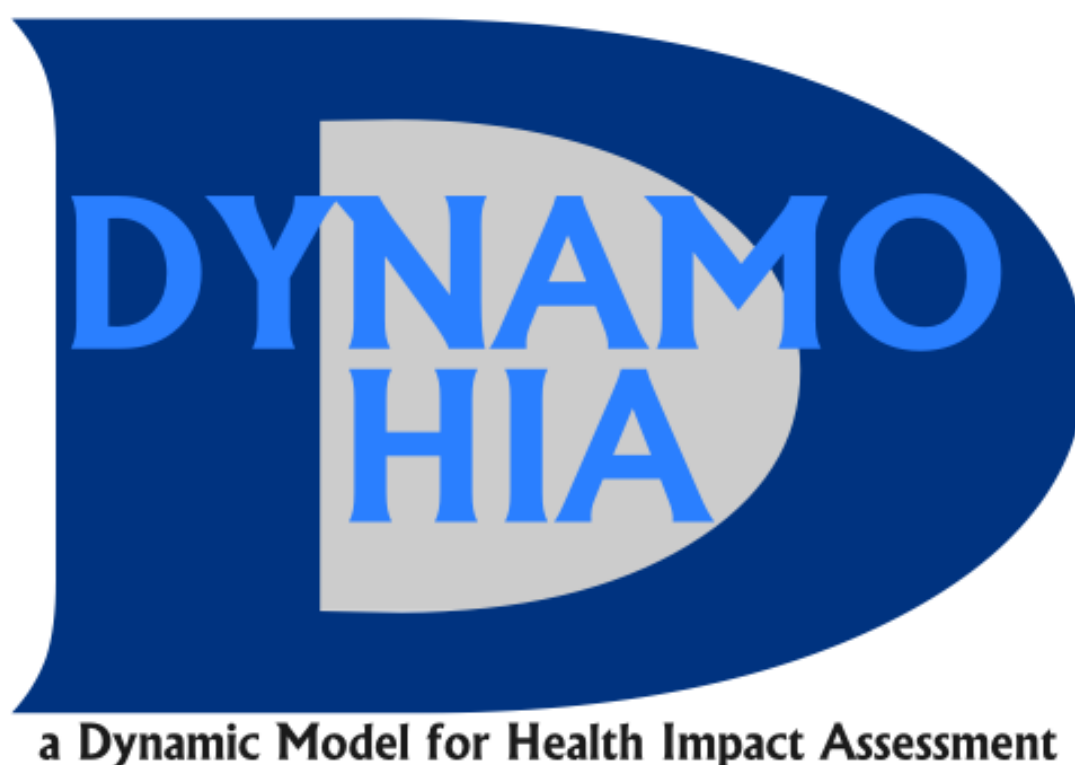


# **DYNAMO-HIA**

## **A Dynamic Model for Health Impact Assessment**

### **USER GUIDE AND MANUAL**

Version 1.2



Stefan K. Lhachimi, Hendriek C. Boshuizen, René L. Mondeel, Wilma J. Nusselder

This program has been developed partially by order and for the account of DG-SANCO, within the framework of grant agreement 2006116

---

## Table of Contents

DYNAMO-HIA – A short Introduction .....	7
Overview.....	7
Installation.....	7
Startup.....	8
Running your first Simulation .....	10
The DYNAMO-HIA user interface .....	16
Reference Data.....	16
Directory Populations .....	16
Directory Risk_Factors .....	18
Directory Diseases .....	20
Configuring Simulations.....	23
Risk Factor Tab.....	26
Diseases Tab .....	27
Relative Risk Tab.....	28
Scenario Tab .....	30
Starting the simulation .....	32
Output Screen in more Detail .....	33
Population Pyramid.....	34
Disease plots .....	36
Risk factor plots .....	38
Life expectancy plots .....	40
Mortality/survival plots.....	42
Write output .....	43
Change scenario settings.....	43
Inspecting the model parameters .....	45

---

Entering Data .....	48
Navigating the Data Tree .....	48
General Mechanics of Data Entry and Manipulating .....	53
Entering by hand .....	53
Using Excel templates and the import function .....	54
Copying files into the working directory .....	55
Specification of reference and intervention scenario's .....	58
Running DYNAMO in batch-mode .....	60
Model Core .....	65
Figures illustrating the DYNAMO-HIA methodology .....	69
Important Notes on using the model .....	72
Negative other cause mortality .....	73
Using continuous risk factors .....	75
Interpreting graphs of disease prevalence by risk factor level over time .....	75
Selective mortality and calculating net transition rates .....	76
Relative risks on death equal to 1 versus no relative risk on death .....	77
Relative risks on death and continuous risk factors .....	78
Other cause mortality and compound risk factors .....	79
Appendices.....	81
Appendix A. System Requirements .....	81
Appendix B: Recommended Naming Conventions .....	82
Appendix C. List of ERROR and WARNING messages .....	84
Errors when installing DYNAMO.....	84
Errors reading files .....	85

---

Errors generated by the parameter estimation module .....	86
Warnings generated by the parameter estimation module: .....	90
Errors generated by the simulation .....	93
Errors generated by the postprocessing module .....	94
Appendix D. Frequently Asked Questions .....	96
General .....	96
Running DYNAMO-HIA.exe (on Windows XP) .....	96
Java heap space.....	97
Reference Data Screens .....	98
Simulation Screen.....	98
Output screen.....	99

---

## List of Figures

Figure 1: Starting Screen of User Interface (detail, text might vary) .....	9
Figure 2: Pre-set simulation configuration screen for Tutorial_1 .....	11
Figure 3: The population pyramid tab of the output screen .....	13
Figure 4: Disease Plots tab of the output screen (here development over time).....	15
Figure 5: Top half of the simulation configuration screen .....	23
Figure 6: Risk Factor tab of simulation configuration screen (detail) .....	25
Figure 7: Specifying a disease in the simulation configuration screen (detail). .....	28
Figure 8: Specifying a relative risk in the simulation configuration screen (detail).....	30
Figure 9: Specifying a scenario in the simulation configuration screen (detail). .....	32
Figure 10: View of the “resultsObject.obj” in the user interface (detail) .....	34
Figure 11: Population Pyramid Screen .....	36
Figure 12: Disease plot screen .....	38
Figure 13: Riskfactor plot screen .....	40
Figure 14: Change scenario settings Tab in output screen (detail) .....	44
Figure 15: Selecting a parameter file for inspection (detail) .....	45
Figure 16: Inspecting the other cause mortality as used by the model in Excel.....	47
Figure 17: Data Tree Navigation Example: Data Tree with all directories collapsed (left panel), Data Tree with the directory Disease expanded (right panel) .....	51
Figure 18: Data Tree: Example of creating a new disease directory: .....	52
Figure 19: Example of data entering window .....	56
Figure 20: A work directory has to be prepared containing the simulations to be run....	61
Figure 21: Example of a text file containing the names of the simulations that should be run in batch-mode .....	61

---

Figure 22: Place of the text file containing the names of the simulations that should be run .....	62
Figure 23: How to open a command window .....	63
Figure 24: Command window, with the eclipse directory as the current directory .....	64
Figure 25: Entering the command running DYNAMO-HIA in batch mode .....	64
Figure 26: Example of risk-factor biographies for a risk factor with three categories....	69
Figure 27: Stylized structure of disease life table .....	70
Figure 28: Stylized cohort life tables (with only one disease, three different biographies, and five time steps) .....	71
Figure 29: Schematic overview of the dimension of a multi-cohort, multistate-life table .....	72

## DYNAMO-HIA – A short Introduction

The document gives an overview about how to use DYNAMO, what it can do and how it works.

We combine this introduction with a practical tutorial using real life data.

### **Overview**

DYNAMO-HIA (DYNAmic MOdeling for Health Impact Assessment) is a generic software tool specially designed to aid the quantification step in health impact assessment. DYNAMO-HIA is generic in the sense that it allows arbitrary chronic diseases or risk-factors that fit the standard causal pathway of the health impact assessment framework to be modeled. The user can import and use his or her own data to add and analyze diseases or populations that are of interest to him or her.

DYNAMO-HIA has been specifically designed to quantify the impact of user-specified risk-factor changes due to policy or interventions on various and multiple diseases on overall population health. Using a Markov-based modeling approach that allows for explicit risk-factor states, it dynamically simulates a real-life population. A built-in parameter estimation module ensures that only standard epidemiological evidence, i.e. data on incidence, prevalence, and mortality are required. DYNAMO-HIA provides a rich model output of summary measures -- such as life expectancy and disease-free life expectancy -- and detailed data -- such as mortality/survival rates and prevalence numbers -- by age, sex, and risk-factor status over time.

This manual gives an introduction in how to use DYNAMO-HIA. The prototype version of DYNAMO is accompanied with an example data set in the “Tutorial\_Data” directory. In this manual we refer several times to this data set using it as step-by-step tutorial to describe the different options of DYNAMO.

### **Installation**

First **install** the DYNAMO-HIA prototype and data for the tutorial on your computer:

1. On the HardDisk/CD/USB-stick: locate and click on the file “setup.exe”.

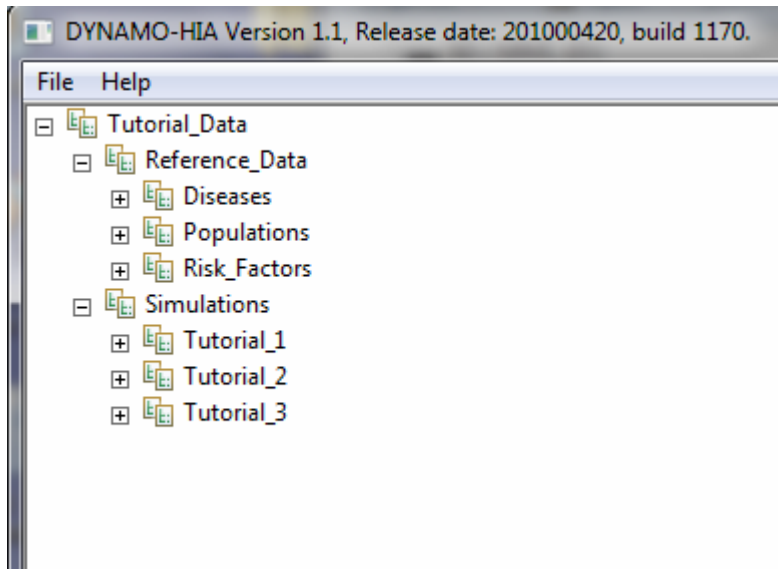
2. The installer asks you to specify the desired installation directory (the software itself requires some 140MB of disk space).
3. After DYNAMO-HIA finished the installations, click “close”. DYNAMO-HIA is installed now and is added to the list of programs in the start menu. The installer can also be used to uninstall DYNAMO-HIA. Click on “setup.exe” again and you can choose to remove or repair the software.

## **Startup**

To open the DYNAMO-HIA prototype:

1. Before you start DYNAMO-HIA, check that the tutorial data is on your computer. After installation, the data should be in the directory `/Program Files/DYNAMO-HIA/Tutorial_Data`. Otherwise, locate on the CD/USB-stick the folder “Tutorial\_Data”, and copy the whole folder to a desired location on your computer.
2. To start the software open the start menu, go the folder “DYNAMO-HIA” and click on the icon “DYNAMO-HIA.exe”.
3. After starting the program, a file browser appears with the sentence “In the DYNAMO-HIA home directory data and simulations are stored”. This window allows you to choose the working directory with the data you want to work with during this session. The working directory has to adhere to a fixed structure, i.e. containing certain directories. For the purpose of this tutorial browse folder “Tutorial\_Data” you just copied on to your computer. If you decide to make a new directory, choose the desired location and type the desired name in the white open space “Folder”, DYNAMO will then create a working directory that follows the required structure. You can choose the working directory during a running session by going to the “File” menu.
4. After choosing an existing or creating a new working directory, the user interface appears (see Figure 1). The user interface allows to open and edit the data files

that are stored in this directory, add new files to them, and setup and run simulations. The structure of the home directory (in this case: “Tutorial\_Data”) mimics the directory structure of the folder specified as the home directory. The home directory always has a *Reference\_Data* and a *Simulations* directory.

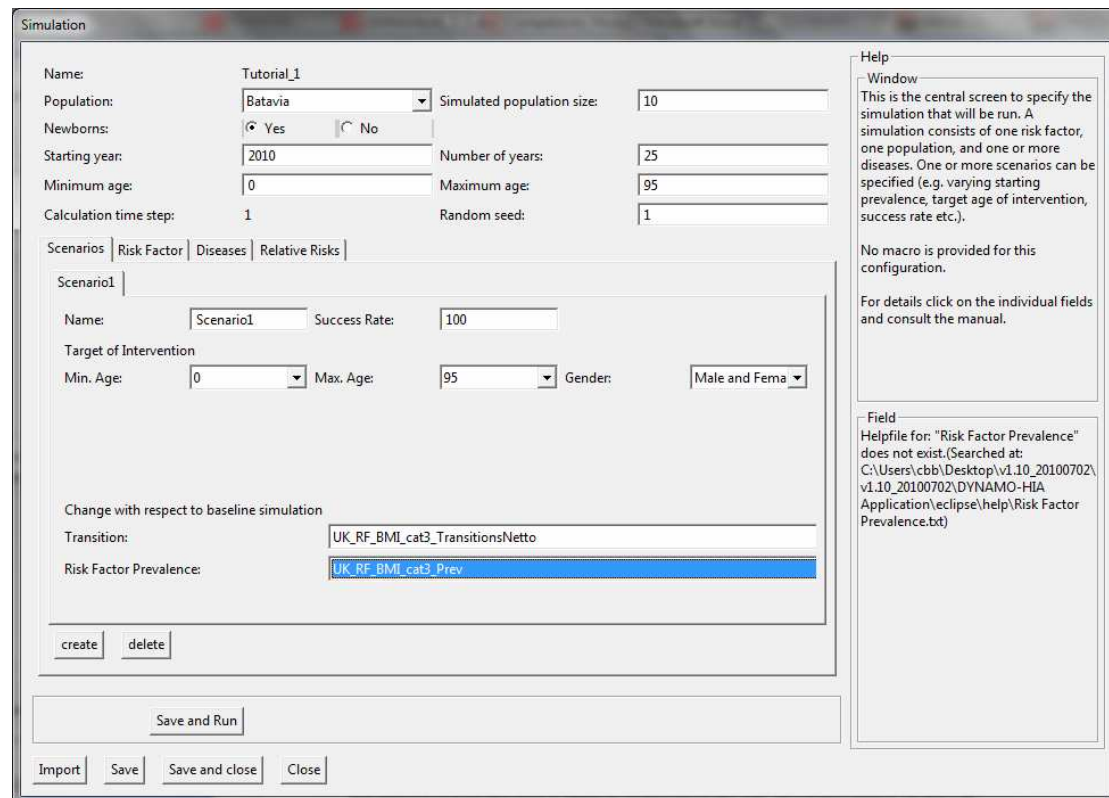


**Figure 1: Starting Screen of User Interface (detail, text might vary)**

### ***Running your first Simulation***

The user interface is split into two main directories. In the directory *Reference\_Data* all the input data required to run simulations is stored. These are files consisting of data about the population, diseases, and risk factors. The example directory “*Tutorial\_Data*” already contains all the data needed to run a simulation. But before proceeding you can explore the *Reference\_Data* directory a bit. By pressing the + sign you can expand a directory and view the content. For example, when pressing the + sign next to the directory *Diseases*, all the disease that are available for simulation in this particular working directory are listed.

Click now the + sign right next to the *Simulations* directory to expand the view. A number of sub-directories are shown. Locate the directory *Tutorial\_1* and click the + sign to expand the directory. Within the *Tutorial\_1* directory, a single file is shown: *configuration*. Right click on this file and choose “*Configure and Run Simulation*” from the context menu. The *simulation screen* appears. In this screen all the technical choices for running simulations can be made.



**Figure 2: Pre-set simulation configuration screen for Tutorial\_1**

Configuring a simulation requires making several choices. For example, which disease to include, the length of a simulation, which risk factor to use, the specification of the intervention scenario and so on. Right now, no choices have to be made as in the *Tutorial\_1* directory a finished simulation configuration is present. In this simulation we use BMI as a risk factor and compare how the population health of Batavia would develop if Batavia would have the risk factor prevalence of the UK. Batavia is a fictional country that shares almost all health and population characteristic of the Netherlands. This intervention affects all age groups and both sexes. We run the simulation for 25 years, include newborns, and made a number of further choices. For now, just click on the button “Save and Run”. Now DYNAMO-HIA runs the first simulation.

After a few second the *output screen* appears. The first image is always the “*Population Pyramid*”, that shows the overall population development over time and presents the share of the population that has a given diseases graphically. The share of the population that has a disease is colored in light red. In Figure 3, the light red area shows the share of the population that has at least one disease, i.e. the total disease burden. Now click on the “*autoRun*” button in the bottom left corner. This starts an animation that shows the development of population and population health for the projection time in one year increments. The population screen view has a number of options: One option is to see the disease burden for a particular disease. From the pull-down menu “*diseases*” another disease can be chosen. For example, when choosing “*IHD*” the light red area changes in shape and size, it now shows the prevalence of IHD in the population.

The pull-down menu “*scenario*” allows choosing different scenarios. In the case of *Tutorial\_1* only two scenarios exist, the “*reference scenario*” and “*Scenario 1*”. When choosing “*Scenario 1*” an additional possibility is to click on the radio button in the middle of the screen and switch the y-axis from “*absolute value for scenario*” to “*difference with reference scenario*”. Activating this button changes the view of the population pyramid. Now the light red area shows the part of the population that has a given disease in both, the “*reference scenario*” and “*Scenario 1*”. The dark red area shows the part of the population that has the disease in “*Scenario 1*” but not in the “*reference scenario*” (a yellow area would show the share of the population that has the disease in “*reference scenario*” but not in “*Scenario 1*”). The black area at the outer margin of the population pyramid shows the number of people that are alive in the in the “*reference scenario*” but not in “*Scenario 1*” (a grey area would show the share of the

population that is alive in the “Scenario 1” but not in “reference scenario”). If you move the mouse over the graph, it shows you the exact numbers in each bar-part. Also you can look more in detail by clicking and holding the left mouse button and then move to the right: a rectangle will appear that shows the area that will be shown in more detail at the moment that you release the mouse button. You can undo this by repeating the procedure, but moving to the left. Right clicking will show a menu, where you can choose to print or save the graph, or change the titles. Note, however, that any such changes to graphs will be temporary, and removed at the moment where you select another graph or tab.

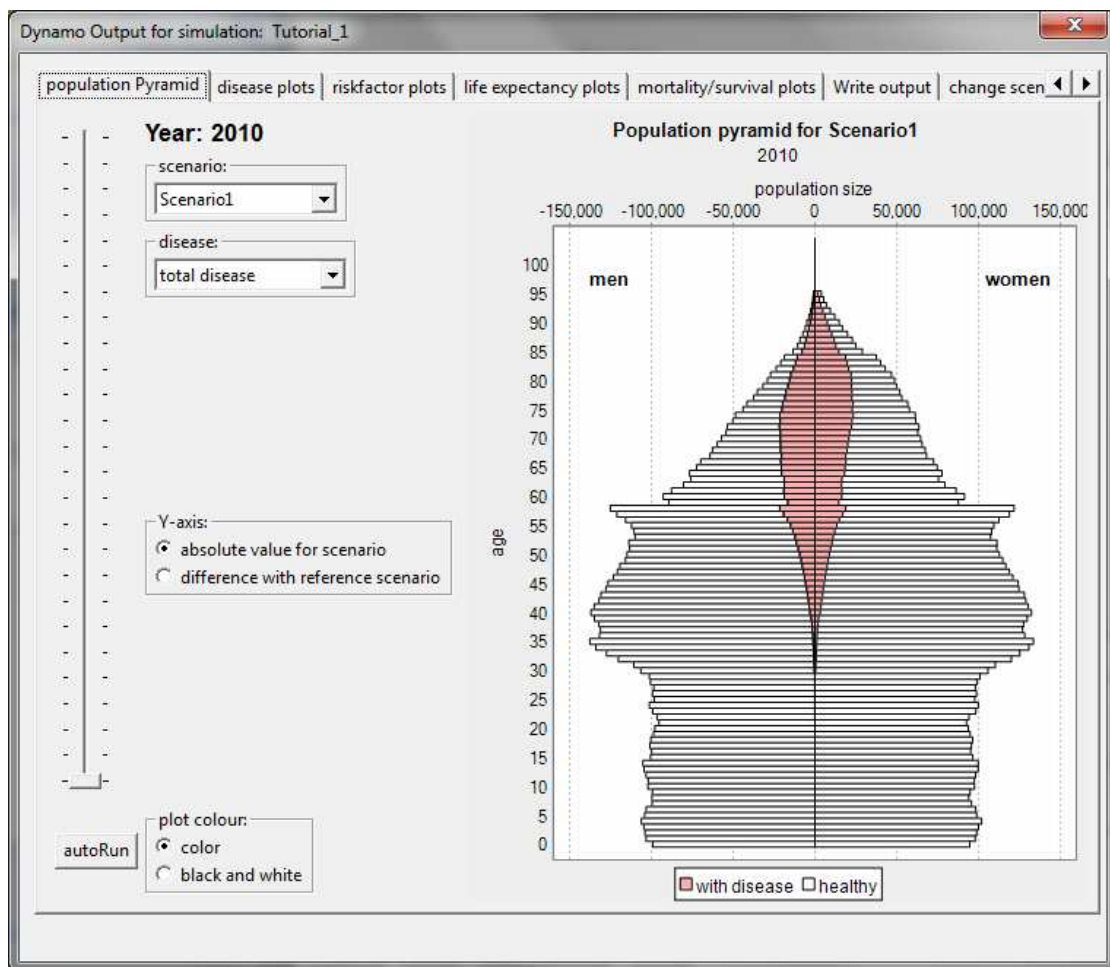
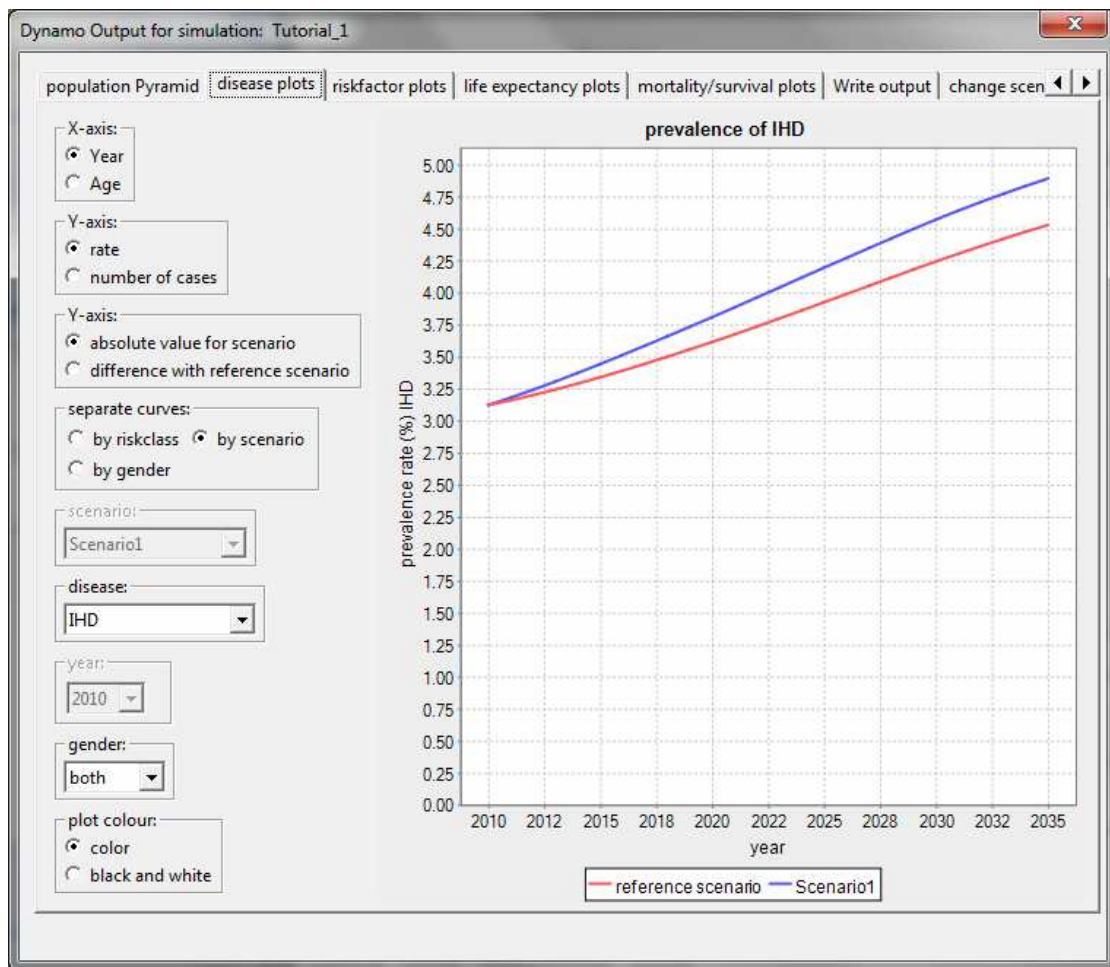


Figure 3: The population pyramid tab of the output screen

On the top of the output interface several different tabs are visible that allow analyzing the simulation results further. For example, the tab “life expectancy plots” shows the life expectancy for the different scenarios, their development over time, and the number of expected life years with a given disease. For a further exploration of the outcomes of “*Tutorial\_1*” click on the tab “disease plots”. This screen gives a graphical overview of the development of disease prevalence for the simulated scenarios. Again this screen allows several different choices. When first viewing the tab “disease plots” after a simulation run, usually the plot graphs the development of the disease prevalence over time for all scenarios. In the case of “*Tutorial\_1*” these are the “reference scenario” and “Scenario 1”. In the pull-down menu “disease”, another of the simulated diseases can be chosen. When selecting the radio button “by gender”, the view changes and the plot shows the prevalence development separately for men, women, and total population. The scenario for which this is done can be selected in the pull-down menu “scenario”. Feel free to explore different options in the output screen.



**Figure 4: Disease Plots tab of the output screen (here development over time)**

As a last step in this tutorial we want to draw your attention to the possibility of exporting the simulated output data. Click on the tab “Write output”. On this screen three different decisions with two options each can be made. First, you can choose to export the data “per year of simulation” or “by cohort”. The second option allows choosing to have the data “separate for man or women” or “total population”. The third option determines whether diseases are shown separately (“per disease”) or diseases clusters (“per combination of disease”) are included in the output. When clicking on “write data”, you can choose a file name and file location where the raw output is saved. The raw output is written in a special format that can be opened using MS Excel.

## The DYNAMO-HIA user interface

### ***Reference Data***

In the starting screen the directory “Reference\_Data” stores all the data needed to run a simulation. DYNAMO comes with a set of data for a large number of EU populations (see the data manuals for details) and also allows to import own data either to augment the already existing data or to enter data for different populations. In this section we will explore the “Reference\_Data” directory in more detail to give an overview of what kind of input data is needed. The data is usually – but not always – needed by age and sex. The age range is from 0 to 95 years of age. When percentages are needed as input, the range is between 0% and 100% (and not a fraction between 0 and 1).

In DYNAMO a directory can contain several sub-directories, which may have some further sub-directories and/or contain files. Within DYNAMO a file holds the actual data and can be recognized by not having a + sign right next to it. A file can be accessed by right-clicking on it and choosing “edit” from the context menu.

Expanding the directory “Reference\_Data” by clicking on the + sign reveals three sub-directories:

- *Populations*
- *Diseases*
- *Riskfactors*

### *Directory Populations*

Expand the view of “Populations” by clicking on the + sign. This directory can contain several populations, if desired, but running a simulation requires only one fully specified

population. In the tutorial, the population directory contains a single sub-directory named “*Batavia*”. This directory holds all the population data of the fictitious country of Batavia (which is surprisingly similar to the Netherlands for many health and population characteristics) needed to run a simulation. The files required to specify a population fully within DYNAMO are:

- *newborns*
- *overalldalyweights*
- *overallmortality*
- *size*

The file *newborns* contains the number of projected newborns for the given population. This is one of the few files in DYNAMO that does not require the data by sex, instead a sex ratio can be set. The sex ratio gives the number of boys born per girl. In European countries this ratio is usually close to 1.05.

The file *overalldalyweights* holds the average disability weight or percentage of disability in the general population. This is a number between 0 and 100, where 0 means that no disabled persons are present in the population, and 100 means that the entire population is disabled. These data are used to calculate DALY-weighted or disability free life expectancies, depending on whether one enters in this window (and other DALY-related windows) a DALY weight or a percentage of disability. The program does not make a distinction between the two, as the mathematical formulae for their calculation is identical. The data that are entered here determine which interpretation should be given to the output.

The file *overallmortality* holds the observed mortality rate for the population in question by age and sex.

The file *size* contains the population size of the population by age and sex. The age range is from 0 to 95.

### Directory Risk\_Factors

The directory *Risk\_Factors* contains all the data needed to specify a risk factor in DYNAMO. To run a simulation at least one risk factor has to be specified. The home directory “Tutorial” has already four different risk factors. Click on the + sign next to the directory “BMI-cat3”: a risk factor directory consist again of a number of sub-directories and contains in addition a file called *configuration*. The file *configuration* becomes important when creating a new risk factor and gives information on the meaning of the categories. In DYNAMO three different kinds of risk factors can be specified (categorical, compounding, and continuous). In this section we focus on categorical risk factors. The subdirectories of a specific risk factor in the directory *Risk\_Factor* are:

- *Prevalences*
- *Relative\_Risk\_For\_Death*
- *Relative\_Risk\_For\_Disability*
- *Transitions*
- *DurationDistributions* (only for compounding risk factors)

The directory *Prevalences* contains files with data about which share of the population is in which risk factor class (by age and sex). To run a simulation in which two situations with different prevalences are compared, at least two files need to be specified: one for the reference scenario and one for the intervention scenario. At least one file must be present to run a DYNAMO simulation.

What the risk factor prevalence looks like, depends on the type of risk factor:

For a categorical or compound risk factor, you have to enter (for each age and gender) the percentage in each exposure category (e.g. % normal weight, % overweight, % obesity) . For a continuous risk factor, you have to enter the mean value and standard deviation (SD) (e.g. mean BMI, SD BMI). For a compound risk factor, you also have to enter additionally information on duration (e.g. the % of former smoking that stopped 1, 2, ...20 year ago), under “DurationDistributions”.

The directory *Relative\_Risk\_For\_Death* contains files with data about the relative risk of the risk factor on total mortality (age and sex specific). This file is optional and not required to run a simulation. If this file is used, the risk factor will influence the “other cause mortality”, that is mortality that is not mediated by the diseases that are included in the simulation.

The directory *Relative\_Risk\_For\_Disability* contains a file with data on the relative risk of becoming disabled from the risk factor in question. Use of this file has not yet been implemented in the DYNAMO model; its presence is anticipating future extensions. Hence, this file is not required to run a simulation.

The directory *Transitions* contains files with data on how people changes their risk factor status. The data consists of the age- and sex specific probability of switching from one risk factor category to another (say, from abstainer to light drinker). At least one file must be present to run a DYNAMO simulation.

The directory *DurationDistribution* only exists when the risk factor is a compounding risk factor (in contrast to a categorical or continuous). This directory contains a file with data about the duration of membership in a risk factor class (e.g. for former smoking the % that stopped 1, 2, ...20 year ago). This is used for risk factors where the relative risk is influenced by the duration of membership, such as former smokers, where the relative

risk declines over time. This file has a standard name (durationPrevalence.xml) that cannot be changed.

### Directory Diseases

The directory *Diseases* contains all the data needed to specify a disease that can be included in a simulation. Expanding the view shows a number of sub-directories, in the case of the working directory “Tutorial\_Data” those are the already included diseases such as “Breast\_Cancer” or “COPD”. Expand the view of a disease specific directory by clicking on the + sign right next to “Breast\_Cancer”. This reveals a number of sub-directories that are the same for all diseases:

- *Daly\_Weights*
- *Excess\_Mortalities*
- *Incidences*
- *Prevalences*
- *Relative\_Risks\_From\_Diseases*
- *Relative\_Risks\_From\_Risk\_Factor*

These sub-directories contain files specifying the different aspects of the chronic diseases that can be simulated by DYNAMO. To include a disease in a simulation run, each of the disease sub-directories needs to contain at least one file with the necessary data (with the exception of the directory *Relative\_Risks\_From\_Diseases* where adding data is optional as it is only applicable for some diseases). More files can be added; allowing running simulations with alternative specifications for a given disease. But in a

single simulation run only one file of each sub-directory can be selected for an included disease.

The directory *Incidences* contains at least one file with the number of cases per person-years for the disease in question (by age and sex).

The directory *Prevalence* contains at least one file with data on the age- and sex specific prevalence of the population in percent (thus a number between 0 and 100).

The directory *Daly\_Weights* contains at least one file with either the DALY weight of the respective disease in percent by age and sex, or the percentage of disability caused by the disease. Even in the case where this information is not known or not intended to be simulated the directory still needs to contain a file. We advise using a file specifying a DALY weight of zero for all ages, i.e. no disability induced by this particular disease).

The directory *Relative\_Risks\_From\_Diseases* may contain files specifying the relative risk of contracting the disease when having another disease (by age and sex). This other disease has to be already specified. A good example is the case of diabetes: having diabetes increases the risk of contracting a heart disease; hence the relative risk of contracting IHD when having diabetes can be specified.

The *Excess\_Mortalities* directory contains a file that specifies the additional mortality when having the disease, i.e. the difference for a person with the disease in question compared with a person without the disease. This is sometimes also called case fatality rate. This can be specified either as a rate or as median survival time. In addition, for a disease either the percentage of the “Acute Fatal” or the percentage of “Cured Fraction” can be specified. This specification, when desired, changes the behavior of the disease from a pure chronic disease to

- 
- either a disease where some people die instantly when contracting the disease (“Acutely Fatal”), e.g. stroke or IHD where some people die instantly
  - or a disease where a share of people is being cured (“Cured Fraction”), e.g. some cancers.

**Only one of these options can be chosen**, and files containing non-zeros for both options will prompt the program to ask you to choose one of them, after which the other will be made zero.

The directory *Relative\_Risks\_From\_Risk\_Factor* contains the files that hold the information of how the underlying risk factor affects the risk of contracting the given disease. The files differ slightly by the type of risk factor. For example, for the risk factor alcohol which has 5 categories, the file contains for each category the relative risk of obtaining the disease in this directory (by age and sex). In the case of a duration dependent risk factor (compound risk factor), the files differs slightly as one needs to enter more information for the category in which the relative risk depends on the duration in this class. In the case of smoking, for example, the risk of contracting a disease usually decreases for a former smoker over time. In this category (the duration category, in the example former smokers) one needs to specify the relative risk at the moment of entering the category (RRbegin), the relative risk after being in the category for a very long time (RRend) and a coefficient that represents how fast the RR is changing from RRbegin towards RREnd (alpha). This alpha is defined so that the relative risk is halfway between RRbegin and RREnd after  $\ln(2)/\alpha$  years.

In case of a continuous risk factor, only a single relative risk is needed for each age and sex combination: this relative risk is the relative risk of increasing the risk factor with 1 unit. So for instance for BMI, it is the relative risk when increasing BMI with 1  $\text{kg.m}^{-2}$ .

---

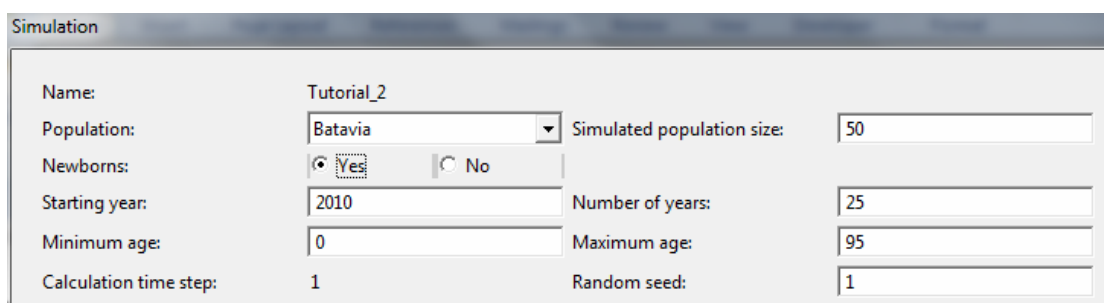
## **Configuring Simulations**

At the core of DYNAMO is the simulation of one (or more) scenarios where changes in the risk factor prevalence or the transition between risk factor states (or both simultaneously) are compared with a reference scenario. This allows quantifying what changes of population health materialize over time when a risk factor is altered. In this section we will talk in more detail about the simulation screen, outlining all possible options. The issue of choosing scenarios is addressed in more detail on page 58.

Expand the directory “*Simulations*” by clicking on the + sign and right click on the directory “*Tutorial\_2*”. In the context menu choose “*Configure and run simulation*”. A screen like in Figure 5 appears. This is the simulation configuration screen and a number of choices are required before running a simulation.

In the bottom half, four different tabs are visible:

- *Scenarios*
- *Risk Factor*
- *Diseases*
- *Relative Risks*



The screenshot shows a window titled "Simulation" with the following configuration options:

Name:	Tutorial_2		
Population:	Batavia	Simulated population size:	50
Newborns:	<input checked="" type="radio"/> Yes <input type="radio"/> No		
Starting year:	2010	Number of years:	25
Minimum age:	0	Maximum age:	95
Calculation time step:	1	Random seed:	1

**Figure 5: Top half of the simulation configuration screen**

On the top half, decisions about the population and some technical aspects of the simulation can be specified. These are:

Name: Shows the name of the simulation run which is taken from the name of the directory and cannot be changed in the simulation screen views. (*It should read "Tutorial\_2"*)

Simulated Population: This is a pull-down menu where the population to be simulated can be selected. When only one population is defined in the directory *Population*, this population appears as the default. (*In Tutorial\_2 it should read "Batavia"*)

Population size: For the risk factor behavior, DYNAMO uses a micro simulation. A number of individuals are simulated and are a representative sample of the whole population. The number entered here is the number simulated for each age/gender combination. A large number usually yields a lower stochastic variation in the risk factor histories. The upper practical limit depends on a number of factors (such as computer memory and complexity of scenario). (*Enter here a 50 for the purpose of the tutorial. This implies that 50 times 95 ((the number of age classes) times 2 (males and females) = approx. 10,000 persons are simulated.)*)

For scenarios with zero-transition rates and categorical risk factors, no stochastic variation is present, so this number can be kept small.

Newborns: Whether or not newborns are included in the simulation. This is only possible when the minimum age is set to zero (as otherwise one would simulate a population with a strange gap between newborns entering the simulation, and the starting age of the simulated population. (*Include newborns by clicking on "yes"*)

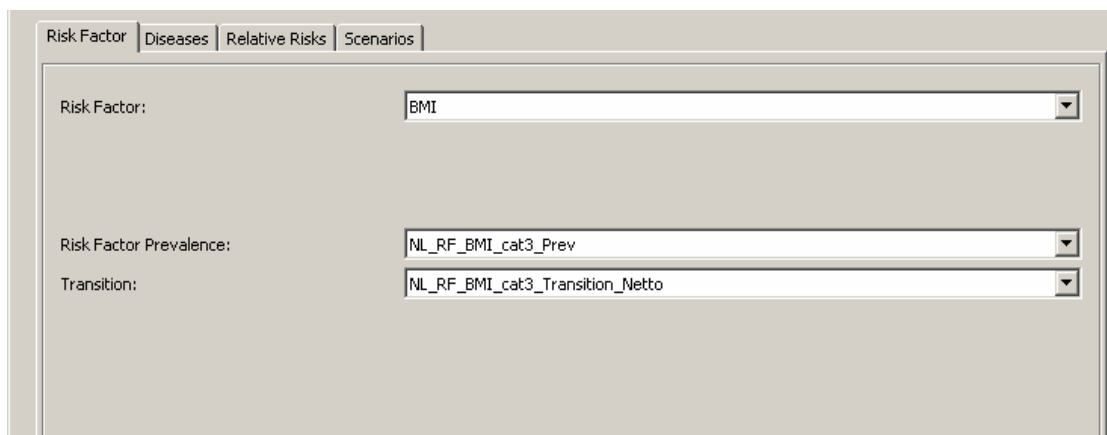
Starting year: The year the simulation starts from. The current calendar year is the default for a new simulation. When newborns are used, the data should provide newborns for all years after this starting year. *(It should read the current year).*

Number of years: The number of years DYNAMO projects the scenarios in the future. *(Use 25 for this tutorial)*

Minimum age: Minimum age of the population you want to simulate. *(Choose “0”)*

Maximum age: Maximum age of the population you want to simulate. The maximum value in the initial population of the DYNAMO model is 95 although the model simulates internally to higher ages. *(Choose “95”)*

Random seed: The value used to initialize the random number generator used during the simulation. Any number will do, but when running two different simulations with exactly the same data, choosing the same random number ensures identical results. Otherwise, random variation alters the simulation outcomes slightly. *(Use “1”).*



The image shows a screenshot of the 'Risk Factor' tab in a simulation configuration interface. The interface has a tabbed header with 'Risk Factor', 'Diseases', 'Relative Risks', and 'Scenarios'. The 'Risk Factor' tab is active. Below the header, there are three rows of configuration options, each with a label and a dropdown menu:

- Risk Factor:** The dropdown menu is set to 'BMI'.
- Risk Factor Prevalence:** The dropdown menu is set to 'NL\_RF\_BMI\_cat3\_Prev'.
- Transition:** The dropdown menu is set to 'NL\_RF\_BMI\_cat3\_Transition\_Netto'.

**Figure 6: Risk Factor tab of simulation configuration screen (detail)**

### Risk Factor Tab

Click on the Risk Factor tab. This tab consists of three pull-down menus. The first on the top, “Risk Factor”, allows choosing the directory that contains the desired risk factor. The other two menus allow choosing the file with data on the risk factor prevalence and the file with the transition probabilities between risk factor states. If only one file exist for the chosen risk factor, this file is the default.

The risk factor prevalence chosen here represents the risk factor exposure in the baseline year in the business-as-usual (reference) scenario.

As DYNAMO is a dynamic tool, in addition the user should specify whether, and if so, how this exposure will change in the future. In other words, what transitions between risk factor categories are persons expected to make in the future. DYNAMO assumes that these transitions remain valid over the entire projection period (25 years in this tutorial).

In DYNAMO there are three options to specify the future transitions:

1. User-specified transitions: the user provides data on transitions between the risk factors categories (e.g. smoking start probabilities and quit probabilities rates, or on trend for continuous exposure (e.g. increase in mean BMI of 0.02 for each age year).
2. Nett-transitions: The user assumes that the age-specific prevalence of exposure in the population will remain the same (thus prevalence by age and sex does not change). This approach is very similar to the use of period life expectancy, where for a newborn the currently observed age-specific mortality pattern is assumed to remain valid. This approach ignores any cohort effects. This approach is named

“net transitions” in DYNAMO-HIA, because DYNAMO derives the minimum transitions that are needed to keep the age-specific prevalence unchanged in the future. DYNAMO can only calculate nett-transitions for the reference scenario. In the case nett transitions are also specified for alternative scenarios, DYNAMO uses the nett transition rates calculated from the prevalence of the reference scenario also for the alternative scenario. In other words, it assumes that the future dynamics of the risk factor remain the same. In order to use nett-transitions based on the prevalence of an alternative scenario, a trick can be used, which is described in the box on page 55.

3. Zero-transitions: Persons are assumed keep the exposure in the baseline year throughout their life until they die. Hence, persons having a normal weight at baseline keep that during the entire period or until they die. This approach is named “zero transitions” in DYNAMO, as there are no transition between risk factor categories or changes in mean BMI in the future when persons age.

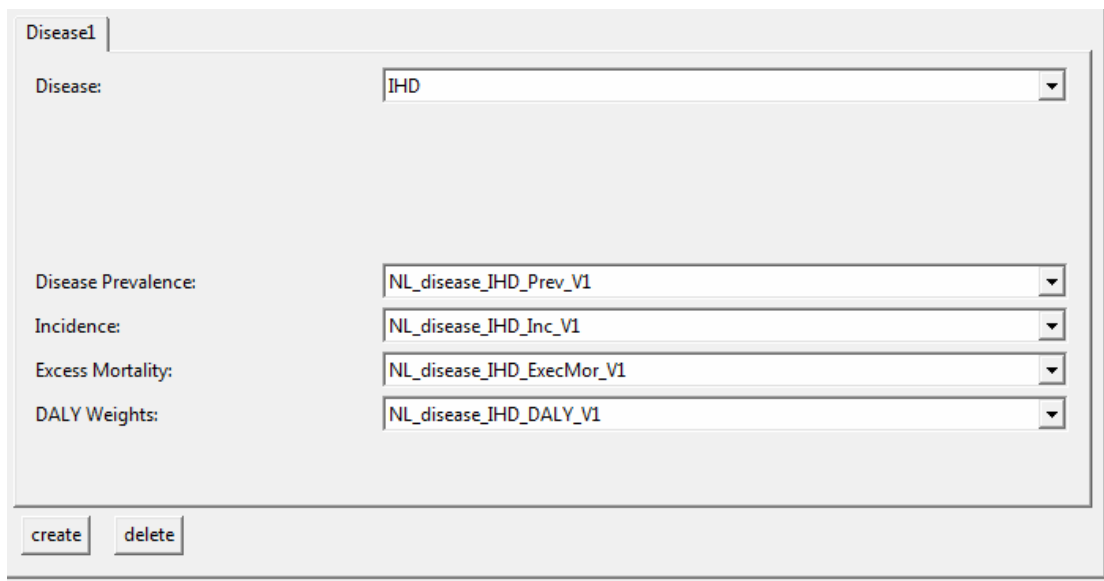
*(Choose “BMI” as the risk factor. For the risk factor prevalence choose the file “NL\_RF\_BMI\_cat3\_Prev”. For transitions choose the file “NL\_RF\_BMI\_cat3\_Transitino\_Netto”.)*

### Diseases Tab

Click on the *Diseases* Tab. This tab allows choosing which diseases to include and further specifies them, when desired. Click on the button “*create*” and a view like in Figure 7 appears. At the top is a pull-down menu, showing the disease that can be included in the simulation. (The names in this pull-down menu are the directory names

in the “Disease” directory of the “Reference\_Data”). For every disease, four files can be specified. The prevalence of the disease (“Disease Prevalence”), the incidence of the disease (“Incidence”), the excess mortality (“Excess Mortality”), and the DALY weights (“DALY Weights”). The pull-down menus shows all the files contained in the respective sub-directory of the chosen disease. This allows, when desired to try out alternative specifications of the same disease in different simulations runs. If only one file exist in each sub-directory, this file is the default.

*(Click nine times on the “create” button. In our tutorial data set, each of the nine included diseases has exactly one file for prevalence, incidence, mortality, and DALY weights. Hence, the default choices are the right files for the simulation run in Tutorial\_2.)*



The screenshot shows a window titled "Disease1" with a tabbed interface. The "Disease:" dropdown menu is set to "IHD". Below it, four dropdown menus are listed for "Disease Prevalence:", "Incidence:", "Excess Mortality:", and "DALY Weights:", each with a default file path: "NL\_disease\_IHD\_Prev\_V1", "NL\_disease\_IHD\_Inc\_V1", "NL\_disease\_IHD\_ExecMor\_V1", and "NL\_disease\_IHD\_DALY\_V1" respectively. At the bottom of the window are two buttons: "create" and "delete".

**Figure 7: Specifying a disease in the simulation configuration screen (detail).**

### Relative Risk Tab

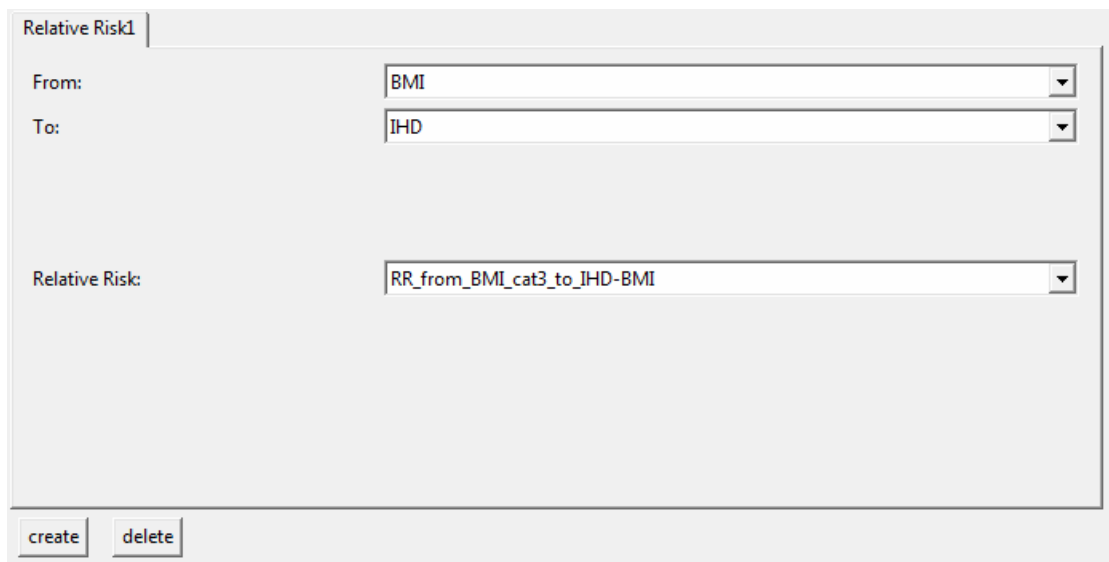
Select the Relative Risk tab. This tab allows determining which relative risks to include. Click on the button “create” and a view like in Figure 8 appears. The view consists of three pull-down menus. The first on the top, “From”, allows choosing the risk factor.

---

This pull-down menu can have several options. The first option is always the risk factor chosen in the “Risk Factor” Tab. When in the reference data, one (or more) relative risk from a disease has been included, then these diseases can be chosen as risk factors as well. This means several relative risks can be specified: one from the risk factor to every included disease, from the risk factor to death, and from one (or more) included disease to one (or more) included disease. The disease is chosen in the pull-down menu “To”. When the risk factor and the disease (or death) are specified, then the pull-down menu “Relative Risk” allows choosing a file that contains the actual data. When only one file has been specified for a given “Risk-Factor-to-Disease-Relationship”, this file is the default selection.

In this tab it is possible to select relative risks that refer to diseases that are not (yet) selected on the disease tab. If a simulation is run with a relative risk for a disease that is not included on the disease tab, this relative risk is ignored in the simulation.

*(Press the “create” button 12 times. This specifies the relative risk from BMI to the nine included diseases, from BMI to death, and the relative risks from diabetes to stroke and IHD, respectively. As we have only one relative risk file for each of these “From”-“To”-combinations the default choices are the right files for the simulation to be run in Tutorial\_2.)*



Relative Risk

From: BMI

To: IHD

Relative Risk: RR\_from\_BMI\_cat3\_to\_IHD-BMI

create delete

**Figure 8: Specifying a relative risk in the simulation configuration screen (detail).**

### Scenario Tab

Click on the Scenario tab: This tab allows configuring the (alternative) scenarios which are being simulated. In effect, by having specified the risk factor (prevalence and transition), the included diseases, and the relative risks, the reference scenario is fully specified. In the Scenario Tab on or more alternative scenarios can be specified by making several, alternative choices. Click on the button “create” and view like in Figure 9 appears. The main choices are in the pull down menu “Transitions” and “Risk Factor Prevalence”, where the alternative scenarios can be specified. The pull-down menus allow choosing from the files which are in the directory of the chosen risk factor. See the description under “risk factor tab” for a general description of these choices.

To specify what is expected in risk factor exposure due to the policy or intervention (=intervention scenario), the user can change the following as compared to the reference scenario:

1. Change the baseline exposure

2. Change the future transitions
3. Change both baseline exposure and transition.

If the user wants to change only one (1 or 2), he has to choose the other input equal as that in the reference scenario (= as selected on the risk factor tab).

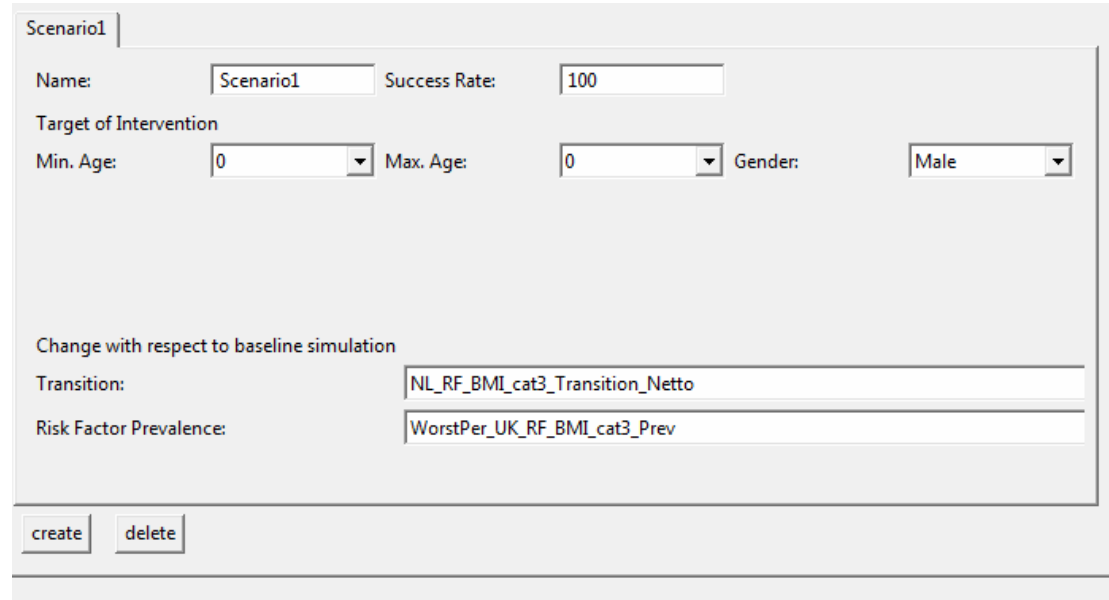
It is important to realize that if, for instance, the user only changes baseline exposure and keeps the transition rates unchanged, due to dynamic behavior, in the long run other prevalence rates are realized. For instance, they may return to the baseline prevalence rates (of the reference scenario) if the latter reflect the steady-state situation of the transition rates. An exception is when nett transitions are used: With nett transitions do not exhibit this type of dynamic behaviour (see {Kasstele J, #3187}). Changing only the transition rates assumes that the intervention changes future behavior. DYNAMO assumes this new behavior to remain during the entire simulation period.

In a scenario you must chose either a different transition dataset or a different risk factor prevalence dataset from that chosen on the risk factor tab. Therefore, if the risk factor prevalence is the same as that on the risk factor tab, the transition dataset from the risk factor tab will not be visible, and visa versa. It can occur that the list of choices is not refreshed correctly after changing the other choice. In that case the dataset does not reappear in the list after changing the other choice. Clicking on the risk factor tab and back to the scenario tab will solve this.

Furthermore, success rate and target of intervention can be specified. The success rate is between 0 and 100% and the target of the intervention can be specified for a desired age range (from 0 to 95) and gender (male, female, or both). This setting

determines to which extent the alternative transitions and risk factor prevalence affect the simulation. This setting, however, can be changed in the output screen, i.e. after the simulation has been run, see the section on Change scenario settings.

(



The screenshot shows a configuration window for a scenario named 'Scenario1'. It includes the following fields and controls:

- Name:** Scenario1
- Success Rate:** 100
- Target of Intervention:**
  - Min. Age:** 0
  - Max. Age:** 0
  - Gender:** Male
- Change with respect to baseline simulation:**
  - Transition:** NL\_RF\_BMI\_cat3\_Transition\_Netto
  - Risk Factor Prevalence:** WorstPer\_UK\_RF\_BMI\_cat3\_Prev
- Buttons:** create, delete

**Figure 9: Specifying a scenario in the simulation configuration screen (detail).**

### Starting the simulation

By pressing the “Save and Run” button, the simulation starts running. Depending on the complexity of the configuration (e.g. chosen population size, number of diseases etc.) the running time may vary. The program does not respond when running but shows the output screen as soon as it is finished. During simulation progress bars appear that indicate the progress. Clicking on a screen during simulation will stop the updating of the progress bar. The simulation, however, will continue, and results will appear in due time.

### ***Output Screen in more Detail***

After running the simulation, an output screen appears. This screen gives an overview (graphically and numerically) about the simulated scenarios. In addition, this screen allows exporting the results as raw data for further analysis in another software (such as MS Excel).

In the directory “Simulations” expand the sub-directory “Tutorial\_3” by clicking on the + sign. “Tutorial\_3” already contains a run simulation that created three sub-directories. The file “configuration” contains all the detailed specification of the simulation run. Click on the + sign next to the directory “results”. This directory holds as content the file “resultsObject.obj”, which stores and allows accessing the simulation output without running a simulation again. Right click on the “resultsObject.obj” and choose “View results” from the context menu (see Figure 10). After a few moments the output screen appears. The output screen has a number of different views that can be accessed via tabs. Those tabs are:

- Population Pyramid
- Disease plots
- Riskfactor plots
- Life expectancy plots
- Mortality/survival plot
- Write output
- Change scenario settings

All plots shown in the output screen share some common technical features: by clicking on a point on the plot and moving the mouse to the right, an area can be selected to be zoomed in. This step can be repeated as desired. By clicking on a graph and moving the mouse to the left, the standard zoom is restored. Right clicking on a

graph opens a context menu with a number of technical options. Most notably, the option “Save as...” allows saving the graph as a separate file for later inclusion in MS Word. But other options also include changing the labels, font type, letter size and so on.

The simulation run in “Tutorial\_3” is similar to “Tutorial\_1” and “Tutorial\_2”. The population is taken from Batavia (a fictitious country very similar to the Netherlands), the risk factor is BMI in three categories (normal, overweight, obese), and the simulation includes nine diseases. The “reference scenario” has the Batavian risk factor prevalence and transition probabilities that keep this risk factor prevalence constant. The intervention scenario, called “UK\_Prevalence”, changes the BMI risk factor prevalence of Batavia to the one of the UK - which has a higher share of overweight and obese – and transition probabilities that keep the UK prevalence constant.

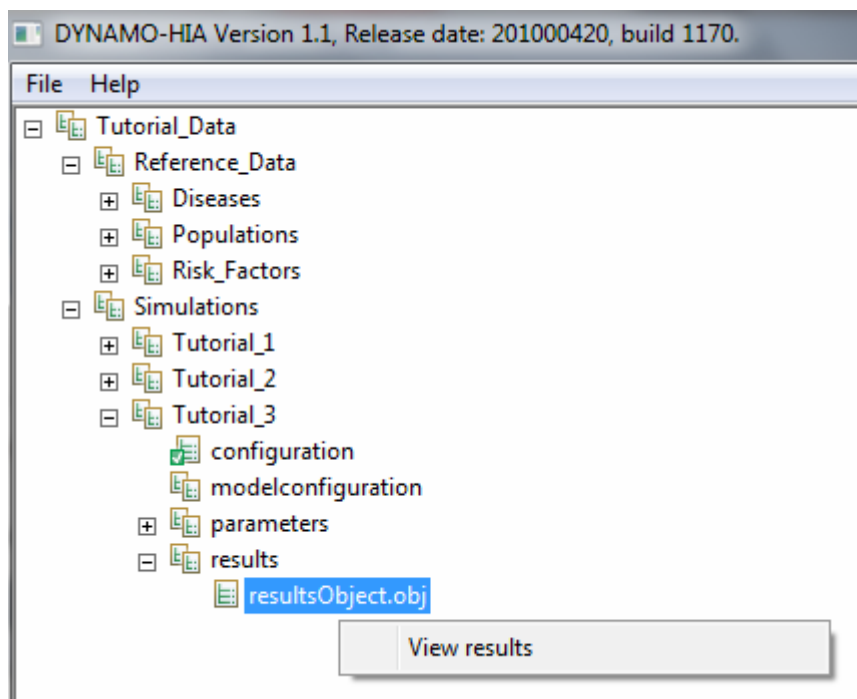


Figure 10: View of the “resultsObject.obj” in the user interface (detail)

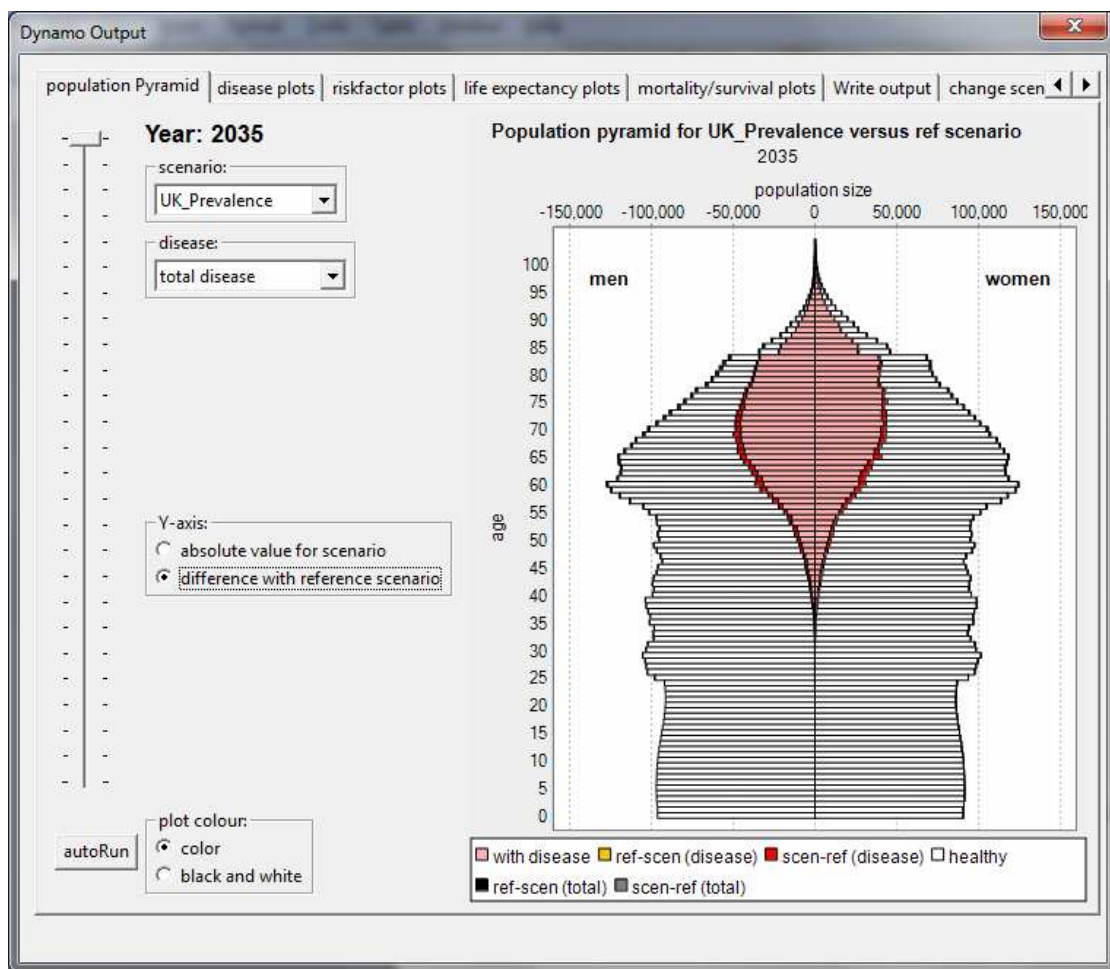
## Population Pyramid

---

The population pyramid screen gives a graphical overview of the total population, coloring the share of the population that is diseased, shows the development over time, and allows comparison between scenarios. This screen has several options that allow altering the plot and analyze different aspect of the data.

Click on the “*autoRun*” button in the bottom left corner. This starts an animation that shows the development of population and population health for the projection time in one year increments. A particular year can be chosen by moving the slider or clicking on the appropriate tick at the left hand ruler.

At the top of the screen, the pull-down menu (“scenario”) allows choosing the scenario for which the graph is plotted. The pull-down menu below (“diseases”) allows choosing which of the simulated diseases are shown. With the further options all persons that are diseased (“total diseases”) or have a disability (“disability”) can be shown. The graph is color coded: the light red area shows all persons that have the selected diseases and the white area are the people that are healthy. Now chose scenario1 under “scenario”, and then click under “Y-axis” on “difference with reference scenario”. Now more colours appear. The light red area now shows the part of the population that has a given disease in both scenarios, the “reference scenario” and “UK\_Prevalence”. The dark red area shows the part of the population that has the disease in “UK\_Prevalence” but not in the “reference scenario” (a yellow area would show the share of the population that has the disease in “reference scenario” but not in “UK\_Prevalence”). The black area at the outer margin of the population pyramid shows the number of people that are alive in the “reference scenario” but not in “UK\_Prevalence” (a grey area would show the share of the population that is alive in the “UK\_Prevalence” but not in the “reference scenario”).



**Figure 11: Population Pyramid Screen**

## Disease plots

The tab *disease plots* graphs the disease prevalence. A number of options can be changed and combined to graph and analyze different aspects of the data. However, not all combinations are possible. In those cases the affected menus are made inaccessible (by graying them out).

The menu “X-Axis” has two radio buttons: either “Year” or “Age”. When “Year” is selected, the development of disease prevalence over time is shown. When switching to “Age”, then the age specific prevalence is shown. In this case, the pull down menu “year” becomes available and the desired simulation year can be chosen for which the age-specific prevalence is shown.

The menu “Y-axis” exists twice. The top “Y-axis” menu has two radio buttons: either “rate” or “number of cases”. When “rate” is chosen, the prevalence is given in percentage of the total population. When “number of cases” is chosen the absolute number of cases is plotted. Right below the “Y-axis” menu has two radio buttons as well. Here the choices are “absolute value for scenario” or “difference with reference scenario”. When “difference with reference scenario” is chosen, the plot calculates and plots the difference between the selected intervention scenario (in the case of “Tutorial\_3” this is “UK\_Prevalence”) and the reference scenario. This difference is either the difference in percentage points (when “rate” is chosen) or absolute numbers (when “number of cases” is chosen).

The menu “separate curves” has three radio buttons: “by riskclass”, “by scenario”, or “by gender”. When selecting “by scenario”, the curves compares the prevalence of a given disease for the included scenarios. When selecting “by riskclass” the curves are drawn for each risk factor class of the simulated risk factor for one scenario (The desired scenario can be chosen from the pull down menu “scenario”). For interpretation of these graphs also see page 75. The choice “by gender” shows the prevalence for males, females and both for one scenario (The desired scenario can be chosen from the pull down menu “scenario”).

The pull down menu “diseases” allows choosing the disease to be plotted.

The pull down menu “gender” allows choosing for which gender (male, female, or both), when applicable.

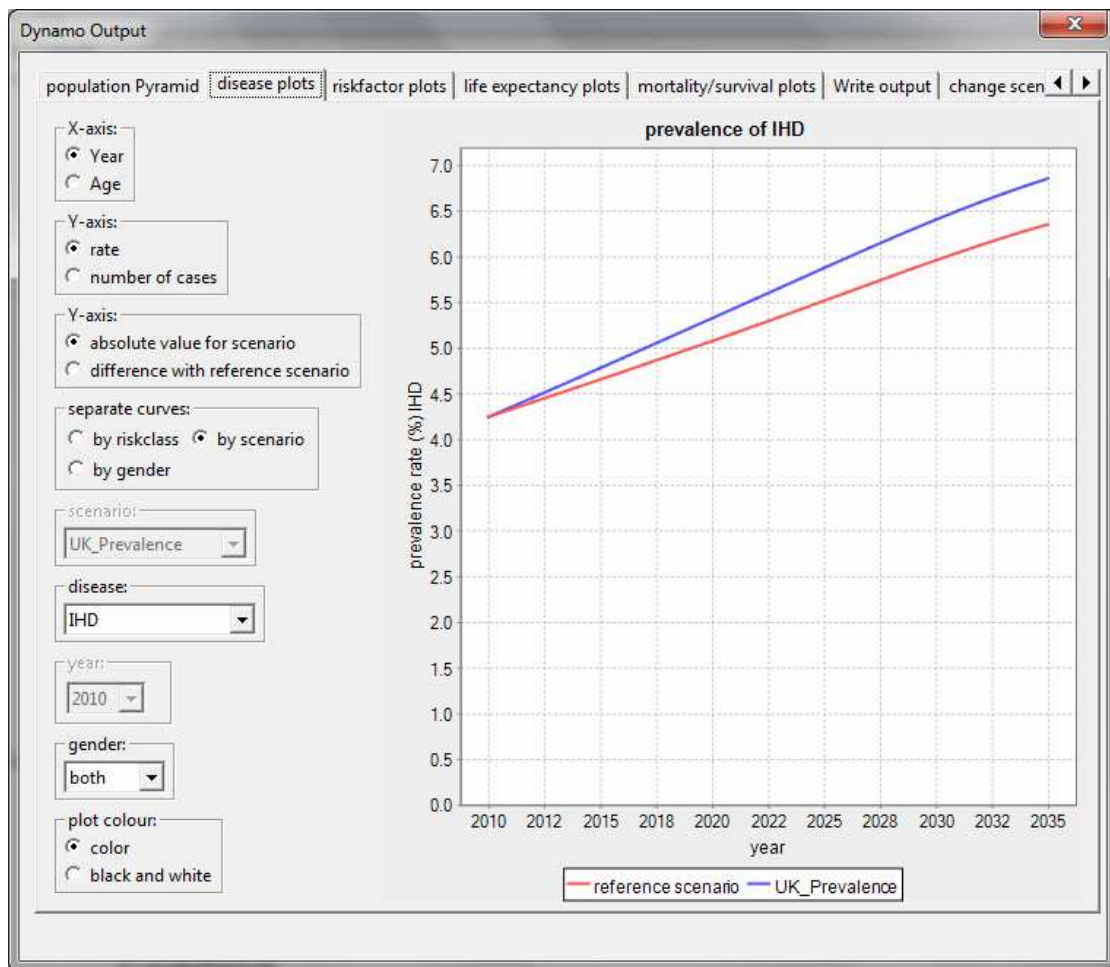


Figure 12: Disease plot screen

## Risk factor plots

The tab “risk factor plots” graphs and compares the risk factor prevalence for all scenarios by risk factor class. A number of options can be changed and combined to graph and analyze different aspects of the data. However, not all combinations are possible. In those cases the affected menus are made in-accessible (by graying them out).

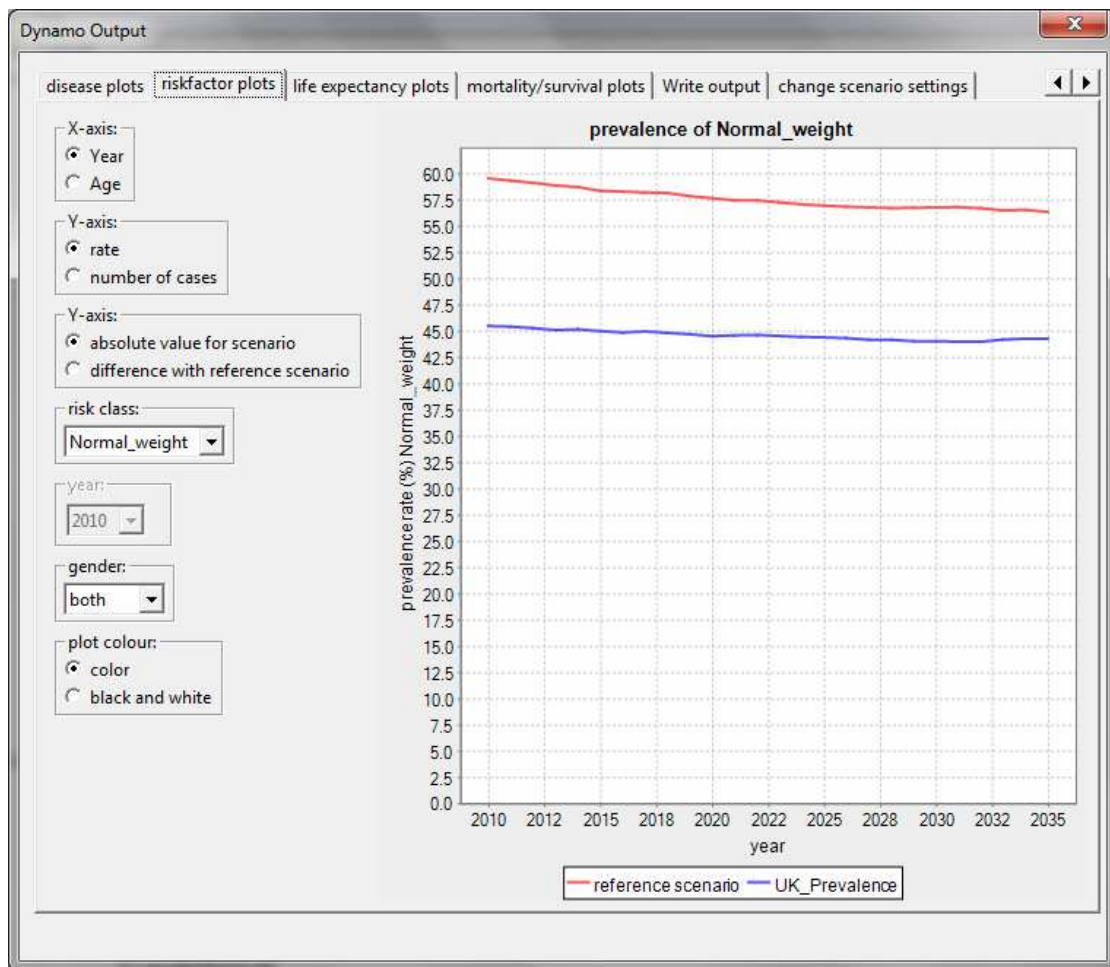
The menu “X-Axis” has two radio buttons: either “Year” or “Age”. When “Year” is selected, the development of risk factor prevalence over time is shown. When switching to “Age”, then the age specific prevalence is shown. In this case, the pull

down menu “year” becomes available and the desired simulation year can be chosen for which the age- specific prevalence should be plotted.

The menu “Y-axis” exists twice. The top “Y-axis” menu has two radio buttons: either “rate” or “number of cases”. When “rate” is chosen, the prevalence is given in percentage of the total population. When “number of cases” is chosen the absolute number of cases is plotted. The lower “Y-axis” menu has two radio buttons as well: Here the choices are “absolute value for scenario” or “difference with reference scenario”. When “difference with reference scenario” is chosen, the plot calculates and plots the difference between the selected intervention scenario (in the case of “Tutorial\_3” this is “UK\_Prevalence”) and the reference scenario. This difference is either the difference in percentage points (when “rate” is chosen) or absolute numbers (when “number of cases” is chosen).

The pull-down menu “risk class” allows choosing the desired risk factor class to be plotted. (In the case of “Tutorial\_3” those are: Normal, Overweight, Obese).

The pull-down menu “gender” allows plotting the risk factor prevalence for one gender only (“men” or “women”) or both combined (“both”).



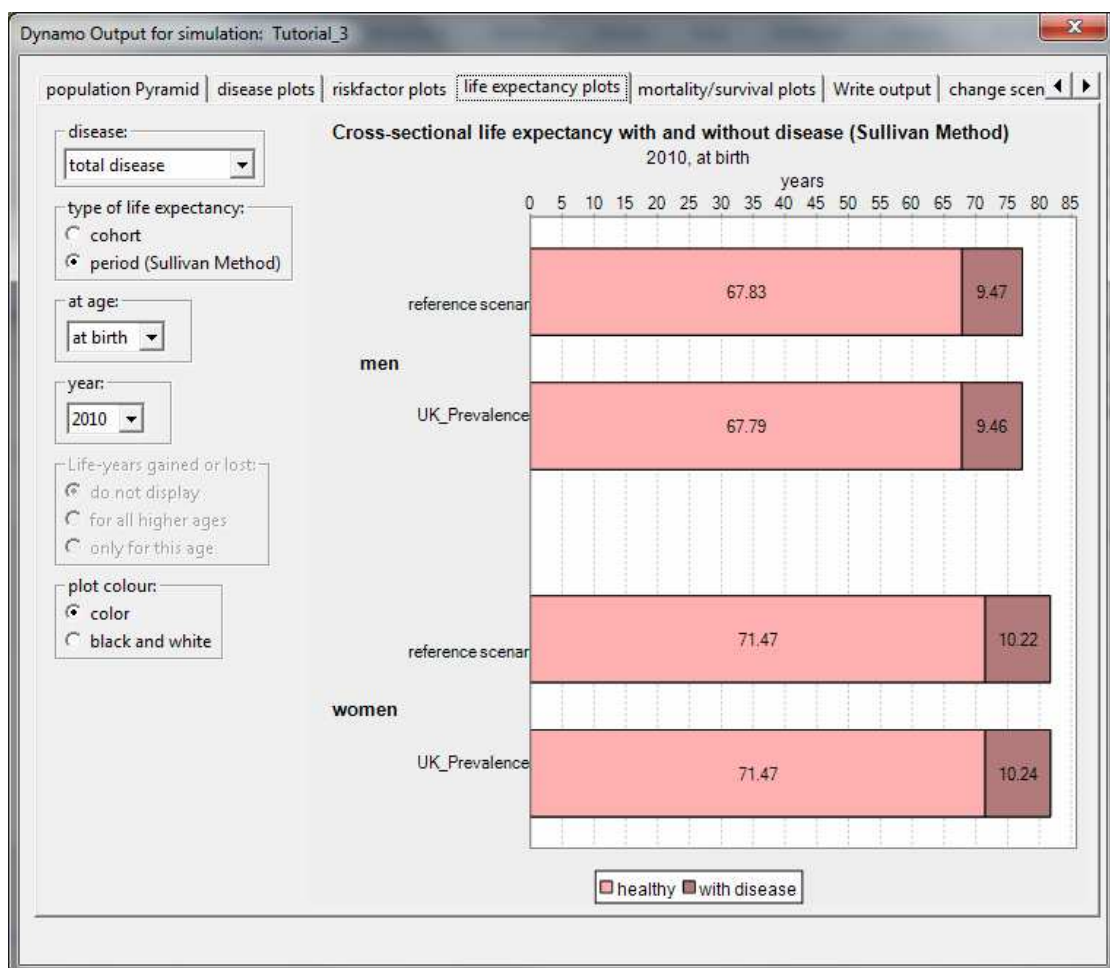
**Figure 13: Riskfactor plot screen**

## Life expectancy plots

The “Life expectancy plots” tab graphs and compares the life expectancy between scenarios by gender. Several choices can be made to alter the plot. The pull-down menu “diseases” allows choosing one of the simulated diseases, “total disease”, or “none”. When choosing the option “none”, the bars reflect total life expectancy. When choosing a particular disease, the bars are split: the lighter color represents the expected life years without disease and darker colors represent the expected life years with the chosen disease.

The menu “type of life expectancy” has two radio buttons: “cohort” and “period (Sullivan Method)”. The cohort life expectancy calculates the life expectancy of a cohort

that would be followed through time. The starting is the starting year of the simulation and the figure reflects the experience of a cohort observed until every member dies. The pull-down menu “age” allows choosing for which cohort this is done. The option “at age: at birth” shows the life expectancy for a cohort born in the starting year of the simulation and followed until everybody dies. The option “at age: 50” would follow the cohort that is 50 years old at the starting year of the simulation until everybody dies. The period life expectancy calculates the life expectancy cross-sectional using the mortality (and disease) numbers of a given year. This can be done for any simulation year by choosing from the pull-down menu “year”. When changing the age, then the plot shows the further life expectancy.



The option “life-years gained or lost” (only available in cohort mode) gives the option to calculate (weighted) life years gained or lost compared to the reference scenario. This can be the years gained or lost by the cohort that has the selected age at the start of simulation and is followed until all have died (“only for this age”), or it can be the sum of all years gained or lost by the total population at the start of simulation that has at least this age and is followed also until all have died.

### **Mortality/survival plots**

The tab “Mortality/survival plots” graphs and compares either the mortality, the population numbers or survival rates for all scenarios. A number of options can be changed and combined to graph and analyze different aspects of the data. However, not all combinations are possible. In those cases the affected menus are made in-accessible (by graying them out).

The menu “X-Axis” has two radio buttons: either “Year” or “Age”. When “Year” is selected, the development of the risk factor prevalence over time is shown. When switching to “Age”, then the age specific prevalence is shown. In this case, the pull down menu “year” becomes available and the desired simulation year can be chosen for which the age- specific prevalence is shown.

The menu “Y-axis” exists twice. The top “Y-axis” menu has two radio buttons: either “rate” or “number of cases”. When “rate” is chosen, the rate is given in percentage of the total population. When “number of cases” is chosen the absolute number of cases is plotted. The lower “Y-axis” menu has two radio buttons as well: Here the choices are “absolute value for scenario” or “difference with reference scenario”. When “difference

with reference scenario” is chosen, the plot calculates and plots the difference between the selected intervention scenario (in the case of “Tutorial\_3” this is “UK\_Prevalence”) and the reference scenario. This difference is either the difference in percentage points (when “rate” is chosen) or absolute numbers (when “number of cases” is chosen).

The menu “outcome” has three radio buttons: “mortality”, “population numbers” or “survival”. When choosing “mortality” the mortality rate is shown, either in percentage when “rate” is selected or in absolute number of deaths when “number of cases” is selected. When “population numbers” is selected, the number of persons in the population is shown (no rate is possible). When “survival” is selected, the development of the initial population over time is shown, either in percentage when “rate” is selected (with the population of the starting year as base) or in absolute number of deaths when “number of cases” is selected.

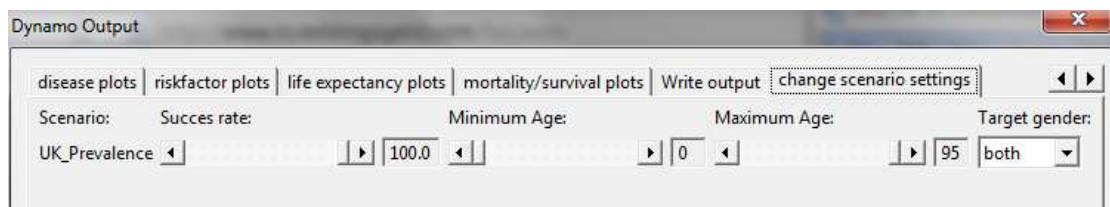
## **Write output**

Click on the tab “Write output”. On this screen three different decisions with two options each can be made. First, you can choose to export the data “per year of simulation” or “by cohort”. The second option allows choosing to have the data “separate for men or women” or “total population”. The third option determines whether diseases are shown separately (“per disease”) or diseases clusters (“per combination of diseases”) in the exported output. When clicking on “write data”, you can choose a file name and file location where the raw output is saved. The raw output is written in a special format that can be opened easily using MS Excel. To do so, right click on the file in window Explore, and chose “open with” and then chose MS Excel.

## **Change scenario settings**

The “change scenario settings” tab allows adjusting the intervention scenarios even after the simulation has been run. Four different choices can be made for each of the interventions scenarios. The success rate of the intervention can be adjusted between 0 and 100 percent. When the success rate is 0 percent, the output shown for the intervention scenario is exactly the same as the reference scenario, with 50 percent success rate the intervention scenario is average between the intervention scenario setting and the reference scenario setting. Furthermore, the minimum and maximum age for which the intervention has been successful can be chosen and if both or only one gender is affected.

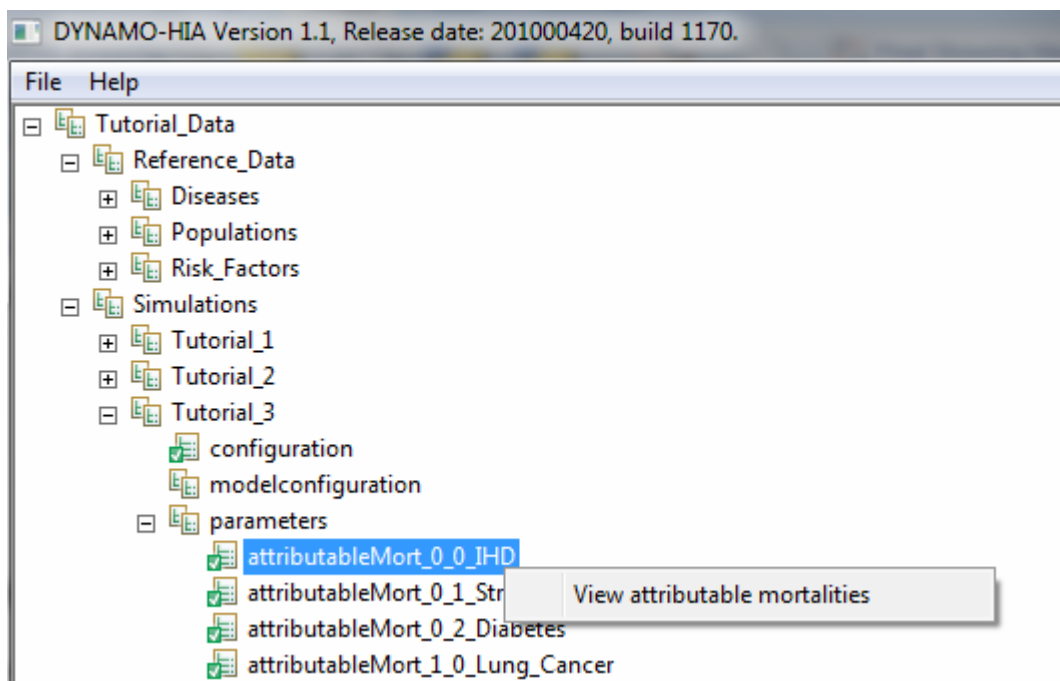
In the example of “Tutorial\_3”, a maximum age of 50 would mean that the in the intervention scenario (“UK\_Prevalence”) only the people of 50 and under would be switched from the Dutch BMI-prevalence to the UK BMI-prevalence. Note that the sliders and buttons on this tab are only present if one or more alternative scenarios are included in the simulation. The tab is empty when only a reference scenario is run.



**Figure 14: Change scenario settings Tab in output screen (detail)**

## ***Inspecting the model parameters***

The DYNAMO model uses the input data to calculate parameters (like disease incidences in those with a relative risk of 1 (baseline incidence) or the mortality that can be attributed to a particular disease). When running the model, these parameters are stored in a directory “parameters” above the “results” directory. After running the model, the value of these parameters can be inspected, by opening the directory and right clicking on the name of the parameter file one wants to inspect.



**Figure 15: Selecting a parameter file for inspection (detail)**

In some situations, the other mortality that will be used in the model could not be made exactly equal to the difference of the total mortality and disease-related mortality as given by the user to the model. In this situation a file “otherMortData.csv” is written to the “parameters” directory. This file can not be seen in this view, but can be opened with

---

for instance excel. After opening this file with excel, use data → filter → autofilter to activate the autofilter. Then, after choosing an age and a sex group in the filter box, and selecting columns C to G, the chart wizard can be used (option XY(scatter)) to plot the data for a particular age and sex combination (figure 16). Data included in this file are:

- Risk factor: depending on the type of risk factor used, this is category number of the risk category (categorical risk factor), the value of the continuous risk factor (continuous risk factor), or the duration (compound risk-factor). For the compound risk factor the value zero is assigned to all non-duration categories
- otherMort: the difference between the total mortality as specified by the user, and the disease related mortality
- otherMortfitted: other cause mortality used by the DYNAMO-model
- diseaseMort: disease related mortality (from the specified by the user in the excess mortality file) used by the DYNAMO model
- totalMort: total mortality as specified by the user

When the effect of other mortality counter-acts the effect of disease-related mortality, the effects on overall mortality are unpredictable. If this happens for more than a few age-groups, we advice not to include a relative risk on mortality in the model. For continuous and compound risk factors see also pages 78 and 79 respectively for further interpretation.

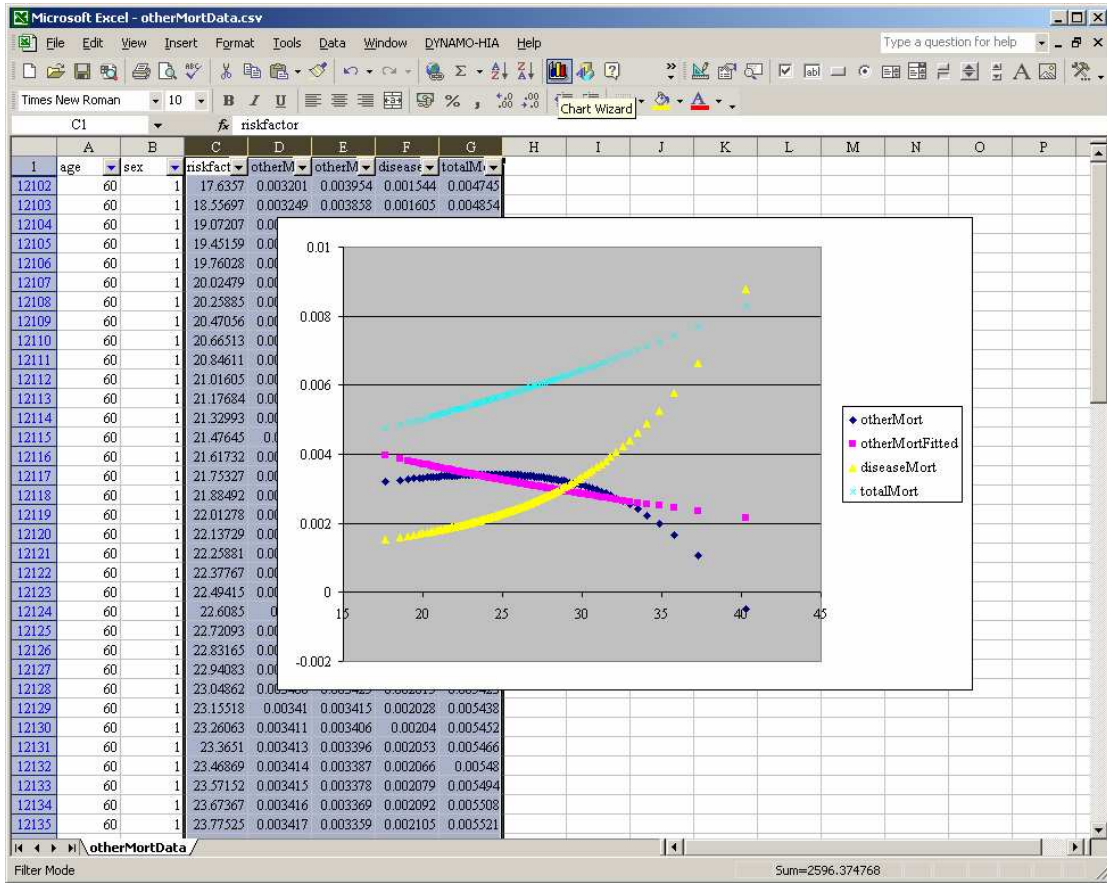


Figure 16: Inspecting the other cause mortality as used by the model in Excel

## Entering Data

*This chapter gives detailed description on how to enter reference data.*

DYNAMO-HIA needs two kinds of inputs from the user: *Reference Data* and *Simulations*. The *Reference Data* consists of data on *Diseases*, *Populations*, and *Risk Factors*. Data can be entered and manipulated in several different ways. The exact procedure depends on the data at hand. Different diseases, population, or risk factors can be specified or the same diseases, population or risk factors can be specified in (slightly) different ways, such as discrete or continuous definition of the same risk factor. The input for *Simulations* configures the desired scenario and initiates the simulation run. In this menu the user chooses the population, the risk factor and the diseases to be simulated.

### ***Navigating the Data Tree***

*This section gives an overview of the mechanics navigating the data tree and how to access a certain section of the input data. It might be skipped by more experienced users.*

The data-tree is the main interface to input, organize, and track the data that are being used in DYNAMO-HIA.

The data-tree is being set up in the chosen working directory and consists of two main folders: *Reference Data* and *Simulations*. In the folder *Reference Data*, all the input data needed to run a simulation is being stored. In the folder *Simulations* the configuration files for the different simulation and the resulting simulation results are being stored.

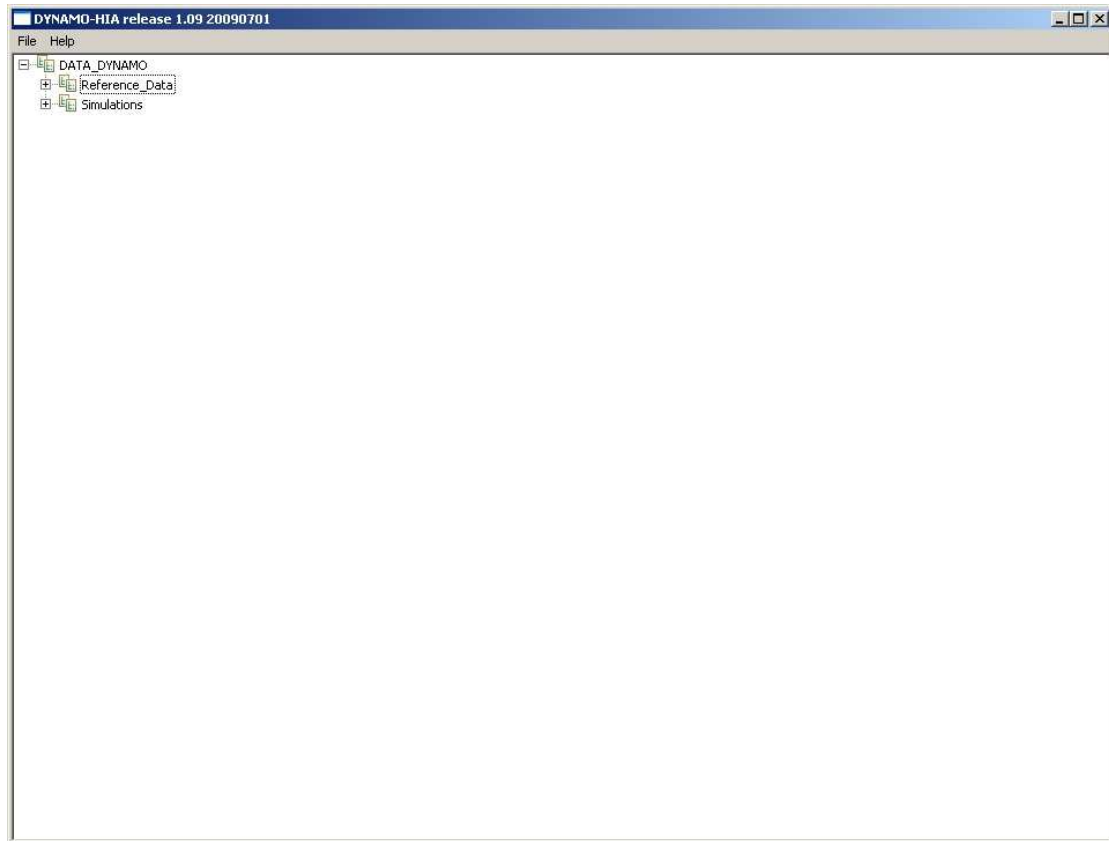
Within the directory *Reference Data*, three sub-directories exist: *Disease*, *Populations*, and *Risk\_Factors*.

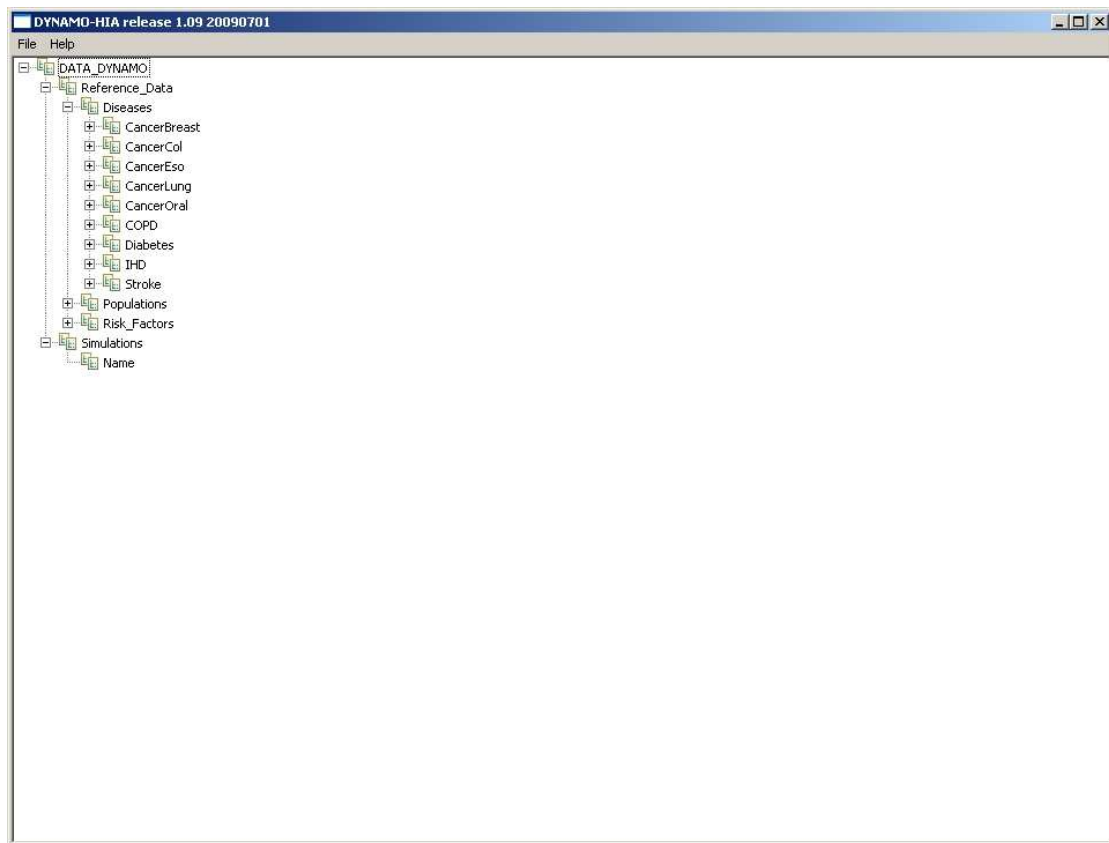
When left-clicking on a node with a plus sign right next to a directory name, the directory tree expands: The node changes now from a plus sign to a minus sign and further directories are listed. In Figure 17 an example is given: First, only the folders *Reference Data* and *Simulations* are visible. When left-clicking on the node next to *Reference Data*, the view expands. Now, the directories *Disease*, *Populations*, and *Risk\_Factors* become visible.

When, for example, left-clicking on the node next to the directory *Disease*, it expands as well and further sub-directories (when already existing) become visible. In the case that the user wishes to create a new disease that should be included in the simulation, a new directory has to be created. The new disease will be created by right-clicking on the directory *Disease*. A context menu with the single option *New Disease* will pop up. When left-clicking on the option *New Disease*, a naming window will appear. In this window a name for the new disease can be assigned (see appendix B for advice on naming). When pressing the *OK-Button*, the sub-directories needed to store the data for a disease are created. Those sub-directories become visible when left-clicking on the node right next to the chosen disease name.

The procedure is the same for the directories *Populations* and *Risk\_Factors*. With a left-click on the node the view is expanded and further directories – when already created – become visible. With a right-click on the directory name a context menu pops up to

allow the creation of new diseases, populations, or risk factors, respectively. Similarly, a new simulation can be specified by right-clicking on the directory name *Simulations*.





**Figure 17: Data Tree Navigation Example: Data Tree with all directories collapsed (left panel), Data Tree with the directory Disease expanded (right panel)**

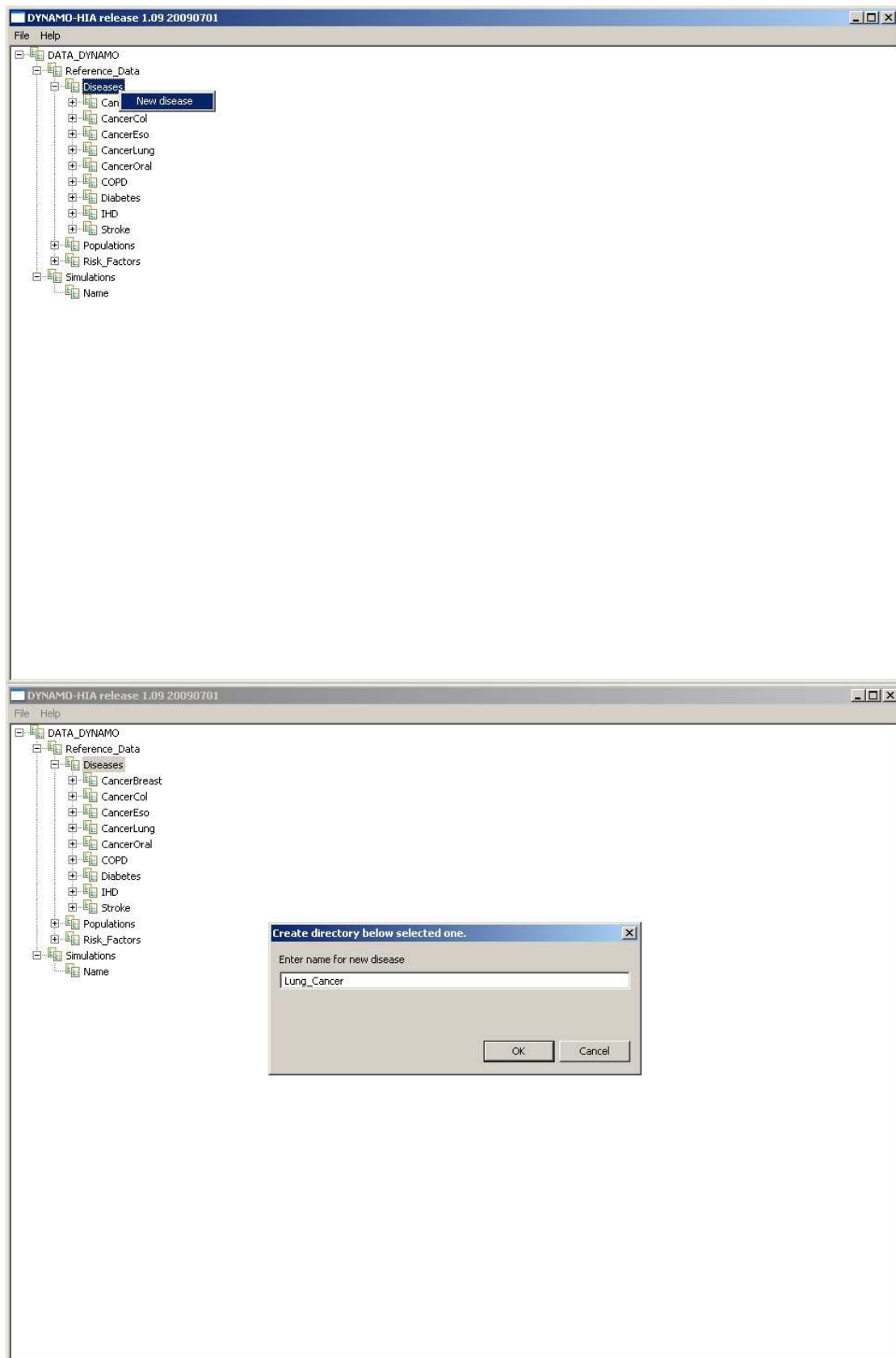


Figure 18: Data Tree: Example of creating a new disease directory:

---

Data Tree showing the context menu that appears right clicking on the directory Diseases (left panel),

Data Tree showing the naming menu for a new disease (right panel)

## ***General Mechanics of Data Entry and Manipulating***

For entering data into DYNAMO-HIA three different ways exist:

1. Entering by hand into the respective data window
2. Using the import function
3. Copying a file into the working directory

We outline here the general mechanics and describe the idiosyncrasies of the respective data windows below.

### Entering by hand

For entering the data by hand, open the respective data window (e.g. *Overall DALY weights*). Enter the desired number in the appropriate field, i.e. by age and sex. To save the results press the *Save* button at the bottom. This can be done repeatedly while entering a large amount of data to ensure that data no is going to be lost in case of a malfunction of the computer (e.g. an electricity black-out). When finished with entering data, the *Save and Close* button closes the window while automatically saving the data. The *Close* button closes the data window without (!) saving the data. DYNAMO-HIA verifies while entering and saving the data whether the entered figure is consistent with the required input, e.g. not negative when a probability is required and so on, and gives a warning message. This, however, does not safe guard for entering wrong data; it only assists in finding errors.

---

### Using Excel templates and the import function

Together with DYNAMO-HIA, Excel templates are available. Those exist for the different data types needed for DYNAMO-HIA and can be used for storage outside of DYNAMO-HIA. The advantage of storing in Excel files is easy checking of the data by making graphs or taking sums. The excel files contain macros that export the content of a given Excel file (e.g. overall DALY weights) into an XML-file. These XML-files can be easily imported into DYNAMO-HIA.

If DYNAMO-HIA has been installed using the installed, the excel notebooks containing these macros can be opened from the start menu (DYNAMO-HIA → Macro). Otherwise they can be downloaded from [www.dynamo-hia.eu](http://www.dynamo-hia.eu). The working of the Excel macros is explained on the first sheet of each excel notebook. In the help text of each DYNAMO-HIA reference data screen (on the right side of the screen) it is indicated which Excel notebook is needed to produce a dataset needed by that screen.

#### **Importing net transition rate files from the parameter directory**

If net transitions are asked from the model, the input file does not contain data, only the message that net transitions should be used. These will always be the net transitions of the reference scenario. However, when running the model, it makes a net transitions matrix for the simulation module, and stores this as an XML file in the parameters directory under the simulation. For categorical (and compound) risk factors, this XML file has the same format as a user specified transition matrix. Therefore it is possible to import these files as user specified transition matrixes.

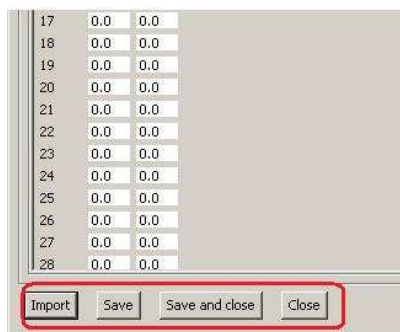
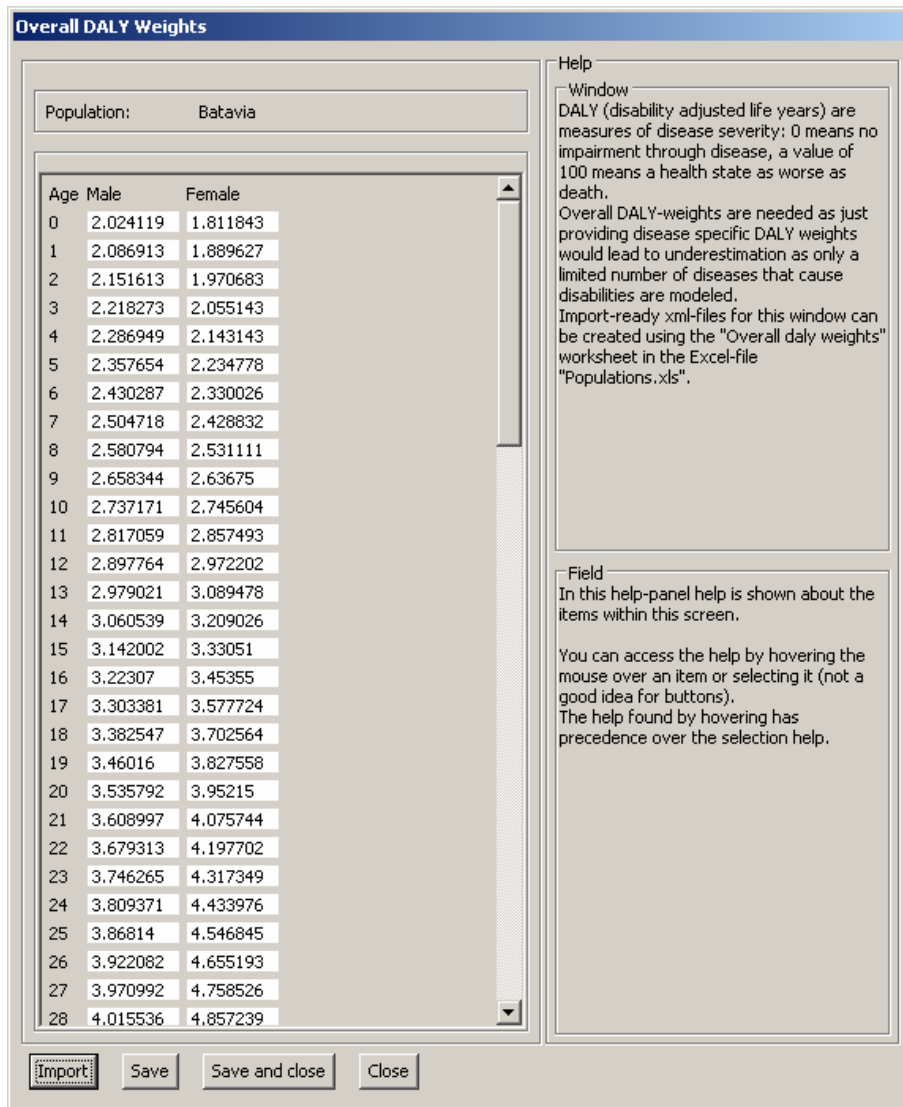
For instance, if you would want an alternative scenario to use transitions that are the net transitions of the prevalence rates of this alternative scenario, you can do so by first running this scenario as a reference scenario, and then (after the model has run) use the import function to import these net transition rates from the parameter-directory.

When the macro in Excel has been used to create an XML-file, go to the respective data window in DYNAMO-HIA. Then press the Import button. The file explorer opens. Choose the XML-file to be imported and open it. The data will appear in the data window and the data window can be closed using the *Save and Close* button. When the XML file does not conform to the required data specification for the respective data window (e.g. the mortality rate template was used but overall DALY weights are required), an error message will appear.

#### Copying files into the working directory

***This approach is only recommended for experienced users.***

DYNAMO-HIA stores the data using a fixed directory structure containing XML-files. When the XML-file conforms to the specification of the respective directory, it is accessible by DYNAMO-HIA. Hence, one can just copy such a XML-file or a whole directory containing several sub-directories with the respective XML-files into the working directory. However, this may lead to serious mistakes destroying the required file structures. Therefore we strongly recommend using the import option.



**Figure 19: Example of data entering window**

Example of data window (here: Overall DALY) (upper panel)

Saving button data window highlighted (here: Overall DALY) (lower panel)



## Specification of reference and intervention scenario's

The most important aspect of running health impact calculation, is to specify the reference and intervention scenario. The challenging part is that, as DYNAMO-HIA is a dynamic model, one needs to specify not only the current simulation, but also what will happen with exposure in the future. The latter should be given to the program in the form of “transition rates”.

In DYNAMO there are three options to specify the future transitions:

1. User-specified transitions: the user provides data on transitions between the risk factors categories (e.g. smoking start probabilities and quit probabilities rates, or on trend for continuous exposure (e.g. increase in mean BMI of 0.02 for each age year).
2. Net transitions: The user assumes that the age-specific prevalence of exposure in the population will remain the same (thus prevalence by age and sex does not change). This approach is very similar to the use of period life expectancy, where for a newborn the currently observed age-specific mortality pattern is assumed to remain valid. This approach ignores any cohort effects. This approach is named “net transitions” in DYNAMO-HIA, because DYNAMO derives the minimum transitions that are needed to keep the age-specific prevalence unchanged in the future. DYNAMO can only calculate net-transitions for the reference scenario. In the case net transitions are also specified for alternative scenarios, DYNAMO uses the net transition rates calculated from the prevalence of the reference scenario also for the alternative scenario. In other words, it assumes that the

future dynamics of the risk factor remain the same. We also describe on (see page 55) how to make net transition rates for the reference scenario.

3. Zero-transitions: Persons are assumed keep the exposure in the baseline year throughout their life until they die. Hence, persons having a normal weight at baseline keep that during the entire period or until they die. This approach is named “zero transitions” in DYNAMO, as there are no transition between risk factor categories or changes in mean BMI in the future when persons age.

To specify what is expected in risk factor exposure due to the policy or intervention (=intervention scenario), the user can change the following as compared to the reference scenario:

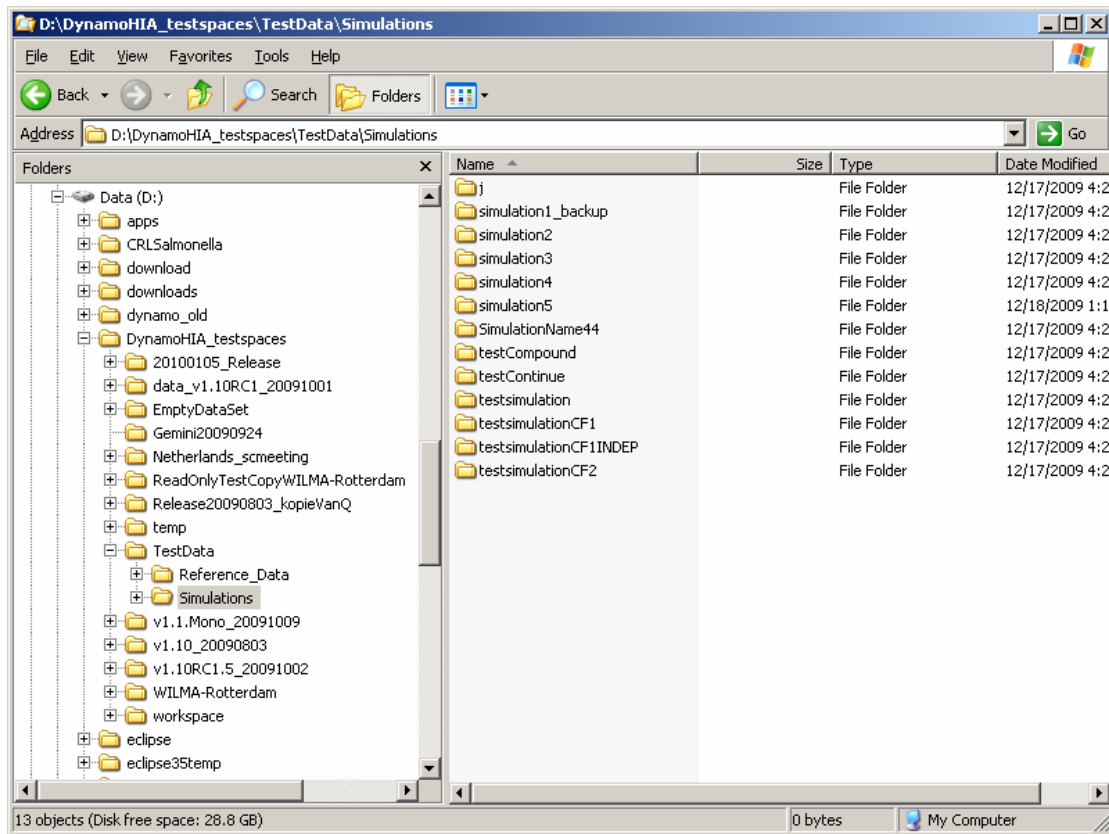
1. Change the baseline exposure, that is the prevalence rates at the start of the simulation
2. Change the future transitions
3. Change both baseline exposure and transition.

It is important to realize that, due to dynamic behavior, generally in the long run other prevalence rates are realized than that where given at baseline. In the long run, the prevalence rates will revert to a kind of “steady state” that is determined only by the transition rates. So if the same transition rates are used for two scenarios, in the long run the prevalence rates will become the same. An exception is when net transitions are used: Net transitions do not exhibit this type of dynamic behavior (see {Kasstele J, #3187}).

## Running DYNAMO in batch-mode

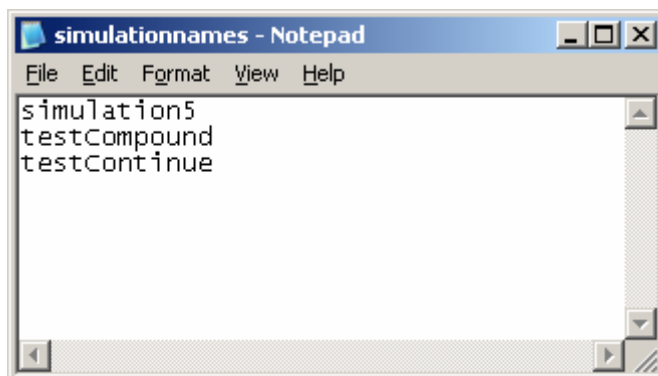
It is also possible to run multiple simulations one after the other outside the graphical Dynamo-HIA software (under Microsoft Windows), that is, in batch mode. This can be done by starting a batch job from the windows command line as described below. It can only be used to run Dynamo-HIA from other applications.

To do so, one must first prepare a work directory for the simulations, that is a directory containing a reference directory with data, and a simulation directory containing the multiple simulations to be run (Figure 20). Since the simulation run is identical to the run initiated from the Dynamo-HIA graphical user interface, the simulations can be tested from the graphical userinterface before a batch-run is attempted.



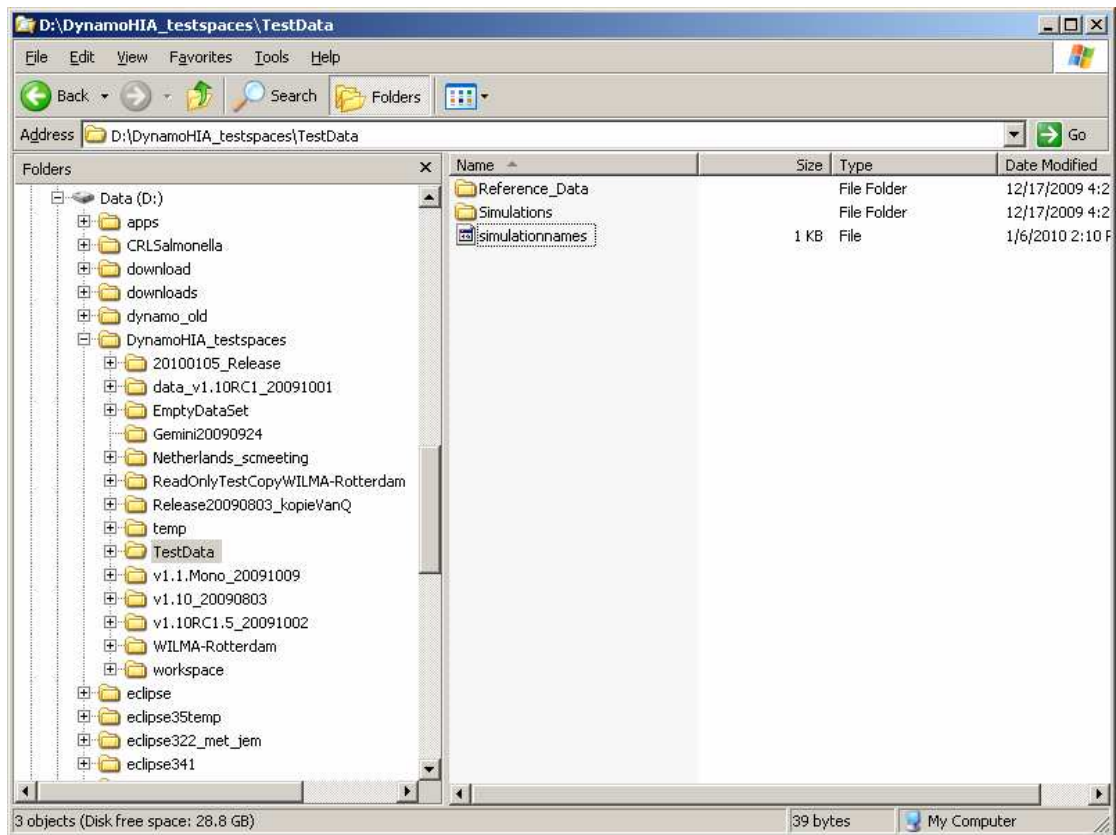
**Figure 20:** A work directory has to be prepared containing the simulations to be run

Now use a plain text editor (notepad, vi ...) to create a text file containing the names of the simulations to be run (Figure 21).



**Figure 21:** Example of a text file containing the names of the simulations that should be run in batch-mode

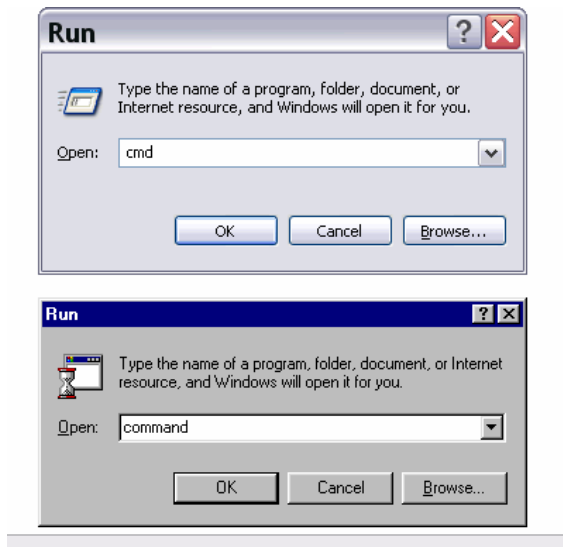
This file must be placed in the base-directory at the same level as the “Reference-Data” and “Simulations” directories (Figure 22). Multiple files can be created there.



**Figure 22: Place of the text file containing the names of the simulations that should be run**

Now open a command line window. To do so, first click the Windows Start menu (located at the very lower-left corner of your computer's desktop) and select "Run...". Then if you are using Windows XP or Vista or Windows 7, type cmd into the Run box and click "OK". You could also type cmd.exe.

Otherwise, if you are using an older version of Windows, type command into the Run box and click "OK". You could also type command.exe. (Figure 23)



**Figure 23: How to open a command window**

Now find to the “eclipse” directory inside the current release (with standard installation this is in the “C:\Program Files\RIVM\DYNAMO-HIA\ Dynamo-HIA Application”) directory. You have to make this directory the "current" directory, which you can do by using the cd command ("cd" is short for "change directory"). With the standard installation you do so by typing:

```
cd c:\programfiles\RIVM\Dynamo-Hia\Dynamo-HIA Application\eclipse
```

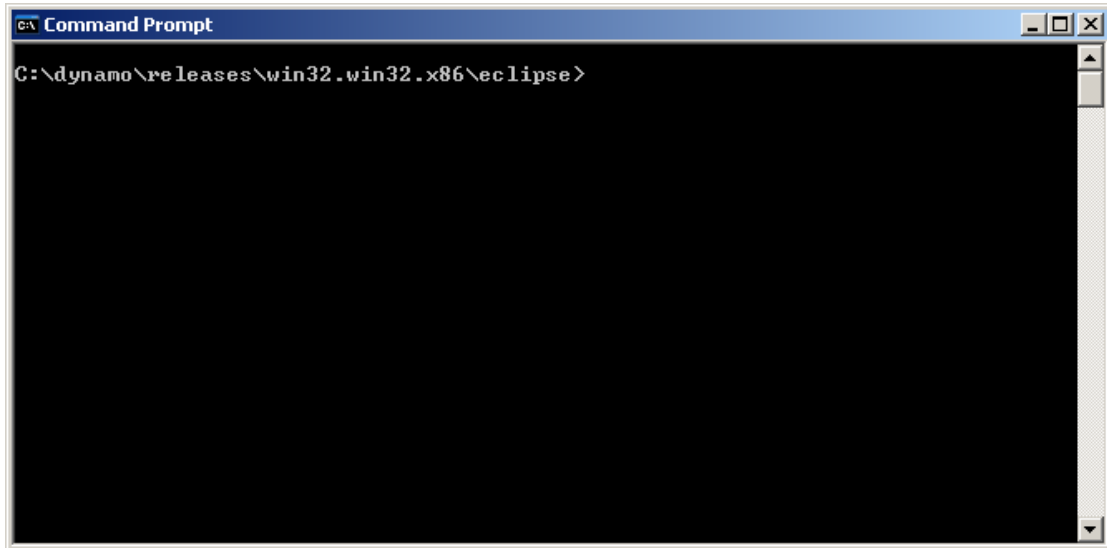


Figure 24: Command window, with the eclipse directory as the current directory

Then enter “runbatch “ plus the path to file we made above.

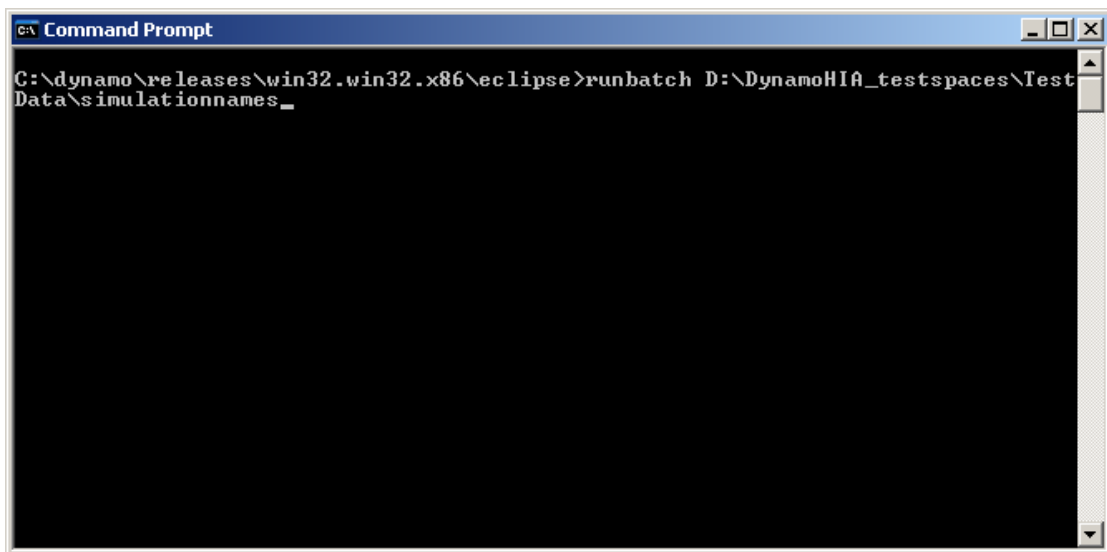


Figure 25: Entering the command running DYNAMO-HIA in batch mode

Press <Enter> and the simulations will be run. Output of each simulation will be written to the file “batchout.csv” in the results directory of the simulation. This is a csv file using ; as separator. Also an results.obj will be made, which can later be inspected with the graphical user interface.

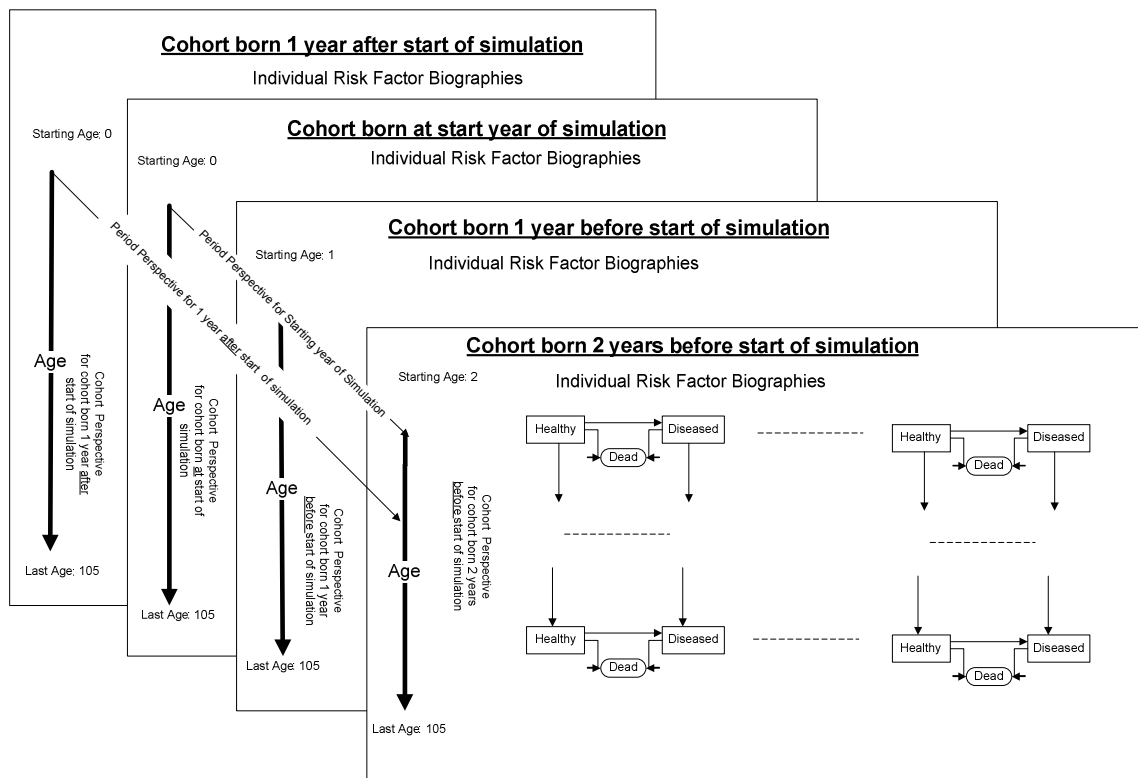
## Simulation Methodology

We briefly summarize the simulation methodology below, while this methodology is described in detail in the document “Detailed description of DYNAMO-HIA calculations” which is also included in the installation package. The simulation methodology is also described in two papers, which were submitted for publication when finalizing this manuscript. Below we first give an intuitive explanation of the core methodology within DYNAMO-HIA, and a series of figures illustrating the methodology and that we think are helpful to gain more insight. Second we will discuss in more detail some of the consequences of our modeling approach, addressing specifically the consequences of several choices that are open to the user.

### ***Model Core***

DYNAMO-HIA is a Markov-type model based on a multi-state model (MSM). The change of the current state depends only on present characteristics (i.e. age, sex, risk-factor status, and health status). The MSM is implemented as a *partial micro-simulation* combining a stochastic micro-simulation to project risk-factor behavior with a deterministic macro approach for the disease life table. In the micro simulation module a large number of distinctive risk-factor biographies are simulated: Given the age and sex-specific transition probabilities between risk-factor states, the risk-factor status of each simulated individual is updated in annual increments (see Figure 26 for details). In the macro module, as many disease life tables as there are risk-factor biographies are constructed. These disease life tables are able to account for competing risks and multiple morbidity. The exact configuration of the disease life tables, i.e. the number and kind of diseases, can be specified by the user (see **Error! Reference source not**

**found.** for details). For every risk-factor biography, the probability of disease incidence and mortality over time is calculated, accounting for the current age, risk-factor and disease status (see **Error! Reference source not found.** for details). These biography-specific life tables are calculated for every cohort, i.e. all individuals that are born in the same calendar year. For example, for a cohort of newborns first the risk-factor biographies are projected and then disease life tables are calculated. Older cohorts, i.e. born before the first simulation year, start out having the disease prevalence specified in the input data, which is then similarly updated. Population values are obtained by aggregating the individual biography/diseases life tables: either across cohorts at a given simulation time point to obtain period measures or along cohorts to obtain cohort specific measures (see



for details). The split into a micro and a macro module is done purely for computational convenience and micro and macro-simulations yield the same result when used with the same data. However, time and memory requirements in macro simulations rise

exponentially when the number of simulated states increases and a micro simulation – unlike a customary multi-state life table – does not require the a priori specification of all theoretically possible combinations of diseases/risk-factor states, but only those states that are actually occupied. But for simulating rare events – such as lung cancer at young ages – micro simulations require the simulation of a large number of individuals, offsetting the savings in time and memory requirements.

The epidemiological model uses relative risks by risk-factor class, i.e. incidence in exposed risk-factor classes is a multiple of the incidence of the non-exposed. The total mortality, i.e. population level mortality by age and sex, is being decomposed in the mortality due to the diseases included in the model and other cause mortality. This decomposition assumes additive mortality: the total mortality rate in the population is explained as the sum of the mortality rate of the included diseases and other-cause mortality, i.e. mortality from all causes/diseases that are not explicitly included in the model.

DYNAMO-HIA simulates the effect of a single risk factor on a population without migration. However, the categorical risk-factor can be used to partition the population in up to ten distinctive categories. For example, a population could be partitioned along a risk-factor – say, non-smokers and smokers – and socio-economic status – say, with college education and without college education, having in total four different groups. This could be used to assess a policy which is known to be more successful for people with certain socio-economic status. The possibility of partitioning the population can also be used to quantify the effect of an environmental hazard. In this case, for example, the population is partitioned according to their proximity to the hazard source – say, noise exposure or air pollution due to a new airport with 5% of the total population

living less than 5km from the hazard source , 5% to 10% living less than 10km and so on. This requires of course sufficient insight into which part of the population is affected and knowledge of the relative risks of the modeled exposure level on the included diseases and total mortality.

A category may also stand for a combination of known risk-factors: For example, smoking status and BMI – smoking/non-smoking and normal weight / overweight / obese – could be modeled by partitioning the population into six distinctive risk-factor categories. However, it requires knowledge about the relative risk of the combined risk-factor class – say, relative risk of being obese and a smoker on the included diseases and total mortality.

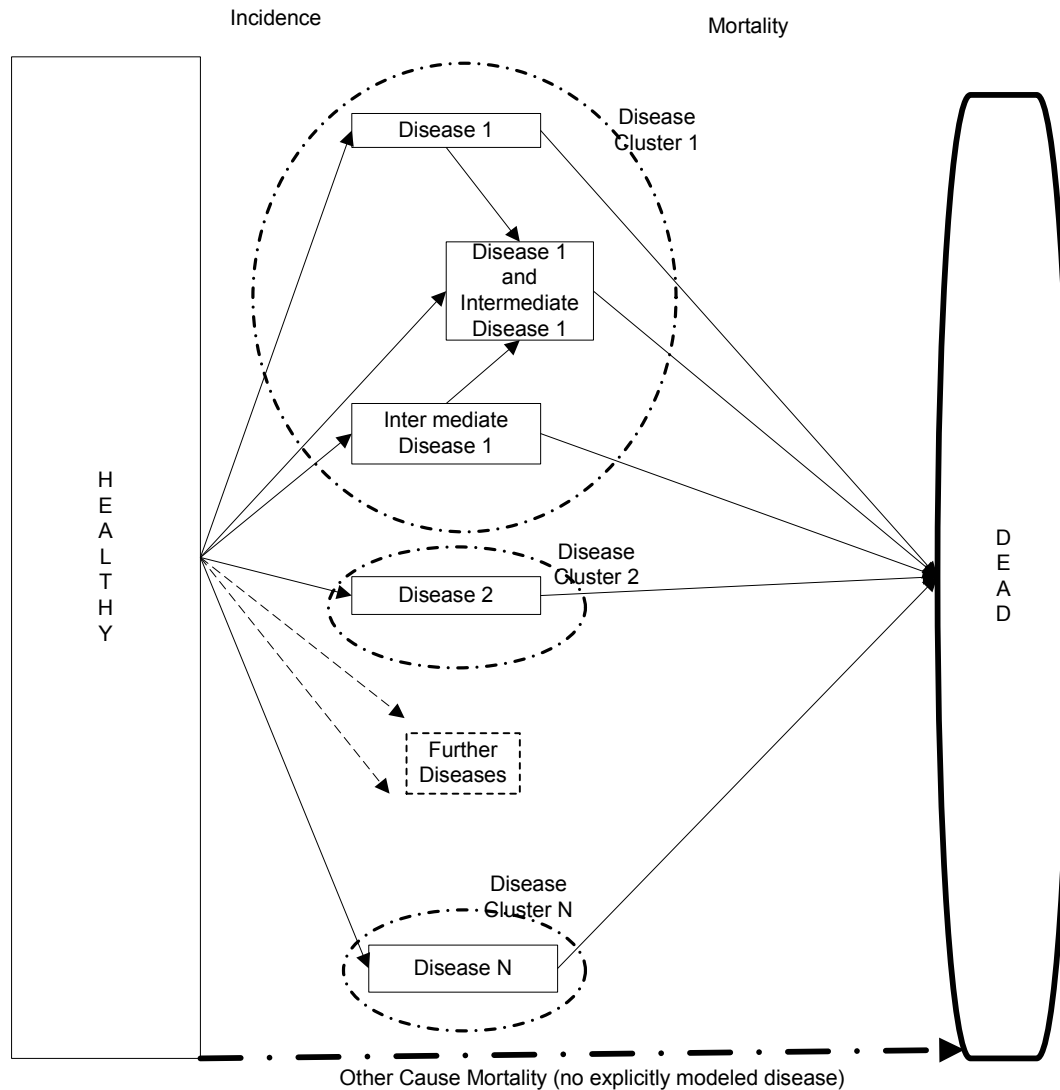
### Figures illustrating the DYNAMO-HIA methodology

risk-factor biography	Age								
	x	x+1	x+2	x+3	x+4				
1	N	→	N	→	P	→	P	→	O
2	O	→	O	→	P	→	N	→	N
3	P	→	P	→	N	→	N	→	N
4	N	→	N	→	P	→	O	→	O
5	N	→	N	→	P	→	O	→	O
6	P	→	P	→	P	→	P	→	P
7	N	→	P	→	P	→	P	→	P
8	N	→	P	→	O	→	O	→	O
9	N	→	N	→	N	→	N	→	N
10	N	→	P	→	P	→	N	→	N

N= Normal Weight, P=Overweight, O= Obese

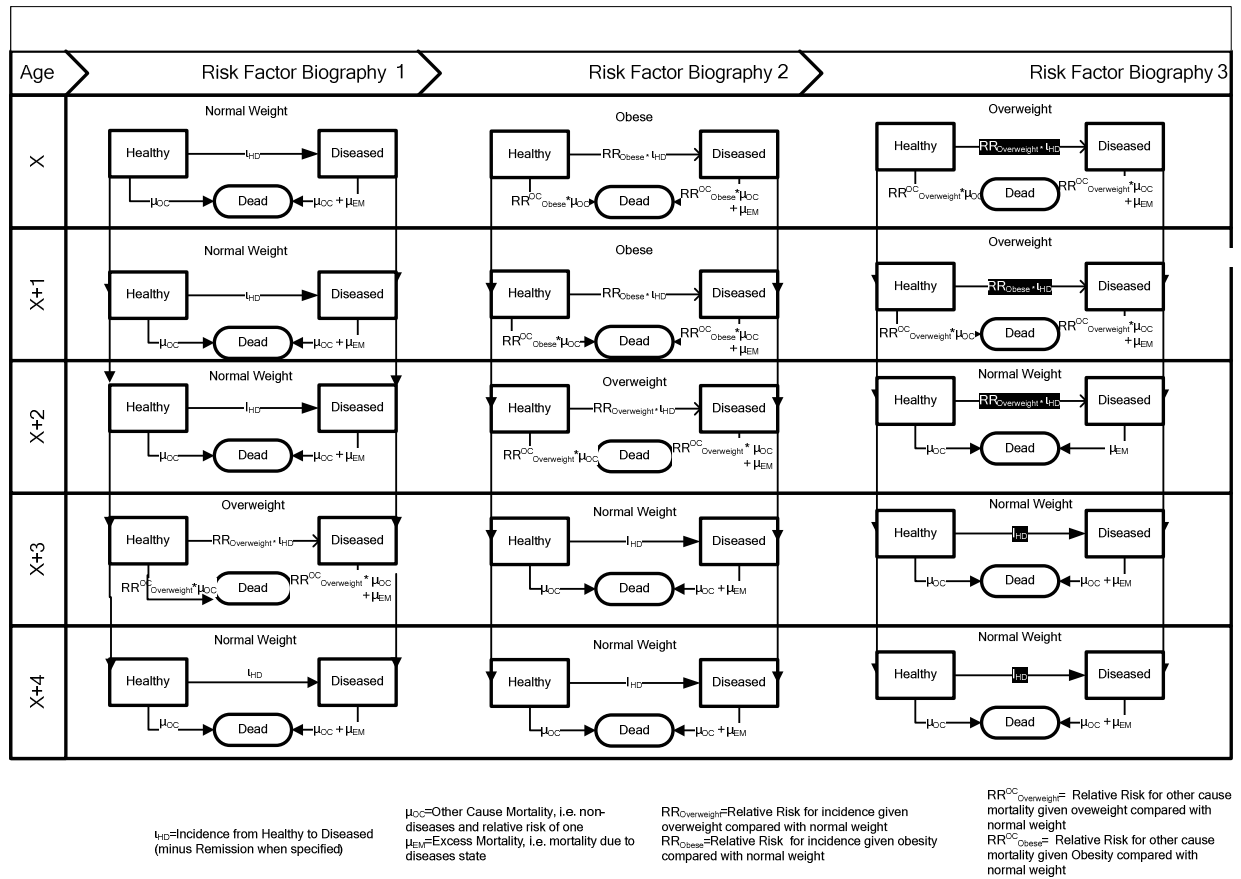
**Figure 26: Example of risk-factor biographies for a risk factor with three categories.**

*DYNAMO-HIA simulates individuals and projects their risk-factor biographies. In annual increments the risk-factor status is being updated, given age- and sex-specific transition risks. The age- and sex-specific risk-factor status determines the relative risk of a person to contract a disease or to die. DYNAMO-HIA allows one risk-factor per scenario. This risk-factor can be either categorical (up to ten categories), duration dependent (up to ten categories of which one is duration dependent, i.e. the risk on disease in this category depends on how long a person is in the category), or a continuous distribution (normal or log-normal, specified by entering mean, standard deviation, and, in the case of the log-normal, skewness).*



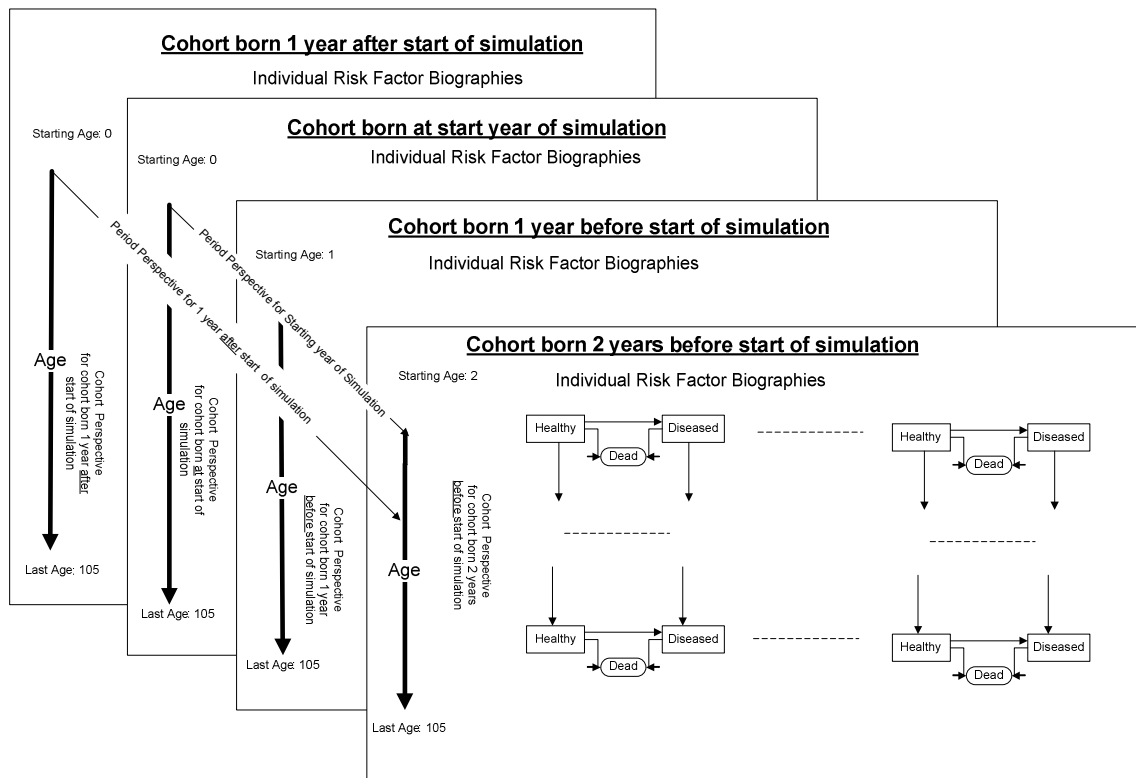
**Figure 27: Stylized structure of disease life table**

*The disease life tables contain diseases clusters. Each disease cluster consists of one or more diseases. Within disease clusters, intermediate diseases - that increase the risk of getting another disease - can be specified (e.g. having diabetes increases the risk of getting IHD). All diseases are chronic diseases, i.e. excess mortality depends on age and sex and not on time since onset of disease. However, acutely fatal and/or cured fraction can be specified for diseases. The disease life table assumes independence between disease clusters. The user can freely specify the relative risks from risk-factor to disease, from risk-factor to death, and from intermediate disease to other diseases.*



**Figure 28: Stylized cohort life tables (with only one disease, three different biographies, and five time steps)**

For every risk-factor biography, a disease life table is constructed. Diseases incidence, i.e. transition from healthy to a disease, equals the baseline incidence, i.e. incidence when in a risk-factor class with a relative risk of one for the specific age- and sex-category, times the relative risk due to the given risk-factor and diseases status (in the case of an intermediate disease). The transition from healthy to dead equals the baseline other-cause mortality of the healthy, i.e. age- and sex-specific total mortality rate minus the excess mortality rate of the diseases included in the disease life table, multiplied by the relative risk due to the given risk-factor status on other cause mortality. The transition from diseased to dead equals the sum of the excess mortality of the disease (given each and sex) and the baseline other cause mortality of the healthy, multiplied by the relative risk in the given risk-factor status. Remission is not explicitly modeled, but for diseases with cured fraction the excess mortality is zero in a “cured”, i.e. user-specified, fraction. Partly acutely fatal diseases, i.e. diseases with very high mortality immediately after contracting the disease while for those who survive this critical period the excess mortality only depends on age and sex, are modeled by specifying the fraction of the incidence cases that die immediately.



**Figure 29: Schematic overview of the dimension of a multi-cohort, multistate-life table**

Each plane is a distinct cohort with varying starting ages for cohorts already existing at the starting year of the simulation and starting age zero for cohorts born during the simulation run. The cohort life tables, consisting of the set of individual risk-factor biographies, follow every already existing birth cohort until the cohort reaches 105 years of age. In addition, every year of the simulation a cohort of newborns is created and – after simulating individual risk-factor biographies for them – is followed through the appropriate disease life tables as well. This allows collecting health data for each cohort according to their risk-factor status (longitudinal) or the health status of the population by age, sex, and risk-factor status by each year of the simulation (cross-sectional).

### ***Important Notes on using the model***

The DYNAMO-model carries out rather complex calculations. Not all details of these calculations are obvious from the users interface, and consequences of some of the

choices that users can make are not always intuitive. Below we highlight some issues that users should be aware of.

### **Negative other cause mortality**

The total mortality (as given in the population data) in DYNAMO is split into “disease related mortality”, that is the mortality due to any of the diseases that are in the model, and “other cause mortality”. The magnitude of the disease related mortality is mainly driven by the prevalence of disease (if there are more persons with lung cancer, more will die because of lung cancer), by the excess mortality and by the fatal fractions of the disease. With many diseases in the model, having high prevalence rates as well as high mortality, it is possible that the sum of the disease related mortality at a particular age exceeds the total mortality at this age. In this case the model will not run, but will ask you to revise the data.

When you specify in DYNAMO a relative risk on death for your risk factor, DYNAMO will attempt to make the total mortality at baseline (= start of simulation in the reference scenario) in each risk factor class equal to that given by that relative risk on total mortality.

This is done by first calculating how high the total mortality in the risk class will be, given this relative risk and the overall mortality rate in the population. Next this is compared to the mortality that is due to the different diseases in the model. In a risk factor class with a higher incidence of for instance lung cancer, the prevalence of lung cancer at baseline will also be higher, and thus mortality from lung cancer will also be higher. So disease-related mortality will be higher in risk factor classes with a higher

risk on disease. After summing the disease-related mortality in each risk factor class, the gap between the total disease-related mortality and the total mortality as calculated from the relative risks on death is taken to be the “other cause mortality”.

This other cause mortality will differ for each risk factor class, and can become negative. In that case it is made zero, while simultaneously the other mortality in other risk factor classes is decreased in order to retain the correct overall population mortality. If other mortality has to be made equal to zero in more than 30% of the population, a warning is given. In all cases, the estimated mortalities (disease-related and other cause mortality) are written to the “othermort.csv” file in the parameter directory, so that they can be inspected by the user. This is especially important for continuous and compound risk factors, where a parametric function is fitted to the other mortality before using it (see page 78 and 79).

It is important to note that in cases where the relative risk on death calculated from the disease information is higher than the relative risk on death as given directly by the user, the algorithm in DYNAMO lowers the other cause mortality in this risk factor class. In other words, it tries to compensate the too high disease-related mortality by a lower other cause mortality (compared to other groups). Only when this is no longer possible (because other cause mortality in this class is already made 0), the relative risk on death will depart from relative risk on death as given by the user.

This can have counter-intuitive effects when running scenarios. This is due to the fact that the dynamics of disease-related mortality is slower than that of other cause mortality, as for disease-related mortality to steps are required: getting the disease and dying from it. This effect takes more time to develop than mortality from the one step process of dying from other cause mortality. We therefore advise caution with

simulations that have negative other mortality warnings. Also, such warnings indicate that the relative risks on total mortality is already covered by the diseases in the model, and thus might be superfluous, so that a model that does not contain a relative risk on death might be preferred.

A good check in case of these warnings is to run the simulations also without a relative risk on death, and see whether conclusions remain the same.

### **Using continuous risk factors**

When using continuous risk factors, the program assumes that the prevalence data have been smoothed over age. This is especially crucial for the standard deviation, as the program increase the variance of the risk factor over time when the standard deviation is increasing with age, but is not able to handle decreasing variance of risk factor in a similar way. When data are not smoothed, this means that the changes between years are too large, and as all negative changes are ignored, there will be considerable bias. Although this would not directly influence the average risk factor value, the exponential relations between risk factor value and disease incidence and other cause mortality will make that it does influence disease incidence and mortality.

### **Interpreting graphs of disease prevalence by risk factor level over time**

The basis of the DYNAMO model is that in each scenario at time 0 (the starting year) either the risk factor prevalence, or the risk factor transition rates, or both are changed compared to the reference scenario. From that moment on, incidence rates and mortality

rates will be based on the new risk factor levels. Disease prevalence, however, is a stock variable: it is the result of past incidences. This means that at the start of follow-up, the disease prevalence in all scenarios will be equal to that the reference scenario, and that over the course of time the prevalence will diverge, as the number of new cases will be determined by the new risk factor status of subjects in the new scenario situation.

The consequence of this is that graphs of disease by risk factor level will show differences in disease prevalence rates between scenarios: As an example, take a scenario that changes part of the smokers into former smokers. In that case, the former smokers in this scenario will be a mixed of subjects that were already former smokers, and of smokers that under the scenario were changed into former smoker. The latter will at time 0 still have the same disease prevalence of smokers, and so the disease prevalence in this mixed group will be higher than that of former smokers. In contrast, the former smokers in the reference scenario will all have the disease prevalence of former smokers. The result is that former smokers in the alternative scenario will have a higher disease prevalence than former smokers in the reference scenario.

The only exception to this rule are newborns: Newborns are given directly the prevalence of the alternative scenario.

### **Selective mortality and calculating net transition rates.**

When net transition rates are calculated, the program uses the relative risks on death to take account of the effects selective mortality. Selective mortality implies that those with high exposure to an adverse risk factor die sooner than those with lower exposure. Therefore the prevalence of such a high exposure in the population will diminish with age, also without any transitions between risk factor classes taking place. This effect can

be taken into account by using the relative risks on death to calculate the amount of selection.

This implies that when no relative risk on death is specified in the simulation configuration screen, net transition rates are calculated without taking selective mortality into account.

### **Relative risks on death equal to 1 versus no relative risk on death**

With relative risks for diseases, not specifying a relative risk on this disease (on the relative risk tab of the model configuration screen) implies that these relative risks are assumed to be 1. A relative risk of 1 implies that there is no effect of the risk factor on the incidence of this disease, that is, the incidence is the same in all risk factor groups. Specifying a relative risk of 1 therefore will give the same result as not specifying a relative risk.

The same, however, is not true for relative risk of death. When a relative risk of death of 1 is specified, the relative risk for other cause mortality in the model is calculated in such a way that no overall effect of the risk factor on initial total mortality is seen. Initial total mortality is the total mortality at the start of the reference simulation. So if there are diseases in the model which increase mortality in e.g. higher exposure groups, the other cause mortality in these groups will be lowered in order to produce the same total mortality in both groups. A relative risk of 1 thus forces a calculation of relative risks for other cause mortality that compensate any mortality effects of diseases.

When no relative risk on death is specified, the relative risk on other mortality is made 1, thus not the relative risk on total mortality. This means that if there are diseases in the model which increase mortality in e.g. higher exposure groups, the total mortality in

---

these groups will also be higher. All exposure groups have the same other mortality, so differences in total mortality are driven by differences in the prevalence of disease.

### **Relative risks on death and continuous risk factors.**

Apart from the effect on nett transitions, relative risks on death are used to estimate a relative risk on other cause mortality. For categorical risk factors this can usually be done exactly. The exception is when total mortality as given to the program is so close to the sum of all mortality related to diseases (also as given to the program) that the other cause mortality (the difference between total mortality and disease related mortality) becomes negative in some risk groups.

For continuous risk factors, first other mortality is calculated for a large range of values of the continuous risk factor. Second an exponential function is fitted, giving other cause mortality as a exponential function of risk factor level. The relative risks on death determine how quickly total mortality rises with risk factor level. This is also an exponential function. In practice it can happen that disease related mortality increases more quickly with risk factor level than total mortality. In that case other cause mortality (the difference between the two) will decrease with risk factor level. That can give strange results in simulations, where a decrease in a deleterious risk factor can lead to more mortality. This is an artifact of the assumed exponential relationship. For continuous risk factors we therefore advise either not to include relative risks on death, or to check in the parameterfile “relative relativeRisk\_OtherMort” whether the relative risks are (mostly) in the expected direction.

A similar effect can also occur for compound risk factors, but as the effect of forcing a particular shape on the relation between duration of exposure and other mortality are limited to those in the “duration class”, effects will be less severe.

## **Other cause mortality and compound risk factors**

For compound risk factors, the relative risks on other cause mortality in the duration class are fitted assuming an exponential decline, starting at “RRbegin”, and decline towards “RRend”. RRbegin and RRend are derived differently depending on the values of the RRbegin and RRend that are given by the user for total mortality.

When the user specifies an RRbegin for total mortality that is equal to the relative risk in a “non-duration” class of the risk factor, RRbegin of other cause mortality is also made equal to the relative risk of other cause mortality in that same class. Similarly, when the user specifies an RRend for total mortality that is equal to the relative risk in a “non-duration” class of the risk factor, RRend of other cause mortality is also made equal to the relative risk of other cause mortality in that same class. Only when it proves impossible to fit the required curve, these restrictions are dropped.

After fitting this relative risk curve, the other mortality figures are calibrated so that the average mortality in the initial reference population is equal to the total mortality specified by the user. If the fitted values for other cause mortality in the duration class are very from the values that they were fitted on, this also changes the mortality in “non-duration” classes, sometimes importantly so.

The user therefore is advised to check the fitted other cause mortality, as written to the file otherMortData.csv (see page 45). One possible solution for improving the fit of the other cause mortality is to lift the restrictions on RRbegin or RRend. This can be done by changing the input RRbegin and/or RRend given for total mortality a little bit, so that they are not exactly the same as the relative risks given for one of the other classes.



## Appendices

### *Appendix A. System Requirements*

The system on which the DYNAMO-HIA application is going to be installed is restricted to the minimum requirements described below.

In the table below the minimum system requirements for installation of the DYNAMO-HIA application on a Windows system are described.

<b>Item</b>	<b>Minimum Requirements</b>
Operating System:	XP (with .NET Framework 3.5 SP1 installed)
Computer Processor:	2,2 Ghz AMD Athlon 64 X2 Dual Core or better (e.g. Intel)
Computer Memory:	1,00 GB of RAM
Screen Resolution:	1024x768

## ***Appendix B: Recommended Naming Conventions***

DYNAMO allows storing and using a large number of files in a single work directory, such as several different incidence files for the same disease. This might occur when having several different populations in the work directory or different incidence data for the same disease to, say, conduct a sensitivity analysis. The xml files within DYNAMO, however, do not carry any additional information about content and origin beyond the name of the file. Hence, we suggest a naming scheme for the created xml-files which could be used within DYNAMO. This naming scheme is not necessary to use DYNAMO and every user is welcome to adjust the scheme to his own needs or devise a completely new one for his use.

This naming scheme classifies the data first by country and then in the three groups of reference data: population, disease, risk factor and in addition the group relative risk, which is assumed to be the same for all countries/regions. Next the actual name is given (either risk factor name or disease name), in the case of risk factors one should consider to include information on the measurement level as one, say, could model BMI with 3 categories or 5 or even more. Finally the characteristics should be included. This naming scheme allows for a distinctive naming of each file and allows ordering them in a file browser in such a way that related data are next to each other.

*Table 1: Suggested Naming Conventions for XML files***Population**

<u>Country/Region</u>	<u>DataSection</u>	<u>Attribute</u>
<i>e.g. UK</i>	<i>Pop</i>	<i>Size</i> <i>Newborns</i> <i>OverallDALY</i> <i>OverallMort</i>

Example:

UK\_Pop\_Size

UK\_Pop\_OverallDALY

**Risk Factor**

<u>Country/Region</u>	<u>DataSection</u>	<u>Name</u>	<u>Measurement Type incl. # of classes</u>	<u>Attribute</u>
<i>e.g. UK</i>	<i>RF</i>	<i>e.g. BMI</i>	<i>{cat10, cont, Duration}</i> <i>{Zero, Net, UserSpec}</i>	<i>Prevalence</i> <i>Transition</i>  <i>In case of compounding RF split up in {Distribution, Prevalence}</i>

Example: UK\_RF\_BMI\_cat5\_Prevalence

**Disease**

<u>Country/Region</u>	<u>DataSection</u>	<u>Name</u>	<u>Attribute</u>
<i>e.g. NL</i>	<i>Disease</i>	<i>e.g. Stroke</i>	<i>DALY</i>  <i>ExcMort</i> <i>Inc</i> <i>Prev</i>

Example: UK\_Disease\_Diabetes\_ExecMort

**Relative Risk**

<u>Data Section</u>	<u>Source</u>	<u>Target</u>
<i>RR</i>	<i>Riskfactor name</i>	<i>Disease</i>
	<i>Disease name</i>	<i>Death</i>
		<i>Disability</i>

Example:

RR\_BMI\_cat5\_Diabetes

### ***Appendix C. List of ERROR and WARNING messages***

In this section we give a list of the known “Error” and “Warning” messages that might appear when running or installing DYNAMO. We do this to give additional information why the error might occur and how severely the warning might affect the model outcome. In many cases an error might indicate inconsistencies in the input data.

#### **Errors when installing DYNAMO**

*The following components failed to install:*

- .NET Framework 3.5 SP1

The MS-dos software .Net Framework 3.5 SP1, needed for installing the software, is not present on the computer. The .Net Framework 3.5 should be installed manually before the Dynamo-HIA software installer is run. These are the steps.

1. Check if the .Net Framework 3.5 is present or not.
  - a. Open the Windows Control Panel under Start;
  - b. Open Add or Remove Programs;
  - c. Look for an entry "Microsoft .NET Framework 3.5 SP1";

Note: versions other than 3.5, like 2.0 will not work with Dynamo-HIA. A version 3.5 without SP1 will have to be upgraded.

2. Download the framework;

- 
- a. Open <http://www.microsoft.com/downloads> and search for "Microsoft .NET Framework 3.5 SP1";
  - b. Change the language, if English is incorrect;
  - c. Click the Download button;
  - d. Save the file dotnetfx35setup.exe to a temporary folder;
  - e. Start dotnetfx35setup.exe and follow the instructions.

## Errors reading files

*Reading error encountered when reading file: [FileName] with message: "[...]".*

This message should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that caused the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting "bug in DYNAMO-HIA" in the subject of the message.

*Disease DISEASENAME is related to another disease and has a cured fraction. This combination is not allowed. Please change this .*

The DYNAMO-HIA model does not allow relations between diseases with a cured fraction and other diseases. So no relative risks of diseases on other diseases can be specified where one of those diseases has a cured fraction. To run the model after this

---

warning, remove (in the relative risks tab of configuration screen) the disease-on-disease relative risks pertaining to the disease named.

*Disease DISEASENAME is both a cause of another disease and is caused itself by another disease. This combination is not allowed. Please change this .*

The DYNAMO-HIA model allow only a single “causal” layer of intermediate diseases. So if there is a relative risk specified for diabetes on IHD, it is not possible to include also a relative risk of IHD on stroke. It is possible, however, to have both a relative risk of diabetes on IHD and a relative risk of diabetes on stroke. In the example, one needs to remove (in the relative risks tab of configuration screen) either the relative risk of diabetes on IHD, or that of IHD on stroke.

### **Errors generated by the parameter estimation module**

*Mortality from Case Fatality is larger than total mortality for age [a] and gender[s] and riskgroup [r].*

*Program will not run unless this problem is solved first.*

*Please change the input*

In risk group  $r$  the total case-fatality, i.e. incidence times acutely fatal fraction for all diseases together, is larger than total mortality. This can be caused by high values of incidence and case-fatality, but also by extremely low relative risks for all cause mortality and might indicate inconsistent input data.

*negative attributable mortality estimated after 10 iterations!!*

*Message given for age [a] and gender[ s].*

*Most common reason is that the mortality from acutely fatal disease is larger than excess mortality*

After adjustment for mortality due to other causes than the disease, the excess mortality from the disease becomes negative. See technical report “detailed model specification, section **3.3.3**.

*FATAL ERROR: Attributable Mortality from diseases exceeds the overall mortality for age [a] and sex[s]*

*Please lower excess mortality rates or case fatality rates or disease prevalence rates, or increase total mortality rate*

The excess mortality from all diseases and from acutely fatal diseases combined is higher than the total mortality in the population. This might indicate inconsistent input data. See technical report “detailed model specification, section **3.3.4**

*Regression for other mortality failed. Average RR for the durationclass is [X] for age [a] and sex [s].*

This message should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that causes the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting “bug in DYNAMO-HIA” in the subject of the message

*The RR for other mortality is put to [X] for all durations. Note that incidence of diseases is still duration dependent as specified.*

The RRbegin and RREnd for other mortality in the duration class could not be estimated. There the RR for other mortality is assumed to be constant. See technical report detailed model specification, section **3.3.4**

*Bug in program when calculating baseline disability odds. Total disability given by user = [X] but calculated from baselineDisabilityOdds [Y];*

This messages should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that causes the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting “bug in DYNAMO-HIA” in the subject of the message.

*Regression for other mortality failed*

This message should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that causes the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting “bug in DYNAMO-HIA” in the subject of the message.

*non-linear regression other cause mortality did not converge in 500 iterations results:  
alpha [A] RR end X RR begin [Y] criterium = [C];*

The regression that estimates the relative risk for the duration class of a compound risk factor has failed. This message should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that causes the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting “bug in DYNAMO-HIA” in the subject of the message.

**Warnings generated by the parameter estimation module:**

*100% of the initial population has the same duration. Therefore it is not possible to estimate a time dependent other mortality or other disability. In case other mortality/disability is requested, those relative risks will be made constant over time.*

See technical report “detailed model specification, section **3.3.4**

*median survival rates for age X and sex 0/1 for disease “diseaseName” are inconsistent with the median survival at the next higher age groups. Please check the data and make sure that survival does not decrease abruptly over age.*

See calculation document section **3.2.1**

**WARNING:**

*RR for disability is not (yet) implemented so RR for disability is ignored*

Use of a relative risk of a risk factor on disability has not yet been implemented. Anticipating future possibilities, however, the user is able to enter such a relative risk in the user interface. In the current implementation, however, this relative risk is ignored and, hence, does not influence the simulation output.

*negative other mortality = [xx] for person [i] for riskclass [r] age: [a] sex: [s]*

For a simulated person in the population on which the parameters are estimated, the other mortality becomes negative. This occurs mostly in case of a continuous risk factor, in those with extreme values of the risk factor.

*negative other mortality in [X] % of simulated cases for age[a] and gender [s].  
no more warnings of this kind will be generated for other age and gender groups*

For [X]% of the population for which the parameters are estimated, other mortality becomes negative. This indicates that, at least for some risk factor groups, the effect of the risk factor on mortality through the modeled diseases is larger than it is implied by the relative risk of the risk factor on all-cause mortality. Leaving out the relative risk on all cause mortality would be an option in this situation, as most of the effects of the risk factor in that case is already modeled by the effects through diseases.

**WARNING:**

*Overall dalyweight/disability is smaller than dalyweight/disability due to diseases for age [a] and gender [s] : disability due to diseases: [X] and overall:[ Y].*

*Other cause disability is set to zero.*

The dalyweight specified for the individual diseases, combined with the prevalence rates specified for these diseases together yield a dalyweight for the population that is higher than the overall dalyweight specified for the entire population. DYNAMO-HIA assumes that the disease data are the accurate data in this case and uses these to calculate DALY-

---

weights. This implies that the persons in the population (of this age and sex) that have none of the diseases that are in the model, are all supposed to be in perfect health.

*different baseline mortalities calculated after calibration nl [XX] after calibration while [YY] before (age= [age] ; sex= [sex] )*

Recalibration of baseline other mortality yields a different number. This is normal for continuous and compound risk factors, but differences should not be extremely large

*Excess mortality of disease [XX] is zero for age [a] and gender [sex]  
The program assumes a zero attributable mortality for this disease  
No more warning messages of this kind are given for other age/gender/disease groups*

If excess mortality is zero, in many cases a negative attributable mortality will be calculated, as in case of a zero attributable mortality in those cases a small positive excess mortality would be present, because those with disease have a worse risk factor pattern than those without the disease. DYNAMO-HIA assumes that in this case the user requests a zero attributable mortality instead of a zero excess mortality, and sets the attributable mortality to zero.

See technical report “detailed model specification, section **3.3.4**, under **Estimation in case excess mortality is zero**

*100% of the initial population has disability due to at least one disease. Therefore it is not possible to estimate the disability from other (not modelled) diseases. This is made 0 (no disability from other diseases)*

*This warning is give for age [a ]and gender[s] and riskgroup [r]*

*No more warnings of this kind will be generated for other risk, age and gender groups*

All persons in the population have at least one modeled disease and therefore it is not possible to estimate the disability (dalyweight) in persons without any disease (as such persons are not present in the population). Persons without any disease (not present at baseline) are all assumed to be perfectly healthy. As it is unlikely that nobody in the population is free of disease, this warning might indicate a inconsistency in the input data.

### **Errors generated by the simulation**

*Incidence and mortality data are unrealistically high for cluster [c] containing disease [XX] and risk factor value [Y].*

The algorithm used to calculate transitions fails. This mostly occurs because risk factor values (of continuous risk factors) became unrealistically high due to errors in the drift or because of errors in the relative risks given to the model. This might indicate an inconsistency in the input data.



The simulation you are running needs more memory than it allowed to have. See the “Running DYAMO-HIA.exe” item on page 96 for how to increase the amount of memory available as a possible solution for this problem.

### Errors generated by the postprocessing module

*" not enough simulated information to calculate scenario [X]. No simulated information on changing riskfactor class from[a] into class [b]*

DYNAMO simulates a scenario in which only the initial prevalence changes by simulating every person under all possible changes in the scenario. (see section 4.3 of the detailed model specification). This error indicates a problem with reconstructing the scenario population from the separate simulated populations.

This message should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that causes the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting “bug in DYNAMO-HIA” in the subject of the message.

*no simulated individuals with riskclass Name and duration [X] in simulation,  
while the prevalence of this riskclass is [xx] for age [a] and gender [s]*

The DYNAMO model does not have any simulated persons in a particular risk class, while there should be such persons as they are present in the “real” population.

This message should not occur when the DYNAMO-HIA model has been used as intended. However, if .xml files have been generated outside the DYNAMO-HIA user-interface, errors made can cause this message. If it occurs in other situations, we would appreciate an E-mail including the file that causes the problem and the full error message to [hendriek.boshuizen@rivm.nl](mailto:hendriek.boshuizen@rivm.nl), putting “bug in DYNAMO-HIA” in the subject of the message.

## ***Appendix D. Frequently Asked Questions***

In this section we given an overview of frequently asked questions from users of DYNAMO.

### **General**

Q: When I click on the names in the explorer tree nothing happens

A: In the DYNAMO program menus appear on *right* clicking only

### **Running DYNAMO-HIA.exe (on Windows XP)**

Q: I want to have some technical background about the software.

A: The DYNAMO-HIA program has been developed using the Java programming language.

Its graphical user interface is based on the Eclipse Rich Client Platform.

WinRun4J has been used to make starting the program easy in Windows and provide icons and JFreeChart has been used for making the output plots.

The software runs on a standard Java Virtual Machine and minimally needs version 1.6 (it is configured to only accept this version). The parameters that are passed to the JVM can be found in the DYNAMO-HIA.ini file that can be found in the same directory as DYNAMO-HIA.exe.

Their lines start with “vmarg.” and they are all about memory:

**-Xms128M**                      Means initially 128 Megabytes of memory are made available for the application.

**-Xmx1024M** Means 1024 Megabytes is the maximum amount the program is allowed to take.

**-XX:MaxPermSize=128M** Means a certain sort of Java memory may not exceed 128 Megabytes.

When you want to run simulations that need more space than the standard configuration allows you may increase the number after `-Xmx`. Under Windows XP the maximum allowed amount of memory is 3 Gigabytes (approx. 3000 Megabytes) and because Windows needs memory as well setting it above 2048M is not a good idea. The amount of physical memory is important. When the amount of required memory exceeds the available physical memory Windows starts making “virtual” memory. This memory space is created by writing the content of a part of the used physical memory to the hard disk and reusing that physical memory. It is nice to have more space, but the price is usually very high: When the content has to be reloaded another part of memory has to be swapped out to hard disk and that process takes orders of magnitude more time than using physical memory. In practical terms: Your simulation will run extremely slow if its memory use (plus Windows’s memory footprint) exceed physical memory.

## Java heap space

Q: When I run a simulation I get the following popup screen:



A: The simulation you are running needs more memory than it allowed to have. See the “Running DYAMO-HIA.exe” on page 96 item above for how to increase the amount of memory available as a possible solution for this problem.

### **Reference Data Screens**

Q: How can I change the risk factor class which has duration dependent relative risks?

A: You can not change this class anymore. This is because otherwise relative risk files that could already have been entered are not usable anymore. However you can make a new risk factor with another class as the duration class, and import the prevalence and transition rates for this risk factor from the old version of the risk factor.

### **Simulation Screen**

Q: I can not choose a risk factor that I have entered in the reference data

A: Risk factors can only be chosen as they have been completely defined in the reference data section. For risk factors this means that there must be minimally a valid prevalence file and a valid transition file present.

Q: I can not choose a disease that I have entered in the reference data

A: Diseases can only be chosen as they have been completely defined in the reference data section. For disease this means that there must be minimally valid prevalence, incidence, excess mortality and dalyweights files present.

Q: I can not chose the right transition or prevalence file name on the scenario tab

A: The first reason for this might be that model does not allow you to chose both the transition file and the prevalence file to be equal to that on the reference tab. So this  
Sometimes version 1.0 does not refresh the dropdown lists

### **Output screen**

Q: On the “change scenario settings” tab I do not see any sliders and buttons to change the scenario

A: These sliders and buttons are only present when one or more an alternative scenario has be requested. When only the “business as usual” (reference) scenario is run, no such buttons are present, as they only apply to alternative scenarios