



HAL
open science

On the ability of the SF-6D to capture the consequences of chronic illnesses on subjective well-being: Evidence from France

Philippe Tessier, François-Charles Wolff

► To cite this version:

Philippe Tessier, François-Charles Wolff. On the ability of the SF-6D to capture the consequences of chronic illnesses on subjective well-being: Evidence from France. *Social Science & Medicine*, 2024, 354, pp.117086. 10.1016/j.socscimed.2024.117086 . hal-04637942

HAL Id: hal-04637942

<https://hal.science/hal-04637942>

Submitted on 12 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License



On the ability of the SF-6D to capture the consequences of chronic illnesses on subjective well-being: Evidence from France[☆]

Philippe Tessier^{a,*}, François-Charles Wolff^b

^a SPHERE, Nantes Université, Univ Tours, INSERM, Methods in Patients-Centered Outcomes and Health Research, IRS2, 22 Boulevard Benoni Goullin, 44000, Nantes, France

^b LEMNA, Nantes Université and TEPP, BP 52231 Chemin de la Censive du Tertre, 44322, Nantes Cedex, France

ARTICLE INFO

Handling Editor: Richard Smith

JEL classification:

I19

I31

Keywords:

SF-6D

Health-related quality-of-life

Chronic illness

Subjective well-being

Mediation analysis

France

ABSTRACT

Using cross-sectional data from a representative sample of the French population (the 2008 Disability Health survey), this paper examines whether the SF-6D, a widely used preference-based measure of health-related quality of life in economic evaluations, fully captures the variation in subjective well-being (SWB) due to chronic illnesses. We conduct a mediation analysis to disentangle the direct and indirect, through the SF-6D, effects of various chronic conditions on SWB (happiness). Our results show that the SF-6D reflects changes in happiness due to most illnesses except mental illness. Changes in SWB mediated by the SF-6D account for 74% of the total effect. The variation unexplained by the SF-6D is significant and increases substantially in the presence of multimorbidity when a chronic illness is combined with anxiety or depression. Overall, our results suggest that the SF-6D incompletely captures the subjective experience of chronically ill patients, especially those with comorbid conditions.

1. Introduction

Cost-effectiveness analysis (CEA) aims to promote efficient resource use by documenting healthcare programs' value for money. In CEA, outcomes are represented by Quality-Adjusted Life Years (QALYs), which are estimated by weighting time with utility values representing the strength of preferences over health states on a scale where 0 corresponds to death and 1 to perfect health (Torrance, 1986).

In applied CEA, health state utilities are not obtained directly from patients but from generic preference-based measures such as the SF-6D, EQ-5D, HUI3, and 15D, among others. These instruments combine a classification and a valuation system. The former consists of a set of health states described by different dimensions of Health-Related Quality of Life (HRQoL). The latter assigns a utility value to each describable health state on the 0–1 “death–perfect health” scale (Brazier et al., 2017). Most national guidelines for the economic evaluation of healthcare programs (HAS, 2020; NICE, 2013) recommend deriving these utility values from the stated preferences of the population over hypothetical health states. The primary justification is that the public

finances healthcare (Versteegh and Brouwer, 2016).

Concerns have been raised about the ability of preference-based HRQoL measures to fully capture the consequences of illness (Brazier et al., 2019). Focusing on HRQoL and hypothetical preferences may not be appropriate for reflecting the subjective experiences of patients. For example, people may adapt to chronic conditions by redirecting their attention to non-health dimensions of life (Dolan and Kahneman, 2007). A proposed alternative is to value the consequences of illness using measures of subjective well-being (SWB) (Dolan, 2011). The term SWB refers to various measures that represent how people think (measures of life satisfaction or satisfaction with a life domain) and feel (measures of positive and negative affect) about their situation (Diener et al., 2018). It corresponds to measures of “experienced utility” as opposed to measures of “decision utility” derived from stated or revealed preferences (Kahneman et al., 1997).

There are several reasons why SWB can capture the experience of illness differently than preference-based HRQoL measures (Brazier et al., 2019). First, SWB encompasses a broad view of a good life, including non-HRQoL dimensions possibly altered by illness, such as social

[☆] The data used were collected by the National Institute of Statistics and Economic Studies in France and are publicly available for research purposes: <https://doi.org/10.13144/lil-0459> Enquête Handicap Santé - Volet ménages (HSM) - 2008, INSEE (producteur), ADISP (diffuseur).

* Corresponding author.

E-mail addresses: philippe.tessier@univ-nantes.fr (P. Tessier), francois.wolff@univ-nantes.fr (F.-C. Wolff).

relationships or meaningful activities (Olsen and Misajon, 2020). Second, SWB is a close concept to mental health, a dimension of HRQoL that does not receive much importance in preference-based instruments such as the EQ-5D and the SF-6D (Brazier et al., 2014). Third, when stating their preferences for hypothetical health states, the public may not be aware of the individuals' ability to adapt to their health conditions (Peeters et al., 2012). This could lead to different weighting of HRQoL dimensions depending on whether decision or experienced utility is used to value health (Dolan and Metcalfe, 2012; Mukuria and Brazier, 2013).

Choosing how health states should be defined and valued in CEA is a normative issue (Brazier et al., 2017). This article does not enter into this debate. Starting from the premise that improving people's SWB is a relevant policy goal – not the sole or ultimate goal –, our study examines the capacity of the SF-6D to fully capture changes in SWB due to chronic illness. The debate about the choice between decision and experienced utility in CEA would become less crucial if the former captures changes in the latter (Richardson et al., 2015). Therefore, this paper seeks to determine whether chronic illness is still associated with SWB when health is controlled for using the SF-6D.

Few articles investigated the possibility that having a chronic illness is correlated with SWB along with preference-based HRQoL measures. In a representative sample of the Finnish population, Böckerman et al. (2011) found significant cross-sectional correlations between chronic conditions and life satisfaction while controlling for the EQ-5D and the 15D. In contrast, a study estimating generalized Logit models in a large UK sample shows that no long-term health condition is consistently associated with life satisfaction along with the EQ-5D (Wu et al., 2014). However, the authors do not consider mental illness because the EQ-5D asks about anxiety and depression. In addition, their models control for the different dimensions of the EQ-5D, not for health state utility values. This means that their test is only related to the EQ-5D descriptive system.

Richardson et al. (2015) considered three measures of SWB and six preference-based HRQoL measures in an international sample. Their results suggest that the HRQoL instruments that include more psychosocial components may be able to capture changes in SWB due to chronic illness. This study also finds that several illnesses (depression, diabetes, cancer) still decrease SWB when HRQoL is controlled for using the SF-6D utility index. In the same vein, Chen and Olsen (2023) find that the EQ-5D lacks some dimensions, such as personal relationships and social isolation, to capture changes in SWB due to illness.

Most studies above suggest that preference-based HRQoL and SWB measures overlap, but represent different concepts. They also provide little evidence on this issue regarding the SF-6D. This paper aims to contribute to this literature in two respects. First, instead of considering chronic conditions in isolation, it examines the association between SWB and a combination of chronic illnesses, with a focus on mental illness. This seems justified since multimorbidity is the rule rather than the exception in most countries (Ofori-Asenso et al., 2019). Second, it proposes a mediation analysis to quantify the direct association between chronic illness and SWB and the indirect association through changes in SF-6D. Examining the issues of multimorbidity and the relative importance of the direct association of chronic illness with SWB may help to determine whether the potential failure of the SF-6D to capture the subjective experience of illness is negligible or should be addressed.

This paper tests three hypotheses. First, it investigates the possibility of a significant association between various chronic conditions and SWB when HRQoL is controlled for using the SF-6D utility index. Such an association would suggest that chronic illness is directly linked to SWB independently from variations in SF-6D (Hypothesis 1). The second hypothesis is whether the indirect association between chronic illness and SWB, captured by the SF-6D, outweighs the direct association (Hypothesis 2). Finally, this paper examines the possibility that the more chronic conditions individuals have, the more significant the negative correlation with their SWB that is not captured by the SF-6D (Hypothesis 3). What motivates this latter hypothesis is the increase over time of the

number of people living with multiple chronic conditions (Uijen and Van De Lisdonk, 2008). In this context, examining whether the number of chronic conditions directly correlates with SWB independently from variations in SF-6D is necessary.

In exploring this latter hypothesis, we emphasize the combination between a mental health condition and at least one chronic physical condition. The reason is twofold. First, people with chronic mental health conditions are more at risk of suffering from chronic physical health problems (Scott et al., 2016). Second, the most common preference-based HRQoL instruments, the EQ-5D and the SF-6D, give less importance to mental health than measures of SWB do (Dolan and Metcalfe, 2012; Mukuria and Brazier, 2013).

We pay close attention to the role of gender in our empirical analysis based on French household data. Some studies suggested that women are more likely to suffer from mental health problems than men (Awaworyi Churchill et al., 2020). It thus seems necessary to check whether the ability of the SF-6D to reflect changes in SWB associated with mental illness remains the same regardless of gender.

In France, national guidelines about cost-effectiveness in health care recommend using the EQ-5D because there are no French tariffs for the SF-6D (HAS, 2020). However, the SF-6D constructed from UK weights may be used in some French studies (Garay et al., 2019), and it may be the only available source of utility measure for retrospective, model-based or international evaluation studies given the widespread use of the SF-36 in clinical trials, patients' cohorts and national surveys.

Specifically, we rely on a French national survey to assess the ability of the UK-weighted SF-6D to capture changes in SWB due to chronic illnesses. When no country-specific tariffs are available, it is common practice to apply UK weights to estimate the SF-6D utility index (Garay et al., 2019; Høgh et al., 2019). Therefore, our findings may be informative for studies in France and of potential interest for research using the SF-6D based on UK weights in other countries.

2. Data and descriptive statistics

2.1. Source of data

We study the impact of chronic illnesses and HRQoL, measured by the SF-6D utility index, on SWB using data from the Disability Health survey. The National Institute for Statistical and Economic Studies (INSEE) conducted this survey in France between April 2008 and October 2008 (Bouvier, 2011). It is based on four different data collection methods: i) a household survey with almost 30,000 respondents living in ordinary housing, ii) an institutional survey with 9000 respondents living in 1550 different institutions, iii) a specific survey of caregivers, and iv) a matching with medical consumption data. Our analysis uses data from the household section. This survey is the only statistical source representative of the French population that includes information on SWB and HRQoL, along with detailed information on various illnesses and chronic diseases for each respondent.

2.2. Measures

We use the SF-6D utility index to represent health. The SF-6D can be estimated from the SF-36 (Ware et al., 1993) or the SF-12 (Ware et al., 1996) HRQoL questionnaires. The Disability Health survey includes part of the SF-36 questionnaire and all SF-12 questions. The SF-6D has six dimensions: physical functioning, social functioning, mental health, role limitation, pain, and vitality. Each dimension has between 4 and 6 levels such that a score of 1 indicates no problem with the dimension, and a higher score represents a more severe problem. The answers are converted to a utility value by combining the various dimensions using weights inferred from the stated preferences of the general population over hypothetical health states. The resulting utility index ranges from 0 (death) to 1 (perfect health). There are no published tariffs for the SF-6D in France, so we applied the UK value set (Brazier and Roberts,

2004).

In the Disability Health survey, the information on chronic conditions is self-reported. The question is: “Do you have or have you ever had any of the following illnesses or health problems?”. If yes, an additional question asked the respondents whether they had had these conditions in the past 12 months. Such an approach may lead to an overestimation of the proportion of chronic illnesses in the survey, as some conditions may have ended in the last 12 months. The survey covers all illnesses reported by the person.

We constructed twelve categories: 1) cardiovascular diseases (heart attack, high blood pressure, heart failure, varicose veins, haemorrhoids, etc.), 2) cancers, 3) respiratory diseases (asthma, bronchitis, allergic rhinitis, etc.), 4) diseases of the bones and joints (back pain, scoliosis, osteoarthritis, osteoporosis, etc.), 5) digestive diseases (ulcers, cirrhosis, etc.), 6) endocrine and metabolic diseases (diabetes, thyroid problems, etc.), 7) neurological diseases (headaches, epilepsy, multiple sclerosis, Alzheimer’s disease, etc.), 8) psychological or mental illnesses (anxiety, depression, autism, schizophrenia, etc.), 9) urinary or genital diseases (incontinence, urinary stones, etc.), 10) skin diseases (psoriasis, eczema, etc.), 11) eye diseases (cataracts, glaucoma, etc.), and 12) other diseases.

Following Mukuria and Brazier (2013), we use a question from the SF-36 about the frequency of happiness feelings to assess SWB: “In the past four weeks, have there been times when you felt happy?”. The five possible answers are “always”, “often”, “sometimes”, “rarely”, and “never”. These answers were converted into an ordered score ranging from 1 for people who never feel happy to 5 for those who always feel happy. We also selected a set of socio-demographic controls as in previous studies: gender, age, marital status, foreign birth, education (seven categories), occupation status (employed, unemployed, student, retired, other inactive), income and urban area segment (nine categories).

2.3. Participants

The self-administered household survey questionnaire was completed by 14,798 respondents. Information on SF-6D items and SWB is available for 12,737 respondents. Detailed information on chronic diseases is available for 23,728 respondents. We restrict the sample to persons aged between 16 and 95. After eliminating observations for which the control variables are missing (2079 participants), this sample contains 21,639 respondents. After matching the different parts of the survey, we obtained a sample of 10,662 people for whom we know SWB, SF-6D, and the various chronic illnesses. Of these, 79.9% (N = 8,154) self-reported at least one condition, with 38.3% reporting one condition, 26.2% reporting two conditions, 16.5% reporting three conditions, and 19.1% reporting at least four conditions.

2.4. Descriptive statistics

According to Table 1, the proportion of women is 56.5%, the average age is 50 (38.7% are over 60 years old and 8.1% are over 80 years old), around 10% of respondents were born abroad, 49.5% have a job, 30.5% are retired, and the average household income is 2,818 euros (the standard deviation is 1,523 euros). There are significant differences in the prevalence of illnesses (see Table A1, online Appendix). The most commonly reported chronic illnesses are bone and joint (39.0%), cardiovascular (32.3%), other (24.8%), respiratory (16.2%) and neurological (15.6%). Mental or psychological illnesses come just behind, with 14.1% of respondents mentioning them. Of the 1,465 respondents who reported a mental or psychological illness, only 2.3% reported an illness other than anxiety or depression (autism, schizophrenia and trisomy 21).

Columns 2 and 3 of Table 1 show large differences in respondents’ characteristics according to whether they report chronic illnesses or not. People reporting at least one chronic illness are more likely to be women (59.0% against 49.0%) and significantly older (51.2 years against 46.9 years). They are more likely to have a low level of education and less

Table 1
Individual characteristics by chronic disease (proportions).

Variables	All	Any chronic illnesses	No chronic illness	Difference
Female	0.565	0.590	0.490	0.100***
Age (average in years)	50.1	51.2	46.9	4.3***
Single	0.295	0.284	0.327	-0.043***
In couple	0.545	0.549	0.533	0.016
Widowed	0.085	0.092	0.064	0.028***
Divorced	0.074	0.074	0.076	-0.002**
Foreign born	0.099	0.101	0.093	0.008
Education: no diploma	0.151	0.157	0.136	0.021***
Education: CEP	0.212	0.222	0.184	0.038***
Education: BAP-CEP	0.230	0.226	0.242	-0.016*
Education: High school	0.155	0.146	0.180	-0.034***
Education: Undergraduate	0.103	0.102	0.106	-0.004*
Education: Graduate	0.071	0.071	0.072	-0.001**
Education: Postgraduate	0.077	0.076	0.081	-0.005***
In employment	0.495	0.467	0.577	-0.110***
Student	0.063	0.060	0.072	-0.012***
Unemployed	0.048	0.044	0.059	-0.015*
Retired	0.305	0.328	0.238	0.090***
Inactive	0.089	0.100	0.054	0.046***
Income (average in euros)	2,817.8	2,751.6	3,011.3	-259.7***
Observations	10,662	8,514	2,148	

Note: significance levels for the mean-comparison tests are 1% (***), 5% (**) and 10% (*).

Source: Disability Health survey 2008, authors’ calculations.

likely to be employed (46.7% against 57.7%). They are also characterized by a lower level of income (-260 euros per month on average). The higher proportion of people unemployed in the group without chronic illness has to be considered in light of the significant proportion of inactive people among those with chronic illnesses.

Regarding SWB, 7.9% of respondents say they are always happy, 36.5% say they are often happy, 15.2% report rarely being happy and 5.6% never being happy. A chi-square test leads to a rejection of independence between SWB and having at least one chronic illness, with a statistic equal to 174.0 (p = 0.000). More precisely, Fig. 1 shows that the correlation between these variables is negative. The proportion of people who are rarely or never happy is 22.8% if they have a chronic illness, compared with 13.41% if they do not. Also, SWB deteriorates significantly as the number of chronic illnesses increases. Of those with at least one disease, 38.3% report exactly one illness, 26.2% have two, 16.5% have three, and almost 20% have at least four. The proportion of people who are never or rarely happy is 15.5% with one chronic illness, 21.0% with two, 28.3% with three, 30.6% with four, and 39.7% with five.

We look at the relationship between SWB and each type of chronic illness in Fig. 2. The proportion of people who are never or rarely happy is significantly higher among respondents who report a mental or psychological illness (42.4%). This is followed by digestive diseases (37.0%) and eye diseases (29.8%). In contrast, there are relatively small differences in SWB for all other types of chronic illness. One concern is that respondents may have multiple conditions. Tables A2 and A3 (online Appendix) describes the association between each condition and between each condition and mental illness. 87.9% of the 1,499 participants who report a mental illness have at least one other condition. For many illnesses (digestive, endocrine or metabolic, neurological, urinary or genital, skin, and eye), more participants report that condition in addition to anxiety and depression (and possibly other conditions) than participants who report only that condition. This seems broadly consistent with observations that anxiety and depression are associated with a higher prevalence of chronic conditions (Bobo et al., 2022).

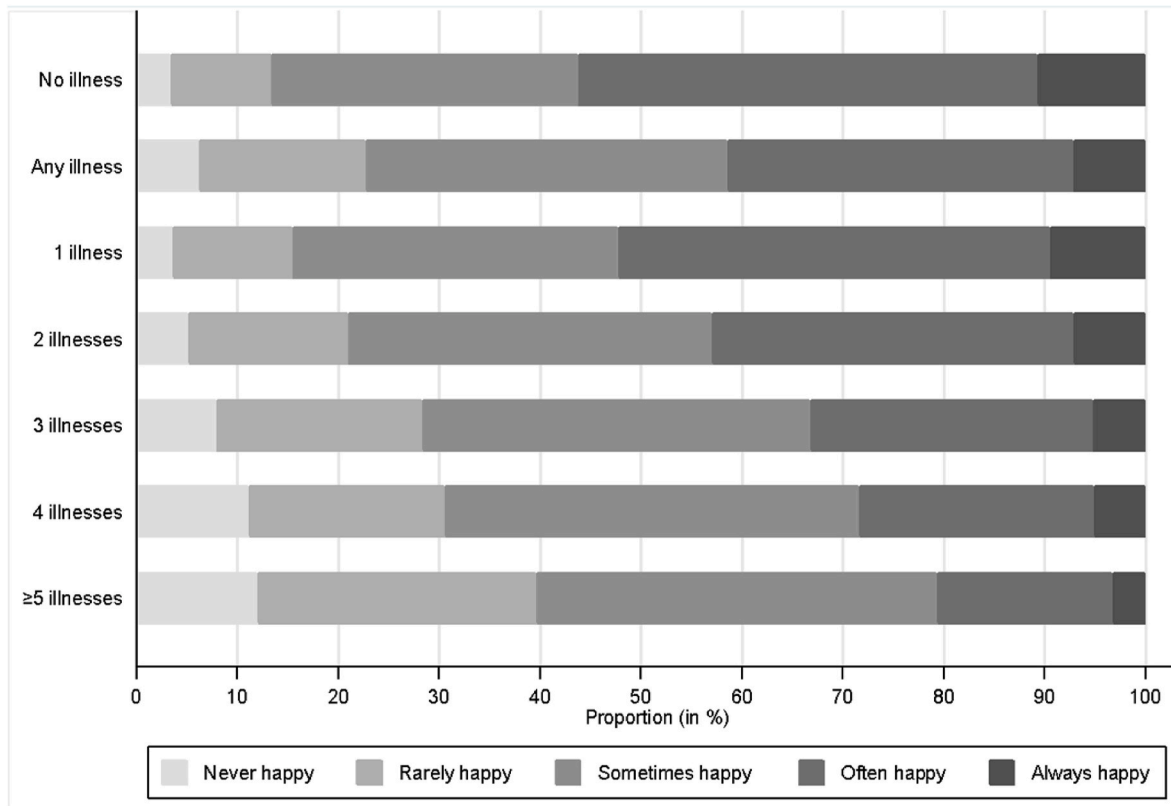


Fig. 1. SWB and chronic illnesses.
Source: Disability Health survey 2008, authors' calculations.

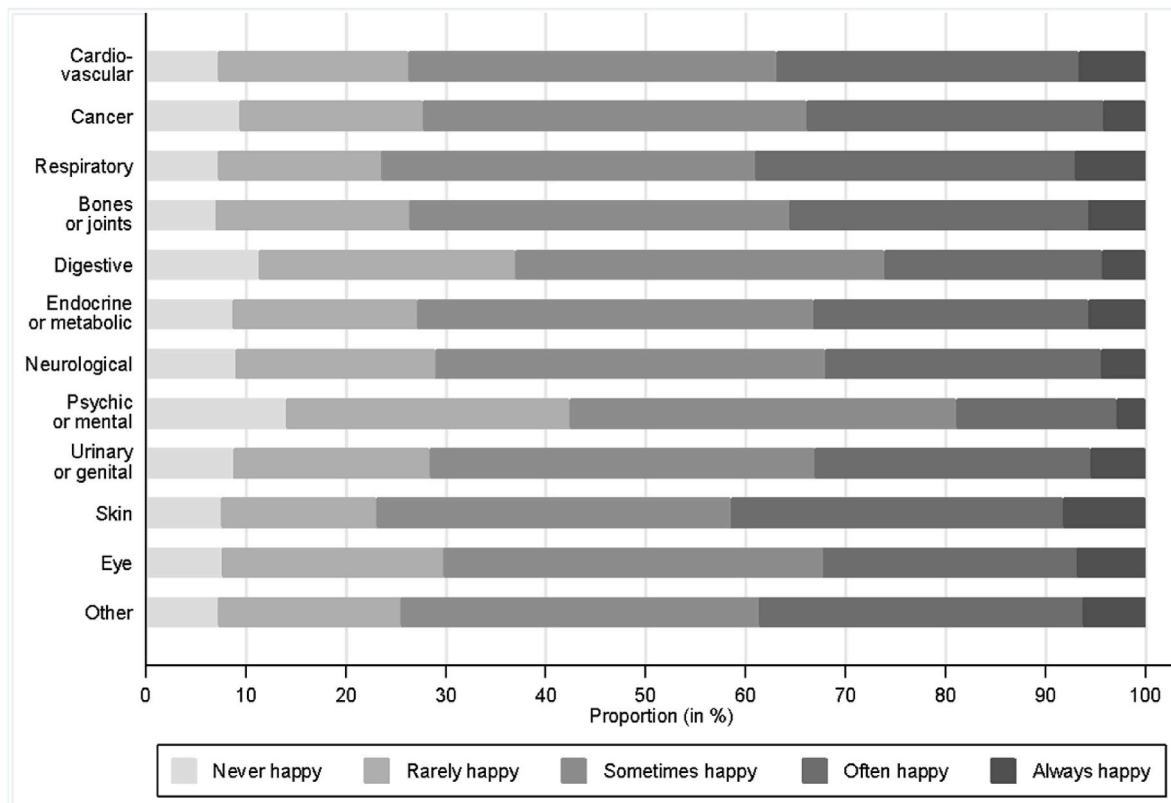


Fig. 2. SWB by type of chronic illness.
Source: Disability Health survey 2008, authors' calculations.

3. The mediation model

We use a mediation analysis to examine the correlation between illness, SF-6D and SWB. Specifically, we examine the magnitudes of the direct and indirect (through SF-6D) associations between chronic illnesses and SWB. A mediation model is a statistical model used to assess the indirect link between an independent variable (the treatment) and a dependent variable (the outcome) through a third variable known as the mediator (Hayes, 2022; Imai et al., 2010; MacKinnon, 2008; Pearl, 2012; VanderWeele, 2016). In a mediation model, the treatment can be correlated with the mediator variable, which is linked to the outcome. We denote by SWB the variable for SWB, $SF6D$ the variable for HRQoL, CI the presence of chronic illnesses, and X a set of individual characteristics.

In our setting, $SF6D$ is a potential mediator through which the treatment CI may influence the outcome SWB . In addition, the treatment CI may be directly linked with SWB , so the total association between CI and SWB is the sum of the direct and indirect links. When the outcome SWB is continuous, the total, direct and indirect links can be obtained by estimating linear regressions or resorting to structural equation modelling. Here, we rely on a regression approach since the outcome and treatment variables are discrete. The mediation model comprises two equations. A first regression explains the outcome SWB :

$$SWB = \alpha_{SWB} + \delta_{CD}CI + \delta_{SF}SF6D + X\beta_{SWB} + \varepsilon_{SWB} \quad (1)$$

where α_{SWB} , δ_{CD} , δ_{SF} and β_{SWB} are the coefficients to be estimated and ε_{SWB} is an error term such that $E(\varepsilon_{SWB}) = 0$. A second regression explains the mediator $SF6D$:

$$SF6D = \alpha_{SF} + \gamma_{CD}CI + X\beta_{SF} + \varepsilon_{SF} \quad (2)$$

where α_{SF} , γ_{CD} and β_{SF} are the coefficients to be estimated and ε_{SF} is an error term such that $E(\varepsilon_{SF}) = 0$. It follows from equations (1) and (2) that the equation explaining SWB can be expressed as:

$$SWB = (\alpha_{SWB} + \delta_{SF}\alpha_{SF}) + (\delta_{CD} + \delta_{SF}\gamma_{CD})CI + (\beta_{SWB} + \delta_{SF}\beta_{SF})X + (\varepsilon_{SWB} + \delta_{SF}\varepsilon_{SF}) \quad (3)$$

Thus, the total correlation between chronic illness CI and SWB is the sum of the direct correlation δ_{CD} and the indirect correlation $\delta_{SF}\gamma_{CD}$ mediated by the SF-6D. Estimating equations (1)–(3) requires overcoming two difficulties.

First, the outcome is ordered, as there are five response categories for the SWB variable, which precludes the estimation of classical linear models. Second, depending on the specifications, we may have either binary or multi-categorical treatments. The former is the case when we consider the prevalence of at least one illness, while the latter is the case when we distinguish between other conditions and mental illness.

Rather than using a parametric mediation estimation strategy, we rely on the inverse odds ratio weighting (IORW) technique originally proposed in Tchetgen Tchetgen (2013) to estimate the direct and indirect association of SWB with chronic illnesses. In this approach, weights obtained from an odds ratio function relating the treatment and the mediator are used in regression models, allowing the method to be applied in complex settings with multiple mediators and discrete outcomes. The IORW estimation of direct and indirect associations involves the following three steps.

First, the total association is obtained by estimating (3) using a regression model with both the treatment and individual characteristics as control variables. Second, the direct correlation is obtained by estimating a weighted version of (3) with IORW weights. The IORW weights correspond to the inverse of the odds ratio association between treatment and mediator, net of the influence of covariates. These weights make the treatment and the mediator independent so that there is no longer an indirect association between the treatment and the outcome. The mediator variable is not introduced in equation (3), but is used in

constructing the IORW weights. Third, the indirect correlation is calculated as the difference between the total and the direct correlations.

The IORW procedure of Tchetgen Tchetgen (2013) has two main advantages. First, because it is a regression-based approach, it can be used with any generalized linear model with possibly nonlinear link functions to handle discrete ordered outcomes. In our setting, the respondent's SWB is explained using an ordered Probit model since there are five response levels. Second, the odds ratio is a symmetric measure of association. According to the invariance property of odds ratios, the odds ratio between two variables is the same regardless of which variable is specified as either the dependent or independent variable. This means that the estimation of the odds ratio linking the treatment and the mediator can be achieved by explaining either the treatment or the mediator. This allows for multiple mediator settings to be considered, or for continuous or discrete mediators to be treated appropriately. The main drawback of the IORW approach is that, compared to parametric mediation approaches, the standard errors may be larger, preventing the detection of indirect associations of small magnitude (Nguyen et al., 2015).

Unlike an instrumental variable framework, which aims to estimate the causal effect of an independent variable on an outcome in the presence of endogeneity, mediation analysis seeks to understand the process by which the independent variable is linked to the outcome (no exogenous instrument is needed). There are three main assumptions for the identification of direct and indirect associations (Imai et al., 2010). First, the consistency assumption states that the observed outcomes for each observation are the same as the potential outcomes under the observed treatment and mediator values. Second, sequential ignorability includes ignorability of the treatment assignment and of the mediator. No unmeasured confounders influence the relationships between the treatment, the mediator and the outcome, given the observed covariates. Third, according to the positivity assumption, there should be sufficient variation in the data such that, for any combination of controls, there is a non-zero probability of receiving any treatment and observing any mediator. Our results are thus valid under selection on observables, but not selection on unobservables.

In our analyses, we begin by estimating the ordered Probit model given by equation (1) of our mediation model, where $SF6D$ is treated as an exogenous covariate. In the first step, we estimate two separate models where only having a chronic illness is regressed on SWB ($\delta_{SF} = 0$) and then only the SF-6D is regressed on SWB ($\delta_{CD} = 0$). In the second stage, we estimate a model where both illness and SF-6D are included, meaning that both δ_{SF} and δ_{CD} can be different from zero (full model). Following Böckerman et al. (2011), we interpret a significant coefficient for chronic illness in this model as evidence that the SF-6D does not fully reflect the subjective experience of illness (Hypothesis 1).

Next, we proceed with the mediation analysis. First, following equation (3), we estimate an ordered Probit model explaining SWB with both CI and X as controls and obtain an estimate of the total correlation. Second, following equation (2), we estimate the probability of reporting at least one chronic illness using a Logit model as a function of the SF-6D utility index and individual characteristics X and use the estimated coefficient of the mediator to derive the IORW weights. Respondents without a chronic illness are assigned a weight of one. Third, we estimate a weighted ordered Probit model explaining happiness with the IORW weights and obtain an estimate of the direct association with chronic illness. Fourth, we subtract this direct correlation from the total correlation to get the indirect one. Regarding inference, we rely on bootstrapping with 1,000 replications to obtain standard errors for the total, direct, and indirect correlations.

Finally, we attempt to assess the cumulative associations and, in particular, the specific link between mental illnesses and SWB. We consider a treatment categorized by the following four cases: i) no chronic illness, ii) only mental illness, iii) at least one chronic illness other than mental, and iv) at least one chronic physical illness in addition to mental illness. The treatment then becomes multi-categorical,

and no single parameter can measure the association of the treatment with the mediator and the outcome. One solution is to define a reference modality for the treatment and calculate relative associations for each treatment modality (Hayes and Preacher, 2014). Using the invariance property of odds ratios, we explain the different treatment categories using a multinomial Logit model that includes the mediator and individual characteristics as explanatory variables. The estimated coefficients of the multinomial model allow us to construct the IORW weights.

4. Results

4.1. The determinants of SWB

Table 2 reports the estimates corresponding to the ordered probit model where the SF-6D is considered as exogenous (equation (1)). The model is estimated with and without sociodemographic controls to assess the robustness of our findings. The corresponding estimates are given for the full sample and women and men separately.

Looking at the whole sample, there is a significant negative correlation between SWB and chronic illness (se = 0.025). We find a strong positive correlation between SWB and the SF-6D utility index (se = 0.089). Consistent with our first hypothesis, the estimates in column 3 indicate that having at least one chronic illness still correlates with SWB when HRQoL is introduced as a control. The correlation between happiness and SF-6D remains strongly positive, and the SF-6D coefficient is hardly reduced (from 4.831 in column 2 to 4.796 in column 3). The chronic illness coefficient is divided by more than 4, from -0.327 to -0.078. Nevertheless, chronic illnesses significantly correlate with happiness. The pseudo-R² statistics in Table 2 are low, but similar in magnitude to those in studies of the correlation between SF-6D and SWB in national survey samples (Dolan et al., 2012).

To allow for comparison with other works, our models included a set of individual sociodemographic characteristics as control variables (column 4). As in previous studies (Dolan et al., 2012; Mukuria and Brazier, 2013), they have almost no effect on the SF-6D and the chronic

Table 2
Ordered Probit estimates of SWB.

Variables	(1)	(2)	(3)	(4)
Panel A. All				
Chronic illness	-0.327*** (0.025)		-0.078*** (0.026)	-0.075*** (0.027)
SF-6D		4.831*** (0.089)	4.796*** (0.090)	4.747*** (0.099)
Control variables	NO	NO	NO	YES
Observations	10,662	10,662	10,662	10,662
Pseudo-R ²	0.006	0.132	0.133	0.143
Panel B. Men				
Chronic illness	-0.341*** (0.037)		-0.073* (0.038)	-0.072* (0.038)
SF-6D		4.817*** (0.139)	4.776*** (0.139)	4.835*** (0.153)
Control variables	NO	NO	NO	YES
Observations	4,557	4,557	4,557	4,557
Pseudo-R ²	0.007	0.131	0.132	0.143
Panel C. Women				
Chronic illness	-0.300*** (0.035)		-0.083** (0.037)	-0.078** (0.037)
SF-6D		4.852*** (0.116)	4.822*** (0.118)	4.704*** (0.129)
Control variables	NO	NO	NO	YES
Observations	6,105	6,105	6,105	6,105
Pseudo-R ²	0.004	0.133	0.133	0.146

Note: estimates from ordered Probit regressions, with robust standard errors in parentheses. Significance levels are 1% (***), 5% (**), and 10% (*). Controls include gender, age (five-year groups), marital status, foreign born, education, occupation status, income quartiles, and urban unit segment. Source: Disability Health survey 2008, authors' calculations.

disease variables coefficients (details available on request). Gender-specific regressions confirm the negative correlation between happiness and chronic illness (column 1) and the positive correlation between happiness and the SF-6D (column 2). Wald tests reject the hypothesis of unequal coefficients for men and women. The coefficient of SF-6D in the happiness equation is only slightly reduced by the introduction of chronic illness as a control (columns 3 and 4). Reporting at least one chronic illness is negatively correlated with SWB, at the 10 percent level (se = 0.038) for men and at the 5 percent level (se = 0.037) for women without control variables.

Next, we explore the possibility of a cumulative association between the number of chronic illnesses and happiness net of the correlation with the SF-6D and individual characteristics (Hypothesis 3). Consistent with this hypothesis, Fig. 3 shows that for a given HRQoL level SWB decreases with the number of chronic illnesses, although there is no significant difference between those with no chronic illness and those with only one. Nevertheless, the different confidence intervals associated with each number of illnesses mostly overlap. We find significant differences only between at least five illnesses and either one illness (p = 0.004) or two illnesses (p = 0.029).

In Table A4 (online appendix), we estimate happiness as a function of the detailed illness dummies. These results show that the largest coefficient (in absolute value) is found for psychic or mental illness. When the SF-6D is not included as a control, 6 out of 12 illnesses are statistically significant and negatively correlated with SWB. The situation is different when the SF-6D is included. The correlation between SWB and mental illness remains large and significant, and there is only one other negative correlation between SWB and neurological illness (for men only). Since, as could be expected, it is mainly having a psychological or mental illness that strongly reduces well-being, we isolate the role of mental illness from other diseases in what follows.

In panel A of Table 3, we introduce two dummy variables for mental illness and other chronic illnesses, respectively. Without the SF-6D control (column 1A), we find a negative and significant correlation between SWB and both types of chronic illnesses. Still, the correlation with mental illness is four times higher than that with other chronic conditions. The results differ when introducing HRQoL as a control (column 1B). The coefficient associated with mental illness is almost half as large, but the correlation between happiness and other illnesses is no longer statistically significant. The results are very similar when we estimate separate regressions for men and women. For a given level of HRQoL, having at least one chronic condition other than mental illness does not play a significant role in explaining SWB (columns 2B and 3B).

In panel B of Table 3, we account for the cumulative association between chronic illnesses and SWB (Hypothesis 3) by distinguishing four cases: no disease (20.1%, reference category), only mental illness (1.7%), at least one chronic illness other than mental (65.8%), and both types of illnesses (12.4%). Without the SF-6D as a control, SWB is negatively correlated with the different combinations of illnesses (column 1A). When the SF-6D is included, having at least one chronic illness other than mental illness does not correlate with SWB (column 1B). In contrast, having a mental illness and another condition significantly reduces happiness, although the marginal correlation is of the same order for the very few respondents who have only a mental illness. Fig. A1 (online Appendix) shows the results for each type of disease. Except for cancer, it is the combination of each condition with mental illness that has the most negative association with SWB.

4.2. Direct versus indirect links

Table 4 reports the results of the mediation analysis, the detailed estimates being in Table A5 (online Appendix). Panel A considers all respondents. The main result supports Hypothesis 2 since the correlation between chronic illnesses and SWB passes mainly through the SF-6D. However, the direct correlation (-0.063) remains non-negligible since it accounts for 25.9% of the total correlation, while the indirect

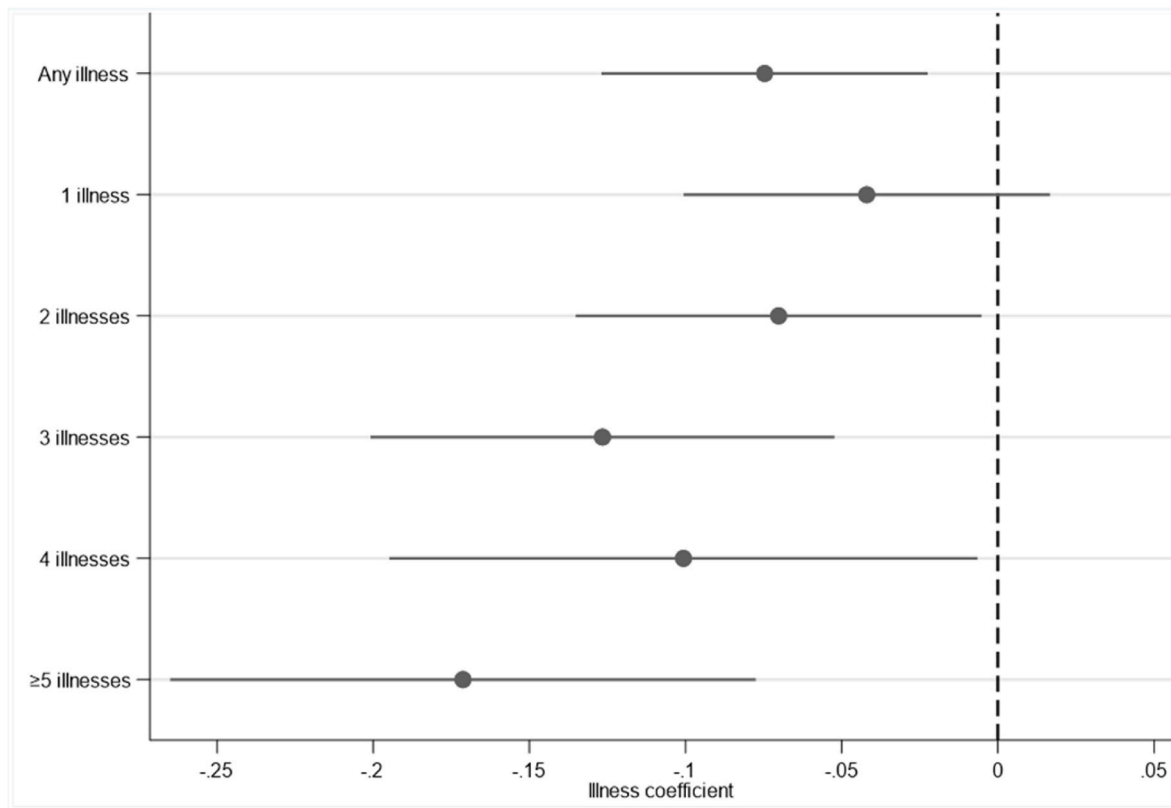


Fig. 3. Ordered Probit estimates of SWB and number of chronic illnesses.

Note: estimates from ordered Probit regressions, with robust standard errors (95% confidence intervals are presented). Controls include gender, age (five-year groups), marital status, foreign born, education, occupation status, quartiles of income, and urban unit segment. Source: Disability Health survey 2008, authors' calculations.

Table 3
Ordered Probit estimates of SWB, with mental illness.

Variables	(1A) All	(1B) All	(2A) Men	(2B) Men	(3A) Women	(3B) Women
Panel A.						
Mental illness	-0.628*** (0.031)	-0.331*** (0.031)	-0.619*** (0.054)	-0.335*** (0.056)	-0.629*** (0.038)	-0.330*** (0.039)
Any other illnesses	-0.152*** (0.025)	-0.023 (0.026)	-0.190*** (0.037)	-0.031 (0.038)	-0.120*** (0.035)	-0.015 (0.036)
SF-6D		4.600*** (0.100)		4.732*** (0.154)		4.527*** (0.131)
Control variables	YES	YES	YES	YES	YES	YES
Observations	10,662	10,662	4,557	4,557	6,105	6,105
Pseudo-R ²	0.050	0.147	0.044	0.145	0.057	0.150
Panel B.						
Mental illness only	-0.615*** (0.083)	-0.385*** (0.085)	-0.585*** (0.115)	-0.367*** (0.127)	-0.620*** (0.118)	-0.398*** (0.114)
Any other illnesses only	-0.151*** (0.027)	-0.029 (0.027)	-0.187*** (0.038)	-0.035 (0.039)	-0.119*** (0.037)	-0.023 (0.038)
Mental and other illnesses	-0.781*** (0.039)	-0.352*** (0.040)	-0.813*** (0.066)	-0.362*** (0.068)	-0.748*** (0.049)	-0.344*** (0.051)
SF-6D		4.601*** (0.100)		4.733*** (0.154)		4.528*** (0.131)
Control variables	YES	YES	YES	YES	YES	YES
Observations	10,662	10,662	4,557	4,557	6,105	6,105
Pseudo-R ²	0.050	0.147	0.044	0.145	0.057	0.150

Note: estimates from ordered Probit regressions, with robust standard errors in parentheses. Significance levels are 1% (***), 5% (**), and 10% (*). Controls include gender, age (five-year groups), marital status, foreign born, education, occupation status, income quartiles, and urban unit segment. Source: Disability Health survey 2008, authors' calculations.

correlation (-0.181) accounts for 74.1%. Both the direct and indirect correlations are statistically significant.

Panels B and C show the correlations for men and women. The results are very similar and three-quarters of the correlation between chronic

illnesses and SWB is mediated by SF-6D: 25.4% for men and 26.9% for women. Following the suggestion of Nguyen et al. (2015), we have also estimated a set of inverse odds weights (IOW). The predicted probability of each respondent having at least one chronic illness is then used to

Table 4
Mediation analysis of chronic illness on SWB, with SF-6D as mediator.

Variables		Direct correlation	Indirect correlation	Total correlation
Panel A. All [N = 10,662]				
Chronic illness	coefficient	-0.063***	-0.181***	-0.245***
	st. error	(0.023)	(0.014)	(0.025)
	%	25.9%	74.1%	100.0%
Panel B. Men [N = 4,557]				
Chronic illness	coefficient	-0.066*	-0.193***	-0.259***
	st. error	(0.034)	(0.021)	(0.039)
	%	25.4%	74.6%	100.0%
Panel C. Women [N = 6,105]				
Chronic illness	coefficient	-0.063**	-0.170***	-0.233***
	st. error	(0.030)	(0.019)	(0.034)
	%	26.9%	73.1%	100.0%

Note: estimates from a mediation analysis with IORW weights, with bootstrapped standard errors in parentheses (1,000 replications). The regression models explaining happiness are ordered Probit regressions. Significance levels are 1% (***), 5% (**), and 10% (*). Controls include gender, age (five-year groups), marital status, foreign born, education, occupation status, income quartiles, and urban unit segment.
Source: Disability Health survey 2008, authors' calculations.

obtain the IOW weights. We reach very similar results since the indirect correlation between chronic illnesses and SWB equals 26.9% with IOW weights against 25.9% using IORW weights.

Table 5 presents the estimates of the mediation analysis considering the possibility of cumulative association between chronic illnesses, with the reference being the absence of chronic illness. We report the direct, indirect, and total correlations for each treatment modality. The first finding is that the largest total correlation with SWB concerns the combination of mental illness and other conditions. Pooling men and women (panel A), the total correlation is about five times smaller for people reporting any illnesses other than mental illness.

A second finding is that there are large differences in the direct

correlation for each treatment category. For people who report only a mental illness, 60.8% of the correlation is direct, which invalidates Hypothesis 2 in this case. Conversely, when the mental illness is associated with one or more other conditions, only one-third of the correlation is direct: the joint association of mental and other conditions is primarily linked to SWB through the SF-6D (64.2%). When no mental illness is reported, 59.3% of the link is indirect.

Panels B and C show some noticeable differences between men and women. First, conditions other than mental illness are only indirectly correlated with SWB for men (93.4%), while about half of the correlation is indirect for women (56.9%). Second, while the total correlation with mental illness alone is very similar for men and women (about

Table 5
Mediation analysis of mental and other chronic illnesses on SWB, with SF-6D as mediator.

Variables		Direct correlation	Indirect correlation	Total correlation
Panel A. All [N = 10,662]				
Other illness only	coefficient	-0.061**	-0.089***	-0.151***
	st. error	(0.030)	(0.023)	(0.026)
	%	40.7%	59.3%	100.0%
Mental illness only	coefficient	-0.373***	-0.241***	-0.615***
	st. error	(0.112)	(0.087)	(0.083)
	%	60.8%	39.3%	100.0%
Mental and other illnesses	coefficient	-0.279***	-0.501***	-0.781***
	st. error	(0.058)	(0.050)	(0.038)
	%	35.8%	64.2%	100.0%
Panel B. Men [N = 4,557]				
Other illness only	coefficient	-0.012	-0.174***	-0.187***
	st. error	(0.049)	(0.038)	(0.040)
	%	6.6%	93.4%	100.0%
Mental illness only	coefficient	-0.572***	-0.013	-0.585***
	st. error	(0.170)	(0.124)	(0.121)
	%	97.7%	2.3%	100.0%
Mental and other illnesses	coefficient	-0.358***	-0.455***	-0.813***
	st. error	(0.109)	(0.087)	(0.068)
	%	44.0%	56.0%	100.0%
Panel C. Women [N = 6,105]				
Other illness only	coefficient	-0.051	-0.068**	-0.119***
	st. error	(0.040)	(0.032)	(0.036)
	%	43.1%	56.9%	100.0%
Mental illness only	coefficient	-0.183	-0.437***	-0.620***
	st. error	(0.154)	(0.128)	(0.117)
	%	29.5%	70.5%	100.0%
Mental and other illnesses	coefficient	-0.284***	-0.464***	-0.748***
	st. error	(0.070)	(0.058)	(0.048)
	%	38.0%	62.0%	100.0%

Note: estimates from a mediation analysis with IORW weights, with bootstrapped standard errors in parentheses (1,000 replications). The regression models explaining happiness are ordered Probit regressions. Significance levels are 1% (***), 5% (**), and 10% (*). Controls include gender, age (five-year groups), marital status, foreign born, education, occupation status, income quartiles, and urban unit segment.
Source: Disability Health survey 2008, authors' calculations.

–0.6), its association with SWB is exclusively direct for men (97.7%) but essentially indirect for women (70.5%). In other terms, regarding mental illness, Hypothesis 2 holds only for women. For men, the SF-6D does not fully capture the variation in SWB associated with illness, leaving most of it unexplained. Finally, when mental illness is combined with other chronic conditions, about 60% of the correlation with SWB is mediated by SF-6D (56.0% for men, 62.0% for women).

5. Discussion and concluding comments

This study tests three hypotheses regarding the ability of the SF-6D utility index to capture the consequences of various chronic illnesses on SWB using a large sample of the French population. It examines whether chronic illness is associated with SWB in addition to its association with the SF-6D (Hypothesis 1), whether the correlation between chronic illnesses and SWB is primarily captured by the SF-6D (Hypothesis 2) and whether the association not mediated by the SF-6D increases with the number of illnesses (Hypothesis 3). Thus, it adds to the literature by investigating the possibility that both the type and the combination of physical and mental conditions matter and by using a mediation analysis to quantify the direct and indirect (through variations in the SF-6D) correlation between illnesses and SWB.

We found that the SF-6D does not fully reflect variations in SWB associated with mental illness. The latter lowers SWB even when the SF-6D utility index is included as a control variable in the regression models. Böckerman et al. (2011) and Richardson et al. (2015) obtained similar results for several preference-based HRQoL instruments and samples from various countries. Additionally, our analyses suggest a gender gap in the ability of the SF-6D to capture changes in SWB associated with mental illness. The SF-6D captures most of the changes in SWB associated with mental illness in women, but misses almost all of the changes in men. The importance of mental illness was partly expected, as the literature shows a strong negative association between mental health and SWB (Dolan et al., 2012; Dolan and Metcalfe, 2012; Mukuria and Brazier, 2013). Most preference-based HRQoL measures give little importance to mental health (Brazier et al., 2014). However, there are exceptions, such as the Danish tariffs for the EQ-5D-5L, that ascribe the most important weight to the anxiety/depression dimension of HRQoL (Jensen et al., 2021).

As stated above, the inability to fully account for the consequences of mental illness has been found in previous studies. However, in contrast to Richardson et al. (2015), we find no significant associations between SWB and other conditions than mental illness when controlling for the SF-6D and not accounting for co-occurrence of diseases. Wu et al. (2014) also found no correlation between chronic illnesses and SWB when they controlled for the descriptive system of the EQ-5D.

Another contribution of our study is to test the possibility of a cumulative direct association between chronic conditions and SWB along the SF-6D (Hypothesis 3). We find that, except for cancer, the negative direct association of any illness with SWB not captured by the SF-6D is larger when this association includes chronic anxiety or depression. This is broadly consistent with studies showing that a higher number of chronic illnesses is associated with lower SWB (Addabbo et al., 2016; Elmståhl et al., 2020). This result qualifies observations, based on considering each chronic illness in isolation, that only mental illness may be linked to SWB independently of SF-6D.

This finding is important because mental illness most often co-occurs with other conditions (Bobo et al., 2022). This is precisely the case in our sample, where having a mental illness alone is uncommon. Thus, the ability of the SF-6D to capture variations in SWB due to chronic illness may be overestimated when multimorbidity is not considered. Furthermore, although our mediation analysis shows that the SF-6D generally accounts for most of the variation in SWB due to chronic illnesses, this is not the case for mental illness.

Our findings further our understanding of the ability of preference-based HRQoL instruments to capture the impact of illness on SWB.

They suggest either that the descriptive system of the SF-6D lacks some psychological/mental dimensions of life that are important in the face of chronic illness, particularly mental illness, or that the weighting of the dimensions in the SF-6D utility index gives too little importance to mental health.

The measure of SWB in our analyses comes from the SF-36 questionnaire. One might wonder whether including this question/dimension in the SF-6D utility score would allow it to capture variations in SWB due to chronic illness (Richardson et al., 2015). However, the question also likely depends on determining the appropriate weighting of the different dimensions of HRQoL to arrive at a utility index. Thus, while our analyses highlight the limitations of the SF-6D to represent experienced utility in the face of chronic illness, they do not provide a clear path as to how this ability could be improved.

Our study has several limitations. First, chronic conditions are self-reported in the Disability Health survey. Using reported information on anxiety and depression may have heightened the correlation with happiness, given the closeness between the concepts of mental health and SWB. Second, we use only one measure of SWB. As Richardson et al. (2015) have shown, the results could have been different for other measures of SWB, such as life satisfaction.

Third, we only have cross-sectional information, which does not allow us to account for unobserved heterogeneity at the individual level or explore reverse causality between chronic illness and SWB. In particular, personality traits may moderate the association between chronic illness and SWB (Aaskoven et al., 2024), and high SWB may be protective against the negative health consequences of chronic illness (Diener et al., 2017). The use of panel data would be necessary to replicate our analyses while accounting for these issues. Fourth, in the Disability Health survey, the questions about self-reported chronic illnesses were administered before the SF-12 and SWB questions. This order may have exacerbated the direct association between chronic illness and SWB. However, the same possibility applies to the correlation between chronic illness and the SF-6D, so we cannot speculate on the overall effect on our findings.

Fifth, our study used a measure of SWB assessed on a Likert scale. Our analyses did not assume that this measure had interval properties. An empirical investigation by Ferrer-i-Carbonell and Frijters (2004) suggested that considering measures of SWB as either ordinal or cardinal does not change the qualitative results of regression analyses. However, this issue remains controversial (Schröder and Yitzhaki, 2017). Finally, our estimates may be biased by selection bias. The response rate for the Disability Health survey was 76.6% (Bouvier, 2011). We cannot exclude that missing responses are correlated with the impact of chronic illness on HRQoL and SWB. Nevertheless, this does not invalidate our finding that the SF-6D does not account for the total correlation between chronic illness and SWB for the individuals included in our analyses.

In conclusion, our analyses highlight the limited ability of the SF-6D to capture changes in SWB due to chronic illness in a representative sample of the French population. This inability does not only concern mental illness, but also multimorbidity when mental illness is associated with other conditions, and it differs for women and men. Although the SF-6D captures most of the association between chronic illness and SWB, our mediation analysis shows that the remaining direct correlation is significant.

Thus, the use of the SF-6D in economic evaluations could lead to suboptimal decisions regarding programs aiming at preventing the incidence of mental illness or improving the quality of life of people who suffer from chronic anxiety and depression in addition to a physical illness. Suppose one aims to reflect the experience of patients in CEA. In that case, our findings suggest that the SF-6D should be revised by considering additional dimensions or by modifying the actual weighting of its dimensions. Another possibility suggested by Richardson et al. (2015) would be to use preference-based HRQoL instruments that give more weight to psychological and mental health.

Funding

We have no funding to declare.

Ethics approval/Statement EA not required

This research did not require Ethics approval, as it relies on a secondary analysis of data made publicly available for research by ADISP (National Archive of Data from Official Statistics). The data disseminated by Adisp are accessible free of charge to researchers, professors, doctoral students, post-doctoral students, and, master's students (in France or abroad) affiliated with a research or educational institution: http://www.progedo-adisp.fr/acces_conditions_en.php.

CRedit authorship contribution statement

Philippe Tessier: Writing – original draft, Methodology, Conceptualization. **François-Charles Wolff:** Writing – original draft, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors have no competing interests to declare.

Data availability

Data were collected by the National Institute of Statistics and Economic Studies in France and are publicly available for research purposes: doi:10.13144/lil-0459 Enquête Handicap Santé - Volet ménages (HSM) - 2008, INSEE (producteur), ADISP (diffuseur).

Acknowledgements

The authors are grateful to Elodie Dejmaï, the discussants at the 40th Journées de Microéconomie Appliquée, and two anonymous referees for their helpful comments.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.socscimed.2024.117086>.

References

- Aaskoven, M.S., Kjær, T., Gyrd-Hansen, D., 2024. Subjective well-being and chronic illnesses: a combined survey and register study. *Intnl. J. Wellbeing* 14, 1–20. <https://doi.org/10.5502/ijw.v14i1.2443>.
- Addabbo, T., Sarti, E., Sciuilli, D., 2016. Disability and life satisfaction in Italy. *Applied Research Quality Life* 11, 925–954. <https://doi.org/10.1007/s11482-015-9412-0>.
- Awaworyi Churchill, S., Munyanyi, M.E., Prakash, K., Smyth, R., 2020. Locus of control and the gender gap in mental health. *J. Econ. Behav. Organ.* 178, 740–758. <https://doi.org/10.1016/j.jebo.2020.08.013>.
- Bobo, W.V., Grossardt, B.R., Virani, S., St Sauver, J.L., Boyd, C.M., Rocca, W.A., 2022. Association of depression and anxiety with the accumulation of chronic conditions. *JAMA Netw. Open* 5, e229817. <https://doi.org/10.1001/jamanetworkopen.2022.9817>.
- Böckerman, P., Johansson, E., Saarni, S.I., 2011. Do established health-related quality-of-life measures adequately capture the impact of chronic conditions on subjective well-being? *Health Pol.* 100, 91–95. <https://doi.org/10.1016/j.healthpol.2010.10.008>.
- Bouvier, G., 2011. L'enquête handicap-santé - présentation générale. Document de travail n° F1109. Insee.
- Brazier, J., Ara, R., Rowen, D., Chevrou-Severac, H., 2017. A review of generic preference-based measures for use in cost-effectiveness models. *Pharmacoeconomics* 35, 21–31. <https://doi.org/10.1007/s40273-017-0545-x>.
- Brazier, J., Connell, J., Papaioannou, D., Mukuria, C., Mulhern, B., Peasgood, T., Jones, M.L., Paisley, S., O' Cathain, A., Barkham, M., Knapp, M., Byford, S., Gilbody, S., Parry, G., 2014. A systematic review, psychometric analysis and qualitative assessment of generic preference-based measures of health in mental health populations and the estimation of mapping functions from widely used specific measures. *Health Technol. Assess.* 18, 1–188. <https://doi.org/10.3310/hta18340> vii–viii, xiii–xxv.

- Brazier, J.E., Roberts, J., 2004. The estimation of a preference-based measure of health from the SF-12. *Med Care* 42, 851–859. <https://doi.org/10.1097/01.mlr.0000135827.18610.0d>.
- Brazier, J.E., Rowen, D., Lloyd, A., Karimi, M., 2019. Future directions in valuing benefits for estimating QALYs: is time up for the EQ-5D? *Value Health* 22, 62–68. <https://doi.org/10.1016/j.jval.2018.12.001>.
- Chen, G., Olsen, J.A., 2023. Extending the EQ-5D: the case for a complementary set of 4 psycho-social dimensions. *Qual. Life Res.* 32, 495–505. <https://doi.org/10.1007/s11136-022-03243-7>.
- Diener, E., Lucas, R.E., Oishi, S., 2018. Advances and open questions in the science of subjective well-being. *Collabra: Psychology* 4, 15. <https://doi.org/10.1525/collabra.115>.
- Diener, E., Pressman, S.D., Hunter, J., Delgado-Chase, D., 2017. If, why, and when subjective well-being influences health, and future needed research. *Appl. Psychol.: Health and Well-Being* 9, 133–167. <https://doi.org/10.1111/aphw.12090>.
- Dolan, P., 2011. Using Happiness to Value Health. *Office of Health Economics*.
- Dolan, P., Kahneman, D., 2007. Interpretations of utility and their implications for the valuation of health. *Econ. J.* 118, 215–234. <https://doi.org/10.1111/j.1468-0297.2007.02110.x>.
- Dolan, P., Lee, H., Peasgood, T., 2012. Losing sight of the wood for the trees: some issues in describing and valuing health, and another possible approach. *Pharmacoeconomics* 30, 1035–1049. <https://doi.org/10.2165/11593040-000000000-00000>.
- Dolan, P., Metcalfe, R., 2012. Valuing health: a brief report on subjective well-being versus preferences. *Med. Decis. Making* 32, 578–582. <https://doi.org/10.1177/0272989X11435173>.
- Elmståhl, S., Sanmartin Berglund, J., Fagerström, C., Ekström, H., 2020. The life satisfaction index-A (LSI-A): normative data for a general Swedish population aged 60 to 93 years. *CIA* 15, 2031–2039. <https://doi.org/10.2147/CIA.S275387>.
- Ferrer-i-Carbonell, A., Frijters, P., 2004. How important is methodology for the estimates of the determinants of happiness? *Econ. J.* 114, 641–659. <https://doi.org/10.1111/j.1468-0297.2004.00235.x>.
- Garay, O.U., Nishimwe, M.L., Bousmah, M.-Q., Janah, A., Girard, P.-M., Chêne, G., Moinot, L., Sagaon-Teyssier, L., Meynard, J.-L., Spire, B., Boyer, S., 2019. Cost-effectiveness analysis of lopinavir/ritonavir monotherapy versus standard combination antiretroviral therapy in HIV-1 infected patients with viral suppression in France (ANRS 140 DREAM). *Pharmacoeconomics Open* 3, 505–515. <https://doi.org/10.1007/s41669-019-0130-7>.
- Has, H.A.S., 2020. *Choix méthodologiques pour l'évaluation économique à la HAS (Guide méthodologique)*. Saint-Denis La Plaine.
- Hayes, A.F., 2022. *Introduction to mediation, moderation, and conditional process analysis: a regression-based approach*. *Methodology in the Social Sciences*, third ed. The Guilford Press, New York London.
- Hayes, A.F., Preacher, K.J., 2014. Statistical mediation analysis with a multicategorical independent variable. *Brit J Math & Statis* 67, 451–470. <https://doi.org/10.1111/bmsp.12028>.
- Høgh, M.B., Kronborg, C., Hansen, J.M., Schaffalitzky De Muckadell, O.B., 2019. The cost effectiveness of *Helicobacter pylori* population screening—economic evaluation alongside a randomised controlled trial with 13-year follow-up. *Aliment. Pharmacol. Ther.* 49, 1013–1025. <https://doi.org/10.1111/apt.15193>.
- Imai, K., Keele, L., Tingley, D., 2010. A general approach to causal mediation analysis. *Psychol. Methods* 15, 309–334. <https://doi.org/10.1037/a0020761>.
- Jensen, C.E., Sørensen, S.S., Gudex, C., Jensen, M.B., Pedersen, K.M., Ehlers, L.H., 2021. The Danish EQ-5D-5L value set: a hybrid model using cTTO and dce data. *Appl. Health Econ. Health Pol.* 19, 579–591. <https://doi.org/10.1007/s40258-021-00639-3>.
- Kahneman, D., Wakker, P.P., Sarin, R., 1997. Back to bentham? Explorations of experienced utility. *Q. J. Econ.* 112, 375–406. <https://doi.org/10.1162/003355397555235>.
- MacKinnon, D.P., 2008. *Introduction to Statistical Mediation Analysis, Multivariate Applications*. Lawrence Erlbaum Associates, New York.
- Mukuria, C., Brazier, J., 2013. Valuing the EQ-5D and the SF-6D health states using subjective well-being: a secondary analysis of patient data. *Soc. Sci. Med.* 77, 97–105. <https://doi.org/10.1016/j.socscimed.2012.11.012>.
- Nguyen, Q.C., Osypuk, T.L., Schmidt, N.M., Glymour, M.M., Tchetgen Tchetgen, E.J., 2015. Practical guidance for conducting mediation analysis with multiple mediators using inverse odds ratio weighting. *Am. J. Epidemiol.* 181, 349–356. <https://doi.org/10.1093/aje/kwu278>.
- NICE, 2013. *Guide to the Methods of Technology Appraisal 2013, NICE Process and Methods [PMG9]*.
- Ofori-Asenso, R., Chin, K.L., Curtis, A.J., Zomer, E., Zoungas, S., Liew, D., 2019. Recent patterns of multimorbidity among older adults in high-income countries. *Popul. Health Manag.* 22, 127–137. <https://doi.org/10.1089/pop.2018.0069>.
- Olsen, J.A., Misajon, R., 2020. A conceptual map of health-related quality of life dimensions: key lessons for a new instrument. *Qual. Life Res.* 29, 733–743. <https://doi.org/10.1007/s11136-019-02341-3>.
- Pearl, J., 2012. The causal mediation formula—a guide to the assessment of pathways and mechanisms. *Prev. Sci.* 13, 426–436. <https://doi.org/10.1007/s11221-011-0270-1>.
- Peeters, Y., Vliet Vlieland, T.P.M., Stiggelbout, A.M., 2012. Focusing illusion, adaptation and EQ-5D health state descriptions: the difference between patients and public. *Health Expect.* 15, 367–378. <https://doi.org/10.1111/j.1369-7625.2011.00667.x>.
- Richardson, J., Chen, G., Khan, M.A., Iezzi, A., 2015. Can multi-attribute utility instruments adequately account for subjective well-being? *Med. Decis. Making* 35, 292–304. <https://doi.org/10.1177/0272989X14567354>.

- Schröder, C., Yitzhaki, S., 2017. Revisiting the evidence for cardinal treatment of ordinal variables. *Eur. Econ. Rev.* 92, 337–358. <https://doi.org/10.1016/j.euroeconrev.2016.12.011>.
- Scott, K.M., Lim, C., Al-Hamzawi, A., Alonso, J., Bruffaerts, R., Caldas-de-Almeida, J.M., Florescu, S., De Girolamo, G., Hu, C., De Jonge, P., Kawakami, N., Medina-Mora, M. E., Moskalewicz, J., Navarro-Mateu, F., O'Neill, S., Piazza, M., Posada-Villa, J., Torres, Y., Kessler, R.C., 2016. Association of mental disorders with subsequent chronic physical conditions: world mental health surveys from 17 countries. *JAMA Psychiatr.* 73, 150. <https://doi.org/10.1001/jamapsychiatry.2015.2688>.
- Tchetgen Tchetgen, E.J., 2013. Inverse odds ratio-weighted estimation for causal mediation analysis. *Stat. Med.* 32, 4567–4580. <https://doi.org/10.1002/sim.5864>.
- Torrance, G.W., 1986. Measurement of health state utilities for economic appraisal. *J. Health Econ.* 5, 1–30.
- Uijen, A.A., Van De Lisdonk, E.H., 2008. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur. J. Gen. Pract.* 14, 28–32. <https://doi.org/10.1080/13814780802436093>.
- VanderWeele, T.J., 2016. Mediation analysis: a practitioner's guide. *Annu. Rev. Publ. Health* 37, 17–32. <https://doi.org/10.1146/annurev-publhealth-032315-021402>.
- Versteegh, M.M., Brouwer, W.B.F., 2016. Patient and general public preferences for health states: a call to reconsider current guidelines. *Soc. Sci. Med.* 165, 66–74. <https://doi.org/10.1016/j.socscimed.2016.07.043>.
- Ware Jr., J.E., Snow, K., Kosinski, M., Gandek, B., 1993. *SF-36 Health Survey: Manual and Interpretation Guide*. Nimrod: Boston.
- Ware, J.E., Kosinski, M., Keller, S.D., 1996. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med. Care* 34, 220–233. <https://doi.org/10.1097/00005650-199603000-00003>.
- Wu, M., Brazier, J., Relton, C., Cooper, C., Smith, C., Blackburn, J., 2014. Examining the incremental impact of long-standing health conditions on subjective well-being alongside the EQ-5D. *Health Qual. Life Outcome* 12, 61. <https://doi.org/10.1186/1477-7525-12-61>.