

Preference-Based Health Valuation for Acute Poisoning: the Challenge of Very Acute Disease and Rapid Reversal of the Health State

Reza Assadi,¹ Bregje A. J. Van Spijker,² Fillip Smit,^{3,4,5} and Reza Afshari^{1,6,*}

¹Clinical Toxicology Research Centre, School of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

²Centre for Mental Health Research, the Australian National University, Canberra, Australia

³Trimbos Institute (Netherlands Institute of Mental Health and Addiction), Utrecht, The Netherlands

⁴Department of Clinical Psychology, EMGO+ Institute for Health and Care Research, VU University, Amsterdam, The Netherlands

⁵Department of Epidemiology and Biostatistics, EMGO+ Institute for Health and Care Research, VU University Medical Centre, Amsterdam, The Netherlands

⁶Addiction Research Centre, School of medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

*Corresponding author: Reza Afshari, Addiction Research Centre, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, IR Iran. Tel: +98-5118535315, E-mail: afsharir@mums.ac.ir

Received 2014 November 01; Revised 2015 April 06; Accepted 2015 April 19.

Abstract

Background: A consistent and comparative description of the burden of diseases, injuries and risk factors that cause them is an important input to health decision-making and planning processes.

Objectives: The aim of this cross-sectional study was to compare the extent and pattern of variation in generic utility measures with respect to capturing the clinical nature of acute poisonings from the moment of onset until restoration of health after treatment.

Patients and Methods: We measured the health status of patients admitted to the emergency medical toxicology ward of our teaching hospital, Mashhad, Iran. We measured their EuroQol both at admission and pre-discharge, and they were asked for time they traded-off for their current illness.

Results: The study enrolled 82 patients (34 males, 48 females) admitted to the emergency medical toxicology department. A questionnaire was completed for all patients at the two time intervals. The results varied from 22222 to 33333 at initial management; at the time of discharge, this rating varied from 11111 to 11122. These significant changes occurred over just a few days.

Conclusions: This study attempted to compare the course of acute poisonings with some other diseases to show how self-induced poisoning affects one's health perception, and how this change takes place over a short time.

Keywords: Preference-Based health Valuation, EQ-5D, Poisoning, Acute Disease

1. Background

Acute poisoning can have an immediate and profound impact on quality of life. However, depending on the type of substance, dosage and treatment given, the majority of patients rapidly return to full health with minimal side effects in few days. Acute poisonings may be inflicted intentionally (suicidal behaviour) or unintentionally (accidental consumption of a poisonous substance or a drug overdose).

Acute poisoning places a large burden on the health system and society in many countries, due to its severity and prevalence (1). Expressed in disability weights (DWs), poisoning is considered mild with a DW of 0.171 (2). The DW is an index between 0 (best imaginable health state) and 1 (worst imaginable health state) that expresses the severity of the disability associated with a specific health state, and it is used in the calculation of disability adjusted life years (DALYs) (3). In 2004, the DWs for poisoning were 0.608 and 0.611 for patients under and above 14 years old, respectively (4). This contrasts the DW of 0.171 in the most recent publication (5), which indicates that there is still uncertainty

about the disability weight for poisoning. One explanation for the change in assigned weight may be that the valuation procedure used to estimate the DW in 2004 was patient and expert panels, while the procedure used in 2013 employed a general population panel. In addition, a variation in health-state definition might have made a contribution (6).

In general, measuring DWs, or utilities (the complement of DWs), involves two main steps: defining a set of health states of interest, and valuing those health states. There are direct and indirect methods of valuation. Most commonly used direct valuation methods include standard gamble, time trade-off, and visual analogue scale, which may use patient or general population panels, depending on the aim of the study and the perspective of the researchers. One of the main indirect valuation methods is the use of generic preference instruments such as EQ-5D, short-form 6 (SF-6D) and the health utilities index (HUI). All these methods have underlying assumptions and continue to be a point of discussion (7). In the UK, the National Institute for Health and Clinical Excellence has specified

the EQ-5D as its preferred method of utility measurement (8).

2. Objectives

Up-to-date, acute poisonings and their specifications (intentional and unintentional) have not been valued separately. This paper aims to provide evaluations for both of these health states using a preference-based method. The current paper is part of an ongoing study which is looking at the extent and pattern of variation in generic utility measures in order to capture the clinical nature of acute poisonings from the moment of onset until recovery following treatment. The purpose of the overall study is to monitor the amount and direction of shift in health state.

3. Patients and Methods

3.1. Design, Participants and Procedures

Participants for this cross-sectional study consisted of patients admitted to the emergency medical toxicology department of a teaching hospital at Mashhad University of Medical Sciences, Mashhad, Iran, from May 2013 to August 2013. All patients admitted to the department due to poisoning (intentional or unintentional) were considered for inclusion in the study by checking their medical records against the inclusion and exclusion criteria.

The inclusion criteria were: 1) being admitted due to intentional or unintentional poisoning (as determined by self-report), 2) not having an intellectual disability, 3) being conscious and able to talk, or having responsive and close relatives, accompanying, 4) not having been diagnosed with a severe mental disorder (as determined by a psychiatrist), 5) being between 10 and 75 years old and 6) consenting to participate. The exclusion criteria were: 1) abusing multiple substances, 2) criminal cases, 3) not consenting to participate, 4) decreased consciousness or mentally incapable for participation, 4) underlying diseases such as malignancies or organ failures based on past medical history (PMH), 5) being younger than 10 or older than 75 and 6) unknown cause of poisoning, mixed substance consumption or poisoning accompanied by other injuries such as trauma.

If eligible for participation, patients were interviewed at their hospital bed by the first author (RA). The head of the hospital and the ward were aware of the study and their permission was obtained in advance. In addition to the EQ-5D questionnaire, patients were asked about demographics, PMH (particularly mental disorders), substance abuse, route of administration, history of suicidal behaviour or self-harm, relevant familial history and the

time they traded off due their current illness (time trade-off method). Measures used in this paper are described in more detail below.

3.2. Assessments

Assessments took place at the time of admission and at discharge. When patients were conscious at the time of admission (90%), self-report assessments were used. In cases where patients were unconscious at the time of admission (10%), their relatives or the medical team were asked to complete the assessment.

3.3. Demographic Information

All participants were asked to provide their age, gender, education, marital status, occupation and source of income.

3.4. EuroQol

The EQ-5D questionnaire is a generic preference-based measure designed to describe and value health-related quality of life in various diseases. The EQ-5D consists of two parts (9). The first part includes five separate domains; mobility, capacity for self-care, conduct of usual activities, pain/discomfort and anxiety/depression. Each domain is rated on three levels: 'no problems' (1), 'some problems' (2) and 'extreme problems' (3). These scores are used to describe patients' health states, expressed as five-digit codes - the so called EQ-5D index. For example, a health state with some problems in walking, no problems with self-care, no problems with performing usual activities, and with moderate pain and moderate anxiety is abbreviated to 21122. With this method, the best health state is expressed as 11111 and the worst health state as 33333. The EQ-5D index ranges from a maximum utility weight of 1 for full health, to death, valued at 0. The worst possible health state ("33333") is -0.59 for the British EQ-5D index (10) So the EQ-5D defines 243 health states and has a range from -0.6 to 1.0 in terms of utility weight, indicating health states valued worse than death (11).

The second part of the EQ-5D consists of a visual analogue scale (VAS) to measure self-perceived health on a vertical scale from 0 to 100, where 0 is the worst imaginable health state, and 100 is the best imaginable health state (9).

3.5. Statistical Analyses

The data gathered in this study were coded and entered to SPSS version 11.5. Demographic information was reported in means, standard deviations and frequencies. Next, a survivorship diagram was drawn for acute poisoning using Microsoft Excel version 2007. In addition, survivorship diagrams were made for four other acute diseases: acute myocardial infarction (DW = 0.422), influenza

(DW = 0.210), multiple sclerosis (DW = 0.445) and bacterial gastroenteritis (DW = 0.281). These conditions were selected based on their similarities to acute poisoning in their course of onset and duration. Finally, a normative survivorship diagram was also included as a point of reference (2). In all statistical measurements, P value less than 0.05 was considered statistically significant.

3.6. Ethical Considerations

All patients were assured that their personal information would be kept confidential and would not be disclosed under any circumstances. Only patients who verbally consented to answer the questionnaire after being informed about the study were enrolled. This study was approved by research committee of our university (approval code 910998).

4. Results

4.1. Participants

This study enrolled 82 patients (34 male, 48 female) admitted to our teaching hospital emergency medical toxicology department. Table 1 describes the characteristics of the sample. Patient ages ranged between 16 - 72 years, with a mean age of 30. The majority of poisonings were intentional (n = 54, 65%). A smaller proportion was unintentional (n = 26, 31%).

The most commonly used substances included benzodiazepines, opiates, salicylates and bites by poisonous animals or insects. The route of poisoning was mainly oral (90%), followed by parenteral routes or bites. The cause of poisoning differed between men and women. Most men were poisoned with opium derivatives, usually unintentional, while most women were poisoned with benzodiazepines and were admitted due to intentional consumption.

4.2. Quality of Life

The EQ-5D questionnaire completed for all patients varied from 22222 to 33333 at initial assessment. At the time of discharge, this rate varied to 11111 to 11122 (Figure 1). The timeframe between admittance and discharge was, on average, two days or less. The exception to this was severely poisoned patients, who developed central nervous suppression or respiratory failure, and were admitted to the intensive care unit. In these cases, the disease lasted longer (up to 30 days) and sometimes resulted in death or discharged with sequelae.

Figure 2 shows the normative survivorship diagram. Area A + B under the bold dashed survivorship curve represents life expectancy at birth. Health expectancies are

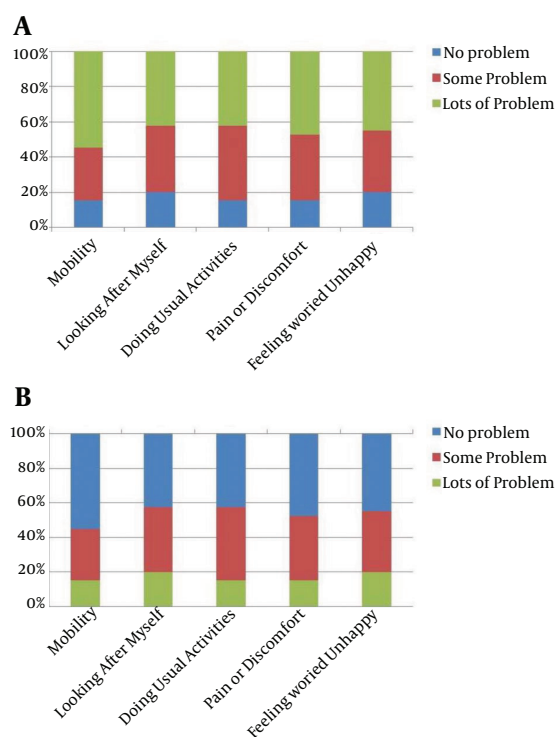


Figure 1. A, the EQ-5D-3L scores of the patients at admission and B, discharge times showing a dramatic change in their health problems, as self-reported.

measures of this area which take into account some lower weights for years lived in health states worse than full health, represented as area B in the diagram. Figure 3 shows the survivorship diagrams for the four selected, acute diseases (influenza, myocardial infarction, acute gastroenteritis, multiple sclerosis) and for acute poisoning. The diagrams show different patterns, despite the approximate similarity of these four conditions to acute poisoning. Compared with the four selected diseases, acute poisoning shows an instant drop in quality of life, but also a speedy recovery (12-15).

5. Discussion

The validity and reliability of the generic usefulness of QoL instruments is always open to debate. The EuroQol is a widely used instrument, due to its simplicity and because it has been evaluated in various cultures and across various health states (16-19). In the current study, we questioned its validity and usability for cases of acute poisoning.

As shown in Figure 3, acute poisoning has an immediate impact on quality of life, a characteristic shared by some other acute diseases. During the early stages, many patients are too ill to measure QoL based on EQ-5D, and

Table 1. Demographics and Characteristics of Admitted Patients With Intentional and Unintentional Poisoning^a

	Total Sample (n = 82)	Intentional Poisonings (n = 58)	Unintentional Poisonings (n = 26)	P Value
Age	30.20 ± 15	23.95 ± 7.2	43 ± 19.4	0.03
Gender				0.027 ^b
Male	34 (41)	14 (17)	20 (24)	
Female	48 (58)	44 (49)	6 (7)	
Marital status				P > 0.05 ^c
Single	15 (18)	10 (12.1)	5 (6)	
Married	55 (67)	40 (48)	15 (18)	
Divorced/Widowed	12 (14.6)	8 (9.7)	4 (4.8)	
Substance used^d				P > 0.05
Benzodiazepines	14 (17)	14 (17)	0	
Opiates	26 (31)	18 (21.9)	8 (9.7)	
Salicylates/Acetaminophen	6 (7.3)	6 (7.3)	0	
Bite by insect/animal	10 (12.1)	NA	10 (12.1)	
Other	22 (26.8)	14 (17)	8 (9.7)	
Route of poisoning				0.01 ^e
Oral	82 (100)	56 (68)	26 (31)	
Other	NA	0	0	
Suicide attempt				0.015
First attempt	NA	37 (45)	NA	
Second or more	NA	19 (23)	NA	

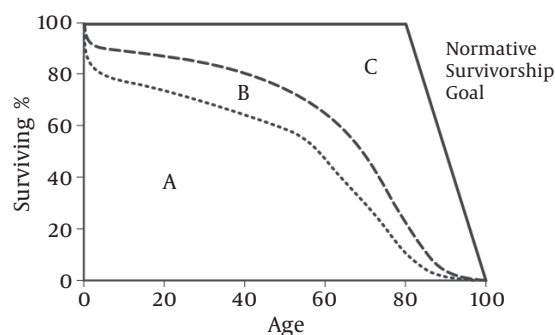
^aValues are expressed as mean SD or No. (%).

^bGender vs. type/cause of poisoning.

^cP-value less than 0.05 has considered statistically significant.

^dThe sum is more than number of subjects due to co-abuse of substances.

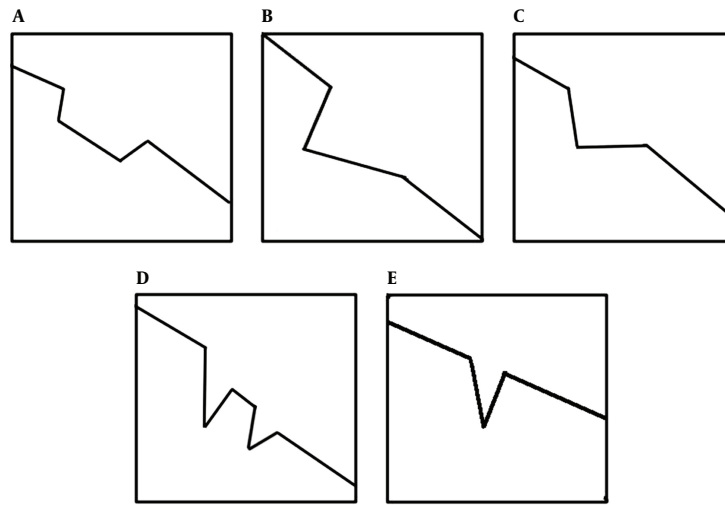
^eRoute of poisoning between the types of poisoning.

Figure 2. Survivorship Curve

Line C is considered normal, while A and B are due to various lifestyles and diseases from which one may suffer. Sources: Murray CJL, Mathers CD, Salomon JA, Lopez AD. Health gaps: an overview and critical appraisal. Summary Measures of Population Health, 2002, Chapter 5.1.

most are, clinically, around 3333* to 2222*, where the asterisk (*) denotes the worry/anxiety question; those patients who were unconscious were incapable of responding to this question (9). In conscious patients, the scores on this question were usually poor (i.e., 2 or 3). However, after appropriate treatment, a rapid improvement occurred in the condition of these patients, making it difficult to measure their QoL. Their health seems to return so fast that most were either not ready to trade off any of their life (based on time trade-off method) or they score it just a little below less than the best imaginable health (score of 100 in VAS scale).

In sum, when many of these patients are detoxified, they feel healthy and are not ready to trade off any life years, due to their health state at the time of discharge. They also score their health in two sections of the EQ-5D as the best possible health state. The only exception consists of few poisonings, such as acetaminophen, where we expect to see longer-term sequelae that do not present in the

Figure 3. The Segmental View of a Survivorship Diagram of Various acute Diseases

A, influenza; B, myocardial infarction; C, acute gastroenteritis; D, multiple sclerosis; E, acute poisoning. Sources: Up-to-date of internal medicine, available from: <http://www.uptodate.com>, accessed 12 Dec. 2013.

initial days, while regionally we observed very few cases of hepatic failure due to toxification of this type (20, 21).

Subsequently, we should take into account that, in cases of super-acute diseases such as poisonings, the EQ-5D measurement does not seem reliable based on patients' statements. Subsequently, despite their poor initial health state, most of these patients improve dramatically after treatment and do not consider themselves ill any more, including many of those who were admitted to the hospital with intentionally suicidal or self-harming thoughts.

Based on the above observations and a review of the literature on the patterns of survivorship of four acute diseases, we extracted and compared those diseases with acute poisoning survivorship lines, and observed a significantly different pattern and length for the latter (12-15).

Comparing the survivorship diagrams of the four acute diseases (Figure 3) with acute poisonings suggests we might need do the following in order to accurately complete the health valuation: 1) score these diseases differently based on criteria more complex than the five dimensions methods of EQ-5D, 2) look after long-term effects, 3) consider the physiopathology sequelae of the illness, or 4) consider the psychological state of the patients (10). As these diseases (intentional poisonings) - due to being commonly mandatory or with a known source (i.e., the substance of toxification is usually known or discoverable) - are induced in formerly (at least physically) healthy subjects, and so are responsive to treatment. However, we should not forget that subjects' mental illness, or impaired coping or problem-solving skills, make them prone to self-harm and

poor will to live or remain healthy (in intentional poisoning cases), and that this adversely affects their health. In addition, it might be that this is the main health state that needs to be considered, rather than the acute onset poisoning (22, 23).

This is the first known epidemiological study attempting to evaluate the validity of routine valuation methods for acute poisonings, to see how these self-induced diseases affect patients' perception of their health. Using two methods - one direct (TTO) and one indirect (EQ-5D) - we demonstrated that special attention should be paid to these diseases, since it seems routine utility measurement tools are not working well and need to be modified or improved (24, 25).

This study population consisted of those who consented to complete the questionnaire, who had with sufficient literacy to understand the study objectives and the complexity of the inquiry methods. Many potential subjects were not mentally aware or otherwise ready to participate in the study, which limited our sampling pool. We also excluded some questionnaires due to mismatched or unreliable replies. Therefore, we recommend further studies with larger samples.

Acknowledgments

We are grateful to Mashhad University of Medical Sciences for approving and supporting this study, and to all of the patients who participated.

References

- Vijayakumar L, Nagaraj K, Pirkis J, Whiteford H. Suicide in developing countries (1): frequency, distribution, and association with socioeconomic indicators. *Crisis*. 2005;26(3):104-11. doi: 10.1027/0227-5910.26.3.104. [PubMed: 16276752].
- Salomon JA, Vos T, Hogan DR, Gagnon M, Naghavi M, Mokdad A, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2129-43. doi: 10.1016/S0140-6736(12)61680-8. [PubMed: 23245605].
- Murray CJL, Lopez AD. Global and regional descriptive epidemiology of disability: incidence, prevalence, health expectancies and years lived with disability. *Glob Burden Dis*. 1996;1:201-46.
- Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2197-223. doi: 10.1016/S0140-6736(12)61689-4. [PubMed: 23245608].
- World health organization. . The global burden of disease 2004. Available from: http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/.
- Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med*. 2001;33(5):337-43. [PubMed: 11491192].
- Schwarzinger M, Stouthard ME, Burstrom K, Nord E. Cross-national agreement on disability weights: the European Disability Weights Project. *Popul Health Metr*. 2003;1(1):9. doi: 10.1186/1478-7954-1-9. [PubMed: 14633276].
- Scalone L, Cortesi PA, Ciampichini R, Belisari A, D'Angiolella LS, Cesana G, et al. Italian population-based values of EQ-5D health states. *Value Health*. 2013;16(5):814-22. doi: 10.1016/j.jval.2013.04.008. [PubMed: 23947975].
- EuroQol. . Valuation of EQ-5D 2013.. Available from: <http://www.euroqol.org/about-eq-5d/valuation-of-eq-5d.html>.
- Sullivan PW, Slejko JF, Sculpher MJ, Ghushchyan V. Catalogue of EQ-5D scores for the United Kingdom. *Med Decis Making*. 2011;31(6):800-4. doi: 10.1177/0272989X11401031. [PubMed: 21422468].
- Sonntag M, Konnopka A, Leichsenring F, Salzer S, Beutel ME, Herpertz S, et al. Reliability, validity and responsiveness of the EQ-5D in assessing and valuing health status in patients with social phobia. *Health Qual Life Outcomes*. 2013;11:215. doi: 10.1186/1477-7525-11-215. [PubMed: 24365384].
- Jenzer HR. [Severe heart insufficiency after acute myocardial infarct: follow up]. *Schweiz Med Wochenschr*. 1981;111(26):980-2. [PubMed: 7268352].
- World Health Organization. . Acute respiratory infections: the forgotten pandemic. *Bull World Health Organ*. 1998;76(1):101-3. [PubMed: 9615503].
- Koch-Henriksen N, Sorensen PS. The changing demographic pattern of multiple sclerosis epidemiology. *Lancet Neurol*. 2010;9(5):520-32. doi: 10.1016/S1474-4422(10)70064-8. [PubMed: 20398859].
- Akinbami FO, Venugopalan P, Elnour IB, Nirmala V, Abiodun P, Azubuike JC. Pattern of chronic diarrhoea in children: a prospective analysis of causes, clinical features and outcome. *Niger Postgrad Med J*. 2006;13(1):53-6. [PubMed: 16633380].
- Kuspinar A, Mayo NE. Do generic utility measures capture what is important to the quality of life of people with multiple sclerosis?. *Health Qual Life Outcomes*. 2013;11:71. doi: 10.1186/1477-7525-11-71. [PubMed: 23618072].
- Yu ST, Chang HY, Yao KP, Lin YH, Hurng BS. Validity of EQ-5D in general population of Taiwan: results of the 2009 National Health Interview and Drug Abuse Survey of Taiwan. *Qual Life Res*. 2015.
- Kontodimopoulos N, Pappa E, Niakas D, Yfantopoulos J, Dimitrakaki C, Tountas Y. Validity of the EuroQoL (EQ-5D) instrument in a Greek general population. *Value Health*. 2008;11(7):1162-9. doi: 10.1111/j.1524-4733.2008.00356.x. [PubMed: 18489492].
- Kimman M, Vathesatogkit P, Woodward M, Tai ES, Thumboo J, Yamwong S, et al. Validity of the Thai EQ-5D in an occupational population in Thailand. *Qual Life Res*. 2013;22(6):1499-506. doi: 10.1007/s11366-012-0251-2. [PubMed: 22926727].
- Asadi R, Afshari R. Applying Global Burden of Diseases in Medical Toxicology. *Asia Pac J Med Toxicol*. 2014;3(1):1.
- Gosselin S, Hoffman RS, Juurlink DN, Whyte I, Yarema M, Caro J. Treating acetaminophen overdose: thresholds, costs and uncertainties. *Clin Toxicol (Phila)*. 2013;51(3):130-3. doi: 10.3109/15563650.2013.775292. [PubMed: 23473457].
- Pajoumand A, Jalali N, Abdollahi M, Shadnia S. Successful treatment of acetaminophen overdose associated with hepatic failure. *Hum Exp Toxicol*. 2003;22(8):453-8. [PubMed: 12948086].
- Afshari R, Majdzadeh R, Balali-Mood M. Pattern of acute poisonings in Mashhad, Iran 1993-2000. *J Toxicol Clin Toxicol*. 2004;42(7):965-75. [PubMed: 15641642].
- Chapman BP, Franks P, Duberstein PR, Jerant A. Differences between individual and societal health state valuations: any link with personality?. *Med Care*. 2009;47(8):902-7. doi: 10.1097/MLR.0b013e3181a8112e. [PubMed: 19543121].
- Rehm J, Frick U. Establishing disability weights from pairwise comparisons for a US burden of disease study. *Int J Methods Psychiatr Res*. 2013;22(2):144-54. doi: 10.1002/mpr.1383. [PubMed: 23716479].