A.T. KEARNEY

GSMA Mobile Health

Improving the evidence for

MOBILE HEALTH

Contents

Foreword

This publication is a follow up to *Mobile Health – Who Pays?* produced by A.T. Kearney in collaboration with the GSMA. *Mobile Health – Who Pays?* highlighted the importance of Mobile Health to achieve adoption in health systems in the developed world and shed light on some of the intricacies of the payment mechanisms within these healthcare systems.

As the overwhelming majority of healthcare expenditure in the developed world is through formalised reimbursement mechanisms (typically funded by governments, insurers or employers), commercial sustainability and success is dependent on Mobile Health stakeholders understanding in detail how such systems work. This is in direct contrast to conventional customers of mobile network operators, who typically pay for mobile products and services from their personal 'out of the pocket' budget.

One of the predominant features of formal reimbursement mechanisms within healthcare is the requirement to justify payment for a product or service upon consideration of the scientific evidence that evaluates the product or service in question.

Although there has been impressive growth in the quantity of evidence for Mobile Health, the commonly held view amongst key healthcare stakeholders is that the evidence does not address the key issues that support the widespread adoption of Mobile Health. A.T. Kearney performed an analysis of all published scientific evidence for Mobile Health which supports this view.

Therefore this publication seeks to address one of the major issues identified for the slow uptake and adoption of Mobile Health; the lack of relevant and robust evidence to support the reimbursement of Mobile Health. This publication is a guide to ensure that future research efforts accurately and effectively substantiate the benefits of Mobile Health.

The intended audience of this paper are Mobile Health managers in their roles as sponsors of research and related stakeholders within mobile telecom operators, although it is equally relevant to any party seeking to gather evidence to support uptake of mobile health technologies. This paper is not an exhaustive academic review of scientific research methodology; rather it is a high-level discussion to guide mobile health stakeholders who are attempting to generate evidence necessary for the increased uptake and payment of Mobile Health products and services.

In this paper Mobile Health is defined as the provision of health related services and information enabled by mobile technologies. The authors recognise that this definition is broad, and may cover a wide variety of solutions. Subsequently, some of the commentary regarding regulatory or reimbursement requirements may not apply to particular Mobile Health solutions or some geographies.

Executive Summary

With the number of mobile health products and services growing rapidly, analysts predict the global mobile health market will be worth between $30bn and $60bn by 2015[1]. Moreover, a number of existing pilots and projects, particularly in the developing world, are having a significant positive impact on local communities. However despite these early successes, mobile health has failed to reach the scale of adoption that many stakeholders have hoped for in the developed world.

Developed world health ecosystems

Healthcare is an industry driven by evidence. Although a market for consumer orientated mobile health and wellness solutions exists, the overwhelming majority of healthcare expenditure in the developed world is through formalised reimbursement mechanisms (typically funded by governments, insurers or employers). To justify payment, these reimbursement mechanisms generally require consideration of the technical and scientific evidence that objectively evaluates the Mobile Health product or service in question.

A recent literature review of Mobile Health evidence conducted by A.T. Kearney on behalf of the GSMA found significant growth in the number of articles published between 2008 and 2010. However, the existing published research has not focused on the issues that drive adoption: the efficacy of clinical outcomes; cost comparisons; and the influence of mobile health on the wider healthcare system (i.e. reduced hospital attendance, resource utilisation, or improved access). Instead, the research has predominantly focused on demonstrating that the technology for mobile health works from a technical perspective and that patients like to use mobile health solutions.

The review also found that only 13% of the available evidence for mobile health has been derived from research methods that are sufficiently robust to be applicable within the context of the formal appraisal mechanisms used in healthcare systems within the developed world.

Commissioning robust research

Future research should focus on the issues that address the key hurdles to adoption such as clinical outcome, cost comparison and wider health system benefits. The quality of the evidence and the strength of the recommendation (for adoption and payment) are critical components of this. This paper includes a guide to help sponsors or commissioners evaluate research proposals to ensure that studies are relevant, use appropriate study designs and employ robust methodologies. The guide is designed to ensure researchers, or those who sponsor research carefully consider the following questions when planning a mobile health research project:

- Does the mobile health research claim address an appropriate hurdle to adoption?
- What existing literature or evidence supports the claim?
- What analysis or research is needed to substantiate the claim?
- Is the proposed research methodology correct?

Improving the evidence base for mobile health will help overcome one of the most challenging barriers to the widespread adoption of mobile health. This paper is a must read for commissioners of mobile health research who want to ensure that their pilots produce high quality and impactful evidence, and want to achieve this as efficiently as possible.

[1] Parks Research, CSMG, McKinsey

1. THE UPTAKE OF MOBILE HEALTH HAS BEEN SLOW

Worldwide, total healthcare spending exceeds $4.2 trillion, consuming an average of 10% of GDP in OECD countries and increasing at an average of 5% every year. However, this spend is highly skewed. The top 20 healthcare consuming countries contain 16% of population, yet spend nearly 90% of every one of those $4.2 trillion. The US alone, with 5% of the population, spends over 45%. The "have-nots," on the other hand — the remaining 84% of the people on the planet — share 11% of health spending, but suffer from nearly 95% of the diseases while devoting around 5% of GDP to health.

This wide disparity in spend means that challenges faced by health systems are somewhat different in the developing and developed world, however there has been considerable excitement regarding the potential of Mobile Healthcare. Commentators on the industry suggest that the global Mobile Health market may be worth up to $30bn by 2015, while others predict a market of $60bn[2]. Although it may be difficult to substantiate some of these claims, there is no doubt that a number of existing pilots and projects, particularly in the developing world, are demonstrating significant impact in local communities.

However despite these early successes, Mobile Health has failed to reach the scale of adoption that many stakeholders have hoped for in the developed world. As described in a previous publication, *Mobile Health – Who Pays?,* the complexities of healthcare systems in the developed world require an appreciation of the intricacies of the funding mechanisms. Typically, healthcare can funded directly by a patient or their family, or indirectly, by privately funded insurance systems, publically funded nationalised health services, or social insurance schemes. The latter option of indirect funding often uses formal reimbursement mechanisms to pay for healthcare services and requires insight into how scientific evidence is used to support the uptake of new interventions or services. This approach is in direct contrast to how telecoms operators typically attract and sustain consumer interests in their conventional products and services which are mostly funded from 'out of the pocket' personal income.

Therefore as healthcare services in the developed world are primarily funded within formal reimbursed mechanisms, operators must understand how the existence of robust and relevant scientific evidence can help accelerate adoption of Mobile Health.

2. KEY HURDLES TO ADOPTION CAN BE OVERCOME WITH EVIDENCE

Within the healthcare industry, new interventions, technologies or services are required to pass through a number of hurdles before widespread adoption is possible. To overcome these hurdles, key questions surrounding safety, benefit, cost, and the overall impact on the healthcare system must be considered. The recommendations to support the use of an intervention or service are typically based on the trade-offs between the proposed benefits versus the risks and economic burden associated with the intervention or service in question. If benefits outweigh the risks and burden, experts are likely to recommend the intervention or service. The uncertainty associated with

[2] Parks Research, CSMG, McKinsey

the trade-off between the benefits, risk and burden will determine the strength of recommendations.[3]

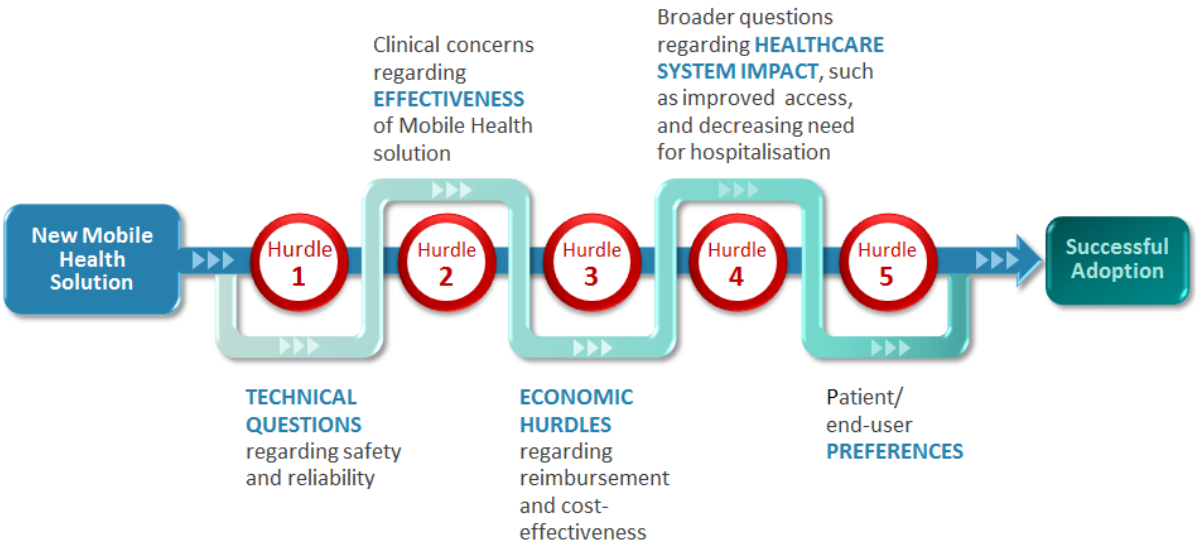


Figure 1: The hurdles to successful adoption

To address these questions stakeholders within the health system either analyse existing evidence or commission new research. High quality research, and the corresponding evidence that it generates, is crucial to present the health and economic impacts of a new intervention, technology or service in the most objective and scientific way as possible. Without this information, healthcare stakeholders are unable to determine whether Mobile Health produces positive benefits such as improved clinical outcome, or offers reduced resource utilisation. If these insights are available, then payers of healthcare (such as governments, insurers or employers) can make a decision to offer reimbursement for Mobile Health services, or providers (such as hospitals, community nursing organisations, family practices or public healthcare organisations) can decide whether it is worthwhile incorporating Mobile Health into their existing service offering.

Therefore to ensure that evidence is effective and powerful, the research must be focussed on producing insights into the key issues that can help overcome the hurdles to adoption, and ensure it is produced using a methodology that is rigorous and appropriate.

3. EVIDENCE MUST ADDRESS KEY STAKEHOLDER CONCERNS

The most influential stakeholders for Mobile Health adoption are regulators, medical professionals and their representative associations, funders of healthcare and healthcare providers. Although patients and carers are important stakeholders they have less direct influence on adoption of Mobile Health in reimbursed healthcare systems. The various stakeholders within the system have different primary concerns which will need to be satisfied before they support the widespread adoption of Mobile Health. Issues that are typically considered to be most important by these stakeholders are safety, benefit, cost, and their combined effect on the overall healthcare system impact. However it should be noted that the relative importance of these issues often varies in different contexts.

[3] Grading of Recommendations, Assessment, Development and Evaluations (GRADE) working group www.gradeworkinggroup.org

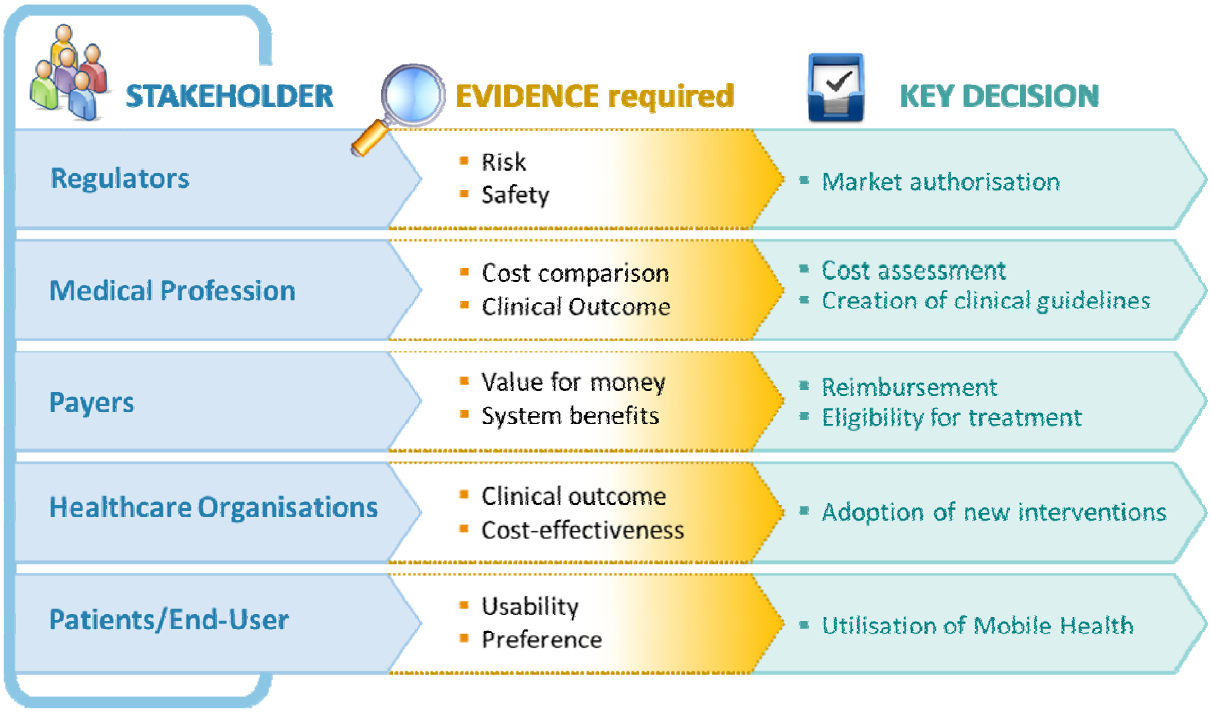


Figure 2: Key stakeholders and related concerns

Hurdle 1: Proving safety

Safety is considered to be the first hurdle for the successful development of any new medical intervention, technology and/or service. Any product that is used for a medical purpose or makes a medically related claim may be subject to regulatory approval, particularly in developed countries. The approval process for market authorisation is generally well understood by manufacturers of conventional medical devices and pharmaceuticals but new entrants from non-healthcare backgrounds may find it a significant undertaking to achieve this regulatory approval.

As Mobile Health offers an increasingly broad spectrum of solutions, ranging from drug compliance to remote heart failure monitoring, national agencies such as the FDA are extending their regulatory oversight to Mobile Health. Historically, the FDA did not have any specific regulation for Mobile Health or related propositions. Therefore early pioneers in Mobile Health who provide remote cardiac monitoring services were required to achieve FDA approval against regulations designed for traditional medical devices rather than regulations that consider the combined range of technology, software, algorithms, and professional services offered within a Mobile Health solution.

This regulatory environment created large hurdles for pioneers in Mobile Health services and delays in gaining market approval and recognition for reimbursement. However recently, regulatory bodies such as the FDA have started to react to market demand by developing specific guidance to provide oversight of 'Mobile Medical Applications'[4] and 'Streamlined review of lower risk, new technology, devices'[5] . Therefore operators should expect that regulatory approval will always be an important part of the pathway to wider adoption and that regulatory guidance will continue to evolve in the coming years. For further information, please see the Appendix for reference current FDA guidelines.

[4] www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm263280.htm
[5] www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm274008.htm

Hurdle 2: Proving benefit

After proving that a Mobile Health solution is safe to use, the value of that solution should be determined by understanding how well it achieves its intended purpose. Proof that Mobile Health solutions have a tangible clinical benefit must be based on robust, non-biased, statistically significant evidence.

Operators should also bear in mind that the benefits of Mobile Health do not necessarily have to be limited to proving a superior clinical outcome compared to existing solutions (although this is clearly beneficial), but could offer *similar* outcomes with a reduced cost or improved access. Typical benefits may include improvement of clinical measurements (e.g. blood pressure, weight, or blood glucose) or change in clinical behaviours (e.g. drug compliance, clinic attendance, or hospitalisation).

For example, pioneers in Mobile Health solutions for diabetics have developed a remote monitoring, compliance and coaching solution for insulin dependent diabetics that successfully lowers blood glucose levels over a sustained period of time. They have not only successfully marketed this proposition in a conventional commercial approach, but have also conducted scientific research to establish the clinical value of their solution compared to existing alternative methods.

This is particularly important in developed countries where structured appraisal systems favouring a pragmatic and sustainable route to adoption are based on scientific evidence. This is particularly apparent within the *Evidence Based Medicine (EBM)* movement which has promoted the use of structured appraisals to assess whether a particular intervention, technology or service has a significant benefit and should be adopted in clinical practice.

Hurdle 3: Evaluating costs to the health care system

Costs within a healthcare system can be considered under the broad categories of direct costs related to patient care, or the indirect costs related to the impact of illness (e.g. loss of income, transport and opportunity costs). Therefore when considering the economic impact of Mobile Health within the healthcare system, there are a number of different perspectives that can be evaluated. The relative priority of each perspective is dependent on the reimbursement structure and funding priorities within the healthcare system in question.

For example, Mobile Health has the potential to reduce transport costs with virtual clinical appointments, but as transport costs are often borne as an ‘out of pocket’ expense by patients, this alone is not likely to be enough for a healthcare funder to invest in a Mobile Health service. Conversely, employers may support and fund such a system if they are the direct funder of care as the Mobile Health service may reduce employee absence from work.

Therefore given the variety of perspectives on cost and impact, the most common evaluation of value in healthcare tends to focus on costs directly attributed to patient care, rather than the indirect costs associated with illness and the provision of healthcare. As pressure on healthcare budgets continues to increase, funders of healthcare are increasingly driven to allocate resources in a manner that is considered to be equitable and achieves the best value for money.

The concept of economic value in healthcare is a critical factor in virtually every healthcare system. In many developed countries with structured reimbursement frameworks, the study of cost, effectiveness, benefit or utility is institutionalised as a formal process that must be considered

before considering the uptake of new interventions, technologies or services. Only when a Mobile Health solution has been deemed to achieve a tangible benefit at a reasonable cost, is it likely to be adopted by providers or reimbursed by healthcare funders.

Hurdle 4: The broader influence of Mobile Health within the health system

Once the Mobile Health solution has been proven to do no harm, has a positive outcome, and has a positive cost impact, stakeholders are in a position to consider the broader influence of the Mobile Health solution. For example, issues such as improved access to hard to reach populations and increased patient satisfaction are benefits that may be difficult to measure but could be attributed to Mobile Health. However, in isolation these factors are not compelling enough to drive adoption unless the preceding hurdles have been overcome.

Hurdle 5: Driving patient use of Mobile Health

Finally, widespread adoption of Mobile Health is dependent on patients successfully interacting with new technologies and appreciating the personal benefits conferred by Mobile Health. This hurdle is in the traditional 'sweet spot' for most mobile telecom operators who tend to have highly sophisticated consumer research capabilities and are experienced at positioning products and services in specific demographic segments.

However, isolated evidence supporting patient desire to adopt a new healthcare service or technology has very little weight in reimbursement decisions, as the overwhelming decision for reimbursement is made on the balance of competing clinical need rather than patient desire. As mentioned previously, in the context of developed healthcare systems, although the patient is the end consumer of healthcare products the direct funders of healthcare have the greatest influence on the adoption of new technologies and services when taking a whole population view into consideration.

4. MOBILE HEALTH RESEARCH SHOULD FOCUS ON KEY ISSUES AND USE THE MOST APPROPRIATE RESEARCH METHODOLOGIES

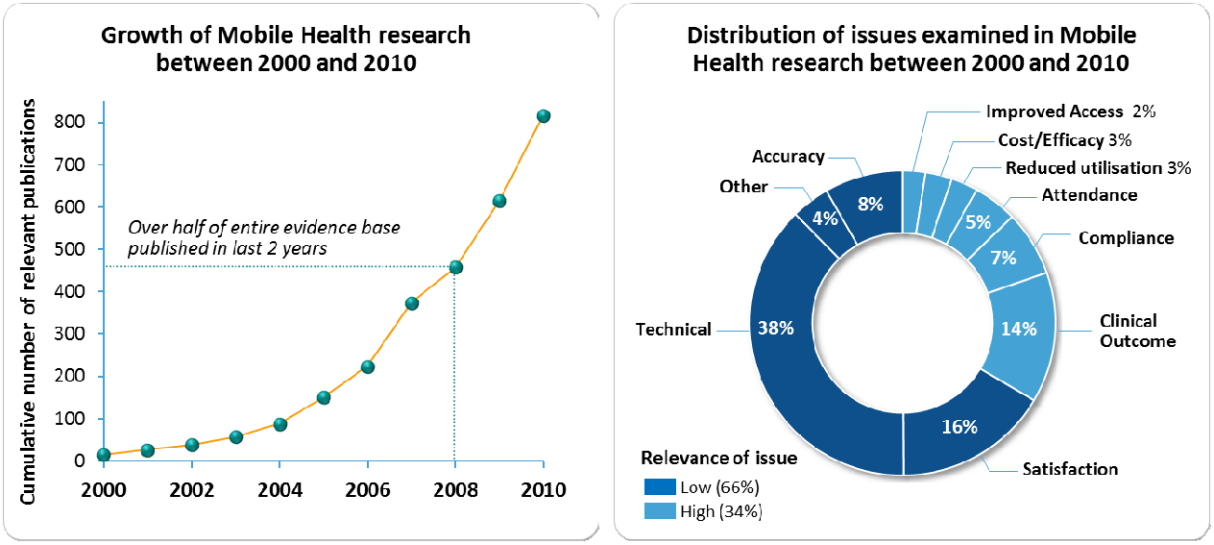


Figure 3: Growth of published Mobile Health research and key issues examined within research

A.T. Kearney conducted a literature review of all available Mobile Health evidence to evaluate the current state and identify the gaps in the evidence required by stakeholders to overcome each hurdle to adoption. The review highlighted a clear growth in number of articles published between 2008 and 2010.

Despite the growth in the quantity of evidence published, the focus of the research has not been on the issues that impact the main hurdles to adoption such as clinical outcome, cost, and the influence of Mobile Health on the wider healthcare system (i.e. reduced hospital attendance, resource utilisation, or improved access). The research has predominantly focussed on demonstrating that the technology for Mobile Health works from a technical perspective and that patients like to use Mobile Health solutions. Although these are interesting findings, as previously described, they are not the most important issues to overcome hurdles that will drive payment of services and increased adoption.

Therefore to accelerate growth and adoption of Mobile Health, future research should focus on the issues that address the key hurdles of clinical outcome, cost impact and wider system benefits such as reduced hospital attendance or improved access.

5. SPONSORS OF MOBILE HEALTH RESEARCH SHOULD USE THE 'MOBILE HEALTH RESEARCH GUIDE'

Beyond the issue that a significant proportion of Mobile Health research does not focus on the hurdles that influence adoption, following the A.T. Kearney analysis of published Mobile Health evidence, only 13% of the available evidence for Mobile Health has been derived from research methods that are sufficiently robust enough to be applicable within the context of the formal appraisal mechanisms used in healthcare systems within the developed world.

These appraisals consider the current evidence ranging from expert opinions and case reports to large complex trials that compare one intervention to another. The latter trial approach often uses specific techniques to avoid bias, such as randomly selecting the individuals who are eligible for testing, and statistical analysis to detect true significance in the results. An example of this type of study is a *Randomised Control Trial.* The outcome of these appraisals often determines best practice, guidelines and protocols. These are published and distributed by respected professional bodies, hold a large influence on professional practice, and are commonly used for supporting efforts to gain acceptance by governments and healthcare funders.

Therefore Mobile Health research should not only focus on key issues that influence adoption, but it should be conducted in a manner that improves the strength and applicability of its conclusions. Therefore, researchers, or those who sponsor research, must carefully consider the following steps when planning a Mobile Health research project:

i. Does the research claim address an appropriate hurdle to adoption?
ii. What existing evidence supports the claim?
iii. What analysis or research is needed to substantiate the claim?
iv. Is the proposed research methodology correct?

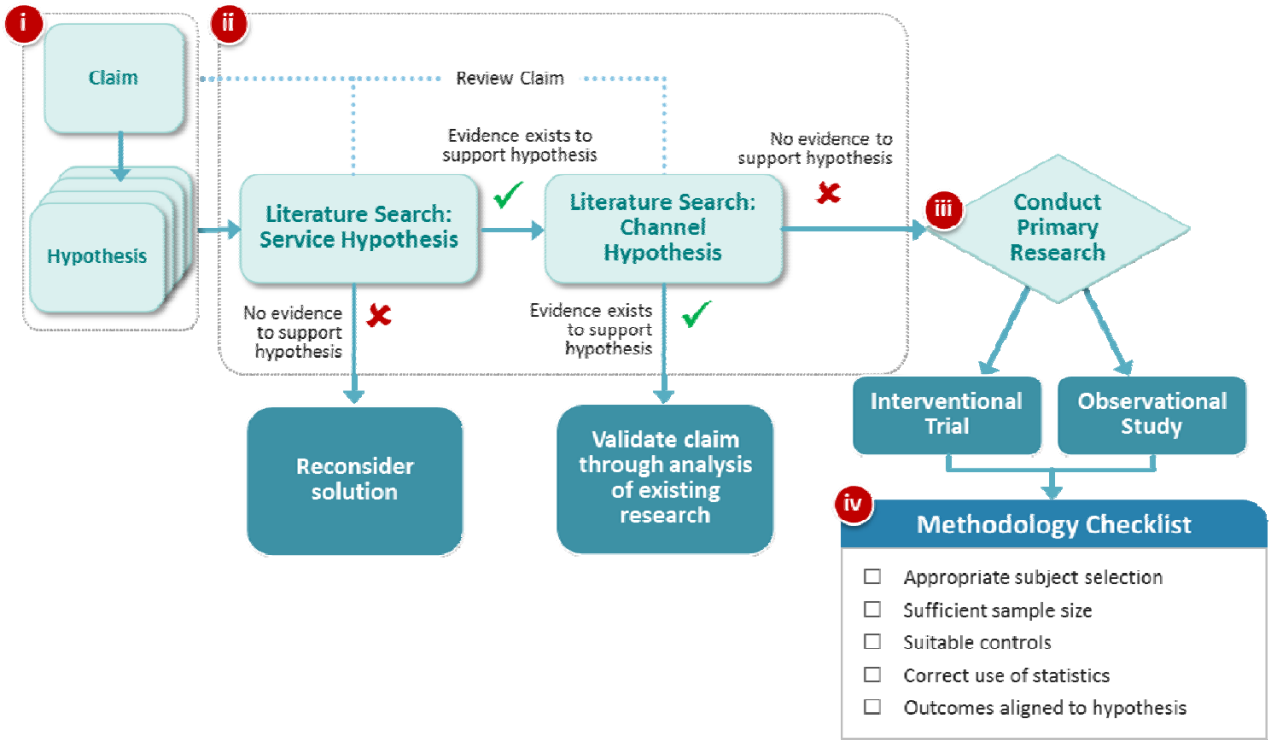


Figure 4: **Mobile Health research guide**

i. What claim is the Mobile Health solution making?

Mobile Health is defined as the provision of health related services and information enabled by mobile technologies. Therefore, Mobile Health can be considered to be a combination of two main elements – a healthcare 'service' and a 'channel' for the service to reach the user (see Figure 5). For example, the 'service' could be patient education, clinical monitoring, or medication reminders. These services are not exclusive to Mobile Health, and are typically provided through other 'channels' such as face to face interactions, patient information leaflets or phone based coaching. Therefore, for Mobile Health to be considered valuable, it must not only provide a 'service' that is proven, but also ensure that the provision of this service through the 'mobile' channel confers an additional advantage over other conventional channels. This is particularly important, as services that are proven to work through existing channels (i.e. face to face) cannot be assumed to work through different channels (i.e. Mobile Health) without further evidentiary support.

Therefore an appropriate starting point for research is to form a claim that serves as a basis for further investigation. Ideally, the claim is based on chain of linked assumptions about the service and channel, informed by the existing evidence. These assumptions are commonly referred to as *hypotheses.* For example:

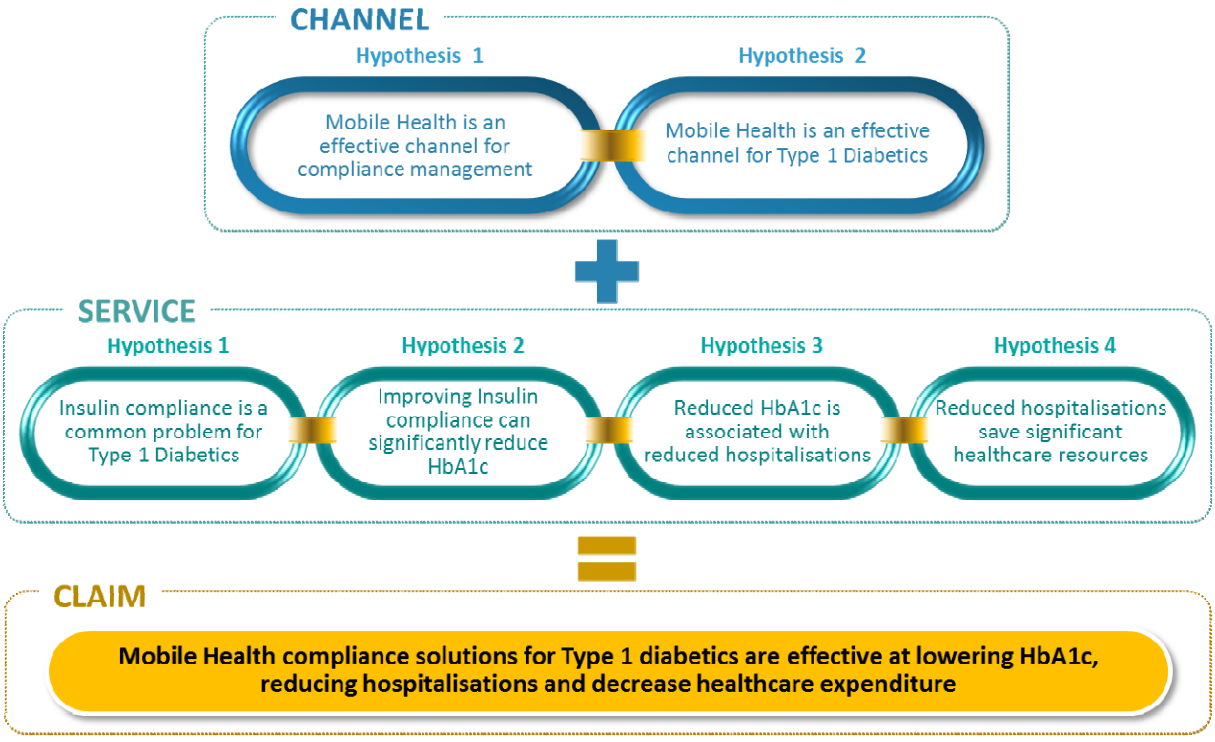


Figure 5: Formation of a Mobile Health claim

Hypotheses that are related to the 'service' are likely to consider issues such as safety and benefit, whereas hypotheses that related to the 'channel' are likely to consider issues such as economic value and wider healthcare system benefits such as access, patient preference, and resource utilisation.

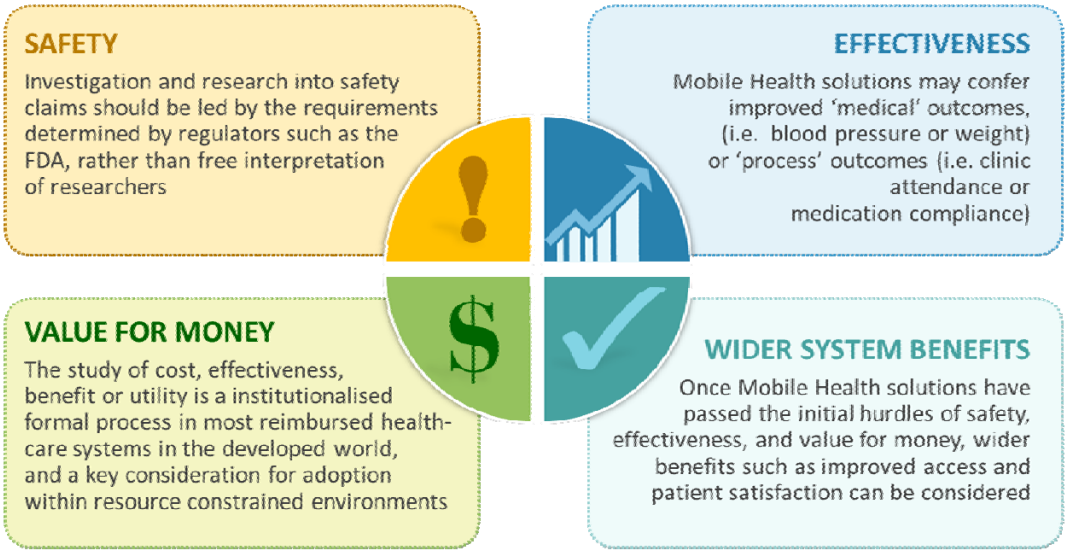


Figure 6: **Key issues for investigation**

Safety

Claims regarding safety and the incidence of adverse events are entirely dependent on the type of Mobile Health solution being investigated. For example, solutions that perform a medical function such as heart monitoring or remote diagnosis may carry a higher risk of actual bodily harm if they fail compared to an appointment reminder or drug compliance solution. This distinction is reflected in the existing regulations governing Mobile Health. Therefore investigation and research into safety claims should be led by the requirements determined by regulators such as the FDA, rather than free interpretation of researchers.

Effectiveness

Like safety, the effectiveness of a Mobile Health solution is entirely dependent on the type of Mobile Health solution being investigated. Solutions may confer improved 'medical' outcomes, such as reduced blood pressure or weight, or 'process' outcomes such as SMS reminders to encourage timely clinic attendance or medication compliance. In each of these cases the research hypothesis should be aligned with the most appropriate type of outcome that proves the effectiveness of the solution. Therefore a solution that offers increased diagnostic effectiveness should have a hypothesis that incorporates outcomes such as accuracy, speed or access, rather than user satisfaction. Likewise, a solution that may offer increased medical effectiveness should have a hypothesis that considers physiological or quality of life outcomes, rather than technical success of the solution.

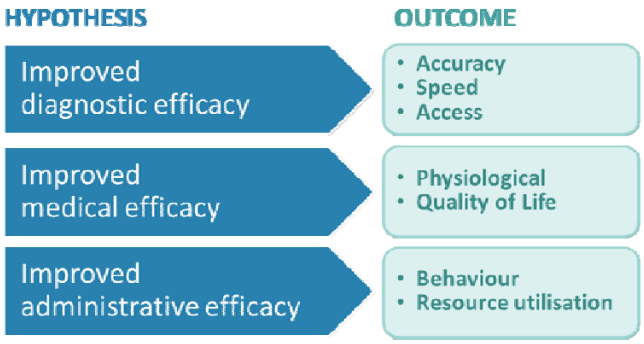


Figure 7: **Link between hypothesis and Outcome**

Value for Money

In the majority of resource constrained healthcare systems, there is an overwhelming pressure to prove that Mobile Health can deliver solutions that provide tangible value. The application of health economic principles, such as (but not limited to) cost-effectiveness, cost-utility, or cost-benefit are increasingly common. These measures are normally determined by collecting existing evidence and modelling the economic impact of the proposed Mobile Health solution within a health system. Therefore research studies create the foundation of evidence upon which economic analysis is performed to determine value for money.

The following potential scenarios can be proposed with regard to cost and effectiveness:

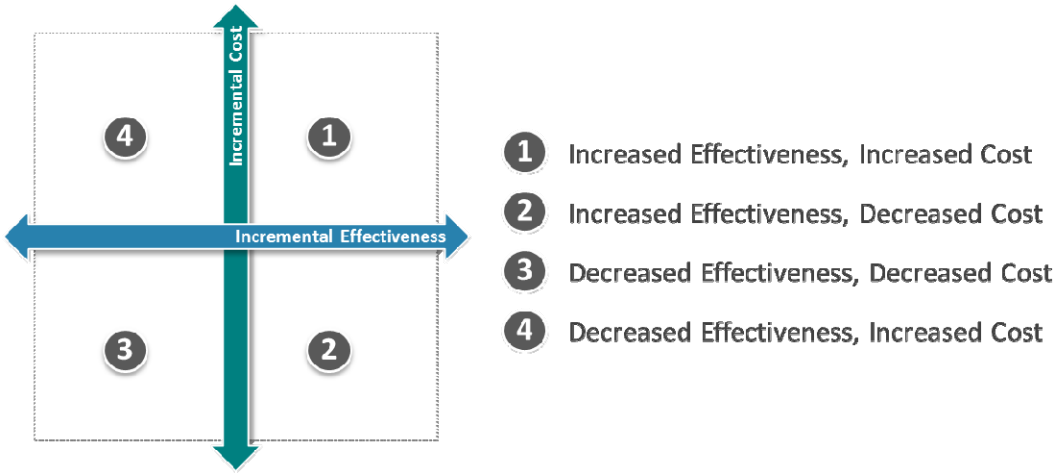


Figure 8: Value scenarios

Scenario 2 is the most desirable outcome, and most Mobile Health solutions should aim for this quadrant. The more tangible, and immediate, the cost reductions are, the more compelling the claim. Mobile Health solutions that require significant upfront investment for long term returns will struggle for adoption when resources are limited.

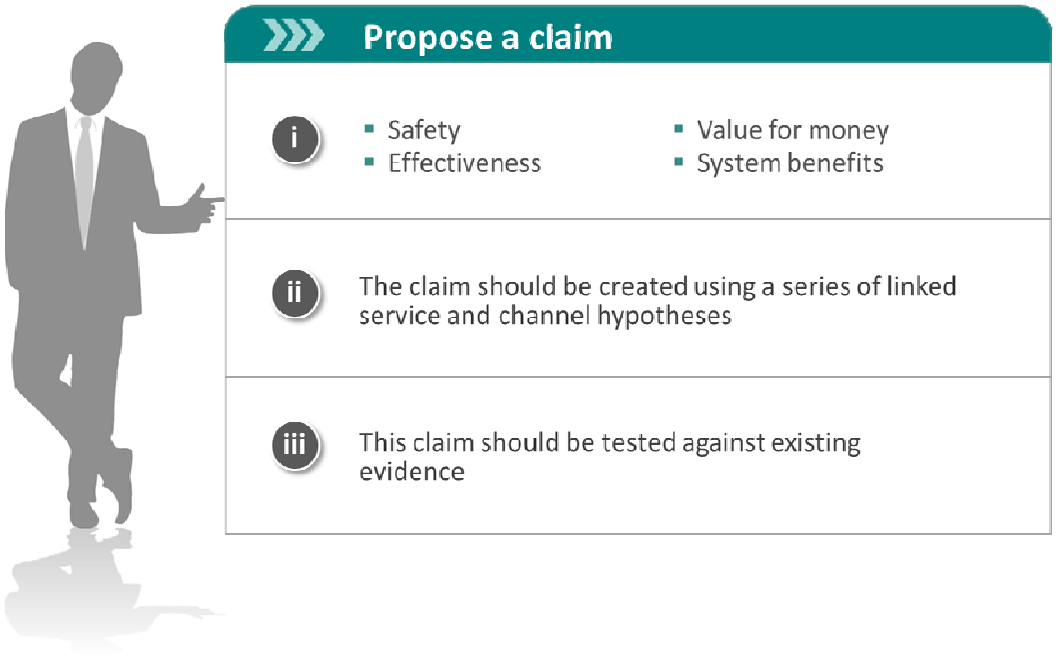
Scenario 1 – increased effectiveness at increased cost – can be satisfactory but will require a more complex analysis of relative value called a Health Technology Assessment. Solutions will be compared against current modes of treatment, for which there may well be large volumes of evidence. In this quadrant, Health Technology Assessment agencies typically use arbitrary value thresholds to decide which solutions are deemed to economically worthwhile, versus those that are not.

Scenario 3 may be acceptable in some scenarios, particularly for public health measures, where limited budgets mean that being able to influence a far larger group, albeit with less impact, is attractive. An example here could be a mobile enabled health information programme, which while less effective than one-to-one nurse based interventions, can be used for large populations at very low cost.

Scenario 4 is clearly unacceptable, but can occur if appropriate measures to evaluate resources and benefits are not implemented.

Wider healthcare system benefits

Once Mobile Health solutions have passed the initial hurdles of safety, effectiveness, and value for money, wider benefits such as improved access to healthcare and patient satisfaction can be considered. Other "societal" benefits can also be considered, but these may be viewed with scepticism by most funders of healthcare. Although there is no doubt that these issues are important and powerful, a Mobile Health solution must first be proved safe, efficacious and cost-effective within the health system.



ii. What evidence already exists for this claim?

Having proposed a claim, and considered the chain of linked hypotheses, a literature search regarding the hypotheses should be performed using respected databases of medical literature. For example, the PubMed database, maintained by the United States National Library of Medicine, has a catalogue of over 21 million records of medical publications from over 5,000 worldwide publications. The literature search should play particular close attention to other literature reviews – called *Systematic Reviews*. These will typically have been carried out by qualified researchers and can be a helpful short-cut to understanding the evidence. There are a number of well-respected sources of systematic reviews, perhaps the best known of which is the *Cochrane Database* based in Oxford, England. A word of caution however - systematic reviews may not be available for some research topics, may be out of date and there can be a significant time lag between actual research and publication.

Therefore performing a literature search will:

a) Reveal the current state of the evidence, including relative strengths and weakness in the chain of hypotheses

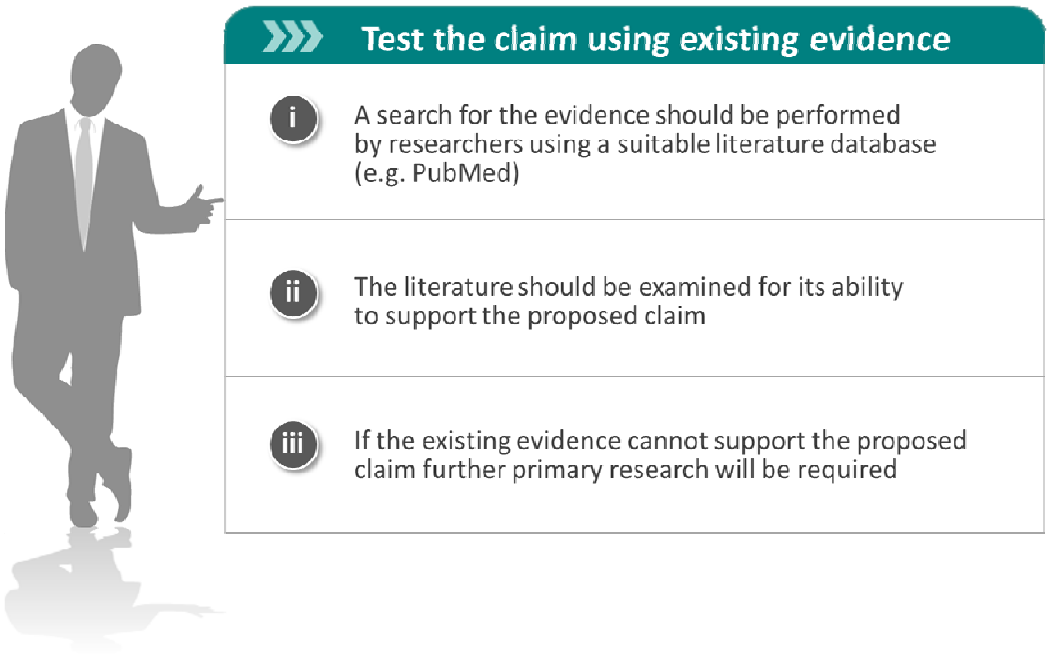
b) Provide an opportunity for the researcher to review and refine the validity of selected hypothesis

c) Provide insight into what type of research or analysis may be required to close gaps in the evidence base and strengthen the claim

The literature search and refinement of the hypotheses is an iterative process, and is an important foundation for the research proposal. The literature search should evaluate the evidence for 'service' related hypotheses first – if there is no supportive evidence for the service, then the provision of the service through an alternative channel such as mobile is unlikely to confer a benefit.

If positive evidence is found for the service, then the literature search should progress to evaluate evidence for the 'channel' i.e. mobile technology. If the evidence for the mobile channel exists, is of sufficient quality, and supports the hypotheses, then no further research may be required- the claim can be substantiated through analysis of existing research. For example an economic model for cost effectiveness can be created if the primary evidence for healthcare system costs and effectiveness of the Mobile Health solution already exist within the evidence base. If, as is most likely, the existing evidence cannot support the hypothesis for the mobile channel, then further primary research will be required to substantiate the claim.

This process will ensure that the proposed research is designed to make a positive contribution to the existing evidence base and help determine the research study design and methodology.



iii. What analysis or research is needed to substantiate the claim?

Once the literature search has been performed, and the hypotheses have been reviewed, the researcher should have an improved view of the state of the existing evidence. At this point, the researcher should also have a clear understanding whether the claim can be supported through analysis of existing research or whether further primary research is required to substantiate the claim.

If further primary research is required, the correct choice of study design will help to ensure that the proposed research will successfully achieve insight into the hypothesis. Some study designs are considered to produce more robust and referenceable evidence than others, and this is often

referred to as a "hierarchy of evidence". In general terms a research study may be either *Interventional* or *Observational*.

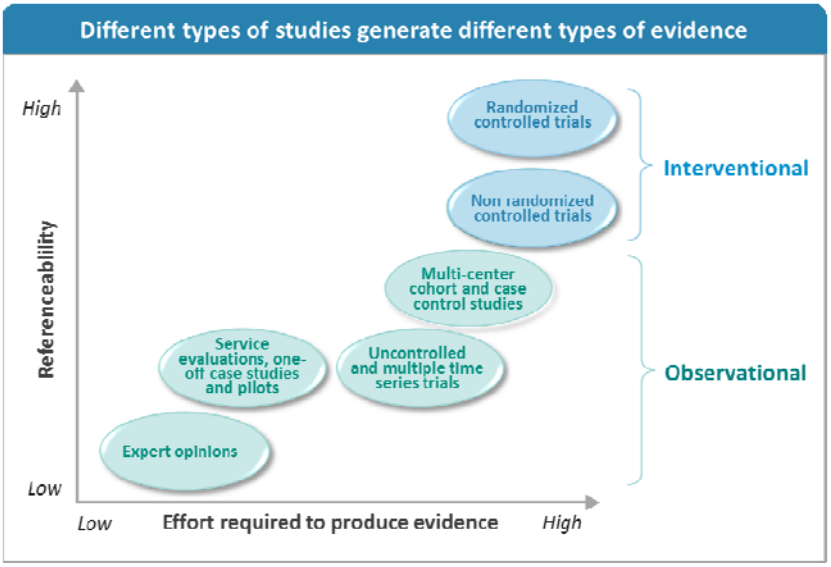


Figure 9: Types of Evidence

Interventional versus Observational Studies

Interventional studies occur when a research investigator assigns individuals to receive a specific intervention (e.g. a medication reminder Mobile Health solution). This group is then monitored for a defined period of time for specific outcomes (e.g. medication adherence or physiological measures). The performance of this 'intervention' group is compared to a 'control' group who receive an appropriate intervention that can be used as a benchmark for performance (e.g. nurse telephone call reminders, or no reminders). The 'control' intervention may range from accepted best practice to a placebo. In some studies, the assignment of individuals into the 'trial' group and the 'control' group is done by randomization. The objective of randomization is to reduce the risk of bias by reducing the risk of any other factor influencing the outcome, except for the intervention being studied. This is called a *Randomised Control Trial (RCT).*

In contrast to an Interventional study, an *Observational* study occurs when the research investigator does not exercise any influence on the intervention, and performs an evaluation and analysis of outcomes within the target population as they naturally occur, rather than in the context of a predetermined 'trial'. This type of study may also be described as a 'non-interventional' study.

Both interventional and observational study designs have advantages and disadvantages in their approach and outcomes.

	Interventional (RCT)	Observational
Applicability	Controlled environment	Real world
Patient Population	Narrowly defined	General
Controls	At all times	Variable
Likelihood of Bias	Low	High
Resource requirement	High	Low

Interventional studies, and in particular Randomised Control Trials, are traditionally considered to be at the top of the 'hierarchy of evidence'. This is because RCTs use specific techniques to reduce bias within the trial. For example, strict inclusion and exclusion criteria ensure that only subjects with specific characteristics are included in the study and these subjects are randomly allocated to a either the intervention or control group. These steps ensure that comparison of outcomes between two groups is a result of an actual difference in the intervention, rather than underlying differences between the subjects of the two groups.

However, a disadvantage of RCTs is that sometimes their inclusion and exclusion criteria can be too narrow. As a result, the subjects selected for the trial are not reflective of the population as a whole. For example, they may under-represent women, the elderly or ethnic minorities. They may only suffer from one particular disease the researcher is interested in (e.g. Diabetes) whereas in the real world most people have multiple diseases or *Co-Morbidities* (e.g. Diabetes and Heart Disease). Therefore the evidence produced from a narrowly defined subject group may not be applicable to a more general population.

In contrast, Observational studies provide an assessment of the impact of an intervention in a population that has not been controlled by a researcher, rather than highly controlled scenario of an RCT. As a result, observational studies are prone to bias as there are no criteria to decide which subjects receives a specific intervention, and a lack of a control group may make it difficult to definitively attribute a positive effect solely to the intervention being assessed.

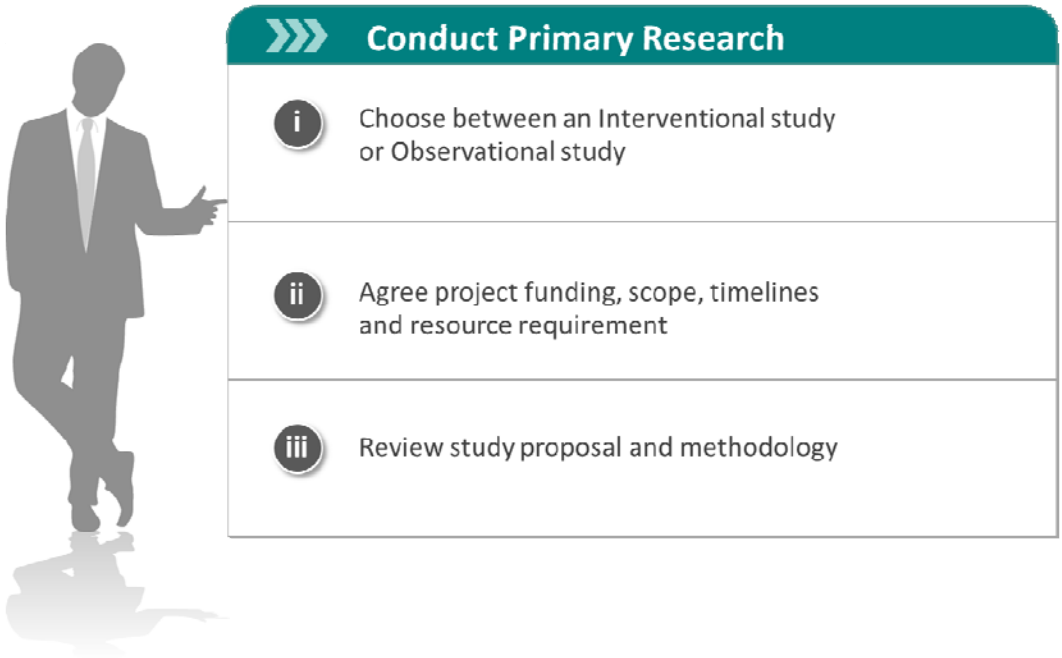
Despite these limitations, observational studies can provide strong insight into how a specified intervention is used in 'real world' practice. For example, one of the criticisms of RCTs is that the research environment often provides support and resources that are not normally found in real life practice i.e. follow up clinics to regularly monitor outcomes or promote adherence to the research protocols. Therefore the results of a RCT may be artificially enhanced compared to results found in 'real world' observational studies where such resources may not be provided. Observational studies can provide a fairer reflection of the effect of an intervention in 'real world' practice, and this is resulting in an increasing challenge to the traditional view of the 'hierarchy of evidence'.[6]

Another important factor is the contrast between the resource and timelines to perform an Interventional versus Observational study. Interventional studies require significant funding to meet regulatory requirements, ethical approval, and staffing to manage and perform the trial. Furthermore, narrow selection criteria can result in slow recruitment of suitable subjects. Within the pharmaceutical industry, the average time taken in RCTs from funding to recruitment of first patient is 621 days, and the median expenditure on NIHR/MRC approved studies was £3.2m.[7]

In contrast, observational studies often rely on analysis of routinely collected clinical data, and are typically subject to lighter regulatory requirements as no actual change is made to routine clinical practice. However, the disadvantage is that the data collected is subject to bias and may be incomplete or inappropriate for statistical analysis, thereby resulting in weaker evidence.

[6] On the evidence for decisions about the use of therapeutic interventions, Michael Rawlins, The Harveian Oration of 2008, Royal College of Physicians

So, what type of study should be used for those looking to prove the value of mobile health? If the solution is aiming to compete against an established treatment for a serious medical condition, or there is significant risk involved, then it is very likely that a randomised trial will be required. If the aim is to prove that an existing service can be delivered more cheaply in the real world, or if there is no existing service (as it often the case in the developing world) then an observational trial may be sufficient, or even superior to a randomised control trial.



iv. Is the proposed methodology correct?

After the appropriate trial design has been chosen, applying the correct methodology will help to ensure that the results of the research are robust and conclusive. We have identified four common methodological faults:

Incorrect Selection and Sample Size

The subjects selected for a trial should ideally reflect the target end user of the proposed Mobile Health solution, and sufficient number of subjects should be enrolled in the study to ensure that the outcomes are statistically significant. If too few subjects are enrolled, the intervention may fail to show any effect on the outcome in statistical analyses, even if an actual effect exists. Therefore the size of a sample should not be chosen arbitrarily but determined by the statistical degree of confidence desired in the results, and this is typically achieved with a *power calculation* (See Appendix).

Unsuitable Control

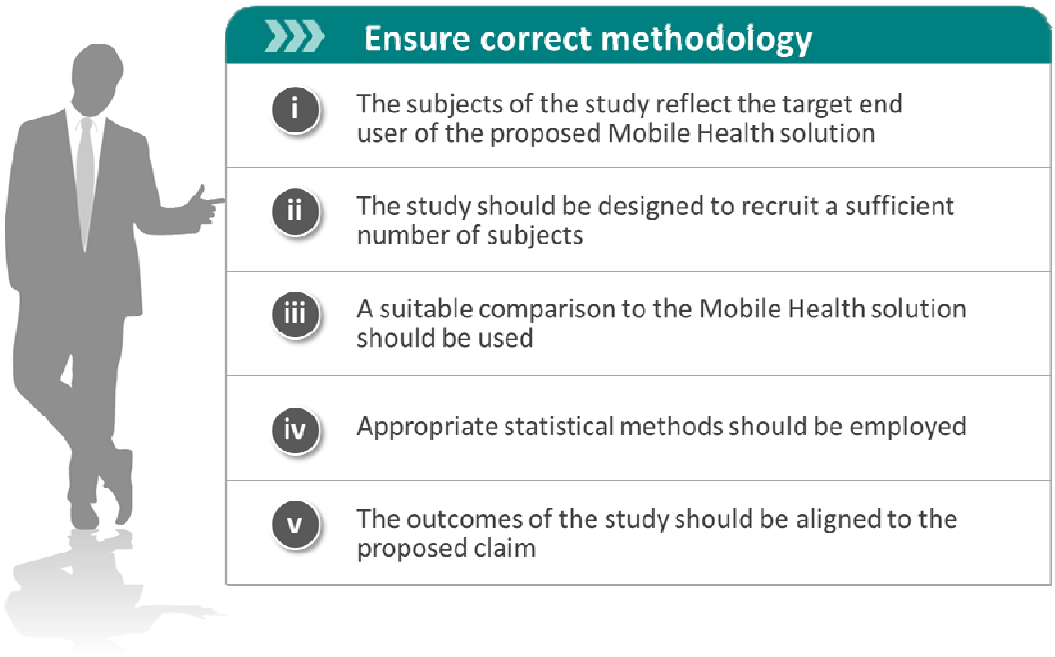
To prove outcomes in a rigorous manner, the Mobile Health solution being tested must be compared to the best alternative. The best alternative may be an existing solution commonly used in clinical practice, a defined 'gold standard' or if appropriate a placebo. This is known as a comparator or control. Applying an appropriate control within a trial is crucial to ensure that the conclusion of the effect of an intervention is accurate. If a control is not used, or is inappropriate, the effect attributed to an intervention is likely to be inaccurate.

Poor use of statistics

A wide range of analytical statistical tests can be used to measure significance of results for both interventional and observational studies. Selecting the correct type of test is important to ensure confidence that the measured outcome is real rather than an erroneous observation.

Measuring inappropriate outcomes

Once the claim in the research hypothesis has been set, it is crucial to ensure that the outcomes measured within the research reflect the subject of the hypothesis. For example, if the hypothesis states that use of a Mobile Health solution under investigation can reduce the blood pressure of the individuals included in the study, then the outcome measured in the study must be blood pressure. This does sound rather simplistic, but unfortunately there are a number of published studies that measure outcomes unrelated to the original hypothesis, whilst neglecting the most appropriate outcome measure. The key to avoid this is to invest significant time and effort prior to commencing the study to assess what data should be collected to appropriately answer the research question.



Illustrative examples of research methods

The authors developed a smoking cessation program using mobile phone text messaging to provide tailored and stage-specific messages to college smokers. The authors recruited **12 daily smokers** who owned smartphones and wanted to quit from a college campus and asked them to use an Internet and mobile phone text messaging program to quit smoking. **Six weeks** after program initiation, **95% smokers felt that they were more likely to quit** and were satisfied with the SMS program. Continued smokers reported significantly reduced smoking rates and dependence. Overall, participants accepted the text messages as **useful aid** to quit smoking.

1

- ✗ Small sample size
- ✗ No control group
- ✗ No use of statistics
- ✗ Inappropriate outcomes

- ✓ Good sample size
- ✓ Control group
- ✓ Appropriate use of statistics
- ✓ Appropriate outcome

2

The authors developed a smoking cessation program using mobile phone text messaging to provide tailored and stage-specific messages to college smokers. The authors recruited 200 daily smokers who desired to quit from a college campus. The smokers were randomised into two groups – one group received nurse counselling and printed information, the other group received daily text message reminders and links to an interactive website. Results were measured at six weeks, 6 months and 1 year after program initiation on an intention to treat basis. 44% reported continued abstinence with 42% abstinent based on cotinine verification in the SMS and internet group, compared to 22% reported abstinence with 20% abstinent based on cotinine verification in the control group. The results demonstrated statistical significance ($p<0.05$). This study demonstrates that SMS based smoking programs confer improved clinical outcome compared to the current best.

6. THE 'MOBILE HEALTH RESEARCH GUIDE' WILL HELP TO ENSURE HIGH QUALITY RESEARCH

Following a review of the existing evidence base and consultation with experts in Mobile Health research, A.T. Kearney and the GSMA have developed a Mobile Health research guide to help address the hurdles to widespread adoption of Mobile Health.

This guide is designed to support sponsors and commissioners of Mobile Health research, to help evaluate research proposals to ensure that studies are relevant, use appropriate study designs and employ robust methodologies.

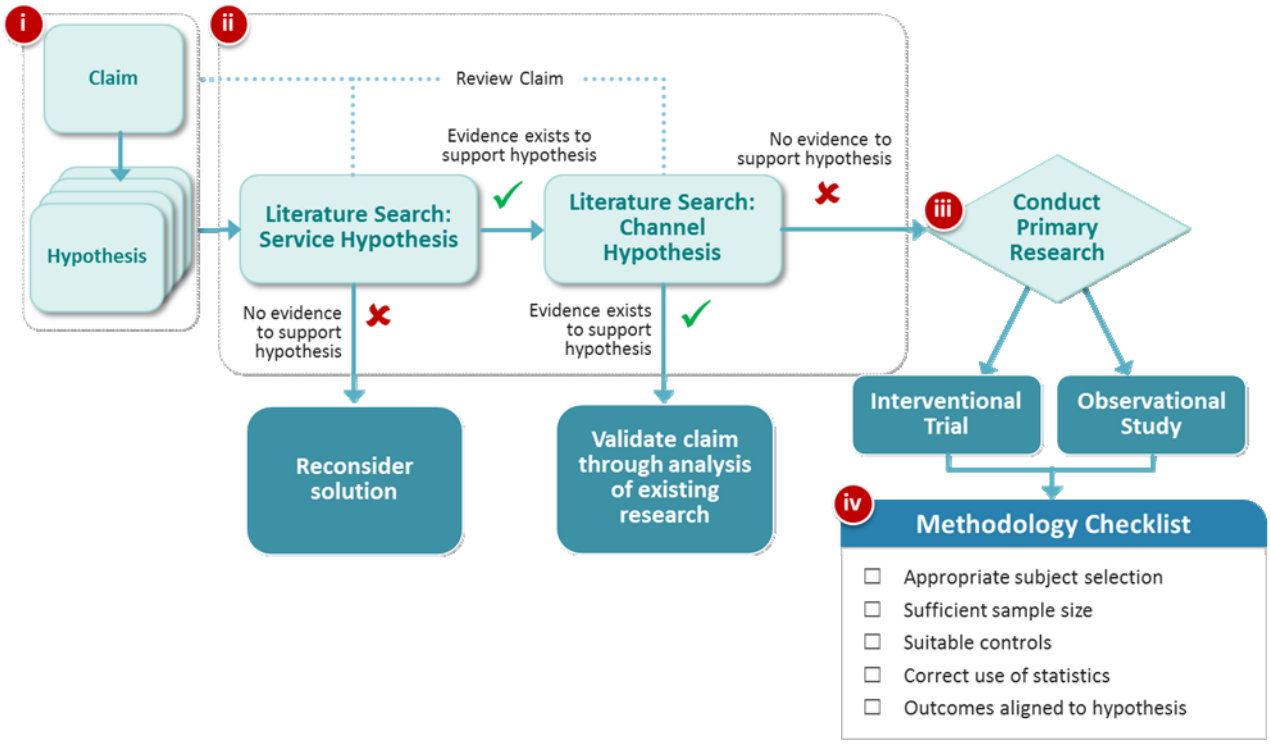
The guide establishes a logical process to support the creation of high quality research defined by four key questions:

i. Does the Mobile Health research claim address an appropriate hurdle to adoption?

ii. What existing literature or evidence supports the claim?

iii. What analysis or research is needed to substantiate the claim?

iv. Is the proposed research methodology correct?



Appendix

Randomised Controlled Trials

RCTs are normally designed to evaluate whether an intervention is superior, equivalent or non-inferior to the control group. A RCT typically follows four stages:

Enrolment Trial participants are assessed for eligibility to take part in the trial. This may include demographic parameters such as gender, age, and ethnicity, or clinical characteristics such as the presence of a specific disease or absence of comorbidities. Subject who do not meet the criteria are excluded from the study.

Randomisation All eligible subjects are allocated at random to receive the intervention or control. Randomisation is performed to minimise *selection bias.*

Follow-up All participating subjects of the trial are monitored at a predetermined interval and period of time, including a log of those subjects who are 'lost to follow up'.

Analysis The results of the follow-up are analysed to identify a statistically significant difference in outcome between the intervention and control subjects of the study.

Following this design, RCTs are capable of producing high degree of certainty on the result of a specific hypothesis. The use of techniques such as eligibility criteria, randomisation, strict monitoring procedures and a protocol-driven approach to experimental enquiry help to eliminate sources of bias and influence that may affect observed outcomes. As a result of this approach, RCTs are often considered to be at the top of the hierarchy of evidence to prove the impact of an intervention within a controlled environment.

Observational Trials

Within the context of Mobile Health research, the most common types of observational study likely to be used are non-randomised contemporaneous controlled trials, before-and-after studies, case series and reports.

Non-randomised controlled trials (NRCT)

This is an experimental study in which subjects are allocated to different interventions using methods that are not random. There is a significant risk of introducing bias in the results of the trial, however as they tend not to have narrow selection criteria, the overall recruitment has the potential of being much larger.

NRCTs have the potential of providing significant insight into the effectiveness of an intervention within a more general context; however the potential for bias must be taken into account.

Before and after studies

This study observes outcomes before and after a specified intervention, whereby the subjects act as their own controls. If a significant response is seen this could be attributed to the intervention. This study is of limited use as it cannot be used in conditions that have random fluctuations in clinical outcome and may be prone to the placebo effect.

Case series and Case reports

This type of study, sometimes referred to as an *uncontrolled longitudinal study*, is an observational study that tracks a group of subjects (or in case reports, a single subject) with a specific health state and their response to an intervention. Although no generalizable conclusions can be derived from a case series or report in isolation, due to selection bias and confounding, they can be useful in helping to validate results from other trials such as RCTs, or informing hypotheses for other research proposals.

Regulatory Approval and Policy for Mobile Health

The GSMA has published a paper that provides an assessment of the policy and regulation issues affecting the adoption of mHealth solutions. This draws on analysis of policy and regulation across four different regions, and identifies opportunities to foster a more supportive regulatory environment. Please consult 'GSMA mHealth: Policy and Regulatory Impact Assessment' for further information.

The FDA has issued draft guidance for the industry for Mobile Medical Applications on 21st July 2011 and is currently seeking industry feedback on this guidance. Further information can be accessed at: www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm263280.htm

Glossary

Cost-Effectiveness analysis is used to determine which program or treatment is the least costly way of obtaining the expected health outcome

Cost-Utility analysis is used to determine which program or treatment is the least costly way of obtaining a standard unit of health

Cost-Benefit analysis can be performed as *Absolute benefit of program*- to evaluate whether it is worth conducting the program of interest, or *Relative performance*- to choose the program producing the largest net benefit as compared to alternative programs

Intention to treat principle is that participants in trials should be analysed in the groups to which they were randomized, regardless of whether they received or adhered to the allocated intervention[7]

Statistical Power is a measure of how likely the study is to produce a statistically significant result for a difference between groups of a given magnitude (i.e. the ability to detect a true difference)[8]

[7] Cochrane Collaboration
[8] Research Methods in Health, A Bowling, OUP

About A.T. Kearney

A.T. Kearney is a global management consulting firm that uses strategic insight, tailored solutions and a collaborative working style to help clients achieve sustainable results. Since 1926, we have been trusted advisors on CEO-agenda issues to the world's leading corporations across all major industries. A.T. Kearney's offices are located in major business centres in 38 countries.

For further information, please contact

Jonathan Anscombe
Partner, A.T. Kearney
jonathan.anscombe@atkearney.com

Aleix Bacardit
Manager, A.T. Kearney
aleix.bacardit@atkearney.com

Imran Hamid
Associate, A.T. Kearney
imran.hamid@atkearney.com

www.atkearney.com

About the GSMA

The GSMA represents the interests of the worldwide mobile communications industry. Spanning 219 countries, the GSMA unites nearly 800 of the world's mobile operators, as well as more than 200 companies in the broader mobile ecosystem, including handset makers, software companies, equipment providers, Internet companies, and media and entertainment organizations. The GSMA is focused on innovating, incubating, and creating new opportunities for its membership, all with the end goal of driving the growth of the mobile communications industry.

For further information, please contact

Craig Friderichs
Director of Health, GSMA
cfriderichs@gsm.org

www.gsma.com