REPUBLIC OF GHANA
MINISTRY OF HEALTH

Reference Case for Health Technology Assessment (HTA) in Ghana

1st Edition 2023

Setting Standards for the Conduct and Reporting of HTA and Economic Evaluations in Ghana

REPUBLIC OF GHANA
MINISTRY OF HEALTH

Reference Case for Health Technology Assessment (HTA) in Ghana

1st Edition

Setting Standards for the Conduct and Reporting of HTA in Ghana

International Decision Support Initiative

London School of Hygiene and Tropical Medicine

The development of this reference case was made possible with support from the international Decision Support Initiative (iDSI) through the School of Public Health (SPH) University of Ghana (UG), as well as technical inputs from the London School of Hygtience and Tropical Medicine (LSHTM).

Reference Case for Health Technology Assessment (HTA) in Ghana, 1st Edition, 2023

ISBN: 978 – 9988 – 3 – 4848 – 9

For all enquiries, write to the publishers:

HTA Secretariat,
Pharmacy Directorate,
Technical Coordination Directorate,
Ministry of Health,
P. O. Box MB-44, Accra, Ghana,
West Africa.
Tel: +233 302 665651
Digital Address: GA-029-4296

E-mail: info@moh.gov.gh
Website: www.moh.gov.gh

Cover Design by:
Dr. Brian Adu Asare (basare100@gmail.com)

Contents

1.1 Acknowledgement

The development of this reference case was made possible with support from the international Decision Support Initiative (iDSI) through the School of Public Health (SPH) University of Ghana (UG), as well as technical inputs from the London School of Hygiene and Tropical Medicine (LSHTM). The following stakeholders and resource persons are acknowledged for their role in developing the HTA reference case for Ghana.

MOH/GHS/other executives

Name	Designation
Hon. Kwaku Agyeman-Manu (MP)	Minister for Health
Hon. Tina Gifty Naa Ayeley Mensah (MP)	Deputy Minister for Health
Hon. Mahama Asei Seini	Deputy Minister for Health
Mr. Hafez Adam	Chief Director, MOH
Mr. Kwabena Boadu Oku-Afari	Fmr. Chief Director, MOH
Dr. Baffour Awuah	Ag. Director, Technical Coordination, MOH
Dr. (Mrs.) Martha Gyansa-Lutterodt	Fmr. Director, Technical Coordination, MOH

Steering Committee for Health Technology Assessment (HTA Steering Committee)

Name	Designation
Mr. Hafez Adam	Chief Director, MOH
Mr. Kwabena Boadu Oku-Afari	Fmr. Chief Director, MOH
Dr. Baffour Awuah	Ag. Director, Technical Coordination, MOH
Dr. (Mrs.) Martha Gyansa-Lutterodt	Fmr Director, Technical Coordination, MOH
Dr. Bernard Okoe-Boye	CEO, National Health Insurance Authority
Dr. Lydia Dsane-Selby	Fmr. CEO, National Health Insurance Authority
Mrs. Delese Darko	CEO, Food and Drugs Authority
Mr. Steve Poku-Kwarteng	Deputy CEO, Ghana Standards Authority
Mrs. Emma Ofori Agyemang	Director, Policy Planning, Monitoring and Evaluation (PPME), MOH
Dr. Emmanuel Ankrah Odame	Fmr. Director, PPME, MOH
Dr. Bismark Attah-Adjepong	Director, Pharmaceutical Services, Ghana Health Service

Name	Designation
Dr. Francis Kasolo	WHO Representative, WHO Country Office for Ghana
Dr. (Mrs.) Joycelyn Azeez	Director, Pharmaceutical Services, MOH
Mr. Peter Yeboah	Executive Director, Christian Health Association of Ghana
Prof. Kwame Ohene Buabeng	Representative, Academia
Prof. Francis W. Offei	Chairperson, National Medicine Selection Committee
Mr. Dan Nuer	Ministry of Finance
Mrs. Cecilia Senoo	Civil Society Organisation
Dr. Vitus Anaab-Bisi	Rep. Ghana Association of Quasi Health Institutions

Technical Working Group for Health Technology Assessment (TWG)

Name	Designation
Prof. Justice Nonvignon	School of Public Health, University of Ghana
Dr. (Mrs.) Joycelyn Azeez	Director, Pharmaceutical Services, MOH
Dr. Augustina Koduah	School of Pharmacy, University of Ghana
Dr. Marc Dzradosi	National Medicines Selection Committee
Dr. (Mrs.) Angela A. Ackon	WHO Country Office for Ghana
Mr. Kwabena Asante Offei	Private Sector Representative
Dr. James Akazili	Research Division, GHS
Mr. Kwadwo Asante	Ghana Statistical Service
Dr. George K. Hedidor	WHO Country Office for Ghana
Dr. Kwame Adu Bonsaffoh	Evidence Summaries Group, NMSC
Dr. Taiba Afaa Jibril	Evidence Summaries Group, NMSC
Dr. Peter Agyei-Baffour	School of Public Health, KNUST
Dr. Mrs Ruby A. Mensah Annan	NHIA
Dr. Daniel Ankrah	Representative, Teaching Hospitals
Mr. Eric Karikari Boateng	Food and Drugs Authority
Dr. Maureen Martey	PPME, MOH
Dr. Brian Adu Asare	Pharmacy Directorate, MOH
Mr. William Omane-Adjekum	NHIA
Mr. Saviour Yevutsey	Head, Drug Policy Unit, Pharmacy Directorate, MOH
Mr. Festus Korang	Pharmacy Directorate, MOH
Ms. Edith E. Gavor	Fmr. Head, Drug Policy Unit, MOH
Dr. Richmond Owusu	University of Ghana, School of Public Health
Mr. Godwin Gulbi	Health Economist
Mrs. Ivy Amankwah	MOH

Name	Designation
Dr. Emmanuella Abassah-Konadu	MOH
Co-opted Expertise	
Mr. Francis Ruiz	London School of Hygiene and Tropical Medicine (LSHTM)
Mr. Joseph Kazibwe	LSHTM
Dr. Sergio Torres Rueda	LSHTM
Ms. Cassandra Nemzoff	Centre for Global Development (CGDEV)

Secretariat for Health Technology Assessment (HTA-Sec)

Name	Designation
Dr. Brian Adu Asare	Pharmacy Directorate, MOH (Head, HTA Secretariat)
Mr. William Omane-Adjekum	NHIA
Mr. Saviour Yevutsey	MOH
Mrs. Ivy Amankwah	MOH
Dr. Emmanuella Abassah-Konadu	MOH
Mr. Festus Korang	MOH
Mr. Nicholas Nyagblornu	PPME, MOH
Mr. Solomon Laryea	PPME, MOH
Mr. Brian Sampram	PPME, MOH

Partners

Name
International Decision Support Initiative (iDSI)
London School of Hygiene and Tropical Medicine (LSHTM)
Centre for Global Development (CGDEV)
Norwegian Institute of Public Health (NIPH)
Access and Delivery Partnership (ADP)
Programme for Appropriate Technology in Health (PATH)
United Nations Development Programme (UNDP)
World Health Organization (WHO)-Geneva, TDR and WHO Country Office for Ghana
Health Intervention and Technology Assessment Programme (HITAP)

1.2 List of abbreviations

BIA	Budget Impact Analysis
CEA	Cost-Effectiveness Analysis
CUA	Cost-Utility Analysis
DALY	Disability Adjusted Life Years
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
LSHTM	London School of Hygiene and Tropical Medicine
HTA	Health Technology Assessment
HTA-SC	Health Technology Assessment Steering Committee
HTA-Sec	Health Technology Assessment Secretariat
HTA-TWG	Health Technology Assessment Technical Working Group
NHIA	National Health Insurance Authority
NHIS	National Health Insurance Scheme
PICO	Population, Intervention, Control/Comparator, Outcome
QALY	Quality Adjusted Life Years
RCTs	Randomised Control Trials
SC	Steering Committee
STG	Standard Treatment Guidelines
TWG	Technical Working Group

1.3 Preface

Health Technology Assessment (HTA) refers to a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. HTA institutionalization in Ghana involves the establishment of structures, processes, methods and standards for the conduct and uptake of HTA outputs and recommendations.

Ghana has developed the HTA strategy, 1st edition, 2020 to strengthen the science and practice of HTA in support of evidence-based decisions for the health sector. This strategy focuses on governance, guidelines and manuals, resourcing and tooling, resource mobilization and funding, collaborations and partnerships, communication and dissemination, topic selection and technical work, capacity development, as well as follow-through implementation actions. Within the context of the above strategy, the development of a reference case for HTA is a specific output under the strategic area: 'Guidelines and Manuals'.

A reference case refers to a set of recommended methodological standards required to conduct an HTA in a given jurisdiction. It lays out formally accepted methods and assumptions underpinning analyses and frames the boundaries of HTAs such as the scope, time horizon, outcome measure(s) as well as resource use and costing.

Ghana's HTA reference case seeks to provide standard guidance for the planning, conduct, and reporting of HTAs and economic evaluations so that the approach to the analyses and the presentation of results is coherent, transparent and consistent. It also seeks to ensure that policy decisions based on HTA evidence are applied equally, and are based on a uniform and transparent technical process in accordance with set standards.

Adherence to these minimum standards would be managed by the HTA secretariat situated within the Pharmacy Directorate of the Ministry of Health.

While Ghana seeks to strengthen the science and practice of HTA to inform policy decisions and priority setting, the need for robust and rigorous analyses in

economic evaluations is critical in meeting the requirements for evidence in health sector decision-making.

It is my hope that HTA conducted or adapted for application to decision-making and health policy in Ghana, would conform to the minimum methodological standards defined in this reference case.

KWAKU AGYEMAN-MANU (MP)
MINISTER FOR HEALTH

1 Introduction

Health Technology Assessment (HTA) institutionalisation has been identified by the World Health Organization (WHO) as one of the decision-making tools that can foster the achievement of Universal Health Coverage (WHO, 2015). Health Technology Assessment is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle (O'Rourke et al., 2020). HTA refers to the systematic evaluation of properties, effects, and/or impacts of health technologies. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology (World Health Organisation, 2016). A health technology may refer to medicines, vaccines, devices, procedures and systems developed to solve a health problem and improve quality of life (HtaGlossary.net, 2021). The purpose of HTA is to inform decision-making in order to promote an equitable, efficient, and high-quality health system. The application of HTA in health systems for priority setting is growing rapidly around the world and there is an increasing commitment to use HTA to allow for more explicit and transparent healthcare priority setting.

Relevant progress has been made in HTA institutionalization since its inception in Ghana. HTAs on hypertension (Gad et al., 2020) and childhood cancers (Ghana HTA TWG, 2022) have been conducted, with several others at various levels of development. The outcomes of these HTAs have informed the Standard Treatment Guidelines on hypertension and reimbursements under the National Health Insurance Scheme (NHIS) for childhood cancers. Other HTA-related analyses include the cost analysis of the COVID-19 vaccine deployment programme, and the assessment of amoxicillin dispersible tablets, among others. In line with the institutionalisation process, the 1st Edition of Ghana's HTA Strategy has been developed. The Strategy serves as an essential tool in strengthening the science and practice of HTA in support of evidence-based decisions for the health sector. In addition, the 1st Edition of Ghana's HTA Process Guidelines has been developed leveraging the evidence-informed deliberative process (Oortwijn et al., 2020) and guided by the context from lessons learnt from the National Medicines Selection Process in Ghana (Koduah et al., 2019). The HTA process guidelines define the stepwise approach to the conduct of HTA and the uptake of HTA

recommendations. Work is also ongoing to explore legislation to support HTA conduct and uptake of recommendations.

A critical feature of any HTA is a high-quality and robust economic analysis that is comprehensive, transparent and reproducible, which includes relevant evidence on resource use and health effects. While acknowledging the need for flexibility, a consistent methodological approach is required for assessments to facilitate comparisons between health technologies and disease areas. HTA methods guidelines should therefore specify the preferred methods or 'reference case' that should be used in the primary analysis for HTA. It is therefore part of Ghana's HTA strategy to further develop a comprehensive methods guideline to support this reference case.

2 Policy perspective on the reference case for HTA in Ghana

Ghana's National Health Policy (revised edition, 2020) (Ghana Ministry of Health, 2020) seeks to promote, restore and maintain good health for all people living in Ghana. The policy defines HTA-related objectives to strengthen the healthcare delivery system to be resilient as well as ensure sustainable financing for health.

The National Medicines Policy (NMP), 3rd edition 2017, expands on the above health policy and defines the policy direction for HTA and associated implementation steps. Among other recommendations, the NMP recommends under section 2.2.2, "There shall be developed and regularly updated HTA guidelines which shall detail methods, processes, benchmarks, perspectives and agreeable standards for the conduction, dissemination and use of HTA in-country." (Ministry of Health, 2017)

The development of the HTA reference case as a methodological and reporting benchmark addresses in part, the above policy recommendation. The reference case is also aligned with the objectives of the HTA strategy which seeks to strengthen the science and practice of HTA to inform policy decisions.

3 The Reference Case for HTA and Economic Evaluations

A) What the reference case is

A reference case refers to a preferred set of methodological standards for a range of items relevant to conducting an economic evaluation or HTA that frames the boundaries of the study, such as the modelled time horizon, outcome measure(s), and the approach to resource use identification and costing.

B) What the reference case does

Ghana's HTA Reference case is developed to:

1. Guide the conduct and reporting of HTAs and economic evaluations so that the approach to the analyses and the presentation of results are coherent, transparent and consistent.
2. Support the HTA Secretariat of the MOH in the planning and management of the conduct of HTA.
3. Harmonise expectations of policy and decision-makers, targeted implementing entities and all relevant stakeholders in relation to HTA findings.
4. Ensure that policy decisions based on HTA evidence are based on a uniform and transparent process and in accordance with set standards.

C) Summary of the Reference Case

Preamble

Ghana's HTA reference case, as summarised in Table 1 below, draws on principles from other reference cases including the iDSI Reference Case, formerly referred to as the Gates Reference Case (Claxton et al., 2014), process guidelines from HITAP (HITAP, 2015), and other guidelines situated within Ghana's context. In presenting the iDSI reference case, Wilkinson et al., 2016 describe the reference case as an aid to thought, but not a substitute, and should not be followed without regard to context, culture or history. This is the context within which adherence to the reference case should be promoted. Promoting adherence to reference cases ensures that they serve as a useful resource for researchers and policy-makers in global health settings (Emerson et al., 2019).

Summary of the Reference Case

Table 1: Summary of the Reference Case for Economic Evaluations and Health Technology Assessment

	Component	Description of Methodological Considerations	Reporting Requirement
A	Evidence Synthesis	Evidence should be synthesized on the various relevant dimensions of an HTA based on the scope of the HTA and the decision problem.	In reporting the outputs, the summary of evidence on the various dimensions of the HTA and the quality of evidence should be captured, as well as Risk of Bias (ROB) assessments.
B	Evaluation type	The preferred evaluation type is a cost-utility analysis (CUA), with the outcomes expressed in terms of Quality Adjusted Life Years (QALYs) gained or Disability Adjusted Life Years (DALYs) averted. Other economic evaluations are acceptable provided a strong justification is made for their adoption.	In reporting the outputs, the reasons for selecting the evaluation type should be clearly stated and justified. A fully executable economic model should be submitted as part of the reporting.
C	Perspective on costs	The preferred perspective is the societal perspective; however, the perspective could be that of the government (defined to include the public-funded health system or the National Health Insurance Authority). Depending on the technology being assessed, a perspective could be analysed to reflect consequences both inside and outside the formal health sector. An impact inventory detailing such consequences may be necessary.	In reporting the outputs, the perspective(s) chosen, various cost inputs, underlying assumptions, and the reasons for selection should be clearly stated and justified.
D	Perspective on outcomes	All relevant effects based on the chosen perspective accruing to individuals, the payer, the health system, the government or society should be included in the	In reporting the outputs, the outcomes selected and the associated perspective as well as the approach to the evaluation of the outcomes

	Component	Description of Methodological Considerations	Reporting Requirement
		outcome analysis and this should be in line with the decision problem (as framed by the PICOT[1] statement).	should be stated and justified.
E	Choice of comparator	The choice of comparator should reflect the decision problem (as framed by the PICOT statement) and should include a comparison with standard practice or the status quo. Having no comparator (having a comparator as "doing nothing") should be justified.	In reporting the outputs, the comparator(s) selected and the associated justification should be stated and justified.
F	Data sources	Systematic reviews, meta-analyses, Randomised Controlled Trials (RCTs) and Real World Evidence are preferred sources of data. However, the use of data from quasi-experimental studies, observational studies, and expert opinion will be considered where appropriate and based on the decision problem. Data from country databases and commissioned studies would be used if necessary.	In reporting data sources for both costs and effects, the effective period of the data and time of access should be clearly stated. The tool used to assess the quality of data should also be stated. The risk of bias (ROB) of the evidence used should be explicitly assessed.
G	Outcome measures	The preferred outcome measure of choice should be DALYs averted or QALYs gained. Other outcome measures are acceptable, provided a strong justification is made for their choice.	In reporting, the choice of outcome measure used should be clearly stated and justified. Alternative measures may be converted into DALYs or QALYs.
H	Discount rate	The applicable discount rate from the Ministry of Finance should be used. Where that is not available,	In reporting, the choice of discount rate for both costs

[1] PICOT – Population, Intervention, Comparator, Outcome, Time Horizon

	Component	Description of Methodological Considerations	Reporting Requirement
		the discount rate should be the standard 3% rate commonly used in global Cost-Effectiveness Analysis (CEA) studies and should be applied to both costs and benefits. Sensitivity analysis should be used to explore the impact of discount rates between 0-10%.	and benefits should be clearly stated and justified.
I	Uncertainty	Uncertainty should be evaluated using scenario analyses for different disease progression paths; deterministic (e.g. one-way or multivariate sensitivity analyses) or probabilistic sensitivity analysis on parameters that have distributions.	In reporting, the choice of sensitivity analysis employed should be clearly stated and justified.
J	Equity considerations	Equity implications and issues should be considered, where necessary, during the economic evaluation.	In reporting, all patient populations considered in the analysis should be stated and justified.
K	Time Horizon	The time horizon or duration should be enough to capture any meaningful differences in the future costs and outcomes likely to accrue or be associated with the competing technologies. A lifetime horizon is recommended for all analyses and when not used, a justification should be provided.	In reporting, the time horizon or duration that adequately captures all relevant costs and benefits should be clearly stated and justified.
L	Heterogeneity	Costs and effects of the health technology on identified sub-groups and populations should be considered.	In reporting, all distinct sub-groups considered in the analysis should be documented. Estimates of heterogeneity in meta-analyses (I^2) should be considered.

	Component	Description of Methodological Considerations	Reporting Requirement
M	Transparency	All measures to ensure transparency and reproducibility of results should be employed.	In reporting, all measures adopted to ensure transparency and reproducibility should be documented.
N	Budget Impact	The Budget Impact Analysis (BIA) should be conducted over a period of 5 years (minimum 3 years) from the perspective of the government/public-funded health system or the NHIA and patients where necessary.	In reporting, a fully executable budget impact model should be submitted to enable confidential third-party validation of the results.

Illustration of the Reference Case

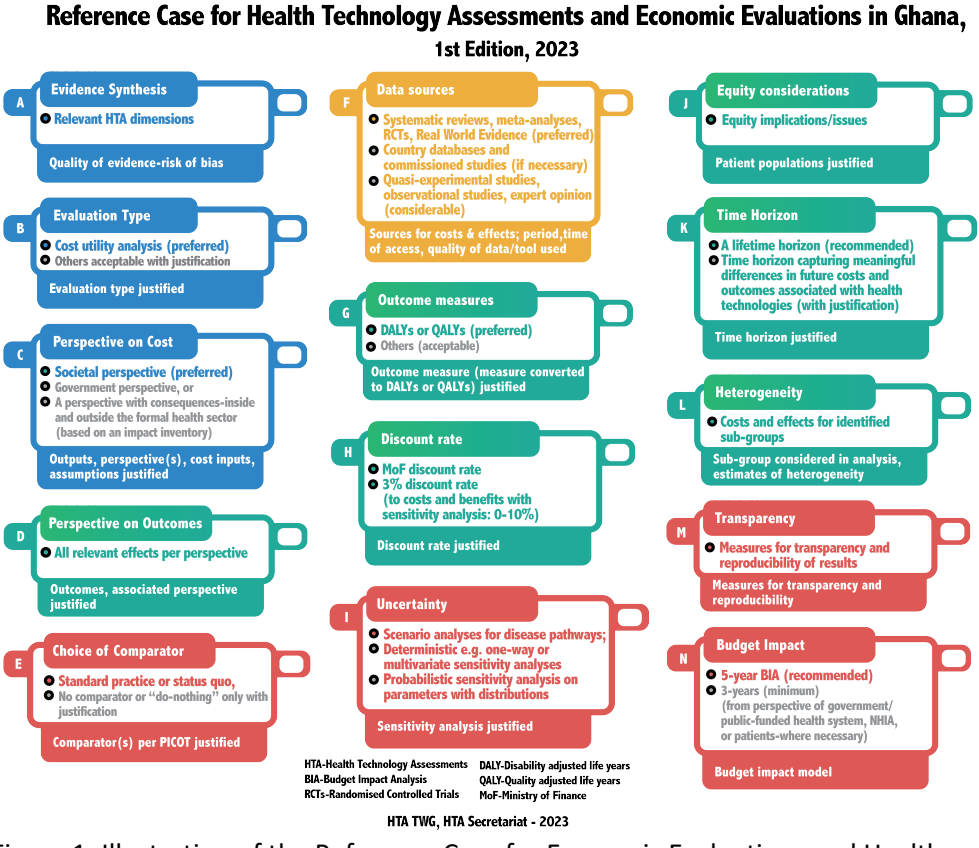

Figure 1: Illustration of the Reference Case for Economic Evaluations and Health Technology Assessment

4 Description of the various dimensions of the Reference Case for HTA and Economic Evaluations

Health Technology Assessment (HTA) including economic evaluations to be considered using this reference case, could be in the following forms:

1. A new economic evaluation to inform decisions
2. An adaptation, transfer or a systematic mapping of existing economic evaluations or HTAs to the Ghana context

A) Evidence Synthesis for Health Technology Assessment

Evidence should be synthesized on the various relevant dimensions of an HTA based on the scope of the HTA and the decision problem.

Evidence synthesis should include: framing the relevant questions (population, intervention, comparator(s), outcome(s)); searching for evidence of efficacy; appraisal of a systematic review; summarizing the results of a systematic review; searching for additional evidence; assessing the 'quality' of evidence; grading of evidence, with due cognizance to the hierarchy of evidence and risk of bias (ROB).

Evidence synthesis summarizes the current body of evidence on a specific question or query. The general outcome of an evidence synthesis on any specific issue should to a large extent be reproducible and repeatable.
The evidence synthesized should be of value to the dimension under consideration. The evidence synthesis may cover health outcomes that are broad enough to capture all socially valued aspects of health and is applicable across various investment types. Where appropriate, the synthesis of evidence can include statistical 'pooling' of results. Bias should be assessed and reported as appropriate.

Preferably, the quality of evidence should be determined using the GRADE approach (G. Guyatt et al., 2011) (G. H. Guyatt et al., 2008). The Jadad or Oxford Quality Scoring System, or any other acceptable tools for evaluating the quality of evidence, may also be used to assess the quality of clinical trials.

In reporting the outputs, the summary of evidence on the various dimensions of the HTA and the quality of evidence should be captured, as well as Risk of Bias (ROB) assessments.

B) Evaluation Type

The preferred evaluation type is a cost-utility analysis (CUA), with the outcomes expressed in terms of Quality Adjusted Life Years (QALYs) gained or Disability Adjusted Life Years (DALYs) averted. Other economic evaluations are acceptable provided a strong justification is made for their adoption.

The use of a generic measure of outcome such as QALYs or DALYs makes it possible to compare outcomes from different technologies across different activities in the healthcare sector. Where patient outcomes in the form of QALYs or DALYs are available, a cost-utility analysis (CUA) will be the preferred evaluation type. Where appropriate, a cost-effectiveness analysis (CEA) where outcomes are measured as life years gained, natural units/intermediate outcomes or any other relevant outcome, may be considered.

In certain circumstances, a cost minimization or cost-benefit analysis may be conducted. Where convincing evidence is available to show that important outcomes of health technologies are similar, a cost minimization analysis will be considered. The health sector interfaces with other sectors such as food and agriculture, aquaculture, finance and economic planning as well as trade and industry. These interactions may necessitate a comparison between health and non-health sector interventions to inform decisions, suggesting a potential consideration for a cost-benefit analysis.

In reporting the outputs, the reasons for selecting the evaluation type should be clearly stated and justified. A fully executable economic model should be submitted as part of the reporting.

C) Perspective on Costs

The preferred perspective is the societal perspective; however, the perspective could be that of the government (defined to include the public-funded health system or the National Health Insurance Authority). Depending on the technology being assessed, a perspective could be analysed to reflect consequences both

inside and outside the formal health sector. An impact inventory detailing such consequences may be necessary.

Most economic evaluations are conducted from a public payer, private payer, individual or societal perspective. The perspective taken is essential in defining the costs, resources and consequences that should be examined, applying the economic principle of forgone welfare/opportunity cost (economic cost is emphasized over accounting cost). To ensure comparability of analyses, the perspective must be clearly stated so that the costs, resources and consequences associated with the perspective adopted can be clearly identified for inclusion in the economic evaluation.
The societal perspective is a broad perspective encapsulating the government/ health system, patients, healthcare providers, etc.

Other costs may also be associated with the implementation of a particular health technology. These may include direct and indirect costs to other public sector agencies, patients and/or their caregivers as a result of a technology.

In reporting the outputs, the perspective(s) chosen, various cost inputs, underlying assumptions, and the reasons for selection should be clearly stated and justified.

D) Perspective on Outcomes

All relevant effects based on the chosen perspective accruing to individuals, the payer, the health system, the government or society should be included in the outcome analysis and this should be in line with the decision problem (as framed by the PICOT statement).

For direct health effects, QALYs gained, DALYs averted, life years gained, and any other relevant measure of health outcome may be used and justified.
For non-health effects, outcomes that fall outside the health budget should be included in the analysis.

In reporting the outputs, the outcomes selected and the associated perspective as well as the approach to the evaluation of the outcomes should be stated and justified.

E) Choice of Comparator

The choice of comparator should reflect the decision problem (as framed by the PICOT statement) and should include a comparison with standard practice or the status quo. Having no comparator (having a comparator as "doing nothing") should be justified.

The preferred comparator for the reference case or standard economic evaluation will be standard/usual/routine care which represents the technology or technologies most widely used in practice e.g. in accordance with Ghana's Standard Treatment Guidelines (STG).

The choice of a comparator is a crucial step in every economic evaluation and must represent the decision problem (framed by the PICOT if applicable). This is because, the costs and effects associated with a particular comparator will be measured, valued and included in the analysis. Comparative incremental analysis against current practice can then most accurately reflect the true nature of the decision problem facing decision-makers. A comparator that does not reflect the decision problem and policy context will lead to spurious conclusions.

While it is best practice to include all relevant comparator technologies in a single evaluation, this may be inefficient and burdensome when there are many available alternatives. It is therefore reasonable to select the best comparator by limiting the choice to usual or standard practice also known as routine care/practice or the technology that would most likely be replaced with the introduction of the new alternative, taking into consideration the decision problem.

In the absence of an active comparator or a not-well-defined standard of care, a comparator of 'no intervention' may be used in addition to 'not standard routine care' as this will provide useful information on the relative benefits of the technology.
In the event that an intervention which is considered as best practice (as defined by evidence-based clinical practice guidelines) differs from routine practice (e.g. as captured by STG), the choice of the comparator should include both the best practice and routine practice. Where only one of them has to be chosen, justification should be provided.

In reporting the outputs, the comparator(s) selected and the associated justification should be stated and justified.

F) Data Sources

Systematic reviews, meta-analyses, Randomised Controlled Trials (RCTs) and Real World Evidence are preferred sources of data. However, the use of data from quasi-experimental studies, observational studies, and expert opinion will be considered where appropriate and based on the decision problem. Data from country databases and commissioned studies would be used if necessary.

Consideration will be given to the hierarchy of evidence in the context of data sources. Systematic reviews and RCTs will be ranked higher than other studies, however, the use of data from other sources such as cohort studies, observational studies and expert opinion will be considered where appropriate and based on the decision problem.

Where commissioned studies are utilized to generate data, the sources should be cited as part of the report. Also, the use of existing country databases is encouraged. While data access and data availability constraints are common in the Ghanaian context, key assumptions in the use of proxy data sets and modified data sets should be reported on. Sources from grey literature should be reported.

In reporting data sources for both costs and effects, the effective period of the data and time of access should be clearly stated. The tool used to assess the quality of data should also be stated. The risk of bias (ROB) of the evidence used should be explicitly assessed.

G) Outcome Measures

The preferred outcome measure of choice should be DALYs averted or QALYs gained. Other outcome measures are acceptable, provided a strong justification is made for their choice.

Health outcomes should be the emphasis of all economic analyses. Therefore, a health outcome measure must be comprehensive enough to capture the most critical and crucial components of health. It should be able to be used consistently throughout the population for various types of health interventions, technologies and programmes.

Where locally relevant QALYs are unavailable, DALYs may be used. Other alternative outcome measures can be adopted where justification is provided. Note that in a cost-benefit analysis, both outcomes and costs are expressed in monetary units.

A measure that captures both length and health-related quality of life is generalizable across disease states and allows for the consideration of opportunity costs across the entire health sector as well as comparisons between health intervention and/or investment types. Sometimes a disease-specific intervention may be the appropriate outcome measure depending on the scope of the decision problem and generalizability may be irrelevant.
Where appropriate, the use of life years gained, natural units/intermediate outcomes or any other relevant outcome may be employed as the outcome measure.

In reporting, the choice of outcome measure used should be clearly stated and justified. Alternative measures may be converted into DALYs or QALYs.

H) Discount Rate

The applicable discount rate from the Ministry of Finance should be used. Where that is not available, the discount rate should be the standard 3% rate (Sharma et al., 2021) *commonly used in global Cost-Effectiveness Analysis (CEA) studies and should be applied to both costs and benefits. Sensitivity analysis should be used to explore the impact of discount rates between 0-10%.* (Sharma et al., 2021).

Discounting is a procedure for adjusting future costs and benefits so as to arrive at their present values. Future predicted costs and health outcomes are usually valued at less than present values, and so best-practice in economic evaluations usually recommend discounting.

In reporting, the choice of discount rate for both costs and benefits should be clearly stated and justified.

I) Uncertainty (Sensitivity Analysis)

Uncertainty should be evaluated using scenario analyses for different disease progression paths; deterministic (e.g. one-way or multivariate sensitivity analyses) or probabilistic sensitivity analysis on parameters that have distributions.

Uncertainty in economic evaluations may arise as a result of how a model is structured. Uncertainty may be introduced through the following:

- how health states are categorised or the representation of care pathways
- bias due to selective use of data sources to inform key parameters, for example, estimates of relative efficacy or selection of cost data
- the precision of the mean parameter values.

To ensure the robustness of the results and conclusions of the economic analysis, uncertainty on the outcome of the economic evaluation should be systematically evaluated.

In reporting, the choice of sensitivity analysis employed should be clearly stated and justified.

J) Equity Considerations

Equity implications and issues should be considered, where necessary, during the economic evaluation.

Equity in health implies that ideally, everyone should have a fair opportunity to attain their full health potential and that no one should be disadvantaged from achieving this potential (World Health Organization, 2019). A starting place for all economic evaluations should be to acknowledge and respect both horizontal and vertical equity. Horizontal equity requires that people with like characteristics (of ethical relevance) be treated the same, while vertical equity allows for people with different characteristics (of ethical relevance) to be treated differently. Equity characteristics include age, gender, socioeconomic status, access to alternative therapies, and prevalence of the condition.

The potential benefits, harms, and costs associated with a health technology are often unevenly distributed across the population. This may be due to differences in treatment effects, risks or incidences of conditions, access to healthcare, or technology uptake in population groups. When the intervention can be provided

selectively to certain subgroups, then cost-effectiveness information can be presented for each subgroup. Any stratified analysis of subgroups motivated by vertical equity considerations must be explained and justified.

Further, groups that are likely to be disadvantaged by the adoption and implementation of the intervention should also be identified, where possible. This may occur, for example, when a change in clinical practice requires that patients be cared for at home rather than at a hospital, thereby shifting costs and burdens to patients and informal caregivers. Given that many decision-makers are concerned about equity, economic evaluations should be presented in a manner that supports equity concerns being reflected in decision-making.

Although the HTA should weigh all outcomes equally (regardless of the characteristics of people receiving the health benefit), the analyses should be presented with full descriptions of the relevant patient populations, to allow for consideration of any subsequent distributional and equity-related policy concerns.

In reporting, all patient populations considered in the analysis should be stated and justified.

K) Time Horizon

The time horizon or duration should be enough to capture any meaningful differences in the future costs and outcomes likely to accrue or be associated with the competing technologies. A lifetime horizon is recommended for all analyses and when not used, a justification should be provided.

For economic evaluations, the study period should be clearly described and appropriate to the disease and its treatment or health program. The time horizon should capture all meaningful differences in costs and outcomes between the various interventions. The time frame adopted should be clearly stated and its choice justified, with the same time horizon being applied to both costs and outcomes.

A lifetime horizon is usually considered appropriate for HTAs, as the majority of technologies have costs and outcomes that impact a patient's lifetime. This is particularly relevant for chronic diseases. A shorter time frame may be considered when the costs and outcomes relate to a relatively short period of time, such as

in an acute infection, and when mortality is not expected to differ between the competing technologies. A decision to use a shorter time frame should be justified and an estimate provided of any possible bias introduced as a result of this decision.

In reporting, the time horizon or duration that adequately captures all relevant costs and benefits should be clearly stated and justified.

L) Heterogeneity

Costs and effects of the health technology on identified sub-groups and populations should be considered.

Economic evaluations should reflect the entire target population as defined by the decision problem. However, it may be necessary in some cases to assess the cost-effectiveness of the intervention in a sub-group of the population.

In conducting an evaluation, potential sources of heterogeneity that may lead to differences in parameter-input values across distinct subgroups should be explored. Heterogeneity may result from differences in the natural history of the disease, effectiveness of the interventions, health state preferences, or costs of the interventions. Heterogeneity may result in different decisions with respect to cost-effectiveness among different subgroups. Care should be taken when representing sub-groups to ensure that ethical issues are considered before the analysis is undertaken.

The evidence supporting the biological or clinical plausibility of the subgroup effect should be fully documented, including details of statistical analyses. Since the goal of the health system is to maximise the potential for health gain from its finite resources, a stratified analysis that allows cost-effectiveness to be modelled separately for each subgroup may contribute important information to the final advice.

In reporting, all distinct sub-groups considered in the analysis should be documented. Estimates of heterogeneity in meta-analyses (I^2) should be considered.

M) Transparency

All measures to ensure transparency and reproducibility of results should be employed.

Economic evaluations conducted should be transparent and reproducible. It should adhere to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement (Husereau et al., 2013) for reporting.

To maximise transparency, the assessment should include a conflict of interest statement in relation to all those involved in the assessment. In assessing evidence, a reproducible search strategy should be employed and two or more reviewers should be involved in the selection process using a pre-defined protocol to maximise objectivity. Data used in the analysis should ideally be publicly available or available upon request, and where possible, unit costs should be detailed separately from the total costs. Undiscounted, disaggregated cost and outcome data should be presented in addition to providing the aggregated, discounted summaries.

Data sources should be identified using a comprehensive and transparent approach that can be replicated by others and the choice of data sources and methods for analyzing data inputs must be clearly stated.
Details on funding partners of the economic evaluation should be disclosed as well as institutions in support.

In reporting, all measures adopted to ensure transparency and reproducibility should be documented.

N) Budget Impact Analysis

The Budget Impact Analysis (BIA) should be conducted over a period of 5 years (minimum 3 years) from the perspective of the government/public-funded health system or the NHIA and patients where necessary.

A budget impact analysis (BIA) is a financial approach designed to estimate, over a specified period, the financial consequences of adopting a health intervention or technology. A budget impact analysis should be submitted along with the economic evaluation of a technology to best inform the needs of the decision-

maker; BIA is often complementary to CEA. The outcome of BIA is the net financial impact, which serves the purpose of determining affordability and informing financial planning for new technologies relative to the status quo. Even though different specifications may be used for a BIA, within the context of this reference case, BIA denotes an analysis of the added financial impact of a new health technology for a finite period. The presentation of BIA should reflect a manner relevant to the decision problem and meet the needs of the decision-maker.

A summary of the conduct of BIA from the perspective of the government of Ghana or the National Health Insurance Authority (NHIA) is detailed below:

Perspective
The BIA should be conducted from the perspective of the government/public-funded health system or the NHIA.

Technology/Intervention
The technology should be described in sufficient detail to differentiate it from its comparators and to provide context for the study.

Choice of comparator(s)
The preferred comparator for the reference case is 'routine care', that is, the technology or technologies most widely used in clinical practice in Ghana in the context of the target population. When both CEA and BIA are conducted, the same comparator(s) should be used in both assessments.

Time Frame/horizon
The core analysis should estimate the annual financial impact over a minimum of three (3) years and ideally five (5) years.

Target Population
The target population should be defined based on the approved indication for the technology. The size of the target population should be guided by the national incidence and prevalence of the indication/disease. Stratified analysis of sub-groups (that have been ideally identified a priori) is appropriate. These should be biologically plausible and justified in terms of clinical and cost-effectiveness evidence, if conducted.

Costing

The costs included should be limited to direct costs associated with the technology that will accrue to the government/public health system and NHIA. The methods used to generate these costs should be clearly described and justified, with all assumptions explicitly tested as part of the sensitivity analysis. As costs are presented in the year they are incurred, no discounting is required.

Budget Impact Model

The budget impact model should be clearly described, with the assumptions and inputs documented and justified. Two primary scenarios should be modelled: the baseline scenario that reflects the current mix of technologies and forecasts the situation should the new technology not be adopted, and the new technology scenario, where it is adopted. The methods for the quality assurance of the model should be detailed and documentation of the results of model validation provided. Key inputs should be varied as part of the sensitivity analysis. The model should be of the simplest design necessary to address the budget impact question using a readily available software package.

Uncertainty

Scenario analyses for a range of plausible scenarios and sensitivity analysis must be employed to systematically evaluate the level of uncertainty in the budget estimates due to uncertainty associated with the model and the key parameters that inform it e.g. the impact on budget by coverage levels. The range of values provided for each parameter must be clearly stated and justified, and justification provided for the omission of any model input from the sensitivity analysis.

Reporting

For the purposes of financial sustainability, a budget impact analysis should be conducted. Input parameters and results should be presented both in their disaggregated and aggregated forms with both incremental and total budget impact reported for each year of the time frame. A five-year budget impact model (three-year minimum) should be submitted to enable (confidential) third-party validation of the results.

In reporting, a fully executable budget impact model should be submitted to enable (confidential) third-party validation of the results.

5 Annexe

5.1 Methodological checklist for the Ghana HTA reference case

	Component	Description of Methodological Considerations	Check	Reporting Requirement	Check
A	Evaluation type	• CUA • Others: e.g. CBA ……	☐ ☐	Reasons/justification for evaluation type:	☐
B	Perspective on costs	• Societal perspective • Payer perspective (Government Or NHIA)	☐ ☐ ☐ ☐	Reasons/justification for outputs, perspective(s), cost inputs as well as assumptions	☐
C	Perspective on outcomes	Relevant effects (outcomes) accruing to -individuals, -the payer, -the health system, -the government (based on chosen perspective)	☐ ☐ ☐ ☐ ☐	Reasons/justification for outcomes, associated perspective, approach to evaluation	☐
D	Choice of comparator	• Standard practice or the status quo	☐	Reasons/justification for comparator(s)	☐
E	Data sources	• Systematic reviews with or without meta-analyses • Randomised Controlled Trials (RCTs) • Observational Studies • Expert opinion • Other ……	☐ ☐ ☐ ☐ ☐	Costs and effects, effective period of data and time of access The tool used to assess the quality of data The risk of bias (ROB) of the evidence	☐ ☐ ☐
F	Evidence Synthesis	Evidence synthesis on relevant HTA dimensions (based on the HTA scope and the decision problem). (See Ghana HTA Process Guidelines)	☐	Summary of evidence on the various dimensions of the HTA and the quality of evidence captured, as well as ROB assessments. (See Ghana HTA Process Guidelines)	☐
G	Outcome measurement	• QALYs • DALYs • Others …….	☐ ☐ ☐	Reasons/justification for the choice of outcome measure	☐
H	Discount rate	• 3% rate for both costs and benefits.	☐	Reasons/justification for the choice of discount rate for both costs and benefits	☐

	Component	Description of Methodological Considerations	Check	Reporting Requirement	Check
		• Sensitivity analysis between 0-10%.	☐		
I	Uncertainty	• Scenario analyses -Deterministic Or -Probabilistic sensitivity analysis	☐ ☐	Reasons/justification for the choice of sensitivity analysis	☐
J	Equity rating	Equity implications and issues	☐	Reasons/justification for patient populations considered	☐
K	Time Horizon	Adequate time period for future costs and outcomes	☐	Reasons/justification for the time horizon chosen	☐
L	Heterogeneity	Costs and effects on sub-groups	☐	Distinct sub-groups documented	☐
M	Transparency	Transparency and reproducibility of results	☐	Transparency and reproducibility measures documented	☐
N	Budget Impact	Five (5)-year budget impact (3-year minimum)	☐	Budget impact model submitted	☐

6 References

Claxton, K. P., Revill, P., Sculpher, M., Wilkinson, T., Cairns, J., & Briggs, A. (2014). *The Gates Reference Case for Economic Evaluation*. The Bill and Melinda Gates Foundation.

Emerson, J., Panzer, A., Cohen, J. T., Chalkidou, K., Teerawattananon, Y., Sculpher, M., Wilkinson, T., Walker, D., Neumann, P. J., & Kim, D. D. (2019). Adherence to the iDSI reference case among published cost-per-DALY averted studies. *PLoS ONE*, *14*(5). https://doi.org/10.1371/JOURNAL.PONE.0205633

Gad, M., Lord, J., Chalkidou, K., Asare, B., Lutterodt, M. G., & Ruiz, F. (2020). Supporting the Development of Evidence-Informed Policy Options: An Economic Evaluation of Hypertension Management in Ghana. *Value in Health*, *23*(2), 171–179. https://doi.org/10.1016/J.JVAL.2019.09.2749

Ghana HTA TWG. (n.d.). *Health Technology Assessment on Burkitt Lymphoma*.

Ghana Ministry of Health. (2020). *National Health Policy* (MOH (ed.); revised edition). MOH.

Guyatt, G. H., Oxman, A. D., Vist, G. E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., & Schünemann, H. J. (2008). GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ : British Medical Journal*, *336*(7650), 924–926. https://doi.org/10.1136/bmj.39489.470347.AD

Guyatt, G., Oxman, A., Akl, E., Kunz, R., & Vist, G. (2011). GRADE guidelines 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*, *64*.

HITAP. (2015). *Health Intervention and Technology Assessment Program (HITAP) HTA Process Guidelines*.

HtaGlossary.net. (2021). *HtaGlossary.net | health technology*. http://htaglossary.net/health-technology

Husereau, D., Drummond, M., Petrou, S., Carswell, C., Moher, D., Greenberg, D., Augustovski, F., Briggs, A., Mauskopf, J., & Loder, E. (2013). Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *The European Journal of Health Economics*, *14*(3), 367–372. https://doi.org/10.1007/s10198-013-0471-6

Koduah, A., Asare, B. A., Gavor, E., Gyansa-Lutterodt, M., Andrews Annan, E., & Ofei, F. W. (2019). Use of evidence and negotiation in the review of national standard treatment guidelines and essential medicines list: experience from Ghana. *Health Policy and Planning*, *34*(Supplement_2), ii104–ii120. https://doi.org/10.1093/HEAPOL/CZZ107

Ministry of Health. (2017). National Medicines Policy, 3rd Edition. In *NMP: Vol. 3rd edition*. Ministry of Health.

O'Rourke, B., Oortwijn, W., Schuller, T., & Group, the I. J. T. (2020). The new definition of health technology assessment: A milestone in international collaboration. *International Journal of Technology Assessment in Health*

Care, *36*(3), 187–190. https://doi.org/10.1017/S0266462320000215

Oortwijn, W., Jansen, M., & Baltussen, R. (2020). Use of evidence-informed deliberative processes by health technology assessment agencies around the globe. *International Journal of Health Policy and Management*, *9*(1), 27–33. https://doi.org/10.15171/IJHPM.2019.72

Sharma, D., Aggarwal, A. K., Downey, L. E., & Prinja, S. (2021). National Healthcare Economic Evaluation Guidelines: A Cross-Country Comparison. *PharmacoEconomics Open*, *5*(3), 349. https://doi.org/10.1007/S41669-020-00250-7

WHO. (2015). *Using Health Technology Assessment for Universal Health Coverage and Reimbursement Systems*.

Wilkinson, T., Sculpher, M. J., Claxton, K., Revill, P., Briggs, A., Cairns, J. A., Teerawattananon, Y., Asfaw, E., Lopert, R., Culyer, A. J., & Walker, D. G. (2016). The International Decision Support Initiative Reference Case for Economic Evaluation: An Aid to Thought. *Value in Health : The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, *19*(8), 921–928. https://doi.org/10.1016/j.jval.2016.04.015

World Health Organisation. (2016). *Health Technology Assessment*. WHO Website. http://www.who.int/health-technology-assessment/about/Defining/en/

ISBN: 978-9988-3-4848-9