



The SIMPATY economic analysis tool: User Guide



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The SIMPATY economic analysis tool: User Guide

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2. Introduction to SIMPATHY

Inappropriate polypharmacy is a major public health issue that needs to be addressed with increasing prevalence of multiple morbidity, particularly in the elderly. The overarching aim of SIMPATHY (Stimulating Innovation Management of Polypharmacy and Adherence in The Elderly) is to stimulate and support innovation across the EU in the management of polypharmacy and adherence in the elderly, with a specific focus on addressing inappropriate polypharmacy by delivering the necessary change management approaches and tools to help manage multi-medication and adherence to prescribed drugs.

Introducing such a change is not easy and will require new ways of working together with public and political acceptance that such a change is important (Moore, 1997). Delivery of such a change will need political and clinical leadership. Kotter's steps can be used to set out the need for change, a vision of what the change will look like and why delivering the change will be important, particularly setting out the sense of urgency for the change (Kotter International, 2017). Setting out the scale of the problem in terms of the economic costs of polypharmacy is an important factor that can help create the sense of urgency in a financially constrained

climate. As work is undertaken to address polypharmacy, it is also important to be able to quantify the economic benefits of the work and report these as quick wins and benefits of the change.

The Economic Analysis Tool introduced by SIMPATHY is intended to add to the package of change management tools provided by the SIMPATHY project. Other tools in the package include templates for PESTEL (Political, Economic, Social, Technological, Environmental and Legal) and SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis and a guidance on how to conduct these. As part of PESTEL and SWOT analyses, the economic factors that will influence the ability to implement a polypharmacy review policy are considered. However, these centre around the overall macro-economic conditions of a region (country) which might impact on policy; the Economic Analysis Tool adds to the package by offering a bespoke analysis of the micro-economic impacts, the costs and benefits of introducing and carrying out reviews. It is thought that this will give a broad overview around resource needs and potential benefits to interested users.

3. Introduction to the Economic Analysis Tool

The economic analysis tool (the tool) provides a simple analysis of the economic costs and benefits associated with carrying out polypharmacy reviews (reviews). The analysis follows the logic outlined in Diagram 1: Activity is driven by the selected population for whom reviews are intended to be carried out; the population can be selected from country geographic area, by age group and sex. The selected group can be further stratified according to their risk of admission or re-admission to hospital. The selected activity therefore represents the maximum number of reviews that would need to be carried out to cover the entire group, and the model estimates maximum costs and benefits based on this.

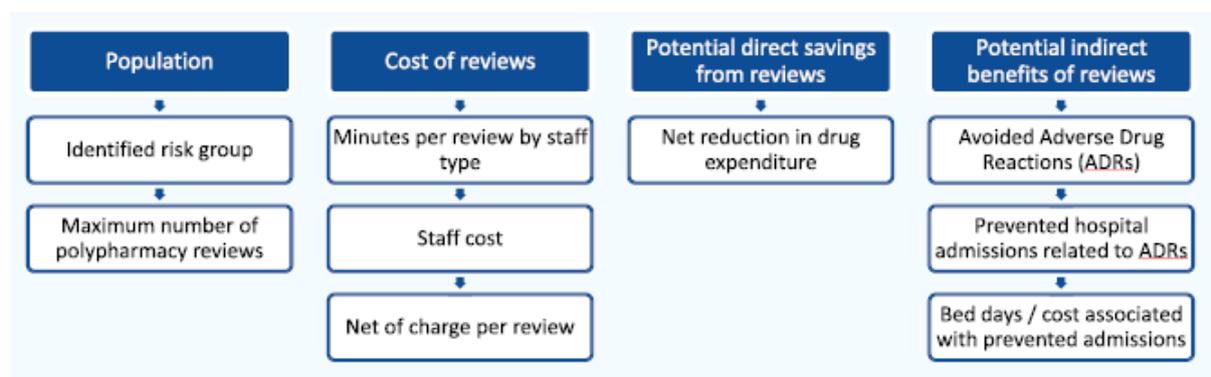
The costs of carrying out the reviews are based on the required time needed by different types of clinicians to carry out individual components of a review, and associated staff cost. This gives a unit cost per review which is then

applied to the selected population group for a maximum total cost, and which can be netted of any review charge that is going to be taken per review.

The direct potential financial benefit of reviews will consist of the net reduction in drugs prescribed (measured in Daily Defined Dose, DDD), and associated expenditure. This is estimated as the net of DDDs started and DDDs stopped per review, and the associated prevented number of repeat prescriptions.

Potential indirect benefits are estimated based on assumptions from Pirmohamed et al (2004), and centre around potentially avoided Adverse Drug Reactions (ADRs), preventable hospital admissions associated with these ADRs, and the associated number of hospital bed days avoided. Appendix A discusses the literature around ADRs and preventable hospital admissions and the decision making process that led to the choice of assumptions in the tool.

Diagram 1: Logic underlying the economic analysis tool



The tool also provides a trend analysis to 2030 in accordance with the SIMPATHY vision, with a simple

exponential autoregressive projection of the selected population by age band into the future. The estimated change

(increase or decrease) in the selected population group to 2030 is applied to the estimated costs and benefits to give a crude overview of how costs and benefits would change to 2030. Note that this is necessarily driven by the change in population, i.e. a 10% increase in the selected population would imply a 10% increase in associated costs and benefits.

As part of the analysis simulation was carried out on some of the key variables in the model, to test the sensitivity around some of the assumptions in the model. Key results for the Scottish case study are presented in Section 8.

It is important to note at this point that not all of the estimated **costs and benefits are necessarily cash releasing** and are estimating the **potential productive opportunity** instead.

The costs that can be cash releasing are the costs of the medicines stopped and reduced, if there had otherwise been a payment if these had carried on as per the baseline. However, the benefits of avoided admissions due to the reduction in inappropriate prescribing should be seen as capacity release and therefore a productive opportunity in the system.

4. Assumptions and caveats

The model is built on an earlier model which informed the original and revised Scottish Polypharmacy Guidances in (2012) and (2015). Since it is built on the Scottish model of review set-up, there will be some limitations as to the flexibility around review set-up and target population. E.g., the model allows for time allocation of four broad types of clinical staff: Primary Care Doctors, Other Doctors, Pharmacists, and Nurses. If there are other staff types involved in local review set-ups, then concessions would need to be made and their allocated time and cost would need to be merged with an existing category.

Likewise, not every region or country will have a risk stratification mechanism such as the Scottish SPARRA¹ (Scottish Patients at Risk of Readmission or Admission) database, and broad assumptions will need to be made around the risk profile of the selected population group. Within the SPARRA algorithm the risk of admission or readmission increases with the number of (high risk) drugs that patients are prescribed, hence the choice of this mechanism as a selection tool.

The model also works with the highest level aggregates of cost, such as an average cost per prescription, an average cost per staff type, and an average cost per inpatient bed day. There will of course be variation in these costs, depending on the distribution of drug costs associated with reviews, profile of staff carrying out reviews, etc.

¹ <http://www.isdscotland.org/Health-Topics/Health-and-Social-Community-Care/SPARRA/>

The model focuses only on direct savings from a net reduction in drugs prescribed, and potential indirect benefits of avoided hospital admissions. There will be numerous other clinical benefits to reviews, such as improved overall health and wellbeing of the patient, drugs optimisation, potential Quality Adjusted Life Years (QALYs) gained, and even prevented deaths from prevented ADRs. These are discussed in broader terms in the SIMPATHY project, but do not feature in this economic analysis.

In calculating the net reduction in drugs prescribed for the Scottish basis, it is currently assumed that a straight translation can be made from individual item prescribed to Daily Defined Dose (DDD). I.e., a net reduction in 1 item prescribed with all its repeats would be equivalent to a reduction of 1 DDD for one year. This is assuming that repeats and doses are following prescription and DDD guidance.

The model also provides a snapshot view of costs and benefits (plus a population trend analysis), i.e. the maximum costs and benefits are set out against each other at one point in time. In reality, the set of reviews will be carried out over a period of time and some of benefits, such as avoided repeat prescriptions and avoided future hospital admissions will occur over the medium to long term.

Also, most of the estimated indirect benefits are based on assumptions from one key paper in the literature (Pirmohamed (2004), see above). There is arguably uncertainty around the applicability of the results from one study onto the entire population of

EU28, which is the main reason that a simulation analysis around these parameters is offered. An assumption is made around the ADRs that are avoidable based on the parameters by (Pirmohamed, et al., 2004) and what proportion of these are avoided by polypharmacy reviews. This proportion can be adjusted in the model to give more or less conservative estimates.

Importantly, and as discussed above, the estimated **costs and benefits are not necessarily cash releasing** and are estimating the **potential productive opportunity** instead. Where polypharmacy reviews are intended to be implemented as part of clinicians' core activity, the time cost associated with that activity would already be covered by the allocated staff cost. However, there might be a case of one clinician type (e.g. a

pharmacist) freeing up the capacity of another clinician (General Practitioner). Similarly, benefits are measured in terms of cost avoidance and preventative potential: A net reduction in drug cost can be cash releasing if future designated payments are reduced or avoided, as well as having the potential for avoided additional costs; a potential future reduction in hospital admission represents the potential future cost that could be avoided (and capacity that could be released).

Tables with a full description of the underlying data and parameters, and the assumptions made around these can be found in Appendix B. A system of equations underlying to economic model is presented in Appendix C.

5. How to use the tool

The main tab for the tool is the 'Summary' tab. When clicking on the button 'Set parameters', the user will

be presented with a set of choices for the parameters outlined in the background note above.

The screenshot shows a 'Parameters' dialog box with the following settings:

- Core Variables:**
 - Population sample: Apply country specific population (dropdown)
 - Country: Scotland (dropdown)
 - Population group: Total (dropdown)
 - Age range: Minimum 65, Maximum 80 (spinners)
- Risk Stratification:**
 - Include Risk Stratification?: Yes (checkbox)
 - if yes, choose Risk Stratification model: Apply Scottish risk profile (dropdown)
- Review setup:**
 - Review setup: Apply Scottish review set-up (dropdown)
 - Staff cost: Apply Scottish profile for staff cost (dropdown)
 - Charge per review: No charge for reviews (dropdown)
 - DDD's stopped / started: Apply Scottish profile for DDD's stopped / started (dropdown)
- Health System Variables:**
 - Average annual cost per DDD: Apply Scottish profile for annual cost per DDD (dropdown)
 - Admission rates: Apply Scottish profile for admission rates (dropdown)
 - Inpatient cost per bed day: Apply Scottish profile for cost per bed day (dropdown)
 - Assumed % of avoidable ADRs avoided through PPH reviews: 60 (text input)

The key element to setting the parameters is choosing the population, by choosing the country region, and selecting the minimum and maximum age bands and sex of the population group that is to be considered for polypharmacy reviews.

The subsequent set of choices follows the same pattern for each parameter:

- choose the Scottish model profile
- choose and enter own data

The model has been set up in this way as data for most variables are not available for each of the EU28 countries. In that case, the user has the option to apply Scottish parameters to his/her selected population, as an approximation of what the costs and benefits in his/her

area might look like; or locally available data can be entered via the data entry forms that can be opened on the main user form.

The subsequent sets of parameters to be determined are:

- First, an option to choose whether a **risk stratification** should be applied to the selected population group, i.e. narrowing down the selection to those identified as at risk of admission to hospital.
- If risk stratification is applied, choose which **risk profile** should be used.
- Choose **review setup options**, including the minutes spent per review by different staff types, staff cost, the anticipated average number of drugs stopped and started per review and subsequent avoided repeats, and an option to impose a charge per review in order to recoup some or all of the cost

- Next, the set of **'health system variables'** offers choices on average drug cost, admission rates, average cost per inpatient bed day (and which type of inpatient admission is used)

Upon clicking 'OK' the tool will automatically estimate the costs and benefits for the selected group, and results are displayed on the 'Summary' tab, along with overall figures of what the chosen parameters would imply across all EU28 countries.

Some of the key results are displayed in diagrams on the tab 'charts'.

The tab 'trend analysis' offers the population based trend to 2030 for the overall costs and benefits estimated as outlined above.

6. Data capture

This feature gives the user the option to capture the results for the combination of parameters set, before changing the parameters. By clicking the button 'record data' on the 'Summary' tab, this will automatically record all choice parameters, input parameters and outputs onto the tab

'Data collection'. Each time the button 'record data' is clicked, another column of data will be added to data collection. This will build a table of cross-sectional data to enable further analysis of various combinations of inputs, if required.

7. Case studies from SIMPATHY consortium countries

7.1 Case study 1 – Scotland

The following set of tables and diagrams provide a case study for Scotland, with a selected population of all persons aged 65 to 80, and include

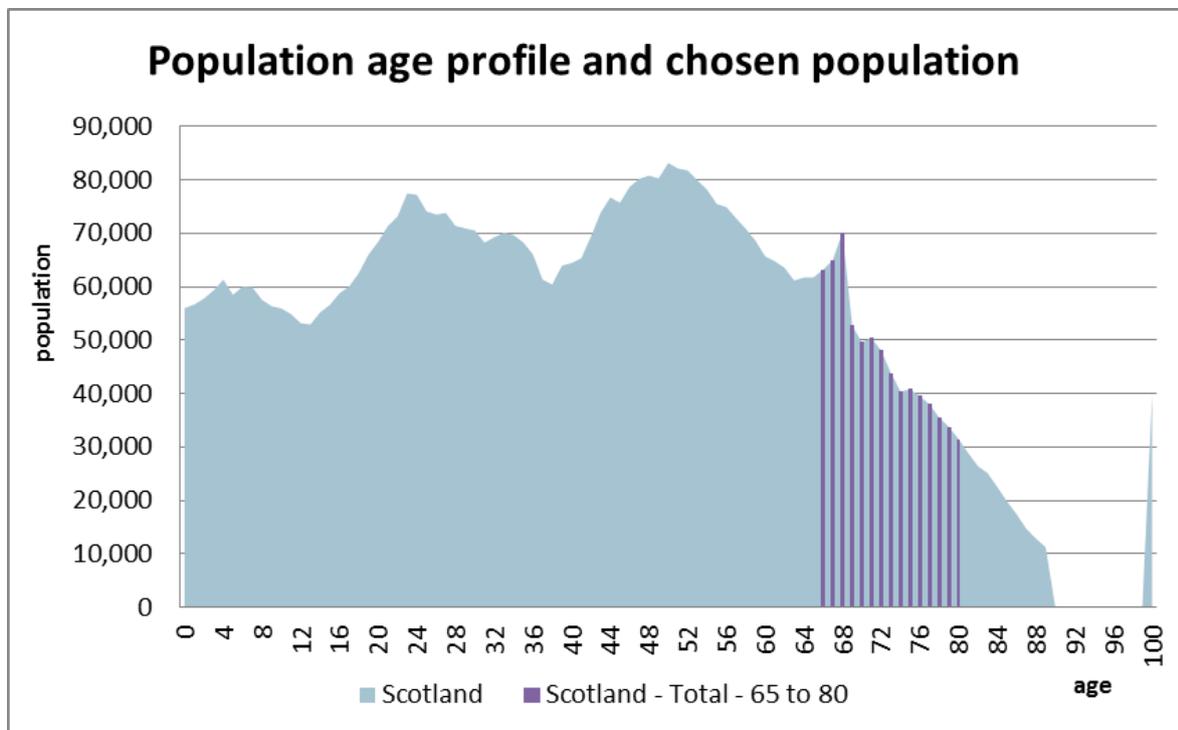
risk stratification according to the Scottish SPARRA profile.

Key parameter selection and population summary

Note that Scottish population data (National Records of Scotland) are recorded for single year of age up to

and including 90 years old, with an additional category of 90+.

Region		Scotland		
Population sex (M/F/Total)		Total		
Population age group		Minimum	Maximum	
		65	80	
No risk stratification		Risk stratification		
BNF10+		BNF10+ & High Risk Med	BNF 5-9 & High Risk Med	BNF 5-9 & High Risk Med
702,559	32,453	31,693	36,807	35,495



Review costs – Minutes and cost per review

The next set of tables show the review set-up, with minutes per review and per staff type needed and the total

associated cost based on staff cost per minute.

Have we not reviewed figure we have for GP time?

Minutes per review	Minutes	Cost per review	€
GPs (Primary Care Doctors)	30.00	GPs (Primary Care Doctors)	€ 30.76
Other doctors	0.00	Other doctors	€ 0.00
Pharmacists	75.00	Pharmacists	€ 47.31
Nurses	0.00	Nurses	€ 0.00
		Total	€ 78.07

Total WTE and cost of reviews, if carried out for entire selected population

results for the number of WTE required of each staff type to conduct reviews for the selected population, and the associated costs.

Based on the selected population and review set-up, the following tables give

WTE required	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
GPs (Primary Care Doctors)	213	10	10	11	11
Other doctors	0	0	0	0	0
Pharmacists	532	25	24	28	27
Nurses	0	0	0	0	0

Total cost of reviews	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
	€m	€m	€m	€m	€m
Total cost of reviews	€ 54.85	€ 2.53	€ 2.47	€ 2.87	€ 2.77
Review charge reclaimed	€ 0.00	€ 0.00	€ 0.00	€ 0.00	€ 0.00
Net total cost of reviews	€ 54.85	€ 2.53	€ 2.47	€ 2.87	€ 2.77

Drug cost avoided

table shows the potential avoided drug cost from reviews.

Based on the underlying assumptions in the Scottish model, the following

Avoided drugs cost	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
	€m	€m	€m	€m	€m
Drugs cost avoided (DDDs)	€ 150.87	€ 6.97	€ 6.81	€ 7.90	€ 7.62

Indirect Benefits

Hospital admissions

The following table shows the number of hospital admissions associated with ADRs in the selected population, and the estimated proportion of those

admissions that could be definitely and possibly avoidable (using assumptions based on (Pirmohamed, et al., 2004)) and an assumption that 60% of these avoidable ADR related admissions can be attributed to the polypharmacy reviews carried out.

Hospital admissions	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
Hospital admissions associated with ADRs 95% confidence interval	13,359 (12742, 14181)	2,151 (2052, 2283)	1,865 (1779, 1980)	2,250 (2146, 2388)	1,918 (1829, 2036)
Proportion of ADRs definitely avoidable through PPH, based on central admission estimate 95% confidence interval (based on central admission estimate)	721 (561, 802)	116 (90, 129)	101 (78, 112)	121 (94, 135)	104 (81, 115)
Proportion of ADRs possibly avoidable through PPH, based on central admission estimate 95% confidence interval (based on central admission estimate)	5,050 (4809, 5290)	813 (774, 852)	705 (671, 738)	850 (810, 891)	725 (690, 759)

Bed days

Based on the average length of stay per hospital admission in Scotland, the following tables show the associated

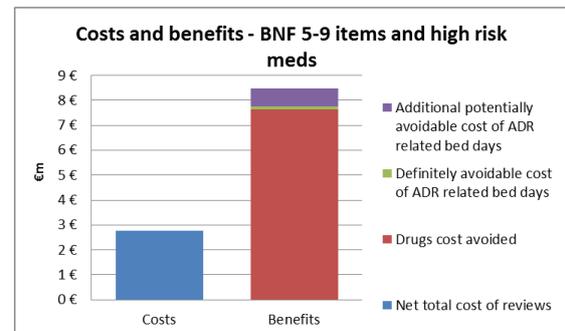
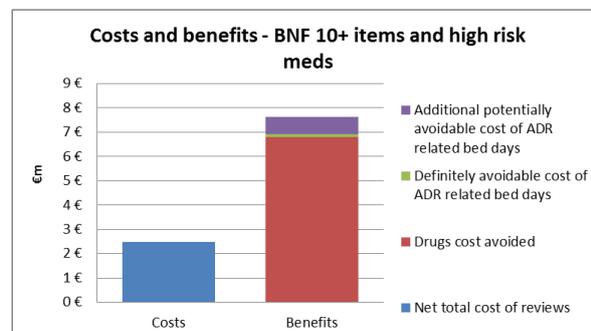
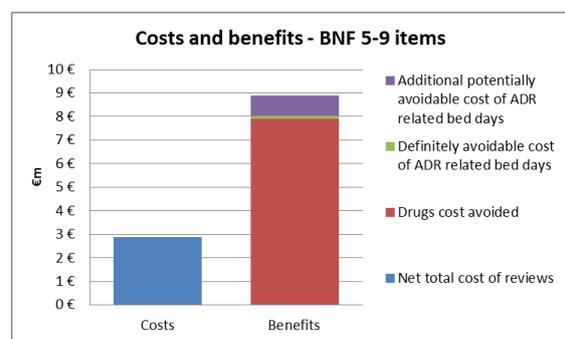
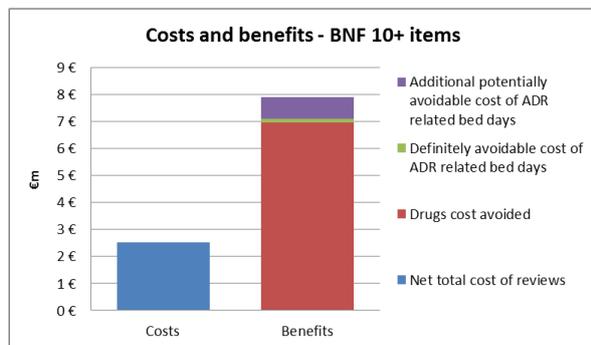
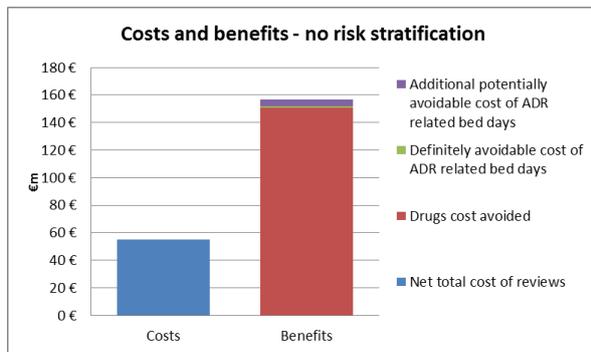
number of bed days and the bed day cost that could be avoided given the above.

Bed Days (BD)	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
BD associated with ADR related hospital admissions, based on central admission estimate	41,413	6,668	5,781	6,974	5,945
BD associated with definitely avoidable ADR related hospital admissions through PPH, based on central admission estimate	2,236	360	312	377	321
BD associated with central estimate of potentially avoidable ADR related hospital admissions through PPH	15,654	2,520	2,185	2,636	2,247

Cost of Bed Days (CBD)	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
		€m	€m	€m	€m
CBD associated with ADR related hospital admissions, based on central admission estimate	€ 15.49	€ 2.49	€ 2.16	€ 2.61	€ 2.22
CBD associated with definitely avoidable ADR related hospital admissions through PPH, based on central admission estimate	€ 0.84	€ 0.13	€ 0.12	€ 0.14	€ 0.12
CBD associated with central estimate of potentially avoidable ADR related hospital admissions through PPH	€ 5.85	€ 0.94	€ 0.82	€ 0.99	€ 0.84

The set of diagrams show the costs and benefits for the different risk groups. In each case the costs of carrying out the reviews are

outweighed by the direct and indirect benefits of avoided drug cost and avoided admissions.



7.2 Case study 2 – Northern Ireland

The following set of tables and diagrams provide a case study for Northern Ireland (NI), with a selected population of all persons aged 65 to 99, and include risk stratification by

superimposing the average Scottish SPARRA profile for the population group onto NI population data.

Key parameter selection and population summary

Region	Northern Ireland			
Population sex (M/F/Total)	Total			
Population age group	Minimum	Maximum		
	65	99		
No risk stratification	Risk stratification			
	BNF10+ & High Risk Med	BNF10+ & High Risk Med	BNF 5-9 & High Risk Med	BNF 5-9 & High Risk Med
	304,000	4,059	3,932	4,932
				4,682

Note that, as the regional population data for NI was inputted manually, an age profile by single year of age cannot be given.

Review costs – Minutes and cost per review

The next set of tables show the review set-up, with minutes per review and per staff type needed and the total associated cost based on staff cost per minute.

Minutes per review	Minutes	Cost per review	€
GPs (Primary Care Doctors)	20.00	GPs (Primary Care Doctors)	€ 20.51
Other doctors	0.00	Other doctors	€ 0.00
Pharmacists	75.00	Pharmacists	€ 47.31
Nurses	0.00	Nurses	€ 0.00
		Total	€ 67.81

Total WTE and cost of reviews, if carried out for entire selected population

Based on the selected population and review set-up, the following tables give

results for the number of WTE required of each staff type to conduct reviews for the selected population, and the associated costs.

WTE required	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
GPs (Primary Care Doctors)	61	1	1	1	1
Other doctors	0	0	0	0	0
Pharmacists	230	3	3	4	4
Nurses	0	0	0	0	0

Total cost of reviews	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
	€m	€m	€m	€m	€m
Total cost of reviews	€ 20.62	€ 0.28	€ 0.27	€ 0.33	€ 0.32
Review charge reclaimed	€ 0.00	€ 0.00	€ 0.00	€ 0.00	€ 0.00
Net total cost of reviews	€ 20.62	€ 0.28	€ 0.27	€ 0.33	€ 0.32

Drug cost avoided

Based on the underlying assumptions adjusted for the case of NI, the

following table shows the potential avoided drug cost from reviews.

Avoided drugs cost	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
	€m	€m	€m	€m	€m
Drugs cost avoided (DDDs)	€ 96.00	€ 1.28	€ 1.24	€ 1.56	€ 1.48

Indirect Benefits

Hospital admissions

The following table shows the number of hospital admissions associated with ADRs in the selected population, and the estimated proportion of those admissions that could be definitely and

possibly avoidable (using assumptions based on (Pirmohamed, et al., 2004)), NI admission rate data, and an assumption that 40% of these avoidable ADR related admissions can be attributed to the polypharmacy reviews carried out.

Hospital admissions	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
Hospital admissions associated with ADRs 95% confidence interval	6,916 (6597, 7342)	92 (88, 98)	89 (85, 95)	112 (107, 119)	107 (102, 113)
Proportion of ADRs definitely avoidable through PPH, based on central admission estimate 95% confidence interval (based on central admission estimate)	249 (194, 277)	3 (3, 4)	3 (3, 4)	4 (3, 4)	4 (3, 4)
Proportion of ADRs possibly avoidable through PPH, based on central admission estimate 95% confidence interval (based on central admission estimate)	1,743 (1660, 1826)	23 (22, 24)	23 (21, 24)	28 (27, 30)	27 (26, 28)

Bed days

Based on NI data for average length of stay and bed day costs, the following

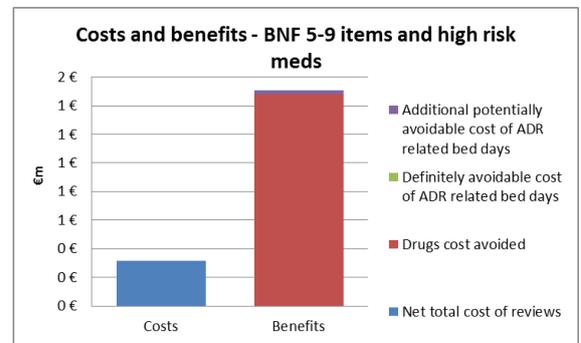
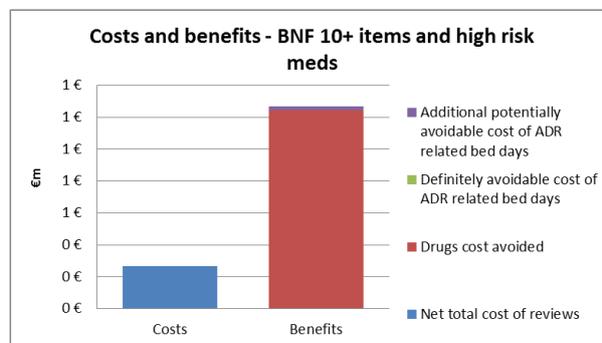
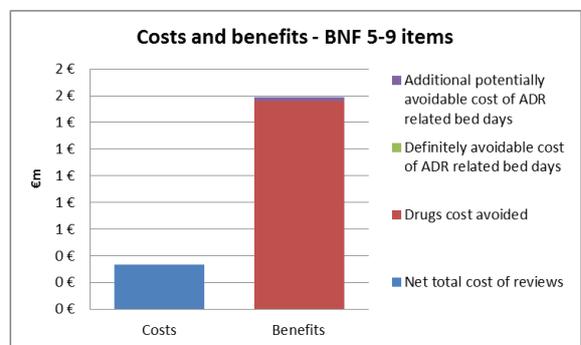
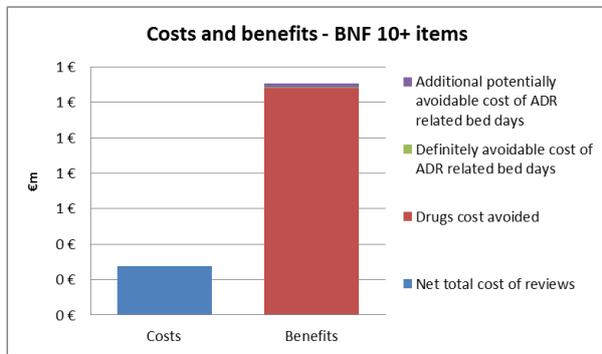
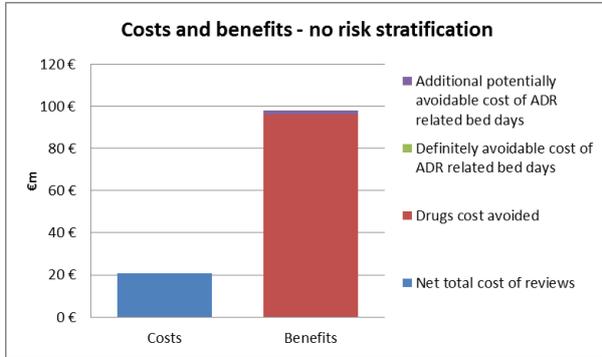
tables show the associated number of bed days and the bed day cost that could be avoided given the above.

Bed Days (BD)	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
BD associated with ADR related hospital admissions, based on central admission estimate	21,440	286	277	348	330
BD associated with definitely avoidable ADR related hospital admissions through PPH, based on central admission estimate	772	10	10	13	12
BD associated with central estimate of potentially avoidable ADR related hospital admissions through PPH	5,403	72	70	88	83

Cost of Bed Days (CBD)	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
	€m	€m	€m	€m	€m
CBD associated with ADR related hospital admissions, based on central admission estimate	€ 29.75	€ 4.68	€ 4.06	€ 4.89	€ 4.17
CBD associated with definitely avoidable ADR related hospital admissions through PPH, based on central admission estimate	€ 1.61	€ 0.25	€ 0.22	€ 0.26	€ 0.23
CBD associated with central estimate of potentially avoidable ADR related hospital admissions through PPH	€ 11.24	€ 1.77	€ 1.53	€ 1.85	€ 1.58

The set of diagrams show the costs and benefits for the different risk groups. In each case the costs of carrying out the reviews are

outweighed by the direct and indirect benefits of avoided drug cost and avoided admissions.



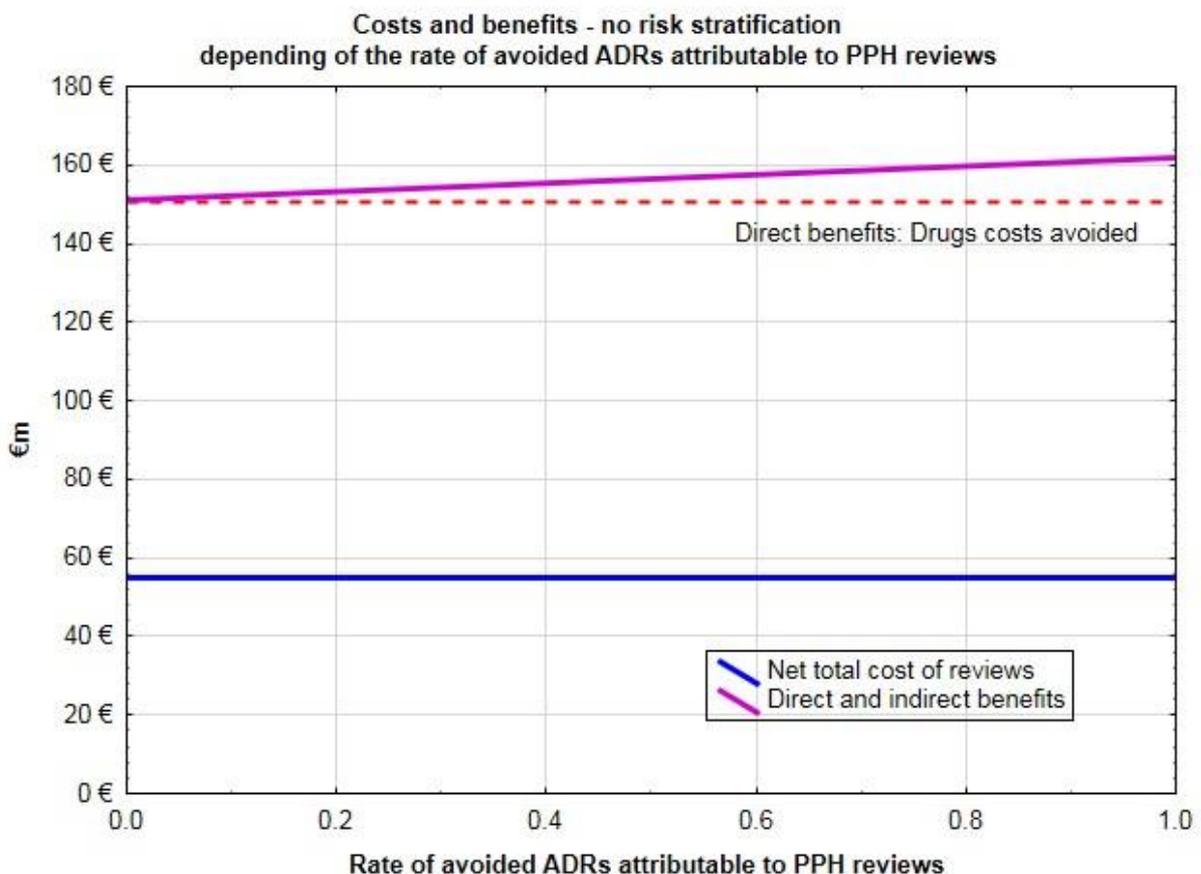
8. Simulation results and testing

The main goal of the simulations is to compare the results for different assumptions which have to be made when using the Economic Analysis Tool. These assumptions are normally based on results from single studies (see (Pirmohamed, et al., 2004)).

To deal with these uncertainties simulations are performed to compare the different results of a range of different assumptions. For every simulation process 1,000 data points were used within a specific range. The software package SPSS Version 24.0 was applied for the simulation programs. Samples of the results were used to test the validity and accuracy of the Economic Analysis Tool.

For the first simulation process the data from Case Study 1 (Scotland) was used with no risk stratification for the chosen population. Only the proportion of avoided ADRs attributable to PPH reviews (ADR_{PPH}) was varied within the range of 0.001 to 1.0, all other values remained constant.

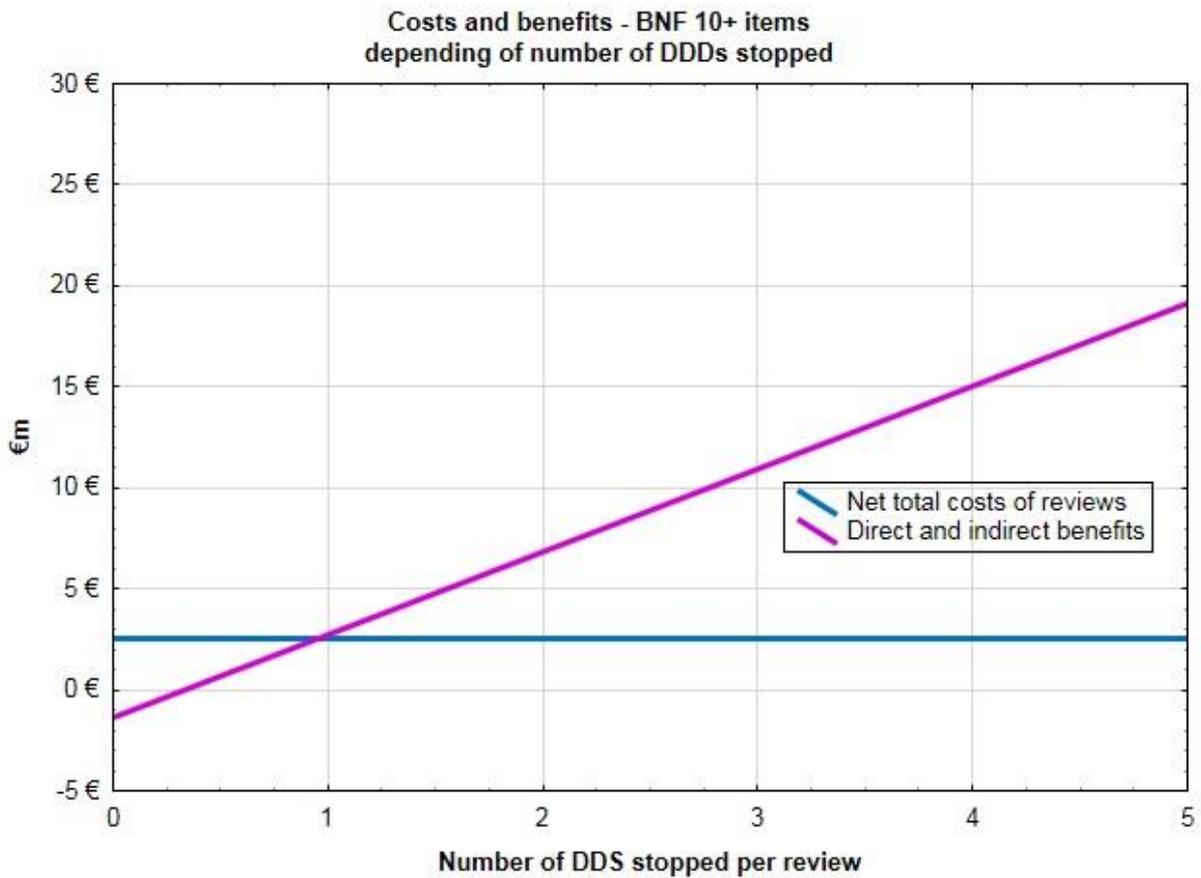
ADR_{PPH} only has an effect on the indirect benefits; therefore a moderate increase in total benefits can be seen in the following graphics. Main parts of the total benefits are the avoided drugs costs.



The second simulation process is also based on the data of case study 1 (Scotland) with the risk stratification for BNF 10+ items on the chosen population.

Here the number of DDDs stopped is varied between 0.01 and 5 while all other values remained constant including the number of DDDs begun after the review (0.4).

The total benefits have a negative value for smaller values of DDDs stopped, because the net decrease DDD per review is negative. At the value of one DDD stopped the total benefits (direct and indirect benefits) exceed the net total costs of reviews (see following graphics).



9. Literature sources

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10. Appendix A – Adverse Drug Reactions and Preventable Hospital Admission: Rapid review of literature post 2006

Most of the estimated indirect benefits in the tool are based on assumptions from (Pirmohamed, et al., 2004) (see above). Pirmohamed et al (2004) conduct a prospective analysis of all admissions to hospital for 18,820 patients to ascertain the current burden of adverse drug reactions (ADRs). They find 1225 admissions related to an ADRs, giving a prevalence of 6.5% (CI, 6.2% to 6.9%), with the ADR directly leading to the admission in 80% of cases. The median bed stay was eight days (interquartile range 4 to 18 days), accounting for 4% of the hospital bed capacity. The overall fatality observed was 0.15% (CI, 0.1% to 0.2%). The authors deem that most reactions were either definitely (9% (CI, 7%-10%)) or possibly (63% (CI, 60%-66%)) avoidable. Overall, they classify 72% of ADRs avoidable.

There is arguably uncertainty around the applicability of the results from one study onto the entire population of EU28, and a rapid review of recent literature was undertaken to compare the findings of (Pirmohamed, et al., 2004) with more recent literature, focussing on systematic reviews and meta analyses undertaken on the issue of preventable Adverse Drug Reactions. However, most of the subsequent reviews reference (Pirmohamed, et al., 2004) or retain the study as one of the selected studies in systematic reviews. It is the study that has by far the biggest underlying sample size and its estimates lie within the range of other studies' findings. It was therefore decided to continue with the results

from (Pirmohamed, et al., 2004) for the tool.

In a systematic review, Howard et al (2006) estimate the percentage of preventable drug-related hospital admissions, as well as the most common drug causes of preventable hospital admissions and the most common underlying causes of preventable drug-related admissions. They find that the median percentage of preventable drug-related admissions to hospital was 3.73% (range 1.36–15.42).

Davies et al (2007) conduct a narrative review of recent literature on epidemiology and adverse drug reactions in hospitals and evaluate the research undertaken to date on preventing ADRs. They cite (Pirmohamed, et al., 2004) and (Howard, et al., 2003) With their findings of about 6.5% of patients being admitted to hospital whilst experiencing an ADR. They also note that this figure is two and a half times that estimated by (Wiffen, et al., 2002) although that review's estimate was based mainly on North American literature, where the ADR rate appears to be about half that of Europe (Wiffen, et al., 2002) as quoted in (Davies, et al., 2007).

A systematic review by Thomsen et al (2007) estimates the incidence and describes characteristics of preventable adverse drug events (pADE) in ambulatory care. They find that the median ADE incidence was 14.9 (range 4.0–91.3) per 1000 person-months, and the pADE

incidence was 5.6 per 1000 person-months (1.1–10.1). The median incidence of ADEs requiring hospital admission was 0.45 (0.10–13.1) per 1000 person-months, and the median incidence of pADEs requiring hospital admission was 4.5 per 1000 person-months. As these findings are given in rates per 1000 person-months, they are not directly comparable with other estimates of ADR or preventable ADR, however, the study also reports a median ADE preventability rate of 21% (11–38%).

In their systematic review of studies that are exclusively observational, Kongkaew et al (2008) determine the prevalence of hospital admissions associated with ADRs and examine differences in prevalence rates between population groups and methods of ADR detection. They find the prevalence rates of ADRs to range from 0.16% to 15.7%, with an overall median of 5.3% (interquartile range [IQR] 2.7–9.0%). Median ADR prevalence rates varied between age groups; for children, the ADR admission rate was 4.1% (IQR 0.16–5.3%), while the corresponding rates for adults and elderly patients were 6.3% (IQR 3.9–9.0%) and 10.7% (IQR 9.6–13.3%), respectively. They attribute the higher overall median rate of ADRs of 5.3% compared to previous studies (including (Wiffen, et al., 2002)) to their focus on prospective observational studies that have used a well-established and consistent ADR definition.

Taché et al's (2011) systematic review of the prevalence of Adverse Drug Events in Ambulatory Care also estimates the proportion of preventable ADEs, compares data for different age groups including children, adults, and elderly patients; and reviews drug classes most commonly

associated with ADEs. The median ADE prevalence rate for retrospective studies was found to be 3.3% (interquartile range [IQR] 2.3-7.1%) vs 9.65% (IQR 3.3-17.35%) for prospective studies. Median preventable ADE rates in ambulatory care-based studies were 16.5%, and 52.9% for hospital-based studies. Median prevalence rates by age group ranged from 2.45% for children to 5.27% for adults, 16.1% for elderly patients, and 3.45% for studies including all ages.

Tsang et al (2012) determine the types of adverse events that are routinely recorded in primary care. They find that approximately 6.5% of adult emergency admissions were due to drug-related events and that between 0.7% and 2.3% of deaths following adverse events were attributed to treatment in primary care. They also stipulate that a large proportion of adverse events resulting in the most severe harm may be preventable.

The systematic review by Hamid et al (2013) investigates the prevalence, causes and major risk factors for Medicine Related Problems (MRPs) leading to hospitalisation in adult patients and identifies the main medicine classes involved. The median prevalence rates of hospitalisation resulting from ADRs, adverse drug events and MRPs were 7% (interquartile range, 2.4–14.9%), 4.6% (interquartile range, 2.85–16.6%) and 12.1% (interquartile range, 6.43–22.2%), respectively. The major causes contributing to MRPs were adverse drug reactions and non-compliance. In addition, the major risk factors associated with MRPs were old age, polypharmacy and comorbidities.

11. Appendix B – data used, parameters, and assumptions made

Data type	Source	Country	Accessed	File name	File link
Population data	Eurostat data	All	19/07/2016	demopjan	http://ec.europa.eu/eurostat/web/population-demography-migration-projections/population-data/database
Population data	NRS Scotland data	Scotland	19/07/2016	table 2	http://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates/mid-2015-and-corrected-mid-2012-to-mid-2014/list-of-tables
Population data	NRS Scotland time series data	Scotland	02/09/2016	table 1	http://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates/population-estimates-time-series-data
Prescription cost data	ISD prescription cost analysis	Scotland	20/07/2016	Jul-16	http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Publications/data-tables.asp?id=1693#1693
Scottish Salary data	AfC salaries	Scotland			HSCA workforce team data
Scottish Salary data	GP salary	Scotland	20/07/2016		https://www.bma.org.uk/advice/employment/pay/general-practitioners-pay
Bed day cost	Cost per bed day	Scotland	25/07/2016	R040	http://www.isdscotland.org/Health-Topics/Finance/Costs/File-Listings-2015.asp
Risk of Admission data	Scottish Patients at Risk of Readmission or Admission data	Scotland	12/09/2016		data request to ISD SPARRA team
Inpatient emergency admissions into General Medicine	ISD hospital data - inpatient and day case activity	Scotland	15/02/2017		http://www.isdscotland.org/Health-Topics/Hospital-Care/Inpatient-and-Day-Case-Activity/
Exchange rates	XE.com	All	03/03/2017		http://www.xe.com/

Parameter overview			
Parameter	Variable type	Variable explanation	Assumptions made
Core Variables			
Population sample	choice / input var	Select either own population sample or pre-set country level population for EU28 or Scotland	Model takes a 'top-down' approach and subsequent variables are applied to total selected population to give estimates of maximum resulting costs / benefits
Geographic Region	choice var	if Country level population chosen, select country	
Age group	choice var	select min / max age group in sample	
sex	choice var	select male / female / total	
Risk stratification			
Risk stratification	choice var	choose whether to apply risk stratification yes / no	
Risk of admission / re-admission	choice / input var	if yes, choose either own blanket risk of admission, or Scottish risk profile for selected population. No data currently for EU28 country setup	Admission risk for Scotland based on algorithm of previous admission history and patient characteristics for different risk groups (different levels of drug prescriptions). Assumption that risk stratified population groups will be impacted on most by PPH reviews

Polypharmacy review setup			
Review setup	choice / input var	Staff types involved with PPH reviews. Choose either own setup with own data input (hours per staff type per activity per review), or Scottish setup. No data currently for EU28 country setup	
Staff cost	choice / input var	Wage cost of staff involved with PPH reviews. Choose either own setup with own data input (annual WTE cost per staff type), or Scottish setup. No data currently for EU28 country setup	In Scotland, reviews are no longer paid by Local Enhanced Service and are part of regular clinician activity. Costs are therefore not additional to overall wage bill and can be seen as opportunity cost. Option to add in travel time and associated staff cost, but not currently including patient time cost.
Charge per review	choice / input var	Choose whether charge per review is applicable (recouping cost per review). Choose yes / no and own input if yes. Not applicable to Scotland and no data currently for EU28 country setup	
DDDs stopped / started	choice / input var	determine average DDDs stopped / started per review. Choose either own setup with own data input, or Scottish setup. No data currently for EU28 country setup	

Health System Variables			
Average annual cost per DDD	choice / input var	Determine average annual cost per DDD to be used. Choose either own input, country specific data, or Scottish data. EU28 country data partially complete (OECD)	
Admission rates	choice / input var	Determine admission rates to be applied to selected population group. Choose own blanket rate applied across entire selected population, or Scottish profile based on SPARRA data. No data currently for EU28 country setup	
Inpatient cost per bed day	choice / input var	Choose between own data input cost per bed day, or Scottish cost. No data currently for EU28 country setup	

Indirect model parameters			
Cost type for inpatient cost	currently fixed to General Medicine Gross direct cost per bed day		
assumed ADR rate associated with stratified population	fixed var	currently based on results of British study, Pirmohamed et al (2004)	most of the estimated indirect benefits based on assumptions from one key paper in the literature. uncertainty around the applicability of the results from one study onto the entire population of EU28
assumed rate of definitely avoidable ADRs	fixed var		
assumed rate of possibly avoidable ADRs	fixed var		
hospital admissions associated with ADRs	fixed var		
assumed proportion of avoidable ADRs avoided through polypharmacy reviews	choice / input var	Imposes what proportion of avoidable ADRs is assumed to be avoided due to a PPH review	PPH reviews will be one of the contributing factors leading towards avoidable ADRs and hospital admissions, but assumptions have to be made around what proportion this factor will take up in local circumstances.
assumed Length of Stay (LOS), bed days per hospital admission	fixed var	based on recent Scottish data (ISD), to give a more up-to-date estimate than the median used by Pirmohamed et al (2004)	

12. Appendix C – System of equations underlying the economic model

Cost of reviews

Constants

$$\text{Staff minutes per year} = SM = \text{work days per yr} \times \text{work hrs per day} = 220 \times 7.5$$

$$\text{Reclaimed review charge} = RRC$$

Variables

$$\begin{aligned} \text{Clinician Type} = CT_i \text{ [for all } i = 1, 2, \dots, n] \text{ where} \\ 1 = GP; \\ 2 = nurse; \\ 3 = \text{community pharmacist, etc} \end{aligned}$$

$$\begin{aligned} \text{Activity (in minutes)} = A_j \text{ [for all } j = 1, 2, \dots, n] \text{ where} \\ 1 = \text{patient review}; \\ 2 = \text{discussion between CT}; \\ 3 = \text{discussion with patient}; \\ 4 = \text{CT travel time} \end{aligned}$$

$$\text{Population (chosen, with or without risk stratification)} = P$$

Formulae

$$\text{Cost per CT per minute} = CTM_i = \frac{\text{annual WTE cost for CT}}{SM} \text{ for all } i$$

$$\text{Activity per review} = AR_i = \sum_{j=1}^n CT_i \times A_j$$

$$\text{Cost per review} = CR_i = \sum_{i=1}^n (CTM_i \times AR_i) - RRC$$

$$\text{Total activity (staff minutes required)} = TA = P \times AR_i \text{ for all } i$$

$$\text{Total cost} = TC = P \times CR_i$$

$$\text{WTE required} = WTE = \frac{P \times AR_i}{SM} \text{ for all } i$$

Direct benefits - drugs saved

Constants

Total Daily Defined Doses for country, per annum (in millions) = DDD

Sales value = SV

Both currently fixed at Scottish levels

$$\text{Annual cost per DDD} = C_{DDD} = \frac{DDD \times SV}{1,000,000}$$

Variables

DDD stopped or decreased per review = DDD_S

DDD begun or increased per review = DDD_B

Population (chosen, with or without risk stratification) = P

Formulae

Net DDD decreased per review = DDD_N = D_S - D_B

Potential savings per review per annum = SPA = DDD_N - C_{DDD}

Total drugs savings for population = TDS = P × SPA

Indirect benefits – avoided hospital admissions

Constants

Adverse Drug Reactions (ADRs) accounting for % hospital admission = ADR_{HA}

Propn of ADRs definitely avoidable = ADR_{DA}

Propn of ADRs possibly avoidable = ADR_{PA}

Bed days (average length of stay) = ALOS

Cost of a bed day = C_{BD}

Variables

Proportion of avoided ADRs attributable to PPH reviews = ADR_{PPH}

Population (chosen, with or without risk stratification) = P

Formulae

$$\text{Hospital Admissions associated with ADRs} = HA_{ADR} = P \times ADR_{HA}$$

$$\begin{aligned} \text{Hospital Admissions definitely avoidable through reviews} &= HA_{DA} \\ &= ADR_{DA} \times ADR_{PPH} \times HA_{ADR} \end{aligned}$$

$$\begin{aligned} \text{Hospital Admissions possibly avoidable through reviews} &= HA_{PA} \\ &= ADR_{PA} \times ADR_{PPH} \times HA_{ADR} \end{aligned}$$

$$\text{Bed days associated with } HA_{ADR} = BD_{ADR} = ALOS \times HA_{ADR}$$

$$\text{Bed days associated with } HA_{DA} = BD_{DA} = ALOS \times HA_{DA}$$

$$\text{Bed days associated with } HA_{PA} = BD_{PA} = ALOS \times HA_{PA}$$

$$\text{Cost of } BD_{ADR} = CBD_{ADR} = C_{BD} \times BD_{ADR}$$

$$\text{Cost of } BD_{DA} = CBD_{DA} = C_{BD} \times BD_{DA}$$

$$\text{Cost of } BD_{PA} = CBD_{PA} = C_{BD} \times BD_{PA}$$

Net benefits – Direct Costs and Benefits only

$$\text{Net Direct Benefit} = NDB = TDS - TC$$

Net benefits – Direct costs, direct benefits and indirect benefits

$$\begin{aligned} \text{Total Net Benefit} &= TNB = TDS + (CBD_{DA} + CBD_{PA}) - TC \\ &= NDB + (CBD_{DA} + CBD_{PA}) \end{aligned}$$