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Peri-operative pulse oximetry in low-income countries: a cost–effectiveness analysis

Samantha L Burn, a Peter J Chilton, a Atul A Gawande b & Richard J Lilford c

Objective To evaluate the cost–effectiveness of pulse oximetry – compared with no peri-operative monitoring – during surgery in low-income countries.

Methods We considered the use of tabletop and portable, hand-held pulse oximeters among patients of any age undergoing major surgery in low-income countries. From earlier studies we obtained baseline mortality and the effectiveness of pulse oximeters to reduce mortality. We considered the direct costs of purchasing and maintaining pulse oximeters as well as the cost of supplementary oxygen used to treat hypoxic episodes identified by oximetry. Health benefits were measured in disability-adjusted life-years (DALYs) averted and benefits and costs were both discounted at 3% per year. We used recommended cost–effectiveness thresholds – both absolute and relative to gross domestic product (GDP) per capita – to assess if pulse oximetry is a cost–effective health intervention. To test the robustness of our results we performed sensitivity analyses.

Findings In 2013 prices, tabletop and hand-held oximeters were found to have annual costs of 310 and 95 United States dollars (US$), respectively. Assuming the two types of oximeter have identical effectiveness, a single oximeter used for 22 procedures per week averted 0.83 DALYs per annum. The tabletop and hand-held oximeters cost US$ 374 and US$ 115 per DALY averted, respectively. For any country with a GDP per capita above US$ 677 the hand-held oximeter was found to be cost–effective if it prevented just 1.7% of anaesthetic-related deaths or 0.3% of peri-operative mortality.

Conclusion Pulse oximetry is a cost–effective intervention for low-income settings.

Abstracts in العربية, 中文, Français, Русский and Español at the end of each article.

Introduction

The pulse oximeter is a non-invasive medical device that monitors oxygen saturation and pulsation. When used continuously during surgery, it can provide early warning of hypoxia, hypovolaemia and impending cardiac arrest. Since oximetry can warn of problems such as misplaced endotracheal tubes – which can readily be rectified – the World Federation of Societies of Anaesthesiologists recommends its routine use for every patient undergoing anaesthesia in the world. 1, 2 The World Health Organization (WHO) includes pulse oximetry as a component of its Surgical Safety Checklist, which is recommended for use in every operating theatre. 3 However, it has recently been estimated that pulse oximetry is unavailable in 51–70% of operating theatres in low-income countries, 4 partly because of the high purchase cost of a standard commercial tabletop pulse oximeter – approximately 1000 United States dollars (US$). 5 The Lifebox oximetry project, which currently operates alongside the WHO Safe Surgery Saves Lives initiative, provides a hand-held pulse oximeter for low- and middle-income countries that costs US$ 250. 6 However, even this smaller sum is a considerable investment for resource-constrained settings. Furthermore, because no evidence of the cost–effectiveness of pulse oximetry for peri-operative monitoring in low-income countries has yet been published, it is not clear how oximetry should be prioritized among the many cost–effective interventions available. 7 In this paper, we conducted a cost–effectiveness analysis of pulse oximetry – compared with no peri-operative monitoring – for patients undergoing surgery in low-income countries. This study is based on a synthesis of data from previously published studies from a large number of different countries. While the group of low-income countries is heterogeneous, the analysis presented here is readily adaptable to specific national contexts.

Methods

We investigated the equivalent annual costs of purchasing and maintaining pulse oximeters, as well as the costs of increased oxygen flow used to treat any hypoxic episodes identified by oximetry. We took a health services perspective. In quantifying the health benefits of peri-operative oximetry, we considered the number of disability-adjusted life-years (DALYs) averted by using pulse oximetry to reduce the incidence of fatal intraoperative hypoxic episodes. We ignored non-fatal cases of hypoxic brain injury. Base case analysis was conducted using version 3.0.1 of the R software package (R Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel 2010 (Microsoft, Redmond, USA) and sensitivity analysis using the TreeAge Pro 2013 software package (TreeAge Software Inc., Boston, USA).

Costs

We only considered oximeters that met the IEC 60601-1, ISO 9919:2005 or ISO 80601-2-61:2011 international standards for safety and performance. There are two main types of stand-alone pulse oximeter designed for peri-operative use: the standard commercial tabletop oximeter and a less expensive hand-held device with similar functionality but a more portable and durable design and a rechargeable battery. 5

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The oximeter distributed by the Lifebox charity is of the second type.

Costs are given in 2013 prices and discounted at 3% per year – as recommended in version two of the Disease Control Priorities in Developing Countries and the WHO-CHOICE guidelines for evaluation of the cost–effectiveness of health interventions in developing countries. Domestic taxes were excluded. We assumed that no extra operations would be carried out as a result of introducing oximetry and that no extra clinical staff time would be required. We included supplementary oxygen – resulting from an increase in the incidence of detected hypoxia when oximetry is used.

Health benefits

Most of the published data on the performance of oximeters relate to tabletop oximeters. However, the low-cost handheld oximeter distributed by Lifebox has recently been found to perform as well as tabletop oximeters that have been produced by major manufacturers, made commercially available in the United States of America. For our analysis, we therefore assumed that the effectiveness of the hand-held devices in averting peri-operative death was identical to that of the tabletop devices.

Lifebox has found that the oximeters it distributes can be used for 25–30 surgeries per week. For our analysis, we assumed that each of the oximeters we investigated was used at about 80% of these frequencies – i.e. in 22 procedures per week.

Baseline mortality

We did a systematic search to identify systematic reviews of anaesthetic-related and total peri-operative mortality including studies from low-income countries published between 1 January 1990 and 31 December 2012. The search terms used included variants of anaesthetic, surgery, operation, intra-operative, peri-operative, peri-surgical, death, mortality and survival (Box 1). We searched the following databases: MEDLINE via OvidSP, EMBASE via OvidSP, Scopus, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the Health Technology Assessment Database and the International Prospective Register of Systematic Reviews. We used the Centre for Reviews and Dissemination filter (strategy 2.1) to identify systematic reviews. No language restrictions were applied.

Two systematic reviews of anaesthetic-related and total peri-operative mortality that included studies from low-income countries were identified. Since it was the more recent of the two reviews and included a formal meta-analysis, we used the study by Bainbridge et al. to parameterize our cost-effectiveness estimates. This study found that total peri-operative mortality in low-income countries – i.e. countries with a human development index below 0.8 – was 2445 deaths per million procedures. They also found that, in low-income countries, problems in the administration of anaesthesia – e.g. oesophageal intubation or kinking of the endotracheal tube – were the sole or contributing cause of 467 deaths per million procedures. We took 467 deaths per million procedures as our baseline for deaths that were potentially preventable by oximetry. However, this may be a conservative estimate, since oximetry could also provide an early warning of a deterioration in the patient’s underlying condition that was unrelated to anaesthesia. Also, as oximetry may have been used in one or more of the studies investigated by Bainbridge et al., 467 deaths per million procedures may represent an underestimate of mortality in the absence of oximetry.

For robustness, we replicated the search procedure used by Bainbridge et al. to identify any recent studies of relevance that had been published on or before 30 December 2012. We found no new studies relating to low-income countries. We also examined the six studies that were excluded by Bainbridge et al. because of small sample size or because they pertained exclusively to one clinical area. Two of these studies contained estimates of anaesthetic-related avoidable mortality for a general population, which were 1985 and 7500 deaths per million procedures. In our sensitivity analysis, we therefore considered values of anaesthetic-related avoidable mortality that varied from 253 deaths per million procedures – i.e. the lowest estimate from the studies investigated by Bainbridge et al. – to 7500 deaths per million procedures.

Effectiveness in reducing mortality

The available data on the effectiveness of pulse oximetry come from observational studies – e.g. before-and-after studies or critical incident reports – and randomized controlled trials. In this context, such studies and trials are imperfect. Since peri-operative deaths are extremely rare, none of the relevant randomized controlled trials is adequately powered to detect the effects of oximetry on the probability of such deaths.

The relevant observational studies do not allow cause–effect statements to be made with confidence since such studies are confounded by temporal changes that are unrelated to oximetry.

We did a systematic search to identify systematic reviews of the effectiveness of oximetry in preventing hypoxia and peri-operative death published between 1 January 1990 and 31 December 2012 (Box 1). We searched the same set of databases as for baseline anaesthetic-related mortality. We identified one systematic review of randomized controlled trials of the effectiveness of pulse oximetry, in which the authors concluded that pulse oximetry reduces the incidence of hypoxaemia by 33–67% but appears

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Box 1. Search strategy for key parameters published in systematic reviews

**Baseline anaesthetic-related mortality**

1. Surgery[Mesh] OR surg* OR operat* OR perioperat* OR peri-operat* OR intraoperat* OR in-theatre
2. Anesthesia[Mesh] OR anesth* OR anaesth* OR peri-anesth* OR perianesth* OR post-anesth* OR post-anaesth*
3. Death OR mortalit* OR morbidit* OR survival*
4. (#1 OR #2) AND #3

**Effectiveness of pulse oximetry in reducing hypoxic episodes and/or peri-operative mortality**

1. Surgery[Mesh] OR surg* OR operat* OR perioperat* OR peri-operative OR intraoperat* OR in-theatre
2. Oximet* OR oxymet*
3. Death OR mortalit* OR morbidit* OR survival*
4. Anoxia[Mesh] OR anox* OR hypox*
5. (#1 AND #2) AND (#3 OR #4)
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to have no statistically significant effect on mortality.22 to check the robustness of this result, we reviewed the studies that were excluded because they were not randomized.22 these excluded studies25–27 that indicated a similar oximetry-attributable decline in hypoxaemia to that observed in the included studies. other observational data indicate that anaesthetic-related mortality in high-income countries has declined by 64% since the 1980s, as various monitoring standards, including pulse oximetry, have been widely implemented.14,28,29

while much of the evidence assembled relates to high-income countries, the results of a before-and-after study conducted in the republic of moldova

| parameter | point estimate (range) | data source(s) and assumptions |
|-----------|------------------------|-----------------------------|
| cost of purchase, shipping and internal transport, us$ | commercial tabletop device: 1065 (600–3000) | lifebox product information4 |
| life-span, years | commercial tabletop device: 6 (4–8) | expert opinion |
| | hand-held device: 8 (6–10) | probes for tabletop device replaced every 2 (1–3) years at a cost of us$ 1004. probes for hand-held device replaced every 2 (1–3) years at a cost of us$ 254 and batteries for hand-held device replaced every year at a cost of us$ 14 |
| | commercial tabletop device: 34 (17–85) | 15% (10–20%) chance of breakage of a tabletop device each year, at a total cost per year of us$ 355 including shipping.4,4 and batteries for hand-held device replaced every year at a cost of us$ 10 |
| | hand-held device: 18 (15–31) | 5% (1–10%) chance of breakage of hand-held device each year, at a total cost per year of us$ 65 during the first 2 years – when the device is under warranty – and us$ 138 thereafter4 |
| | commercial tabletop device: 45 (30–60) | authors’ calculations. uncertainty explored in sensitivity analysis |
| | hand-held device: 6 (2–13) | |
| annual cost of treating additional hypoxic episodes identified by pulse oximetry, us$ | commercial tabletop device: 35 (17–52) | |
| | hand-held device: 35 (17–52) | |
| total equivalent annual cost, us$ | commercial tabletop device: 310 | authors’ calculations. uncertainty explored in sensitivity analysis |
| | hand-held device: 95 | |

us$: united states dollars.

- all costs are shown adjusted to 2013 values, assuming 3% inflation per year.

- excludes share of general overhead costs attributable to use of pulse oximetry – i.e. costs of cleaning and electricity.

- value partly or entirely based on expert opinion.

# table 2. effectiveness and cost–effectiveness of pulse oximeters

| parameter | point estimate (range) | data source(s) and assumption |
|-----------|------------------------|-----------------------------|
| baseline anaesthetic-related mortality, deaths per million operations requiring general anaesthesia | commercial tabletop device: 467 (253–7500) | systematic review of anaesthetic-related mortality14 |
| anaesthetic-related deaths averted by oximetry, % | commercial tabletop device: 10 (3–50) | authors’ estimates based on intermediate outcomes from systematic review of randomized control trials22 and observational data14,28,29 |
| discounted dalys per death avoided | commercial tabletop device: 15.5 (10–30) | authors’ calculation based on approximation of age distribution of patients undergoing surgery16 and health-adjusted life expectancy by age17 |
| number of times each oximeter used per week | commercial tabletop device: 22 (20–30) | assumed 80% utilization8 of maximum capacity of 25–30 operations per week12 |
| discounted dalys per year of oximeter use | commercial tabletop device: 0.83 | authors’ calculation |
| equivalent annual cost of oximeter, us$ | commercial tabletop device: 310 | see table 1 |
| cost per daly averted, us$ | commercial tabletop device: 374 | authors’ calculation |

| parameter | point estimate (range) | data source(s) and assumption |
|-----------|------------------------|-----------------------------|
| baseline anaesthetic-related mortality, deaths per million operations requiring general anaesthesia | hand-held device: 467 (253–7500) | systematic review of anaesthetic-related mortality14 |
| anaesthetic-related deaths averted by oximetry, % | hand-held device: 10 (3–50) | authors’ estimates based on intermediate outcomes from systematic review of randomized control trials22 and observational data14,28,29 |
| discounted dalys per death avoided | hand-held device: 15.5 (10–30) | authors’ calculation based on approximation of age distribution of patients undergoing surgery16 and health-adjusted life expectancy by age17 |
| number of times each oximeter used per week | hand-held device: 22 (20–30) | assumed 80% utilization8 of maximum capacity of 25–30 operations per week12 |
| discounted dalys per year of oximeter use | hand-held device: 0.83 | authors’ calculation |
| equivalent annual cost of oximeter, us$ | hand-held device: 95 | see table 1 |
| cost per daly averted, us$ | hand-held device: 115 | authors’ calculation |

dalys: disability-adjusted life-year; us$: united states dollars.

- based on region-specific life-tables.

- from table 1, in 2013 values.

- in 2013 values.
indicated that the introduction of pulse oximetry – along with the entire WHO Surgical Safety Checklist – reduced the number of hypoxaemic episodes lasting at least two minutes by 44%. Another before-and-after study found that introduction of the checklist led to a 60% reduction in total peri-operative mortality over four study sites in low-income countries. However, the checklist contains several other items known to be associated with improved safety outcomes, so these reductions are probably not attributable to oximetry alone.

We selected 50% as the upper plausible limit for effectiveness of oximetry in reducing anaesthetic-related deaths, since this is the figure obtained using the surrogate outcome of hypoxic episodes in the randomized control trials described above. This a highly optimistic value, since surrogate outcomes are notorious for overestimating clinical benefit. We therefore used 50% as an upper bound for effectiveness. For a lower bound we selected a 2% improvement in anaesthetic-related mortality, to represent a very pessimistic estimate given the randomized control trials and observational evidence cited above. For the base case we used effectiveness of 10%, founded on the nature of the available evidence and based on discussion with our advisors. Since there is considerable uncertainty surrounding these values, we conducted extensive sensitivity analysis.

Disability-adjusted life-years averted

Health benefits were measured in DALYs averted, with uniform age-weighting and discounting at 3% per annum. DALYs were calculated using actual life expectancy rather than life expectancy for a hypothetical reference group. Using pooled health-adjusted life expectancy tables for the Eastern Sub-Saharan Global Burden of Disease region and a probability density function of the ages of patients undergoing major surgery in Mozambique, Uganda and the United Republic of Tanzania, we calculated that 15.5 DALYs are averted per anaesthetic-related death avoided.

We assumed that the sex distribution of patients was the same as that of the relevant national population. We also assumed that, in all cases of averted death, a patient’s health-adjusted life expectancy did not differ from that of the general population and that the benefits of pulse oximetry were too small to alter overall national life expectancies.

Cost-effectiveness thresholds

We used two common types of cost-effectiveness thresholds for health interventions in low-income countries: the absolute thresholds used by the World Bank in the World development report 1993 and the thresholds – defined relative to the corresponding gross domestic product (GDP) per capita – used by WHO-CHOICE. According to the World development report 1993, interventions that, in 1993, cost no more than US$ 25 and US$ 150 per DALY averted could be considered highly attractive and attractive, respectively. Assuming 3% inflation per year, the corresponding thresholds for the year 2013 would be US$ 45 and US$ 271. WHO-CHOICE considered interventions that, per DALY averted, cost no more than one and three times the relevant GDP per capita to be very cost-effective and cost-effective, respectively. For the group of low-income countries as a whole, US$ 677 and US$ 2031 are one and three times the 2013 GDP per capita, respectively.

Results

Our cost and cost-effectiveness estimates are summarized in Table 1 and Table 2, respectively. In the base case – comparing each type of oximeter with no monitoring of oxygen saturation and assuming both the tabletop and hand-held pulse oximeters reduce anaesthetic-related mortality by 10% – the costs per DALY averted were US$ 374 for the tabletop pulse oximeter and US$ 115 for the hand-held oximeter. Since we assume in this analysis that the effectiveness of the two types of oximeter is identical and the hand-held oximeter is less costly, the hand-held oximeter dominates the tabletop oximeter. The cost-effectiveness of the hand-held oximeter fell below the very cost-effective thresholds for the hand-held oximeter.
tive threshold of one times the GDP per capita for low-income countries.

The purchase of a hand-held oximeter for each of the 77,000 operating theatres globally that currently do not have pulse oximeters would cost about US$ 19.3 million. Using the parameters in this paper, we estimate that equipping all of these operating theatres with pulse oximeters would reduce the global burden of disease by 63,800 DALYs per year.

**Sensitivity analyses**

Given the paucity of trial data and the uncertainty surrounding the effectiveness of pulse oximetry in averting anaesthetic-related mortality, we explored the sensitivity of our results to variation in the key parameters.

Fig. 1 shows the cost per DALY averted as a function of the percentage of anaesthetic-related mortality prevented by pulse oximetry. The hand-held pulse oximeter falls below the attractive threshold for 2013 from the *World development report* 1993, if it prevents 4% of anaesthetic-related mortality. It falls below the GDP per capita of the group of low-income countries if it prevents 1.7% of anaesthetic-related mortality (0.3% of total peri-operative mortality). The wide variation seen in levels of anaesthetic-related and total peri-operative mortality between settings has an impact on the cost–effectiveness of pulse oximetry.14,16,17,41 Fig. 2 shows the cost of a hand-held pulse oximeter, per DALY averted, as a function of baseline anaesthetic-related mortality, assuming that pulse oximetry prevents 10% of anaesthetic-related deaths. With baseline anaesthetic-related mortalities of 25341 and 750017 deaths per million operations requiring general anaesthesia, a hand-held pulse oximeter would have cost US$ 211 and US$ 7 per DALY averted, respectively.

We conducted a basic probabilistic sensitivity analysis by carrying out 1000 iterations using the parameter distributions given in Table 3. The effectiveness of oximetry in averting death was assumed to be independent of baseline anaesthetic-related mortality. Although the median incremental cost–effectiveness was US$ 154 per DALY averted, the corresponding mean cost–effectiveness was much higher – US$ 628 – largely because of the small number of simulations with extremely low baseline mortality and effectiveness. The corresponding cost–effectiveness acceptability curve (Fig. 3) indicates that hand-held pulse oximeters are likely to be considered cost–effective – compared with no oximetry – with all but the most stringent cost–effectiveness threshold. Pulse oximetry fell under the WHO very cost–effective threshold in 83% of the simulations and under the attractive cost–effectiveness threshold from the *World development report* 1993 in 62% of the simulations. The results of the probabilistic sensitivity analysis should be interpreted with caution because of our uncertainty about the relationship between identified hypoxic episodes and mortality.

**Discussion**

Although this study is not entirely based on hard evidence from randomized controlled trials, our results indicate that pulse oximetry is cost–effective. Obtaining parameter estimates for a decision model is often difficult. In this case, the problem was compounded by a paucity of evidence relating to use of oximetry in low-income settings and the very low frequency of the outcome of interest. To estimate the effectiveness of oximetry in averting peri-operative death, it was necessary to extrapolate from surrogate outcomes and from observational studies in high income countries. Another possibility would have been to estimate this parameter by means of a Bayesian elicitation, but the estimate would still have been an informed guess. Our approach instead was to carry out extensive sensitivity analysis. In our base case, the hand-held pulse oximeter appeared to be very cost–effective for low-income countries if it prevented just 1.7% of anaesthetic-related deaths or 0.3% of total peri-operative deaths. It is worth

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**Fig. 2. Cost–effectiveness of pulse oximetry as a function of baseline anaesthetic-related mortality**

DALY: disability-adjusted life-year; GDP: gross domestic product; US$: United States dollars.

Note: The cost–effective thresholds were for the year 2013. Attractive interventions were based on the *World development report* 1993.20 Cost–effective interventions were based on World Health Organization guidelines, with very cost–effective and cost–effective interventions below one (US$ 677) and three (US$ 2031) times the GDP per capita for the group of low-income countries, respectively.20

The base case, lower bound and upper bound report levels of the baseline anaesthetic-related mortality that occurs – or might occur – in the absence of pulse oximetry.
noting that to detect an improvement of this magnitude in total peri-operative mortality in a randomized controlled trial would require a sample size of almost 1.5 billion patients – and such a trial will never be conducted. The aim of the WHO Global Pulse Oximetry Project is to make pulse oximetry more widely available is based on best practice from high-income countries and the results of informal analysis – rather than on an explicit calculation of what oximetry would have to achieve to be cost–effective.

In this paper, we only considered deaths averted by oximetry. Our estimates of the cost–effectiveness of pulse oximetry would probably have increased if we had also considered non-fatal brain damage. Discussions with doctors working in low-income countries highlighted several additional points. First, pulse oximetry may actually reduce overall oxygen use, since flow rate can be reduced where saturation is adequate. Second, the availability of oximetry may change clinical practice. For example, only practitioners with access to oximetry may be willing to use alternatives to general anaesthesia that may be safer in some situations – e.g. spinal blocks in obstetrics. Third, there is a role for oximetry outside the operating theatre – e.g. in monitoring patients in the recovery room and mothers and neonates during vaginal delivery, and reducing oxygen use in patients with pneumonia who are tachypnoeic but well saturated.42,43

Our analysis considered only stand-alone tabletop and hand-held oximeters. A third type of oximeter, the fingertip oximeter, is even cheaper than the hand-held devices – with a purchase cost of US$3044 – but is designed only for spot-checks in primary care and probably has limited usefulness in operating theatres, since it lacks an audible tone that changes with oxygen saturation, an alarm to indicate desaturation and a plethysmograph display. As well as stand-alone pulse oximeters, pulse oximetry may be built into other devices – e.g. anaesthesia machines or sphygmomanometers – or combined with electrocardiography or capnography in a multivariable monitor.45 In practice the choice of which type of oximeter to purchase is likely to depend on a variety of setting-specific considerations. For example, in a setting with only intermittent electricity supply, a standard tabletop oximeter would be unsuitable because of its inability to function for long periods without mains electricity. The presence of combined capnography or other functionality in an expensive unit that can be used for oximetry is only valuable if the requisite expertise is present.46

| Parameter                                                                 | Point estimate | Distribution | Distributional parameters | Data source(s)                                    |
|--------------------------------------------------------------------------|----------------|--------------|----------------------------|---------------------------------------------------|
| Anaesthetic-related mortality, deaths per million operations requiring general anaesthesia | 467            | Log–normal   | µ = 6.0; σ = 0.56          | Systematic review, with variance increased to take into account higher mortality for excluded studies14 |
| Proportion of anaesthetic-related deaths averted by pulse oximetry       | 0.1            | Beta         | α = 1; β = 9               | Authors’ estimates based on intermediate outcomes from review of randomized control trials22 and observational data14,28,29 |
| Annual equivalent cost of purchasing and maintaining a hand-held pulse oximeter, US$ per 1000 operations requiring general anaesthesia | 83             | Log–normal   | µ = 4.4; σ = 0.81          | Authors’ calculation                                |

**Table 3. Parameters included in probabilistic sensitivity analysis**

**Fig. 3. Cost–effectiveness acceptability curve for pulse oximetry**

DALY: disability-adjusted life-year; GDP: gross domestic product; US$: United States dollars.

Note: The cost–effective thresholds were for the year 2013. Attractive interventions were based on the World development report 1993.20 Cost–effective interventions were based on World Health Organization guidelines, with very cost–effective and cost–effective interventions below one (US$ 677) and three (US$ 2031) times the GDP per capita for the group of low-income countries, respectively20,38,39
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There is a large body of literature relating to cost–effectiveness of health interventions in low-income countries. Much of this literature relates to evaluations of complex interventions that are of little value in specific device-procurement decisions. There is also an emerging interest in frugal innovation – i.e. the adaptation of existing medical technologies to make them more affordable and more suitable for use in low-resource settings. We hope that analysis of the type presented here – in which the types and grades of device available for a particular purpose are made explicit – could help bridge the gap between the literature on cost-effectiveness of health interventions and the literature on technical specifications for devices, allowing decision-makers to proceed beyond the prioritization of complex interventions to the selection of specific devices for different clinical settings.

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Competing interests: AAG is the Chair of the Lifebox Foundation Board. The other authors declare no competing interests.

Malzah

Cost–effectiveness of pulse oximetry

Purpose

The objective of this study was to assess the cost–effectiveness of pulse oximetry in the perioperative period in low-income countries. The study was conducted in a series of two studies. The first study was a systematic review of the literature on pulse oximetry in the perioperative period. The second study was a cost–effectiveness analysis of pulse oximetry in low-income countries. The study was conducted using a decision tree model. The results of the study showed that pulse oximetry was cost–effective in the perioperative period in low-income countries. The study was funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care for Birmingham and the Black Country, and the NIHR Senior Investigator Award granted to RJL.

Method

The study was conducted using a decision tree model. The decision tree model was used to estimate the cost–effectiveness of pulse oximetry in the perioperative period in low-income countries. The model was based on the literature review and the results of the cost–effectiveness analysis. The results of the study were presented in a cost–effectiveness analysis report.

Results

The results of the study showed that pulse oximetry was cost–effective in the perioperative period in low-income countries. The study was funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care for Birmingham and the Black Country, and the NIHR Senior Investigator Award granted to RJL.

Conclusion

The results of the study showed that pulse oximetry was cost–effective in the perioperative period in low-income countries. The study was funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care for Birmingham and the Black Country, and the NIHR Senior Investigator Award granted to RJL.

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Résumé

Oxymétrie de pouls périopératoire dans les pays à revenu faible: une analyse de la rentabilité

Objectif E valuer la rentabilité de l’oxymétrie de pouls par rapport à l’absence de surveillance périopératoire lors d’une chirurgie dans les pays à revenu faible.

Méthodes Nous avons considéré l’utilisation d’oxymètres de pouls à poser et d’oxymètres de pouls portatifs chez des patients de tous âges ayant subi une opération chirurgicale importante dans des pays à revenu faible. À partir d’études antérieures, nous avons obtenu la mortalité de référence et l’efficacité des oxymètres de pouls pour réduire la mortalité. Nous avons considéré les coûts directs de l’achat et de l’entretien des oxymètres de pouls, ainsi que le coût de l’oxygène supplémentaire utilisé pour traiter les épisodes hypoxiques identifiés par oxymétrie. Les avantages pour la santé ont été mesurés en espérance de vie corrigée de l’incapacité (EVC I) évitée, et les avantages et les coûts ont été actualisés à 3% par an. Nous avons utilisé les seuils de rentabilité recommandés – à la fois de manière absolue et relative par rapport au produit intérieur brut (PIB) par habitant – afin d’évaluer si l’oxymétrie de pouls était une intervention de santé rentable. Pour tester la solidité de nos résultats, nous avons effectué des analyses de sensibilité.

Résultats Avec les prix de 2013, les oxymètres à poser et les oxymètres portatifs présentaient des coûts annuels de 310 et 95 dollars, respectivement. En supposant que les deux types d’oxymètre ont une efficacité identique, un seul oxymètre utilisé pour 22 interventions par semaine permettrait d’éviter 0,83 EVC I par an. Les oxymètres à poser et les oxymètres portatifs coûtaient 374  et 115 $ par EVC I évitée, respectivement. Pour tous les pays avec un PIB par habitant supérieur à 677 $, l’oxymètre portatif s’est avéré rentable s’il évitait seulement 1,7% des décès liés à l’anesthésie ou 0,3% de mortalité périopératoire.

Conclusion L’oxymétrie de pouls est une intervention rentable pour les pays à faible revenu.

Resumen

Perioperatoria pульсовая оксиметрия в странах с низким уровнем доходов: анализ экономической эффективности

Цель Оценить экономическую эффективность пульсоксиметрии — в сравнении с отсутствием периоперационного мониторинга — при проведении операций в странах с низким уровнем доходов.

Методы Было рассмотрено использование как настольных, так и портативных ручных пульсоксиметров среди пациентов любого возраста, перенесших обширное оперативное вмешательство, в странах с низким уровнем доходов. Данные об исходном уровне смертности и эффективности пульсоксиметров для снижения смертности были получены из предыдущих исследований. Учитывались прямые затраты на приобретение и обслуживание пульсоксиметров, а также стоимость дополнительного кислорода, используемого для устранения эпизодов гипоксии, выявленных с помощью оксиметрии. Позиция для здоровья определялась спасенными годами жизни, скорректированными на инвалидность (индекс DALY), при этом полученные значения позиции и затрат снижались на 3% в год. Были использованы рекомендованные пороговые значения показателя «затраты-эффективность» — как абсолютные, так и относительные, с учетом валового внутреннего продукта (ВВП) на душу населения — для оценки того, является ли пульсоксиметрия экономически эффективной лечебной мерой. Чтобы проверить надежность полученных результатов, был проведен анализ чувствительности.

Результаты Было установлено, что в ценах 2013 года годовые затраты на использование настольных и ручных оксиметров составили 310 и 95 долларов США соответственно. Если предположить, что два типа оксиметров имеют одинаковую эффективность, то один оксиметр, применяемый для 22 процедур в неделю, спас 0,83 DALY за год. Стоимость настольного и ручного оксиметра на спасенный DALY составила 374 и 115 долларов США соответственно. Для любой страны с ВВП на душу населения свыше 677 долларов США использование ручного оксиметра оказалось экономически эффективным, если он позволял предотвращать как минимум 1,7% анестезиологических или 0,3% периоперационных смертей.

Вывод Пульсоксиметрия является экономически эффективной лечебной мерой для стран с низким уровнем доходов.

La oximetría de pulso perioperatoria en los países de ingresos bajos: un análisis de la rentabilidad

Objetivo Evaluar la rentabilidad de la oximetría de pulso en comparación con la ausencia de vigilancia perioperatoria durante la cirugía en países de ingresos bajos.

Métodos Se tuvieron en cuenta oxímetros de pulso manuales, tanto de mesa como portátiles, entre los pacientes de todas las edades sometidos a una intervención quirúrgica importante en países de ingresos bajos. A partir de los estudios anteriores se obtuvo la mortalidad inicial y la eficacia de los oxímetros de pulso para reducir la mortalidad. Se consideraron los costes directos de la adquisición y del mantenimiento de los oxímetros de pulso, así como el coste del oxígeno complementario que se utiliza para tratar los episodios de hipoxia identificados mediante la oximetría. Se midieron los beneficios para la salud en años de vida con discapacidad (AVAD) evitados, mientras que los beneficios y los costes se descontaron al 3% por año. Utilizamos los umbrales de rentabilidad recomendados, tanto absolutos como relativos, respecto al producto interno bruto (PIB) por cápita para evaluar si la oximetría de pulso es una intervención de salud rentable. Por último, se realizó un análisis de sensibilidad para poner a prueba la solidez de los resultados.

Resultados En 2013, se halló que los precios de los oxímetros de mesa y portátiles suponían unos costes anuales de 310 y 95 dólares estadounidenses (US$), respectivamente. En el supuesto de que ambos tipos de oxímetro tengan la misma eficacia, el uso de un único oxímetro para 22 procedimientos por semana evitó 0,83 AVAD por año. Los oxímetros de mesa y manuales costan 374 US$ y 115 US$ por AVAD evitado, respectivamente. Para cualquier país con un PIB per cápita superior a 677 US$, el oxímetro manual resultó ser rentable con tan solo impedir un 1,7% de las muertes relacionadas con la anestesia o el 0,3% de la mortalidad perioperatoria.

Conclusión La oximetría de pulso es una intervención rentable para entornos de ingresos bajos.
References

1. Merry AE, Eichhorn JH, Wilson IH. Extending the WHO’s Safe Surgery Saves Lives’ project through global oximetry. Anaesthesia. 2009;64(10):1045–8. doi: http://dx.doi.org/10.1111/j.1365-2044.2009.06104.x PMID: 19735392

2. Enright A, Merry A. The WFA and patient safety in the perioperative setting. Can J Anaesth. 2009;56(1):8–13. doi: http://dx.doi.org/10.1016/S0140-6736(08)-90010-X PMID: 19247772

3. Funk LM, Weiser TG, Berry WR, Lipsitz SR, Merry AE, Enright AC, et al. Global operating theatre distribution and pulse oximetry supply: an estimation from reported data. Lancet. 2010;376(9746):1055–61. doi: http://dx.doi.org/10.1016/S0140-6736(10)60932-3 PMID: 20598894

4. Our product. Lifebox. saving lives through safer surgery [Internet]. London: Lifebox Foundation; 2013. Available from: http://www.lifeboxfoundation.org/about-lifebox/our-products/ [cited 2013 Jul 17].

5. Jamison DT, Breman JG, Measham AR, Alleyne G, Garside R, Cawthorne A, et al. Disease control priorities in developing countries. Washington: World Bank; 2006.

6. Pulse oximeter: technology opportunity assessment. Seattle: Program for Appropriate Technology in Health; 2013. Available from: http://sites.path.org/mnhtech/files/2013/06/Proofed-Pulse-oximeter_FINAL_27June2013.pdf [cited 2014 Aug 18].

7. Edger T, Balaban V, Adam R, Hutubessy R, Acharya A, Evans DB, et al. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: World Health Organization; 2003.

8. Hutubessy R, Chisholm D, Edger TT. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. Cost Eff Resour Alloc. 2003;1(18). doi: http://dx.doi.org/10.1111/j.1476-7547.1-8 PMID: 14687420

9. Howie SR, Hill S, Bonyon A, Krishnan G, Njie O, Sannah M, et al. Meeting oxygen needs in Africa: an options analysis from the Gambia. Bull World Health Organ. 2009;87(10):763–71. doi: http://dx.doi.org/10.2471/BLT.09.014271 PMID: 19786543

10. Moller JT, Johannesen NW, Espensen K, Ravlo O, Pedersen BD, Jensen PF, et al. Randomized evaluation of pulse oximetry in 20,802 patients. II. Perioperative events and postoperative complications. Anesthesiology. 1993;78(3):445–53. doi: http://dx.doi.org/10.1097/00000542-199303000-00002 PMID: 8457045

11. Dubowitz G, Breyer K, Lipnick M, Sall JW, Feiner J, Ikeda K, et al. Accuracy of the Lifebox pulse oximeter during hypoxia in healthy volunteers. Anesthesiology. 1993;78(3):445–53. doi: http://dx.doi.org/10.1097/00000542-198904000-00002 PMID: 2929993

12. Moller JT, Johannessen NW, Espensen K, Ravlo O, Pedersen BD, Jensen PF, et al. Randomized evaluation of pulse oximetry in 20,802 patients: II. Perioperative events and postoperative complications. Anesthesiology. 1993;78(3):445–53. doi: http://dx.doi.org/10.1097/00000542-198904000-00002 PMID: 2929993

13. Kwok AF, Funk LM, Balbata R, Lipsitz SR, Merry AE, Dziekan G, et al. Implementation of the World Health Organization surgical safety checklist, including introduction of pulse oximetry, in a resource-limited setting. Ann Surg. 2013;257(4):633–9. doi: http://dx.doi.org/10.1097/SLA.0b013e3182777674 PMID: 23207242

14. Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breslau AH, Dellinger EP, et al. Safe Surgery Saves Lives Study Group. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med. 2009;360(5):419–9. doi: http://dx.doi.org/10.1056/NEJMc0801199 PMID: 1944931

15. D’Cunha LM, Bondi S, Melzer-Dweis H, Díaz AE, Starfield B, et al. Comparison of treatment effect sizes associated with surrogate and final patient relevant outcomes in randomized controlled trials: meta-epidemiological study. BMJ. 2013;346:f547. doi: http://dx.doi.org/10.1136/bmj.f547 PMID: 23360719

16. Moynihan R. Surrogates under scrutiny: fallible correlations, fatal consequences. BMJ. 2011;343:d5160. doi: http://dx.doi.org/10.1136/bmj.d5160 PMID: 21844159

17. Yudkin JS, Lipska KJ, Montori VM. The idolatry of the surrogate. BMJ. 2011;343:d7995. doi: http://dx.doi.org/10.1136/bmj.d7995 PMID: 22205706

18. Salomon JA, Wang H, Freeman MK, Vos T, Flaxman AD, Lopez AD, et al. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2144–62. doi: http://dx.doi.org/10.1016/S0140-6736(12)61690-0 PMID: 22345606

19. Galukande M, van Schreeb J, Wladis A, Mibekanti N, de Miranda H, Kruk ME, et al. Essential surgery at the district hospital: a retrospective descriptive analysis in three African countries. PLoS Med. 2010;7(3):e1000243. doi: http://dx.doi.org/10.1371/journal.pmed.1000243 PMID: 20211871

20. Shillcutt SD, Walker DG, Goodman CA, Mills AJ. Cost effectiveness in low- and middle-income countries: a review of the debates surrounding decision rules. Pharmacoeconomics. 2009;27(11):903–17. doi: http://dx.doi.org/10.2165/10899580-000000000-00000 PMID: 19888791

21. World development report 1993: investing in health [Internet]. Washington: Oxford University Press; 1993. Available from: http://books.google.co.uk/books?id=syVuGAAMAAJ [cited 2014 Jul 25].

22. World development indicators. Washington: World Bank; 2014.

23. Reardon S. Frugal science gets DIY diagnostics to world’s poorest. New Sci. 2013;219(2933):20–1. doi: http://dx.doi.org/10.1016/S2042-0701(13)62184-3

24. McKenzie KG. Mortality associated with anaesthesia at Zimbabwean teaching hospitals. S Afr Med J 1996;86(9):338–42. PMID: 8693367
42. Duke T, Wandi F, Jonathan M, Matai S, Kaupa M, Saavu M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet. 2008;372(9646):1328–33. doi: http://dx.doi.org/10.1016/S0140-6736(08)61164-2 PMID: 18708248

43. Matai S, Peel D, Wandi F, Jonathan M, Subhi R, Duke T. Implementing an oxygen programme in hospitals in Papua New Guinea. Ann Trop Paediatr. 2008;28(1):71–8. doi: http://dx.doi.org/10.1179/146532808X270716 PMID: 18516953

44. Savage A. Why are the chosen pulse oximeters so expensive? BMJ. 2012;344:e210, discussion e219. doi: http://dx.doi.org/10.1136/bmj.e210 PMID: 22252691

45. Core medical equipment. Geneva: World Health Organization; 2011. Available from: http://whqlibdoc.who.int/hq/2011/WHO_HSS_EHT_DIM_11.03_eng.pdf [cited 2014 Jul 25].

46. Medical devices: managing the mismatch. An outcome of the priority medical devices project. Geneva: World Health Organization; 2010. Available from: http://whqlibdoc.who.int/publications/2010/9789241564045_eng.pdf [cited 2014 Jul 25].

47. Compendium of innovative health technologies for low-resource settings 2011–2013. Geneva: World Health Organization; 2014. Available from: http://apps.who.int/iris/bitstream/10665/108781/1/9789241564731_eng.pdf?ua=1 [cited 2014 Jul 25].