations based on confounds. Many of the studies have done a thorough job measuring and adjusting for baseline health, lifestyle factors, and sociodemographics, and in doing so provide reasonably persuasive evidence that these variables are not creating a spurious association between IS and health. Of course, there may be other confounds that have not been considered, and for that reason it's impossible to make any definitive causal inferences from the human findings. But when the human findings are considered in conjunction with data from SIV animal paradigm, which is much more tightly controlled, the weight of the evidence suggests that a cautious causal conclusion may be in order, at least for infectious diseases. Third, the review of evidence suggests that the effects of IS are accentuated in contexts that activate social-evaluative concerns. This was most apparent in studies of introversion, a construct that showed weak links to disease outcomes, except in socially threatening circumstance. In particular, introversion was significantly associated with disease when participants were exposed to early life residential mobility (Oishi & Schimmack, 2010), when they were quarantined with strangers in a novel environment (as in the viral challenge studies; Broadbent et al., 1984; Cohen et al., 1997; Totman et al., 1980), and when they were living with the stigma of HIV (Ironson et al., 2008). As we noted earlier, introverts are generally able to create social environments in which they feel comfortable—that is, niche-pick (Scarr & McCartney, 1983)—and this may explain most of the null findings in studies that assessed introversion. Other IS constructs may show more direct linkages to health outcomes because they are rooted in concerns about social evaluation and aren't as easily coped with by selecting into comfortable environments. We now explain these findings in more detail as they relate to the research questions posed at the beginning of the article.

Are Interpersonally Sensitive Individuals at Risk for Adverse Health Outcomes?

We found evidence for an association between IS and morbidity and mortality, but its strength varied across disease settings. The most uniformly positive evidence was in studies of infectious disease, where eight of the nine studies (89%) indicated that IS was associated with adverse outcomes, ranging from accelerated progression of HIV to increased susceptibility to the common cold. There were also consistent findings in studies of CVD, where 15/19 articles (79%) reported detrimental outcomes among those high in IS. However, these patterns were most robust in Type D studies, which as noted pose numerous interpretational problems. By contrast, studies looking at cancer outcomes and overall mortality yielded mostly null results. However, this pattern of results may be a function of the types of IS measures used in each disease category, a hypothesis that we discuss in detail below.

What Is the Nature of the Association Between IS and Disease?

Temporal precedence. There is strong evidence from the animal model of HIV and the viral challenge studies to indicate that IS precedes the onset of disease. For example, the studies on SIV progression in macaques measured personality prior to infection, and in the viral challenge studies, healthy participants rated

personality dimensions prior to inoculation. Thus, it is unlikely that disease-rated factors influenced the personality assessments in this domain. In contrast, it's difficult to determine the temporal ordering of events in the long-term studies of humans, especially those that are based on patients with medical illnesses like HIV and CVD. More work is needed to determine whether the associations observed in this literature are truly from IS to health. To do that, future studies will need to measure IS in the early stages of disease, carefully control for disease factors that may influence self-reports of personality and use long follow-up times. However, we recognize the challenges of implementing these types of studies, especially when it comes to disentangling personality factors from disease-related psychological changes.

Potential confounders. Given that we cannot manipulate IS experimentally, and we have to rely on quasiexperimental and longitudinal designs to examine its relationship to health, there is no way of definitively ruling out all third variables. In general, the studies did a good job of accounting for potential third factors. For instance, most of the studies statistically adjusted for socioeconomic status and other demographic variables. There was no evidence that the findings were driven by gender, ethnicity, or socioeconomic status, although any of these factors may represent important moderating variables. Unfortunately, the majority of studies in the review did not test such models. There is burgeoning evidence that gender has a moderating influence, especially in regard to studies of submissiveness and CVD (Newton, 2009), and it will be important for future research to explore this more fully with respect to other IS constructs.

In regard to other potential confounders, IS constructs are associated with lifestyle factors that could affect disease. Introversion has been linked to reduced physical activity but also a reduced likelihood of cigarette smoking (Hampson, Goldberg, Vogt, & Dubanoski, 2007; Kikuchi et al., 1999; Nakaya et al., 2010; Plouhidis & Grundy, 2009). Moreover, recent studies have linked IS components to treatment adherence in HIV/AIDS (Pereira et al., 2004). However, the majority of studies in this review showed effects of IS constructs over and above health-related behaviors. For instance, one study showed that the introversion-mortality association was reduced by 8% after controlling for physical activity, yet introversion remained an independent predictor of mortality (Wilson et al., 2005). In sum, health behaviors may be an important pathway linking IS to health, but they do not fully explain this association.

Baseline disease severity represents another health-related variable that may confound the association between IS and health outcomes, especially in patient populations. The majority of survival studies in this review statistically controlled for disease severity, although some did a better job than others. For example, some of the samples were too small to support the number of covariates needed to fully account for baseline illness. This was particularly true in the studies of cardiac prognosis. Moreover, it's difficult to adequately control for how sick patients are at baseline, because in most cases markers of prognosis are rough, and even when several are combined they tend to be highly collinear. These problems even plague studies that start with healthy young people and track the emergence of later disease because conditions like CVD and cancer develop over lengthy periods of time and noninvasive measures of subclinical disease (e.g., intima-media thick-

ness as a marker of carotid atherosclerosis) have only recently become available.

There are a number of other potential third variables (e.g., birth complications and pollution exposures) that could give rise to inflated and spurious associations between IS and disease risks. These are very tough to rule out unless one does a very thorough birth cohort study that follows people over the life course. However, Capitano's SIV studies (Capitano et al., 2008, 1998) provide initial evidence that a construct related to IS can have effects on health that are not dependent on these mechanisms. This is because the animals are housed in well-controlled environments, and factors like health behaviors and medication use don't come into play. Moreover, the three studies that revealed significant personality by context interactions (two from the human literature and one based on Capitano's SIV model) provide indirect evidence that IS is acting causally. Specifically, it's difficult to conceive of a plausible alternative explanation for why personality would be associated with health in some contexts but not others (e.g., introversion in the context of high but not low residential mobility in early life).

Related psychological constructs. Even though studies in this area have tested for many of the plausible explanations related to confounding, an issue that's been less thoroughly considered is how elements of IS might overlap with other psychological constructs that have been related to disease. Of particular importance in this regard are variables reflecting negative emotions. Constructs reflecting IS reliably covary with negative mood (Ayduk et al., 2001; Cole et al., 1997; Heiser et al., 2003). And there is abundant evidence for a role of specific mood states (depression, anxiety) and clusters of these states in the development and progression of CVD (Carney & Freedland, 2003; Cohen et al., 1995; Suls & Bunde, 2005). As we noted above, negative emotions represent an especially important alternative explanation for the Type D findings, which if substantiated, would limit their relevance to IS.

With that said, studies of IS in other disease contexts have tested for mediating and confounding influences of negative emotions and found little evidence of it. For instance, concealment of homosexual identity continued to predict risks of cancer and infection, independent of depression, anxiety, and negative affect (Cole, Kemeny, Taylor, & Visscher, 1996). Moreover, in two distinct studies inhibition was associated with faster HIV progression, independent of anxiety and depression (Cole et al., 2003; Cole, Kemeny, Taylor, Visscher, & Fahey 1996). Finally, Shen et al. (2008) reported that social anxiety predicted a greater risk of MI in a large sample, independent of depression and negative emotion more generally. These findings are consistent with evidence from the neuroimaging literature, which shows that social inhibition and negative affectivity have distinct neural correlates in response to socially threatening stimuli (Kret, Denollet, Grezes, & de Gelder, 2011). With that said, the IS literature to date has considered a fairly narrow set of mood states and would benefit from a more thorough examination of where they overlap with IS. Of special importance here is low positive emotionality, one of the defining features of introversion (Costa & McCrae, 1992b) and also a risk factor for infectious disease (Chida & Steptoe, 2008; Pressman & Cohen, 2005).

IS also has some overlap with the personality dimension of hostility, which has been identified as a predictor of morbidity and

mortality from CVD. Hostility sits in a similar region of the interpersonal circumplex as IS constructs. In fact, the Cook-Medley questionnaire that's typically used to measure hostility is composed of four subscales, one of which taps social avoidance (Barefoot et al., 1989). A few of the studies reviewed here recognized this overlap and attempted to disentangle the constructs. In one of those studies all of the subscales of the Cook-Medley were administered, and analyses explored whether social avoidance predicted CVD while statistically controlling for the other dimensions (hostile affect, aggressive responding, and cynicism; Berry et al., 2007). Results indicated that social avoidance was an independent predictor, providing initial evidence that IS is an important variable in its own right. Yet other studies in the review reported evidence to the contrary. In particular, one study showed that social avoidance was unrelated to mortality, whereas the other three Cook-Medley subscales emerged as significant predictors (Barefoot et al., 1989). And in a third study by Hearn et al. (1989), none of the Cook-Medley subscales were significantly associated with mortality (Hearn et al., 1989). Despite the mixed nature of these findings, studies of other IS concepts suggest that the patterns observed herein are not simply due to overlap with hostility. For example, recent evidence indicates that social anxiety is associated with risk of myocardial infarction, independent of anger and hostility (Shen et al., 2008). Together, these findings suggest that IS's health effects partially, though not completely, overlap with those of hostility. There seems to some independent influence of each trait. All that being said, too much focus on this question of independence may be counterproductive, in the sense that impedes progress toward an understanding of where the psychological "action" really is. That's because recent evidence suggests that health effects may be most potent at the juncture where these constructs intersect. Specifically, in one study it was the overlap between social inhibition and cynical hostility that most strongly related to HIV pathogenesis (Cole et al., 2003). This finding suggests that when studies attempt to isolate these constructs' effects through statistical control, they are likely to be "throwing the baby out with the bath water," by removing the common variance that is most influential in shaping later disease outcomes.

Elements of IS also share variance with trait dominance, which has been linked to coronary heart disease. Submissiveness is particularly relevant here because submissiveness and dominance are often viewed as opposite poles on a continuum, thus measures of them are expected to be negatively correlated (Newton, 2009). However, we would argue that low dominance is not necessarily equivalent to high submissiveness, and vice versa and that the constructs do not lie on a perfect linear continuum. For example, Moskowitz and Cote (1995) reported a correlation of -0.47 between IAS-R submissiveness and dominance, which reflects an overlap of around 22%. Even assuming these correlations are attenuated due to measurement error, the evidence does not support the interpretation that these constructs are on opposite ends of a single bipolar continuum (Wiggins, Trapnell, & Phillips, 1988). However, we recognize that we cannot draw any firm conclusions based on a single correlation and that more research is needed to delineate the extent of overlap between submissiveness and dominance. Moreover, the body of evidence linking dominance to CHD risk is inconsistent with our hypothesis that submissiveness is associated with increased risk of morbidity and mortality, thus more studies that actually measure submissiveness (rather than

inferring it from a lack of dominance) are needed to get traction on this issue.

Finally, elements of IS by definition overlap with the kinds of social niches that people create for themselves, and how they subjectively experience those environments. And in almost every domain of health studied to date, benefits of high-quality relationships have been found (Cohen & Wills, 1985; Hawkey & Cacioppo, 2010; Seeman, 1996). This raises the question of whether IS might simply be acting as a proxy for constructs like social isolation, trait loneliness, or perceived support. To address this possibility studies have adjusted for social constructs when considering the health effects of IS. For example, the research linking concealed homosexual identity to accelerated HIV progression documented associations after adjustment for social support (Cole, Kemeny, Taylor, Visscher, & Fahey, 1996). Another study found that introversion was associated with mortality risk in older adults, even after the number of regular social activities was statistically controlled (Wilson et al., 2005). These studies provide preliminary evidence that IS has an independent association with disease outcomes.

But as was the case with hostility, too much focus on independence could be problematic here. It seems quite likely that social behavior is one of the major routes through which IS comes to affect health. Those who possess elements of IS tend to have less diverse networks, perceive less support from those networks and report feeling more lonely (Cohen et al., 1997; Cohen, Sherrod, & Clark, 1986; Denollet et al., 1996; London et al., 2007; Swickert, Rosentreter, Hittner, & Mushrush, 2002). These experiences may have direct biological consequences (Cacioppo & Hawkey, 2003; Cohen et al., 1997; Seeman, Berkman, Blazer, & Rowe, 1994) with relevance for disease. Consistent with this line of reasoning, one study in the review found support for a meditational hypothesis, wherein introversion predicted mortality in older adults by reducing the number of socially engaging activities in which they participated (e.g., attending religious services, part-time or full-time employment; Wilson et al., 2005). Findings like these suggest the importance of future research that considers more complex accounts of how IS and other social risk factors act together to influence health outcomes. See Gallo and Smith (1999) for a more detailed discussion of the interplay between personality and social context in relation to health.

Do the IS Constructs Share a Common Health-Relevant Core?

The review found that each of the concepts reflecting IS components related to increased risk of morbidity and/or mortality. However, findings were more consistent for some concepts than others. Here we comment on what can be learned from these differential associations.

Introversion. Just under half of the studies in this review focused on a single feature of IS- the introversion-extraversion dimension. Although introversion emerged as a significant predictor in several studies, it was not consistently associated with health risk. In general, the findings for introversion were very strong in the infectious disease category, but very weak across the all-cause morbidity/mortality studies. How do we explain these findings? Introversion has been defined and measured as a preference for social situations, and unlike the other IS constructs, it does not

specifically tap concerns about negative social evaluation or psychological inhibition. However, there is a subgroup of introverts who have these tendencies (Bienvenu et al., 2004; Downey & Feldman, 1996; Heiser et al., 2003; Pilkonis, 1977), and this heterogeneity may explain why the effects are weaker (or “watered down”) for introversion compared to some of the other constructs.

Consistent with this hypothesis, the results of multiple studies reviewed here suggest that introversion’s effects on health are most pronounced (and may only be apparent) when people are forced into situations with the potential for negative social evaluation. These situations don’t match the situational preferences held by most introverts. Specifically, introversion was consistently associated with worse health outcomes when participants had been forced into settings that involved early life residential mobility, being quarantined with strangers for 5 days (as in the viral challenge studies), or living with the stigma of HIV. In addition, Capitanio’s group showed that low-sociable monkeys who were assigned to an unstable social condition showed SIV-related immune changes, whereas low-sociable monkeys in the stable condition and highly sociable monkeys did not. Thus, it appears to be the combination of introversion and a potentially aversive social environment that most strongly affects health outcomes.

As mentioned above, introverts may be especially good at seeking out nonthreatening environments, and to the extent that they are successful at doing so may avoid some of the health damaging effects of IS. However, people are sometimes forced into environments that are a mismatch for their preferences. This could happen as a consequence of job relocations or financial crises that force people into undesirable employment or crowded housing. Even job promotions or societal pressures to follow certain career paths may result in personality-environment mismatches. More work focusing on what kinds of social contexts are good vs. bad matches for introverts, and people high in IS more generally, would help clarify the mechanisms that underlie these patterns and may also help to guide applied efforts to direct people to environments where they are most likely to realize their potential.

Given that IS individuals are sensitive to threat in their social worlds, we expect social context to be an important moderator across the various constructs. In other words, we’d expect to see main effects of the IS constructs characterized by social fears and insecurities because individuals are likely to carry these concerns across social situations. Although these individuals may seek out suitable environments (similar to what we described for introverts), it may be impossible to avoid fears of disapproval and rejection entirely. In addition, we’d expect to see exaggerated effects of these IS constructs in the context of objectively threatening social environments. In fact, B. W. Smith and Zautra (2002) have already shown evidence for this type of interaction in a study of arthritis patients. Their findings indicated that IS was positively associated with disease activity, and this association was amplified during times of increased interpersonal stress. Similarly, Cole’s group showed that rejection sensitivity was significantly associated with accelerated disease progression and that the effect was exaggerated among men who were “out of the closet” (and more fully exposed to the threat of homophobic social rejection; Cole et al., 1997).

Other constructs. Given that there were fewer studies on other indicators of IS, like inhibition, social avoidance, rejection

sensitivity, and submissiveness, there is a less strong basis for making inferences about their relative associations with health. Measures of inhibition emerged as a relatively strong predictor of disease. First, concealment of homosexual identity and a composite measure of social inhibition (including introversion, social avoidance and emotional inexpression) related to risks for infectious disease (although these studies have the added component of exposure to stigma (HIV, homosexuality)). Second, Type D (the combination of social inhibition and negative affect) consistently predicted outcomes among cardiac patients, albeit in studies with some important weaknesses. Third, there was some indication that inhibition may play a role in cancer development and progression. In particular, measures of concealment of homosexual identity and Type D personality were associated with adverse disease outcomes.

Very few studies in the review actually measured cognitive and affective components of IS directly. The one study that focused specifically on rejection sensitivity revealed an association with HIV progression (Cole et al., 1997). However, the findings were mixed for studies that examined social anxiety/insecurity. Two studies found that social anxiety/insecurity predicted CVD risk (Räikkönen et al., 2001; Shen et al., 2008), another found a protective effect of social anxiety on all-cause mortality (Trumbetta et al., 2010), and another focused on cancer yielded null results (Persky et al., 1987). It is unclear whether these mixed findings reflect differential influences of IS across disease settings, or a somewhat unstable phenomenon. Clearly, more prospective studies with measures of these constructs are needed to clarify the nature of these associations. This is important because constructs like rejection sensitivity and social anxiety directly tap social-evaluative concerns, which may be at the heart of the IS disposition.

There was hardly any evidence for health effects of submissiveness. Moreover, research suggests a link between dominance and risk of CHD, which is inconsistent with the view that IS as we’ve described it has repercussions for health (see above for a more detailed discussion). It remains unclear whether these null/inconsistent findings mean that our model of IS is wrong about the relevance of submissiveness, or whether the studies just haven’t done the phenomenon justice by failing to measure it well or consider the distinction between voluntary and involuntary submissiveness. In particular, involuntary submissive responses are more likely to occur in the context of social threat, and they may be more taxing to the body (Gilbert & McGuire, 1998; Newton, 2009). Based on Newton’s review (2009), of submissiveness/dominance and CV functioning both gender and social context may be important moderating factors, yet we cannot begin to sort this out within the scope of our review, because there is too little evidence available. In regard to the remaining IS concepts, all but one of the seven studies on social avoidance, shyness, and childhood behavioral inhibition (ratings of shyness and withdrawal) yielded null findings. It is unclear what to make of these findings given that social avoidance and shyness capture aspects of social inhibition, which was more clearly associated with risk.

Can this pattern of findings teach us anything about what’s common and unique about these indicators of IS and what exactly matters for health? At this point, the best we can do is draw some tentative conclusions. While it remains unclear whether there is a toxic core that’s common across the IS constructs, we would

hazard a guess that social and psychological inhibition fall within the toxic core and that submissiveness and shyness falls outside of this zone. As for the other IS constructs, the evidence isn't pointing either way.

We found evidence that both the cognitive-emotional and behavioral aspects relate to health outcomes, especially in regard to rejection sensitivity, social anxiety, and inhibition. However, with the likely covariance between the cognitive/emotional and motivational/behavioral aspects of IS, it may be difficult to disentangle one from the other in an observational study. In this regard, experimental studies are needed to manipulate the various components and hone in on what exactly drives biological changes. However, our findings point to the importance of distinguishing between constructs that represent preferences for social situations (e.g., introversion) and those that capture social fear/anxiety (e.g., social anxiety, rejection sensitivity) and/or its behavioral correlates (e.g., social inhibition). Whereas the former may only be detrimental in the context of social threat, the latter may be more directly associated with poor health.

Of course, these findings beg the question of whether introversion should be included in the IS style. On the basis of the empirical evidence, we believe that IS underlies some manifestations of introversion, yet introversion is too broad to capture IS specifically. In fact, if we were to create a measure of IS, we would not include introversion - we would focus on more specific motivational, cognitive/affective, and behavioral factors. Despite this, including introversion in the review led to a number of interesting observations, which merit further investigation. For example, it will be informative for later research to examine whether the observed interaction between introversion and social context is driven by a subgroup of high IS individuals or if there is a tendency for introverts to respond to socially threatening situations with IS cognitions, emotions, and behaviors.

Mechanisms Linking IS to Health

The evidence linking IS to adverse outcomes, particularly in infectious and coronary diseases, raises questions about underlying mechanisms. In this section we offer some initial thoughts on this issue, with the hope that they provide an agenda for later research. We note up front that little is currently known about the biological correlates of IS. So, much of this discussion is speculative in nature, and derives from generic biobehavioral models of the stress response.

Functional significance. To start, it might help to ask why sensitivity to others would influence whether a person gets sick? One answer to this question comes from research that considers the value of social relationships from an evolutionary perspective. According to Baumeister and Leary (1995), concerns about negative social evaluation may serve the basic human need for belongingness and acceptance. Belongingness needs are thought to have evolved from our ancestors' dependence on group membership for survival and reproduction. Specifically, in the environment of evolutionary adaptation, the motive to create and maintain social bonds would have increased the chances of group membership (and all of the benefits a group has to offer) and decreased the chances of social isolation. Thus, a great deal of human thought, emotion, and behavior is likely to have evolved to serve this fundamental interpersonal motive. In this regard, a focus on neg-

ative social evaluation may promote social connectedness by increasing sensitivity to social cues. In particular, if a person is able to detect signs of disapproval from others, she is in a better position to repair the social damage.

But how does this relate to health? According to Dickerson and Kemeny (2004) the selective pressures to belong have resulted in the evolution of a social self-preservation system. These authors maintain that situations that signal a threat to one's social status or social self-esteem (e.g., rejection, loss of status) trigger feelings of shame, which in turn, activate the HPA axis and proinflammatory pathways in the immune system. These biological adjustments elicit disengagement-related behavioral, cognitive, and motivational changes that are relevant to maintaining status within the group. Although these adjustments are short-lived, they can exact a toll on the body over time. In particular, repeated activation of adrenocortical and inflammatory pathways is thought to increase vulnerability to a variety of mental and physical illnesses (Cohen et al., 2012; Libby, 2006; Mohr & Pelletier, 2006; Slavich, O'Donovan, Epel, & Kemeny, 2010).

Plausible mechanisms. With this conceptual framework as a foundation, we now speculate about some behavioral and biological mechanisms that could underlie the associations we've observed between IS and certain disease outcomes. Throughout the article we've argued that the IS disposition is characterized by concerns about negative evaluation and defensive social behaviors. We also maintain that these tendencies predispose those who are interpersonally sensitive to experience aversive social interactions marked by rejection, disapproval, and conflict. For example, the tendency of IS persons to be vigilant for negative social evaluation may color their perception of others' behavior, setting the stage for an unintended misunderstanding, or the escalation of an already-tense interaction. As these encounters unfold, IS individuals may also become submissive or defensive, and by doing so further worsen the situation or its outcome. They'd also presumably be more threatened by any such abrasive interactions. This reasoning is consistent with previous models describing the impact of personality on exposure to social stimuli, as well as cognitive appraisals of and biological responses to those stimuli (Bolger & Zuckerman, 1995; Gallo & Smith, 1999; Millon & Lerner, 2003). As a consequence of these interactional tendencies, IS individuals will have difficulty establishing and maintaining close relationships, resulting in a more chronic sense of subjective isolation (see work by Downey and colleagues on rejection sensitivity in the context of intimate relationships; Downey & Feldman, 1996; Downey et al., 1998).

This characterization suggests that IS might be thought of as having both acute and chronic repercussions that affect health through somewhat distinct mechanisms. On an acute basis, both concerns about negative evaluation and abrasive social encounters would be expected to activate the SNS and the HPA axis, and reduce parasympathetic nervous system drive on some organ systems. There is considerable evidence from laboratory studies documenting effects of this nature (Bosch et al., 2009; Dickerson & Kemeny, 2004; Dickerson et al., 2004; Kiecolt-Glaser et al., 2010; Repetti, Robles, & Reynolds, 2011). Moreover, laboratory studies have also shown that individuals higher in IS constructs such as introversion and Type D personality show exaggerated autonomic responses to social threat compared to their less sensitive counter-

parts (Habra et al., 2003; Hinton & Craske, 1977; Houtman & Bakker, 1991; Williams et al., 2009).

On a chronic basis, stable difficulties with social isolation, lack of social support, and recurrent conflict within established relationships are likely to be important mediating variables. Indeed, socially isolated persons display higher levels of cortisol, epinephrine, and norepinephrine in everyday life than their more integrated peers (Adam, Hawkley, Kudielka, & Cacioppo, 2006; Cacioppo et al., 2002; Hawkley & Cacioppo, 2007), and similar patterns are observed among those who are integrated but in abrasive relationships (Repetti, Wang, & Saxbe, 2011; Saxbe, Repetti, & Nishina, 2008), and those who report decreased social support (Seeman et al., 1994). More generally, people who score high on constructs that map onto IS show greater daily epinephrine and norepinephrine output (Miller, Cohen, Rabin, Skoner, & Doyle, 1999) and increased ANS activity (Cole et al., 2003). In contrast, a recent study linked rejection sensitivity to hypocortisolism, which may be due to a history of high cortisol responses among these individuals (Tops, Riese, Oldehinkel, Rijdsdijk, & Ormel, 2008).

As we noted earlier, this physiologic milieu would presumably have implications for the functioning of bodily tissues regulated by the HPA axis and the ANS (McEwen & Stellar, 1993). Receptors for the products of these circuits are found in the cardiac, vascular, metabolic, skeletal, immune, and nervous systems, among others. With recurrent perturbations these systems would be expected to manifest various forms of dysregulation. Of particular relevance here are the impairments in antiviral defenses that typically accompany interpersonal stress (Bailey et al., 2003; Glaser & Kiecolt-Glaser, 2005; Irwin & Cole, 2011), which could underlie the heightened vulnerability of IS individuals to the common cold and accelerated HIV progression. Also of relevance here are the metabolic consequences—like fat accumulation, insulin resistance, and cholesterol imbalance—thought to result from prolonged stress-related activation of the HPA and ANS (Bjorntorp & Rosmond, 1999; Brindley, McCann, Niaura, Stoney, & Suarez, 1993; Marques et al., 2009; Thayer & Sternberg, 2006). Persons who endorse elements of IS, like social anxiety, display more atherogenic lipid profiles and higher waist-hip ratio (Landén et al., 2004). If prolonged, metabolic alterations of this nature might accelerate the early stages of atherosclerosis, and help to explain the differential vulnerability to CVD that we observed in the literature. Also of likely importance in explaining CVD vulnerability is chronic inflammation, a process that contributes to the progression of all phases of the atherosclerotic process (Libby, Ridker, & Hansson, 2009). IS constructs have been associated with relatively elevated levels of inflammatory biomarkers, like C-reactive and IL-6 (Chapman et al., 2009; Conraads et al., 2006; Denollet et al., 2003, 2009). Moreover, various downstream psychosocial consequences of the IS disposition, like abrasive encounters and social isolation, have been repeatedly linked to inflammation (Cole et al., 2007; Kiecolt-Glaser et al., 2010; Miller, Rohleder, & Cole, 2009; Repetti, Robles, & Reynolds, 2011). Finally, the physiologic milieu recurrently evoked by IS might also be expected to have direct influences on the function of the myocardium and vasculature, as manifest by markers of preclinical cardiovascular disease, like endothelial dysfunction, arterial stiffness, and carotid atherosclerosis, and later in clinical manifestations, like episodes of ischemia, arrhythmias, and myocardial infarction (Harris & Matthews,

2004; Krantz & Manuck, 1984; Manuck et al., 1995; Thayer & Sternberg, 2006; Treiber et al., 2003).

Consistent with this reasoning, there is evidence that social inhibition is associated with elevated total peripheral resistance (Howard & Hughes, 2012) and that public self-consciousness is prospectively associated with increased carotid atherosclerosis (Matthews, Owens, Kuller, Sutton-Tyrrell, & Jansen-McWilliams, 1998). However, not all of the evidence points in this direction. Some prospective studies have failed to detect links between IS constructs and markers of preclinical CVD (Niaura et al., 2000).

We emphasize that much of this mechanistic discussion is speculative. On the basis of the broader literature on stress physiology (Glaser & Kiecolt-Glaser, 2005; Miller, Chen, & Cole, 2009; Sapolsky, Romero, & Munck, 2000) we suspect the broad contours of our arguments are accurate. However, there has been very little mechanistic research dedicated to IS per se, and as a result we've only been able to assemble strands of evidence to substantiate our hypotheses. Moreover, it is important to keep in mind that IS is not itself a disease-causing entity; it acts in conjunction with genetic liabilities, relevant exposures, and other factors to move pathogenesis forward. In summary, the arguments we've outlined here are suggestive of mechanistic hypotheses that future research should pursue, as opposed to firm convictions.

In the course of doing so, one of the difficult questions future research will have to address is why IS seems to have disease-specific associations. The mechanistic routes we have speculated about are thought to be gateways to a broad array of medical conditions (McEwen, 1998; Miller, Chen, & Cole, 2009). And indeed, research in animals indicates that HPA and SNS dysregulation can heighten vulnerability to diseases across the spectrum we've considered, including respiratory infection, various cancer, autoimmune conditions, and atherosclerosis (Manuck et al., 1995; Sheridan et al., 1998; Sternberg et al., 1989; Thaker et al., 2006). Assuming this is the case, it remains unclear why IS would show effects in infectious and coronary diseases, but not in cancer. This will be a difficult but important question for later research to address. That said, the disease-specific pattern of findings observed here bears much similarity to the broader literature on stress and health, where consistent associations are seen for infectious and coronary disease, but not cancer (see Cohen, Janicki-Deverts, & Miller, 2007).

Future Directions

This area of research is in its infancy. Though our review suggests that IS heightens vulnerability to certain medical problems, much remains to be learned about the nature of this association. In this section we outlined seven areas of inquiry that we believe are essential for progress.

One of the first priorities for research in this area is instrument development. To progress, the field needs a validated method for measuring IS, which captures the motivational, affective, cognitive, and behavioral components we've specified. Assuming that IS has dispositional structure we suggest, this measure should display high test-retest stability over time. It should also correlate with the measures in our review that we argue tap parts of it (e.g., rejection sensitivity, social inhibition, and social avoidance). Moreover, it should correlate with how people behave in social contexts and how they respond physiologically. Specifically, peo-

ple who score high on IS should display vigilance for social threat, be defensive and inhibited and have an exaggerated response to social rejection. Finally, a measure of IS should show evidence of discriminant validity, such that its impact can be distinguished from that of related but distinct constructs such as hostility and negative affect.

A second priority, once a good measure is established, is to reexamine the prospective relationship between IS and health outcomes, particularly in the case of cancer and all-cause mortality. Although many of the studies that looked at these outcomes reported null findings, the majority of them focused on introversion, which is an imprecise measure of IS. Thus, we expect that a solid measure of IS (as opposed to introversion) will emerge as an important predictor of both cancer and overall mortality. We also predict that this measure of IS will be consistently associated with cardiac outcomes, and thereby strengthen our confidence in the CVD findings. This is important because most of the current evidence on CVD comes from studies of Type D personality, which provide a suboptimal test of the IS-CVD relationship.

A third priority is to situate our measure of IS empirically with respect to other relevant constructs, such as negative affectivity, hostility, dominance, and social isolation. We must determine whether IS is acting independently of—or synergistically with—each of these constructs. On the basis of current theory and research, we expect IS to have some overlap with these constructs, inasmuch as many of them could function as partial mediators of its effects on disease-relevant biology, e.g., IS acting via perceived social isolation to diminish positive affect and thereby alter HPA outflow. But IS should also have distinct relations with health outcomes, which are not fully explained by other constructs, and reflect its unique capacity to shape experiences of the social world.

A fourth priority should be to evaluate whether the health effects of IS are magnified in contexts that activate social evaluative concerns. For example, common cold studies could be conducted where IS (rather than introversion) is measured and acute biological measures are taken in quarantine, where participants spend five to 7 days living with strangers in a novel environment. Given that this social context is likely to trigger social-evaluative concerns among high IS participants, we predict that these individuals will be more vulnerable to infection than their low IS counterparts. Thus, we expect to replicate the common cold findings shown with introversion, although the magnitude of the effect will likely be stronger in the case of IS. Finally, additional field studies similar to that of Oishi and Schimmack (2010) would shed light on the interaction between IS and real-world contextual factors.

A fifth priority would be to identify plausible motivational, cognitive/emotional, and biological mediators of disease risk. For example, a laboratory study could be conducted to examine how high IS individuals respond to ambiguous social situations. We expect these individuals to show increased vigilance, biased cognitive appraisals, and aberrant HPA and SNS responses, yet it is unclear whether hormonal activity will be exaggerated or blunted given the inconsistencies in the current literature. Moreover, in the context of a common cold study, participant cognitive/emotional, behavioral, and biological responses to the quarantine scenario could be measured as possible mediators of the association between IS and risk of infection. We expect that perceptions of negative social evaluation and aversive social interactions will

emerge as important mediators and that they will be accompanied by biological changes that set the stage for disease risk.

A seventh priority is to unravel the levels at which the social environment moderates the relationship between IS and health. It is unclear whether the moderating role of the social environment is most likely to act at the cultural, group, or dyadic level. For example, we may see effects at the cultural level of analysis when there is a mismatch between IS traits and cultural norms or values. This could manifest such that the effects of IS on health are more profound in cultures that value individualism compared to collectivism. Moreover, we may see stronger effects of IS in males compared to females given gender stereotypes that emphasize instrumentality and agency for men, and expressiveness, IS, and submissiveness for women (Prentice & Carranza, 2004). At the group level of analysis, we would expect the early family environment to play an important role, especially given the link between insecure early attachment and later IS tendencies (Downey & Feldman, 1996). On the other hand, we may also be able to identify particular social roles (e.g., specific occupations) that represent a good “fit” for IS individuals, and at the same time, clarify what it means to be a successful “niche-picker.” Finally, at the dyadic level of analysis, factors such as relationship quality, trust, and social support are likely to emerge as important moderators of the IS-health relationship.

Conclusions

This review suggests three conclusions about IS and health. First, the work to date provides initial evidence that individuals with nagging concerns about negative social evaluation are at increased risk for morbidity and mortality. However, the pattern of findings across studies suggests that the relationship differs across conditions; such that IS heightens susceptibility to negative outcomes from infectious diseases and maybe CVD, but not cancer. Second, temporal precedence has been established and many plausible confounds have been ruled out, at least for infectious outcomes, suggesting a tentative causal conclusion is in order. Third, the effects of IS are accentuated and may only become apparent, in contexts that activate social-evaluative concerns.

Despite these findings more work is needed to definitively establish the causal nature of this association, evaluate the role of other related constructs, identify the conditions where the effects of IS are more versus less pronounced, and explore the potential social, emotional, and biological mediators of these effects.

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