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Opinion
Is evidence-based medicine enough?

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Summary

This paper deals with the gap existing between efficacy and effectiveness. While evidence-based medicine (EBM) has improved our knowledge on 'what' works and what does not, there is still a knowledge gap on 'how' and 'why' an efficacious intervention can work in practice. What works in ideal circumstances may not produce the same effect in everyday practice, especially if we do not know why and how the effect was obtained in experimental conditions.

The application of results from EBM into clinical practice should take into account feasibility according to local circumstances. EBM should be used as a tool to aid decisions and not as a bland rule applicable in all circumstances. Therefore, the fact that certain interventions have been found cost-effective in the literature can create the feeling that the solution is around the corner and that these interventions will be easily implementable and will be cost-effective. However, these assumptions can lead to disillusionment when the critical conditions that allowed those results are missing in operational conditions.

Cost-effectiveness needs to be considered together with efficacy, effectiveness, feasibility and adverse events. An intervention that was efficacious in trial or pilot conditions was such because there were human and financial resources, compliance and other conditions that allowed for efficacy to take place. Not considering these critical conditions will lead to failure in reproducing the same efficacy in operational conditions (effectiveness). Estimating the minimum factors needed for an efficacious intervention to be effective and assessing their presence in operational conditions should be part of risk analysis and health planning.

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Cost-effectiveness and rationing

Judgment over how to use the evidence and apply it to local situations is required. Decisions need to be well thought out, otherwise scarce resources are wasted. All evidence needs to be critically assessed for its appropriateness and applicability. EBM can only produce general results applicable to the situations assessed in the trials or systematic reviews. Low implementation capacity should be taken into consideration in the cost-effectiveness analysis.

Any rationing of resources should take into account how efficacy relates to effectiveness through feasibility. If an intervention had a high efficacy in trial or pilot conditions but it has a high risk of failure in operational conditions, the effect is likely to be much lower or nil and the intervention can result unfeasible. This is what happens when 'cost-effective' but ambitious programs are damped on weak health systems that do not even have the capacity to implement much less ambitious programs. Instead of asking why the expected results did not come, planners should ask themselves why any result should have come without the necessary human and financial resources. As it is easier to go ahead and produce more projects that are too theoretical without asking what minimum conditions should be in place, failure is bound to follow. Risk of failure increases with the complexity of health endeavours and more realistic approaches would have a better chance of producing results than the theoretical planning agenda.

Rationale behind EBM

Available information from Randomised Control Trials (RCTs) and best practices provide the criteria for selecting priority interventions and for improving the rationing of resources. The assumption is that the results obtained in experimental conditions (efficacy) will be obtained in the average clinical practice (effectiveness). For clarity sake, we can define effectiveness as the proportion of efficacy that has been found in RCT or in pilots. Therefore, an intervention can be both efficacious and effective, if the results from clinical trials are easily transferable in clinical practice, and ineffective if critical conditions are missing.

Evidence-based medicine has become the main basis to accept an intervention as worth funding. Meta-analysis and systematic reviews on the efficacy of treatments have increased the use of already published data to screen for effective interventions. Most EBM specialists take for granted that once there is evidence that an intervention has been found efficacious, the same efficacy can be effectively obtained in clinical practice. This attitude provides an oversimplified approach to the complex problem of transferring good practices into clinical practice. What the EBM specialists look at is 'what' has been obtained without questioning 'why' and 'how' it was obtained.

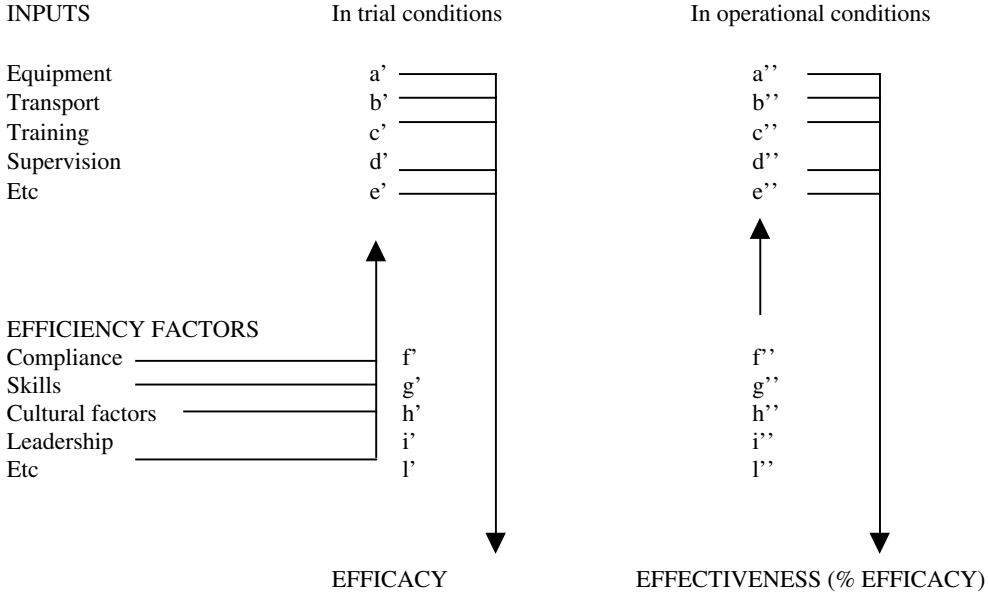
The efficacy of an intervention can vary considerably across multi-centre trials and the transfer of the same effect in operational conditions is likely to vary even more. However, when an effect is obtained in RCT or pilot projects we should ask ourselves what

were the conditions that allowed such efficacy in the first place. The identification of these conditions helps to understand why and how the efficacy was obtained, and why there was a high variation in the efficacy, which is likely to increase with the complexity of the intervention. These conditions are easier to identify when there is a direct link between an intervention and its efficacy such as in pharmacological trials where the key variables can include training and supervision, type of personnel, compliance and so on. When the intervention becomes more comprehensive and its complexity increases, such as in primary health care programs, the link between the intervention and the efficacy found in primary health care pilots is less direct and more blurred. In this case it becomes more difficult to single out the conditions required for efficacy to be repeated outside the experimental settings and the transferability from pilot to operational settings becomes much more cumbersome and uncertain.

Efficacy versus effectiveness and the risk of failure

Evidence-based efficacy can be misleading if the risk of failure related to the absence of critical factors allowing for the efficacy to take place are not taken into account. Figure 1 simplifies the relationship between efficacy and effectiveness, which is a by-product of inputs and efficiency factors. The probability of obtaining a certain effect through health services (operational conditions) depends on the presence of the same inputs/factors that allowed the efficacy in trial or pilot conditions. If the mix of inputs/factors is

Figure 1. Conditions in RCT and in operational setting



far from those present in the trial conditions, the probability of obtaining the effect declines until a critical point under which no effect is obtained.

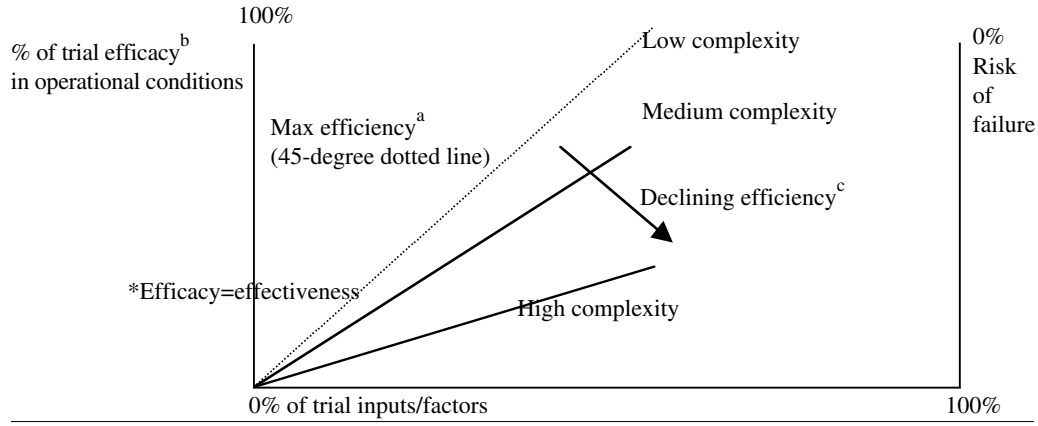
Figure 2 shows the relationship between efficacy and effectiveness as a by-product of the interaction of inputs and efficiency factors. The 45% dotted line shows the ideal situation in which inputs and factors, and thus efficacy and effectiveness are the same in trial and operational conditions. However, the input mix and their efficient use are far from ideal in the health services (straight lines) and the proportion of efficacy transferred at operational level declines with declining levels of input/factors mix. For a given mix of inputs/factors, the efficiency is likely to decline with the increasing complexity of the intervention because of the stretching of material and human resources. With the declining efficiency, the risk of failure, shown in the second Y axis, increases.

Possible solutions

The complexity of an intervention is likely to be one major risk factor for increasing inefficiency and failure. This is related to the fact that the direct link between inputs/factors/effect is more straightforward for a pharmacological than for a health education intervention. In fact it is much easier to be near the mix of inputs/factors that allowed for the effect obtained in a pharmacological trial than to recreate the high levels of social marketing skills or the peculiar factors (i.e. cultural values) that allowed for the behavioural change obtained in a pilot intervention of health education.

Further analytical work could be done to investigate the relationship between inputs/factors and efficacy in trial conditions. This could help identify the influential mixes, which are behind the efficacy variation and the critical mixes needed to maintain a minimum level of inputs/factors allowing for

Figure 2. Transfer of efficacy into effectiveness



[a] The 45 degree line is an ideal situation where inputs/factors/skills of trial and operational conditions coincide and efficacy and effectiveness are the same.
[b] The % efficacy transferred into operational effectiveness declines with increasing complexity.
[c] Efficiency is a by-product of inputs/factors/skills.

effectiveness. Statistical modelling could be used to help policy formulation and decision making, though this should be used with some caution in order not to be misleading. Careful use is required to ensure that any modelling shows clinical differences as well as statistically significant differences. This caution extends to interpretation of all evidence. The modelling could help identify the critical conditions when the effect declines below critical levels that are not worth the costs. These critical conditions would help establish the minimum requirements needed for the intervention to take place. These would be compared with the local conditions before deciding if and how the intervention could be implemented.

This exercise could begin with few key interventions, which are richer in data, and the methodology could be validated at the operational level. This could be done through the identification of trials with sufficient data on a number of key input/factor mixes or organising such data collection in ongoing trials. The development of such methodology could provide better clues to understand why many health programs fail to deliver and to match the implementation requirements with local conditions. This could be part of the risk analysis to compare the minimum requirements of interventions with the local conditions and assess their probability of failure, providing a better rationale for resource rationing. Finally, the accuracy of the predictions from the models could be validated in operational conditions.

The methodology based on effectiveness models would help planners and managers to assess whether the local conditions are likely to cause a fall in efficiency below the critical threshold where no effect is likely to be produced. This could help avoid the risk of over-optimistic expectations which could overburden an already weak health system with subsequent failure to deliver. In terms of opportunistic costs, this would avoid the problem of scarce resources being wasted because of too theoretical planning, while the same resources could be better employed in more feasible endeavours. The effectiveness of an efficacious intervention depends on critical mixes of inputs and factors allowing for a minimum level of efficiency below which efficacy is not possible. If this is not possible, good intentions and theoretical interventions will have scarce results even if the intervention is efficacious according to EBM criteria.