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Discussion Paper

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value of further research? A
review of methods used to
estimate uptake in population
expected value of information
analyses**

[Sabine Grimm](#), [Simon Dixon](#), [John W Stevens](#)

DP 13/15

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Are we over-estimating the value of further research? A review of methods used to estimate uptake in population expected value of information analyses

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Abstract

Background: There is a lack of guidance on how population estimates should be obtained for expected value of information (EVI) analysis. We argue that disregarding uptake may lead to over-estimation of the population EVI (PEVI).

Aims: To investigate how population estimates for PEVI analyses were obtained, whether they were adjusted by uptake and what methods were employed to obtain the uptake estimates.

Methods: A literature search and review was conducted using the NHS Economic Evaluation Database (EED) and prior knowledge of relevant publications. Publications were excluded when they did not report PEVI estimates or were duplicates.

Results: Out of 43 records resulting from the CRD search and 3 relevant publications that were known to us prior to this study, 29 studies were included. Out of these, 27 had not adjusted their population estimate by uptake levels. The remaining 2 studies had obtained their uptake estimates from uptake levels reported in trials and based on assumption. Only 5 studies acknowledged uncertainty associated with the population estimate used.

Conclusion: Based on the result that very few PEVI studies had adjusted their population estimate by uptake and taking into account the large downward effect that uptake adjustments could have on the value of PEVI estimates, there is a need for discussion and further research around uptake adjustments in PEVI analyses.

Keywords

Expected Value of Information, EVI, VOI, Uptake, Implementation, Health Technology Assessment

Background

There is a lack of guidance on how population estimates should be obtained for expected value of information (EVI) analysis. The EVI is used in economic evaluations to assess the value of reducing decision uncertainty through further research. To obtain the overall value that can be derived from research in a health system or society, the EVI is then often aggregated over the population that may potentially benefit and the time horizon that research may be relevant to, resulting in the population EVI (PEVI). While there has been some discussion on what time horizon to apply in EVI analyses (Philips, Claxton et al. 2008), methods of obtaining population estimates are less clear.

We argue here that disregarding uptake may lead to over-estimation of PEVIs. Not all patients will benefit from research on a new intervention as technology uptake may be low. This has previously been acknowledged by Fenwick, Claxton et al. (2008). Furthermore, technology implementation is rarely an instantaneous process resulting in 100% of uptake in the period after research results became available. A variety of NICE implementation uptake reports suggest that health technologies in the British National Health Service diffuse gradually over time (see for instance NICE (2010) or NICE (2009)). Adjusting the PEVI by uptake estimates of static or, ideally, dynamic nature would therefore result in more realistic estimates of the value of further research.

Complexity is added through the potential inter-dependence between uptake and information. Uptake may be dependent on the level of information available to adopters and therefore be larger (or smaller) with perfect information than with less than perfect information. This has been discussed previously by Hoomans, Fenwick et al. (2009). In such a setting, two uptake estimates or curves would be needed for current and perfect information.

With this background, the objective of this research was to investigate how population estimates for EVI analyses were obtained and whether uptake estimates or dynamics were used and what methods of obtaining them were employed. We therefore conducted a review of PEVI analyses with the following research questions in mind: how was the population estimate obtained? Was the population estimate adjusted by uptake? How was the estimate of uptake obtained? Was the issue of uncertainty associated with the population estimate discussed?

Methods

The search was conducted using the NHS Economic Evaluation Database (EED). Search terms were: ((Value of Information) OR EVI OR VOI). Titles and abstracts were screened and publications excluded when they did not report PEVI analyses or in the event of duplicates. Full texts of the included publications were then reviewed according to the research questions. Additional PEVI analyses that were known to us but did not come up through this small-scale search were also included.

Results

The NHS CRD search resulted in 43 hits. The titles and abstracts of all results were screened and 10 publications were excluded as no EVI analysis had been performed and another 4 were excluded as no population EVI had been reported. Another publication was excluded because it resulted from an analysis already described in another included publication. One publication stated that EVI analysis had been conducted but did not detail methods or results and instead referenced another publication. Hence, the former was excluded and the latter included. For 2 other publications, full texts could not be obtained and they were therefore excluded. Three additional publications with EVI analyses that had not come up through this search but were known to us from elsewhere were included.

We therefore included a total of 29 publications and examined them with regards to the research questions. Results are shown in detail in Table 1 in the appendix and are described below.

In 27 out of the included 29 publications, the population size was not adjusted by uptake of the intervention. In those analyses, the population estimate was mainly obtained through the incidence and prevalence of the condition or the number of annual procedures. An uptake level of 100% was implicitly assumed in those cases.

Only 2 studies had adjusted the population estimate by uptake. One of these, on thrombo-prophylaxis in post-hip replacement patients, acknowledged the dependence of uptake on information and reported 2 different estimates of uptake: one conditional on perfect information and one for current information (McCullagh, Walsh et al. 2012). The uptake estimate for perfect information was obtained from a trial that had reported the proportion of patients receiving American College of Chest Physicians recommended prophylaxis and, for the current information scenario, an assumption was made.

The second study used an uptake estimate which was obtained from a trial that had reported the use of trastuzumab adjuvant to chemotherapy in early stage breast cancer (Hall, Hulme et al. 2011). Neither

of the two studies had used a dynamic estimate of uptake or accounted for uncertainty associated with it.

Five studies mentioned the issue of uncertainty associated with the population estimates in their PEVI analysis; four in their discussion and one implicitly by reporting different PEVI results with varying population estimates. In 1 of the 5 studies, it was stated that implementation of research results may not automatically happen after they became available and further exploration of this topic was recommended. None of the 5 studies, however, fully accounted for uncertainty by modelling the population estimate probabilistically.

Discussion

Our review has shown that the majority of EVI analyses do not consider uptake adjustments in their population estimates. The implication is that most reported values for the PEVI are likely to be an over-estimate of the actual value of further research as low uptake causes the population benefitting from further research to be smaller than the potentially eligible population.

As the PEVI is viewed as an upper ceiling to the value of further research, assuming an uptake level of 100% is not wrong per se. It could simply be argued that this reflects the value of further research in a best-case and full uptake scenario. It should, however, be highlighted that this value might never be reached due to barriers to implementation. In cases where an uptake level of 100% is unachievable, potentially due to strong competition or other barriers, ignoring uptake from the PEVI estimate would result in a drastic over-statement of the value of further research and therefore have the potential to mislead decision-makers.

With this study, we would like to spark a discussion on the need for adjusting population estimates by uptake. In the case that research is technology-specific and the level of uptake of that technology is foreseen to be below 100%, we think it essential to acknowledge this in the development of PEVI estimates. We also think that further research is needed on how uptake estimates can be obtained to inform such analyses.

Limitations of this study include the small scope of the search. It is improbable that all PEVI analyses in health technologies have been captured with the adopted search strategy and there may be further examples out there that incorporated uptake estimates in their analysis. We do think, however, that with 27 out of 29 analyses estimating the population without an uptake adjustment and none including uptake dynamics, our findings are fairly representative of common practice and can be used as the basis for this discussion.

Further research could include, firstly, a broadening of the review and secondly, exploring and developing methods to include uptake estimates in PEVI analysis. The former could be achieved by broadening the search to other databases which would likely lead to inclusion of more PEVI analyses. The inclusion of related methodology papers could also be considered. We do not, however, anticipate a significant change in results.

As for exploring how to include uptake estimates in PEVI studies, we see two main areas of research. One is to address the question of how uptake estimates of both, static and dynamic nature, can be obtained. The two studies in this review that had used uptake estimates had obtained them from available trials and assumed that this level of uptake would hold throughout the time horizon adopted. Other ways of obtaining uptake estimates may include modelling future uptake probabilistically, with probability distributions obtained from using elicitation of expert opinions. As technology implementation is regarded as a dynamic process, there is further research potential on the way a dynamic uptake model could be estimated.

More scope for further research is seen in the modelling implications of incorporating uptake into PEVI analysis. As was highlighted above, uptake levels may depend on information and, for instance, differ from current to perfect information. It is not unthinkable that, conversely, information may be dependent on uptake in that further research would only be conducted if patients are using an intervention. Exploring the modelling of such inter-dependencies between uptake and information provides potential direction for further research.

In conclusion, we think that based on the result that very few PEVI studies had adjusted their population estimate by uptake and taking into account the large downward effect that uptake adjustments could have on the value of PEVI estimates, there is a need for discussion and further research around uptake adjustments in PEVI analyses.

Appendix

Table 1. Review of PEVI analyses and the role of uptake in population estimates

Entry number	Author (Year)	Condition	Comparators	Population estimate based on:	PEVI uptake-adjusted?	Uptake level or pattern used	Uptake estimate based on:	Issue of uncertainty around population estimate discussed?
1	McCullagh, Walsh et al. (2012)	Prophylaxis of venous thromboembolism after hip replacement	Rivaroxaban, dagibatran etexilate, enoxaparin sodium	THR procedures in acute public hospitals in Ireland and uptake	Yes	a) 64% for perfect information, b) 50% for current information	a) Trial that reported proportion of patients receiving American College of Chest Physicians recommended prophylaxis, b) assumption	It was acknowledged that population estimates for PEVI were themselves subject to uncertainty, however this was not explored.
2	Welton, Ades et al. (2008)	Low uptake of breast cancer screening	Do nothing, send letter, flag in patient record, letter and flag	Women eligible for screening	No	100% (implicitly)	-	-
3	Fleurence (2007)	Two case studies: 1. risk of fracture in osteoporosis patients and 2. pressure ulcers	1. Hormone replacement therapy, bisphosphonates, vitamin D with or without calcium, hip protectors, 2. High-spec foam mattress, alternating pressure mattresses and overlays	Number of patients entering the decision in each year	No	100% (implicitly)	-	The implementation of research results will not automatically follow the logical implications of the cost-effectiveness evidence and should therefore be explored further in EVI analysis.
4	Pandor, Eastham et al. (2004)	Neonatal screening for inborn errors of metabolism	Neonatal tandem mass spectrometry, no treatment	Number of neonates per annum	No	100% (implicitly)	-	-
5	Soares, Welton et al. (2012)	Severe sepsis and septic shock	Adjuvant intravenous immunoglobulin, current care	Incidence	No	100% (implicitly)	-	-
6	Hall, McCabe et al. (2012)	Early stage lymph node positive breast cancer	Oncotype DX 21-gene assay directed chemotherapy, chemotherapy for all	Incidence	No	100% (implicitly)	-	-
7	Gurusa my, Wilson et al. (2012)	Gallbladder and common bile duct stones (CBD)	Intra-operative versus pre-operative endoscopic sphincterotomy (ES)	Number of patients with laparoscopic cholecystectomy with CBD stones and the number of ES performed each year	No	100% (implicitly)	-	-

Entry number	Author (Year)	Condition	Comparators	Population estimate based on:	PEVI uptake-adjusted?	Uptake level or pattern used	Uptake estimate based on:	Issue of uncertainty around population estimate discussed?
8	Pham, Teague et al. (2011)	Pressure ulcers in elderly patients admitted through emergency departments	Pressure re-distributing foam mattresses, standard hospital mattresses	Elderly admitted emergency department patients in Ontario	No	100% (implicitly)	-	-
9	Purmonen, Pankalainen et al. (2011)	Human epidermal growth factor Receptor 2 (HER2)-positive early breast cancer	Adjuvant trastuzumab, conventional treatment after chemotherapy	Number of HER2-positive breast cancer patients	No	100% (implicitly)	-	-
10	Nosyk, Sharif et al. (2011)	Influenza in patients with human immunodeficiency virus	Three influenza vaccine dosing strategies, previous dosing strategy	Prevalence of HIV positive individuals in Canada	No	100% (implicitly)	-	-
11	Hall, Hulme et al. (2011)	Human epidermal growth factor Receptor 2 (HER2)-positive early breast cancer	Adjuvant trastuzumab, conventional treatment after chemotherapy	Annual incidence of breast cancer and rate of over-expression of HER2 and uptake	Yes	67%	Estimates of use of chemotherapy with adjuvant trastuzumab from a study	-
12	Petrou, Dakin et al. (2010)	Otitis media with effusion	Topical intranasal steroids, no treatment	Number of children potentially eligible based on a trial	No	100% (implicitly)	-	-
13	Wilson, Gurusa my et al. (2010)	Acute cholecystitis	Early versus delayed laparoscopic cholecystectomy	Number of laparoscopic cholecystectomy per annum	No	100% (implicitly)	-	-
14	Eddama, Petrou et al. (2010)	Pre-term birth in twins	Progesterone gel, no treatment	Estimated number of twin pregnancies per annum	No	100% (implicitly)	-	-
15	Stevens on, Scope et al. (2010)	Post-natal depression (PND)	Group Cognitive Behavioural Therapy, routine care	Annual incidence of PND	No	100% (implicitly)	-	-
16	Genders, Meijboom et al. (2009)	Suspected coronary artery disease	Computer-tomographic coronary angiography prior to conventional angiography, conventional coronary angiography	Incidence	No	100% (implicitly)	-	-

Entry number	Author (Year)	Condition	Comparators	Population estimate based on:	PEVI uptake-adjusted?	Uptake level or pattern used	Uptake estimate based on:	Issue of uncertainty around population estimate discussed?
17	Bansback, Ara et al. (2009)	Rheumatoid arthritis (RA)	Statin therapy in addition to conventional treatment, conventional treatment	Number of RA patients	No	100% (implicitly)	-	-
18	Ramsey, Blough et al. (2008)	Emphysema	Lung-volume reduction surgery, medical treatment	Number of procedures per annum	No	100% (implicitly)	-	Acknowledged that there was uncertainty associated with the number of procedures but did not address this in the model.
19	Wailoo, Sutton et al. (2008)	Influenza	Amantadine, zanamivir, oseltamivir	Influenza attack rate in healthy population and rate of influenza like illness	No	100% (implicitly)	-	Acknowledged uncertainty associated with the population estimate but did not address this in the model.
20	Singh, Nosyk et al. (2008)	Patients with chest discomfort presenting to emergency department	Early Disposition Prediction Rule, standard care	Number of individuals presenting to emergency departments with chest discomfort each year	No	100% (implicitly)	-	EVPI was reported with different levels of incidence; implementation was not discussed.
21	Griebisch, Knowles et al. (2007)	Newborn screening for congenital heart defects	Clinical examination, pulse oximetry, echocardiography	Number of newborns	No	100% (implicitly)	-	-
22	Girling, Freeman et al. (2007)	End-stage heart failure	Left-ventricular assist device implantation vs. optimal medical management	Cases of ESHF per annum	No	100% (implicitly)	-	-
23	Colbourn, Asseburg et al. (2007)	Prevention of group B streptococcal and other bacterial infections in early infancy	Prenatal screening and treatment strategies	UK population	No	100% (implicitly)	-	-
24	Wight, Chilcott et al. (2003)	Preserving kidneys prior to transplantation	Pulsatile machine perfusion, cold storage	Transplant population	No	100% (implicitly)	-	-
25	Maheswaran and Barton (2012)	Tuberculosis in HIV infected individuals	9 different screening strategies in combination with Isoniazid Preventative Therapy	Annual HIV incidence	No	100% (implicitly)	-	-

Entry number	Author (Year)	Condition	Comparators	Population estimate based on:	PEVI uptake-adjusted?	Uptake level or pattern used	Uptake estimate based on:	Issue of uncertainty around population estimate discussed?
26	McKenna, Walker et al. (2012)	Post-myocardial infarction (MI) heart failure	Eplerenone, spironolactone	Prevalence and incidence of post-MI heart failure	No	100% (implicitly)	-	-
27	Mohseni nejad, van Baal et al. (2013)	Prevention of depression	Opportunistic screening and contact psychotherapy, no screening	Prevalence of subthreshold depression	No	100% (implicitly)	-	-
28	Dallat, Hunter et al. (2013)	Quality of life and absenteeism from work	Monitoring physical activity at work, not monitoring	All current Northern Ireland employees	No	100% (implicitly)	-	-
29	Murphy, Fenwick et al. (2013)	Severe aortic stenosis	Transcatheter aortic valve implantation, medical management	Annual number of patients ineligible for surgery	No	100% (implicitly)	-	-

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