PRACTICAL APPLICATION TO INCLUDE FUTURE DISEASE COSTS (PAID) USER MANUAL PAID 1.1

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Terms of use

PAID is a toolkit that enables researchers to incorporate future unrelated medical costs in their economic evaluations. PAID consists of a series of worksheets in Excel in which users can select diseases they want to exclude if they have already modelled costs of these diseases. In this document, it is briefly explained how to use PAID version 1.1. PAID is open access and can be used free of charge and downloaded from www.imta.nl/paid. However, when reporting results produced with PAID please refer to: *van Baal, P.H., Wong, A., Slobbe, L.J., Polder, J.J., Brouwer, W.B.,de Wit G.A. (2011) Standardizing the inclusion of indirect medical costs. Pharmacoeconomics Mar 1;29(3):175-87.*

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INTRODUCTION

WHAT IS PAID?

Medical interventions that increase life expectancy may create additional consumption of medical goods and services in so-called 'added life years'. Added years are those years that would not have been lived without the intervention. A part of this medical consumption in added years is directly related to the intervention. In case in of a successful heart transplantation costs of visiting the cardiologist in life years gained are considered related. These costs are typically included in economic analyses. Other costs in added years are not directly related to the intervention and are termed 'future unrelated medical costs'. This would for instance be the case for costs resulting of dementia care in added life years after the same heart transplantation. These costs are also referred to as 'indirect medical costs' and are typically excluded from economic analyses. PAID is a Microsoft Excel file which is especially developed to facilitate inclusion of future unrelated medical costs in economic evaluations. PAID contains of a large number of worksheets containing cost data. Using a simple user-interface the user can make various selections so that he/she gets the costs needed as input for the economic evaluation. The output of PAID consists of per capita annual health care expenditure for the Netherlands summed over all disease categories and health care providers that the user has selected in PAID stratified by sex, age and proximity to death. These estimates of annual per capita health care expenditures can be used in economic evaluations to estimate incremental future unrelated medical costs. For instance, the output of PAID can be combined with survivor curves for different treatment scenarios calculated with the use of Markov models (see later chapter for more information on how to do this).

To produce consistent estimates of disease specific costs per capita taking into account proximity to death we combined information from several data sources. As backbone we used the Costs of Illness (COI) study data for the Netherlands (www.kostenvanziekten.nl). In that study total direct health care costs in different health care settings in the Netherlands were uniquely attributed to 107 disease categories (including rest categories as 'not disease related') and 8 categories of healthcare providers, specified by gender and age. In PAID the annual health care expenditures per capita are partitioned into annual per capita expenditure in the last year of life and all other years for all diseases and five categories of health care providers. For more details on how this is accomplished we refer to van Baal et al. 2011.

CONCEPTUAL MODEL UNDERLYING PAID

In PAID it is assumed that total health care expenditure can be explained by age, sex and time to death and that the relation between costs and these three variables differs per disease and per health care provider. Based on this assumption lifetime health care costs can be estimated by summing up annual age specific costs specified by disease and health care provider distinguishing the last year of life and other years:

$$lhc(g) = \sum_{a}^{n-1} \sum_{i} sc_i(a,g) + \sum_{i} dc_i(n,g) \qquad (1)$$

where *lhc*(*g*) = lifetime healthcare costs for an individual of sex *g*; *a* = age in years; *n* = age at death; *dc* = decedent costs (per capita healthcare costs in the last year of life); *sc* = survivor costs (per capita healthcare costs in all other years); and *i* = index for diseases. Equation 1 simply states that individual healthcare expenditures are the sum of per capita disease-specific expenditures in the last year of life and 'other' years,

and can be thought of as lifetime health expenditures if the current health expenditure pattern would remain constant and if the person incurs average health care use (conditional on age, gender and time to death). It is important to realize that both *sc* and *dc* refer to per capita costs and not costs per patients. Furthermore, please note that the assumption regarding average health care use can be relaxed (see the last chapter).

Now suppose an intervention that increases life expectancy influences the health expenditures for *Z*, a set of related diseases. The costs of all other diseases can then be simply estimated by summing over the remaining disease categories (equation 2):

$$\sum_{a}^{n-1}\sum_{i\notin Z} sc_i(a,g) + \sum_{i\notin Z} dc_i(n,g) \qquad (2)$$

where *Z* = the set of related diseases. To avoid double counting, total lifetime healthcare expenditures are broken down into disease components. This enables to exclude the costs of the diseases at which the intervention is targeted (i.e. the related medical costs).

PAID 1.1 VERSUS PAID 1.0

Cost estimates in PAID 1.0 were based on the Costs of Illness study in the Netherlands from 2005. These age and gender specific per capita average costs per disease and health care provider were decomposed into costs that are incurred in the last year of life and costs that are incurred in other years using various data sources. In PAID 1.1 data from the Costs of Illness study of 2013 and also mortality rates from 2013 were used. All other data sources and steps in the decomposition used to construct PAID 1.1 are the same as in PAID 1.0 (see van Baal et al. 2011)

The user interface has also changed a bit in PAID 1.1 compared to PAID 1.0. Besides selecting disease categories PAID 1.1 also allows to select health care providers included. Furthermore, per capita costs of unselected diseases and an estimate of the costs of dying one year later are also shown. Costs of dying one year later (denoted $c_i(a,g)$ for a particular disease) are defined in the following manner:

$$c_i(a,g) = sc_i(a,g) + sc_i(a+1,g) - dc_i(a,g) \qquad (3)$$

It is recommended that costs of dying one year later are used in economic evaluations in which models are used with a short time horizon (see last chapter for more details).

PAID USER INTERFACE

PAID consists of a series of worksheets in Excel in which users can select diseases and health care providers for which they want to include costs. The idea is that users select all diseases and health care providers for which they have not calculated costs yet in their analysis (the set of unrelated diseases). The set of related diseases should be deselected (NB: in a lot of cases there will be just one related disease). Conditional on these selections PAID calculates cost per capita stratified by age, gender and the last year of life/other years for both related (deselected) and unrelated diseases (selected). Furthermore, PAID 1.1 also calculates the costs of living exactly one additional year longer (see next chapter for more details on how to use these numbers). The user interface of PAID 1.1 consists of three worksheets (sheets with data are hidden from the user but are available upon request):

- the 'Main' worksheet: this worksheet displays estimates of per capita annual health expenditures summed over the selected diseases. Furthermore, estimates of per capita costs of living exactly one year longer are displayed. In this worksheet the user can also select the health care providers one wants to include;
- the 'Select diseases' worksheet: on this worksheet the user can select the diseases he/she wants to include in the calculation of per capita health expenditures;
- the 'Graphs' worksheet: this worksheet displays graphically the estimates of the per capita annual health expenditures summed over the selected diseases.

Figure 1 displays screenshots of the PAID 1.1 'Main' worksheet.

PAID 1.1

Select health care providers to include

2013 price level

Number of unrelated disease 106

Number of related diseases: 1

- [x] Hospitals
- [x] Nursing and residential care facilities
- [ ] Retail sale and other providers of medical goods
- [ ] Providers of ambulatory health care
- [ ] Other health care providers

Per capita annual health care expenditure

	Unrelated diseases				Related diseases					Per capit	
	Last year of life		Other years			Last year of life		Other years		Costs of livin	
										Unrelated di	
Age	Men	Women	Men	Women	Age	Men	Women	Men	Women	Age	Men
81	30,188	37,922	6,384	7,843	81	7,867	11,521	1,231	2,147	81	5,323
82	29,126	37,749	6,768	8,580	82	8,182	12,375	1,417	2,541	82	5,863
83	28,221	37,657	7,222	9,408	83	8,512	13,273	1,629	2,997	83	6,634
84	27,634	37,826	7,796	10,366	84	8,960	14,272	1,883	3,527	84	7,750
85	27,588	38,526	8,527	11,478	85	9,558	15,363	2,200	4,145	85	9,078
86	28,139	39,781	9,489	12,784	86	10,375	16,589	2,594	4,863	86	10,666

Per capita health care expenditure

Costs of living one additional year

	Unrelated diseases		Related diseases	
Age	Men	Women	Men	Women
81	5,323	7,670	1,547	3,001
82	5,863	8,488	1,747	3,439
83	6,634	9,578	2,077	3,996
84	7,750	11,066	2,482	4,618
85	9,078	12,733	3,017	5,371
86	10,666	14,617	3,654	6,265

Figure 1: Screenshots of the PAID 1.1 'Main' worksheet

From Figure 1 it can be seen that not all health care providers are included (only costs of hospitals, nursing and residential care facilities are included) and costs of 106 diseases are selected. To check which diseases are selected and deselected Figure 2 displays a screenshot of part the 'Selections' worksheet. The 'Selections' worksheet is nothing but a series of checkboxes (107 in total corresponding to the number of disease categories distinguished in the Dutch Costs of Illness study) indicating whether a disease is unrelated (then the box is checked) or related (then the box is unchecked). In Figure 2 all checkboxes are except 'Dementia' are checked.

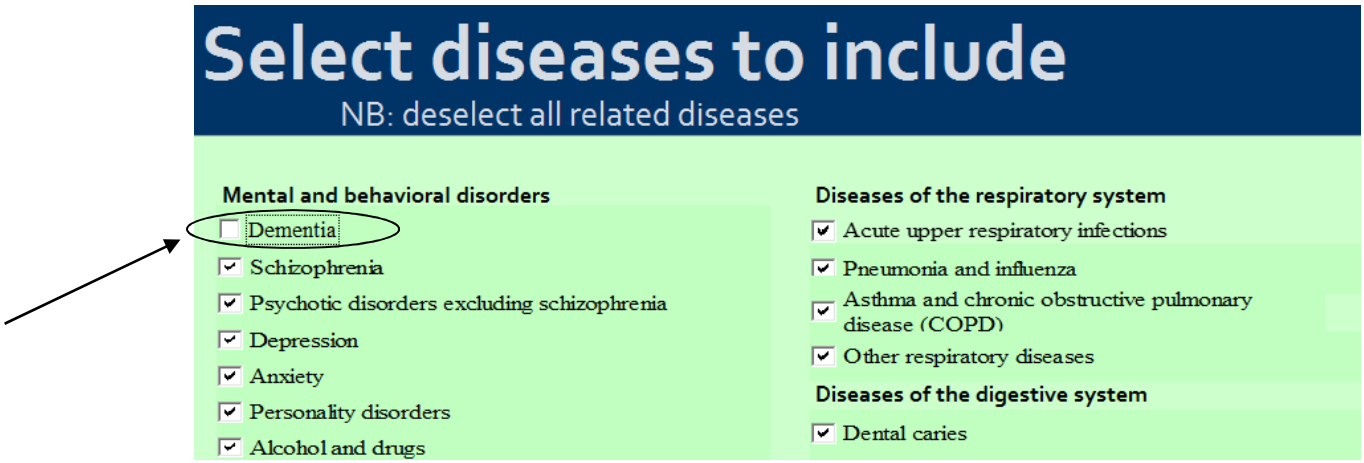
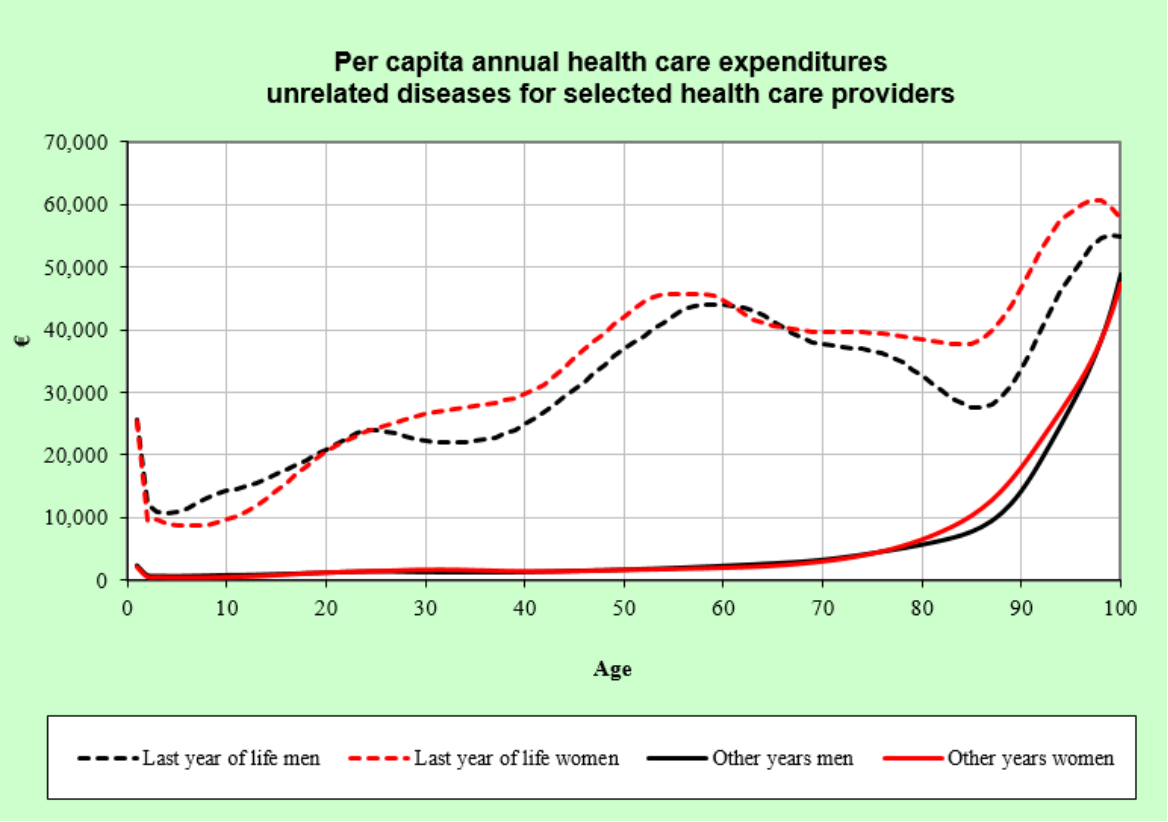


Figure 2: Screenshot of part of the PAID 1.1 'Selections' worksheet. Excluding the costs of Dementia

The yellow area in Figure 1 displays the output generated by PAID 1.1 conditional on the selections made. For instance, if we look at the first yellow column on the left we can see that the average per capital health care expenditures for a men aged 81 for all unrelated diseases incurred in hospitals, nursing and residential care facilities equals €6,384 if he does not die at that age but equals €30,188 if he dies at that age. The average per capital health care expenditure for all related diseases (Dementia in this example) incurred in hospitals, nursing and residential care facilities equals €1,231 if he does not die at that age but equals €7,867 if he dies at that age. Male costs incurred in hospitals, nursing and residential care facilities for dying at age 82 rather than 81 equal €5,323 for unrelated diseases and €1,547 for related diseases. Please again note that all output of PAID refers to costs per capita rather than costs per patient.

The 'Graphs' worksheet consists simply of a series of graphs that graphically display the numerical data of the 'Output' worksheet. Figure 3 displays two graphs displayed in the 'Graphs' worksheets. From this figure it can be seen that per capita annual health expenditures are much larger in the last year of life compared to other years.



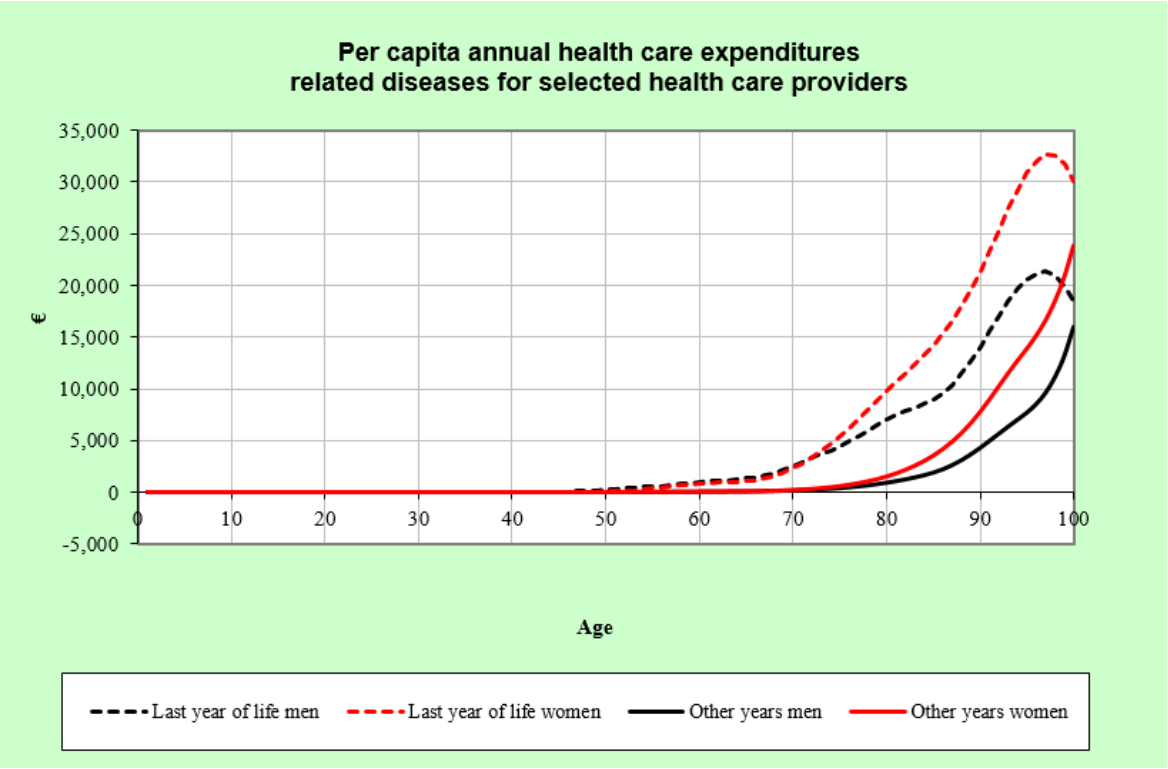


Figure 3: Screenshots of part of the PAID 1.1 'Graphs' worksheet

USING PAID IN ECONOMIC EVALUATIONS

In this chapter we illustrate how PAID can be used in economic evaluations. As the output of PAID concerns estimates of per capita annual health care costs the easiest way to use PAID is when the model has a long time horizon (as a rule of thumb one can use > 5 years) and the costs for unrelated diseases can be assumed to be similar to the average Dutch person conditional on age, gender and time to death. In the next section, we will show a worked out example for this situation. Thereafter, it is shortly discussed how to use PAID in economic evaluations with a very short time horizon. In the last section a framework is provided to adjust estimates of PAID in case it is unreasonable to expect that the health care use for unrelated diseases of the population at which the interventions are targeted resembles the average Dutch population.

What is crucial in all applications is that in order to get sensible results using PAID is that a lifetime horizon is adopted and that in all scenarios everybody of the target population should die. Furthermore, in case a Markov model is employed with time steps smaller than one year is employed one must ensure that all persons incurs the high costs in the entire last year of life!

WORKED OUT EXAMPLE

Table 2 on the next page displays a worked out example. Here the analogy are two treatments (treatment A and treatment B) targeted at a patient with dementia. The patient starts treatment at age 75 and with treatment A the patient dies at age 81 while with treatment B he dies at age 85. The gain in lifeyears is thus 4 years for this patient. Under treatment A the patient incurs the high costs in the last year of life at age 81 while if he has treatment B these high costs are incurred at age 85. At other ages, the patient incurs 'survivor' costs. It is interesting to note that the results in Table 2 illustrate that life prolonging interventions will result in short run savings in costs of unrelated diseases (due to postponement of the expensive last year of life) but in additional costs in the longer run (i.e. the added years). The impact of including unrelated costs on the ICER can be understood if we look at equations (4a) and (4b):

$$ICER = \frac{\Delta non\ medical\ \ costs + \Delta related\ medical\ costs + \Delta unrelated\ medical\ costs}{\Delta Qalys} = \qquad (4a)$$

$$\frac{\Delta non\ medical\ \ costs + \Delta related\ medical\ costs}{\Delta Qalys} + \frac{\boldsymbol{\Delta unrelated\ medical\ costs}}{\boldsymbol{\Delta Qalys}} \qquad (4b)$$

Using the numbers of the last row of table 2 we can calculate the impact of including unrelated medical costs on the ICER which are displayed in Table 1. From Table 1 it can be seen that the impact of including unrelated costs has a smaller impact on costs per life year gained than on costs per QALY gained in this example. A general rule is that the impact of unrelated costs on the ICER is bigger the higher the ratio (life years gained) / (QALYs gained).

Table 1: impact of including unrelated costs on the ICER based on the example presented in table 2

	Undiscounted	Discounted
Unrelated medical costs per LY gained	10,006	7,299
Unrelated medical costs per QALY gained	22,486	16,381

Table 2: worked out example

	Per capita costs of unrelated diseases from PAID 1.1 for all health care providers (all diseases except dementia)		*Life years*				*Costs unrelated diseases*				*QALYs*			
Age	Last year of life	Other years	A	B	B -/- A	B -/- A Discounted*	A	B	B -/- A	B -/- A Discounted**	A	B	B -/- A	B -/- A Discounted*
75	42,503	7,815	1	1	0	0	7,815	7,815	0	0	0.70	0.70	0.00	0.00
76	41,968	8,158	1	1	0	0	8,158	8,158	0	0	0.67	0.67	0.00	0.00
77	41,222	8,504	1	1	0	0	8,504	8,504	0	0	0.64	0.64	0.00	0.00
78	40,277	8,849	1	1	0	0	8,849	8,849	0	0	0.61	0.61	0.00	0.00
79	39,199	9,200	1	1	0	0	9,200	9,200	0	0	0.58	0.58	0.00	0.00
80	38,033	9,563	1	1	0	0	9,563	9,563	0	0	0.55	0.55	0.00	0.00
81	36,900	9,948	1	1	0	0	36,900	9,948	-26,952	-21,301	0.52	0.52	0.00	0.00
82	35,868	10,365		1	1	0.90		10,365	10,365	7,876		0.49	0.49	0.44
83	34,976	10,846		1	1	0.89		10,846	10,846	7,925		0.46	0.46	0.41
84	34,388	11,436		1	1	0.87		11,436	11,436	8,035		0.43	0.43	0.38
85	34,332	12,166		1	1	0.86		34,332	34,332	23,194		0.40	0.40	0.34
Sum					**4**	**3.52**			**40,026**	**25,728**			**1.78**	**1.57**

**Discounted with 1.5% annually **Discounted with 4% annually*

USING PAID IN CASE OF A SHORT TIME HORIZON

The default way of using PAID was described in the previous pages. However, if the time horizon of the economic evaluation is short (as a rule of thumb one can use < 5 years) and there are big differences in survival in the first year using costs stratified by the last year of life and other years may lead to strange results. In that case it is advised to use the costs of dying one year later instead ($c_i(a, g)$). To illustrate what can go wrong if PAID is used in these circumstances consider the example described in textbox 1.

Textbox 1: using PAID output in case there is short time horizon

Suppose that a male person who had a stroke at age 80 dies after 4 months with treatment A but dies after 13 months with treatment B. Decedent and survivor costs from PAID for a man aged 80 (selecting all health care providers and deselecting stroke) equal €42,859.- and €9,986.- respectively. Using the default way of applying PAID lifetime unrelated medical costs would equal 4/12 x €42,859.- under treatment A and 1/12 x €9,986.- + €42,859.- under treatment B. The difference would equal €29,405.- which equals €39,206.- per life year gained. However, using survivor and decedent costs would create big differences in costs at baseline between treatment A and B for unrelated diseases which is implausible and in conflict with the definition of unrelated. Conceptually, this would also make no sense as this implies a different past trajectory of costs for the same person before getting the stroke treatment. Therefore, in these circumstances it is advised to use the costs of living one year longer and to make no distinction between survivor and decedent costs anymore Under treatment A lifetime costs of unrelated diseases would equal 4/12 x €9,172 and under treatment B these would equal 13/12 x €9,172 (or €9,172 +1/12 x €9,720 if you are very precise ☺) resulting in €9,172 (or €9,233) per lifeyear gained.

ADJUSTING PAID OUTPUT

In case it is unreasonable to expect that the health care use for unrelated diseases of the population at which the interventions is targeted resembles the average Dutch population the output of PAID can be still be useful if they are properly adjusted. In order to adjust the estimates produced by PAID it is good to realize that per capita costs can be viewed as a product of having the disease or dying with the disease times the costs conditional on the disease (costs per patient):

$$\begin{aligned} sc(a)_i &= p(a,i) \times sc(a \mid i)_i \\ dc(a)_i &= m(a \mid i) \times dc(a \mid i)_i \end{aligned} \qquad (5)$$

Where $p(a,i)$ denotes the probability of having disease *i* at age *a* (conditional on being alive at age *a*); $sc(a \mid i)_i$ survivor costs for disease *i* age *a* conditional on having disease *i* ; $m(a \mid i)$ denotes the mortality rate at age *a* conditional on having disease *i* ; $dc(a \mid i)_i$ decedent costs for disease *i* age *a* conditional on dying at age *a* with disease *i* . Equation provides a framework to adjust estimates of $sc(a)_i$ and $dc(a)_i$ if the target population of the intervention is likely to differ in terms of health care costs for unrelated diseases. This could for instance be done using estimates of hazard ratios for acquiring a disease or dying with a disease in a particular target group. Please note that the user is responsible for adjusting PAID estimates in a sensible manner.