Mapping future directions to test biopsychosocial pathways to health and well-being

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Author Note

Keywords: biopsychosocial model; theory; subjective well-being; societal well-being; mental health; physical health; development

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Abstract

The original biopsychosocial (BPS) model by Engel, although important for challenging the biomedical model and adding psychological and social factors to the study of health, has long been criticized for being too vague and untestable. The BPS-Pathways model introduced by Karunamuni, Imayama, and Goonetilleke (2020) builds on the original model by making the model more specific and testable. The authors cite research that provides support for individual pathways between biological, psychological, and social variables that influence subjective well-being and physical health. The current commentary discusses three considerations for scientists and practitioners using the model, including 1) expanding the range of outcomes that should be considered within the model to include mental health and societal well-being, 2) considering how certain factors may fall into more than one category (biological, psychological, and/or social), and 3) considering ways that social factors may directly affect biology independent of psychological mediation. Future directions are discussed, which include considering biopsychosocial pathways across development, studying individual differences in susceptibility to specific biological, psychological, or social factors, and using rigorous methods such as randomized controlled trials and advanced statistical tools at the biological, psychological, and societal levels to test these pathways and create more effective interventions.

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Introduction

The introduction of the biopsychosocial (BPS) model was revolutionary for challenging the prevailing biomedical model when Engel proposed the BPS model in the 1970s (Engel, 1977). Engel originally proposed the BPS model to highlight the psychological and social factors that influence health, which were not considered in the biomedical model prominent in medicine at the time. Although the introduction of the BPS model was innovative and led to greater incorporation of social and psychological factors into medicine and health research, many have criticized the model for being too vague and untestable (Benning, 2015; Farre and Rapley, 2017; Ghaemi, 2010). As a result, an update to the BPS model outlining specific pathways linking biological, psychological, and social factors in a specific and testable manner is needed.

Overview

The BPS-Pathways model proposed by Karunamuni, Imayama, and Goonetilleke (Karunamuni et al., 2020) in this issue carefully examines the interrelationships among factors across 3 domains—biological, psychological, and social—to understand how these factors contribute to health and well-being. The purpose of the model is to better delineate these pathways between biological (B), psychological (P), and social (S) factors in order to make more specific and testable predictions than Engel's original BPS model (Engel, 1977; Karunamuni et al., 2020). The authors present causal evidence, consider epidemiological criteria, and use analytical reasoning to examine

each of the pathways in the model (B→P [i.e., biological factors to psychological factors pathway], B→S, P→S, P→B, S→B, S→P). In the literature, there are fewer studies focusing on some pathways than others. For example, there are many experimental studies demonstrating that changes in psychological factors cause biological changes in the brain, immune system, and epigenetics. There are fewer studies examining direct biological to social changes, for example, health conditions influencing social factors such as social norms or stigma. Karunamuni et al. (2020) effectively highlight the limitations and challenges of using the BPS-Pathways model and some future directions for using the model.

Biological, psychological, and social factors interact in this model to predict subjective well-being and physical health. However, subjective well-being and physical health can also influence each other as well as influence biological, psychological, and social factors in the BPS-Pathways model. Importantly, there is no set of factors (biological, psychological, or social) that has greater importance in the model than others. Rather, the strength of associations between individual factors across biological psychological, and social domains can be investigated individually. As a result, biological factors are not prioritized over psychological factors, for example. Clinicians and health practitioners can instead consider the range of biological, psychological, and social factors that may be influencing health and well-being. Based on the patient or client's particular circumstances, there may be factors with well-researched, robust influences on health that may guide clinicians to focus on that particular factor to most effectively improve health and well-being. The BPS-Pathways model uses analytical reasoning and considers causal evidence to present links between BPS factors while

the original biopsychosocial model separately considered how biological, psychological, and social factors were associated with health. The BPS-Pathways model carefully considers subjective experiences, or psychological factors, which is particularly important for understanding individual differences in response to factors. For example, a social factor such as a surprising life event may be interpreted positively by some, resulting in positive affect and excitement, while others may react to a surprise with fear and anxiety, thus leading to different behavioral (S→P pathway) and biological responses (S→B pathway mediated by psychological factors, as described in the BPS-Pathways model). Similarly, high levels of biological arousal may be interpreted positively by some, leading to more positive affect, but may be interpreted negatively by others as anxiety, leading to more negative affect (B→P pathway). The BPS-Pathways model stresses the importance of psychological interpretations of biological, psychological, and social factors.

I argue that the BPS-Pathways model answers the need for a more specific and testable model for understanding pathways between biological, psychological, and social factors. I further argue that researchers and clinicians who want to better understand and test these biological, psychological, and social pathways should consider using the BPS-Pathways model due to its improvement upon previous models in specificity, testability, and attention to how subjective experiences may change pathways in the model. The goals of this commentary are to 1) outline additional considerations for those looking to use the BPS-Pathways model in their own work, and 2) to present promising future research directions while using the model.

Considerations for the BPS-Pathways model

The BPS-Pathways model improves upon the main critiques of Engel's biopsychosocial model by making the model more specific and testable and providing specific examples of BPS factors that are associated with one another. Considerations for scientists and practitioners using the model include: 1) expanding the range of outcomes that should be considered within the model beyond subjective well-being and physical health, 2) considering how certain factors may fall into more than one category (biological, psychological, and/or social), and 3) considering ways that social factors may directly affect biology independent of psychological mediation. These considerations are discussed below.

First, the paper by Karunamuni and colleagues (2020) focuses on the outcome of subjective well-being, which is predicted by biological, psychological, and social factors in the model, though there is a secondary focus on physical health as an outcome in the model. Subjective well-being was chosen as the primary outcome because Engel's model emphasizes the importance of considering an individual's subjective experience within their life context. Subjective well-being is dynamic over time due to changing conditions. Subjective well-being incorporates mental health measures that are not typically included in physical health outcomes, though subjective well-being and physical health are typically correlated with one another (Cross et al., 2018). Subjective well-being as an outcome is situated within the psychological domain in the BPS-Pathways model. Although subjective well-being is an umbrella term that incorporates aspects of mental health including negative and positive affect, life satisfaction and eudaimonic well-being, it would be informative to use the model to test aspects of mental health that do not fall under the umbrella of subjective well-being. Subjective

well-being inherently depends on one's own self-rated assessments, which do not always align with one's functioning. For example, some individuals with psychological disorders such as personality disorders or those experiencing a manic episode do not report any issues with affect, life satisfaction, or well-being even though they are experiencing significant disruptions in functioning (Berk et al., 2007; Hart et al., 2018). Some individuals with anorexia nervosa may be dangerously underweight yet still do not acknowledge they have a problem nor report deficits in subjective well-being (Gregertsen et al., 2017). Another example is an individual with a substance use disorder or gambling disorder who does not report that their addiction interferes with their subjective well-being yet may have significant problems with functioning (el-Guebaly et al., 2012). As a result, though subjective well-being does significantly overlap with mental health, there are aspects of mental health that are distinct from subjective well-being. I argue that the model will be useful to researchers studying psychological disorders that do not result in deficits in subjective well-being as outcomes. Considering these outcomes will broaden the clinical utility of the model, guiding researchers testing the biological and social inputs to subjective well-being, psychological functioning, and mental health. In this way, the model will be especially useful to researchers and practitioners in psychiatry, clinical psychology, and counseling psychology.

Physical health is within the biological domain though it is affected by psychological and social factors. As Karunamuni and colleagues (2020) suggest, it will be important for those testing the BPS-Pathways model to break physical health down into components. For example, researchers may separately examine cardiovascular

health, nutrition status, neurological health, and dental health to consider how factors may differentially affect various aspects of physical health. For example, high perceived discrimination may be detrimental to cardiovascular health (Lockwood et al., 2018), though associations with dental health may not be as strong. Understanding how BPS pathways differentially affect various aspects of physical health, and what factors affect the strength and direction of these paths across individuals will be important to consider.

Social factors such as social policies and social circumstances are considered in the model, though there are no society-level outcomes mentioned. *Societal well-being* (Allin, 2007), including measures such as life expectancy, rates of health problems, social welfare, gross domestic product (GDP), and rates of unemployment, poverty, and homelessness, may be influenced by biological, psychological, and social factors. Societal well-being should be considered as a social outcome for this model, though it is likely more difficult to test associations between biopsychosocial factors and societal well-being than for individuals' subjective well-being, mental health, and physical health. Similar to physical health, different aspects of societal well-being (e.g., life expectancy, poverty, unemployment) may be differentially affected by BPS factors. For example, a country may have high life expectancy while also having a low GDP just as an individual could have good neurological health but poor cardiovascular health. It will be important to better understand these outcomes by considering the individual components that make up health and well-being. Biological, psychological, and social factors all contribute to societal well-being, and developing a completer understanding which of these pathways may lead to the largest improvements in societal well-being will be important for researchers and policymakers. Examining societal well-being as an

outcome in the social factors system will make this model useful for guiding research in sociology, economics, political science, and other social sciences where society-level factors are targeted as outcomes. As subjective and societal well-being, and physical and mental health, are intertwined, it will be fruitful to investigate factors that robustly predict all four of these outcomes so that we can target these factors in interventions to produce more favorable outcomes. Figure 1 provides an expanded model adapted from Karunamuni et al. (2020) that examines subjective and societal well-being and mental and physical health as outcomes.

Second, given the complexity of human behavior and health, it is unsurprising that certain factors may be difficult to categorize as solely biological, psychological, or social. Karunamuni and colleagues (2020) list the accurate classification of factors as biological, psychological, or social as one of the challenges of using the model. Certain social factors are identified as being particularly challenging to classify. The accurate classification of BPS factors is a challenge for researchers using a BPS framework. An example of a challenging factor to categorize is behavior. Behavior is categorized as a psychological variable in the BPS-Pathways model as it is certainly heavily influenced by cognition, emotion, and other psychological factors at the individual level. However, there are strong biological and social components of behavior that make it challenging to only classify behavior as a psychological factor. For example, a reflex is a behavior that is an automatic response to a stimulus that occurs without conscious thought. In this instance, behavior can be classified as a biological factor when it occurs without conscious processing or moderation by psychological factors. In the case of addiction, strong biological impulses may override psychological factors to give rise to drug-

seeking behaviors even at the risk of negative future consequences (Volkow and Li, 2004). There may be different points during the stages of substance use disorders where psychological or social factors have stronger influences on behavior. At more advanced stages of the disorder, strong biological influences such as brain alterations due to long-term drug use (Gould, 2010) or compulsions (Lüscher et al., 2020) may override psychological or social influences on behavior. The BPS-Pathways model can be used guide research on substance use disorders where there are strong biological, psychological, and social influences on behavior. For example, psychological strategies or mindfulness-based interventions may be used to change cognitive, affective, and psychophysiological processes that could reduce craving for substances and produce changes in the brain that may lead to lower substance use (Garland and Howard, 2018).

Poverty is another complex factor that has biological, psychological, and social components, which is considered by Karunamuni and colleagues (2020) in the context of the BPS-Pathways model. Social factors include both social circumstances and sociocultural influences (Karunamuni et al., 2020), and as a result, poverty can broadly be thought of as a social factor that can influence one's daily experiences, resources, life circumstances, neighborhood, and community. However, poverty has multiple components, and all of these components may not clearly fall into the category of a social factor. As Karunamuni and colleagues state, poverty may be understood as both *material deprivation*, which can affect physical health through B→B pathways, and as a *social circumstance* that affects health through mediation by psychological factors (S→P→B pathway). In addition, poverty can be measured in terms of *absolute poverty*

or *relative poverty* (one's level of poverty compared to others in the community). Greater income inequality in a society (social factor) may contribute to lower *subjective socioeconomic status* by individuals (psychological factor), which is one's perception of their socioeconomic standing relative to others (Murali and Oyebode, 2004). The perception of lower socioeconomic status relative to others may lead to greater perceived stress and negative emotions (psychological factors), which can lead to deleterious mental and physical health outcomes over time (Evans and English, 2002; Evans and Kim, 2007). Subjective socioeconomic status may differ from objective measures of poverty or socioeconomic status and uniquely contribute to health (Adler et al., 2000), demonstrating the importance of considering the psychological perception of socioeconomic status as an additional component of poverty. In addition, poverty as a social circumstance may determine what type of neighborhood an individual lives in. If poverty makes an individual more likely to live in an unsafe neighborhood or a neighborhood with a lack of resources (social factors), that individual may experience negative influences on their physical health through poor nutrition, lack of exercise, or injury (biological factors). Individuals living in unsafe or low-resource neighborhoods may have greater perceptions of threat or hopelessness (psychological factors) (Bolland, 2003; Farver et al., 2000), which can in turn affect subjective well-being, mental health, and physical health.

Additionally, the factors of sex and gender are closely intertwined (Hyde et al., 2019) and can have biological, psychological, and social meaning. Sex may have important implications for biological and brain development (McEwen and Milner, 2017). Gender may be thought of as a psychological construct as it includes an individual's

gender identity, though there are biological inputs to gender identity (Polderman et al., 2018) and social implications if others interact with an individual in a gender-dependent manner (Dedovic et al., 2009; Fagot et al., 2012). As a result, scientists and practitioners using the BPS-Pathways model will have to consider whether factors fit neatly within one category or if the factor may fit within multiple categories. These considerations do not invalidate the model. Instead, the classification of factors should be carefully thought through when using this interdisciplinary model to plan future studies, analyses, and interventions in order to properly consider all BPS pathways that may be affecting outcomes.

Third, Karunamuni and colleagues (2020) assume that social factors (e.g., life events, social circumstances) are largely—but not solely—mediated through psychological factors such as perceived stress or negative affect. However, when designing research studies or public policies, researchers and policymakers must consider the direct pathways by which social factors might impact biological factors, such as living in a social environment or neighborhood where one is exposed to toxins that directly affect the brain (direct S → B path), which does not require psychological factors such as cognitive appraisal to operate. A recent example is the Flint water crisis where families in Flint, Michigan have been affected by high lead levels in the water for the past several years, which is associated with higher blood lead levels in children (Hanna-Attisha et al., 2016), a known predictor of cognitive and behavioral problems (Kordas, 2010). In this instance, the social environment—living in neighborhoods with high lead levels, which are typically more socioeconomically disadvantaged (Hanna-Attisha et al., 2016)—directly affects biology without a psychological mediator. A social

policy that could theoretically be implemented to reduce lead in water in a community is an example of a social factor that would directly affect a biological factor (lead levels in the body) without needing to affect psychological processes to produce change. It is still possible that the social policy may change psychological factors that further influence biology through an indirect pathway, but it is important to acknowledge both the direct and indirect pathways by which social factors influence biology. Likewise, living in certain neighborhoods may affect access to food (e.g., food deserts), which then directly affect nutrition, brain development, and health. Social factors such as neighborhood location and prevalence of community violence may also directly impact whether an individual is injured (a biological factor), which is another way that social factors may directly impact biology. Although individuals across the SES gradient can experience injury or toxic exposures, individuals in low SES neighborhoods are the most likely to experience these biological factors (Evans, 2004). Psychological mediators such as cognitive interpretations of threat, deprivation, or unpredictability from living in low-resource neighborhoods may lead to higher levels of stress, which could also affect biology, so there are likely both direct and indirect pathways by which social factors affect biology.

As Karunamuni et al. (2020) suggest, it will also be important to understand placebo and nocebo effects that may change the effects of a factor. An example of a nocebo is knowing one has been exposed to a toxin versus not knowing. Similarly, an example of a placebo is receiving an intervention to mitigate exposure to a toxin while being told it is an effective intervention versus receiving an intervention but being given no information on its effectiveness to better understand P→B pathways. Expectations

about side effects of a toxin or of better outcomes following successful mitigation of a toxin could change cognitive, affective, and neurobiological pathways, which then influence outcomes (e.g., Webster et al., 2016). Comparing outcomes across placebo and nocebo conditions will allow us to better understand S→B, P→B, and S→P→B effects. Future research should test what portion of social influences on biology operates directly or indirectly through psychological factors in order to understand which factors are most important to change in the context of interventions.

Future directions

Karunamuni and colleagues (2020) reviewed causal evidence to support direct associations between BPS factors in the model, though future research using experimental or randomized controlled trial (RCT) designs to test paths in this model are needed. Conducting experimental research is often more difficult in humans than in animals and introduces unique ethical considerations that can prevent experimentation. As a result, correlational studies are often used for research in humans. Some of these correlational studies are longitudinal, allowing us to test directionality of paths over time. A growing number of these studies are in large, nationally representative cohorts followed over years that measure biological, psychological, and social factors. Two examples of such cohorts, each of which have publicly available data, are the National Longitudinal Study of Adolescent to Adult Health (Harris, 2013) and the Fragile Families and Child Wellbeing Study (Reichman et al., 2001). However, the strongest evidence for causal effects require large RCTs, which are notoriously difficult to conduct and often introduce special ethical concerns. RCTs allow us to isolate factors that may cause changes in BPS pathways over time. It is important to note that not all variables can be

experimentally manipulated in humans (e.g., death of a loved one, maltreatment), and as a result, rigorous non-experimental study designs are needed to isolate the impact of the BPS factor of interest. Two examples of ongoing projects using RCT designs in humans to test causal BPS pathways (e.g., S→B, S→P, P→B, S→P→B) are 1) a poverty reduction RCT in families with young children to test whether changing socioeconomic factors improves child brain, biological, and psychological development (S→B and S→P pathways) (Noble, 2017; Rojas et al., 2020), and 2) a RCT testing whether reducing prenatal maternal depression improves infant mental health and brain development (P→B and P→P pathways) (Davis et al., 2018). In the first example of the unconditional cash transfer RCT for low-income mothers, researchers can test whether increasing family socioeconomic status through cash transfers improves childhood cognitive function (S→P), leads to more optimal brain development (S→B), and improves physical health (S→B). Due to the longitudinal nature of the work, researchers will also be able to test whether these effects operate through reducing maternal financial stress (S→P), improving the quality of maternal caregiving behaviors (S→P), improving child nutrition (S→B), increasing access to healthcare (S→S), or reducing toxin exposure by improving living conditions (S→B). In the second example of the prenatal maternal depression RCT, researchers can test how reducing prenatal maternal depressive symptoms improves child cognition and emotionality (P→P), leads to more optimal brain development (P→B), and improves offspring physical health (P→B). Researchers can test whether reducing prenatal maternal depressive symptoms improves child outcomes through improving the prenatal environment (P→B) or through

improving maternal caregiving behaviors due to continued reductions in postnatal depressive symptoms (P→P).

More research using rigorous designs will allow us to test the BPS model and test causality between biological, psychological, and social factors in humans. To understand how social factors influence psychological and biological factors, these tests should involve removing factors hypothesized to cause harm or adding factors hypothesized to improve health. This rigorous evidence is likely to have the biggest impact on policy and interventions by experimentally manipulating biological, psychological, and social factors in humans to improve health. For example, finding that a simple poverty reduction RCT positively impacts child development in a cost-effective manner (Noble, 2017) will provide some of the strongest evidence to date that improving social factors (e.g., socioeconomic status) leads to positive changes in psychological and biological factors. These designs will also allow for testing the strength of specific pathways to compare which mediating factors may have greater influence on health and well-being. Results from these studies can be used to guide interventions by identifying BPS factors and both direct and indirect BPS pathways that can be targeted in interventions to create the most positive change. These studies will also be helpful in ruling out alternative explanations for outcomes and identifying who may be most likely to benefit from interventions. Thus, studies with RCT designs should be used to test the BPS-Pathways model to better understand the pathways by which BPS factors influence health and well-being, and produce policy-relevant research findings.

Longitudinal structural equation modeling (SEM) is another method that should be used to assess pathways from BPS predictors to mediators and to outcome variables over time while controlling for potential confounding variables. Another promising option is to combine RCT and SEM methodology by using longitudinal SEM to examine changes in BPS pathways following an RCT to allow us to understand both causality and the direction of BPS pathways over time. Other favorable options for testing the BPS-Pathways model include simulation modeling and N-of-1 trials for understanding health and behavior of individuals (Vieira et al., 2017). Different scientific fields use differing methods depending on their research questions and various constraints, such as the impossibility of using RCTs to manipulate certain factors, including abuse, divorce, or other life events. These considerations are important when evaluating specific BPS pathways.

Individual differences in susceptibility to specific biological, psychological, or social factors must also be considered (Boyce and Ellis, 2005; Ellis et al., 2011). Individual differences could arise from a number of genetic, psychological, or social factors. Further, interactions between factors may influence the strength of paths in the model, so it is important to look beyond main effects. Karunamuni et al. (2020) discuss the moderation of BPS pathways by psychological factors including subjective experience and an individual's likes and dislikes, which is an important consideration. Moderation of BPS pathways by both biological and social factors should also be assessed. For example, recent evidence suggests that being born small for gestational age (biological factor), typically thought of as a developmental vulnerability, predicts greater susceptibility to differences in maternal sensitivity (Nichols et al., 2020). Infants

born small for gestational age attain lower wealth by age 26 years compared to their appropriate for gestational age peers if they are exposed to low maternal sensitivity. However, small for gestational age children attain higher wealth than their appropriate for gestational age peers if they are exposed to high maternal sensitivity (Nichols et al., 2020). Similarly, increasing evidence suggests that individual differences in neurobiological sensitivity to social context are important factors predicting psychopathology and well-being in adolescents (Guyer, 2020). Brain structure and function may be important biological moderators of social context when predicting psychological outcomes across development (Guyer, 2020), which must be considered in BPS models. Examining only main effects of social contexts or the quality of social interactions may lead to incorrect assumptions about the effect sizes of these variables on our outcomes of interest as a number of biological factors may be moderating these associations. Thus, carefully examining biological and social moderators of BPS pathways will lead to more precise estimates of effect sizes and a better understanding of risk and resilience.

Future research using the BPS-Pathways model should consider how the strength of associations between BPS factors may change across development. For example, the role of parents or caregivers likely has different implications for psychological and biological development in infancy than in adulthood, when other social partners may gain in importance for affecting psychological or biological factors. Sensitive periods of development during which BPS factors may have a larger impact on each other—and on health and well-being—than at other times in development should also be considered using the model. For example, the role of nutrition status in

predicting lifelong psychological well-being and neurodevelopment is strongest in the prenatal and early postnatal periods when the brain is rapidly developing compared to adulthood when much of brain development is complete (Doom and Georgieff, 2016). Of course, experimental work in children is even more challenging than in adults due to greater ethical concerns, which will make some of the pathways more difficult to test across development. Considering the role of development in the BPS-Pathways model will lead to more precise estimates about the strength and direction of associations over time. This developmental specificity will also inform the timing and type of interventions that should be implemented to improve health and well-being.

Conclusions

Understanding how biological, psychological, and social factors interact across development to influence health and well-being is crucial for creating effective interventions that improve functioning across multiple outcomes. The BPS-Pathways model effectively translates Engel's biopsychosocial model into a model that is more specific, testable, and provides scientific evidence for each of the pathways in the model. Future research using advanced statistical methods and rigorous research designs, including experimentally manipulating biological, psychological, and social factors and measuring changes in mental and physical health, subjective well-being, and societal well-being will be integral for testing this model, informing interventions, and producing policy-relevant results.

Research connecting the social sciences and medicine has been greatly influenced by Engel's biopsychosocial model in the past 40 years despite its limitations. The BPS-Pathways model improves upon the foundations of the biopsychosocial model

by creating a broad yet testable framework for analyzing associations between biological, psychological, and social factors that influence health and well-being. Although we must consider where complex factors like poverty, behavior, sex, and gender fit into the model, how factors may interact to predict health and well-being, and how paths may change across development, the BPS-Pathways model improves upon the original biopsychosocial model by making it more specific and ultimately testable. Researchers will benefit by using the model to plan future studies and interventions and to guide analyses of existing data. As a result, researchers studying interactions between BPS factors and practitioners working with patients and clients will benefit from using this framework to guide future research and practice.

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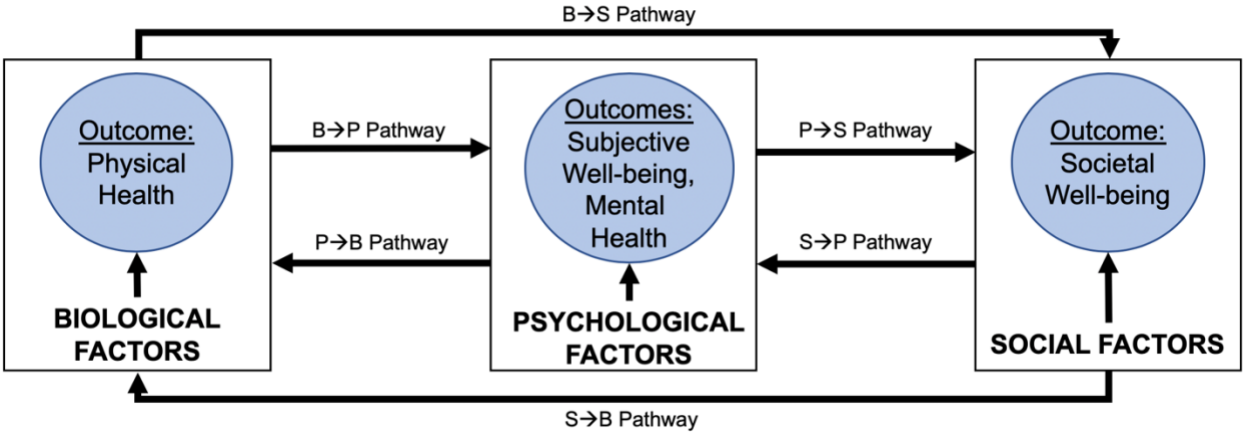

Figure 1. The BPS-Pathways model expanded to outcomes in the biological (physical health), psychological (mental health), and social domains (societal well-being). Biological, psychological, and social factors may interact to influence each of these outcomes. Adapted from Karunamuni, Imayama, and Goonetilleke (2020).