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ACRONYMS AND ABBREVIATIONS

BCR	Benefit-Cost Ratio
BIA	Budget Impact Analysis
CBA	Cost-Benefit Analysis
CCA	Cost Consequences Analysis
CDS	Clinical Decision Support
CEA	Cost-Effectiveness Analysis
CMA	Cost-Minimization Analysis
CUA	Cost-Utility Analysis
DALYs	Disability-Adjusted Life Years
DCER	Decremental Cost-Effectiveness Ratio
DHI	Digital Health Intervention
DHIS2	District Health Information System 2
EMR	Electronic Medical Records
HIS	Health Information System
ICER	Incremental Cost-Effectiveness Ratio
IIS	Immunization Information System
IO	Interoperability
IT	Information Technology
LIS	Laboratory Information System
LMIC	Low- and Middle-Income Countries
OpenMRS	Open Medical Records System
PSA	Probabilistic Sensitivity Analysis
QALYs	Quality-Adjusted Life Years
ROI	Return on Investment
SOC	Standard of Care
WHO	World Health Organization

1. INTRODUCTION

Through expenditures by governments, bilateral and multilateral organizations, and private organizations, investments in digital health have been increasing in low- and middle-income countries (LMICs). These investments in the health sector mirror a broad global movement to toward an information economy across sectors, from manufacturing to agriculture to education, where productivity depends upon generating, processing, and efficiently applying information. The goal of investments in digital health information systems (HIS), which are included under the larger umbrella of digital health interventions (DHIs), is to generate timely, complete, easy-to-use, and relevant information to help understand the operational needs and gaps of health programs and to increase their operational efficiency.

HIS are recognized as a foundational building block of health systems; many innovations in the DHI space have been introduced in LMICs. However, DHIs sometimes fail to succeed; this is due to poor design, mismatches between technology and infrastructure, gaps in human resources capacity, and either a lack of or a failure to adhere to national standards for system interoperability, privacy, and security. Transforming DHIs from their early promise to stable, enduring success at the national level remains a challenge.

To make decisions about DHI investments and scale-up, stakeholders—in government, bilateral and multilateral organizations, private organizations, industry, and academia—require evidence from careful evaluation to ascertain what does and doesn't work, particularly in settings of extreme resource constraints. However, despite clear guidance on evaluation principles,[1, 2] rigorous evaluation of DHI effectiveness seldom occurs in LMICs. Additionally, limited research has been done on the costs and value of digital health investments of DHIs versus traditional methods of managing, or communicating information in the health sector.[3, 4]

Despite vast and expanding literature on economic evaluation of health care interventions, most studies focus more on predominantly indication-specific technologies, such as medications and devices, and less cross-cutting, systems-level technologies such as DHIs. Consequently, although a few economic evaluations of DHIs exist in the literature, they cover limited ranges of methods and types. As a result, the evidence base on budget impact, return on investment, cost effectiveness, and cost utility of DHIs remains fairly limited and many questions remain unanswered about near and long-term costs and value of HIS investments.

One reason for the limited evidence on economic value of DHIs is that economic evaluation and health informatics are distinctive areas of expertise, with few individuals and thought leaders with intersecting expertise. Another reason is the methodologic complexity of economic evaluation of DHIs as cross-cutting health systems interventions. In this monograph, we aim to respond to these challenges by presenting an accessible overview of economic evaluation methods, as applied to DHIs as complex interventions, by reviewing the literature, and by presenting case studies that demonstrate the methodologic and analytic considerations for planning, conducting, and reviewing studies. The monograph will provide a framework to guide

planning, conduct, and consumption by stakeholders of economic evaluations of DHIs, and build familiarity with health economic evaluation concepts among health informatics experts.

1.1 Digital Health Interventions

DHIs are characterized by the use of computer systems (including smartphones) to receive, store, process (analyze), and communicate health and health care-related information. DHIs are used by patients, health care providers, health care managers, and other health care stakeholders (such as researchers) for a wide spectrum of health care services. These interventions are replacing legacy systems of information collection, processing, and communication (e.g., paper-based medical records) with contemporary network-based systems (electronic medical records). Network-based DHIs connect patients, health care workers, and other health care stakeholders through devices (computers and smartphones) and health care infrastructure (clinics, laboratories, and administration offices). Software programs help to automate systems, optimize processes, promote adherence to care guidelines, connect infrastructure units, and disseminate information.

1.2 Classification of Digital Health Interventions

The World Health Organization (WHO) *Classification of Digital Health Interventions v1.0* classifies digital technologies for health by their users or uses: clients, health care providers, health system managers, and data services.[5]

Clients may send or receive information (e.g., targeted and untargeted health communication, client-to-client communication, personal health tracking, health status and related reporting, and on-demand information services), or manage finances (e.g., transmission of payments and receipt of vouchers, subsidies, and incentives for health care services).

Health care providers may use DHIs for client identification, registration, and record management; health care worker decision support, remote consultation (e.g., telemedicine), communication, health care coordination, and activity planning; training; prescription and medication management; and laboratory and diagnostic imaging management.

Health care system managers may use DHIs for human resources and supply chain management, public health notification, civil registration and vital statistics, health financing, equipment and asset management, and facility management. Additionally, DHIs may be used for data services—collection, management, and use; coding; location mapping; and data exchange and interoperability.

Arguably the most pervasive digital technology with respect to provider-client communication is the mobile phone. Health-related applications for mobile devices are commonly referred to as *mHealth*. A review of mHealth applications in Africa found a wide range of applications, including patient follow-up and medication adherence; staff training, support, and motivation; staff evaluation, monitoring, and compliance; supply chain management; patient education; disease surveillance and intervention monitoring; and data collection, transfer, and reporting.[6] Another review of mHealth interventions for chronic diseases revealed their potential as tools

to increase access and coverage of health care interventions.[7] The growing use of these types of interventions makes the economic evaluation of their application ever more necessary for identifying cost-effective mHealth tools.

1.3 Complex Interventions

Digital health interventions vary in scale and complexity. DHIs may be designed to target a single condition (e.g., sending text messages to improve adherence to antihypertensive medications) or multiple conditions (e.g., electronic pharmacy management and decision support to prevent drug interactions), or to be part of the infrastructure of local, subnational, or national health systems (e.g., nationwide laboratory information systems).

Complex health care interventions may be defined by the following attributes:[8]

1) Multiple interacting components
2) Multiple (often difficult) behaviors required for successful delivery or consumption
3) Targeting of multiple groups or organizational levels
4) Multiple (often variable) outcomes
5) Tolerance to flexibility or tailoring of the intervention.

Many DHIs can be considered complex interventions.[9]

Using electronic medical records (EMRs) as an example, we can break down the attributes of complex interventions:

1) EMRs consist of hardware, software, and multiple personnel types (e.g., clinicians, data clerk, computer scientists) interacting together.
2) All personnel types must play specific roles and demonstrate specific behaviors to deliver a successful EMR system.
3) EMRs target multiple groups (e.g., clinicians and patients) and multiple organizational levels (e.g., administrators, physician, nurses, data clerks).
4) EMRs are amenable to customization, with substantial flexibility, to health care methods (curative or preventive), services (inpatient or outpatient), clinic sizes (small or large), and contexts (rural or urban).

1.4 Economic Evaluation in Health Care

In the health care field (including public health), *economic evaluation* is defined as the comparative analysis of two or more health care interventions in terms of both costs and consequences.[10]

Economic evaluations are performed from a specific perspective, usually that of the individual or group with an interest or stake in the results of the analysis. This perspective is the guide to which costs and outcomes the analysis will consider. The evaluations consider costs incurred and outcomes accrued over different time horizons, which may vary from days to years, depending on the interests of analysts and stakeholders.

All economic evaluations have one characteristic in common: estimation of the costs of interventions. Costs are usually estimated as a product of the quantity of resources used and the unit cost of the product, service, or activity, on a per person or per use basis for a specified period. For example, the per patient cost of text message reminders for antihypertensive medication adherence is a product of the number of messages (sent to one patient in, say, one year) and the cost per message. Costs may also be estimated in using "top-down" approaches, in which the total cost of a (usually shared) good or service is allocated to different units, and ultimately to individual patients.

Outcomes of complex interventions are estimated in a variety of ways, based on the mechanism of action of the intervention, and depending on the needs of analysts and stakeholders. For example, a national laboratory information system (LIS) may reduce the cost of personnel dedicated to data entry. A government's ministry of health may be interested exclusively in how the LIS reduces personnel time use and costs, whereas an analyst might estimate other consequences, such as reduced time from sample collection to receipt of results, or increased quality of patient care due to prompt receipt and use of laboratory results.

An analyst might compare the costs and consequences of a new EMR system to those of an existing paper-based system. The costs of the EMR system over a one-year period would be calculated as a product of the resources needed to run the system for a year, and the unit costs of those resources. For instance, the implementation of a new EMR system may require a health facility to hire a new computer technician. The cost of this component of the system is a product of the number of hours of service provided by the computer technician for one year and the technician's hourly wage. The EMR system might lead to several potential outcomes—reduced personnel costs, automated appointments, reduced patient wait times—that could be evaluated.

2. COSTS: ANALYSIS AND ESTIMATION

Cost estimation can occur as part of stand-alone analyses independent of intervention outcomes. However, in most applications, cost estimation occurs as part of different types of economic evaluations in which costs are assessed relative to the outcomes generated by interventions. If the primary interest is costing only, the methods described herein can be applied without seeking to estimate the value of outcomes or consequences.

2.1 Cost Descriptions

The estimation of costs may occur for a single intervention, or for an intervention relative to one or more comparator interventions. Studies that examine the costs of interventions without comparison are called *cost descriptions*.[10] Examples of cost descriptions include a study of the cost per patient record of a population-based immunization information system (IIS) in the United States,[11] a study of the cost per patient for an informatics-based (e.g., registry and disease management) diabetics program,[12] and a study of the financial and nonfinancial costs of implementing an EMR system in a primary care setting in the United States (US).[13]

2.2 Cost Analyses

Studies that compare the costs of two or more interventions without assessing outcomes are called *cost analyses*. An example of a cost analysis is the study by Adler-Milstein et al., in which they compared the annual cost per diabetic patient for information technology-enabled management of diabetes using registries with reminders, EMRs with clinical decision support (CDS), remote monitoring of care, and a self-management platform.[14] Other examples of cost analyses include a study that compared the U.S. IIS to the standard of care (non-US IIS reporting) with a focus on the opportunity cost of time spent performing administrative tasks,[15] and the study by McKenna et al. that compared an IIS with the prevailing manual registry system.[16]

2.3 Cost Categories

In general, three kinds of costs are incurred for health care interventions: direct medical, direct nonmedical, and indirect costs.[17] However, there is some flexibility in the ways costs are grouped in economic evaluation, and choices about categories may differ from one economic evaluation to another. The discussion below is intended to cover a range of cost types to consider in economic evaluation of DHIs.

Direct medical costs go directly into providing patient care, and include such costs as those incurred to procure medicines, diagnostics, and other medical supplies. An example of direct medical costs for a DHI is the time cost incurred by clinicians to update a patient's EMR. Direct medical costs can be borne by the provider, the health system, the patient, or others.

Direct nonmedical costs are incurred by patients, healthcare payers, or society but do not go directly into patient care. They include such items as overhead and capital costs incurred by facilities and the costs incurred by patients for transportation and upkeep while seeking care. DHIs are usually associated with direct nonmedical costs, such as utilities and personnel costs

for management and administration at the facility level. DHIs may also affect patient-level direct nonmedical costs, for example, by reducing patient wait times, and thereby reducing caregiver time and cost.

Indirect costs are the (opportunity) costs of lost productivity by patients, due to their illness (e.g, missed work or suboptimal performance), or while seeking care (e.g, travel to care and time spent at health facilities). Indirect costs may also be impacted if DHIs affect wait times and care efficiency.

Other program costs may be incurred in some interventions, such as demand creation for health care services (e.g., television advertisements) and outreach (e.g., travel by health workers to provide community-based services). Both demand creation and outreach costs are affected by DHIs. For example, mobile phone applications and text messages may replace television advertisements, and remote teleconsultation may replace community outreach. The choice of which costs to include depends on the perspective of the evaluation.

Costs can also be categorized as *startup* (fixed) and *recurring costs*. These cost categories are relevant to an evaluation of DHIs. Startup costs would include DHI hardware and software, and training the personnel assigned to run it; and recurring costs would include salaries, utilities, and so on. For an intervention requiring the purchase of equipment, first-year costs are usually higher than the recurring costs for subsequent years due to the initial (often high) cost of equipment.

An additional dimension of cost specifically relevant to evaluation of DHIs is the concept of *sunk costs*—costs that have already been incurred and cannot be recovered. Such costs usually have no bearing on the decision of whether or not to implement an intervention, so they may be safely excluded from analyses. For example, a particular health center may already have a building with enough space to accommodate paper-based, data-related activities as well as a new EMR system. Since the cost of the building has already been incurred, it would be considered a sunk cost. As a result, the space cost for the new EMR system would not be included in the analysis.

2.4 Cost Estimation

There are two basic methods of cost estimation: microcosting (bottom-up costing) and gross costing (top-down costing).[18]

In *microcosting*, costs, for purposes of estimation, are a factor of the quantity of resource use and unit costs (prices). For example, personnel costs are a factor of time spent performing certain tasks (in hours) and unit costs or hourly wages. Cost estimation, therefore, proceeds through the three steps of identification of resources used to achieve an intervention, valuation of the quantity of resources used, and measurement (the combination of resource use and unit costs).[18] Unit costs for goods and services are usually obtained from price lists or market surveys, but may also be obtained from financial records such as invoices or expenditure records within health organizations. Information on volume or quantities of resources used is

usually obtained from the analysis of treatment patterns in primary studies (e.g., time-motion studies) or secondary studeis (e.g., chart reviews and database analyses).

In *gross costing*, analysts obtain estimates of total costs incurred for a facility and allocate them to care bundles (e.g., costs per outpatient visit or per hospital day) and units of service provision (e.g., costs per cardiac unit or cardiac patient).[18]

To estimate the costs of personnel required to run a digital health intervention using microcosting methods, the quantity of resources used might be measured in a *time-motion survey*, which is a method of tracking health worker and patient time use as patients progress through the careseeking process. Times measured using paper forms or electronic devices,such as low-power Bluetooth and near-field communication, are multiplied by the hourly wage of providers to estimate the cost of providing care. Similarly, time-motion surveys can be used to estimate patient time spent seeking care as a basis for estimating the opportunity cost to the patient of seeking care.

For example, Were et al. used a time-motion study to demonstrate the change in the percentage of health worker days spent on different clinical and administrative activities, and the time savings that accrue from a change from paper-based medical records to an EMR system.[19] Data from Were et al. may be combined with wage data to estimate the cost savings that accrue from introducing the EMR system.

Using gross costing methods to estimate the personnel costs involved in running a DHI, an analyst might calculate the sum of wages paid to facility staff members responsible for delivering the intervention. This sum is then allocated to the amount of time spent by staff members on delivering the intervention, and the number of patients to whom it is delivered, resulting in an estimate of the cost of personnel time per patient.

In many cases, to estimate the costs of such facility-based interventions as EMR and laboratory information systems, resource-use data for both fixed and recurring costs may be collected from administrative and accounting records. These resource-use estimates can be combined with unit costs or prices for goods and services.

2.5 Currency Conversion, Reference Years for Costing, and Discounting

Analysts also need to consider currencies and dates when estimating costs. To allow for comparison with other studies in the literature, most evaluations use U.S. dollars. However, it may sometimes be necessary to report amounts in local currency units.

Cost estimates may be collected or observed in multiple years. Because of inflation, costs need to be converted to a specific base (reference) year using the appropriate country-specific consumer price index.

Analysts must also consider the discount rate when estimating costs and outcomes that occur across multiple years. The discount rate is a representation of time preference for money—i.e., individuals prefer money today rather than tomorrow because they can invest money in hand and see a return on their investment. The recommended discount rate is 3%.[20]

3. OUTCOMES—TYPES OF ECONOMIC EVALUATION

The techniques for defining and valuing the outcomes or consequences of an intervention depend upon the type of economic evaluation method used. Analysts have a choice of different types of economic evaluation methods:[20]

1) Cost-effectiveness analysis
2) Cost-utility analysis
3) Cost-minimization analysis
4) Cost-consequence analysis
5) Cost-benefit analysis

What distinguishes these different types of analyses is how they characterize the health and other benefits that accrue as a result of implementing an intervention. It is also important to note that it is common for studies to use multiple methods, and that there is often a lack of methodological purity or clarity with regard to studies as reported in the literature.

Other types of economic evaluations include return-on-investment analysis and budget impact analysis, which are predominantly used for fiscal and planning purposes.[20, 21]

3.1 Cost-Effectiveness Analysis

Cost-effectiveness analysis (CEA) measures outcomes in "natural units," such as reductions in morbidity (e.g., symptom-free days), metrics of illness (mm of Hg for hypertension), or mortality (increases in life expectancy).[10, 20] CEA allows comparison of interventions within a given indication—for example, management of patients with HIV. In a clinical intervention setting, CEA may estimate outcomes for a particular indication, such as management of hypertension, in which the outcome is expressed as a percentage reduction in mmHg as a result of a given intervention.

In the case of EMRs, analysts might consider such outcomes as reductions in total time spent per patient in the clinic, or in the percentage of patients not reminded of the dates of their next visits. Other possible choices of outcomes in the context of a CEA of an EMR system include completeness of records, adherence to guidelines, and quality of care. If an EMR system were installed in an HIV clinic, outcomes of interest for CEA might include linkage to care (if the EMR is connected to testing data, or if there is a clear reference pathway); occurrence and timeliness of HIV testing; timeliness of antiretroviral therapy initiation, detection of treatment failure, or return of laboratory results; appropriateness of regimen; or detection of drug interactions or adverse events and allergies.

Kopach et al. performed a CEA of an automated documentation system at a Canadian hospital, comparing it against the existing manual system. [22] [22] [22] The outcome of the analysis was the average time in days from patient discharge to note completion; the metric of cost-effectiveness was the incremental daily cost of reducing average completion time per discharge order by one day.[22] Wu et al. performed an analysis of electronic medication ordering and administration,

also in Canada, in which the outcome was the prevention of adverse drug events, and the value metric was cost per adverse drug event avoided.[23]

3.2 Cost-Utility Analysis

Cost-utility analysis (CUA) in the health care field estimates outcomes as a combination of length of life and quality-of-life, either as quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs).[10, 20] QALYs combine gains from reduced morbidity (quality gains) and gains in reduced mortality (quantity gains) into a single metric. Similarly, DALYs combine gains from reduced morbidity (disability reductions) and gains in reduced mortality (quality gains) into a single metric. Because they combine both length and quality of life, QALYs and DALYs allow for comparison of the value of interventions for both diseases in which morbidity predominates, such as anxiety, and diseases in which mortality predominates, such as suicide—thereby allowing comparison of interventions across the health care sector.

While it is often difficult to ascribe health outcomes in terms of DALYs and QALYs to complex, system-level interventions, one can identify specific avenues by which such interventions might lead to increases in either length of life (DALYs), quality of life (QALYs), or both. An EMR system deployed at an HIV clinic might be customized to send automatic reminders to patients who fail to fill their prescriptions, thereby leading to increased adherence to treatment. Increased rates of adherence may lead to better viral load control, better quality of life, and increased life expectancy. Economic evaluations may be able to leverage intermediate outcomes,such as increased adherence, to calculate health outcomes in terms of DALYs and QALYs, making CUA potentially useful as an analytic tool in applications where the ultimate impact of the EMR system is of interest to analysts and stakeholders.[10, 20]

For example, O'Reilly et al. conducted a CUA in which they compared computerized decision support linked to EMRs against the standard of care for diabetes in Canada.[24] They used data from a randomized trial to parameterize a patient-level computer simulation model of major diabetes complications.[24] The main outcome of the analysis was cost per QALY saved over a 40-year time horizon.

3.3 Cost-Minimization Analysis

Cost-minimization analysis (CMA) assumes or leverages evidence of equivalent health or other outcomes, and compares only costs.[10, 20] Therefore, under CMA, the better intervention is the least costly one. CMA is neither commonly used nor recommended. The presence of uncertainty regarding the estimates of costs or outcomes means that this method is rarely chosen as a unique, pre-specified method of analysis. CMA is most commonly used to compare drugs within the same therapeutic class.[10]

Although CMA is unlikely to be applicable in evaluating digital health interventions in general, or EMR systems in particular, one can think of specific stakeholders whose interests would be unaffected by migration to an electronic platform. In such a case, the cheaper of the two systems, electronic or paper-based records, would be chosen.

3.4 Cost-Consequence Analysis

Cost-consequence analysis (CCA) presents a multidimensional listing of outcomes, and places the onus of deciding whether interventions are desirable on the consumers of the analysis.[10, 20] Different health and system-level outcomes may be presented alongside costs of interventions without aggregation of either costs or outcomes. This kind of analysis may be particularly suited for the evaluation of complex interventions, such as DHIs in general or EMR systems in particular, given the wide range of possible outcomes that can result from implementing HIS interventions.

In comparing a new EMR system to an existing paper-based system using a CCA, an analyst may present the cost of both systems on a per patient or per facility basis. The analyst would then present multiple outcomes, such as reduction in patient wait times; percentage increases in completion of records, attendance at scheduled visits, or adherence; and increases in perceived quality of care. This then allows different stakeholders to examine the costs and outcomes of interest specific to their perspective. For example, a patient advocate might be interested in reduced patient wait times, while a government bureaucrat might be interested in ensuring that patients attend scheduled clinic visits.

3.5 Cost-Benefit Analysis

Cost-benefit analysis (CBA) estimates outcomes in monetary units and allows comparison of interventions across the entire economy.[10, 20] For clinical interventions, CBA monetizes health outcomes using a variety of methods, such as discrete choice experiments, contingent valuation, and value-of-a-statistical-life. Often policymakers and other stakeholders do not encourage or readily accept the explicit monetization of health benefits; this makes cost-benefit analyses relatively rare in the literature on economic evaluation of health care interventions and programs.

Some analysts perform CBA in which they monetize intermediate outcomes. For example, cost-benefit analyses in the EMR space have reported monetized benefits in terms of reductions in the costs of paper chart storage areas and medical transcriptionist wages;[25] the monetized benefits of reduced need to create medical records; decreased labor costs; and reductions in adverse drug events, dosage errors, full-time equivalent personnel, and medical billing errors.[26] In the LIS space, Chae et al. monetized the reduction in laboratory data processing time per test.[27] At the broader health system level, Byrne et al. compared the net value of investments in IT infrastructure by the US Department of Veterans Affairs with that of the private sector.[28]

3.6 Return-on-Investment Analysis

Return-on-investment (ROI) analysis estimates the financial return accrued from investment in an intervention over a given period. ROI analysis compares the timing and quantity of financial returns to the timing and quantity of costs, and is therefore dependent on time horizon. ROI analysis is not recommended for economic evaluations of health care programs, since health outcomes are not considered independent of their impact on costs and cost savings.[20]

With EMR systems, however, ROI analysis may have a role to play, given the difficulty of ascribing health effects to a system- or provider-level intervention. For example, Driessen et al. modeled the potential ROI of a hospital-wide EMR system. Although they considered a limited set of cost savings—in length of hospital stay, transcription time, and laboratory use—Driessen estimated a net financial gain in the third year of operation of the EMR system, and a financial return of over half a million dollars over five years. [29]

3.7 Budget Impact Analysis

Budget impact analysis (BIA) estimates the expected change in health system expenditures after the adoption of a new intervention; it can be used for budget or resource planning.[21] In a budget impact analysis, the costs of health care in the new (post-intervention) environment are compared with those in the old (pre-intervention) environment. The difference between the two is the budget impact. BIA is usually performed after analysts have already ascertained that an intervention is cost-effective. Given cost-effectiveness, the BIA is performed to determine the intervention's fiscal feasibility or affordability. It is important to note that some cost-effective interventions have prohibitively large budget impacts; that is, they are efficient but unaffordable.

BIA can be performed to assess the affordability of a new health information system for planning purposes. The estimate of the expected change in costs between the pre- and post-EMR periods can be used to determine whether cash flow from revenues or government disbursements would be sufficient to maintain the EMR system. In a planning context, the BIA can be the main factor determining whether or not the EMR system is implemented.

There are multiple examples of budget impact analyses of digital health interventions in the literature. Following the report that evidence-based clinical decision support reduced primary care prescription costs,[30] McMullin et al. performed a BIA in which they reported the per-member per-month savings in prescription drug costs over a twelve-month period.[31] Ohsfeldt et al. conducted a BIA of implementation of a hospital computerized order entry system in rural Iowa.[32]

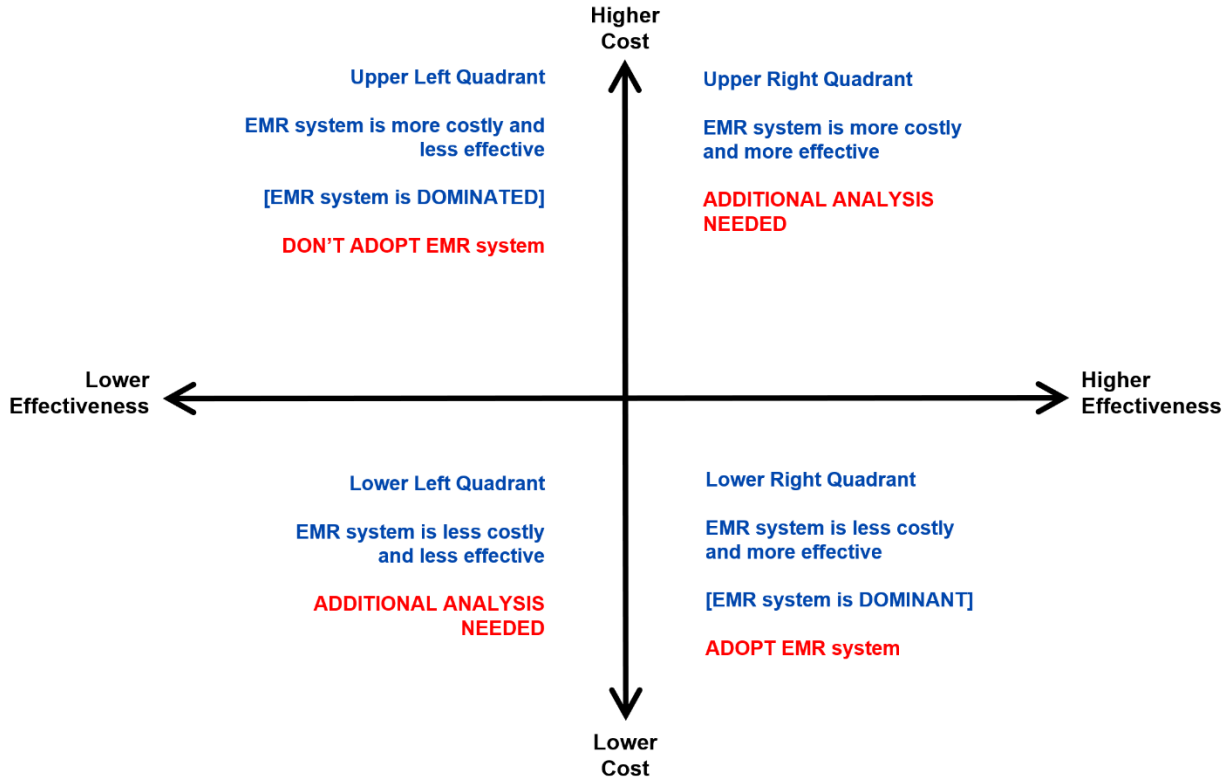
4. ASSESSMENT OF VALUE

Once costs are estimated and outcomes are measured and valued, the next step in an economic evaluation is to compare cost and outcomes in an assesement of intervention value.

4.1 Assessing Value in Economic Evaluations

Given cost and outcomes estimates of two or more digital health interventions, when is the DHI under evaluation considered cost-effective? As mentioned above, economic evaluation compares two or more interventions in terms of costs and outcomes. The analysis underpinning the determination of cost-effectiveness proceeds in a pairwise manner. In the case of an economic evaluation comparing a new EMR system to the paper-based record system, there are four possible outcomes; these are shown in Figure 1 below.

Figure 1. Cost-effectiveness plane comparing an EMR system to the standard of care (SOC)



In the upper left quadrant, the EMR system leads to higher costs and lower effectiveness. The EMR system is said to be "dominated," and is therefore not recommended for implementation.

In the upper right quadrant, the EMR system leads to higher costs and greater effectiveness. The extent to which the increase in effectiveness is worth the increase in costs is subject to additional analysis. The additional analysis involves calculation of an incremental cost-effectiveness ratio, or ICER: *(cEMR – cPaper-based)/(eEMR – ePaper-based)*.

In the lower left quadrant, the EMR system leads to lower costs and reduced effectiveness. The extent to which the reduction in effectiveness is worth the additional cost savings is subject to additional analysis. The additional analysis involves the calculation of a decremental cost-effectiveness ratio, or DCER: *(cEMR – cPaper-based)/(eEMR – ePaper-based)*.

In the lower right quadrant, the EMR system leads to lower costs and higher effectiveness. The EMR system is said to be "dominant," and is thus recommended for implementation.

Most interventions are expected to increase both costs and effectiveness (upper right quadrant); accordingly, we can usually expect manufacturers and innovators to charge a premium for new products. Based on ICER values, there are three ways to determine whether the ICER meets the criteria for cost-effectiveness:[33]

- *Thresholds*—pre-specified ICER values that are acceptable in a given setting
- *Benchmarks*—ICERs for other interventions that are considered broadly acceptable in a given setting
- *League Tables*—listings of interventions by ICER, in ascending order, with the interventions implemented in order until the budget is exhausted

Thresholds, benchmarks, and league tables are commonly, but not exclusively, applied to economic evaluations that measure combined length-of-life and quality-of-life, i.e., QALYs and DALYs. For other outcomes, the decision as to what is considered cost-effective is usually left to the relevant stakeholder or budget holder.

4.2 Expanded Value Framework

An expanded basis for value assessment has recently been published that considers other dimensions beyond net costs and outcomes as described above, such as labor productivity and adherence improvement. The expanded framework does not suggest that existing economic evaluations have not considered some of these dimensions, but rather seeks to classify them.[34] The economic evaluation of DHIs, given their wide range of uses and complexity, may be expanded to more formally include, or at least consider, some of these dimensions of economic value.

Labor productivity as a metric of value refers to the extent to which a health care intervention affects the ability of individuals to participate in the workforce, i.e. productivity gains and losses. It is a product of labor force participation, time spent in the workforce, and wages. One can imagine how, by improving patient management, DHIs may lead to productivity gains in a single indication of interest, or across several indications. For instance, an EMR system may improve antiretroviral medication adherence and control of viral loads, and reduce opportunistic infections and absenteeism. An alternative labor force effect is related to health workers that interface directly with DHIs: they may incur a higher time cost initially due to learning curves (e.g., when first using an unfamiliar EMR system), and a lower time cost in the long run thanks to efficiency gains because the introduction of an EMR system enables paper-based systems to be bypassed. Learning effects were demonstrated in a study of hospital information systems, in which there was an association between cost decreases and lagged intervention.[35]

Adherence-improving factors refers to interventions (or aspects of interventions) that affect behavior, lead to increased adherence to treatment, and thereby improve health outcomes.[34] A wide variety of DHIs are designed for this very purpose; these include the use of mobile phones to promote adherence to antiretroviral therapy,[36] mobile applications to improve adherence to hypertension medication,[37] and multiple digital tools to tackle nonadherence in autoimmune diseases.[38] Interventions such as EMRs may also be used as the interface for push notifications that act as reminders for the purpose of attempting to improve adherence to treatment.

In the diagnostics arena, the reduction in uncertainty due to companion diagnostics refers to the value of selecting responders or nonresponders and predicting treatment effectiveness and its attendant economic cost and outcome benefits,such as reductions in treatment costs and number of adverse events, respectively. DHIs don't often play the role of direct complements to accompanying treatments; their potential effect may instead be realized through such avenues as prompt relay of results to clinicians using laboratory information systems, and the use of electronic reminders to reduce the amount of time between when results are available to clinicians and when they are accessible by patients. However, DHIs can be configured to identify patients who need targeted services using, for instance, clinical and phenotypic data and predictive modeling, thereby behaving like traditional diagnostic tests.[46]

Equity refers to the achievement of more equal health outcomes across, for example, income groups or healthy and sick groups. DHIs as health care interventions may promote equity indirectly by improving access to a broader range of health care interventions, and by creating efficiencies that lead to increased access among marginalized groups. For example, an EMR system may lead to reduced patient waiting and an increase in clinician full-time equivalents by speeding up the process of retrieving and updating records in the clinic setting, thereby increasing the number of patients that a given clinic can see on a given day.

Economic evaluations of DHIs should also consider that the efficiency gains achieved by DHIs must be weighed against the opportunity cost of emerging threats (e.g., cyberattacks) to data safety and patient confidentiality that either did not exist or were minimal when legacy systems were the norm.

5. CONDUCTING AN ECONOMIC EVALUATION

Individual economic evaluations are usually performed to match a specific intervention and the perspective of a particular stakeholder. Therefore, each study is unique. This section discusses some general considerations for performing economic evaluation studies.

5.1 Framing the Economic Evaluation

5.1.1 Definition of Comparators

Full economic evaluation studies are by definition comparative, encompassing two or more interventions. Although the number of interventions is usually determined by best practice, it is important to both include all relevant comparators, lest the evaluation be irrelevant, and limit comparators for analytic simplicity. It is also essential to define the intervention and comparators in detail. Sometimes the intervention is simple, as in the example of a text message service to provide reminders for antiretroviral medications, in which the comparator is the absence of an adherence-enhancing intervention. Sometimes the intervention and comparator are complex, as when hardware and software are added to affect IO between EMRs, LIS, and patient cellphones in order to quickly transmit HIV viral load results from the laboratory to patients and clinicians. In this example, the comparator is the unlinked, stand-alone EMR, LIS, and patient cellphone systems. In both cases, it is important is to clearly define both the intervention and the comparator; it is this definition that determines which costs to consider, and which inventory of possible outcomes to choose from when the evaluation is conducted.

5.1.2 Perspective

Perspective refers to the viewpoint from which an analysis is conducted; that viewpoint is usually that of the stakeholder on whose behalf the analysis is performed.

Two major perspectives are recommended: the health care sector perspective, and the societal perspective.[20] Analysts may choose one or use both perspectives. The *health care sector perspective* includes health care sector medical and non-medical costs borne by payers and out-of-pocket costs borne by patients.[20] In many low-income countries, the payer is the ministry of health, although most countries have substantial private (including insurance) and nonprofit health care markets. The *societal perspective* is broader, and includes not only the medical costs described in the health care sector perspective, but also the time costs of patients seeking and receiving care, and of informal (unpaid) caregivers; transportation costs; the effects of future productivity and consumption; and other outside costs and effects.[20] One or both of the perspectives may be chosen.

It is recommended that analysts quantify nonhealth consequences of interventions in an impact inventory—a list of disaggregated consequences across different sectors.[20] The impact inventory is of interest in the evaluation of DHIs, particularly complex DHIs. A given DHI might have impacts outside of the health sector, as in the example

of the possible use of an EMR system as part of government planning for services unrelated to health care.

Other perspectives are also possible, depending on stakeholder needs. A key stakeholder in LMICs is the community of bilateral and multilateral donors; this may necessitate an analysis from a donor perspective. Analysts may also conduct analyses from a patient perspective, or a public health (as opposed to clinical) perspective.

5.1.3 Reference Case

The *reference case* in an economic evaluation defines the typical entity in an analysis. In analyses of disease-specific therapies, the base case is usually the typical patient in the population of interest.[39] However, there are different kinds of entities possible, for example, a specific blood sample in the economic evaluation of handling of laboratory orders and test information for routine viral load tests as part of HIV treatment. Although DHIs may be configured for a specific disease, most DHIs will be configured for several diseases. The reference case may then be defined as a generic patient straddling multiple disease areas.

5.1.4 Time Horizon

The *time horizon* of the analysis is the period for which the costs and outcomes of the intervention and comparator are considered. The time horizon is chosen to be adequate to capture all the potential benefits of an intervention; what qualifies as adequate depends on the specific intervention and the stakeholder. Therefore, analysts need to tailor the time horizon of each analysis to the intervention and the needs of the stakeholder. Sometimes interventions happen over a short period, with consequences unfolding over a long(er) period. Decision-modeling methods allow analysts to extrapolate data from shorter periods to longer periods in order to estimate benefits.

5.1.5 Consideration of Intervention and Analytic Complexity

Regardless of complexity, each evaluation should be considered a unique analysis guided by the perspective of the stakeholder of interest. As discussed above, many DHIs are complex interventions operating within complex systems.[9, 40, 41] This has several possible effects on how economic evaluations are designed and conducted. Analysts must decide whether a traditional analysis (as described above) is sufficient, or if a more complex evaluation, one which explicitly considers intervention and system complexity, is warranted.[41] Evaluations that explicitly consider the complexity of an intervention differ from traditional analyses in their modeling of patient-system-network relationships.[41]

To perform an economic evaluation that properly considers intervention complexity, analysts need to consider the impact of intervention complexity on cost estimates. The types of costs that are relevant may depend on the perspective being applied. Other resource use and cost considerations include the opportunity cost of learning: DHIs may initially result in high upfront labor costs as personnel learn to work with

them, but later result in labor cost savings as the efficiency of DHI-based systems kicks in.

When it comes to assessment of outcomes, analysts must decide which outcomes are of interest to the relevant stakeholders. In the case of complex interventions, analysts might compare the outcomes of reminders received by auto-generated text messages to those received by telephone with respect to implementation outcomes (e.g., the percentage of patients receiving each type of message), service outcomes (e.g., percentage of patients retained in care due to each type of message), and patient outcomes (e.g., percentage of patients with reduced viral loads due to each type of message). Analysts also need to consider the impact of the interventions to generate economies of scale whereby efficiency and productivity improve when services are provided at higher volume, such as when an EMR allows more patients to be served in a health facility, and economies of scope whereby efficiency and productivity improve when multiple products or services are provided, such as when an EMR addresses both outpatient and inpatient care within a hospital. Analysts also need to consider that the intervention may produce spinoffs, cause feedback loops or negative effects, or lead to impacts beyond the disease area or health system in which the evaluation is conducted.[40, 41]

5.2 Collecting and Organizing Data

Economic evaluations of DHIs can be conducted by using primary data collected in a trial or observational study, such as an impact evaluation (trial-based analysis), or by using decision-analytic models to combine data from multiple sources (model-based analysis). [20]

5.2.1 Trial-Based Economic Evaluations

Trial-based evaluations are conducted using primary data on costs and outcomes collected from individual patients in trials or observational studies. Either during or after the study, data are collected on resource use and health care utilization. The limitation of trial-based analyses is that they seldom include all possible analytic comparators or patient groups, or all relevant evidence, and they seldom use time horizons that are long enough to capture all relevant costs and benefits.[8]

5.2.2 Model-Based Economic Evaluations

Model-based evaluations use estimates from a variety of sources, including primary studies, databases, and estimates from published literature.[20] Models provide a framework for decision-making under conditions of uncertainty, and are useful for extrapolating beyond the time horizon of available data; extrapolating from intermediate to ultimate outcomes (e.g., from blood pressure to life expectancy); extrapolating to population subgroups not observed in primary studies; extrapolating to interventions (comparators) that were not analyzed in primary studies; (5) weighing benefits, harms and costs; and assessing the implications of uncertainty on decisions.[20]

Although models are useful and potentially powerful analytic tools, they have limitations worth pointing out. For one thing, models are only as good as the data that are used to parameterize them, and how well the data are used, which determines the degree to which the biases of observational data are included in the models themselves. For another, modeling methods lack standardization, regulation, and (sometimes) transparency, which may affect their validity.

The choice of modeling framework depends on the application or question of interest, time horizon (long, short, lifetime), and unit of analysis (individual, cohort, or population), and whether entities in the model are allowed to interact with each other, or with other components of the model. Analysts have five different decision modeling types to choose from: decision trees, state-transition models, microsimulation models, dynamic transmission models, and dynamic simulation models. [20] These modeling methods are discussed in detail elsewhere.[10, 18, 20, 42]

5.3 Sensitivity Analysis

Sensitivity analysis is important in economic evaluations because of the presence of *uncertainty*. There are four kinds of uncertainty:

1) *Analytic*—whether the chosen methods fit the economic evaluation question
2) *Parameter*—whether analysts have statistical confidence in estimates used in a study
3) *Structural*—whether the analytic structure fits the problem, e.g., using short-term clinical trial data to extrapolate to long-term outcomes
4) *Generalizable*—whether the results of the analysis are applicable to real-world settings

The most basic type of sensitivity analysis is *univariate (one-way) sensitivity analysis*, which examines the impact of changing a single parameter estimate through its plausible range of values on costs, outcomes, or metrics of cost-effectiveness, such as ICERs or benefit-cost ratios (BCRs).

Multivariate sensitivity analyses (such as two- and three-way sensitivity analyses) examine the impact on outcomes of varying two or more parameters simultaneously.

Probabilistic sensitivity analyses (PSAs) are conducted to reflect overall uncertainty in the model. In PSAs, all parameter inputs are varied simultaneously in the model by using probability distributions to characterize their uncertainty, and propagating that uncertainty through the analysis or model using Monte Carlo simulation. The result of PSAs is a distribution of the results or outcomes of the analysis.

6. CASE STUDIES

In this section we present a series of three case studies to illustrate how to pragmatically apply the concepts of economic evaluation to specific digital health interventions. The case studies are designed around existing real-world interventions that have been implemented, or are being implemented, in LMICs. The case scenarios were purposely chosen to illustrate interventions of current interest, and common types of analyses that may be of interest to DHI implementers, evaluators, and decision makers. Each case study includes a table of analytic options to demonstrate how to assess outcomes and costs under different types of economic evaluation studies. The case studies demonstrate the methods and analytic considerations for estimating costs and outcomes, and determining the cost-effectiveness of DHIs. The methods proposed reflect the authors' choices, and do not demonstrate all the available analytic options for economic evaluations of DHIs.

The case studies are divided into two parts: (1) a detailed description of a specific economic evaluation analysis that could be selected for the intervention, and (2) a description of a wider range of analytic methods, choices, and considerations for economic evaluation of the intervention.

Summary of Case Studies

	Case 1: Economic evaluation of an EMR system at the point of service delivery in an outpatient HIV clinic	**Case 2: Economic evaluation of an IO platform between a health facility EMR system and a national aggregate data system**	**Case 3: Economic evaluation of IO of EMR and LIS for access to timely and accurate HIV viral load results**
Topic	Replacing a paper-based system with a digital solution	IO to facilitate transmission of reports from the facility to the national database	Linkage of patient information across multiple systems
DHI	EMR system	EMR and aggregate data reporting systems	EMR and LIS
Analysis Type	CEA	CEA	CUA
Comparators	Paper-based medical records system vs. EMR system	Manual indicator reporting vs. automated indicator reporting	Independent systems vs. interoperable systems
Perspective	Payer	Payer	Society
Outcome	Retention of patients in clinical care	Time required to report aggregate data following data collection	QALYs or DALYs
Time Horizon	1 year	6 months	Patient lifetime
Considerations	Identifying one-time and recurrent resources using administrative and financial records, along with time	Identifying costs of personnel, software, overhead; need data from an impact evaluation to assess the outcome.	Identifying one-time and recurrent resources using administrative and financial records, along with time estimates; include costs of seeking care incurred by

	estimates; need data from an impact evaluation to assess the outcome.		patients, and opportunity costs of lost productivity while seeking care.
Results	1) Costs of each comparator 2) Incremental costs 3) Percentage of patients retained in care 4) Change in percentage of patients retained in care	1) Costs of each comparator 2) Incremental costs 3) Time from record creation to record aggregation 4) Changes in time	1) Costs of each comparator 2) Incremental costs 3) QALYs gained or DALYs averted 4) Incremental QALYs or DALYs
Additional Design and Analytic Considerations	• Use of a different perspective • Alternative outcomes could be assessed using a CCA • The time horizon could be reduced or increased, depending on the perspective	• Use of a different perspective • Alternative outcomes could be assessed using a CEA or CCA • The time horizon could be reduced or increased, depending on the perspective	• Use of a different perspective • Alternative outcomes could be assessed using a CEA or CCA • A shorter time horizon could be used

6.1 Economic Evaluation of an Electronic Medical Record System at the Point of Service Delivery in an Outpatient HIV Clinic

6.1.1 Background

EMRs can improve the quality of care provided by health facilities. EMRs provide a framework for repeated data analysis and use, thereby improving quality of care (e.g., increasing the likelihood that services required by patients will be received), improving patient management (e.g., increasing retention in care), and supporting program management (e.g., reporting of indicators of program progress and success). EMRs can be configured to provide such services as clinical decision support to potentially reduce adverse drug events and drug interactions.

Low-income countries have begun to introduce EMRs despite facing severe resource constraints, often using disease-specific funding from donors. For example, in Kenya, EMRs have been used in projects that mainly support HIV care, leading to well-developed systems for this disease area. Kenya has been implementing an EMR system in public health care facilities across the country.[43] We describe below the considerations for an economic evaluation of the EMR system in an outpatient HIV clinic.

6.1.2 Cost-Effectiveness Analysis of an EMR System in an Outpatient HIV Clinic in Kenya

6.1.2.1 Comparators

The comparators (the items the analysis will compare) would be an EMR system and a paper-based medical records system.

6.1.2.2 Perspective

The perspective is that of the payer, which would be either the government of Kenya or donors. This means that only costs incurred by the specific payer would be included in the analysis. This perspective would, for instance, exclude costs incurred by patients and other payers (such as donor staff). Additionally, the government may be interested specifically in increasing the rate of retention of HIV patients in clinical care.

6.1.2.3 Outcome of Interest—Type of Economic Evaluation

Given the outcome of interest to the government—increased retention in clinical care—the economic evaluation will take the form of a CEA. That is, the outcome occurs "naturally" as a result of the intervention.

6.1.2.4 Reference Case

Given the outcome of interest, the reference case is a newly-diagnosed HIV patient who has been started on antiretroviral therapy.

6.1.2.5 Time Horizon

The time horizon of the analysis is one year. Therefore, the measurement of retention in care would be measured for one year following initiation of antiretroviral therapy.

6.1.2.6 Intervention Complexity

As discussed above, EMRs are complex interventions. They consist of multiple components and personnel types interacting together, require different personnel types to demonstrate specific behaviors in order to deliver the intervention successfully, target different groups of stakeholders and organizations, and are amenable to customization, with substantial flexibility, to different types of health care. For example, an EMR may include automated alerts, reminders, or reports about patients who have missed appointments, and may affect a clinic's care practices or staffing mix, such as by reducing the need for data clerks to compile lists of patients with missed visits. In this specific CEA, the impact of the EMR system on retention of patients in clinical care necessitates explicit consideration of the costs, outcomes, and avenues of impact affecting personnel cadres involved in the system and departments in the clinic (e.g., clinical, administration, and recordkeeping).

6.1.2.7 Cost Considerations

Costs to be considered when implementing an intervention include those for such one-time resources as hardware and software, and for such recurrent resources as physical space, software updates, IT system administration and maintenance services, electricity, telecommunications and internet data fees, and personnel (IT personnel, clinical personnel, and managers), and staff training costs.

To estimate the costs of these resources, an analyst would combine primary data collection and analysis of administrative and financial records. For instance, the upfront costs of hardware and software and the recurring cost of utilities can be obtained from expense account records. For personnel costs, the analyst could conduct a time-motion survey before and after implementation of the intervention and compare time use. Time estimates could then be combined with data on wages for different cadres to estimate the intervention and comparator costs.

Intervention Costs

- **One-time**
  - *Software development*: salaries for developers to design, build, test, deploy
  - *Hardware*: desktop computers, printers
- **Recurrent**
  - *Physical space*: rent for location housing system
  - *Software updates*: salary for developer to troubleshoot and fix issues
  - *System administration*: salaries for administrators and supervisors
  - *Maintenance services*: fees to maintain and house server
  - *Electricity*: fees to power the system
  - *Telecommunications*: staff phone bills
  - *Internet data fees*: data bundles for system's online functionality
  - *Personnel*: staff salaries for completing intervention-related activities
  - *Staff training*: trainer per diem, printed materials, transport

Costs of the comparator condition, a paper-based data system, could be estimated using similar techniques in specific health facilities before EMR implementation, or could be estimated contemporaneously in health facilites which are similar but where only paper-based data systems are used.

6.1.2.8 Data and Analytic Considerations

Given the outcome of interest, a trial-based economic evaluation, with data from a previously conducted impact evaluation or a primary data collection effort, would be the best analytic choice.

6.1.2.9 Results and Uncertainty

The results of the analysis would be presented as: the costs of each comparator, incremental costs, the percentage of patients retained in care for each comparator, the change in percentage of patients retained in care, and an ICER in the form of a cost per percentage increase in retention in care, comparing the intervention to the comparator. A univariate sensitivity analysis would be performed and presented to show which paramaters had the greatest impact on costs, outcomes, and the ICER, and a probabilistic sensitivity analysis would be performed and presented to show the combined uncertainty in the model and its impact on cost-effeciveness results.

6.1.3 Additional Design and Analytic Considerations for an Economic Evaluation of an EMR System in an Outpatient HIV Clinic in Kenya

Although the comparators remain unchanged, the analysis may be performed from alternative perspectives, include donor and societal perspectives. It is possible for analysts to choose from a range of possible outcomes, and select the particular economic evaluation type that fits with the outcome of interest (Table 1). Some examples of the alternative outcomes of interest include patient satisifaction, HIV viral load supression, and improved completeness and timeliness of patient records. The study can also take on the form of a CCA, presenting multiple outcomes from different perspectives in addition to estimates of the costs of the interventions.

If a stakeholder is interested in completeness and timeliness of records, the alternative reference case to the patient is a unique patient record. The choice of reference case will depend on the interests of the stakeholder. Depending on the perspective and outcome of interest, the time horizon may be reduced (e.g., to one month for a CEA with record accuracy as an outcome) or increased (to enable a lifetime horizon CUA). The different perspectives and time horizons also have implications for which costs to include, and for the choice between trial- and model-based analyses. For instance, by including all costs from the payer perspective plus direct nonmedical and indirect costs, the societal perspective would generate higher costs for both comparators.

Table 1. *Analytic options for economic evaluation of an EMR system at the point of service delivery in an outpatient HIV clinic*

Analysis Type	Comparator?	Costs to Consider	Outcomes
Cost Description	No	EMR system	No
Cost Analysis	Yes	EMR system and paper-based record system	No
Cost-Minimization Analysis	Yes	EMR system and paper-based record system	Known or assumed to be equal by comparator
Cost-Effectiveness Analysis	Yes	EMR system and paper-based record system	Retention in care or other outcomes, such as patient satisfaction, HIV viral load

			supression, completeness of records
Cost-Utility Analysis	Yes	EMR system and paper-based record system	Extrapolation of patient-related outcomes to DALYs or QALYs
Cost-Benefit Analysis	Yes	EMR system and paper-based record system	Monetized patient and other outcomes
Cost-Consequence Analysis	Yes	EMR system and paper-based record system	All relevant and evaluable outcomes assesed and presented—for example, patient waiting time, completeness of data in records, patient compliance with scheduled visits, adherence to medication, fidelity to care guidelines, patient satisfaction, and perceived quality of care

6.2 Economic Evaluation of an Interoperability Platform Between a Health Facility Electronic Medical Records System and a National Aggregate Data System

6.2.1 Background

Health services data are vital inputs to the planning, delivery, evaluation, and accountability of health systems. Although Kenya has begun the process of introducing EMR systems and an aggregate national data system, they initially existed in silos as stand-alone systems. The lack of interoperability between electronic data systems at the different levels of the health care system (facility, county/district, national) means that data are printed out from the EMR systems, and then reentered into the national aggregate data reporting system. This manual process has several disadvantages: it is labor intensive, prone to transcription errors, and increases the amount of time between collection of data and its reporting and use.

An automated indicator reporting process for a subset of PEPFAR's next generation indicators was implemented to link the Open Medical Records System (OpenMRS) system at a district hospital to the District Health Information System (DHIS2) aggregate data reporting system in Kenya.[44] We describe below the considerations for an economic evaluation of this intervention to establish interoperability.

6.2.2 A Cost-Effectiveness Analysis of Interoperability Between a Health Facility EMR System and National Aggregate Data System In Kenya

6.2.2.1 Comparators

The comparators in this analysis would be independent OpenMRS and DHIS2 systems with manual reporting of indicators, and OpenMRS and DHIS2 linked through an interoperability framework with automated reporting of indicators.

6.2.2.2 *Perspective*

The perspective of the analysis would be that of the payer, which in this case is PEPFAR. This means that only costs incurred by PEPFAR would be included in the analysis. Additionally, PEPFAR is specifically interested in reducing the time between data collection in facilities and aggregation, reporting, and use of that data by the national PEPFAR office for planning purposes.

6.2.2.3 *Outcome of Interest—Type of Economic Evaluation*

Given the outcome of interest—reduced amount of time between data collection and aggregate data reporting—the economic evalution will take the form of a CEA. That is, the outcome is a "natural" occurrence as a result of the intervention.

6.2.2.4 *Reference Case*

Given the outcome of interest, the reference case is a monthly patient report generated for review and incorporation into the DHIS2 in a format appropriate for aggregation and reporting.

6.2.2.5 *Time Horizon*

The time horizon of the analysis is six months, which is the longest possible gap between creation of a record for a unique facility visit and entry of that record in a national database to allow for automated indicator reporting.

6.2.2.6 *Intervention Complexity*

Automated indicator reporting through interoperability between OpenMRS and DHIS2 is a complex intervention. First, there is an interaction between an EMR and a national data system. Then there is the need for several cadres of personnel, health care, and otherwise, to work together to develop, deploy, and test the intervention. There are multiple system levels and many possible outcomes, and the intervention can be tailored to deliver outcomes besides accuracy, completeness, and timeliness of clinical indicator reporting. For example, the system could be extended to enable interoperability between other clinical information systems, such as LIS, and DHIS2.

A clear scoping definition of the intervention itself is important. For example, does the EMR system have strong underlying data completeness and data quality attributes beyond paper-based registers or other primary data collection tools, or is reinforcing data quality within the EMR part of the intervention?

Given such complexity, it is important for an analyst to limit analyses to the specific avenues of intervention impact, costs, and outcomes spelled out by the stakeholders or ultimate users of the results. In this specific evaluation, the impact of interoperability to expedite the creation of data in a format necessary for automated indicator reporting necessitates explicit consideration

of the costs, outcomes, and avenues of impact for multiple levels and personnel cadres involved in the system.

6.2.2.7 Cost Considerations

Given the payer (PEPFAR) perspective, and the outcome of interest, the following costs would be included: personnel, trainers, supervisors, clinical personnel that enter OpenMRS records, data entrants that enter records manually into the DHIS2 system, and IT administrators; software (purchase and updates), and applicable capital and overhead costs (e.g., additional server hardware, additional space, and IT network cabling, and other supplies). To estimate these personnel costs, analysts would conduct a time-motion survey before and after the implementation of the intervention, and compare time use for generating and transmitting monthly indicator reports from health facilities to district (county) and national databases via DHIS2. Time estimates would then be combined with data on wages for different cadres to estimate intervention and comparator costs.

Intervention Costs

- **One-time**
  - *Software purchases*
  - *Hardware*: server, IT network cabling, supplies
- **Recurrent**
  - *Personnel*: salaries of trainers, supervisors, and clinical personnel who perform intervention-related activities
  - *Software updates*: salary for developer to troubleshoot and fix issues
  - *Physical space*: rent for location housing system
  - *Electricity*: fees to power the system
  - *Telecommunications*: staff phone bills
  - *Internet data fees*: data bundles for system's online functionality

6.2.2.8 Data and Analytic Considerations

Given the short time horizon, a trial-based analysis would be sufficient to perform an economic evaluation of the intervention. That is, data for costs and outcomes would be obtained from a primary impact evaluation of the intervention. The analyst would either utilize data from an exisiting impact evaluation, or perform a new one as part of this economic evaluation.

6.2.2.9 Results and Uncertainty

The results of the analysis would be presented as: the costs of each comparator, incremental costs, amounts of time between record creation and aggregation for each comparator, changes in amounts of time between record creation and aggregation, and an ICER in the form of a cost per unit reduction (e.g., minutes, hours, days, or percentage points) in the amounts time between record creation to aggregation, comparing the intervention to the comparator. A univariate sensitivity analysis would be performed and presented to show

which paramaters had the greatest impact on costs, outcomes, and the ICER, and a probabilistic sensitivity analysis would be performed and presented to show the combined uncertainty in the model and its impact on cost-effectiveness results.

6.2.3 Additional Design and Analytic Considerations for an Economic Evaluation of Interoperability Between a Health Facility EMR System and the National Aggregate Data System in Kenya

Although the comparators remain unchanged, the analysis may be performed from alternative perspectives. For instance, many LMICs have de facto national health systems despite a substantial proportion of health spending occuring in the private sector. This often necessitates analyses from the governmental perspective. The other rationale for the governmental perspective is that most donors commit to limited time-bound investments with the expectation that governments will take over for purposes of sustaining DHIs. Another possible perspective is the all-inclusive societal perspective, which has the advantage of presenting policymakers with a complete picture of the opportunity costs of the intervention.

It is possible for analysts to consider multiple outcomes, and thereby use multiple economic evaluation types (Table 2). The specific outcomes that might be considered in this case study include in the context of a CEA include data completeness, transcription errors, and personnel time use. The study can also take on the form of a CCA presenting several outcomes from different perspectives in addition to estimates of intervention costs.

The alternative reference case to the patient record for a unique visit would be either a comprehensive patient record that includes multiple visits or the patient. The choice of reference case will depend on the interests of the stakeholder. Depending on the perspective and outcome of interest, the time horizon may be expanded, for example, to one year in order to appeal to administrators, or to a lifetime horizon to enable a CUA. The different perspectives and time horizons also have implications for which costs to include, and for the choice between trial- and model-based analyses.

Table 2. *Analytic options for an economic evaluation of an interoperability (IO) platform between a health facility EMR system and a national aggregate data system*

Analysis Type	Comparator?	Costs to Consider	Outcomes
Cost Description	No	IO platform	No
Cost Analysis	Yes	IO platform and independent systems	No
Cost-Minimization Analysis	Yes	IO platform and independent systems	Known or assumed to be equal by comparator
Cost-Effectiveness Analysis	Yes	IO platform and independent systems	Examples: data completeness, transcription errors, quality of care metrics
Cost-Utility Analysis	Yes	IO platform and independent systems	Extrapolation of patient-related outcomes to DALYs or QALYs
Cost-Benefit Analysis	Yes	IO platform and independent systems	Monetized patient and other outcomes
Cost-Consequence Analysis	Yes	IO platform and independent systems	All relevant and evaluable outcomes assesed and presented—for example, accuracy, completeness, and timeliness of reported data; appropriate allocation of health sector commodities and human resources that reflect health services utilization patterns

6.3 Economic Evaluation of EMR-LIS Interoperability for Access to Timely and Accurate HIV Viral Load Results

6.3.1 Background

Routine HIV viral load testing is a pillar of HIV care: it enables the tracking of viral suppression, and triggers regimen changes in the event of virologic failure. Although some clinics in low-income countries are using point-of-care technology, it is still relatively expensive. The majority of clinics continue to rely on central (reference) laboratories equipped with the machinery and expertise that allow for sample batching, which is cheaper on a per-test cost basis than point-of-care testing.

Batch testing of samples for viral load at central laboratories is challenging for several reasons, not least of which is the lack of accurate and timely transfer of viral load testing orders and samples from peripheral clinics, not to mention the transmission of results back to those clinics. To remedy this, countries that have invested in both EMR and LIS are seeking to establish interoperability between the two. The goal of EMR-LIS interoperability is to facilitate linkage of patient information across multiple systems for improved continuity of care**.** We describe below the considerations for the economic evaluation of an EMR-LIS interoperability solution in an outpatient HIV clinic.

6.3.2 Cost-Utility Analysis of EMR and LIS Interoperability

6.3.2.1 Comparators

The analysis would compare implementation of independent EMR and LIS with implementation of interoperable EMR and LIS.

6.3.2.2 Perspective

The government, through a joint committee of the ministries of finance and health, has asked for a comprehensive analysis of the impact of investments in EMR-LIS interoperability. Therefore, the analysis would be perfomed from the societal perspective. This means that all possible costs incurred as a result of implementing EMR-LIS interoperability would be included in the analysis. The joint committee has also asked that analysis be performed to allow them to compare the value of EMR-LIS interoperability with that other health-related investments.

6.3.2.3 Outcome of Interest—Type of Economic Evaluation

The outcome of interest to allow the comparison of investment in the EMR-LIS interoperability platform would be either QALYs or DALYs, making the evaluation a CUA.

6.3.2.4 Reference Case

Given the outcome of interest, the reference case is a an HIV patient on antiretroviral therapy.

6.3.2.5 Time Horizon

The time horizon is the lifetime of patients, a time horizon that captures all the potential costs and benefits of patients attending clinics with EMR-LIS interoperability.

6.3.2.6 Intervention Complexity

EMR-LIS interoperability is a complex intervention. First, there is interaction between an EMR system and the LIS, and potentially with other systems such as the DHIS. Then there is the need for several cadres of personnel, both health care and otherwise, to work together to implement the intervention. There are multiple system levels and possible outcomes, and the intervention can be leveraged to either transmit a wider array of lab test orders and results, or to link data with other systems, such as logistics management information systems for laboratory supply chain management. Given the perspective of the analysis, the analyst would attempt to model all avenues of complexity to capture a holistic view of costs and benefits.

6.3.2.7 Cost Considerations

Costs to be considered when implementing EMR-LIS IO include those for such one-time resources as hardware and software (e.g., biometric identification devices, barcode readers, printers, cables, personal computers), and for such

recurrent resources as cloud services, software updates, electricity, telecommunications and internet data fees, and personnel (e.g., IT, clinical and laboratory staff, data clerks, and managers).

To estimate the costs of these resources, an analyst would combine primary data collection and analysis of administrative and financial records. For instance, the upfront costs of hardware and software and the recurring cost of utilities can be obtained from expense account records. For personnel costs, the analyst could conduct a time-motion survey before and after implementation of the intervention and compare time use. Time estimates could then be combined with data on wages for different cadres to estimate the intervention and comparator costs.

Intervention Costs

- **One-time**
  - *Software development*: salaries for developers to design, build, test, deploy
  - *Hardware*: desktop computers, printers, biometric identification devices, barcode readers, cables
- **Recurrent**
  - *Software updates*: salary for developer to troubleshoot and fix issues
  - *Maintenance services*: fees to maintain and house server, fees for cloud-based data storage
  - *Electricity*: fees to power the system
  - *Telecommunications*: staff phone bills
  - *Internet data fees*: data bundles for system's online functionality
  - *Personnel:* staff salaries for completing intervention-related activities

In an an economic evaluation from the societal perspective, other relevant costs may also apply, including costs incurred by patients seeking care or for upkeep while they are seeking care, and the opportunity costs of lost productivity by patients while seeking care. These costs would apply if EMR-LIS interoperability led to differences in the patient experience while seeking care, for example, as a result of differences in waiting times.

Costs of the comparator condition, independent EMR and LIS systems, could be estimated using similar techniques in specific health facilities before EMR and LIS interoperability is established, or could be estimated contemporaneously in health facilites which are similar but no EMR-LIS interoperability exists.

6.3.2.8 Data and Analytic Considerations

Given the outcome of interest (QALYs or DALYs) and the time horizon, a model-based analysis would be required. A decision model would be developed and parameterized using data from several sources, including primary and secondary data. Decision models provide a framework for decision making under uncertain conditions.[45] There are multiple types of decision models that

may be used to consider, in this case, the probability that samples or sample orders are unusable, and the probability of a change of treatment regimen contingent upon laboratory diagnosis of virologic failure. Other parameters that would be needed in the analysis include health-related quality of life in terms of utility or disability weights.

6.3.2.9 Results and Uncertainty

The results of the analysis would be presented as: the costs of each comparator, incremental costs, QALYs gained or DALYs averted for each comparator, incremental QALYs or DALYs, and an ICER in the form of a cost per QALY gained or DALY averted comparing the intervention to the comparator. A univariate sensitivity analysis would be performed and presented to show which paramaters had the greatest impact on costs, outcomes, and the ICER, and a probabilistic sensitivity analysis would be performed and presented to show the combined uncertainty in the model and its impact on cost-effectiveness results.

6.3.3 Additional Design and Analytic Considerations for an Economic Evaluation of EMR-LIS Interoperability

The conduct of an economic evaluation from the societal perspective gives analysts the flexibility to perform and present analyses from other, comparatively limited perspectives, such as the payer perspective, by excluding certain kinds of costs. Therefore, multiple perspectives are possible for this analysis.

Analysts might also consider multiple outcomes, and thereby use several economic evaluation types (Table 3). Specific outcomes of interest include accurate transmission of viral load test orders, and accurate receipt of viral load results. These outcomes would imply the use of a CEA. The study could also take the form of a CCA, presenting multiple outcomes from different perspectives in addition to estimates of intervention costs. Alternative, shorter time horizons are also possible, depending on the outcome of interest.

Table 3. *Analytic options for an economic evaluation of EMR-LIS interoperability (IO)*

Analysis Type	Comparator?	Costs to Consider	Outcomes
Cost Description	No	EMR-LIS IO	No
Cost Analysis	Yes	EMR-LIS IO and both of the separate systems (EMR, LIS)	No
Cost-Minimization Analysis	Yes	EMR-LIS IO and both of the separate systems (EMR, LIS)	Known or assumed to be equal by comparator
Cost-Effectiveness Analysis	Yes	EMR-LIS IO and both of the separate systems (EMR, LIS)	Examples: accurate transmission of viral load test orders, and accurate reception of viral load results
Cost-Utility Analysis	Yes	EMR-LIS IO and both of the separate systems (EMR, LIS)	Extrapolation of patient-related outcomes to DALYs or QALYs
Cost-Benefit Analysis	Yes	EMR-LIS IO and both of the separate systems (EMR, LIS)	Monetized patient and other outcomes
Cost-Consequence Analysis	Yes	EMR-LIS IO and both of the separate systems (EMR, LIS)	All relevant and evaluable outcomes assesed and presented —for example, increased patient awareness of health status, accuracy of diagnoses, appropriateness of clinical management, reduced waste of lab supplies and duplication of tests, patient satisfaction, and perceived quality of care

CONCLUSION

Digital health interventions, including HIS, will play increasingly important roles in the transformation of exisiting health care systems. As investments in digital health interventions increase, the demand for evaluations, particularly economic evaluations, is likely to increase. Such analyses have potential to inform health system managers about budget planning for implementation and maintenance of DHIs, and to guide in decisions based on the relative value of different types of DHI investments as compared to other health system investments. This increased demand will be acompanied by an increase in demand for both analysts and informed consumption of analyses. This monograph contributes to meeting this demand by empowering analysts with practical information relevant for performing analyses, and enabling stakeholders to become informed consumers of analyses, and ultimately, to enable better decisions about allocating resources to DHIs.

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ANNOTATED BIBLIOGRAPHY

Summary of Background Articles

	Article
Methods	Classification of digital health interventions v1.0: A shared language to describe the uses of digital technology for health. World Health Organization (Link)
	Developing and evaluating complex interventions: the new Medical Research Council guidance (Link)
	Methods for the Economic Evaluation of Health Care Programs (Book)
	Evaluating digital health interventions: key questions and approaches (Link)
	Cost-effectiveness in Health and Medicine (Book)
	Budget Impact Analysis—Principles of Good Practice: Report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force (Link)
	Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3] (Link)
	Complex interventions or complex systems? Implications for health economic evaluation (Link)
	Introduction to health economics for physicians. (Link)
	Applied Methods of Cost-effectiveness Analysis in Healthcare (Book)
	Thresholds for the cost–effectiveness of interventions: Alternative approaches (Link)
	Decision Modelling for Health Economic Evaluation (Book)
Reviews	Systematic review on what works, what does not work and why of implementation of mobile health (mHealth) projects in Africa. (Link)
	The impact of mobile health interventions on chronic disease outcomes in developing countries: a systematic review. (Link)
	A Systematic Review on Promoting Adherence to Antiretroviral Therapy in HIV-infected Patients Using Mobile Phone Technology (Link)
	Use of mHealth Systems and Tools for Non-Communicable Diseases in Low- and Middle-Income Countries: a Systematic Review. (Link)
	Assessing the Effect of mHealth Interventions in Improving Maternal and Neonatal Care in Low- and Middle-Income Countries: A Systematic Review. (Link)
Commentaries and Other Resources	Designing and Undertaking a Health Economics Study of Digital Health Interventions. (Link)
	The Bellagio eHealth Evaluation Group. Call to Action on Global eHealth Evaluation. Consensus Statement of the WHO Global eHealth Evaluation Meeting, Bellagio, September 2011. (Link)
	World Health Organization. Monitoring and evaluating digital health interventions: A practical guide to conducting research and assessment. (Link)

Table of Empirical Studies by Analysis Type

Type Of Analysis	Author(s)	Title
Cost Descriptions	Bartlett	Economics of immunization information systems in the United States: assessing costs and efficiency (Abstract)
	Blanchfield	Cost of an informatics-based diabetes management program (Abstract)
	Fleming	The financial and nonfinancial costs of implementing electronic health records in primary care practices (Abstract)
Cost Analysis	Adler-Milstein	The cost of information technology-enabled diabetes management (Abstract)
	Barlett	Cost savings associated with using immunization information systems for Vaccines for Children administrative tasks (Abstract)
	McKenna	Immunization registries: costs and savings (Abstract)
Cost-Effectiveness Analysis	Kopach	Cost-effectiveness analysis of medical documentation alternatives (Abstract)
	Wu	Cost-effectiveness of an electronic medication ordering and administration system in reducing adverse drug events (Abstract)
Cost-Utility Analysis	O'Reilly	Cost-effectiveness of a shared computerized decision support system for diabetes linked to electronic medical records (Abstract)
Cost-Benefit Analysis	Choi	Cost-benefit analysis of electronic medical record system at a tertiary care hospital (Abstract)
	Li	Study of the cost-benefit analysis of electronic medical record systems in general hospital in China (Abstract)
	Chae	The development of an intelligent laboratory information system for a community health promotion center (Abstract)
	Byrne	The value from investments in health information technology at the U.S. Department of Veterans Affairs (Abstract)
Return-on-Investment Analysis	Driessen	Modeling return on investment for an electronic medical record system in Lilongwe, Malawi (Abstract)
Budget Impact Analysis	McMullin	Impact of an evidence-based computerized decision support system on primary care prescription costs (Abstract)
	McMullin	Twelve-month drug cost savings related to use of an electronic prescribing system with integrated decision support in primary care (Abstract)
	Ohsfeldt	Implementation of hospital computerized physician order entry systems in a rural state: feasibility and financial impact (Abstract)
Cost Estimation	Were	Evaluating a scalable model for implementing electronic health records in resource-limited settings (Abstract)

1. **Methods, Reviews, and Commentaries**

   a. **Methods**

      i. **Classification of digital health interventions v1.0: A shared language to describe the uses of digital technology for health. World Health Organization.** http://www.who.int/reproductivehealth/publications/mhealth/classification-digital-health-interventions/en/ (Accessed on 05/01/2018).

      From the Abstract
      The classification of digital health interventions (DHIs) categorizes the different ways in which digital and mobile technologies are being used to support health system needs. Historically, the diverse communities working in digital health—including government stakeholders, technologists, clinicians, implementers, network operators, researchers, donors—have lacked a mutually understandable language with which to assess and articulate functionality. A shared and, standardized vocabulary was recognized as necessary to identify gaps and duplication, evaluate effectiveness, and facilitate alignment across different digital health implementations. Targeted primarily at public health audiences, this classification framework aims to promote an accessible and bridging language for health program planners to articulate functionalities of digital health implementations.

      ii. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M: **Developing and evaluating complex interventions: the new Medical Research Council guidance.** *BMJ* 2008, 337.

      From the Abstract
      Complex interventions are widely used in the health services, in public health practice, and in areas of social policy that have important health consequences, such as education, transport, and housing. They present various problems for evaluators, in addition to the practical and methodological difficulties that any successful evaluation must overcome. In 2000, the Medical Research Council (MRC) published a framework[1] to help researchers and research funders to recognize and adopt appropriate methods. The framework has been highly influential, and the accompanying BMJ paper is widely cited.[2] However, much valuable experience has since accumulated of both conventional and more innovative methods. This has now been incorporated in comprehensively revised and updated guidance recently released by the MRC (www.mrc.ac.uk/complexinterventionsguidance). In this article we summarize the issues that prompted the revision and the key messages of the new guidance.

      Summary points:

      - *The Medical Research Council guidance for the evaluation of complex interventions has been revised and updated.*
      - *The process of developing and evaluating a complex intervention has several phases, although they may not follow a linear sequence.*

- *Experimental designs are preferred to observational designs in most circumstances, but are not always practicable.*
- *Understanding processes is important, but does not replace evaluation of outcomes.*
- *Complex interventions may work best if tailored to local circumstances, rather than being completely standardized.*
- *Reports of studies should include a detailed description of the intervention to enable replication, evidence synthesis, and wider implementation.*

iii. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. **Methods for the Economic Evaluation of Health Care Programmes. Fourth Edition. Oxford University Press. 2015.**

From the Abstract
The purpose of economic evaluation is to inform decisions intended to improve health care. The new edition of Methods for the Economic Evaluation of Health Care Programmes equips the reader with the essential hands-on experience required to undertake evaluations by providing a "tool kit" based on the authors' own experiences of undertaking economic evaluations.

Building on the strength of the previous edition, the accessible writing style ensures the text is key reading for the nonexpert reader, as no prior knowledge of economics is required. The book employs a critical appraisal framework, which is useful both to researchers conducting studies and to decision-makers assessing them. Practical examples are provided throughout to aid learning and understanding.

The book analyzes the methodological and policy challenges that face health systems in seeking to allocate resources efficiently and fairly. New chapters include "Principles of economic evaluation" and "Making decisions in health care," which introduces the reader to core issues and questions about allocation, and provides an understanding of the fundamental principles which guide decision making.

A key part of evidence-based decision making is the analysis of all the relevant evidence to make informed decisions and policy. The new chapter "Identifying, synthesizing and analysing evidence" highlights the importance of systematic review, and how and why these methods are used. As methods of analysis continue to change, the chapter on "Characterizing, reporting and interpreting uncertainty" introduces the reader to recent methods of analysis and why uncertainty matters for health care decisions.

iv. Murray E, Hekler EB, Andersson G, Collins LM, Doherty A, Hollis C, Rivera DE, West R, Wyatt JC: **Evaluating digital health interventions: key questions and approaches.** *American journal of preventive medicine* 2016, **51**(5):843-851.

From the Abstract
Digital health interventions have enormous potential as scalable tools to improve health and health care delivery by improving effectiveness, efficiency, accessibility,

safety, and personalization. Achieving these improvements requires a cumulative knowledge base to inform development and deployment of digital health interventions. However, evaluations of digital health interventions present special challenges. This paper aims to examine these challenges and outline an evaluation strategy in terms of the research questions needed to appraise such interventions. As they are at the intersection of biomedical, behavioral, computing, and engineering research, methods drawn from all of these disciplines are required. Relevant research questions include defining the problem and the likely benefit of the digital health intervention, which in turn requires establishing the likely reach and uptake of the intervention, the causal model describing how the intervention will achieve its intended benefit, key components, and how they interact with one another, and estimating overall benefit in terms of effectiveness, cost effectiveness, and harms. Although RCTs are important for evaluation of effectiveness and cost effectiveness, they are best undertaken only when: (1) the intervention and its delivery package are stable; (2) these can be implemented with high fidelity; and (3) there is a reasonable likelihood that the overall benefits will be clinically meaningful (improved outcomes or equivalent outcomes at lower cost). Broadening the portfolio of research questions and evaluation methods will help with developing the necessary knowledge base to inform decisions on policy, practice, and research.

v. Cost-effectiveness in Health and Medicine. By P.J. Neumann, G.D. Sanders, L.B. Russell, J. E. Siegel, and T. G. Ganiats (eds). New York: Oxford University Press, 2016.

From the Abstract
Produced by the Second Panel on Cost-Effectiveness in Health and Medicine—a team of 13 experts from fields including decision science, economics, ethics, psychology, and medicine—this new edition is a comprehensive guide to the use of cost-effectiveness analysis as an evaluative tool at the institutional and policy levels. As health care systems face increasing pressure to derive maximum value from expenditures, the guidelines in this new text represent not just the best information available, but a vital guide to health care decision-making in a challenging new era.

vi. Sullivan SD, Mauskopf JA, Augustovski F, Jaime Caro J, Lee KM, Minchin M, Orlewska E, Penna P, Rodriguez Barrios J-M, Shau W-Y: **Budget Impact Analysis—Principles of Good Practice: Report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force**. *Value in Health* 2014, **17**(1):5-14.

From the Abstract
BACKGROUND: Budget impact analyses (BIAs) are an essential part of a comprehensive economic assessment of a health care intervention and are increasingly required by reimbursement authorities as part of a listing or reimbursement submission.

OBJECTIVES: The objective of this report was to present updated guidance on methods for those undertaking such analyses or for those reviewing the results of

such analyses. This update was needed, in part, because of developments in BIA methods as well as a growing interest, particularly in emerging markets, in matters related to affordability and population health impacts of health care interventions.

METHODS: The Task Force was approved by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Health Sciences Policy Council and appointed by its Board of Directors. Members were experienced developers or users of BIAs; worked in academia and industry and as advisors to governments; and came from several countries in North America and South America, Oceania, Asia, and Europe. The Task Force solicited comments on the drafts from a core group of external reviewers and, more broadly, from the membership of the International Society for Pharmacoeconomics and Outcomes Research.

RESULTS: The Task Force recommends that the design of a BIA for a new health care intervention should take into account relevant features of the health care system, possible access restrictions, the anticipated uptake of the new intervention, and the use and effects of the current and new interventions. The key elements of a BIA include estimating the size of the eligible population, the current mix of treatments and the expected mix after the introduction of the new intervention, the cost of the treatment mixes, and any changes expected in condition-related costs. Where possible, the BIA calculations should be performed by using a simple cost calculator approach because of its ease of use for budget holders. In instances, however, in which the changes in eligible population size, disease severity mix, or treatment patterns cannot be credibly captured by using the cost calculator approach, a cohort or patient-level condition-specific model may be used to estimate the budget impact of the new intervention, accounting appropriately for those entering and leaving the eligible population over time. In either case, the BIA should use data that reflect values specific to a particular decision maker's population. Sensitivity analysis should be of alternative scenarios chosen from the perspective of the decision maker. The validation of the model should include at least face validity with decision makers and verification of the calculations. Data sources for the BIA should include published clinical trial estimates and comparator studies for the efficacy and safety of the current and new interventions as well as the decision maker's own population for the other parameter estimates, where possible. Other data sources include the use of published data, well-recognized local or national statistical information, and, in special circumstances, expert opinion. Reporting of the BIA should provide detailed information about the input parameter values and calculations at a level of detail that would allow another modeler to replicate the analysis. The outcomes of the BIA should be presented in the format of interest to health care decision makers. In a computer program, options should be provided for different categories of costs to be included or excluded from the analysis.

CONCLUSIONS: We recommend a framework for the BIA, provide guidance on the acquisition and use of data, and offer a common reporting format that will promote standardization and transparency. Adherence to these good research practice

principles would not necessarily supersede jurisdiction-specific BIA guidelines but may support and enhance local recommendations or serve as a starting point for payers wishing to promulgate methodology guidelines.

vii. Lakdawalla DN, Doshi JA, Garrison LP, Jr., Phelps CE, Basu A, Danzon PM: **Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report [3].** *Value in Health* 2018, **21**(2):131-139.

From the Abstract
The third section of our Special Task Force report identifies and defines a series of elements that warrant consideration in value assessments of medical technologies. We aim to broaden the view of what constitutes value in health care, and to spur new research on incorporating additional elements of value into cost-effectiveness analysis (CEA). Twelve potential elements of value are considered. Four of them—quality-adjusted life-years, net costs, productivity, and adherence-improving factors—are conventionally included or considered in value assessments. Eight others, which would be more novel in economic assessments, are defined and discussed: reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real option value, equity, and scientific spillovers. Most of these are theoretically well understood and available for inclusion in value assessments. The two exceptions are equity and scientific spillover effects, which require more theoretical development and consensus. A number of regulatory authorities around the globe have shown interest in some of these novel elements. Augmenting CEA to consider these additional elements would result in a more comprehensive CEA in line with the "impact inventory" of the Second Panel on Cost-Effectiveness in Health and Medicine. Possible approaches for valuation and inclusion of these elements include integrating them as part of a net monetary benefit calculation, including elements as attributes in health state descriptions, or using them as criteria in a multicriteria decision analysis. Further research is needed on how best to measure and include them in decision-making.

viii. Shiell A, Hawe P, Gold L: **Complex interventions or complex systems? Implications for health economic evaluation.** *BMJ* 2008, **336**(7656):1281-1283.

From the Abstract
Health researchers commonly use the notion of complexity to indicate the problems faced in evaluating the effectiveness of many nondrug interventions.[1][2][3] However, although it is rarely delineated, complexity has two meanings. In the first it is a property of the intervention, and in the second it is a property of the system in which the intervention is implemented. We examine the implications of these two views for economic evaluation.

Summary points

- *Health research often uses complexity to refer to multicomponent interventions.*

- *An alternate view is that complexity refers to systems.*
- *Interventions implemented in complex systems are likely to have diverse, far-reaching, and nonlinear effects.*
- *Distinguishing the two types of complexity is important for economic evaluation.*

ix. Meltzer MI: **Introduction to health economics for physicians**. *The Lancet* 2001, **358**(9286):993-998.

From the Abstract
Since the 1960s, expenditure on health care in developed countries has risen faster than the general rate of inflation, thus making economic assessment of interventions an integral part of decision making in health services. This paper is the first in a series whose goal is to provide some basic principles of health economics that will allow practising physicians to understand better the economic relations between their practice of medicine, the health-care sector, and the national economy. Some of the most important principles described in this paper include opportunity costs, identifying the appropriate perspective, correctly categorising costs, and discounting costs and non-monetary benefits (eg, lives saved) over time. Economic analyses of medical interventions must also take into consideration the difference between efficacy and effectiveness. Efficacy is the maximum possible benefit, often achieved with carefully controlled trials, and effectiveness is the actual decrease in disease achieved when the intervention is applied over a large, non-homogeneous population. This introduction ends with three methods of assessing the costs and benefits of an intervention—namely, cost-benefit, cost-effectiveness, and cost-utility analyses.

x. Alistair M. Gray, Philip M. Clarke, Jane Wolstenholme, and Sarah Wordsworth. Applied Methods of Cost-effectiveness Analysis in Healthcare. Oxford University Press. 2010.

From the Abstract
The third volume in the Handbooks in Health Economic Evaluation series, this book provides the reader with a comprehensive set of instructions and examples of how to perform an economic evaluation of a health intervention. It focuses solely on cost-effectiveness analysis in health care. The book is developed out of the Advanced Methods in Economic Evaluation course taught at the University of Oxford, and the four main sections mirror the four principal components of the course: Outcomes, Costs, Modelling using decision trees and Markov models, and Presenting cost-effectiveness results.

xi. Marseille E, Larson B, S Kazi D, G Kahn J, Rosen S: **Thresholds for the cost-effectiveness of interventions: Alternative approaches,** vol. 93; 2015.

From the Abstract
Many countries use the cost-effectiveness thresholds recommended by the World

Health Organization's Choosing Interventions that are Cost-Effective project (WHO-CHOICE) when evaluating health interventions. This project sets the threshold for cost–effectiveness as the cost of the intervention per disability-adjusted life-year (DALY) averted less than three times the country's annual gross domestic product (GDP) per capita. Highly cost-effective interventions are defined as meeting a threshold per DALY averted of once the annual GDP per capita. We argue that reliance on these thresholds reduces the value of cost-effectiveness analyses and makes such analyses too blunt to be useful for most decision-making in the field of public health. Use of these thresholds has little theoretical justification, skirts the difficult but necessary ranking of the relative values of locally-applicable interventions and omits any consideration of what is truly affordable. The WHO-CHOICE thresholds set such a low bar for cost-effectiveness that very few interventions with evidence of efficacy can be ruled out. The thresholds have little value in assessing the trade-offs that decision-makers must confront. We present alternative approaches for applying cost-effectiveness criteria to choices in the allocation of health-care resources.

xii. **Andrew Briggs, Karl Claxton and Mark Sculpher. Decision Modelling for Health Economic Evaluation. Oxford University Press. 2006**

From the Abstract

In financially constrained health systems across the world, increasing emphasis is being placed on the ability to demonstrate that health care interventions are not only effective, but also cost-effective. This book deals with decision modelling techniques that can be used to estimate the value for money of various interventions including medical devices, surgical procedures, diagnostic technologies, and pharmaceuticals. Particular emphasis is placed on the importance of the appropriate representation of uncertainty in the evaluative process and the implication this uncertainty has for decision making and the need for future research. This highly practical guide takes the reader through the key principles and approaches of modelling techniques. It begins with the basics of constructing different forms of the model, the population of the model with input parameter estimates, analysis of the results, and progression to the holistic view of models as a valuable tool for informing future research exercises. Case studies and exercises are supported with online templates and solutions. This book will help analysts understand the contribution of decision-analytic modelling to the evaluation of health care programmes.

b. Reviews

i. Aranda-Jan CB, Mohutsiwa-Dibe N, Loukanova S: **Systematic review on what works, what does not work and why of implementation of mobile health (mHealth) projects in Africa.** *BMC Public Health* 2014, **14**(1):188.

From the Abstract

BACKGROUND: Access to mobile phone technology has rapidly expanded in developing countries. In Africa, mHealth is a relatively new concept, and questions

arise regarding reliability of the technology used for health outcomes. This review documents strengths, weaknesses, opportunities, and threats (SWOT) of mHealth projects in Africa.

METHODS: A systematic review of peer-reviewed literature on mHealth projects in Africa, between 2003 and 2013, was carried out using PubMed and OvidSP. Data was synthesized using a SWOT analysis methodology. Results were grouped to assess specific aspects of project implementation in terms of sustainability and mid/long-term results, integration to the health system, management process, scale-up and replication, and legal issues, regulations and standards.

RESULTS: Forty-four studies on mHealth projects in Africa were included and classified as: "patient follow-up and medication adherence" (n = 19), "staff training, support and motivation" (n = 2), "staff evaluation, monitoring and guidelines compliance" (n = 4), "drug supply-chain and stock management" (n = 2), "patient education and awareness" (n = 1), "disease surveillance and intervention monitoring" (n = 4), "data collection/transfer and reporting" (n = 10) and "overview of mHealth projects" (n = 2). In general, mHealth projects demonstrate positive health-related outcomes and their success is based on the accessibility, acceptance and low cost of the technology, effective adaptation to local contexts, strong stakeholder collaboration, and government involvement. Threats such as dependency on funding, unclear health care system responsibilities, unreliable infrastructure, and lack of evidence on cost-effectiveness challenge their implementation. mHealth projects can potentially be scaled up to help tackle problems faced by health care systems like poor management of drug stocks, weak surveillance and reporting systems or lack of resources.

CONCLUSIONS: mHealth in Africa is an innovative approach to delivering health services. In this fast-growing technological field, research opportunities include assessing implications of scaling up mHealth projects, evaluating cost-effectiveness, and impacts on the overall health system.

ii. Beratarrechea A, Lee AG, Willner JM, Jahangir E, Ciapponi A, Rubinstein A: **The impact of mobile health interventions on chronic disease outcomes in developing countries: a systematic review**. *Telemedicine Journal and e-Health: the Official Journal of the American Telemedicine Association* 2014, **20**(1):75-82.

From the Abstract

INTRODUCTION: Rates of chronic diseases will continue to rise in developing countries unless effective and cost-effective interventions are implemented. This review aims to discuss the impact of mobile health ([mHealth]) on chronic disease outcomes in low- and middle-income countries (LMIC).

MATERIALS AND METHODS: Systematic literature searches were performed using CENTRAL, MEDLINE, EMBASE, and LILACS databases and gray literature. Scientific literature was searched to identify controlled studies evaluating cell phone voice and

text message interventions to address chronic diseases in adults in low- or middle-income countries. Outcomes measured included morbidity, mortality, hospitalization rates, behavioral or lifestyle changes, process of care improvements, clinical outcomes, costs, patient-provider satisfaction, compliance, and health-related quality of life (HRQoL).

RESULTS: From the 1,709 abstracts retrieved, 163 articles were selected for full text review, including 9 randomized controlled trials with 4,604 participants. Most of the studies addressed more than one outcome. Of the articles selected, six studied clinical outcomes, six studied processes of care, three examined health care costs, and two examined HRQoL. [mHealth] positively impacted on chronic disease outcomes, improving attendance rates, clinical outcomes, and HRQoL, and was cost-effective.

CONCLUSIONS: [mHealth] is emerging as a promising tool to address access, coverage, and equity gaps in developing countries and low-resource settings. The results for [mHealth] interventions showed a positive impact on chronic diseases in LMIC. However, a limiting factor of this review was the relatively small number of studies and patients enrolled, highlighting the need for more rigorous research in this area in developing countries.

iii. Quintana Y, Gonzalez Martorell EA, Fahy D, Safran C: **A Systematic Review on Promoting Adherence to Antiretroviral Therapy in HIV-infected Patients Using Mobile Phone Technology.** *Applied Clinical Informatics* 2018, **9**(2):450-466.

From the Abstract

OBJECTIVE: Adherence to antiretroviral therapy (ART) is paramount to successful long-term suppression of human immunodeficiency virus (HIV). For poorly adherent patients with HIV, barriers to remaining adherent may be overcome by the implementation of targeted interventions delivered via mobile devices. This systematic review is focused specifically on mobile phone technologies to deliver adherence interventions in HIV/acquired immunodeficiency syndrome (AIDS) populations.

METHODS: This review (PROSPERO #CRD42017065131) systematically extracted data from published literature from five databases on mobile phone interventions to improve adherence to ART for HIV. The reported studies had been conducted between 2007 and 2017. Risk of bias was assessed using the Cochrane method, ranking each criterion as low, high, or unclear risk of bias.

RESULTS: Of the 835 articles returned, we identified 26 randomized controlled trials (RCTs), retrospective and prospective cohort trials, or mixed method studies with a comparison group that fit criteria for inclusion. No standard measure of adherence was consistent throughout the examined studies, and assessments by self-report, pill counting, and medication event monitoring system (MEMS) were utilized. The studies reported mixed results, with 17 reporting significant improvements to

adherence, 3 reporting improvements without supplying p-values, and 6 reporting no significant change or a reduction in adherence.

CONCLUSION: The mixed nature of the results exemplifies the need for more comprehensive approaches and larger-scale trials to confirm results observed in limited cohort sizes. To better retain satisfactory adherence within the HIV population, and especially in low-resource settings, we recommend that future interventions incorporate multiple strategies: mobile-based reminders, social support structures, and personalized content.

c. Commentaries and Other Resources

i. McNamee P, Murray E, Kelly MP, Bojke L, Chilcott J, Fischer A, West R, Yardley L: **Designing and Undertaking a Health Economics Study of Digital Health Interventions**. *American Journal of Preventive Medicine* 2016, **51**(5):852-860.

From the Abstract

This paper introduces and discusses key issues in the economic evaluation of digital health interventions. The purpose is to stimulate debate so that existing economic techniques may be refined or new methods developed. The paper does not seek to provide definitive guidance on appropriate methods of economic analysis for digital health interventions. This paper describes existing guides and analytic frameworks that have been suggested for the economic evaluation of health care interventions. Using selected examples of digital health interventions, it assesses how well existing guides and frameworks align to digital health interventions. It shows that digital health interventions may be best characterized as complex interventions in complex systems. Key features of complexity relate to intervention complexity, outcome complexity, and causal pathway complexity, with much of this driven by iterative intervention development over time, and uncertainty regarding likely reach of the interventions among the relevant population. These characteristics imply that more -complex methods of economic evaluation are likely to be better able to capture fully the impact of the intervention on costs and benefits over the appropriate time horizon. This complexity includes wider measurement of costs and benefits, and a modeling framework that is able to capture dynamic interactions among the intervention, the population of interest, and the environment. The authors recommend that future research should develop and apply more flexible modeling techniques to allow better prediction of the interdependency between interventions and important environmental influences.

ii. The Bellagio eHealth Evaluation Group. Call to Action on Global eHealth Evaluation. Consensus Statement of the WHO Global eHealth Evaluation Meeting, Bellagio, September 2011. Accessed on 08 22 2018 at https://www.ghdonline.org/uploads/The_Bellagio_eHealth_Evaluation_Call_to_Action-Release.docx

From the Abstract

Bellagio eHealth Evaluation Principles

1. *Core principles underlie the structure, content, and delivery of an eHealth system independent of the rapidly changing technology used.*
2. *High quality data collection, communication and use are central to the benefits of eHealth systems.*
3. ***Evaluating eHealth both demonstrates its impact and fosters a culture that values evidence and uses it to inform improvements in eHealth deployments.***
4. *To ensure the greatest benefit from eHealth and enhance sustainability and scale, eHealth evaluations should recognize and address the needs of all key constituencies.*
5. *Evidence is needed to demonstrate costs and benefits of eHealth implementations, and maximize eHealth's beneficial impact on health system performance and population health.*
6. *value of a complete evaluation program is enhanced through research that is attuned to the differing requirements throughout the life-course of the project, whether at needs assessment, pilot-, facility level-, regional and national scale-up stages.*
7. *Independent and objective outcome-focused evaluation represents the ideal of impact evaluation.*
8. *Country alignment and commitment to a clear eHealth vision, plan, and evaluation strategy is essential.*
9. *Improving the eHealth evidence base requires more than increased numbers of studies but also improved quality of eHealth research studies.*

iii. World Health Organization. Monitoring and evaluating digital health interventions: A practical guide to conducting research and assessment.

From the Abstract

This resource on Monitoring and Evaluating Digital Health Interventions provides step-wise guidance to improve the quality and value of monitoring and evaluation (M&E) efforts in the context of digital health interventions, also commonly referred to as mHealth or eHealth interventions. This Guide is intended for implementers and researchers of digital health activities, as well as policy-makers seeking to understand the various stages and opportunities for systematically monitoring implementation fidelity and for evaluating the impact of digital health interventions.

2. Empirical Studies by Type

a. Cost Descriptions

i. Bartlett DL, Molinari N-AM, Ortega-Sanchez IR, Urquhart GA: **Economics of immunization information systems in the United States: assessing costs and efficiency**. In: *Cost Eff Resour Alloc.* vol. 4; 2006: 15.

Country	United States
Purpose of Study	To evaluate the economic determinants of immunization information system (IIS) performance by estimating the influence of development and management costs of in-house and contracted labor and nonlabor and resources used by IIS centralized systems. Also, to measure the effect of standards and other factors affecting the functioning of such systems, determine the threshold of patient records needed to minimize average cost per patient record (CPR), and identify strategies to increase efficiency.
Type of Digital Health Intervention	Immunization information system
Business Setting	Primary care setting
Comparator	IIS not meeting all standards
Time Horizon	8 years
Perspective	Government
Inputs/Estimation of Costs	Labor and nonlabor resources used in development and operations tasks
Outcomes	Impact of information technology, local provider participation, and compliance with federal IIS performance standards.
Key Conclusions	Efficiently increasing the number of records in IIS would require additional resources and careful consideration of various strategies to minimize CPR, such as boosting provider participation.

ii. Blanchfield BB, Grant RW, Estey GA, Chueh HC, Gazelle GS, Meigs JB: **Cost of an informatics-based diabetes management program**. *International Journal of Technology Assessment in Health Care* 2006, **22**(2):249-254.

Country	United States
Purpose of Study	To identify the costs to design, develop, implement, and operate an innovative informatics-based system.
Type of Digital Health Intervention	Registry and disease management system for managing type 2 diabetes (POPMAN)
Business Setting	Primary care setting
Comparator	N/A
Time Horizon	3.5 years
Perspective	Health care sector
Inputs/Estimation of Costs	Direct and indirect costs incurred by the hospital to develop and implement the program; identification of the various cost components of the program and their potential sensitivity to change if the program were recreated or modified in the future.
Outcomes	Cost to develop and operate, cost per patient for a 1,200 patient registry.
Key Conclusions	The cost of POPMAN is comparable to the costs of other quality-improving interventions for patients with diabetes. Modifications to POPMAN for adaptation to other chronic diseases or to interface with new EMR systems will require additional investment but should not be as high as initial development costs.

iii. Fleming NS, Culler SD, McCorkle R, Becker ER, Ballard DJ: **The financial and nonfinancial costs of implementing electronic health records in primary care practices**. *Health affairs (Project Hope)* 2011, **30**(3):481-489.

Country	United States
Purpose of Study	To report the cost of implementing an electronic health record system in twenty-six primary care practices in a physician network.
Type of Digital Health Intervention	Electronic health record system
Business Setting	Primary care setting
Comparator	N/A
Time Horizon	1 year
Perspective	Health care sector
Inputs/Estimation of Costs	Direct and indirect costs
Outcomes	Total cost of implementation and maintenance
Key Conclusions	For an average five-physician practice, implementation cost an estimated $162,000, with $85,500 in maintenance expenses during the first year. We also estimate that the HealthTexas network implementation team and the practice implementation team needed 611 hours, on average, to prepare for and implement the electronic health record system, and that end users—physicians, other clinical staff, and nonclinical staff—needed 134 hours per physician, on average, to prepare for use of the record system in clinical encounters.

b. Cost Analysis

i. Adler-Milstein J, Bu D, Pan E, Walker J, Kendrick D, Hook JM, Bates DW, Middleton B: **The cost of information technology-enabled diabetes management**. *Disease Management : DM* 2007, **10**(3):115-128.

Country	United States
Purpose of Study	To estimate the cost of various approaches to diabetes disease management to inform purchasing decisions.
Type of Digital Health Intervention	IT-enabled diabetes management approaches (5): stand-alone point-of-care registry with clinical reminders, electronic health records with diabetes-specific clinical decision support, device-based remote monitoring, Internet-based diabetes self-management platform, remote management by specially trained nurses or health coaches using IT systems to compare patient data.
Business Setting	Various
Comparator	Compared provider practice size categories; all practices and payers start with no diabetes-specific IT and no disease management intervention.
Time Horizon	1 year
Perspective	Sponsoring organization
Inputs/Estimation of Costs	Acquisitions and annual costs for each approach (does not include costs incurred by other organizations).
Outcomes	Acquisition cost and costs incurred annually for each size of practice.
Key Conclusions	Provider-sponsored diabetes registries are estimated to be the least-expensive approach for small- and medium-sized practices. For large practices with electronic health record systems, modifying such systems with diabetes-specific clinical decision support capabilities is projected to be the most economical approach.
Notes	Used decision modeling

ii. Bartlett DL, Washington ML, Bryant A, Thurston N, Perfili CA: **Cost savings associated with using immunization information systems for Vaccines for Children administrative tasks**. *Journal of public health management and practice : JPHMP* 2007, **13**(6):559-566.

Country	United States
Purpose of Study	To investigate the potential cost savings of immunization information systems (IIS) in performing some administrative tasks associated with the federal Vaccines for Children (VFC) program at state and practice levels.
Type of Digital Health Intervention	IIS or registries are confidential, population-based, computerized information systems that collect vaccination data about persons, especially children, within a geographic area.
Business Setting	Primary care, point of care
Comparator	Paper tally sheets
Time Horizon	1 year
Perspective	Health care sector and Government
Inputs/Estimation of Costs	Time spent to record the child's eligibility category, age group, and quantity of VFC vaccines administered; time required to prepare and submit the report; salary data for clinical staff by job title and practice location.
Outcomes	Costs and time for a private practice to perform VFC-related reporting per year; government time and costs for doses administered and vaccination assessments.
Key Conclusions	Median cost savings to the state health department could be as much as $11,740 annually. VFC practices could save up to a maximum of $446 annually per practice by using USIIS for VFC tasks. If applied to the 218 enrolled private practices statewide, this would result in a median total cost savings of $17,615 ($15,519 for reports and $2,096 for pulling medical charts).

iii. McKenna VB, Sager A, Gunn JE, Tormey P, Barry MA: **Immunization registries: costs and savings**. *Public Health Reports* 2002, **117**(4):386-392.

Country	United States
Purpose of Study	To quantify the actual costs of developing, maintaining, and operating the Boston Immunization Information System (BIIS), an electronic registry and tracking system, and to compare the registry's costs with those of performing the same functions manually.
Type of Digital Health Intervention	Immunization information system
Business Setting	Primary care
Comparator	Manual functionality for completing immunization history, pulling and reviewing records
Time Horizon	4 years
Perspective	Government
Inputs/Estimation of Costs	Costs of developing and operating the IIS, time to complete each registry-related activity.
Outcomes	Development and maintenance costs, operating costs, 1998 cost comparison, costs per child, projected costs and savings of a hypothetical expanded registry in 1999.
Key Conclusions	Electronic immunization registries potentially offer an efficient tool for delivery of immunization services. The total annual cost of developing, maintaining, and operating BIIS in 1998 was $345,556. Annual total cost per record was $5.45 for all children under 2–3 years of age, and $10 when costs were distributed only among active users (children under the age of 8). Operating BIIS saved $26,768 in 1998 compared with manual performance. The hypothetical projected total cost of an expanded BIIS in 1999 would have been $577,919, with a projected savings of $689,403 compared with manual costs.

c. Cost-effectiveness analysis

i. Kopach R, Sadat S, Gallaway ID, Geiger G, Ungar WJ, Coyte PC: **Cost-effectiveness analysis of medical documentation alternatives**. *Int J Technol Assess Health Care* 2005, **21**(1):126-131.

Country	Canada
Purpose of Study	To compare the relative cost-effectiveness of an automated medical documentation system to the current system in place at a Canadian hospital. There are significant expenditures associated with choice of medical documentation system, yet the benefit to the patient population has not been studied.
Type of Digital Health Intervention	Automated medical documentation system, incorporating speech recognition software and electronic signatures
Business Setting	Primary care setting
Comparator	Transcription of digital voice file
Time Horizon	4 years
Perspective	Health care sector
Inputs/Estimation of Costs	Time for medical documentation and signature tasks; costs of maintenance, transcription wages, notification, distribution, hardware, licensing, and infrastructure.
Outcomes	Average length of time (delay) between patient discharge and completion of final note per discharge.
Key Conclusions	Although the automated documentation system was more expensive than the current system, it also provided qualitative benefits that were not considered in the cost-effectiveness analysis. The automated documentation system was associated with higher costs than the current system—but better outcomes. The incremental cost-effectiveness ratio used for comparing the automated medical documentation system with the traditional system indicated that the incremental daily cost for decreasing a day in average note completion time per discharge note was Can$0.331/day over the study period (4 years).

ii. Wu RC, Laporte A, Ungar WJ: **Cost-effectiveness of an electronic medication ordering and administration system in reducing adverse drug events.** *Journal of evaluation in clinical practice* 2007, **13**(3):440-448.

Country	Canada
Purpose of Study	To examine the costs of introducing an electronic medication ordering and administration system, and evaluate its potential impact on reducing adverse drug events (ADE).
Type of Digital Health Intervention	Electronic medication ordering and administration system
Business Setting	Primary care setting
Comparator	Standard paper ordering system
Time Horizon	10 years
Perspective	Health care sector
Inputs/Estimation of Costs	The new system incurred not only costs related to its implementation, but also possible costs related to increased workload. Included possible savings that have been documented with CPOE due to reduced inappropriate ordering of medications. Costs common to both approaches were excluded.
Outcomes	Defined effectiveness as the ability of the system to reduce ADEs and ADE-associated deaths. The overall effectiveness of the UHN electronic ordering/administration system was determined by three factors: (1) the incidence of ADEs, (2) how many ADEs are preventable, and (3) the effectiveness of the new system at reducing preventable ADEs.
Key Conclusions	The incremental cost-effectiveness of the new system was $12,700 (USD) per ADE prevented. The cost-effectiveness was found to be sensitive to the ADE rate, the effectiveness of the new system, the cost of the system, and costs due to possible increases in doctor workload.

d. Cost-utility analysis

i. O'Reilly D, Holbrook A, Blackhouse G, Troyan S, Goeree R: **Cost-effectiveness of a shared computerized decision support system for diabetes linked to electronic medical records**. *Journal of the American Medical Informatics Association* 2012, **19**(3):341-345.

Country	Canada
Purpose of Study	To measure the long-term cost-effectiveness of a community-based computerized decision support system for diabetes, shared between patients and physicians, using a decision-analytic model, the Ontario Diabetes Economic Model.
Type of Digital Health Intervention	Computerized decision support systems (CDSS)
Business Setting	Primary care setting
Comparator	Usual care from physician
Time Horizon	40 years
Perspective	Government and societal
Inputs/Estimation of Costs	Ontario-specific diabetes-related health care costs, program development and implementation costs
Outcomes	Occurrence of complications, mean lifetime cost/patient, life years, quality-adjusted life years (QALYs)
Key Conclusions	The web-based prototype decision support system slightly improved short-term risk factors. The model predicted moderate improvements in long-term health outcomes. This disease management program will need to develop considerable efficiencies in terms of costs and processes or improved effectiveness to be considered a cost-effective intervention for treating patients with type 2 diabetes. The cost of implementing the intervention was $483,699. The one-year intervention reduced HbA1c by 0.2 and systolic blood pressure by 3.95 mmHg, but increased body mass index by 0.02 kg/m^2, resulting in a relative risk reduction of 14% in the occurrence of amputation. The model estimated that the intervention resulted in an additional 0.0117 quality-adjusted life year; the incremental cost-effectiveness ratio was $160,845 per quality-adjusted life year.

e. Cost-benefit analysis

i. Choi JS, Lee WB, Rhee P-L: **Cost-Benefit Analysis of Electronic Medical Record System at a Tertiary Care Hospital.** *Healthcare Informatics Research* 2013, **19**(3):205-214.

Country	South Korea
Purpose of Study	To analyze the economic effects of electronic medical record (EMR) systems using a cost-benefit analysis based on the differential costs of managerial accounting.
Type of Digital Health Intervention	Electronic medical record system
Business Setting	Primary care setting
Comparator	Paper chart system
Time Horizon	8 years
Perspective	Health care sector
Inputs/Estimation of Costs	There are two cost categories: system costs and induced costs. System costs include the direct costs of building the system infrastructure, developing the EMR applications, and purchasing office supplies. Induced costs were required to facilitate EMR adoption.
Outcomes	The benefits of EMR adoption included cost reductions, plus additional revenues from both remodeling of paper-chart storage areas and the efforts of medical transcriptionists.
Key Conclusions	Although EMR adoption resulted in overall growth in administrative costs, since the cumulative net present value was positive it has proven cost-effective. The positive net present value was attributed to both cost reductions and additional revenues. Where EMR adoption is not so attractive to management is that the discounted payback period is longer than five years (6.18) and the benefit-cost ratio is near 1 (1.23). However, given that this study did not include any qualitative benefits and the paper-chart system was cost-centric, an EMR system is a worthwhile investment.

ii. Li K, Naganawa S, Wang K, Li P, Kato K, Li X, Zhang J, Yamauchi K: **Study of the cost-benefit analysis of electronic medical record systems in general hospital in China**. *Journal of medical systems* 2012, **36**(5):3283-3291.

Country	China
Purpose of Study	Document financial effects of an electronic medical record (EMR) system at a general hospital.
Type of Digital Health Intervention	Electronic medical record system
Business Setting	Primary care setting
Comparator	Paper-based medical record
Time Horizon	6-year period
Perspective	Health care sector
Inputs/Estimation of Costs	EMR system costs based on information supplied and literature from the general hospital. Costs associated with system implementation were categorized as system basis costs and running costs. System costs consist of the one-time implementation cost of installing the hardware, software, and network. Running costs are included in the one-time costs: the transition from paper to electronic medical records, the temporary decrease in hospital productivity after implementation, and training; and the durative costs: ongoing maintenance, support, electricity, system change, and running and replacement costs.
Outcomes	Net financial benefits of implementing the system; reasons for accruing benefits.
Key Conclusions	The total net benefit to the general hospital assessed from implementing an EMR system for the 6-year period was $559,025. Benefits accrue primarily from savings in new medical record creation, reductions in the number of full-time-equivalent (FTE) employees, fewer adverse drug events (ADEs) and dose errors, improved charge capture, and decreased billing errors.

iii. Chae YM, Lim HS, Lee JH, Bae MY, Kim GH, et al: **The development of an intelligent laboratory information system for a community health promotion centre.** *Asia-Pacific journal of public health* 2002, **14**(2):64-68.

Country	South Korea
Purpose of Study	To analyze the economic feasibility of the intelligent laboratory information system (ILIS) based on the information economics approach.
Type of Digital Health Intervention	Laboratory information system
Business Setting	Primary care setting
Comparator	Paper-based system
Time Horizon	1 year
Perspective	Health care sector
Inputs/Estimation of Costs	One direct benefit of using the ILIS was a reduction in personnel costs by automating laboratory data processing tasks, such as test order entry, interpretation of results, prescriptions, and entry of test results. Value acceleration refers to improved performance of a system for speeding up the flow of information. In ILIS, the increased revenue from one additional person per day for screening due to the reduction of laboratory data processing time falls into this category. Finally, value linkage is closely related with value acceleration, but it has more to do with the combined effects of an information system rather than the time factor alone. It represents the ripple effect of an improvement in an overall function. In ILIS, savings from the reduction in reporting error and misdiagnosis may be viewed as value linkage.
Outcomes	Total system costs, personnel costs, costing the average number of screens per day, and cumulative benefit.
Key Conclusions	The results showed that the ILIS not only helps screen more people by increasing a health promotion center's capacity, but also brings in more revenue to the center.
Notes	Cost is only one component of analysis.

iv. Byrne CM, Mercincavage LM, Pan EC, Vincent AG, Johnston DS, Middleton B: **The value from investments in health information technology at the U.S. Department of Veterans Affairs**. *Health Affairs (Project Hope)* 2010, **29**(4):629-638.

Country	United States
Purpose of Study	To conduct a benchmarking analysis comparing the adoption, cost, and quality-related impacts of health IT across the Veterans Affairs (VA) relative to private health care sector norms or benchmarks. Also, to compose cost-benefit models that estimate the financial value of key components of the Veterans Health Information Systems and Technology Architecture (VistA).
Type of Digital Health Intervention	Computerized patient records/electronic health records, radiological imaging, and laboratory and medication ordering and administration.
Business Setting	Primary care setting
Comparator	Private health care sector, not having the VA's integrated health IT system component or similar tools
Time Horizon	6 years
Perspective	Health care sector
Inputs/Estimation of Costs	IT spending, IT adoption, IT-related quality of care
Outcomes	Annual and cumulative net value, benefits in terms of prevention of adverse events and eliminating redundancies, and total costs.
Key Conclusions	The VA spent proportionately more on IT than did the private health care sector, but achieved higher levels of IT adoption and quality of care. The potential value of the VA's health IT investments is estimated at $3.09 billion in cumulative benefits net of investment costs.

f. Return-on-investment analysis

i. Driessen J, Cioffi M, Alide N, Landis-Lewis Z, Gamadzi G, Gadabu OJ, Douglas G: **Modeling return on investment for an electronic medical record system in Lilongwe, Malawi**. *Journal of the American Medical Informatics Association* 2013, **20**(4):743-748.

Country	Malawi
Purpose of Study	To model the financial effects of implementing a hospital-wide electronic medical record (EMR) system in a tertiary facility.
Type of Digital Health Intervention	Electronic medical record system
Business Setting	Primary care setting
Comparator	Paper-based system
Time Horizon	5 years
Perspective	Health care sector
Inputs/Estimation of Costs	Collected data on expenditures for length of stay, transcription time, and laboratory use under the (pre-EMR) paper-based system, then estimated reductions in each category based on findings from EMR systems in the USA and backed by ambulatory data from low-income settings.
Outcomes	Evaluated three areas of impact: length of stay, transcription time, and laboratory use. Compared these potential savings accrued over a period of five years with the costs of implementing the touchscreen point-of-care EMR system at that site.
Key Conclusions	Estimated cost savings in length of stay, transcription time, and laboratory use totaled US$284,395 annually. When compared with the costs of installing and sustaining the EMR system, there is a net financial gain by the third year of operation. Over five years the estimated net benefit was US$613,681.

g. Budget impact analysis

i. McMullin ST, Lonergan TP, Rynearson CS, Doerr TD, Veregge PA, Scanlan ES: **Impact of an evidence-based computerized decision support system on primary care prescription costs**. *Annals of Family Medicine* 2004, **2**(5):494-498.

Country	United States
Purpose of Study	To evaluate the impact of a commercially available CDSS on the cost of medications prescribed by primary care clinicians in a community-based, ambulatory setting.
Type of Digital Health Intervention	Computerized decision support system (CDSS) for electronic prescribing process. The CDSS provides diagnosis-specific, evidence-based messages during the electronic prescribing process. Most messages focus on the comparative efficacy, safety, and cost of different treatment options.
Business Setting	Primary care
Comparator	Clinicians not using the CDSS
Time Horizon	6 months
Perspective	Health care system
Inputs/Estimation of Costs	Pharmacy claims data
Outcomes	Difference in new prescription costs between groups during the six-month post-implementation period. Secondary outcomes included differences in costs for medications in the 10 high-cost drug categories.
Key Conclusions	Providing electronic, evidence-based decision support during the prescribing process can shift prescribing decisions toward more evidence-based care and significantly decrease primary care prescription costs. Clinicians who received evidence-based messages had significantly lower prescription costs than those in the control group. The average cost per new prescription was $4.16 lower (P = .02) in the intervention group, and the average cost for new prescriptions and refills was $4.99 lower (P = .01). The six-month savings from new prescriptions and their refills are estimated to be $3,450 (95% CI, $1,030–$5,863) per clinician.

ii. McMullin ST, Lonergan TP, Rynearson CS: **Twelve-month drug cost savings related to use of an electronic prescribing system with integrated decision support in primary care.** *Journal of Managed Care Pharmacy: JMCP* 2005, **11**(4):322-332.

Country	United States
Purpose of Study	To determine if the six-month savings on new prescriptions were sustained during a longer follow-up observation period (12 months), and to evaluate the impact of the CDSS on all pharmacy claims (i.e., new prescriptions plus older prescriptions that were active prior to the intervention) and per-member-per month (PMPM) expenditures. Also evaluated the utilization of drugs within eight high-cost therapeutic categories that were targets of the CDSS messaging function.
Type of Digital Health Intervention	Computerized decision support system for electronic prescribing process. The CDSS provides diagnosis-specific, evidence-based messages during the electronic prescribing process. Most messages focus on the comparative efficacy, safety, and cost of different treatment options.
Business Setting	Primary care
Comparator	Clinicians not using the CDSS
Time Horizon	1 year
Perspective	Health care system
Inputs/Estimation of Costs	Pharmacy claims data
Outcomes	To determine if the savings on new prescriptions were sustained during 12 months of follow-up, and to assess the impact of the CDSS on the cost of all pharmacy claims (i.e., including chronic medications that were active prior to CDSS implementation), per-member-per month drug expenditure was an important secondary measure. Also evaluated the prescribing patterns for the intervention and control groups during the 12-month follow-up period by comparing new prescriptions (and their refills) for specific high-cost drug classes and preferred-drug classes within eight therapeutic categories.
Key Conclusions	An electronic prescribing system with integrated decision support shifted prescribing behavior away from high-cost therapies and significantly lowered prescription drug costs. The savings associated with altered prescribing behavior offset the monthly subscription cost of the system. During 12 months of follow-up, clinicians using the electronic prescribing system continued to have lower prescription costs than the controls. Clinicians using the electronic prescribing system had average costs for 26,674 new prescriptions

	that were $4.12 lower (95% confidence interval, $1.53–$6.71; P=0.003) and PMPM expenditures that were $0.57 lower than expected based on the changes observed for 24,507 new prescriptions written by clinicians in the control group. The average cost savings on new prescriptions were $482 per prescriber per month (PPPM) based upon prescription cost, and $465 PPPM based upon PMPM analysis. When all pharmacy claims (156,429) were analyzed, the intervention group's average prescription cost was $2.57 lower and their PMPM expenditures were $1.07 lower than expected based on the changes observed in the control group. The average drug cost savings on all pharmacy claims were $863 PPPM based on average prescription cost and $873 PPPM based on PMPM analysis. The proportion of prescriptions for high cost drugs that were the target of the CDSS messages to prescribers was 17.5% lower among the intervention group (35.8%) compared with the control group (43.4%; P=0.03).

iii. Ohsfeldt RL, Ward MM, Schneider JE, Jaana M, Miller TR, Lei Y, Wakefield DS: **Implementation of hospital computerized physician order entry systems in a rural state: feasibility and financial impact**. *Journal of the American Medical Informatics Association: JAMIA* 2005, **12**(1):20-27.

Country	United States
Purpose of Study	To estimate the costs of implementing computerized physician order entry (CPOE) systems in hospitals in a rural state, and to evaluate the financial implications of statewide CPOE implementation.
Type of Digital Health Intervention	Computerized physician order entry (CPOE)
Business Setting	Primary care
Comparator	Model simulations on the scenarios use the vendor's lower cost estimates (“low” cost) or higher cost estimates (“high” cost).
Time Horizon	5 years
Perspective	Health care sector
Inputs/Estimation of Costs	Determination of the current IT infrastructure within Iowa hospitals; costs of CPOE implementation.
Outcomes	Costs of CPOE implementation, financial impact of implementation, impact on third-party payers, and cost savings from improved safety and efficiency.
Key Conclusions	Implementation of CPOE in rural or critical access hospitals may depend on net increase in operating costs. Adoption of CPOE may be financially infeasible for these small hospitals in the absence of increases in hospital payments or ongoing subsidies from third parties. CPOE implementation would dramatically increase operating costs for rural and critical access hospitals in the absence of substantial costs savings associated with improved efficiency or improved patient safety. For urban and rural referral hospitals, the cost impact is less dramatic but still substantial. However, relatively modest benefits in the form of patient care cost savings or revenue enhancement would be sufficient to offset CPOE costs for these larger hospitals.

h. Cost Estimation

i. Were MC, Emenyonu N, Achieng M, Shen C, Ssali J, Masaba JP, Tierney WM: **Evaluating a scalable model for implementing electronic health records in resource-limited settings**. *Journal of the American Medical Informatics Association: JAMIA* 2010, **17**(3):237-244.

Country	Uganda
Purpose of Study	To describe an alternative and scalable model for implementing EHRs in resource-limited settings. This model directly addresses the human-resource constraints in these settings. Also, to describe the application of this model in three OpenMRS implementations in Uganda. We assessed the impact of OpenMRS implemented using this model on health care delivery with a formal time-motion study of providers and patients at one site.
Type of Digital Health Intervention	Electronic health records
Business Setting	Primary care
Comparator	Time before EHR implementation
Time Horizon	N/A
Perspective	Health care sector
Inputs/Estimation of Costs	Followed 100 established adult HIV-positive patients and 20 newly diagnosed adult HIV-positive patients from the time they presented to the registration clerk at the center, using a list of provider tasks and patient activities.
Outcomes	Time use
Key Conclusions	Providers spent a third less time in direct and indirect care of patients ($p < 0.001$) and 40% more time on personal activities ($p = 0.09$) after EHRs implementation. Time spent by previously enrolled patients with nonclinician staff fell by half ($p = 0.004$); time spent with pharmacy staff fell by 63% ($p < 0.001$). This model offers a viable approach for broadly implementing EHRs in resource-limited settings.