Keeping score: fostering accountability for children’s lives

We live in a remarkable era of accelerated progress in reducing child deaths in the poorest countries. The death rate in children younger than 5 years in low-income countries has dropped by 28.1% since 2000. The Millennium Declaration set an ambitious goal of reducing the death rate in this age group by two-thirds in each country. Progress has not been even, but since the year 2000 reductions were recorded in 136 of 138 low-income and middle-income countries. In the few months remaining until the end of the Millennium Development Goal period, even more can be achieved. Continued progress will benefit from a focus on results. Where are we making progress and where not? Where can more resources make the biggest difference?

We propose a Lives Saved Scorecard to drive funding and policy attention to where it is most needed. The ideal scorecard would track all investments by donors and governments, the coverage of each life-saving intervention, the quality of interventions delivered, and the link to child deaths averted in a cross-country, comparable manner. Among donor organisations, this scorecard would measure effects, incentivise progress, and help to ensure that collective gaps are filled. Across partner countries, it can help to identify urgent funding shortfalls and show where expected progress has not been realised, as well as foster shared learning.

We propose beginning with a simple and pragmatic strategy for a scorecard: understanding the relationship between expenditures and effects. Estimates of child mortality are available for nearly all countries. Likewise, donor expenditure for child health can be tracked, as can national health expenditure targeting children. For most countries, we can generate a reasonable time trend for expenditure on child health (appendix).

<table>
<thead>
<tr>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHE-S</td>
<td>1105973</td>
<td>1130650</td>
<td>1131982</td>
<td>1148547</td>
<td>1207419</td>
<td>1177436</td>
<td>1222566</td>
</tr>
</tbody>
</table>

Development assistance by channel:

<table>
<thead>
<tr>
<th></th>
<th>GAVI</th>
<th>Global Fund</th>
<th>UNICEF</th>
<th>UK</th>
<th>US bilateral</th>
<th>World Bank</th>
<th>Others</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>10599</td>
<td>3946</td>
<td>36658</td>
<td>53579</td>
<td>57980</td>
<td>83491</td>
<td>77418</td>
<td>206235</td>
</tr>
<tr>
<td>2001</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>16635</td>
<td>15871</td>
<td>57625</td>
<td>68530</td>
<td>10735</td>
</tr>
<tr>
<td>2002</td>
<td>51136</td>
<td>72741</td>
<td>68158</td>
<td>66859</td>
<td>71725</td>
<td>102496</td>
<td>60511</td>
<td>80767</td>
</tr>
<tr>
<td>2003</td>
<td>30243</td>
<td>3015</td>
<td>28667</td>
<td>26466</td>
<td>9071</td>
<td>28437</td>
<td>36935</td>
<td>31825</td>
</tr>
<tr>
<td>2004</td>
<td>112779</td>
<td>143814</td>
<td>61392</td>
<td>45494</td>
<td>17361</td>
<td>41017</td>
<td>42575</td>
<td>54071</td>
</tr>
<tr>
<td>2005</td>
<td>139940</td>
<td>145313</td>
<td>160822</td>
<td>153684</td>
<td>187198</td>
<td>161253</td>
<td>102775</td>
<td>96596</td>
</tr>
<tr>
<td>2006</td>
<td>101760</td>
<td>112700</td>
<td>168927</td>
<td>210274</td>
<td>251493</td>
<td>226235</td>
<td>275882</td>
<td>310534</td>
</tr>
<tr>
<td>2007</td>
<td>427867</td>
<td>517009</td>
<td>524624</td>
<td>572991</td>
<td>616009</td>
<td>700554</td>
<td>663726</td>
<td>887663</td>
</tr>
</tbody>
</table>

Development assistance by source:

<table>
<thead>
<tr>
<th></th>
<th>Australia</th>
<th>BMGF</th>
<th>Canada</th>
<th>France</th>
<th>Germany</th>
<th>Norway</th>
<th>Japan</th>
<th>UK</th>
<th>USA</th>
<th>Others</th>
<th>Total</th>
<th>GHE-S and DAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>2425</td>
<td>30203</td>
<td>6530</td>
<td>6266</td>
<td>18771</td>
<td>4583</td>
<td>39121</td>
<td>42047</td>
<td>156016</td>
<td>124330</td>
<td>472867</td>
<td>1533840</td>
</tr>
<tr>
<td>2001</td>
<td>2929</td>
<td>58346</td>
<td>4064</td>
<td>7806</td>
<td>21009</td>
<td>9014</td>
<td>45760</td>
<td>24594</td>
<td>201475</td>
<td>144941</td>
<td>517009</td>
<td>1647659</td>
</tr>
<tr>
<td>2002</td>
<td>3931</td>
<td>42548</td>
<td>15631</td>
<td>11934</td>
<td>25906</td>
<td>18638</td>
<td>23740</td>
<td>47303</td>
<td>185433</td>
<td>154184</td>
<td>524624</td>
<td>1656606</td>
</tr>
<tr>
<td>2003</td>
<td>3402</td>
<td>67499</td>
<td>15451</td>
<td>16992</td>
<td>16265</td>
<td>1900</td>
<td>29634</td>
<td>52974</td>
<td>103040</td>
<td>308121</td>
<td>572991</td>
<td>1721538</td>
</tr>
<tr>
<td>2004</td>
<td>4461</td>
<td>21912</td>
<td>23903</td>
<td>7514</td>
<td>24133</td>
<td>28795</td>
<td>35905</td>
<td>39823</td>
<td>125993</td>
<td>299711</td>
<td>616009</td>
<td>182428</td>
</tr>
<tr>
<td>2005</td>
<td>10122</td>
<td>59712</td>
<td>48565</td>
<td>17841</td>
<td>19449</td>
<td>24783</td>
<td>36302</td>
<td>66323</td>
<td>127868</td>
<td>262630</td>
<td>700554</td>
<td>187990</td>
</tr>
<tr>
<td>2006</td>
<td>4434</td>
<td>50302</td>
<td>21620</td>
<td>52993</td>
<td>23771</td>
<td>20713</td>
<td>35353</td>
<td>85551</td>
<td>110793</td>
<td>370206</td>
<td>663726</td>
<td>1886291</td>
</tr>
<tr>
<td>2007</td>
<td>6183</td>
<td>73784</td>
<td>47224</td>
<td>54193</td>
<td>34500</td>
<td>37797</td>
<td>17653</td>
<td>118044</td>
<td>134262</td>
<td>2151655</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2014 estimates are preliminary. GHE-S=government health expenditure from their own revenue sources. DAH=development assistance for health. BMGF=Bill & Melinda Gates Foundation.

Table 1: Lives saved in children younger than 5 years by channel-specific spending on child health, 2000-07
Comment

finding highlights how other factors can intervene in the relation between investment and child deaths averted: everything from wars and disasters to changes in health system efficiency could be causes of decreases in health expenditure and reductions in child deaths. The key point is that changes in death counts and changes in health expenditures, and thus the ratio of expenditures to lives saved, are observable.

Ratios of changes in expenditures to changes in deaths can be used to approximate the incremental cost per life saved. Using statistical methods (appendix), we have computed for each country in the period 2000 to 2013 the incremental cost per child life saved through health expenditures. To save a child’s life, the cost is US$4205 in low-income countries, $6496 in lower-middle-income countries, and $10 016 in upper-middle-income countries. Although costs are highest in upper-middle-income countries, there are many justifications to maintain and increase expenditures in these settings—such as disease eradication, funding of other public goods, and other important objectives.

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

<table>
<thead>
<tr>
<th>Year</th>
<th>Low-income countries</th>
<th>Lower-middle-income countries</th>
<th>Upper-middle-income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>$4205</td>
<td>$6496</td>
<td>$10 016</td>
</tr>
<tr>
<td>2014</td>
<td>$4205</td>
<td>$6496</td>
<td>$10 016</td>
</tr>
</tbody>
</table>

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less

We propose using this resources-to-lives-saved ratio as the basis for an initial Lives Saved Scorecard. Increased dollars spent by a national government or a donor in a country would be converted into estimated child deaths averted. By connecting investments to improvements in health, we can see the true stakes of any increased or decreased investments in health expenditure.

Tables 1 and 2 show the application of this approach to the period 2000–14 as a demonstration of principle. From 2000 to 2013, health expenditure increased by $1·2 billion, saving an additional 170 000 lives. Among donors agencies, over the period 2000 to 2014, USAID, the World Bank, GAVI, UNICEF, and the Global Fund all saved more than a million child lives each. Developing country governments themselves spent vastly more than donors on child health, but the number of deaths averted by donor funds is only 29·9% less
because of the concentration of donor funding in the poorest countries, where the cost per life saved is lower.

Our scorecard makes some strong but reasonable assumptions. First, for a given country in a given year, we assume that all dollars irrespective of the source make the same contribution to saving child lives. Credit for reductions in child deaths is shared among funders in proportion to their investment. Second, we assume that the 2010–13 cost per child death averted in a country is a reasonable basis for predicting the present. If efficiency gains occur quickly from one year to the next, estimating cost per death averted from the recent past might overestimate current costs per life saved. Third, we assume that not all reduction in child mortality is due to expenditure on health interventions. The well established and strong association between maternal education and income per person and child mortality might partly be related to increased access to health interventions, but some of this association is probably related to other factors such as housing, nutrition, clean water and sanitation, indoor air pollution, birth spacing, child-rearing practices, hygiene, and other factors.

In practice, we propose computing and reporting using the expenditure-to-effect ratio as a quarterly Lives Saved Scorecard. Donors and national governments would need to be able to track quarterly spending or estimated disbursement on the basis of budgets or obligations. This scorecard can keep attention focused on further progress. It can also help in other ways, such as to identify where the greatest funding gaps exist.

Future versions of the scorecard can address important limitations in an iterative fashion. First, careful retrospective assessment in some countries of investments, changes in coverage, effective coverage, and changes in child mortality can strengthen the estimates of the cost per life saved for each country. Second, the effect of maternal health investments on newborn babies and children, including in reducing stillborn deaths, should be explored and potentially incorporated. Third, in this model, the current period’s spending has an effect on mortality in the current period. Many investments will continue to have an effect beyond the period in which they are made, and this approach does not intend to divert resources away from such longer-term investments. Overall, the scorecard can be annually revised and improved with better data.

This simple but practical Lives Saved Scorecard can be an important tool for fostering accountability and accelerating progress toward the crucial goal of preventing suffering throughout the world. We believe that this scorecard can and should be used after the end of 2015 to aid in tracking progress on the Global Goals for Sustainable Development. We know that despite the efforts of governments and donors to improve health in low-income and middle-income countries, too many children die before the age of 5 years. Without a way to monitor progress regularly, we will miss the opportunity to build on the momentum we have seen since the Millennium Declaration.

Christopher Murray, *Ray Chambers
Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA (CM); UN Secretary General’s Special Envoy for Financing the Health MDGs and Malaria, New York, NY 10019, USA (RC)
Ray.Chambers@mdghealthenvoy.org

We declare that we have no conflicts of interest.


Final results from a pivotal phase 3 malaria vaccine trial

In The Lancet, the RTS,S Clinical Trials Partnership[1] report the most recent results from the pivotal phase 3 trial of RTS,S/AS01 malaria vaccine, the fourth major publication from this randomised controlled trial.2–4 The trial enrolled 15,459 infants and young children at 11 centres in seven sub-Saharan African countries: Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, and Tanzania. Two age groups were included: 6–12 weeks and 5–17 months at first dose. The schedule involved a primary series of three monthly

Published Online
April 24, 2015
http://dx.doi.org/10.1016/S0140-6736(15)60767-X

See Online/Articles
http://dx.doi.org/10.1016/S0140-6736(15)60721-8
doses, with a booster dose given 18 months later in one of the three trial groups. The partnership responsible for undertaking this trial, consisting of GlaxoSmithKline and PATH, are to be congratulated on the quality of the study. Industry involvement in malaria vaccine development has been crucial to the promising next-generation malaria vaccine work that is underway. The generous funding from the Bill & Melinda Gates Foundation to PATH for clinical trials of RTS,S/AS01 has been very important, as has the continued commitment of a large pharmaceutical company to this project despite the absence of a market for this product in high-income settings. GlaxoSmithKline and PATH worked with many of the leading scientists in sub-Saharan Africa in a clinical trial partnership model, through a committee in which many of the decisions were taken together with and by local investigators. The strengthening of clinical trial capacity in sub-Saharan Africa to support the trial has already left a strong legacy.

The new results show that the vaccine induces partial protection against clinical malaria in the older age group (5–17 months) at all 11 sites over the follow-up period of the trial, and shows benefit of the 18-month booster.

The new results show that, with a booster of the vaccine, the overall efficacy against severe malaria in 5–17-month-old children was 32·2% (95% CI 13·7–46·9), and efficacy was detected against both malaria hospital admission (34·6%, 22·5–44·9) and all-cause hospital admission (16·5%, 7·2–24·9). Unlike many illnesses of infancy, the risk of death from malaria continues through early childhood, even in the face of repeated infection, although the mortality rate drops from the age of 2 years in high-transmission settings.

For every new malaria intervention, discussions about potential increased disease incidence after the effect of the intervention wanes have been intense at the time of initial policy decisions. Another key question, which does not need to be addressed in pre-licensure trials of vaccines, is whether the intervention will reduce childhood mortality. Malaria models predict that the RTS,S/AS01 vaccine will reduce mortality, but we will only know whether or not this is the case if larger datasets become available.

From the perspective of the immunisation programme, there are added challenges with the delivery of this vaccine through new immunisation contacts. The required booster will need to be administered in settings 14 months from the first dose. Efficacy against clinical and severe malaria endpoints in 6–12-week olds was lower, and no significant efficacy against severe malaria was noted in the 6–12 week age group, even with a booster, over the duration of the trial.

Two WHO advisory groups—the Strategic Advisory Group of Experts on Immunization (SAGE) and the Malaria Policy Advisory Committee (MPAC)—will formulate their recommendations to the WHO Director-General with regard to introduction of the RTS,S/AS01 vaccine into the vaccination schedule of children in Africa. These two groups will meet in open joint session if the European Medicines Agency provides a positive scientific opinion on its regulatory assessment, which is underway. The earliest month for the SAGE and MPAC recommendation is October, 2015, depending on timing of the European Medicines Agency’s decision.

One key question SAGE and MPAC will consider is the duration of protection of the vaccine. Without a booster dose of vaccine, the new results do not show overall efficacy against severe malaria in the 5–17 month age group, with cases prevented in the first 20 months of the trial shifted to older age groups. The new results show that, with a booster of the vaccine, the overall efficacy against severe malaria in 5–17-month-old children was 32·2% (95% CI 13·7–46·9), and efficacy was detected against both malaria hospital admission (34·6%, 22·5–44·9) and all-cause hospital admission (16·5%, 7·2–24·9). Unlike many illnesses of infancy, the risk of death from malaria continues through early childhood, even in the face of repeated infection, although the mortality rate drops from the age of 2 years in high-transmission settings.

For every new malaria intervention, discussions about potential increased disease incidence after the effect of the intervention wanes have been intense at the time of initial policy decisions. Another key question, which does not need to be addressed in pre-licensure trials of vaccines, is whether the intervention will reduce childhood mortality. Malaria models predict that the RTS,S/AS01 vaccine will reduce mortality, but we will only know whether or not this is the case if larger datasets become available.

From the perspective of the immunisation programme, there are added challenges with the delivery of this vaccine through new immunisation contacts. The required booster will need to be administered in settings...
where the booster platform is weak and needs to be strengthened. If recommendations were to support use of the vaccine with booster in the 5–17 months age range, at least two new visits for immunisation and a new visit for the booster would be needed.

Malaria remains an ongoing public health crisis in many settings in sub-Saharan Africa. Every day, on average, about 1200 children die in sub-Saharan Africa from malaria.1 This figure is a substantial reduction from mortality estimates 15 years ago, and the decline has been associated with scale-up in longlasting insecticidal nets, access to effective artemisinin-combination treatments, and other WHO recommended control measures. Nevertheless, present mortality owing to malaria is unacceptable. Drug and insecticide resistance are major threats, and new malaria interventions are necessary.

The donor community would need to coordinate any financing for the RTS,S/AS01 vaccine carefully, should it reach that stage. In particular, funding must not be redirected away from meeting adequate access to artemisinin-combination treatments, rapid diagnostic tests, longlasting insecticidal nets, and other malaria control measures already in place in some settings, and financial resources might be better raised through the GAVI Alliance, if their board chooses to support such a role. GAVI has a strong track record for financing the delivery of new vaccines in sub-Saharan Africa. Finally, strong guidance is needed about the role of the vaccine in the context of existing malaria control measures, and about which malaria transmission intensity settings are best suited for vaccine use. The outcomes of regulatory and global policy assessments will no doubt be of interest to policy makers in malaria-endemic countries and multilateral financing agencies. WHO has a major responsibility to articulate evidence-based policy recommendations for use to support decision making in malaria-endemic countries.

*Vasee S Moorthy, Jean-Marie Okwo-Bele
Department of Immunization, Vaccines and Biologicals, World Health Organization, Geneva 1211, Switzerland
moorthyv@who.int

We declare no competing interests.

© 2015, World Health Organization. Published by Elsevier Ltd/Inc/BV. All rights reserved.


AVERT: a major milestone in stroke research

Prevention of stroke is, of course, the ideal scenario, but with more than 10 million major strokes every year worldwide, acute treatment and rehabilitation should also be optimised. Organised acute stroke care within dedicated stroke units reduces death and dependency after stroke,1 but which elements of such care confer this benefit is uncertain. Systematic prevention of common complications and more expert nursing care undoubtedly contribute, but in the physiologically unstable setting of acute stroke, the benefits and harms of each specific element of care need to be reliably assessed.

How soon and how intensively patients with acute stroke should be mobilised is an obviously important question. Early mobilisation after stroke, whether sitting, standing, or walking, is recommended in many guidelines, but, as with most nursing and therapist interventions, the evidence base has been weak. The rationale for early and more intensive mobilisation is that bed rest might increase immobility-related complications and could slow neurological recovery by impairing early brain plasticity and repair. On the other hand, forced sitting and standing might lead to falls and injury and could reduce cerebral perfusion, autoregulation being impaired in acute stroke, and thereby exacerbate ischaemia. Early mobilisation might also worsen any post-stroke hypertension and increase the risk of rebleeding after intracerebral haemorrhage or after thrombolysis for ischaemic stroke.

In The Lancet, the AVERT Collaboration group randomly assigned 2104 patients within 24 h of onset of acute stroke to early mobilisation or usual care.2 The


Comment

THELANCET-D-15-02486
SO140-6736(15)60906-0

Embargo: May 11, 2015—00:01 (BST)
that reported in previous acute stroke trials, perhaps the 3 month mortality rate of only 8% was less than half of and patient refusals (n=446) were remarkably low. The frequent in the intervention group (adjusted odds ratio outcome at 3 months (the primary outcome) was less and the usual care group, and a good overall functionalwalking recovery between the early mobilisation group

The investigators hypothesised that more intensive, early out-of-bed activity would improve functional outcome at 3 months, reduce immobility-related complications, and accelerate walking recovery, with no increase in neurological complications. None of these predictions proved correct. There was no difference in walking recovery between the early mobilisation group and the usual care group, and a good overall functional outcome at 3 months (the primary outcome) was less frequent in the intervention group (adjusted odds ratio [OR] 0·73, 95% CI 0·59–0·90). The unadjusted result for the primary outcome was less convincingly adverse (OR 0·85, 95% CI 0·72–1·00), but the adjustment for age and stroke severity was robust to different analysis methods. The absence of a difference between the groups in immobility-related complications might partly be due to improvements in stroke-unit practice in the past few years and a move away from prolonged bed rest, such that only 7% of patients in the usual care group stayed in bed for more than 48 h after stroke onset. However, the adverse effect of the intervention on the primary outcome seems to have been driven at least partly by a non-significant increase in neurological deterioration in the intervention group as compared with the usual care group. The non-significant increase in mortality in the intervention group was driven mainly by progression or recurrence (42 such deaths in the intervention group vs 26 deaths in the usual care group). The overall increase in mortality in the intervention group was non-significant, and remains so when combined with the few data (15 deaths in 81 patients with early mobilisation vs six deaths in 78 patients with usual care) from three small previous trials (fixed-effects OR 1·35, 95% CI 0·99–1·83). Nevertheless, it seems reasonable to conclude that a beneficial effect on mortality is unlikely.

In view of the clinical, causal, and physiological heterogeneity of acute stroke, subgroup–treatment effect interactions might well be expected, and many clinicians had a-priori concern about starting mobilisation early in patients with intracerebral haemorrhage. Therefore, that both the primary outcome (adjusted OR 0·48, 95% CI 0·25–0·92) and 3 month mortality (0·31, 0·11–0·88) were significantly better in the usual care group than the early mobilisation group in patients with intracerebral haemorrhage is noteworthy. The investigators are cautious in their interpretation of this finding on the basis that they did not stratify for stroke subtype at randomisation and did not pre-specify any expected subgroup effects themselves, and because no subgroup–treatment effect interaction was statistically significant. However, significance is a poor measure of the validity of subgroup effects, partly because most trials are substantially underpowered to detect them (AVERT recruited only 258 patients with intracerebral haemorrhage). Further analyses of frequency and dose of intervention received in relation to apparent harms could be informative, but updated clinical guidelines should not overestimate the statistical obstacles to interpretation of what seems to be potentially substantial harm in patients with intracerebral haemorrhage, particularly in view of the a-priori clinical concern and evidence that excessive variability in blood pressure, which might be exacerbated by early and intensive mobilisation, is associated with a poor outcome in acute intracerebral haemorrhage. There also seems to be little to lose by a cautious approach to early mobilisation in this group.

AVERT is a milestone in stroke research in that it has shown that large, international, high-quality trials of complex interventions in stroke care, led by physiotherapists and nurses, are possible. The trial contributes several other important lessons. First, it reminds us that high-quality randomised controlled trials of acute stroke so often confound expectations—the overall balance of benefits and harms of any intervention are almost impossible to predict reliably from first principles. Second, it shows
In The Lancet, Mark Barone and colleagues report the results of their study aimed at establishing whether 7 day bladder catheterisation is non-inferior to 14 day catheterisation in terms of fistula breakdown after repair, in women with simple genital fistulas. The traditional 14 day duration of catheterisation after fistula repair has been challenged over the years, although this duration has been widely used in practice. A survey of 40 fistula surgeons by Arrowsmith and colleagues reported variability of postoperative catheter drainage strategies ranging from 5 to 42 days.

Barone and colleagues carried out their randomised, controlled, open-label study in hospitals in eight African countries. With 261 patients in the 7 day group and 263 in the 14 day group in the study, no significant difference in fistula repair breakdown, the trial’s primary endpoint, was noted between the 7 day and 14 day bladder catheterisation groups (ten [4%] of 250 patients in the 7 day group had repair breakdown vs eight [3%] of 251 in the 14 day group, risk difference 0.8% [95% CI −2.8 to 4.5], falling within the predefined non-inferiority margin of 10%). Additionally, no significant differences were noted in secondary outcomes of repair breakdowns 7 days after catheter removal or thereafter; urinary retention the effect that simple interventions can have on outcome in this physiologically complex and unstable disorder. Findings from the ongoing HeadPoST trial (ClinicalTrials.gov, NCT02162017), comparing the effectiveness of the lying flat (0°) head position with the sitting up (≥30°) head position in the first 24 h of admission to hospital with acute stroke, are likely to be similarly important in this regard. Finally, the low rate of patients refusing to participate in AVERT shows that patients also see the importance of simple, pragmatic research questions. Ironically, the main barriers to more such research are those put up by agencies intended to represent the public interest: the trial regulators with their unnecessarily complex bureaucratic framework for trial performance, which often results in trial prevention, and the medical research funding agencies that in many countries have little interest in the needs of patients and clinicians for answers to pragmatic questions about making the best use of existing interventions in routine clinical practice. Thankfully, those agencies in Australia and the UK that funded AVERT took a different view.

**Peter M Rothwell**

Stroke Prevention Research Unit, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford OX2 6HE, UK

peter.rothwell@clneuro.ox.ac.uk

I declare no competing interests.

Copyright © Rothwell. Open Access article distributed under the terms of CC BY-NC-ND.


2 The AVERT Trial Collaboration Group. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. Lancet 2015; published online April 17. http://dx.doi.org/10.1016/S0140-6736(15)60690-0.


1, 3, or 7 days after catheter removal; infections and febrile episodes potentially related to treatment; catheter blockage; extended hospital stay; and residual incontinence at 3 months. 7 day bladder drainage after repair of simple fistulas was therefore found to be non-inferior to 14 day drainage, indicating that 7 day drainage is a safe and effective way to manage postoperative bladder drainage without any substantial increase in complications. The crucial stage in wound healing, that is mobilisation of fibroblasts, granulation formation, and neovascularisation, occurs at 5 days, with inflammation generally resolving after 7 days.2,3

The findings of Barone and colleagues’ study1 will be welcome news to fistula surgeons who have agonised over the absence of capacity to care for patients, and the fact that patients with fistulas are often relegated to the bottom of theatre lists4 that are frequently loaded with emergencies. Reduction of postoperative catheterisation from 14 days to 10 days without a substantial increase in failure has been estimated to increase the number of patients with fistulas undergoing surgical repair by almost 30% without any increase in capital investment.3,4 Because duration of bladder catheterisation is a key determinant of the length of hospital stay, which affects treatment costs and use of hospital beds,6,7 a halving of the duration of bladder drainage would increase the turnover of women getting the opportunity for care. However, possible confounding factors such as inadequacy of consumable supplies, anaesthesia, and nursing services would need to be addressed4,7 for the full benefits of such a change in practice to be realised. The socioeconomic benefit of reduced hospital stay, from the perspectives of both patients and health systems, can be enormous in the setting of poorly resourced countries.4

A shortened duration of bladder drainage after simple fistula repair without an increase in the number of breakdowns is most welcome news to patients with fistulas and their caregivers. If the results of Barone and colleagues’ study can be reproduced in another multicentre randomised controlled trial, adoption of its conclusions into clinical practice would substantially expand our capacity to care for patients with fistulas. My hope is that, in the near future, obstetric fistula surgeons will have the evidence-based confidence to reduce the duration of postoperative bladder drainage without any anxiety about increased repair breakdowns.

Anyetei Tonyeli Lassey
Department of Obstetrics and Gynaecology, Korle-Bu Teaching Hospital, PO Box KB 36, Korle-Bu, Accra, Ghana
atlassey@yahoo.co.uk

I declare no competing interests.


Depression relapse: importance of a long-term perspective

Emil Kraepelin’s demarcation between dementia praecox and manic depressive illness defined affective disorder as a remitting and recurring disease. He considered that only long-term outcome was useful in assessing accuracy of diagnosis and treatment response in patients.1 The more recent interest in the outcome of single mood episodes probably indicates motives to register and market drugs rather than assisting clinical practice. This interest has resulted in many 4–8 week randomised trials but few well designed long-term studies in patients with depression.

There is now increasing evidence that Kraepelin was right. Mood disorders are generally recurring, and the relevant measure of clinical success is long-term...
functioning rather than the outcome of a single mood episode. In secondary and tertiary care, less than a third of patients recover and remain well in the 18 months after an episode of depression, whereas in general practice and community studies, the proportion of patients with recurrence is between 35% and 65%. Treatment needs to focus on maintenance and prevention of relapse as well as on the acute mood episode.

The most established treatment for prevention of relapse and recurrence is maintenance antidepressant medication. Studies have consistently reported a reduction in the odds of relapse of about 50–70%. However, many patients might not wish to remain on medication or cannot tolerate the side-effects. Alternative non-medication strategies would obviously be desirable.

Mindfulness-based cognitive therapy (MBCT) was developed as an explicit intervention to reduce relapse and recurrence in depression. MBCT teaches people who have had depression that negative feelings and thoughts will recur and that, rather than worrying or ruminating about these experiences, it is possible to become aware of and disengage from them, thereby preventing a downward spiral into depression. Although cognitive behavioural therapy and interpersonal therapy also have evidence of efficacy in the prevention of relapse in depressed patients neither were developed specifically for this purpose.

Willem Kuyken and colleagues’ study, published in The Lancet, of mindfulness-based cognitive therapy in the prevention of depressive relapse or recurrence is therefore timely. It is a pragmatic long-term study done in general practice, where most depression is treated. The randomised trial compared MBCT with maintenance antidepressants in a large sample of patients with recurrent depression in the UK. 212 patients were randomly assigned to MBCT and 212 to maintenance antidepressant treatment, and the time to relapse or recurrence of depression did not differ between treatment groups over 24 months (hazard ratio 0·89, 95% CI 0·67–1·18). The authors’ interpretation of the findings is carefully worded: there is no support for MBCT being superior to maintenance antidepressants in preventing depressive relapse. Despite this apparent negative result, the findings have substantial clinical significance.

Kuyken and colleagues’ findings, if benchmarked against the studies of maintenance antidepressant therapy, provide evidence that MBCT might offer a similar ongoing protective effect as that of maintenance antidepressants. MBCT therefore provides an alternative effective treatment for patients who cannot tolerate or do not wish to have maintenance antidepressant therapy. Because it is a group treatment that reduces costs and the number of trained staff needed, it might be feasible to offer MBCT as a choice to patients in general practice. Pooling all trial data comparing MBCT and maintenance antidepressant treatment (which is limited to three studies), as Kuyken and colleagues did, resulted in a risk reduction of 24% for MBCT compared with maintenance antidepressants (risk ratio 0·76 95% CI 0·59–0·98). Perhaps all patients with recurrent depression should be offered MBCT.

We therefore have a promising new treatment that is reasonably cost effective and applicable to the large group of patients with recurrent depression. The next obvious question is whether there are specific effects of MBCT that confer this decreased risk of relapse or whether any structured group psychotherapy would produce similar results. Ongoing studies of mechanism of action are promised by the authors. If the research in long-term treatment of personality disorders is any guide, they are likely to find that general factors such as a manualised approach, active supportive therapists, a focus on patients’ sense of agency and management of life situations are most important, rather than specific factors related to mindfulness theory.
Depression remains a disabling condition with high prevalence and a large clinical burden. Despite the increased use of drugs, the long-term outcome of mood disorders has not improved in the modern era. Having an alternative non-medication strategy to reduce relapse is an important means to help patients with depression.

Roger Mulder
Department of Psychological Medicine, University of Otago, Christchurch 8140, New Zealand
roger.mulder@otago.ac.nz

I declare no competing interests.

Copyright © Mulder et al. Open Access article distributed under the terms of CC BY.


The Wakley Prize, 2015: what do you know?

What do I know? That question was the impulse behind Michel de Montaigne’s essays. Whether he was writing about illness, vanity, drunkenness, or sleep, Montaigne wrote with informality, intimacy, and incisive knowledge. As another great essayist William Hazlitt said of Montaigne, “he did not set up for a philosopher, wit, or orator or moralist but he became all these by merely daring to tell us whatever passed through his mind”. In the centuries since Montaigne mastered this form, the essay, a discursive and intimate form of personal reflection, has remained a powerful way to inform, engage, and entertain readers.

So what do you know? And why does it matter to clinical medicine or global health now? We want you to tell us by entering The Lancet’s annual essay completion, the Wakley Prize. The Prize will be awarded to the best essay on any clinical topic of importance to health. Whether your focus is global or local, we expect provocative originality, fine writing, and invigorating argument. We’re looking for fresh writing that engages both our hearts and minds about what matters most to you in contemporary medicine.

We invite submissions from anyone around the world working in a health-related field, whether you’re a student, established in mid-career, or approaching the end of a lifetime of service in health care or biomedical science. Allow your imagination the freedom to develop your idea into the informal prose of an excellent essay.

Essays of no more than 2000 words should be submitted via The Lancet’s electronic submission system by Oct 26, 2015, with “Wakley Prize” selected as the publication type. Essays should not contain any information that might identify individual patients. Entries will be anonymised, and judged by the editors of The Lancet. The winner of The Lancet Wakley Prize will receive £2000, and the essay will be published in The Lancet and feature in our podcast. We will only accept one submission per author. We look forward to reading your essays and finding out what you know and why it matters.

Joanna Palmer, Philippa Berman, Priya Venkatesan
The Lancet, London EC2Y 5AS, UK
Highlights 2015: a picture of health

It’s that time of year again when we ask Lancet readers to submit photographs for our annual Highlights photography competition. We are looking for striking images that arrest our attention about any topic in medicine, from global health to clinical medicine, from the individual person to populations. An image can be a powerful way to tell a story, and as we have seen with past Highlights winners over the years your photographs about the health stories that speak to you capture important moments in clinical and global health. Last year’s beautiful selection of winning photographs included images about neonatal care in Africa, the work of midwives in Afghanistan, the life of sex workers in India, and the importance of community health workers in bringing health care to homes.

We are interested in photographs from any country and invite readers to submit photographs to Highlights 2015 that capture any health issue in a powerful way. As in previous years, The Lancet and The Lancet Global Health will run the competition together. Winning photographs will be published in The Lancet’s final issue of 2015 and might also be selected for the front cover of The Lancet Global Health.

Each entry should be submitted with 300 accompanying words that put the image in context. Submissions should not have been previously published in print or online.

If a person or patient is featured then you must obtain and keep written consent from the individual or, where this is not an option, their next of kin. Please complete the patient consent section of the Author statements form while retaining copies of the signed forms. We also encourage you to submit any additional media to support your submission online, such as video or audio features.

All photographs—colour or black and white—should be submitted through our online editorial submission system, along with the required text and any supporting material for online publication. Please select Lancet Photograph as the article type. If a digital camera is used please set it to the highest possible quality setting and submit images as JPEG files. If you are using a film camera please submit an 8 × 11 inch glossy print to The Lancet in the post. The entries will be judged by Lancet editors and there will be a £300 prize for winning entries. The deadline for entries is Nov 12, 2015. So share your photos with The Lancet and The Lancet Global Health: we look forward to seeing what health stories you capture.

*Joanna Palmer, Zoë Mullan
joanna.palmer@lancet.com
Offline:

Paragraph 1:

Paragraph 2

Paragraph 3

Paragraph 4