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Pain and Fifty Six Subsequent Wellbeing and Life Outcomes in a Multicountry Longitudinal Study

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Abstract

Background: Pain is a universal problem, with millions of people around the world experiencing some kind of pain. Despite its importance, rigorous longitudinal evidence on the longer-term effects of pain across various countries remains scarce.

Methods: This study takes one step toward addressing this gap by examining how pain predicts 56 diverse wellbeing and life-related outcomes using longitudinal data from 22 countries and one territory (N = 207,989). Country-specific regression analyses were conducted, with estimates pooled using random-effects meta-analyses.

Results: Adjusting for demographic and childhood factors, we find that pain in Wave 1 negatively predicts flourishing, happiness, life satisfaction, inner peace, mental health, purpose, relationship satisfaction, belonging, orientation to promote good, delayed gratification, hope, gratitude, showing love, physical health, physical exercise, financial and material security, financial comfort, owning home, and being in the top income quintile in Wave 2. Conversely, pain in Wave 1 significantly predicts higher traumatic distress, anxiety, depression, suffering, loneliness, perceived discrimination, health problems, and pain in Wave 2. Pain in Wave 1 has the largest positive effects on subsequent pain, health problems, and suffering, and the largest negative effects on subsequent secure flourishing, mental health, and financial security.

Conclusions: This study offers some of the most comprehensive country-wide evidence to date on the potential enduring impact of pain, providing valuable insights for policymakers, healthcare providers, and global organizations focused on reducing health inequalities and enhancing human wellbeing.

Plain Language Summary: Understanding the long-term consequences of pain in different countries is highly important. Here, we used rigorous statistical techniques to explore the link between pain and subsequent wellbeing and life outcomes across 22 countries. We found that pain is negatively linked to subsequent flourishing, happiness, life satisfaction, inner peace, mental health, purpose, relationship satisfaction, belonging, orientation to promote good, delayed gratification, hope, gratitude, showing love, physical health, physical exercise, financial and material security, financial comfort, owning home, and being in the top income quintile. Conversely, pain is positively linked to subsequent traumatic distress, anxiety, depression, suffering, loneliness, perceived discrimination, health problems, and pain. These findings inform future research on potential mechanisms as well as health policy design.

Introduction

Pain (i.e., an uncomfortable bodily sensation) is a universal problem. Pain is a common reason for visiting the emergency room with between 55% and 78% of people reporting pain upon arrival [1]. Pain management is costly: The United Kingdom spends nearly £5 billion annually on treating pain [2], underscoring the economic pressure on the national healthcare system. Beyond its financial toll, pain has detrimental consequences for different aspects of people's lives, threatening the goal of many national governments and global initiatives (e.g., Sustainable Development Goals) to promote human wellbeing. This situation suggests that robust evidence on how pain can affect wellbeing and life outcomes is critical for the development of nations. The present study contributes to that goal.

Previous research has looked at the effect of pain on wellbeing, demographic, and socioeconomic outcomes. However, much of the existing research has used cross-sectional data, which may overestimate the true effect of a predictor on an outcome [3]. Although longitudinal studies have been conducted, they have focused on specific countries and limited outcomes. For example, one study showed that, in the United States, pain was strongly associated with drug misuse [4] while other studies showed that, in Australia, people with pain tend to subsequently report lower life satisfaction [5]. While important, focusing on a single outcome can make it difficult to compare effects across different outcomes since samples and analytic choices may vary. Similarly, focusing on a single country or on countries within the same world region limits our understanding of whether the relationship between pain and wellbeing can be shaped by social and economic factors.

Here, we explore the association of pain with 56 subsequent outcomes across 22 countries and one territory using the first two waves of data from the Global Flourishing Study (N = 207,989) and the same participants across two waves. By examining the association of pain in Wave 1 with various wellbeing and life outcomes in Wave 2 (assessed approximately

one year later), this study sheds new and important light on the potential longer-term implications of pain. This "outcome-wide" analytic approach [6,7] allows us to compare the potential effect of pain on different outcomes in the same sample. Given limited resources, the ability to determine the direction of relationships and to robustly compare effects across outcomes is key for effective policy and intervention design.

In the health and wellbeing literature, a number of outcome-wide analyses have been conducted focusing on predictors unrelated to pain. For example, using longitudinal data from the United Kingdom, Steptoe and Zaninotto [8] found that socioeconomic status (SES) was associated with accelerated aging across six outcomes including physical capability, sensory function, physiological function, cognitive performance, emotional wellbeing and social function. In a different study, Steptoe and Fancourt [9] also used data from the UK and found that greater meaning in life was linked to better health, emotional, behavioural, and social outcomes. Using cohort data from the Nurses' Health Study II (NHSII), Chen et al. [10] found that greater parent-child relationship satisfaction was linked to better emotional well-being, lower risk of mental illness, and less eating disorders, overweight and marijuana use in young adulthood. Using volunteering as the predictor in a study with US adults over 50 years of age, Kim et al. [11] showed that volunteering was associated with better outcomes including risk of mortality, physical functioning, physical activity, and psychosocial outcomes like optimism and purpose. Despite this evidence, no prior outcome-wide study has been conducted with pain as the focal predictor.

The present study contributes to addressing this gap by adding the first outcome-wide study of pain involving 56 subsequent wellbeing and life outcomes. We do this using a sample of 22 countries and one territory; 207,989 participants; and two waves of panel data. We explore the following hypotheses:

1) Pain in Wave 1 will show statistically significant associations with numerous wellbeing and life outcomes in Wave 2.
2) The strength of associations between pain and wellbeing outcomes approximately one year later will vary to some extent by country.

This study finds that pain in Wave 1 negatively predicts flourishing, happiness, life satisfaction, inner peace, mental health, purpose, relationship satisfaction, belonging, orientation to promote good, delayed gratification, hope, gratitude, showing love, physical health, physical exercise, financial and material security, financial comfort, owning home, and being in the top income quintile in Wave 2. Conversely, pain in Wave 1 significantly predicts higher traumatic distress, anxiety, depression, suffering, loneliness, perceived discrimination, health problems, and pain in Wave 2.

Methods

This study was preregistered before data access at https://doi.org/10.17605/OSF.IO/4RGCA
The methodology for the analyses follows that described in Padgett et al. [12] and VanderWeele et al. [13]. The study design, sampling, and survey development for the Global Flourishing Study (GFS) are described elsewhere [14–17].

Here, we employ this data in an outcome-wide longitudinal design [6] incorporating Wave 2 data as part of a coordinated set of outcome-wide studies [18] to assess associations of pain on subsequent outcomes, minimizing individual researcher degrees of freedom, and maintaining a consistent analytic framework from which to compare across outcomes and studies.

Study sample

Wave 1 of the GFS included nationally representative samples from 22 countries and one territory: Argentina, Australia, Brazil, China, Egypt, Germany, Hong Kong (Special

Administrative Region of China), India, Indonesia, Israel, Japan, Kenya, Mexico, Nigeria, the Philippines, Poland, South Africa, Spain, Sweden, Tanzania, Turkey, the United Kingdom, and the United States (N = 207,919). The countries were selected to (1) maximize coverage of the world's population, (2) ensure geographic, cultural, and religious diversity, and (3) prioritize feasibility in Gallup's existing data collection infrastructure. Data for Wave 1 were collected from March 2022 to January 2024, except in China (March/April of 2024) [19]. Data for Wave 2 were collected from January 2024 to December 2024, with data in China collected at least six months after Wave 1 [19]. The GFS survey assesses aspects of wellbeing, including happiness, health, meaning, character, relationships, and financial security [20], along with other demographic, social, economic, political, religious, personality, childhood, community, health, and wellbeing variables. Gallup translated the GFS survey into multiple languages following the TRAPD (translation, review, adjudication, pretesting, and documentation) model for cross-cultural survey research [21]. Details about the translation, cognitive interviewing, and pilot testing phases of the GFS can be found elsewhere [16,22,23].

Sampling design

The precise sampling design varied by country to ensure samples were approximately nationally representative [17,21]. Follow-up for Wave 2 data collection relied on the respondent-provided contact information, with a minimum of three contact attempts. Additional information about the sampling design and weighting scheme for Wave 2 is available elsewhere [18,19].

Outcome-wide Analytic Design

An outcome-wide analytic approach [6,7] was employed to examine the associations of a single exposure (i.e., pain) with a range of subsequent outcomes. The outcome-wide analytic design has strengths of reducing researcher subjectivity/degree-of-freedom [24] in analysis by ensuring a consistent analytic strategy and the same set of covariates across models for all outcomes;

mitigates publication bias by reporting of results for all examined outcomes simultaneously; and provides insights into beneficial, detrimental, and null associations with the exposure [7].

Measures

Focal Wave 1 predictor variable

Pain in past 4 weeks was assessed using the question, "How much bodily pain have you had during the past 4 weeks?", with response options, A lot(1), Some(2), Not very much(3), and None at all(4). The responses to this item were collapsed with A lot/Some = 1; Not very much/None at all=0 as analysed in Wave 1 analyses for comparability of results [see 25].

Covariates

Country-specific analyses adjusted for 16 covariates (9 demographic and 7 childhood variables). Additional details on all variables can be found in the GFS Codebook (https://osf.io/cg76b) or Crabtree et al. [22]. Demographic variables included gender, year of birth (i.e., a set of dummy-coded variables with "1998-2005 (current age: 18-24 years)" used as the reference group; see all categories in Table 1), marital status, employment, education, religious service attendance, immigration status, religious affiliation (categories varied by country) and race/ethnicity. Retrospectively assessed childhood covariates included relationship with mother during childhood, relationship with father, parental marital status, subjective childhood financial status, abuse, feeling like an outsider growing up, self-rated childhood health; and childhood religious service attendance.

Outcome variables

Fifty-six outcomes were examined across domains of psychological wellbeing, psychological distress, social wellbeing, social participation, social distress, character and prosocial behaviour, physical health and health behaviours, and socioeconomic outcomes. The list of Wave 2 outcomes is given in tables below. Further details on item wording can be found in Crabtree et al. [22]. The outcomes included a flourishing index using two items in each of six

domains: happiness, health, meaning, character, close social relationships, and financial security [15,20,26,27], along with results of this index without financial security as this particular dimension is sometimes considered a means rather than an end. In the GFS sample, coefficient alpha for the twelve-item index was 0.88 and ranged from 0.75 in Nigeria to 0.94 in Japan.

Statistical analysis

Regression analyses with complex survey weights

Analyses were performed using R 4.5 [28] and the *Rglobalflourishing* package [29]. Weighted descriptive statistics for the sample (N=207,989) were estimated for each of the sociodemographic and outcome variables at both waves. All analyses, including imputation and attrition modeling described below, accounted for complex survey design by including weights, primary sampling units, and strata [19,30]. Within each country, we conducted a series of weighted linear, or weighted modified Poisson (for binary outcomes), multivariate regression analyses. Two models were used for each outcome, regressing each outcome on the focal exposure, first (Model 1) controlling only for the demographic and childhood variables, and second (Model 2) controlling also for principal components extracted from all contemporaneous Wave 1 variables (including baseline outcome) other than the focal exposure. Principal components were used to reduce the dimensionality of predictors to mitigate multicollinearity [31], while accommodating complex survey weights and missing data. The first seven principal components were used, and accounted for an average of 51.2% of the variability in all covariates [30], with additional principal components each explaining only 1-2%.

Meta-analysis

All analyses were conducted by country (results in Online Supplement) and random-effects meta-analyses were used to pool estimates across countries and to estimate heterogeneity (tau).

For each outcome, a global p-value for an omnibus test of evidence of association in any country is reported [32]. All meta-analyses were conducted using the metafor package [33].

Sensitivity to unmeasured confounded

We report E-values for all associations to evaluate the sensitivity of results to potential unmeasured confounding. An E-value is the minimum strength of the association on the risk ratio scale that an unmeasured confounder would need to have with both the outcome and the predictor, above and beyond all measured covariates, to explain away an association [34]. A high E-value signifies that an unmeasured confounder would need to have a strong association with both the predictor and the outcome to explain away the observed association. Approximate E-values can be obtained for continuous outcomes through scale conversions [34].

Missing data

The primary analyses utilize all participants from Wave 1, including those not reporting in Wave 2 by imputing missing data [35]. Multiple imputation (MI) by chained equations [36,37] was used for exposures, covariates, and outcomes. Twenty imputed datasets were used. Imputation was conducted separately by country to account for variation in the assessment of certain variables across countries (e.g., race/ethnicity and income). As a sensitivity analysis for possible misspecification of the imputation models [38], analyses were conducted using only Wave 2 respondents (complete case analysis [39]), with attrition weights [40] multiplied by the sampling weights for use in the analysis. Attrition weights were estimated using logistic regression models to calculate stabilized inverse probability of retention weights [41], incorporating a broad range of predictors [7,42,43].

Results

Table 1 shows summary statistics of sample demographic characteristics and the focal predictor. Overall, 12.1% of people reported a lot of pain, 32.1% some pain, 32.1% not very

much pain, and 23.6% no pain at all. Most people were middle age (19.4% were 30-39 years old, 16.8% were40-49 years old, 15.6% were 50-59 years old), 51.1% were female, 55.8% had between 9 and 15 years of education, and the countries with the greater percentage of people in the sample were the United States (18.4%), Japan (9.9%), and Sweden (7.2%). Summary statistics of demographic, childhood, and outcome variables can be found in Tables S1-4 in the Online Supplement by wave or attrition status and in Table S32 and S33 across countries and waves.

Tables 2 and 3 show the meta-analysed associations between pain at Wave 1 and wellbeing and life outcomes at Wave 2. Model 1 accounted for demographic characteristics and childhood circumstances and shows that pain in Wave 1 was significantly negatively associated with the following outcomes at Wave 2: Secure flourishing index (*B* -0.15; 95%CI -0.17, -0.13), flourishing index (*B* -0.14; 95%CI -0.16, -0.12), happiness (*B* -0.11; 95%CI -0.12, -0.09), life satisfaction (*B* -0.11; 95%CI -0.12, -0.09), current life evaluation (*B* -0.09; 95%CI -0.11, -0.07), future life evaluation (*B* -0.07; 95%CI -0.09, -0.05), optimism (*B* -0.06; 95%CI -0.08, -0.05), freedom to pursue what's important (*B* -0.08; 95%CI -0.10, -0.06), inner peace (*RR* 0.97; 95%CI 0.97,0.98), life balance (*RR* 0.97; 95%CI 0.96,0.98), sense of mastery (*RR* 0.98; 95%CI 0.97,0.99), meaningful activities (*B* -0.08; 95%CI -0.10,-0.07), understanding purpose (*B* -0.08; 95%CI -0.09,-0.06), self-rated mental health (*B* -0.12; 95%CI -0.14,-0.09), relationship contentment (*B* -0.07; 95%CI -0.09, -0.06), relationship satisfaction (*B* -0.08; 95%CI -0.09, -0.06), social support (*B* -0.06; 95%CI -0.07, -0.04), close friendships (*RR* 0.99; 95%CI 0.99, 0.99), government approval (*RR* 0.99; 95%CI 0.98, 1.00), say in government (*RR* 0.99; 95%CI 0.99, 1.00), belonging in country (*B* -0.05; 95%CI -0.06, -0.04), city/place satisfaction (*RR* 0.98; 95%CI 0.97, 0.98), trust within country (*RR* 0.99; 95%CI 0.98, 1.00), orientation to promote good (*B* -0.05; 95%CI -0.07, -0.03), delayed gratification (*B* -0.04; 95%CI -0.05, -0.03), hope (*B* -0.07; 95%CI -0.09, -0.05), gratitude (*B* -0.05; 95%CI -

0.07, -0.04), showing love/care (*B* -0.02; 95%CI -0.03, -0.01), self-rated physical health (*B* -0.18; 95%CI -0.21, -0.14), days exercise per week (*B* -0.03; 95%CI -0.04, -0.02), financial security (*B* -0.10; 95%CI -0.11, -0.08), material security (*B* -0.09; 95%CI -0.10, -0.07), financially comfortable/getting by (*RR* 0.97; 95%CI 0.96, 0.97), having own home (*RR* 0.99; 95%CI 0.99, 0.99), and being in the top income top quintile (*RR* 0.99; 95%CI 0.99, 0.99).

The same model 1 shows that pain at Wave 1 was significantly positively associated with the following outcomes at Wave 2: Traumatic distress (*RR* 1.06; 95%CI 1.05, 1.07), depression symptoms (*RR* 1.06; 95%CI 1.05, 1.07), anxiety symptoms (*RR* 1.06; 95%CI 1.05, 1.07), suffering (*RR* 1.09; 95%CI 1.08, 1.11), loneliness (*B* 0.10; 95%CI 0.08, 0.11), perceived discrimination (*RR* 1.02; 95%CI 1.02, 1.03), helping strangers (*RR* 1.01; 95%CI 1.00, 1.01), health problems (*RR* 1.07; 95%CI 1.06, 1.09), and pain (*RR* 1.13; 95%CI 1.11, 1.16).

Model 1 also shows that pain at Wave 1 had the largest positive effects on subsequent pain (*RR* 1.13), health problems (*RR* 1.07), and suffering (*RR* 1.09), and the largest negative effects on subsequent secure flourishing (*B* -0.15), flourishing *(B* -0.14), mental health (*B* -0.12), and financial security (*B* -0.10).

Model 2 in Tables 2 and 3 control for demographic, childhood, and other Wave 1 confounding variables. In these models, associations were substantially attenuated. Some persisted though at notably weaker levels. Even under this very extensive covariate control, and quite possibly over-control, pain at Wave 1 was significantly negatively associated with subsequent secure flourishing (*B* -0.02; 95%CI -0.03, -0.01), flourishing (*B* -0.02; 95%CI -0.03, -0.01), life satisfaction (*B* -0.01; 95%CI -0.01, 0.00), current life evaluation (*B* -0.01; 95%CI -0.02, 0.00), future life evaluation (*B* -0.01; 95%CI -0.02,0.01), freedom to pursue what's important (*B* -0.01; 95%CI -0.02,-0.00), self-rated mental health (*B* -0.01; 95%CI -0.02,-0.00), number of children (*B* 0.01; 95%CI 0.00,0.02), orientation to promote good (*B* -0.01; 95%CI -0.02,-0.00), delayed gratification (*B* -0.01; 95%CI -0.02,-0.00), self-rated physical

health (*B* -0.09; 95%CI -0.11,-0.07), financial security (*B* -0.01; 95%CI -0.02,-0.00), and material security (*B* -0.01; 95%CI -0.02,-0.01).

In Model 2, pain at Wave 1 was significantly positively associated with subsequent traumatic distress (*RR* 1.03; 95%CI 1.02, 1.03), depression symptoms (*RR* 1.01; 95%CI 1.00, 1.02), anxiety symptoms (*RR* 1.01; 95%CI 1.00,1.01), suffering (*RR* 1.05; 95%C 1.04,1.06), health problems (*RR* 1.04; 95%CI 1.03,1.05), and pain (*RR* 1.10; 95%CI 1.08,1.13).

Although some effects in Model 2 were substantially reduced, becoming pulled towards a null with *B* 0.00 or *RR* 1.00, many variables kept their significance including those with the largest effects such as pain (*RR* 1.10), suffering (*RR* 1.05), health problems (*RR* 1.04), and traumatic distress (*RR* 1.03). Supplemental meta-analytic results based on country-level complete-case analyses can be found in Tables S5-8, providing similar conclusions about the magnitude of effects.

It is worth noting that, across the two models, we did not find associations between pain and marital status, having more than 16 years of education, being employed, smoking, and measures of prosocial behaviour like donating and volunteering one year later.

Overall, the meta-analytic results based on Model 1 and Model 2 provided evidence in favour of hypothesis 1 of this study that pain at Wave 1 showed statistically significant associations with numerous wellbeing outcomes at Wave 2.

Figure 1 shows the effect of pain at Wave 1 on Secure Flourishing Index scores at Wave 2 in each country. In models that did control for only demographic variables and childhood variables as confounders (Model 1), the effects were significantly negative in all countries. After additionally adjusting for principal components from all Wave 1 outcomes (Model 2), the effect was significantly negative in the United States, Sweden, the United Kingdom, Poland, Israel, Japan, Tanzania, and Australia. In all the other countries, the 95% confidence

interval for the effect estimate included 0. The Flourishing Index models showed similar results (Figure S2).

Similar levels of country heterogeneity in effect sizes were observed across many other outcomes. For example, after additionally adjusting for principal components, the effect of pain and happiness & life satisfaction was significantly negative in Poland and significantly positive in Japan (Figure S3) whereas the effect of pain and meaning was only significantly negative in Poland (Figure S5). On the other hand, the effect of pain and physical and mental health was significantly negative in several countries including Israel, Australia, Brazil, Japan, the United Kingdom, Sweden, Poland, Indonesia, Mexico, Germany, and Spain (Figure S4). Moreover, the effect of pain and character and virtue was significantly negative in Poland, Japan, the United States (Figure S6), while the effect of pain and financial and material security was significantly negative in Australia and Sweden (Figure S8). Yet the link between pain and close social relationships in the fully adjusted models seems to be insignificant in all countries (Figure S7). Pain was significantly positive associated with number of children in Sweden and Mexico (Figure S40) as well as significantly positive associated with perceived discrimination in the United States and Sweden (Figure S44). All country-specific results can be found in Tables S9a to S31i, Table S34, and in Figures S1-S78. These findings provide some support for hypothesis 2 of this study, in which the strength of associations between pain and the outcomes was expected to vary to some extent by country.

The presence of unmeasured confounding is an inherent issue from this type of analysis. To shed light on this possibility, we conducted E-value sensitivity analysis for unmeasured confounding for the association between pain at Wave 1 and subsequent wellbeing and life outcomes. In Model 1 of Tables 4 and 5, the E-value for the outcomes with the strongest effects was quite substantial, for example, self-rated physical health (1.63), secure flourishing (1.56), flourishing (1.54), pain (1.52), mental health (1.46), suffering (1.41), financial security (1.41),

health problems (1.35), and traumatic distress (1.32). This suggests that an unmeasured confounder would need to have a somewhat strong association with both Wave 1 pain and the respective Wave 2 outcome to shift the effect estimate for their association to include the null. For example, to explain away the association between pain at Wave 1 and higher self-rated physical health at Wave 2, an unmeasured confounder associated with both pain at Wave 1 and self-rated physical health at Wave 2 with risk ratios of 1.63 each, conditional on the measured covariates, could suffice, but weaker joint confounder association could not. To reduce the 95% confidence interval to include the null, an unmeasured confounder associated with both pain at Wave 1 and higher self-rated physical health at Wave 2 with risk ratios of 1.53 each could suffice, but weaker joint confounder association could not. In Model 2 of Tables 4 and 5, the E-value for the variables mentioned earlier was reduced but still remained substantial: Self-rated physical health (1.38), secure flourishing (1.16), flourishing (1.16), pain (1.44), mental health (1.11), suffering (1.27), financial security (1.12), health problems (1.24), and traumatic distress (1.19). These findings support the idea that some of the observed associations between pain and the outcomes are relatively robust to potential unmeasured confounding.

Discussion

We used a longitudinal, representative dataset with 22 countries and one territory to explore the association between pain and 56 subsequent wellbeing and life outcomes. We conducted two types of analytical models: Model 1 adjusting for demographic factors, and childhood characteristics, and Model 2 adjusting for demographic factors, childhood characteristics, and principal components based on all prior values of the outcomes.

While analyses with fewer control variables showed that pain at Wave 1 was strongly associated with almost all wellbeing and life outcomes at Wave 2, analyses with more extensive covariate control also provided evidence that people who experienced greater pain at Wave 1,

reported lower secure flourishing, flourishing, life satisfaction, current life evaluation, future life evaluation, freedom to pursue what's important, mental health, orientation to promote good, delayed gratification, physical health, financial security, and material security at Wave 2 than those who reported lower pain.

These more extensively adjusted models also showed that people who experienced greater pain at Wave 1 reported higher traumatic distress, depression symptoms, anxiety symptoms, suffering, number of children, health problems, and pain at Wave 2 than those who reported lower pain at Wave 1.

While the strongest association was that of pain at Wave 1 and pain at Wave 2, the fact that pain at Wave 1 was strongly linked to other wellbeing aspects at Wave 2 highlights the potential impact of pain on other dimensions of wellbeing, including the widely studied aspects of flourishing and life satisfaction.

These results are in line with prior work that explored the association between pain and different outcomes in specific countries using varied analytical methods. For example, longitudinal work in Australia [5] and the United Kingdom [44] found a link between pain and life satisfaction, cross-sectional work with several countries showed a link between pain and loneliness [45], and with pain and income quintiles [46]. Other related work has shown a strong link between pain and negative emotions [47–49] or chronic pain and disability, poor mental health and poor cognitive functioning [50].

Some aspects of psychological wellbeing (e.g., optimism, inner peace, life balance, sense of mastery, meaningful activities, and understanding purpose), social wellbeing (e.g., relationship contentment, relationship satisfaction, social support, close friendships, government approval, say in government, belonging in country), character and prosocial behaviour (e.g., hope and gratitude), and socioeconomic circumstances (e.g., feeling financially comfortable, owning home, being in the top income quintile) had much smaller

effects and confidence intervals that included 0 in Model 2. However, model 2 included numerous variables that may have been on the pathway between the pain exposure and subsequent outcomes. Model 2 may thus constitute fairly substantial over-control with regard to the covariates. More work could be done with subsequent waves of data to understand how the additional covariates might act as mediators of the link between pain at Wave 1 and these outcomes at Wave 2.

While prior work has shown a relationship between education [51], employment [52], and prosocial behaviour [53], we did not find associations between pain and these aspects. It might happen that these relationships are present in different groups of the population or that other categories within the same variable were driving the results in prior work, for example, being unemployed or having low education. Regarding prosocial behaviour, most of the prior work has shown that prosocial behaviour tend to ease pain whereas, here, we looked at the effect of pain on subsequent prosocial behaviour. Future research should examine these points in greater detail.

At the country level, pain at Wave 1 and Secure Flourishing Index scores at Wave 2 were significantly negatively associated in the United States, Sweden, the United Kingdom, Poland, Israel, and Australia after controlling for potential confounders. These findings may reflect the influence of diverse sociodemographic, economic, and health contexts. Future research should examine country-specific circumstances that may be mediating or moderating these results, including gender and income distributions, access to healthcare, the use of prescribed or over-the-counter painkillers, macroeconomic conditions such as unemployment and inflation, and underlying health inequalities. National governments and international organisations that design interventions and policies for pain reduction should consider country-specific findings to tailor future intervention and policymaking strategies.

This study has several limitations that warrant discussion. For instance, these findings cannot be interpreted as strictly causal. Although our methodological approach advances causal inference relative to much of the existing literature, the associations reported here should not be construed as definitive evidence of causation. Nevertheless, this work provides a strong foundation for future studies explicitly designed to assess causality, for example, through epidemiological or econometric causal modelling approaches. Similarly, because the fully adjusted models controlled for a large number of sociodemographic characteristics as well as baseline levels of the outcomes, the standardized effect sizes were generally small. This is expected, as the models estimate the independent contribution of baseline pain after accounting for many competing predictors of future wellbeing. Importantly, even small effects can have meaningful public health implications particularly when they affect large populations and accumulate over time. Moreover, the observed associations were remarkably consistent across a broad range of outcomes and countries, supporting the robustness of the findings. The analyses using E-values also suggested that the observed associations were unlikely to be fully explained by unmeasured confounding.

Our pain measure, which asks about pain in the last four weeks, with four response categories, deserves some considerations. First, this single-item measure does not provide substantial insight into the severity of the pain, the type of pain, or the extent of pain in more specific moments like 'yesterday' or when performing certain activities. This is important because different types of pain can have more impactful consequences than others [54,55]. However, this measure enabled us to examine general pain at the population level, addressing a significant gap in the existing pain research literature. Second, pain reports might be influenced by cultural norms and language interpretation. Although country-specific data analysis and meta-analysis helped reducing cross-cultural comparability issues, biases within each country may persist. Future research should test these possibilities. Similarly, since all

variables were self-reported, they may be vulnerable to self-report bias, and the associations observed may partly reflect correlated response styles. However, participants were blind to the study hypotheses and the survey was anonymous, reducing the likelihood that respondents could tailor their answers or that individual responses could be identified.

As mentioned in the results section, the relationships presented in this study may be driven by omitted variables such as chronic health conditions associated with pain. Although our models control for an extensive number of covariates, including baseline outcome in model 2, we investigated the robustness of our results to potential unmeasured confounding using E-values. Even in the fully adjusted model (Model 2), some E-values for some associations suggested at least moderate robustness of the potential association of pain at Wave 1 to potential unmeasured confounding. Nonetheless, E-values are a descriptive sensitivity metric: while informative, they do not rule out residual confounding, and unmeasured factors may still partly explain the associations reported here.

It is also worth noting that while our study is based on data from 22 countries and one territory encompassing approximately two-thirds of the global population, the results we present may not generalise to other countries [56]. Future research should extend this work to other nations. Moreover, although the study employed a longitudinal design, it included only one year of follow-up. If some effects of chronic pain unfold over longer periods, they may not be fully captured here. Future research should also examine how changes in pain within individuals are associated with changes in wellbeing over longer periods of time. Certain outcomes, such as socioeconomic circumstances, tend to change slowly in relatively stable societies. As a result, some risk of reverse causation or simultaneity cannot be entirely ruled out.

Despite these limitations, our study is the first to explore the link between pain and 56 subsequent wellbeing and life outcomes in a multi-country, representative sample, using a

consistent statistical approach across the 56 associations, and confirming the robustness of the results to unmeasured confounding.

Our findings point to some potential practical applications. Interventions and policies for reducing pain have been at the centre of debates in policymaking, healthcare, and even in corporate sectors. We show that pain may negatively affect key aspects of human wellbeing (from flourishing to suffering) suggesting that interventions to reduce pain are more important than ever. In a world where societal wellbeing is increasingly becoming a central goal of national governments and international initiatives, designing effective interventions for pain reduction is of utmost relevance [57].

By showing that pain is strongly associated with several subsequent wellbeing and life outcomes, this study offers some of the most comprehensive country-wide evidence to date on pain's potential enduring impact. One of the most important conclusions of this study is that pain can have detrimental consequences for people's health, and quality of life, and overall societal wellbeing. While pain tends to reduce flourishing, life satisfaction, mental and physical health, pain also tends to increase distress, anxiety, depression, and suffering.

These findings provide valuable insights for policymakers, healthcare providers, and global organizations focused on reducing health inequalities and enhancing societal wellbeing. We also hope that this work guides future research on the effect of pain on subsequent wellbeing outcomes and life circumstances.

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Additional details

Data Availability

Data for Waves 1 and 2 of the Global Flourishing Study is available through the Center for Open Science (https://www.cos.io/gfs).

The data that support the findings of this article are openly available on the Open Science Framework: https://osf.io/ge2x5/overview Under files preview, select "Waves 1 and 2 Global Data" and the datasets will be displayed to download in different formats. Embargo periods may apply. Johnson, B. R., Ritter, Z., Fogleman, A., Markham, L., Stankov, T., Srinivasan, R., Honohan, J., Ripley, A., Phillips, T.A., Wang, H., & VanderWeele, T. J. (2024, February 8). The Global Flourishing Study.

Code for analyses

OSF Project: https://doi.org/10.17605/OSF.IO/RBCMP. This links to the Wave 2 Methodology paper, code shared in the zip file for running analyses, and is connected to the GitHub repository which stores to the core R package code.

GutHib Repository Directly: https://github.com/noah-padgett/Rglobalflourishing. This directly links to the code of the R package.

Competing Interests Statement

Tyler J. VanderWeele reports consulting fees from Gloo Inc. along with shared revenue received by Harvard University in its license agreement with Gloo Inc. according to the University IP policy. We also note that Byron Johnson is a senior fellow at the Religious Freedom Institute and receives no compensation for this courtesy appointment.

We have been asked to provide other disclosures including, for example, non-academic honoraria that we do not consider conflicts of interest with the Global Flourishing Study, but which we are providing as requested. From 2016-2026, Tyler J. VanderWeele declares prior consulting fees from Aetna Inc. and the Analysis group, prior license agreements with Flerish and Flourishing Metrics Inc. through Harvard, similar to that currently held with Gloo Inc., and non-academic honoraria and fees from Statistical Horizons, the Veritas Forum, Made to Flourish, New York Times, Psychology Today, WBUR CitySpace Forum, Asia Calling, the Gathering, Cura Foundation, Institute for Family Studies, Abigail Adams Institute, Order of Malta, and Montrose School LifeCompass Speaker Series. Byron Johnson is a senior fellow at the Sagamore Institute and receives a stipend for this appointment. Byron Johnson also received non-academic lecture honoraria 2016-2026 from Citygate Network, Relational Values Alliance, National Religious Broadcasters, and Christian Alliance for Orphans.

The other authors have no disclosures to report.

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Papers under consideration
This manuscript at Communications Medicine is the only paper under consideration that reports these results.

Overlapping data across publications
Descriptive statistics for the observed sample in Table 1 are reproduced from the descriptive statistics in Cowden et al. (2026) Table 1. Further descriptive statistics for the observed sample in Tables 1-4, 32-33, and by country (9-31a-f), in the Online Supplement Tables 1-4, in the "a" Tables (Tables 1a-22a) are reproduced from the corresponding descriptive tables of the Online Supplement of Cowden et al. (2026); cf. Padgett et al. (2026) and VanderWeele et al. (2026) for common methodology.

Cowden, R. G., Worthington Jr, E. L., Padgett, R. N., Felton, C., Weziak-Bialowolska, D., Wilkinson, R., ... & VanderWeele, T. J. Longitudinal associations of dispositional forgivingness with multidimensional well-being: a two-wave outcome-wide analysis in the Global Flourishing Study. *npj Mental Health Research* ***5***(1), 3, (2026).
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Ethics approval and consent to participate
Ethical approval was granted by the institutional review boards at Baylor University (IRB Reference #: 1841317) and Gallup (IRB Reference #: 2021-11-02). Gallup is a multi-national corporation, and its IRB covers all countries included in the GFS. All participants provided informed consent. The research conformed to the principles of the Helsinki Declaration.

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Author contributions
L.M. Conducted the data analysis, wrote the paper.
N.P. Creates code to analyse the data and provided helpful comments to the written drafts
R.C. Provided helpful comments to the written drafts.
B.R.J. Coordinated data collection, participated in survey design, coordinated creation of code for analysis, provided helpful comments to the written drafts.
T.J.V. Coordinated data collection, participated in survey design, coordinated creation of code for analysis, provided helpful comments to the written drafts.

Tables and figures

Table 1. Weighted sample demographic summary statistics.

Characteristic	Wave 1 N = 207,919	Wave 2 N = 128,868
Pain, n (%)		
A lot	25,137 (12.1%)	16,416 (12.7%)
Some	66,705 (32.1%)	42,749 (33.2%)
Not very much	66,696 (32.1%)	42,467 (33.0%)
None at all	49,011 (23.6%)	27,034 (21.0%)
(Missing)	370 (0.2%)	202 (0.2%)
Year of birth, n (%)		
1943 or earlier (current age: 80+ years)	4,047 (1.9%)	3,446 (2.7%)
1943-1953 (current age: 70-79 years)	16,902 (8.1%)	12,684 (9.8%)
1953-1963 (current age: 60-69 years)	29,031 (14.0%)	19,539 (15.2%)
1963-1973 (current age: 50-59 years)	32,409 (15.6%)	20,497 (15.9%)
1973-1983 (current age: 40-49 years)	34,970 (16.8%)	21,996 (17.1%)
1983-1993 (current age: 30-39 years)	40,297 (19.4%)	24,640 (19.1%)
1993-1998 (current age: 25-29 years)	20,325 (9.8%)	12,310 (9.6%)
1998-2005 (current age: 18-24 years)	29,920 (14.4%)	13,757 (10.7%)
(Missing)	18 (<0.0%)	1 (<0.0%)
Gender, n (%)		
Male	100,661 (48.4%)	62,165 (48.2%)
Female	106,349 (51.1%)	66,137 (51.3%)
Other	523 (0.3%)	370 (0.3%)
(Missing)	386 (0.2%)	197 (0.2%)
Education (years), n (%)		
Up to 8	46,842 (22.5%)	22,656 (17.6%)
9-15	116,015 (55.8%)	72,945 (56.6%)
16+	44,904 (21.6%)	33,256 (25.8%)
(Missing)	158 (0.1%)	11 (<0.0%)
Country of respondent, n (%)		
Argentina	6,724 (3.2%)	2,876 (2.2%)
Australia	3,844 (1.8%)	2,578 (2.0%)
Brazil	13,203 (6.4%)	4,222 (3.3%)
China	5,022 (2.4%)	4,575 (3.6%)
Egypt	4,729 (2.3%)	3,044 (2.4%)
Germany	9,506 (4.6%)	5,585 (4.3%)
Hong Kong (S.A.R. of China)	3,012 (1.4%)	608 (0.5%)
India	12,765 (6.1%)	6,353 (4.9%)
Indonesia	6,992 (3.4%)	2,661 (2.1%)
Israel	3,669 (1.8%)	2,495 (1.9%)
Japan	20,543 (9.9%)	13,966 (10.8%)
Kenya	11,389 (5.5%)	7,712 (6.0%)
Mexico	5,776 (2.8%)	2,264 (1.8%)
Nigeria	6,827 (3.3%)	3,143 (2.4%)
Philippines	5,292 (2.5%)	2,684 (2.1%)
Poland	10,389 (5.0%)	6,544 (5.1%)
South Africa	2,651 (1.3%)	962 (0.7%)
Spain	6,290 (3.0%)	2,917 (2.3%)
Sweden	15,068 (7.2%)	11,663 (9.1%)
Tanzania	9,075 (4.4%)	5,588 (4.3%)
Turkey	1,473 (0.7%)	497 (0.4%)
United Kingdom	5,368 (2.6%)	3,621 (2.8%)
United States	38,312 (18.4%)	32,310 (25.1%)

Note. N (%); this table is based on non-imputed data; cumulative percentages for variables may not add up to 100% due to rounding; S.A.R., Special Administrative Region. Expanded summary tables of all demographic characteristics and outcome variables are provided the online supplement in Tables S1-2 aggregated over the full sample and Tables S9a-32a and S9b-32b are summary tables by country.

Table 2. Meta-analysed associations of Pain at Wave 1 with the following outcomes at Wave 2: Human flourishing, psychological wellbeing, psychological distress, social wellbeing.

	Model 1: Demographic and Childhood Variables as Covariates					Model 2: Demographic, Childhood, and Other Wave 1 Confounding Variables (Via Principal Components) as Covariates				
Outcome	RR	ES	95% CI	τ	Global p-value	RR	ES	95% CI	τ	Global p-value
Human Flourishing										
Secure flourishing index		-0.15	(-0.17,-0.13)	0.05	3.4e-16***		-0.02	(-0.03,-0.01)	0.02	3.02e-07***
Flourishing index		-0.14	(-0.16,-0.12)	0.05	3.92e-16***		-0.02	(-0.03,-0.01)	0.02	1.21e-06***
Psychological Wellbeing										
Happiness		-0.11	(-0.12,-0.09)	0.04	1.28e-15***		-0.00	(-0.01,0.00)	0.01	0.029*
Life satisfaction		-0.11	(-0.12,-0.09)	0.03	1.28e-15***		-0.01	(-0.01,0.00)	0.01	0.010*
Current life evaluation		-0.09	(-0.11,-0.07)	0.04	1.7e-15***		-0.01	(-0.02,0.00)	0.01	4.62e-06***
Future life evaluation		-0.07	(-0.09,-0.05)	0.05	1.02e-15***		-0.01	(-0.02,0.01)	0.02	4.51e-04***
Optimism		-0.06	(-0.08,-0.05)	0.04	2.51e-15***		-0.01	(-0.01,-0.00)	<0.01†	0.050
Freedom to pursue what's important		-0.08	(-0.10,-0.06)	0.03	1.7e-15***		-0.01	(-0.02,-0.00)	0.01	9.84e-06***
Inner peace	0.97		(0.97,0.98)	0.02	2.54e-15***	1.00		(1.00,1.01)	<0.01†	0.068
Life balance	0.97		(0.96,0.98)	0.02	1.7e-15***	1.00		(1.00,1.00)	<0.01†	0.085
Sense of mastery	0.98		(0.97,0.99)	0.01	2.55e-15***	1.00		(1.00,1.00)	<0.01†	0.490
Meaningful activities		-0.08	(-0.10,-0.07)	0.04	1.7e-15***		-0.00	(-0.01,0.00)	<0.01†	0.314
Understanding purpose		-0.08	(-0.09,-0.06)	0.03	2.55e-15***		-0.01	(-0.02,-0.00)	<0.01†	0.158
Self-rated mental health		-0.12	(-0.14,-0.09)	0.06	8.23e-16***		-0.01	(-0.02,-0.00)	0.01	4.79e-03**
Psychological Distress										
Traumatic distress	1.06		(1.05,1.07)	0.02	1.39e-15***	1.03		(1.02,1.03)	0.01	1.07e-10***
Depression symptoms	1.06		(1.05,1.07)	0.02	9.55e-16***	1.01		(1.00,1.02)	0.01	0.006*
Anxiety symptoms	1.06		(1.05,1.07)	0.02	1.26e-15***	1.01		(1.00,1.01)	0.01	0.007*
Suffering	1.09		(1.08,1.11)	0.04	4.57e-16***	1.05		(1.04,1.06)	0.02	1.6e-15***
Social Wellbeing										
Relationship contentment		-0.07	(-0.09,-0.06)	0.03	2.55e-15***		0.00	(-0.01,0.01)	<0.01†	0.493
Relationship satisfaction		-0.08	(-0.09,-0.06)	0.02	2.43e-15***		-0.01	(-0.01,0.00)	<0.01†	0.349
Social support		-0.06	(-0.07,-0.04)	0.02	3.06e-15***		-0.00	(-0.01,0.00)	<0.01†	0.547
Intimate/close friend	0.99		(0.99,0.99)	<0.01†	0.051	1.00		(1.00,1.00)	<0.01†	0.911
Government approval	0.99		(0.98,1.00)	<0.01†	1.41e-04***	1.00		(0.99,1.00)	<0.01†	0.623
Say in government	0.99		(0.99,1.00)	0.01	1.25e-04***	1.00		(0.99,1.00)	<0.01†	0.300
Belonging in country		-0.05	(-0.06,-0.04)	0.01	4.88e-15***		-0.01	(-0.02,-0.00)	<0.01†	0.756
City/place satisfaction	0.98		(0.97,0.98)	<0.01†	5.11e-15***	1.00		(0.99,1.00)	<0.01†	0.027*
Trust within country	0.99		(0.98,1.00)	0.01	4.17e-11***	1.00		(0.99,1.01)	0.01	0.006*

Notes. N=207919; Reference for focal predictor: None at all/Not very much; RR, risk-ratio, null effect is 1.00; ES, effect size measure for standardized regression coefficient, null effect is 0.00; CI, confidence interval; τ (tau, heterogeneity), estimated standard deviation of the distribution of effects; Global p-value, joint test of the null hypothesis that the country-specific Wald tests are null in all countries. P-value significance thresholds: $p < 0.05$*, $p < 0.005$**, (Bonferroni) $p < 0.00077$***, correction for multiple testing to significant threshold; † Estimate of τ (tau, heterogeneity) is likely unstable. See our online supplement forest plots for more detail on heterogeneity of effects.

Table 3. Meta-analysed associations of Pain at Wave 1 with wellbeing and the following outcomes at Wave 2: Social participation, social distress, character and prosocial behaviour, physical health and health behaviour, socioeconomic outcomes.

	Model 1: Demographic and Childhood Variables as Covariates					Model 2: Demographic, Childhood, and Other Wave 1 Confounding Variables (Via Principal Components) as Covariates				
Outcome	RR	ES	95% CI	τ	Global p-value	RR	ES	95% CI	τ	Global p-value
Social Participation										
Ever been married	1.00		(1.00,1.00)	<0.01†	0.955	1.00		(1.00,1.00)	<0.01†	0.925
Currently divorced	1.00		(1.00,1.00)	<0.01†	0.950	1.00		(1.00,1.00)	<0.01†	0.985
Number of children		0.01	(-0.00,0.01)	<0.01†	0.148		0.01	(0.00,0.02)	0.02	5.54e-13***
Weekly+ community participation	1.00		(1.00,1.00)	<0.01†	0.172	1.00		(1.00,1.01)	<0.01†	0.313
Weekly+ religious attendance	1.00		(1.00,1.00)	<0.01†	0.383	1.00		(1.00,1.00)	<0.01†	0.494
Social Distress										
Loneliness		0.10	(0.08,0.11)	0.02	2.54e-15***		0.01	(-0.00,0.01)	<0.01†	0.370
Perceived discrimination	1.02		(1.02,1.03)	<0.01†	5.11e-15***	1.00		(1.00,1.01)	<0.01†	0.020*
Character & Prosocial Behaviour										
Orientation to promote good		-0.05	(-0.07,-0.03)	0.03	5.11e-15***		-0.01	(-0.02,-0.00)	0.01	0.036*
Delayed gratification		-0.04	(-0.05,-0.03)	0.02	5.11e-15***		-0.01	(-0.02,-0.00)	<0.01†	0.009*
Hope		-0.07	(-0.09,-0.05)	0.03	2.53e-15***		-0.00	(-0.01,0.01)	0.01	0.292
Gratitude		-0.05	(-0.07,-0.04)	0.02	4.84e-15***		-0.00	(-0.01,0.00)	<0.01†	0.097
Showing love/care		-0.02	(-0.03,-0.01)	0.02	3.94e-08***		0.01	(-0.00,0.02)	0.01	0.028*
Forgivingness	1.00		(0.99,1.00)	0.01	1.8e-04***	1.00		(1.00,1.01)	<0.01†	0.006*
Charitable giving	1.00		(1.00,1.01)	<0.01†	5.15e-04***	1.00		(1.00,1.01)	<0.01†	0.158
Helping strangers	1.01		(1.00,1.01)	0.01	2.19e-05***	1.00		(1.00,1.01)	0.01	1.95e-04***
Volunteering	1.00		(0.99,1.01)	0.01	0.121	1.00		(1.00,1.00)	<0.01†	0.314
Physical Health & Health Behaviour										
Self-rated physical health		-0.18	(-0.21,-0.14)	0.08	4.64e-16***		-0.09	(-0.11,-0.07)	0.05	1.69e-15***
Health problems	1.07		(1.06,1.09)	0.04	6.71e-16***	1.04		(1.03,1.05)	0.02	1.7e-15***
Pain in past 4 weeks	1.13		(1.11,1.16)	0.07	3.65e-16***	1.10		(1.08,1.13)	0.06	6.19e-16***
Daily smoker	1.00		(1.00,1.01)	<0.01†	2.92e-03**	0.99		(0.99,1.00)	<0.01†	1.39e-12***
Number of drinks per week		0.00	(-0.01,0.01)	<0.01†	0.356		0.00	(-0.01,0.01)	<0.01†	0.434
Days exercise per week		-0.03	(-0.04,-0.02)	0.02	5.11e-15***		-0.00	(-0.01,0.00)	<0.01†	0.318
Socioeconomic Outcomes										
Financial security		-0.10	(-0.11,-0.08)	0.03	1.7e-15***		-0.01	(-0.02,-0.00)	0.01	2.71e-04***
Material security		-0.09	(-0.10,-0.07)	0.03	1.7e-15***		-0.01	(-0.02,-0.01)	<0.01†	0.011*
Educational attainment (16+ years)	1.00		(1.00,1.00)	<0.01†	0.860	1.00		(1.00,1.00)	<0.01†	0.983
Currently employed	0.99		(0.99,1.00)	<0.01†	0.487	1.00		(1.00,1.00)	<0.01†	0.922
Financially comfortable/getting by	0.97		(0.96,0.97)	0.01	2.55e-15***	1.00		(1.00,1.00)	<0.01†	0.577
Own home	0.99		(0.99,0.99)	<0.01†	4.44e-04***	1.00		(1.00,1.00)	<0.01†	0.631
Income -- top quintile	0.99		(0.99,0.99)	<0.01†	3.55e-03**	1.00		(1.00,1.00)	<0.01†	0.966

Notes. N=207919; Reference for focal predictor: None at all/Not very much; RR, risk-ratio, null effect is 1.00; ES, effect size measure for standardized regression coefficient, null effect is 0.00; CI, confidence interval; τ (tau, heterogeneity), estimated standard deviation of the distribution of effects; Global p-value, joint test of the null hypothesis that the country-specific Wald tests are null in all countries. P-value significance thresholds: $p < 0.05$*, $p < 0.005$**, (Bonferroni) $p < 0.00077$***, correction for multiple testing to significant threshold; † Estimate of τ (tau, heterogeneity) is likely unstable. See our online supplement forest plots for more detail on heterogeneity of effects.

Additional notes for Tables 2 and 3: Multiple imputation was performed to impute missing data on the covariates, exposure, and outcomes. All models controlled for sociodemographic and childhood factors assessed at Wave 1: relationship with mother growing up; relationship with father growing up; parent marital status around age 12; experienced abuse growing up (except for Israel); felt like an outsider in family growing up; self-rated health growing up; subjective financial status growing up; religious affiliation at age 12; frequency of religious service attendance around age 12; year of birth; gender; education, employment status, marital status, immigration status; and racial/ethnic identity when available. For Model 2 with PC (principal components), the first seven principal components of the entire set of contemporaneous confounders assessed at Wave 1 were included as additional covariates of the outcomes at Wave 2. An outcome-wide analytic approach was used, and a separate model was run for each outcome. A different type of model was run depending on the nature of the outcome: (1) for each binary outcome, a weighted generalized linear model (with a log link and Poisson distribution) was used to estimate a RR; and (2) for each continuous outcome, a weighted linear regression model was used to estimate an ES. All effect sizes were standardized. For continuous outcomes, the ES represents the change in SD on the outcome between the lower and upper categories of the binary focal predictor. For binary outcomes, the RR represents the change in risk of being in the upper category compared to the lower category between the lower and upper categories of the binary focal predictor.

Table 4. E-value sensitivity analysis for unmeasured confounding for the association between Pain and the following outcomes: Human flourishing, psychological wellbeing, psychological distress, social wellbeing, social participation.

	Model 1: Demographic and Childhood Variables as Covariates		Model 2: Demographic, Childhood, and Other Wave 1 Confounding Variables (Via Principal Components) as Covariates	
Outcome	E-value	E-value for CI	E-value	E-value for CI
Human Flourishing				
Secure flourishing index	1.56	1.50	1.16	1.12
Flourishing index	1.54	1.48	1.16	1.11
Psychological Wellbeing				
Happiness	1.44	1.39	1.07	1.00
Life satisfaction	1.43	1.39	1.08	1.00
Current life evaluation	1.38	1.33	1.08	1.00
Future life evaluation	1.33	1.27	1.07	1.00
Optimism	1.31	1.25	1.09	1.01
Freedom to pursue what's important	1.36	1.31	1.10	1.03
Inner peace	1.19	1.15	1.05	1.00
Life balance	1.20	1.16	1.01	1.00
Sense of mastery	1.17	1.13	1.01	1.00
Meaningful activities	1.37	1.32	1.07	1.00
Understanding purpose	1.35	1.30	1.11	1.07
Self-rated mental health	1.46	1.39	1.11	1.04
Psychological Distress				
Traumatic distress	1.32	1.29	1.19	1.16
Depression symptoms	1.31	1.28	1.11	1.07
Anxiety symptoms	1.31	1.27	1.09	1.04
Suffering	1.41	1.36	1.27	1.23
Social Wellbeing				
Relationship contentment	1.33	1.29	1.02	1.00
Relationship satisfaction	1.35	1.31	1.08	1.00
Social support	1.29	1.25	1.05	1.00
Intimate/close friend	1.10	1.08	1.03	1.00
Government approval	1.11	1.07	1.06	1.02
Say in government	1.09	1.03	1.06	1.00
Belonging in country	1.25	1.22	1.09	1.03
City/place satisfaction	1.18	1.16	1.06	1.00
Trust within country	1.12	1.07	1.01	1.00
Social Participation				
Ever been married	1.03	1.00	1.04	1.02
Currently divorced	1.01	1.00	1.01	1.00
Number of children	1.08	1.00	1.11	1.03
Weekly+ community participation	1.04	1.00	1.06	1.01
Weekly+ religious attendance	1.04	1.00	1.03	1.00

Notes. N=207919; The formula for calculating E-values can be found in VanderWeele and Ding (2017). E-values for estimate are the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to fully explain away the observed association between the exposure and outcome, conditional on the measured covariates. E-values for the 95% CI closest to the null denote the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to shift the CI to include the null value, conditional on the measured covariates.

Table 5. E-value sensitivity analysis for unmeasured confounding for the association between Pain and the following outcomes: Social distress, character and prosocial behaviour, physical health and health behaviour, socioeconomic outcomes.

	Model 1: Demographic and Childhood Variables as Covariates		Model 2: Demographic, Childhood, and Other Wave 1 Confounding Variables (Via Principal Components) as Covariates	
Outcome	E-value	E-value for CI	E-value	E-value for CI
Social Distress				
Loneliness	1.41	1.37	1.08	1.00
Perceived discrimination	1.18	1.16	1.07	1.05
Character & Prosocial Behavior				
Orientation to promote good	1.27	1.21	1.11	1.03
Delayed gratification	1.22	1.18	1.10	1.05
Hope	1.33	1.28	1.05	1.00
Gratitude	1.28	1.24	1.06	1.00
Showing love/care	1.16	1.10	1.09	1.00
Forgivingness	1.03	1.00	1.03	1.00
Charitable giving	1.02	1.00	1.07	1.00
Helping strangers	1.10	1.05	1.07	1.00
Volunteering	1.03	1.00	1.02	1.00
Physical Health & Health Behavior				
Self-rated physical health	1.63	1.53	1.38	1.32
Health problems	1.35	1.30	1.24	1.20
Pain in past 4 weeks	1.52	1.45	1.44	1.37
Daily smoker	1.07	1.05	1.09	1.04
Number of drinks per week	1.03	1.00	1.04	1.00
Days exercise per week	1.19	1.15	1.07	1.00
Socioeconomic Outcomes				
Financial security	1.41	1.36	1.12	1.07
Material security	1.38	1.33	1.12	1.07
Educational attainment (16+ years)	1.00	1.00	1.00	1.00
Currently employed	1.08	1.06	1.05	1.00
Financially comfortable/getting by	1.22	1.20	1.03	1.00
Own home	1.12	1.10	1.03	1.00
Income -- top quintile	1.11	1.09	1.02	1.00

Notes. N=207919; The formula for calculating E-values can be found in VanderWeele and Ding (2017). E-values for estimate are the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to fully explain away the observed association between the exposure and outcome, conditional on the measured covariates. E-values for the 95% CI closest to the null denote the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to shift the CI to include the null value, conditional on the measured covariates.

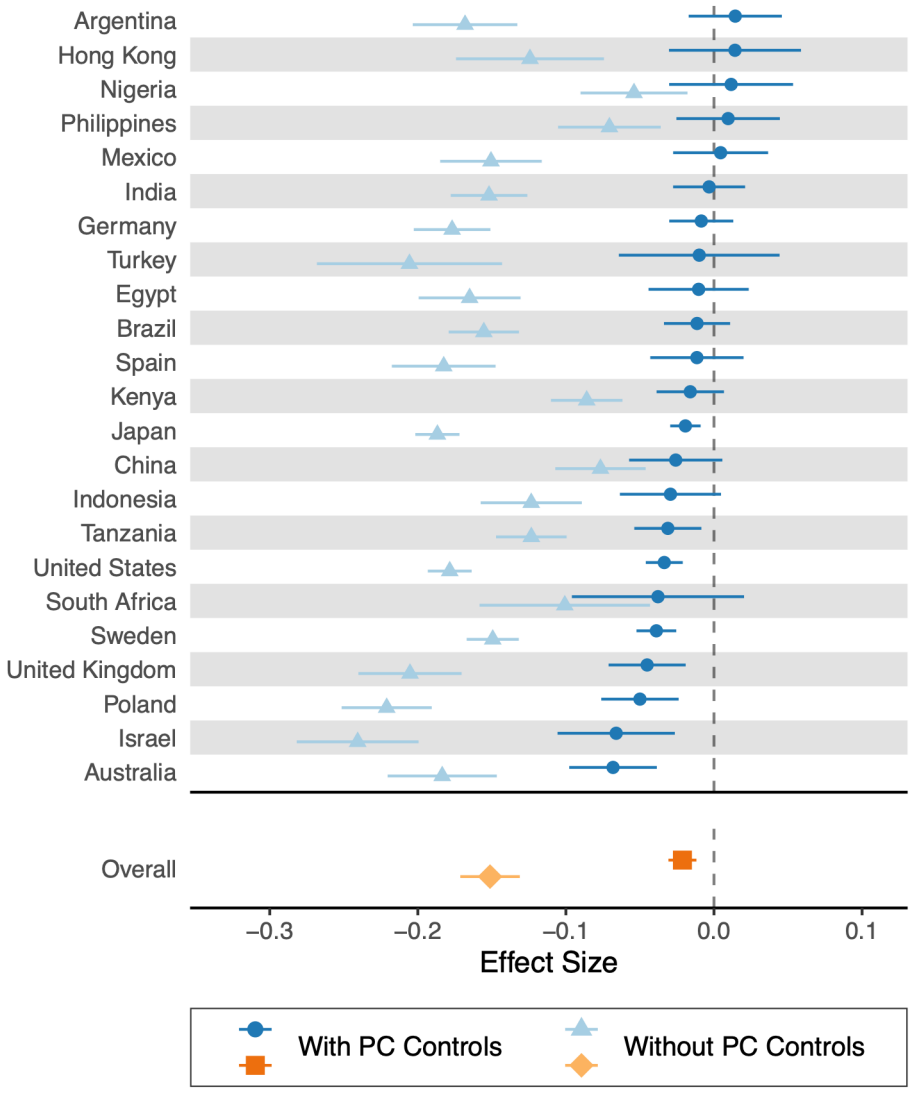


Figure 1. *Heterogeneity in the effects of Pain at Wave 1 on Secure Flourishing Index scores at Wave 2 across countries (N=207919).* The plot compares the estimates between Model 1 which controls for demographic and childhood variables only and Model 2 which controls for demographic variables, childhood variances, and the entire set of Wave 1 potential confounders. The potential confounders were included using principal components. The points represent the estimated effect size in each country. The lines represented the confidence interval obtained via est+/-t(df)*SE, standard error; the overall pooled mean is represented by the points and intervals in the 'overall' row near the bottom. See our online supplemental material for more information regarding the tests of heterogenetiy. The source data for this figure is in https://www.cos.io/gfs.