UNIVERSIDAD DEL CEMA
Buenos Aires
Argentina

Serie
DOCUMENTOS DE TRABAJO

Área: Economía

SIMPLE ANALYTICS OF DISABILITY ADJUSTED LIFE YEARS (DALYS)

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Septiembre 2014
Nro. 545

www.cema.edu.ar/publicaciones/doc_trabajo.html
UCEMA: Av. Córdoba 374, C1054AAP Buenos Aires, Argentina
ISSN 1668-4575 (impreso), ISSN 1668-4583 (en línea)
Editor: Jorge M. Streb; asistente editorial: Valeria Dowding <jae@cema.edu.ar>

Simple Analytics of Disability Adjusted Life Years (DALYs)

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Disability adjusted life years lost (DALYs) are one of the most usual health outcome metrics in environmental and health assessments and cost-effectiveness or cost/benefit analysis of interventions in those two areas. The methodology for DALYs´ calculation has been evolving under the Global Burden of Disease Project. The objective of this paper is to show in a simple way what lies behind DALYs´ method. The dependence of DALYs´ metric from parameter values and estimates is illustrated using as a base the Fox-Rushby and Hanson (2001) example for depression.

I. Introduction

At the beginning of the 90s, the World Bank commissioned a Global Burden of Disease (GBD) study to quantify the world burden of diseases and injuries and the risk factors that cause them for its World Development Report (WB, 1993). The study provided estimates for 1990, which were then subsequently updated, until the present. Each GBD publication implies work by thousand of specialists. Those estimates have not only generated policy discussions, but also a very large body of academic literature (see the review by Polinder et al, 2012).

Burden of disease in the GBD project is measured as the number of years of life lost due to premature mortality plus the time lived in less than perfect health.[1] According to the supporters of this approach, the main advantage of DALYs (Disability Adjusted Life Years) is that they present, with a single number, the impact of a risk factor on health of a particular population. The target of health policies is clearly to reduce DALYs. Hence, their number could serve as an input to set health priorities, since it allows health outcomes to be measured in a comparable way along time and among countries or regions.

The main goal of this document is to explain in detail how DALYs are calculated and to perform a probabilistic multivariate sensitivity analysis with DALYs´ formulae using an Excel complement that performs Monte Carlo simulations. The article is organized as follows. Section II describes the methodology and the key parameter and other estimates needed to calculate Disability Adjusted Life Years. Section III summarizes the Fox-Rushby and Hanson (2001) depression example and its univariate and bivariate sensitivity analysis.[2] Section IV

* The author thanks funding from the Nexus Fulbright Program to visit as a scholar the Institute for Health Metric and Evaluation at the University of Washington (Seattle) and comments from Vanesa D´Elia. The views and opinions expressed in this publication are those of the author and do not necessarily represent those of the Universidad del CEMA or any other institution.

[1] This "less than optimal state" is referred to as "disability" by the GBD studies. Some authors discuss the use of the term "disability" for this case (see, for example, Grosse et al 2009).

[2] Univariate sensitivity analysis constitute the simplest form of sensitivity analysis: vary one input in the model by a given amount, and examine the impact that this change has on the model's result.

gathers from the literature alternative estimate and parameter values that are used to run a probabilistic multivariate sensitivity analysis. Finally, Section V summarizes and concludes.

II. The Disability Adjusted Life Years (DALYs)

II.1. Methodology

The Disability Adjusted Life Years (DALYs) were developed as a unit of measurement to capture "one lost year of healthy life" (Murray, 1994). DALYs are a combination of two concepts (Years of Life Lost, YLL and Years of Life with Disability, YLD) into a single number:

$$DALY(c,s,a,t) = YLL(c,s,a,t) + YLD(c,s,a,t)$$

Where *c* stands for cause, *s* for sex, *a* for age and *t* for year. Hence, DALYs combine the number of years lost due to premature mortality in a population and the duration and severity of illnesses attributable to a given cause.

A premature death occurs when it happens before the age at which a person could have expected to survive. The number of years between the premature death and the expected life are the *YLL*. This means that:

$$YLL(c,s,a,t) = N(c,s,a,t) \cdot L(s,a)$$

Where *N* is the number of deaths to a given cause (c) at a point in time and *L* is the life expectancy at the age that the death occurs (i.e., the years of life lost due to premature death). Both *N* and *L* vary with gender and age.

The time period in years that is lived in state of disability (less than ideal health) due to a disease is *YLD*. There are severity weights for each disability, going from 1 (death) to 0 (perfect health). YLD requires duration of disability and the severity weight to be given to disability (how strong it is):

$$YLD = I(c,s,a,t) \cdot D(c,s,a) \cdot L(c,s,a,t)$$

Where *I* is the number of cases of a disease, *D* is the disability weight and *L* is the average duration of the disease until remission or death.[3]

If *N* and *I* are not incorporated in the calculation, it is possible to derive the DALYS for a particular individual, with a given health story. This was done, for example, by Fox-Rushby and Hanson (2001).

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[3] With respect to *YLD*, it is important to distinguish prevalence from incidence. Incidence is the rate of new (or newly diagnosed) cases of the disease. It is generally reported as the number of new cases occurring within a period of time (e.g., per month, per year). Prevalence is the actual number of cases alive with the disease during a period of time. Incidence tells us about a change in status from non-disease to disease, thus being limited to new cases. Prevalence includes both new cases and those who contracted the disease in the past and are still surviving. For a disease that takes a long time to cure, this disease would have both high incidence and high prevalence in the year it occurs, then, it would have a low incidence but continue to have a high prevalence (because it takes a long time to cure, so the fraction of individuals that are affected remains high). In contrast, a disease that has a short duration may have a low prevalence and a high incidence. Some studies incidence (1990 and previous to last update) and some use prevalence (GBD 2010).

In the standard DALYs used in the GBD, DALYs calculations follow from this general formula:

$$\int_{x=a}^{x=a+L} D \cdot \{K \cdot C \cdot x \cdot e^{-\beta \cdot x} + (1-K)\} \cdot e^{-r \cdot (x-a)} \cdot dx \tag{1}$$

Where *x* is the age, *a* is the age of onset of a disease, *L* is the life-expectancy if calculating YLLs or the average duration of disease until remission or death if calculating YLDs, *D* is the disability weight (*D = 1,* for death, D = 0 for perfect health and $0 < D < 1$ for illness), *K* is an age-weighting modulation constant (*K = 0* if no age weights, *K = 1* when full age weights), C is an age-weighting correction constant, β is an age-weighting constant, and r is a discount rate.

Solving the integral in (1), yields the following result, that we derive in Appendix A and is stated in Murray and Lopez (1996: p.65):

$$DALYs(c,s,a,t) = D \cdot \left\{\frac{K \cdot C \cdot e^{r \cdot a}}{(r+\beta)^2} \cdot \left[e^{-(r+\beta)\cdot(L+a)} \cdot (-(r+\beta)\cdot(L+a)-1) - e^{-(r+\beta)\cdot a} \cdot (-(r+\beta)\cdot a - 1)\right] + \frac{1-K}{r} \cdot (1-e^{-rL})\right\} \tag{2}$$

There has been extensive debate in the literature on all the assumptions incorporated in the DALYs formula (Anand and Hanson 1997, Lyttkens 2003, Arnesen and Kapiriri 2004, Airoldi and Morton 2009, Hausman 2012, Nord 2013, among others): years lost (*L*), disability weights (*D*), age weights (*K*, *C*, β) and time discounting (*r*). In part, because of the criticisms received, the GBD has been changing the value of those inputs along time.

II.2. Estimates and parameters behind DALYs

Strictly, DALYs formula inputs are of two different types: estimates (age of onset of disease – *a* -, expected age of death with and without treatment – *a + L* – and disability weights – *D* -) and parameters (age weights – *K, C,* β - and discount rate – r -). This section discusses the changing values attributed to those key inputs in different GBD studies. A summary of that evolution can be seen in Table 1.

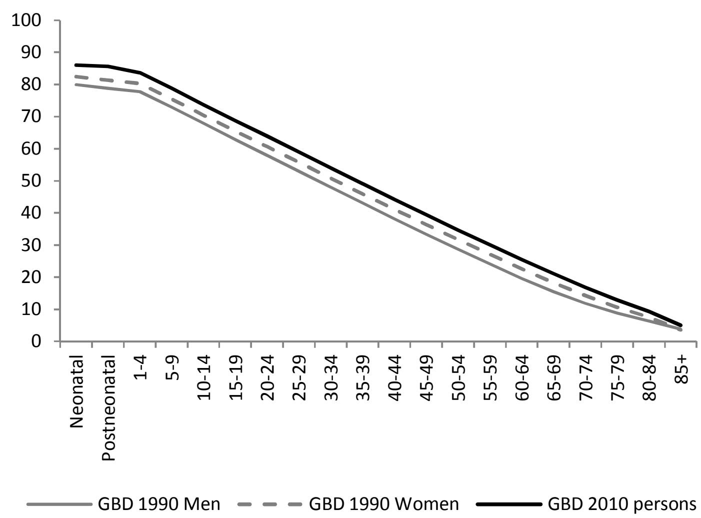
Table 1. Parameter values in the GBD study

	1990	2001	2004	2010
Life table (*L*)	Standard West 25 (males) and 26 (females)	Standard West 25 (males) and 26 (females)	Standard West 25 (males) and 26 (females)	Synthetic life table (the same for men and women)
Discount rate (*r*)	3%	3%	3%	0%
Age-weighting (*K, C,* β)	Non-uniform weighting	Uniform weighting	Non-uniform weighting	Uniform weighting
Adjustment for comorbidity	No	No	No	Yes

Source: http://www.who.int/healthinfo/global_burden_disease/daly_disability_weight/en/. "a" and "D" are not included because they vary depending on each health outcome.

With respect to L, the survival table used in several of the GBD studies intended to represent the world maximum life span of individuals at each age differentiating women and men. In its origin (GBD 1990) that reference was the Japan´s life expectancy at birth of 80 and 82.5 for males and females respectively (Standard West Table 25 for males and 26 for females). Critics state that the table did not necessarily represent the situation of less developed countries. In addition, since on average men die before women, their health ends up counting less (which could appear as unfair). Both issues were changed in GBD 2010 by using a synthetic table for both genders, based on the lowest observed death rate for each age group in countries of more than 5 million inhabitants. Figure 1 shows the differences between GBD 1990 and GBD 2010 life expectancy tables by age groups.

Figure 1. Life expectancy by age group (*L*)



Source: from Table 2.1. in WHO (2013).

With respect to D, its value ranges from 0 (indicating perfect health) to 1 (equivalent to no health, or death). A disability weight of d means that the condition the individual suffers implies a d % reduction in DALYs with respect to good health. There are several sets of D (for different health conditions). As described in Salomon (2013), the first GBD disability weights correspond to GBD 1990 and were derived from weights assigned to 6 different disability classes by a panel of public health experts where each disabling sequel was defined in terms of those classes. For the 1996 revision, again a panel of health professionals defined the Ds, based on "person trade-off" questions. Based on those questions, 22 indicators conditions were ranked and then grouped into 7 classes of severity level. Then, the panel defined the percentage of time an individual with a given health problem would spend in each of those classes (making clear the difference between treated and non treated individuals).[4]

[4] When weights are not available, they are usually complemented with Ds from a Dutch Disability Weights (DDW) study (Stouthard et al, 1997) or from the Australian Burden of Disease study (Salomon, 2013). According to Polinder et al (2012), DDW covers less health outcomes, but with more details than the GBD studies.

The GBD disability weights were updated subsequently using this same type of methodology up until 2008. For the 2010 study, a large study was undertaken (it gathered approximately 30,000 observations). The study was based on household surveys in five different countries of the world (Bangladesh, Indonesia, Peru, Tanzania and the United States) and an open-access world internet survey (in English, Spanish and Mandarin). The web survey included respondents from many countries of the world. The method of eliciting weights is based on a “pairwise comparison” of sequelae. Participants have to indicate for each pair which one they believe corresponds to a healthier state. The main criticism to the derivation of *D*s is that they involve individuals´ judgements about the relative value of different health states, and so, are not objective but rather depend on the context (Hausman 2012; Nord 2013; Voigt and King 2014). The results from GBD 2010 elude this criticism by indicating that their study shows that *D*s do not change much across cultures (Salomon et al, 2013).

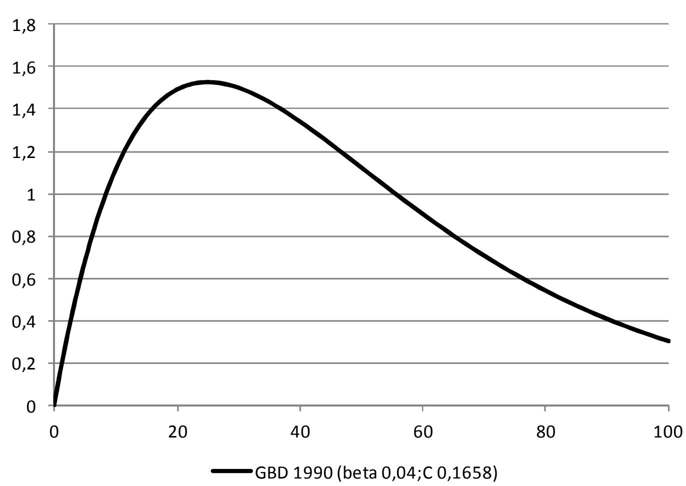
With respect to *K, C* and β, years lost can be assigned different weights depending of age (*K* in DALYs equations (1) and (2) allows elimination of age-weights when *K = 0*). More precisely, time lived at different ages is valued according to an exponential function of the form:

$$C \cdot x \cdot e^{-\beta \cdot x}. \tag{3}$$

This means that years in DALYs can be valued differently at different ages. The idea behind this approach is that, because young and often elderly depend on the rest of society for (physical, emotional and financial) support, the value of a year lived by a young adult could be said to be worth more than that of a very young or old individual (Murray and Acharya, 2002).

According to Mathers et al (2006, p.401), “C is a parameter chosen to ensure that the total global DALYs are the same with and without age weighting, estimated at C = 0.1658 for the 1990 GBD study”. Choosing that value of C implies the weights for each age shown in Figure 2. According to the Polinder et al (2012) review of DALYs studies, half of them use age-weighting. Many, erroneously, use the C corresponding to GBD 1990, which is not correct since C is a parameter that was calibrated for that specific GBD study.

Figure 2. Age weights in GBD 1990



This age-weighting issue deserves more analysis. In fact, the age-weighting function (3) has a maximum at $x = \frac{1}{\beta}$ since its first derivative ($C \cdot e^{-\beta \cdot x} + C \cdot x \cdot e^{-\beta \cdot x} \cdot (-\beta)$) equals zero for that value of *x*. Hence, for the value of β chosen in GBD 1990 (i.e., $\beta = 0.04$), individuals of 25 years of age (i.e., 1/0.04 = 25) are those given the maximum weight (see Figure 2). On the other side, when $\beta = 0.01$, the maximum weight would be given to those individuals who are 100 years old, while for $\beta = 0.1$, people aged 10 would be those with the highest weight. Usually, when sensitivity analysis is undertaken, GBD authors use βs between 0.02 (highest weight at 50 years) and 0.06 (highest weight at 16.67 years).

It is also clear that the age-weighting curve has a sort of inverted U shape since the first derivative is positive before the maximum and negative after the maximum. This is, $C \cdot e^{-\beta \cdot x} - \beta \cdot C \cdot x \cdot e^{-\beta \cdot x} > 0$ when $C \cdot e^{-\beta \cdot x}(1 - \beta \cdot x) > 0$. Since, an exponential is always greater than 0 ($e^{-\beta \cdot x} > 0$) and C > 0, it has to hold that $(1 - \beta \cdot x) > 0$ and that happens for $x < \frac{1}{\beta}$. The only age-weighting curve that increases monotonically is the one for $\beta = 0.01$.

Moreover, as stated above, β is closely linked to C. The mechanism to choose alternative *C*s suggested by GBD authors in Mathers et al (2006) and followed by Larson (2013) is to ensure the same area (100) under the age weighting curve from age 0 to 100 years. That would imply that each age is given the same weight (weight = 1).

For the area under the curve $C \cdot x \cdot e^{-\beta \cdot x}$ to be equal to 100, it has to hold that the definite integral of that function is 100. This means that:

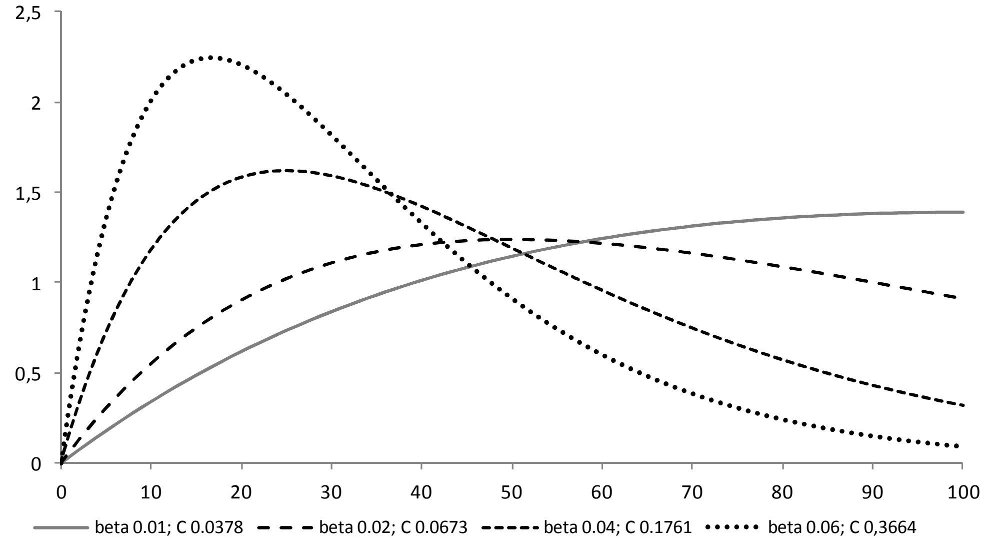
$$\int_{x=0}^{x=100} C \cdot x \cdot e^{-\beta \cdot x} dx = 100 \tag{4}$$

Solving by parts, as derived in Appendix B, the value of *C* is:

$$C = 100 / \left[\frac{e^{-100 \cdot \beta}}{\beta} \cdot \left(-100 - \frac{1}{\beta}\right) + \frac{1}{\beta^2}\right]. \tag{5}$$

Once this calculation is acknowledged, *C* and β are indeed only one parameter (β, since C depends on it). Figure 3 depicts different age-weighting schemes using alternative β (with the corresponding Cs that ensure that the integral below the curve is 100 using or not using age weights).

Figure 3. Alternative age-weights

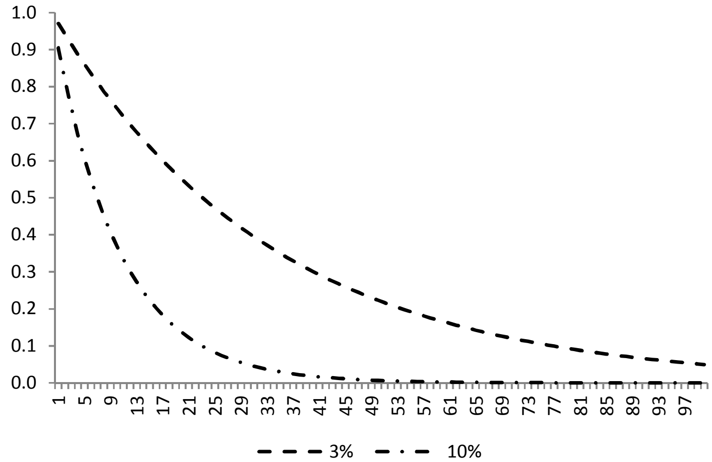


Finally, the use of discounting to sum years in the present and in the future is also usual in this literature. The conceptual basis of discounting is individuals´ preferences that future outcomes have less value than today´s outcomes. Hence, "years now are worth more than years in the future". Discounting is continuous and exponential: $e^{-r \cdot t}$, where r is the discount rate and t is time.[5,6] According to Polinder et al (2012), 80% of the studies use a non negative discount rate and the most usual is 3%. Discounting is usual in economics and reflects individuals´ preference for the present with respect to the future. The difference is that, in DALYs, discounting is used for health and not for money. The higher the discount rate, the lower is the impact of health problems in the future. For example, as can be seen in Figure 4, using a 3% discount rate, a year of life in 25 years is worth half what is worth a year of life today. If the rate used for discounting is 10%, a year of life in 25 years is worth one tenth of what is worth a year of life today.

[5] Recently, some authors have shown how would be DALYs with discrete time discounting (Elbasha 2000 and Larson 2013).

[6] Exponential discounting implies using a constant discount rate. There are alternative ways of discounting. For example, hyperbolic discounting implies that the rate decreases through time (Doyle, 2013).

Figure 4. Implications of exponential discounting



There is a large literature using DALYs for the calculation of the burden of disease in specific countries, for calculation of the burden of disease or for cost-effectiveness or cost-benefit analysis of various environmental and health interventions. But, not in all studies that use the GBD methodology, the values of the described parameters are made clear. And, not all the calculations run sensitivity analysis on the parameters and estimates they use (21 of the 31 studies reviewed by Polinder et al 2012 do so). In the next section, the simple Fox-Rushby and Hanson (2001) example is replicated and a multivariate probabilistic sensitivity analysis using an Excel complement is performed. This allows making clear that difference in input values yield substantial differences in the DALYs obtained (this adds to the uncertainty behind epidemiological data: variables *N* and *I* in equation (2)).

III. The Fox-Rushby and Hanson (2001) example and its sensitivity analysis

In Fox-Rushby and Hanson (2001), the calculation of DALYs is illustrated with a specific example. It consists of a woman in Chile, who, when she is 35 years old is diagnosed with major depression.[7] The authors calculate DALYs that would be averted if a woman of that age is treated versus the situation of no treatment. They assume that, if she is treated, this person will live the rest of her life with a chronic condition, but if she is not, she will die at 45 (10 years after the onset of the disease). The authors use the disability weights in Murray et al (1996) and the United Nations Chilean Pattern Model Life Tables (United Nations, 1982) for life expectancy.[8]

[7] The burden of major depressive disorder has been increasing in importance since GBD 1990 (Murray et al 2012: p. 2212). It was the 15th contributor to world DALYs in 1990 (it represented 15.2% of the total) and was 11 in the rank in 2010 (it contributed with 10.8% to total DALYs).

[8] Note that the disability weights taken from Murray et al (1996, p.145), correspond in fact to “unipolar major depression” and not “bipolar depression” as the authors state on page 327.

Table 2. Assumptions in Fox-Rushby and Hanson example and corresponding results

	No treatment		Treatment	Averted
	YLD	***YLL***	***YLD***	***DALYs***
Input values				
Beta	0.04	0.04	0.04	
r	0.03	0.03	0.03	
D	0.6	1	0.302	
C	0.1658	0.1658	0.1658	
K	1	1	1	
L	10	34.73	44.13	
Calculation results				
Base case	6.95	14.80	7.94	13.81
No age-weighting	5.18	15.98	7.39	13.78
No discounting	8.02	30.07	13.02	25.07
No age weights and no discount	6.00	34.73	13.33	27.40

Using equation (2) with the values in Table 2, the DALYs that can be attributed to the years this woman lives with the illness (YLD) are:

If not treated:

$$0.6 \cdot \left\{ \frac{1 \cdot 0.1658 \cdot e^{0.03 \cdot 35}}{(0.03+0.04)^2} \cdot \left[e^{-(0.03+0.04)\cdot(10+35)} \cdot (-(0.03+0.04)\cdot(10+35)-1) - e^{-(0.03+0.04)\cdot 35} \cdot (-(0.03+0.04)\cdot 35 - 1) \right] \right\} = 6.95$$

If treated:

$$0.302 \cdot \left\{ \frac{1 \cdot 0.1658 \cdot e^{0.03 \cdot 35}}{(0.03+0.04)^2} \cdot \left[e^{-(0.03+0.04)\cdot(44.13+35)} \cdot (-(0.03+0.04)\cdot(44.13+35)-1) - e^{-(0.03+0.04)\cdot 35} \cdot (-(0.03+0.04)\cdot 35 - 1) \right] \right\} = 7.94$$

Then, under the no treatment scenario, this woman dies prematurely (at age 45), hence there are also years of life lost (YLL):

$$1 \cdot \left\{ \frac{1 \cdot 0.1658 \cdot e^{0.03 \cdot 45}}{(0.03+0.04)^2} \cdot \left[e^{-(0.03+0.04)\cdot(34.73+45)} \cdot (-(0.03+0.04)\cdot(34.73+45)-1) - e^{-(0.03+0.04)\cdot 45} \cdot (-(0.03+0.04)\cdot 45 - 1) \right] \right\} = 19.97$$

But, those years of life lost occur from 45 on, hence they have to be discounted to the moment of the calculations (when the woman is 35 years). To do so, the authors discount 19.97 as:

$$19.97 \cdot e^{-0.03\cdot(45-35)} = 14.80$$

Table 2 also summarizes DALYs calculated in this example, using the assumptions in the same Table. If the person is treated, 13.81 DALYs are averted (6.95+14.80-7.94).

Fox-Rushby and Hanson (2001) perform then a simple type of sensitivity analysis: they calculate DALYs without age weighting, without discounting and without both. The results are reproduced (and completed) in Table 2 and show that, dropping discount, results in a doubling of the DALYs averted.[9]

[9] DALYs´ formula when discount is eliminated is also shown in Appendix A.

IV. Multivariate probabilistic sensitivity analysis

However, a more complete sensitivity analysis is needed in order to assess the impact of changes in input values on DALYs. It is important to study how the variation in DALYs can be due to the alternative estimates and parameter values (and not only to the complete exclusion of one or two parameters from DALYs´ formula). This section illustrates to what extent uncertainty around estimates and parameter values change the DALYs averted result and which inputs impact more on its variation.

The first issue to consider for a sensitivity analysis is the alternative value that each of the inputs in DALYs calculation have in the related literature.

IV.1. Alternative input values from the literature

With respect to life expectancy, as stated above, Fox-Rushby and Hanson (2001) base their estimation on the United Nations Model Life Table Chilean Pattern for females published in 1982. However, there are many alternatives to that table. On one side, in the 2010 GBD standard life table (same for both genders and global), life expectancy at age 35 is 51.53 years and at age 45 is 41.80 years. When the United Nations (WHO, 2013) projected frontier life expectancy table for 2050 is considered, those value change to 57.15 and 47.27 respectively.[10]

With respect to Disability weights, Haagsma et al (2014) review all studies that derive DW in the past 16 years (not only those of the GBD) and conclude that the values of *D*s vary greatly. For the particular case of depression, they report the DW summarized in Table 3.

Table 3. Disability weights for depression

Authors of study	Region	Disability weight *Mild*	*Moderate*	*Severe*
Kruijshaar et al (2005, p.446)	Netherlands	0.19 (C.I. 0.16-0.22)	0.51 (C.I. 0.46-0.55)	0.84 (C.I. 0.80-0.88)
Lai et al (2009, p.544)	Estonia		0.140	
Salomon et al (2012, p.2135)	Global	0.159 (C.I. 0.107-0.223)	0.406 (C.I. 0.276-0.551)	0.655 (C.I. 0.469-0.816)
Stouthard et al (1997, p.74)	Netherlands	0.14 (C.I. 0.086-0.194)	0.35 (C.I. 0.272-0.425)	0.76 (C.I. 0.556-0.971)

Note: Adapted from Table 3 in Haagsma et al (2014). Individual articles were checked (and information was added when available: precise page of the paper and DW confidence intervals). These DW exclude "depression with psychotic features".

Note that Murray et al (1996), the reference that Fox-Rushby and Hanson (2001) use for their DW, calculates DW for treated and untreated depression. However, the rest of the DW studies report DW depending on health states (mild, moderate and severe).[11] Here, the DW for

[10] An alternative could have been the 1999 WHO updated Life Table for Chile, in which women from 35 to 39 years have a life expectancy of 46.06 and those from 45 to 49 are expected to live 36.46 more years (Lopez et al, 2001).

[11] As defined in Ferrari et al (2013), depression state lay descriptions would be: for mild depression (person "has constant sadness and has lost interest in usual activities. The person can still function in daily life with extra effort, but sleeps badly, feels tired, and has trouble concentrating"), for moderate depression (person "has constant sadness and has lost interest in usual activities. The person has some difficulty in daily life, sleeps badly, has trouble concentrating, and sometimes thinks about harming himself"), and for severe depression (person has overwhelming, constant sadness and cannot function in daily life. The person sometimes loses touch with reality and wants to harm or kill himself").

treated patients is taken to be that of mild to moderate depression, while the severe depression DW is taken as the reference for untreated cases.[12]

With respect to age-weighting, Mathers et al (2006) suggest alternative betas from 0.02 to 0.06 and the same is done here (the corresponding *C* is calculated, using the formula explained above). Discount rate is usually set at 3%, here the options of 1% and 5% are also considered. Those relatively low rates are usual in long term discounting as when environmental or health impacts have to be considered (see Cline 1999, for example).

Knowing a most likely value, in addition to a range (a lower bound and an upper bound from that value) it is standard to assign a triangular distribution to each of the inputs, as it is done here. The following step is then to perform a Monte Carlo simulation for DALYs.[13] The result is a distribution for DALYs averted (not a single number) that reflects the combined effects of the inputs uncertainties.

IV.2. Results of the Monte Carlo simulations

The results (summarized in Table 4) correspond to a Monte Carlo simulation with 10.000 iterations, based on the assumptions in Section IV.1. The uncertainty behind the number of years of life lost due to premature mortality (YLL), the time lived in less than perfect health (YLD) and the corresponding DALYs averted if the person is treated are shown in Figure 5.

Table 4. Uncertainty in inputs and outputs

Inputs	**Deterministic value**	**Range**	**Distribution**	**Source**
Beta	0.04	0.02-0.06	triangular	Murray et al (1996)
r	3%	1%-5%	triangular	GBD and own estimate
D treated	0.293	0.179-0.387	triangular	Haagsma et al (2014)
D untreated	0.752	0.469-0.971	triangular	Haagsma et al (2014)
L Death treated	41.8	34.73-47.27	triangular	WHO (2013) and GBD 2010
L Death untreated	51.53	44.13-57.15	triangular	WHO (2013) and GBD 2010
D death	1		deterministic	GBD
L Disability treated	10		deterministic	Fox-Rushby and Hanson (2001)
K	1		deterministic	GBD
Outputs	***Min***	***Mean***	***Max***	***Variance***
YLD treated	*3.80*	*8.26*	*16.37*	*3.12*
YLD untreated	*5.11*	*8.84*	*12.78*	*1.76*
YLL untreated	*19.76*	*30.03*	*44.35*	*16.85*
DALYs Averted	*18.64*	*30.61*	*43.67*	*13.75*

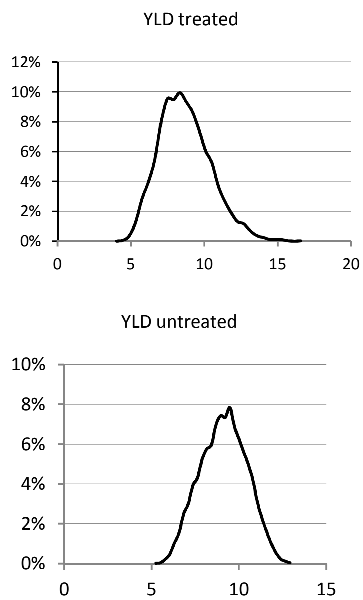
Note: Normal fonts are assumptions. Script indicates calculations. DALYs averted are calculated independently from YLD and YLL.

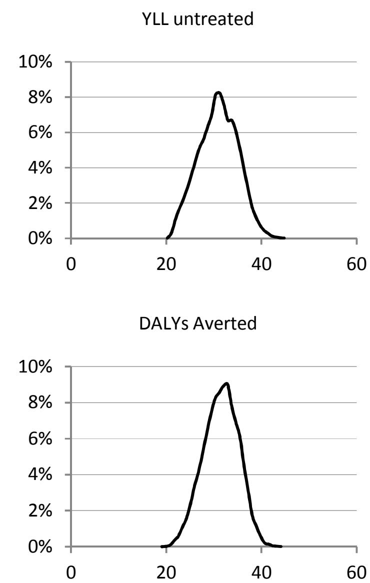
[12] Another estimate to consider is the average duration of the disease until death. Fox-Rushby and Hanson (2001) assume that, if it goes untreated, the person dies 10 years later. This is not necessarily representative of the evolution of major depression (see, for example, Vos et al, 2004). Nevertheless, for simplicity, this estimate is kept constant.

[13] Monte Carlo simulation is a standard method to perform sensitivity analysis. There are numerous Excel applications to do so. It consists of selecting a random set of input data values drawn from their individual probability distributions. Those values are used to obtain the ouputs (here, YLL, YLD and DALYs). This process is repeated many times and the result is a probability distribution for the output variables.

As can be seen in Figure 5 and Table 4, there is an impact of uncertainty on DALYs. While averted DALYs attributable to the person being treated is approximately 31 years, when alternative parameter and estimates values are considered, it turns out that this number can be as low as 18 and as high as 43. This means that considering uncertainty about the true numerical values of the inputs in DALYs´ formula, there may be a divergence of approximately 40% with respect to the deterministic calculations. The gap between DALYs averted central and extreme values not only can have an impact in policy decisions regarding a specific health outcome, but it also may have consequences in how different diseases are ranked in terms of health policy priorities (see Arnesen and Kapiriri 2004 for that discussion).

Figure 5. Distribution of outputs given uncertainty in inputs





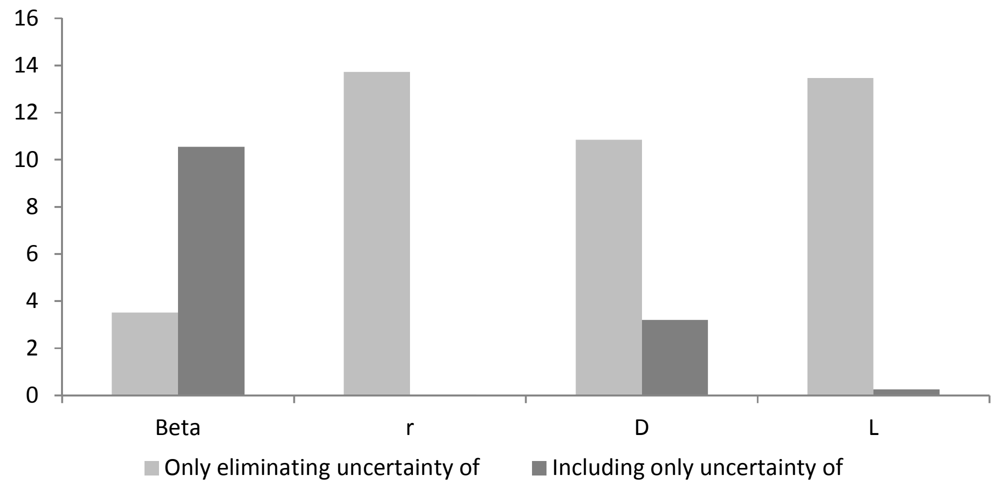
But, the uncertainty in the different inputs can influence DALYs in a different way. This point can be seen by eliminating the uncertainty of each of the inputs one by one or adding the uncertainty on one input while holding the other inputs at their deterministic value. As depicted in Figure 6 (and Figure 7), the parameter with the highest impact on DALYs uncertainty is age –weighting. When only uncertainty regarding β is eliminated, DALYs´ variance goes from 13.75 to 3.52. The latter value is the lowest, when compared to DALYs´ uncertainty when r, D or L variation is eliminated. This result is related to the one obtained if only β uncertainty is included in the sensitivity analysis. In that case, DALYs´ variance is the highest (10.55) when compared to the simulations where other parameters or estimates are assumed to be uncertain but β is not. This is also in line with the fact that the correlation between the DALYs averted and β is higher (-0.85) than the correlation with any of the other inputs.[14]

[14] The correlation between DALYs averted and the rest of the inputs is: 0.34 for D untreated, -0.32 for D treated, 0.14 for L of treated,-0.03 for L of untreated and -0.05 for r. This means that, for example, when the disability weight that is assumed for a person not treated for depression increase, the number of averted DALYs due to treatment increases. Similarly, when the discount rate increases (i.e., years in the future are worth less), this decreases the number of DALYs if a person is treated (because survival at older ages is given less value).

As can also be deduced from Figure 6, the second factor that affects the precision implicit in DALYs calculation are disability weights and the less important factors are the survival assumptions taken from life tables and the discount rate. Note that Fox-Rushby and Hanson (2001) finding that eliminating discounting yielded a doubling of DALYs averted gives more importance to discounting than it seems to have in his example.

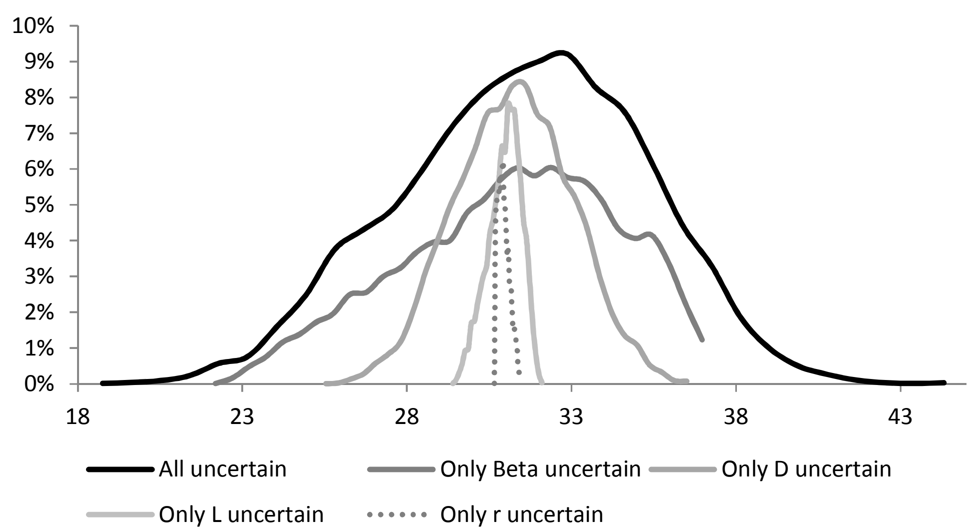
In summary, when age weighting and discounting are eliminated (as suggested by GBD 2010), the highest and the lowest source of uncertainty are avoided. But, it still leaves disability weights, which are a non marginal source of noise. The problem with disability weights (beyond criticisms on how they are calculated) is that they cannot be removed from DALYs calculations because if that was done, mortality and morbidity could not be presented as a single number (allegedly, the main advantage of DALYs).

Figure 6. Change in DALYs averted´s variance when inputs uncertainty is removed or added



This same result can be assessed in Figure 6, where each line represents DALYs´ averted distribution adding uncertainty over all variables.

Figure 7. Distribution of DALYs averted under different uncertainty conditions



V. Summary and Conclusions

Disability adjusted life years are an attractive indicator for health policy decisions. This is so because it is a metric that was designed to combine mortality and morbidity estimates. Hence, it synthesizes, in a single number, information about the severity and duration of adverse health outcomes.

However, this work shows in detail what is behind DALYs and the uncertainty that surrounds its calculation. The Fox-Rushby and Hanson (2001) major depression example is taken as a base case illustration. Then, alternative inputs values are gathered from published sources. A multivariate and univariate probabilistic uncertainty analysis is carried out in order to account for uncertainty on the true input values for averted DALYs´ calculation. Each parameter and estimate value is varied according to a pre-specified distribution and Monte Carlo simulations with 10,000 trials are run for each case. This analysis shows that averted DALYs can be 40% higher or lower when uncertainty on all key inputs is considered. It also shows that, in this case, the main factors that affect the precision implicit in DALYs´ calculation are age weighting and disability weights and the less important factors are the survival assumptions taken from life tables and the discount rate.

Many authors have criticized DALYs. This article pretends to contribute to increase awareness towards assessing what they mean and facilitate harmonization among studies that use this specific metric. This is more important now than it was before because many applied work based on DALYs is being increasingly performed using pre designed software (as the one suggested in Devleesschauwer 2012, among others).

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Appendix A. Derivation of DALYs´ formula

A.1. DALYs formula with age-weighting and discounting

DALYs (complete) formula comes from solving the following integral:

$$\int_{x=a}^{x=a+L} D \cdot \{K \cdot C \cdot x \cdot e^{-\beta \cdot x} + (1-K)\} \cdot e^{-r \cdot (x-a)} \cdot dx$$ (equation (1) in the text)

This integral can be rewritten as a sum of two integrals:

$$\int_{x=a}^{x=a+L} D \cdot K \cdot C \cdot x \cdot e^{-\beta \cdot x} \cdot e^{-r \cdot (x-a)} \cdot dx + \int_{x=a}^{x=a+L} D \cdot (1-K) \cdot e^{-r \cdot (x-a)} \cdot dx \qquad \text{(A.1)}$$

The second term, can be integrated as:

$$D \cdot (1-K) \cdot \frac{e^{-r \cdot x + r \cdot a}}{-r}\Big]_{x=a}^{x=a+L}$$

Then, applying Barrow´s rule, the result is:

$$D \cdot (1-K) \cdot \left(\frac{e^{-r \cdot (a+L) + r \cdot a}}{-r} - \frac{e^{-r \cdot a + r \cdot a}}{-r} \right)$$

$$= D \cdot (1-K) \cdot \left(\frac{e^{-r \cdot L}}{-r} + \frac{1}{r} \right)$$

$$= \frac{D \cdot (1-K)}{r} \cdot (1 - e^{-r \cdot L}) \qquad \text{(A.2)}$$

This expression corresponds to the right-hand side of equation (2) in the text.

On the other side, the first term in equation (1) in the text can be rewritten as:

$$\int_{x=a}^{x=a+L} D \cdot K \cdot C \cdot x \cdot e^{-x \cdot (r+\beta) + r \cdot a} \cdot dx$$

Choosing $u = x; v' = e^{-x \cdot (r+\beta) + r \cdot a}$, integrating by parts using the corresponding formula ($\int u \cdot v' \, dx = u \cdot v - \int u' \cdot v \, dx$), it results (knowing $u' = 1; v = e^{-x \cdot (r+\beta) + r \cdot a} / -(r+\beta)$) that:

$$D \cdot K \cdot C \cdot x \cdot \frac{e^{-x \cdot (r+\beta) + r \cdot a}}{-(r+\beta)}\Bigg]_{x=a}^{x=a+L} - D \cdot K \cdot C \cdot \int_{x=a}^{x=a+L} 1 \cdot \frac{e^{-x \cdot (r+\beta) + r \cdot a}}{-(r+\beta)} \cdot dx$$

Solving the second term, it happens that:

$$D \cdot K \cdot C \cdot \left\{ x \cdot \frac{e^{-x \cdot (r+\beta) + r \cdot a}}{-(r+\beta)} - \frac{e^{-x \cdot (r+\beta) + r \cdot a}}{[-(r+\beta)]^2} \right\} \Bigg]_{x=a}^{x=a+L}$$

$$= D \cdot K \cdot C \cdot \left\{\frac{e^{-x\cdot(r+\beta)+r\cdot a}}{[-(r+\beta)]^2} \cdot [-(r+\beta)\cdot x - 1]\right\}\Bigg]_{x=a}^{x=a+L}$$

$$= \frac{D\cdot K\cdot C\cdot e^{r\cdot a}}{[-(r+\beta)]^2} \cdot \left\{e^{-x\cdot(r+\beta)} \cdot [-(r+\beta)\cdot x - 1]\right\}\Big]_{x=a}^{x=a+L}$$

$$= \frac{D\cdot K\cdot C\cdot e^{r\cdot a}}{(r+\beta)^2} \cdot \left\{e^{-(r+\beta)\cdot(L+a)} \cdot [-(r+\beta)\cdot(L+a) - 1] - e^{-(r+\beta)\cdot a} \cdot [-(r+\beta)\cdot a - 1]\right\} \text{(A.3)}$$

Hence (A.3) plus (A.2) is equivalent to equation (2).

A.2. DALYs formula without discounting

When discounting is eliminated, formula (1) in the text becomes:

$$\int_{x=a}^{x=a+L} D \cdot \left\{K \cdot C \cdot x \cdot e^{-\beta\cdot x} + (1-K)\right\} \cdot dx$$

This expression can be rewritten as:

$$\int_{x=a}^{x=a+L} D \cdot K \cdot C \cdot x \cdot e^{-\beta\cdot x} \cdot dx + \int_{x=a}^{x=a+L} D \cdot (1-K) \cdot dx$$

The right hand-side integral is easy to solve:

$$D(1-K) \cdot x]_{x=a}^{x=a+L}$$

$$= D(1-K) \cdot L]_{x=a}^{x=a+L} \qquad \text{(A.4)}$$

The left hand-side can be solved by parts taking $u = x; v' = e^{-\beta\cdot x}$, integrating by parts using the corresponding formula ($\int u \cdot v'\, dx = u \cdot v - \int u' \cdot v\, dx$), it results (knowing $u' = 1; v = e^{-\beta\cdot x}/-\beta$) that:

$$D \cdot K \cdot C \cdot x \cdot \frac{e^{-\beta\cdot x}}{-\beta}\Bigg]_{x=a}^{x=a+L} - D \cdot K \cdot C \cdot \int_{x=a}^{x=a+L} 1 \cdot \frac{e^{-\beta\cdot x}}{-\beta} \cdot dx$$

Then:

$$D \cdot K \cdot C \cdot \left\{x \cdot \frac{e^{-\beta\cdot x}}{-\beta} - \frac{e^{-\beta\cdot x}}{[-\beta]^2}\right\}\Bigg]_{x=a}^{x=a+L}$$

$$= \frac{D\cdot K\cdot C\cdot e^{-\beta\cdot x}}{-\beta} \cdot \left\{\left[x - \frac{1}{(-\beta)}\right]\right\}\Bigg]_{x=a}^{x=a+L}$$

$$= \frac{D\cdot K\cdot C\cdot e^{-\beta\cdot(a+L)}}{-\beta} \cdot \left\{\left[(a+L) - \frac{1}{(-\beta)}\right]\right\} - \frac{D\cdot K\cdot C\cdot e^{-\beta\cdot a}}{-\beta} \cdot \left\{\left[a - \frac{1}{(-\beta)}\right]\right\}$$

$$= \frac{D\cdot K\cdot C\cdot e^{-\beta\cdot a}}{-\beta} \cdot \left\{e^{-\beta\cdot L} \cdot \left[\frac{-\beta\cdot(L+a)-1}{-\beta}\right] - \left[\frac{-\beta\cdot a-1}{-\beta}\right]\right\}$$

$= \frac{D \cdot K \cdot C \cdot e^{-\beta \cdot a}}{(-\beta)^2} \cdot \{e^{-\beta \cdot L} \cdot [-\beta \cdot (L + a) - 1] - [-\beta \cdot a - 1]\}.$ (A.5)

Hence (A.5) plus (A.4) is the formula used for DALYs when discounting is eliminated from DALYs.

Appendix B. Formula to determine C for age-weighting

Based on $\int_{x=0}^{x=100} C \cdot x \cdot e^{-\beta \cdot x} dx = 100$.

Knowing that $u = C \cdot x; v' = e^{-\beta \cdot x}$, integrating by parts using the corresponding formula ($\int u \cdot v' \, dx = u \cdot v - \int u' \cdot v \, dx$), it results (knowing $u' = C; v = e^{-\beta \cdot x}/-\beta$) that:

$$-\frac{C \cdot x \cdot e^{-\beta \cdot x}}{\beta}\Bigg]_0^{100} - \int_0^{100} \frac{C \cdot e^{-\beta \cdot x}}{-\beta} \, dx = 100$$

$$-\frac{C \cdot 100 \cdot e^{-\beta \cdot 100}}{\beta} + \frac{C \cdot 0 \cdot e^{-\beta \cdot 0}}{\beta} + \frac{C}{\beta} \int_0^{100} e^{-\beta \cdot x} \, dx = 100$$

$$-\frac{C \cdot 100 \cdot e^{-\beta \cdot 100}}{\beta} + \frac{C}{\beta} \cdot \frac{e^{-\beta \cdot x}}{-\beta}\Bigg]_0^{100} = 100$$

$$-\frac{C \cdot 100 \cdot e^{-\beta \cdot 100}}{\beta} - \frac{C}{\beta} \cdot \frac{e^{-\beta \cdot 100}}{\beta} + \frac{C}{\beta} \cdot \frac{e^{-\beta \cdot 0}}{\beta} = 100$$

$$-\frac{C \cdot 100 \cdot e^{-\beta \cdot 100}}{\beta} - \frac{C}{\beta} \cdot \frac{e^{-\beta \cdot 100}}{\beta} + \frac{C}{\beta} \cdot \frac{1}{\beta} = 100$$

$$C \cdot \left[\frac{e^{-\beta \cdot 100}}{\beta} \cdot \left(-100 - \frac{1}{\beta}\right) + \frac{1}{\beta^2}\right] = 100$$

$$C = 100 \Bigg/ \left[\frac{e^{-\beta \cdot 100}}{\beta} \cdot \left(-100 - \frac{1}{\beta}\right) + \frac{1}{\beta^2}\right]$$