Action Line 3: *Evaluation of Health Care 2.0: Setting the Landscape for a Full Benefit HTA Decision-Making Framework* **– Summary**

1.   **Background and vision:**

The basic objective of any economic evaluation in a health technology assessment (HTA) framework is to identify, measure, value, and compare the costs and benefits of health interventions. However, full benefit assessment is one of the greatest challenges facing economists.

In recent years, the interest in valuing the benefits of health interventions has shifted from the common health-focussed quality-adjusted-life-year (QALY) model towards capturing the full benefit of interventions by identifying additional dimensions of value beyond health. Ignoring such benefits selectively might lead to non-optimal or wrong HTA decisions. This shift has led to the exploration of more appropriate and broader outcome measures in terms of overall quality of life (i.e., wellbeing and the wellbeing-adjusted-life-year 'WALY' framework). Such an outcome measure would allow (i) the evaluation of a wider scope of interventions in and between health sectors (i.e. prevention, cure and care), (ii) improve welfare economic evaluations in health care, and (iii) optimize HTA decision making. However, the exploration of such a broader outcome measure is still in its infancy. In the Erasmus Initiative 'Smarter Choices for Better Health' 2017-2021 (i.e. SCBH 1.0), a first important step towards a broader outcome measure has been made that should make **measuring benefits beyond the QALY** possible. That is, based on literature and a theoretical framework, the Wellbeing Instrument Ten Domains (i.e. WiX) was developed in the Netherlands. However, several urgent and relevant research questions must be tackled before the WiX can be used in policy-decision making (see our research agenda below).

Additionally, full benefit assessment requires insights into **patients' preferences and uptake predictions.** Evidence showed that many health interventions are used by fewer patients and with less frequent intervals than recommended by clinical guidelines. When health interventions (including health and non-health benefits) are not aligned with patients' needs, this low uptake and poor adherence can squander limited resources. Scientists and HTA bodies both agree on the importance of incorporating patients' preference information into HTA decision making; a recent paper identified five applications of preferences in HTA: endpoint selection, clinical benefit rating, predicted uptake, valuation of benefits in economic evaluations, and multi-criteria decision analysis (MCDA). Yet there is little guidance how to systematically elicit and incorporate patient preferences in a scientifically valid way to optimise HTA decision making. Besides, the action line 'Evaluation of Health Care' of SCBH 1.0 provided an evidence-based research agenda with 37 research questions that should be addressed to integrate patient preferences in HTA procedures in a robust and scientific manner. Although SCBH 1.0 successfully answered a handful of research questions, many remaining research questions – among them methodological and procedural questions – require further investigation (see our research agenda below).

Lastly, a full-benefit HTA decision making framework requires a rethink of **policy-related preconditions**. Research is needed to determine when a HTA decision is sensitive to including other benefits than QALY as well as preferences. Research is also required to investigate whether an economic evaluation in terms of costs per WALY can act as a substitute for the costs per

QALY evaluation and to determine the cut-off values (i.e. willingness to pay) for a WALY. Finally, existing economic evaluation and priority setting frameworks are insensitive to **distributional considerations** over QALY which likely matter more when incorporating more benefits such as WALYs. A unified welfare economics method could be used to guide decisions-makers to reach equitable distributions of QALYs and WALYs. Questions asked are for instance: how to make HTA decisions when the average cost per QALY/WALY reduces but the variability of QALYs/WALYs across individuals increases. Such a framework might be further extended to decide on allocation rules that an equity-sensitive decision maker can use to optimally target health care and public health interventions on groups that display heterogenous responses (such as varying uptake of health interventions depending on patient preferences, or health interventions having differential effectiveness across patients). Successful application of such equity sensitive HTA decision rules requires elicitation of social preferences to establish the trade-offs that the general public and decision makers are prepared to make between using available resources to maximize WALYs and to equalize the distribution of WALYs (see our research agenda below)

Evaluation of Health Care 2.0 has the ambition to pave the way for a full benefit HTA decision-making framework, to enable a fair and transparent evaluation of a wider scope of interventions in and between health sectors (i.e. prevention, cure and care). Our goal is to set the landscape for a full benefit   HTA decision-making framework   by measuring benefits   beyond   the   QALY, incorporating   preferences   and   distributional   considerations,   and   setting   policy-related preconditions.

2.   **Our research agenda:**

Three pillars will be taken forward into further research. The **first pillar** relates to **measuring benefits beyond the QALY**. In this pillar the research conducted in SCBH 1.0 will be continued. The developed WiX instrument will be validated and valuated in the Netherlands and subsequently in other EU countries and, after that, beyond EU. In doing so the additional benefit of including WALY instead of QALY in HTA decision will be quantified. The developed WiX instrument will also be compared to the existing wellbeing instrument developed by EuroQol-Sheffield (EQ-HWB). The EQ-HWB was developed at the same time as the WiX in collaboration with the EuroQol but does not have the thorough theoretical basis of the WiX. Additionally, it will be determined in which sector(s) of health (in prevention, cure, and care) the difference between WALY and QALY is most substantial.

The **second pillar** covers **preferences and uptake predictions.** Although preference elicitation studies have been conducted for decades, several fundamental methodological and procedural research questions remain before HTA stakeholders are able and willing to trust such study outcomes and include preferences in their policy decision making. Previous studies in SCBH 1.0 and other EU wide consortia showed that external validity, internal validity (or data quality assessments), as well as transferability of preference study outcomes are especially relevant themes for further exploration. On top of that, the impact of the described choice context, social environment, educational material and framing and presentation of risks and benefits in such experiments lack evidence-based guidance. Finally, uptake predictions might differ based on for instance demographic characteristics of the population, accurate predictions should

therefore account for such heterogeneity. Different mechanisms, modelling and estimation techniques (e.g. DCE, Impact Evaluation) exist in health economics and welfare economics to measure the impact of heterogeneity on uptake predictions. These methods will be compared, which provides insights into best-practice applications of uptake predictions.

The **third pillar** concerns **policy-related preconditions** for moving to a full-benefit HTA decision making framework. First and foremost: when is a HTA decision sensitive to including other benefits than QALY as well as preferences? Based on evidence from pillar 1 and 2, a definition will be developed on wellbeing and preference-sensitive HTA decisions. Second, if other than QALY measures of benefit are used to evaluate care, cure and prevention, it should be investigated at what thresholds such treatments or interventions will be considered cost-effective. Third, even with benefits broadly measured, healthcare policy decisions should not only consider mean benefits, but also their **distribution**. Are large benefits that are only obtained by a few preferred over large benefits for many? Are benefits early in life preferred over benefits at old age? How to account for inter-individual differences in the benefits derived from similar interventions? Using welfare economic theory, the issue of evaluating distributions over the lifecycle in combination with heterogenous responses to health interventions (heterogenous impact evaluation) will be explored. In doing so, it will be evaluated whether this framework can be applied in conjunction with the QALY and WiX instrument in the Netherlands and beyond. Fourth, social preferences over QALY/WALY distributions will be elicited to determine if and how they might differ from patient preferences as well as how they might be used for priority setting in HTA decision-making. From there, derivation of optimal allocation rules will be introduced in situation where patients are likely not to follow clinical guidelines or when health interventions have different effectiveness across individuals.

Finally, this action line will **take part in methodological research across action lines that connects the different pillars of this action line with several research lines** (for instance Action Line 2 where it is often unclear how healthcare provider ranks could be used in policy). Research and policy are often interested in rankings of units such as countries, neighborhoods, hospitals, treatments, etc. However, these rankings contain a lot of statistical uncertainty. For instance, the first ranked unit may not be statistically better than the second ranked unit. This research considers extending and empirically applying previously set concepts in Mogstad et al. (2021); using results on i) ranges of ranks for units, and ii) the number of units that belong to the x-best %, it will be considered how to reliably rank and group medical treatments based on their outcomes.

3.   **Our impact:**

Setting the landscape for a full benefit HTA decision-making framework inevitably means creating impact. This action line's impact will be threefold. Firstly, the action line requires input from patients, health care providers, industry, decision-makers as well as society in order to set the landscape. We will sample from these populations to ensure outcomes are relevant for all stakeholders. Secondly, we will engage and communicate with the general public and academia. We will engage with the public via the infrastructure set up in SCBH 1.0, namely via blogs and social media. We will seek academic engagement by presenting and networking during national

and international conferences, seminars and workshops. Thirdly, the research of this action line will exploit multidisciplinary to enhance impact. The core team will seek collaborations with other action lines and Universities to gain knowledge and expertise from many different perspectives. Examples of multidisciplinary efforts are the methodological research that connects different pillars and convergence initiatives between Erasmus MC, TU Delft and Erasmus University. Collaborations with partners outside of academia will also actively be sought.

4. **Methodology:**

In line with the diversity of topics proposed in this action line and the expertise of the different researchers involved, a mixed-methods approach will be used for the proposed studies. Methods range from qualitative methods (e.g., semi-structured interviews, focus group discussions, nominal group technique) to quantitative survey methods (e.g., DCE and Likert-scales). Furthermore, we will use existing data from previous action line research and registries. Additionally, different analytical techniques (e.g., content analysis, theoretical analysis, direct comparisons, rankings, statistical choice modelling, validations) will be used. More specifically, to address the aims in the **first pillar,** surveys will be developed and administrated. Data will be analyzed to validate the WiX and compare outcomes between WiX and EQ-HWB. In the **second pillar**, qualitative studies will be used to develop different DCE surveys, and quantitative methods will be used to analyze the survey data. These surveys will contain methodological components, wherever possible, in the form of RCT studies. Besides formal statistical comparison of study arms, debriefing interviews with research respondents will be applied to attain in-depth information on respondents' personal views towards decision strategies and the potential impact of topics investigated (e.g., risk and benefit presentation, social influences). To research the **third pillar**, first a set of interviews with experts will be conducted to establish preference- and WALY-sensitive decisions in HTA. Depending on the consensus reached during these interviews, and additional round using these interviews, an additional round using the Delphi-method (or similar consensus methodology) will be applied to establish a final definition. To make distributional comparisons, and to elicit social preferences for QALY/WALY distributions, social welfare functions will be used in conjunction with experimental and secondary data.

5. **Core team:**

Action Line Leaders: Jorien Veldwijk (ESHPM), Vacancy (ESE)
Postdoctoral researchers: Samare Huls (ESHPM), Raf Van Gestel (ESE/ESHPM)
PhD students: ESE (vacancy); ESHPM (vacancy)
Affiliated MT members: Esther de Bekker-Grob (ESHPM), Tom Van Ourti (ESE)
Affiliated steering group members: Job van Exel (ESHPM), Werner Brouwer (ESHPM)
Visiting professor (part-time): Joffre Swait (ESHPM) (Affiliated to ESHPM otherwise retired (DoB: 17-01-1954) and not formally employed anymore at MIT nor UniSA (his previous appointments). Joffre Swait is an experienced statistician & econometrician / leading scholar in choice modelling research, he is highly engaged and therefore provides valuable input for SCBH 2.0 AL#3)