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### How is depression valued?

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# Chapter 5

Is depression valued differently when it co-occurs with a somatic condition?

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## **ABSTRACT**

**Background:** Health state valuation can be used for economic evaluations of depression interventions that are also offered to somatic patients. This study aimed to examine the effect of the presence of a somatic condition on the general population's valuation of depression. Additionally, whether this effect depends on depression severity and characteristics of the somatic condition was also examined.

**Methods:** A sample of 1268 participants performed an online time-trade-off task to value depression (range 0 to 1, with higher values indicating less-negative valuations). A generalized linear mixed model was used for data analysis.

**Results:** A significant effect of a somatic condition on depression valuations ( $p < .01$ ) was observed, with lower estimated mean values for co-occurring (.60) compared to solitary (.66) depression. A significant interaction effect of a somatic condition with the severity of depression ( $p = .003$ ) was found, with lower values of co-occurring depression for mild and moderate depression states but not for severe depression states. A main effect of the type ( $p < .01$ ), severity ( $p < .01$ ) and order ( $p < .01$ ) of the somatic condition was also observed, with significantly lower valuations of co-occurring depression when the somatic condition followed depression, when it was cancer (vs. diabetes) and moderate (vs. severe).

**Conclusions:** The presence of a somatic condition relates to more negative depression valuations, depending on depression severity and on the characteristics of the somatic condition. Future randomized controlled trials should consider this effect, as it can affect conclusions on the benefits of depression intervention when offered to somatically healthy individuals compared to somatic patients.

## INTRODUCTION

Depression is a highly prevalent condition (Kessler et al., 2003) that may have a substantial impact on health-related quality of life (HRQoL), and moreover, it is expected to evolve to the second major cause of disease burden by 2020 (Lopez & Murray, 1998). While approximately 7% of primary care patients are diagnosed with depression (12-month prevalence), it is found to be two or three times higher for patients with conditions such as cancer (Fann et al., 2008; Reich, Lesur, & Perdrizet-Chevallier, 2008) and diabetes (Ali, Stone, Peters, Davies, & Khunti, 2006; Knol et al., 2006). This co-occurring depression may impose an additional burden on those patients and is also related to lower levels of HRQoL and poorer medical outcomes (Katon, 2003; Katon, Lin, & Kroenke, 2007; Ruo et al., 2003). Accordingly, psychological interventions are offered to chronically ill patients with the primary aim to alleviate co-occurring depression (Beltman, Voshaar, & Speckens, 2010).

Most Randomized Controlled Trials on psychological interventions for depression in chronically ill patients examine the efficacy of the intervention in terms of reductions in depression (Bortolotti, Menchetti, Bellini, Montaguti, & Berardi, 2008). Information on these benefits together with the evaluation of their costs is necessary to inform policy decision making. Cost effectiveness and cost utility have been recommended for this purpose (Drummond, Sculpher, Torrance, O'Brien, & Stoddart, 2005). Cost utility is a type of economic analysis that allows for comparing not only different interventions for the same condition (for example, two different types of psychological interventions for depression) but also different interventions for different conditions (for example, comparing a psychological intervention for depression to a pharmacological intervention for hypertension). This is possible due to the use of a common metric to assess the benefits of health care interventions, namely, quality-adjusted life years, a combination of health state valuations and life years (Drummond et al., 2005).

Health state valuations represent an individual's preference for living in a specific health state, rescaled to range from 0 to 1, which is equivalent to dead and full health, respectively. To elicit valuations, the health state of interest is first described and then a value is attached to it. Most commonly, generic preference-based measures composed of generic classification systems, including domains useful to describe a great range of health conditions, are used to value health states. Values can be obtained either from patients who experience the relevant states or from the general population who are asked to imagine them (Gold, Siegel, Russel, & et al., 1996). The general population perspective is often recommended from an economic perspective based on the argument that resource allocation in the health

care field should be guided not only by those who gain health (i.e., patients) but also by those who pay for it (i.e., general population) (Gold et al., 1996).

Currently, the application of cost-utility analyses for depression interventions is limited (Barrett, Byford, & Knapp, 2005; Mohiuddin & Payne, 2014; Pirraglia, Rosen, Hermann, Olchanski, & Neumann, 2004), and there only a few studies of cost-utility analyses of depression interventions offered to patients with somatic conditions. In these studies, however, generic instruments were applied to conduct the analyses used (Horn et al., 2007; Jonkers et al., 2009; Katon et al., 2006). The appropriateness of using such generic preference-based measures to value mental health conditions such as depression has been called into question. Thus, condition-specific measures, such as the McSad (Bennett, Torrance, Boyle, Guscott, & Moran, 2000), have been developed and recommended for this purpose. While depression-specific valuations can be used for depression among chronically ill patients, it is necessary to examine whether the presence of a somatic condition affects depression valuations, an area that has yet to be examined.

Existing studies suggest that co-occurring conditions affect condition-specific valuations (Nease, 1996). Similarly, it is possible that the presence of a somatic condition affects depression-specific valuations or, in other words, affects how the burden of depression is perceived. It is hypothesized that depression is perceived as more burdensome for an individual who also copes with cancer as compared to a somatically healthy individual with depression. Accordingly, depression would be valued lower (more negatively) in the earlier case. Conversely, it can be argued that the burden of depression might be perceived as less severe when experienced by an individual who also copes with cancer due to a change in the internal standards of comparison given that the presence of cancer might change what is considered good health and what is considered bad health. For example, symptoms associated with depression, such as fatigue and lack of sleep, could be perceived as extremely burdensome by someone who is normally in a good health, while the same symptoms could be considered less burdensome when compared with cancer-related pain. In this latter case, depression would be valued higher (less negatively). In this context, it is important to determine whether the depression or the somatic condition is perceived as the primary condition. Although the issue of which of two co-occurring conditions is considered the primary condition and whether this plays a role in depression valuations has not been the focus of any studies to date, a potential effect of a somatic condition cannot be ruled out.

Understanding the effect of the presence of a somatic condition on valuation of depression is crucial. If the effect of a somatic condition on depression valuations does not exist, then we can use depression valuations by individuals from the general population also in assessing the benefits of interventions for depression

when offered to patients with somatic conditions. If a somatic condition does have an effect, this may have serious implications given that health state valuations are increasingly being used to guide resource allocation in the health care field. If, for example, depression is valued less negatively in the presence of cancer, then this would mean that an intervention that would alleviate depression among chronically patients with somatic conditions would be evaluated as less beneficial compared to when the same intervention would be offered to somatically healthy individuals.

This study aims to examine the effect of the presence of a somatic condition on the general population's valuations of depression. We have chosen two types of somatic conditions - cancer and diabetes. These two chronic somatic conditions are highly prevalent and both are related to a high risk for depressive symptomatology (Ali et al., 2006; Reich et al., 2008). Although the burden of disease is considerable for both conditions, the two conditions also differ in some important aspects (Sprangers, te Velde, Aaronson, & European Org Res Treatment Canc Study Grp Quali, 1999). For example, cancer is more directly related to the risk of death, and its treatment is often intensive, e.g., surgery or chemotherapy (World Health Organization). Diabetes, on the other hand, is not directly related to the risk of death, and its primary treatment involves the management of glucose levels and the adherence to strict lifestyle regimes that include the taking of medications (World Health Organization). The second aim was to test whether this potential effect of the somatic condition is dependent on its characteristics, such as its type (cancer vs diabetes), its severity (moderate vs severe) and it is presented prior or secondary to depression). A valuation study was conducted among the general Dutch population to address these objectives.

## METHOD

### Participants and procedures

The final sample consisted of 1268 participants who were recruited through an existing panel of an international company that specialized in sampling for marketing and academic research (Survey Sampling International), a panel that had been used in previous relevant studies (Damschroder, Zikmund-Fisher, & Ubel, 2008; Lamers, Bouwmans, van Straten, Donker, & Hakkaart, 2006). Participants were required to be 18 years of age or older, to understand Dutch and to sign an informed consent form. Of the 2378 participants initially invited to participate in the study, 1840 (80.7%) agreed to participate and signed the informed consent form and 1268 (53.4%) completed the survey. The characteristics of the final sample were as follows: mean (sd) age of 46.66 (17.41), 51.1% female, residence and educational background. The

majority (64.1%) of the participants was married or in partnership and 58.8% had children. The study was administered online, and the study protocol was finalized after an in-depth pilot study that included ten participants was conducted in June 2011 (Papageorgiou et al., 2014). This was followed by a quantitative pilot study in August 2012 that involved two hundred members of the general population. The final protocol of the study was reviewed by the Medical Ethical Committee of the University Medical Center Groningen and a waiver was provided (M12.119685). Data collection took place in December 2012 and January 2013.

### **Vignettes of co-occurring depression states**

Each participant was asked to value two vignettes randomly selected from 24 available vignettes that describe depression co-occurring with a somatic condition. Each vignette was valued, on average, by 169 participants (range: 155 to 183). We first developed twelve vignettes for co-occurring depression, differing with regard to the severity of depression (mild, moderate, severe) as well as the somatic condition (cancer vs diabetes) and the severity (moderate vs severe) of the somatic condition (3x2x2). Reversing the order of the depression and the somatic condition in the vignette resulted in 24 vignettes of co-occurring depression. Descriptions of the three depression states (mild, moderate, severe) were based on the McSad depression-specific classification system, validated Dutch version (Papageorgiou, Vermeulen, Schroevers, Buskens, & Ranchor, 2013). The McSad states 222222, 3333333 and 444444, which represented mild, moderate and severe levels of dysfunction in the six McSad domains, were used to develop the descriptions of mild, moderate and severe depression. Descriptions of the somatic conditions (type and severity) were based on available disease-specific HRQoL measures (Grimison, Simes, Hudson, & Stockler, 2009; Sundaram, Smith, Revicki, Elswick, & Miller, 2009) and were refined, following a systematic procedure, by an expert panel comprised of eight doctors and two nurses who had extensive experience working with cancer and diabetes patients.

### **Vignettes of solitary depression states**

Participants also valued vignettes describing depression as a solitary condition. For the purposes of the current study, three vignettes describing mild, moderate and severe depression states, based on the McSad states 222222, 3333333 and 444444, were included, to compare with valuations for the exact same states, when presented as co-occurring with a somatic condition. Each of the three vignettes describing depression as a solitary condition was valued, on average, by 166 participants.

## **Valuation elicitation**

Valuations were elicited using the time-trade-off (TTO) method, an established method with proven reliability and validity (Green, Brazier, & Deverill, 2000), in valuations of depression (Koenig, Guenther, Angermeyer, & Roick, 2009). In the TTO method, participants must imagine themselves in the health state described in the vignette and choose between living in this state for another 10 years or recovering from this state but living for less than 10 years. The maximum number of years one is willing to trade in the second option ( $x_{max}$ ) is used to calculate the value attached to this state based on the formula  $1 - (x_{max}/10)$ . To obtain depression-specific values in the case of vignettes describing depression co-occurring with a somatic condition, it is noted that participants were asked for the maximum years they would trade to recover from depression, while the description of the somatic condition remained unchanged (Fryback & Lawrence, 1997). Participants were trained in the use of the TTO method by valuing an asthma-related vignette, a procedure commonly used in valuation protocols.

## **Measures**

### ***Demographic Characteristics***

Information was collected with respect to participant gender, age, nationality, place of residence, education, family situation, occupation and religious background.

### *Health status*

Generic health status was assessed using the EQ-5D+C variant health status classification system and the visual analogue scale (Krabbe, Stouthard, Essink-Bot, & Bonsel, 1999; Wolfs et al., 2007). The classification system is comprised of six domains - mobility, self-care, daily activities, pain/discomfort, anxiety/depression and cognition. Respondents were first asked to choose the level - no, moderate, or severe problems - that best reflects their current level of functioning. Participants were then asked to rate their health state on a visual analogue scale ranging from 0 to 100 (0 representing the worst and 100 representing the best imaginable health state).

The presence of a chronic condition was assessed using an extended list that included 23 somatic chronic conditions that were assessed separately, such as diabetes, cancer, stroke and heart disease. This information was used to determine whether the participant had experience with a chronic somatic condition.



**Depression**

Current level of depression was assessed by means of the Patient Health Questionnaire (PHQ-9), a scale with established psychometric properties among the general population (Chronbach's  $\alpha = 0.89$ ) (Kroenke, Spitzer, & Williams, 2001; Kroenke & Spitzer, 2002). The PHQ-9 is an established scale that has been previously validated in the Dutch language (Zuithoff et al., 2010). It consists of nine items corresponding to the DSM-IV criteria based on which diagnosis of depression is made, such as reduced interest or sleep problems. Questions assess the frequency of depressive symptoms during the last two weeks and answers are reflected on a 4-point scale ranging from 0 = not at all to 3 = almost every day. Item scores are summed and a total score is calculated that ranges from 0 to 27, with higher scores representing higher levels of depression.

Self-reported previous diagnoses of depression by a psychiatrist or psychologist were also included on the questionnaire. To assess the history of depression, participants were provided with a description of what constitutes a depressive episode and then asked whether they have ever experienced such an episode. Finally, participants were asked whether they had experience with depression via close friends or family members. Information on depression was used to describe our sample and to control for its effect when examining the effect of the presence of a somatic condition on valuations of depression.

**Analysis**

The sample was described with regard to their demographic characteristics and health status. Average values were computed for depression (mild, moderate, severe) either as a solitary or as a co-occurring condition with a somatic condition. The frequency distribution of the valuations was approximated in the analyses with a binomial distribution where the proportion represents a 0 to 1 scale. This option was made given that the valuations represent a scale from 0 to 1 using discrete increments of .05. Therefore, when there are no floor or ceiling effects, a binomial distribution approximates a normal distribution. A logit link function was used to model the binomial proportion and a random intercepts for subjects was included to account for the correlation among the multiple valuations per subject. This generalized linear mixed model was estimated using the GLIMMIX of SAS/STAT@ software, version 9.3 (SAS Institute Inc.).

The Wald test was used to answer the first research question concerning the effect of the presence of the somatic condition on valuations of depression. The presence of a somatic condition was the predictor variable, and the value was the valuation of the outcome. As a second step, an interaction term of the presence of the somatic condition with the severity of depression state on valuations was included in the

model to determine whether the effect of the somatic conditions on depression valuations depends on the severity of depression.

To answer the second research question - whether the effect of the somatic condition on depression valuation depends on characteristics of the somatic condition – the three variables concerning characteristics of the somatic condition were independently examined as predictors in our model in the following order: the type (cancer vs diabetes), the severity (moderate vs severe) and the order (prior vs following the depression).

Statistical significance was assessed and a level of .05 and difference in valuations of .05 were considered meaningful, consistent with current valuation research (Dolan & Roberts, 2002; Obrien & Drummond, 1994).

## RESULTS

### Effect of a somatic condition on valuations of depression

The participant's age, family situation, personal experiences with depression and with somatic conditions were found to affect depression valuations, and thus, they were controlled for in the analyses.

Average observed values showed that mild depression was valued higher (meaning less burden), followed by moderate and severe depression, when presented either as a solitary or as a co-occurring condition (Table 1). After applying our model, we found a significant effect of the presence of the somatic condition on valuations of depression ( $F = 62.83, p < .01$ ). Estimated mean values were lower for co-occurring (.60), compared to solitary (.66) depression, and this difference is considered meaningful ( $> .05$ ). This implies that in the presence of a chronic somatic condition, depression is valued more negatively or, in other words, depression is considered more burdensome. A significant interaction effect of the presence of a somatic condition with the severity of the depression state on depression valuations was also observed ( $F = 5.85; p < .01$ ). Specifically, mild and moderate, but not severe depression, as a co-occurring condition was valued significantly lower than depression as a solitary condition (Table 2). This implies that, when taking the severity level of depression into account, the presence of a chronic somatic condition is related to more negative valuations of mild and moderate depression, but such presence has no effect on valuations of severe depression.

### Effect of the characteristics of the somatic condition

A main effect of the type ( $F = 76.06, p < .01$ ) of somatic condition (i.e., cancer vs diabetes) on depression valuations was observed. Estimated mean values for solitary

**Table 1** Average values for depression states (mild, moderate, severe), when depression is presented either as a solitary or as a co-occurring condition

severity of the depression state	Depression solitary M (SD)	Depression co-occurring M (SD)
mild	N=162 .68 (.30)	N=886 .65 (.30)
moderate	N=167 .60 (.30)	N=821 .58 (.30)
severe	N=169 .58 (.31)	N=829 .55 (.31)

**Table 2** Estimated mean values\* for depression states (mild, moderate, severe), when depression is presented either as a solitary or as a co-occurring condition

severity of the depression state	Depression solitary M (SD)	Depression co-occurring M (SD)	p value
mild	.73 (.02)	.67 (.02)	<.01
moderate	.66 (.02)	.58 (.02)	<.01
severe	.57 (.05)	.55 (.02)	.057

\*based on the *glimm*

\*controlled for age, family situation, experience with chronic conditions

depression (estimated mean = .66) differed significantly ( $p < .01$ ) from estimated mean values for co-occurring depression when the somatic condition was cancer (estimated mean = .58) or diabetes (estimated mean = .64). However, the difference was meaningful ( $> .05$ ) only in the case of cancer, thus suggesting that the presence of cancer, but not diabetes, was related to meaningful and more negative valuations of depression.

The severity of the somatic condition was also found to have a main effect ( $F = 29.33$ ,  $p < .01$ ) on depression valuations. Estimated mean values for solitary depression (estimated mean = .66) differed significantly ( $p < .01$ ) compared to estimated mean values for co-occurring depression when the somatic condition was either moderate (estimated mean = .63) or severe (estimated mean = .58). However, the difference was clinically meaningful ( $> .05$ ) only when the somatic condition was severe. This implies that the presence of a severe somatic condition, but not a moderate somatic condition, was related to clinically meaningful more negative valuations of depression.

Finally, a main effect of the presenting order of the somatic condition on depression valuations was found ( $F = 36.80$ ,  $p < .01$ ), thus implying that the effect of the somatic condition on depression valuations varied depending on whether the somatic condition presented prior to or secondary to depression. Specifically, estimated mean values for solitary depression (estimated mean = .66) differed significantly ( $p < .01$ )

and clinically meaningfully to estimated mean values for co-occurring depression only when the somatic condition was presented following depression (estimated mean = .58). This indicates that the presence of the somatic condition was related to more negative valuations of depression only when it was presented secondary to depression.

## DISCUSSION

With respect to economic evaluations, valuations of depression are useful to assess the benefits of psychological interventions aiming to alleviate depression as well as when patients with chronic somatic conditions experience depression. Our results indicate that mild and moderate depressive states, but not severe depressive states, are valued more negatively, and thus are considered more burdensome, when in the presence of a somatic condition. Furthermore, the presence of a somatic condition is related to more negative valuations of depression only when it presents as secondary to depression, and not when the somatic condition presents prior to depression; only when it is cancer, and not when it is diabetes; and only when it is severe, and not when it is moderate.

To our knowledge, this is the first study to examine the effect of the presence of a somatic condition on valuations of depression. Findings from previous literature on the effect of comorbidities on condition-specific valuations are scarce as most of the studies on the topic of co-morbidity in valuations focus on understanding the interaction of the two conditions on determining the overall value (Dale, Basu, Elstein, & Meltzer, 2008; Hu & Fu, 2010). Similar to a previous study that reports that depression was related to more negative diabetes valuations (Brown et al., 2000), we also find that the somatic condition can affect valuations of depression. However, our results contradict previous findings that report a null effect of comorbid somatic conditions in the case of angina specific populations (Nease, 1996).

Our findings support an initial hypothesis - when a somatic condition is present, depression is perceived as more burdensome. This may be because having to cope with an adverse health condition requires a great deal of one's personal resources, which, in turn, makes other conditions more difficult to manage. Our findings, therefore, contradict our alternative hypothesis - depression is considered less burdensome in the presence of an adverse health condition due to a change in internal standards that the latter evokes. Our finding that the effect on depression valuation is present when the somatic condition is more burdensome (cancer vs diabetes (Sprangers et al., 1999); severe vs moderate) is consistent with the confirmed hypothesis. Furthermore, when the burden of depression is already at its

maximum, the somatic condition makes little difference in the valuation (Brown et al., 2000). However, a second, more methodological explanation could be suggested based on our findings. When valuing co-occurring depression, participants may be eager to trade life years, thus resulting in more negative valuations, not because they consider depression as more burdensome compared to solitary depression, but because the life years that are traded are not healthy years and are therefore considered to be of less value (Fryback & Lawrence, 1997; Nease, 1996). Our finding that the effect of the somatic condition is only observed when it presents secondary to depression provides support for the first, more conceptual explanation rather than for the second, more methodological explanation, as we would not expect an effect of order if more negative valuations of co-occurring depression are due to increased eagerness to trade non-healthy years.

What explains the finding that the presence of a somatic condition leads to more negative valuations of depression only when the somatic condition presents secondary to depression? One explanation might be that when depression presents prior to the somatic condition, it – the depression - is considered more burdensome as it might be perceived as being related to the development of the somatic condition.

If our findings reflect that people genuinely perceive depression more burdensome when cancer is present, then this means that the same intervention that would alleviate depression could be considered more beneficial when offered to specific groups of somatic patients. It also implies that depression-specific valuations elicited in the absence of somatic conditions might not be appropriate to represent valuations of depression when co-occurring with a somatic condition. If, however, the finding that increased negative valuations of co-occurring depression is an artefact of the methodology due to greater willingness to trade years when these years are not spent in full health, then this needs to be taken into account when comparing benefits between the two populations. Second, this study provides insight useful for the understanding of co-morbidity in valuations. We find that a co-occurring somatic condition can affect valuation specific to depression. Additionally, our finding that the effect of co-morbidity depends on characteristics of the conditions, such as the severity, might explain the complexity reported by studies that modelled the valuations of co-occurring health states (Dale et al., 2008; Hu & Fu, 2010).

Among the strengths of the current study is the large sample, as it is representative of the general Dutch population with respect to gender, age, education and residence and thus supports the generalizability of our findings. Furthermore, to give special attention to the construction of the vignettes of the health states of interest, an established classification system was used to describe depression and

a systematic method conducted by a panel of experienced health care professionals was employed to describe the somatic conditions. This resulted in a number of vignettes that combined health conditions with varied characteristics. Furthermore, we used the TTO, the most recommended strategy, with an expansively pilot-tested protocol to elicit valuation.

Certain limitations of the study must also be noted. An online administration of the valuation task was chosen as it was a particularly cost-effective method with established feasibility and validity regarding valuation research (Buitinga, Braakman-Jansen, Taal, & van de Laar, 2011; Lenert, Sturley, & Watson, 2002; van Nooten, Koolman, & Brouwer, 2009). Furthermore, it underwent pilot testing. Nonetheless, given that the TTO may be cognitively demanding for some participants (Devlin, Hansen, & Selai, 2004) and an interviewer administration would ensure better comprehension, the interviewer effect could also impose a bias. Additionally, the range of values assigned to the different states of depression was rather small, thus perhaps making it more difficult to detect differences between the various states.

Future studies could build on the findings of this study. An issue that warrants more research is whether the observed differences in valuations of solitary and co-occurring depression reflect a true difference or whether the differences are an artefact of the method. For example, future studies could add to our methodology by applying the TTO for the somatic condition and then examining whether the number of years traded for the somatic condition affects valuations of depression. Future studies could employ other techniques of valuation elicitation, such as the Standard gamble rating method and the visual analogue scale, and examine whether differences occur under these varied techniques. Finally, in-depth interviews could examine how individuals value depression in the presence of a somatic condition, a study that has been previously attempted (Papageorgiou et al., ). It is also important to test whether differences in the valuations between solitary and co-occurring depression exist not only when the general population values hypothetical states but also when patients value the states that they are actually experiencing.

The findings of the current study support that while depression is valued more negatively in the presence of a somatic condition, this valuation depends on the severity of the depression and on the characteristics of the somatic condition. These findings should be further investigated and should be considered when applying valuation methodology to evaluate depression interventions when offered to patients with somatic conditions.

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