Health Technology Assessment – What's in it for Stats?

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Joint BBS/EFSPI Seminar, Basel, 4th June 2013

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- The views expressed herein represent those of the presenter and do not necessarily represent the views or practices of Eli Lilly.

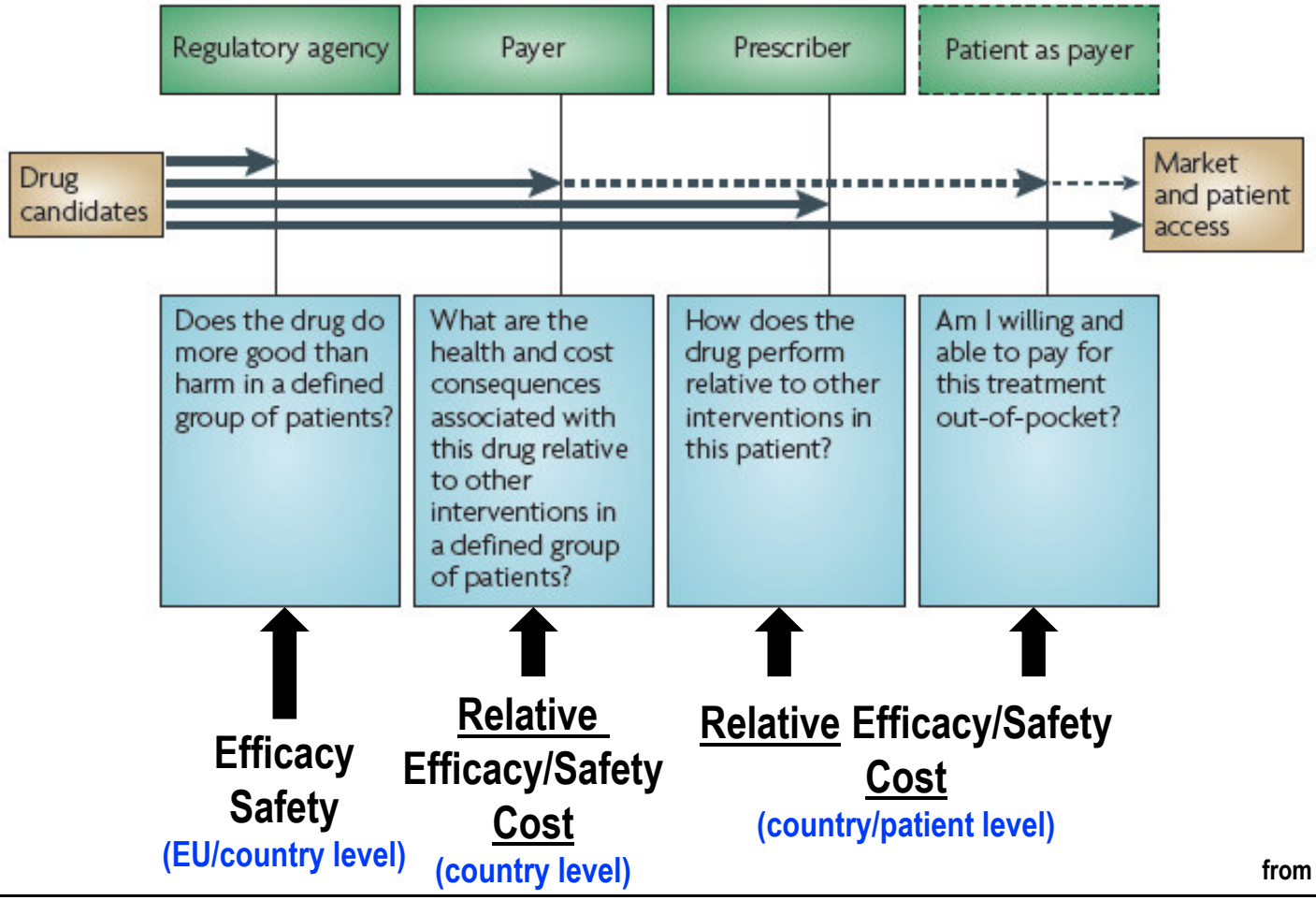
Abstract

Health Technology Assessment (HTA) has become increasingly important during recent years and will continue to do so in the future.

HTA is comprised of a wide variety of disciplines, data sources, methods and analytical challenges.

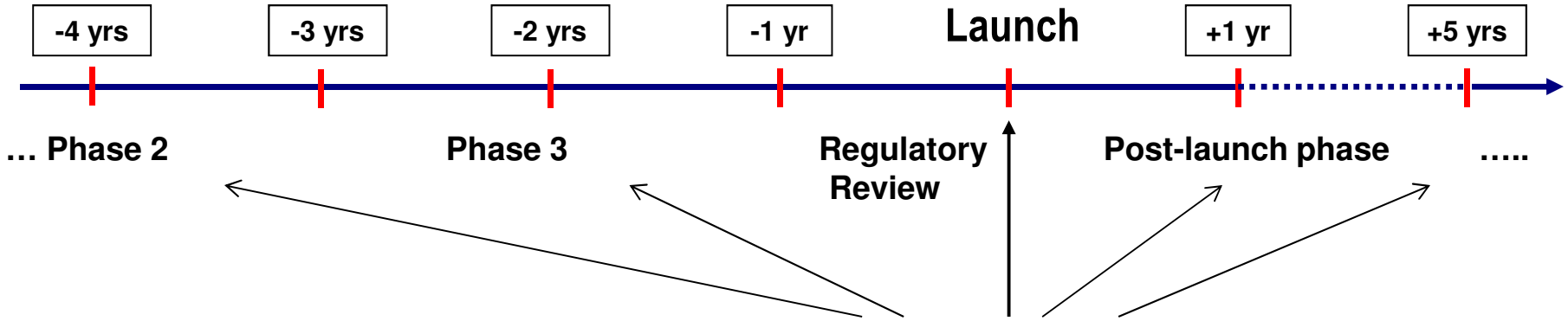
This presentation provides an overview of the current state in HTA with a focus on the area of reimbursement, highlighting the opportunities for statisticians to provide substantial contributions and guidance.

Market & Patient Access



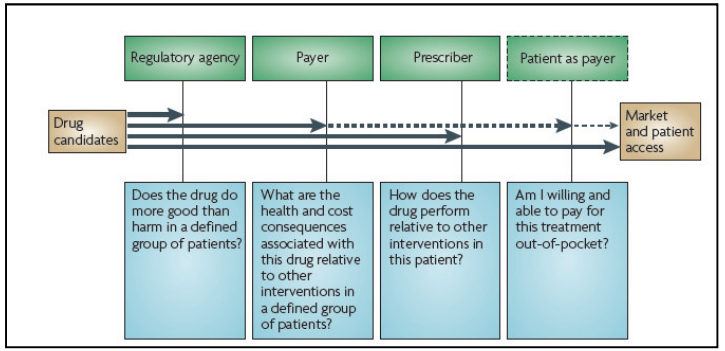
from Eichler et al. 2010

HTA activities …
… from pre-launch to patent loss



Key Skills/Strengths:

- ❖ Understanding Data
- ❖ Statistical Methods / Handling Uncertainty
- ❖ Business acumen/ Communication



from Eichler et al. 2010

Market Access & HTA Activities

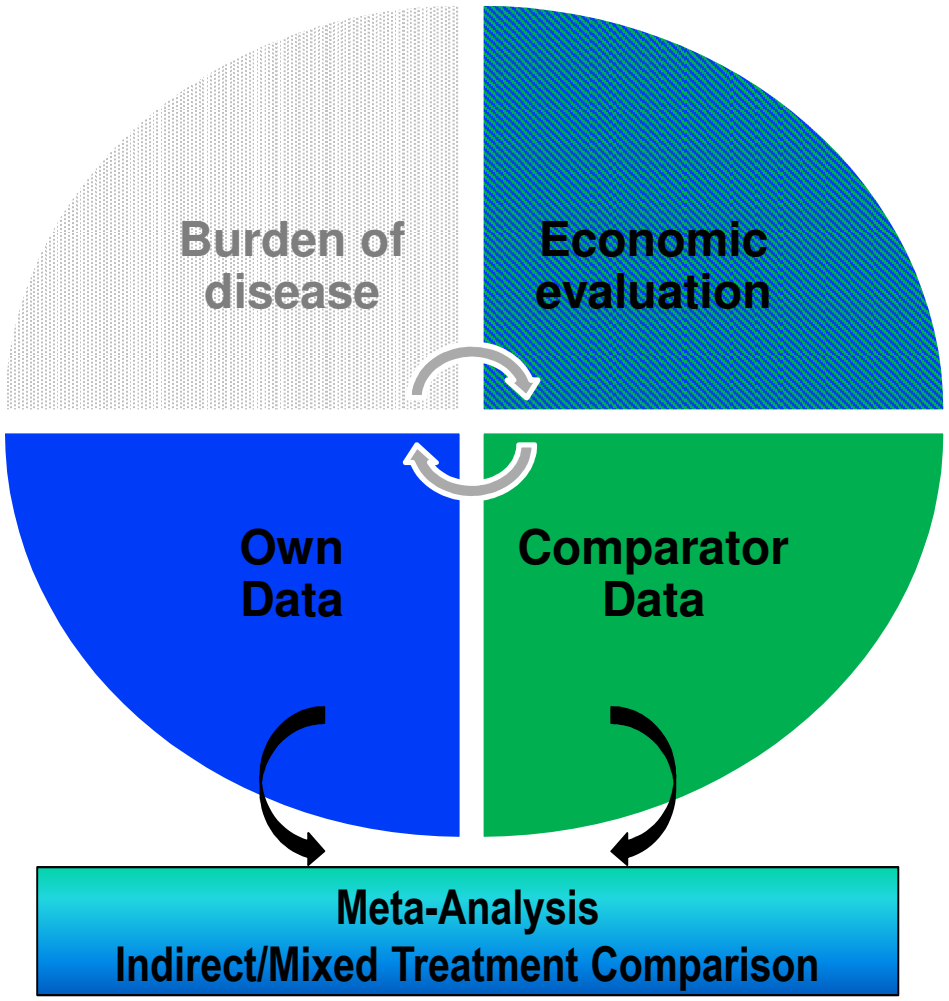
Market & Patient Access: different players/stakeholders with different views of & needs from a therapy.

Market & Patient Access and with it HTA work does not happen only at launch, it definitely continues after launch. And like regulatory requirements influence the earlier phases of drug development, so does HTA.

So, where does the statisticians come into play? EVERYWHERE!

Only the combination of all the above skills/strengths enables us as statisticians to provide solutions for the requirements and needs in this complex & ever changing environment.

HTA Dossier



In general, these are the main parts of an HTA or reimbursement dossier as it needs to be submitted in an European country and in other countries, e.g. Australia and Canada.

What are the skills & strengths that statisticians can bring to the different parts of an HTA dossier?

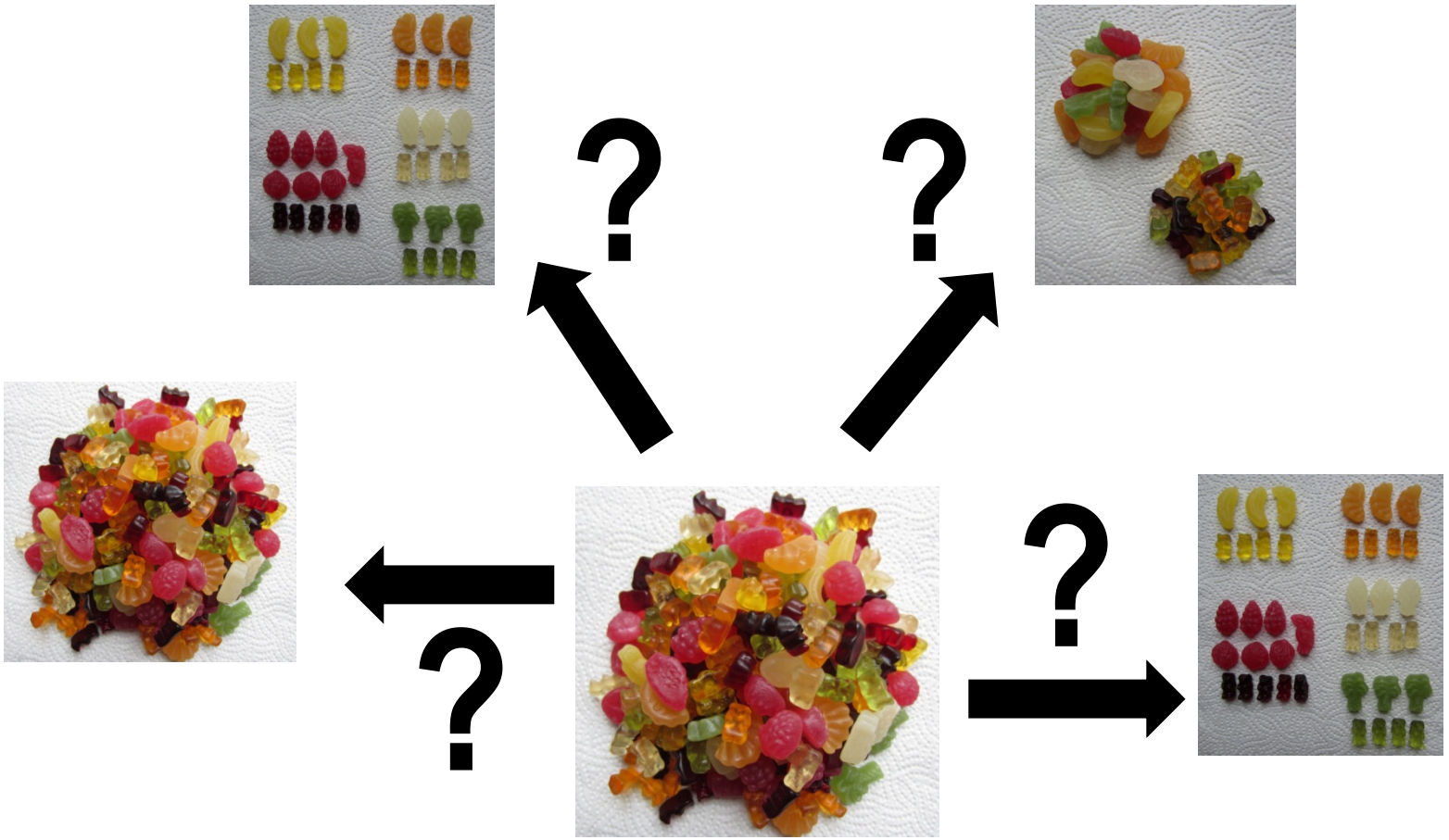
Own Data

Understanding Data is one of the core competencies of statisticians.

Keywords here are e.g.

- Variability
- Heterogeneity
- Prognostic factors
- Patient subgroups

Own Data



Own Data

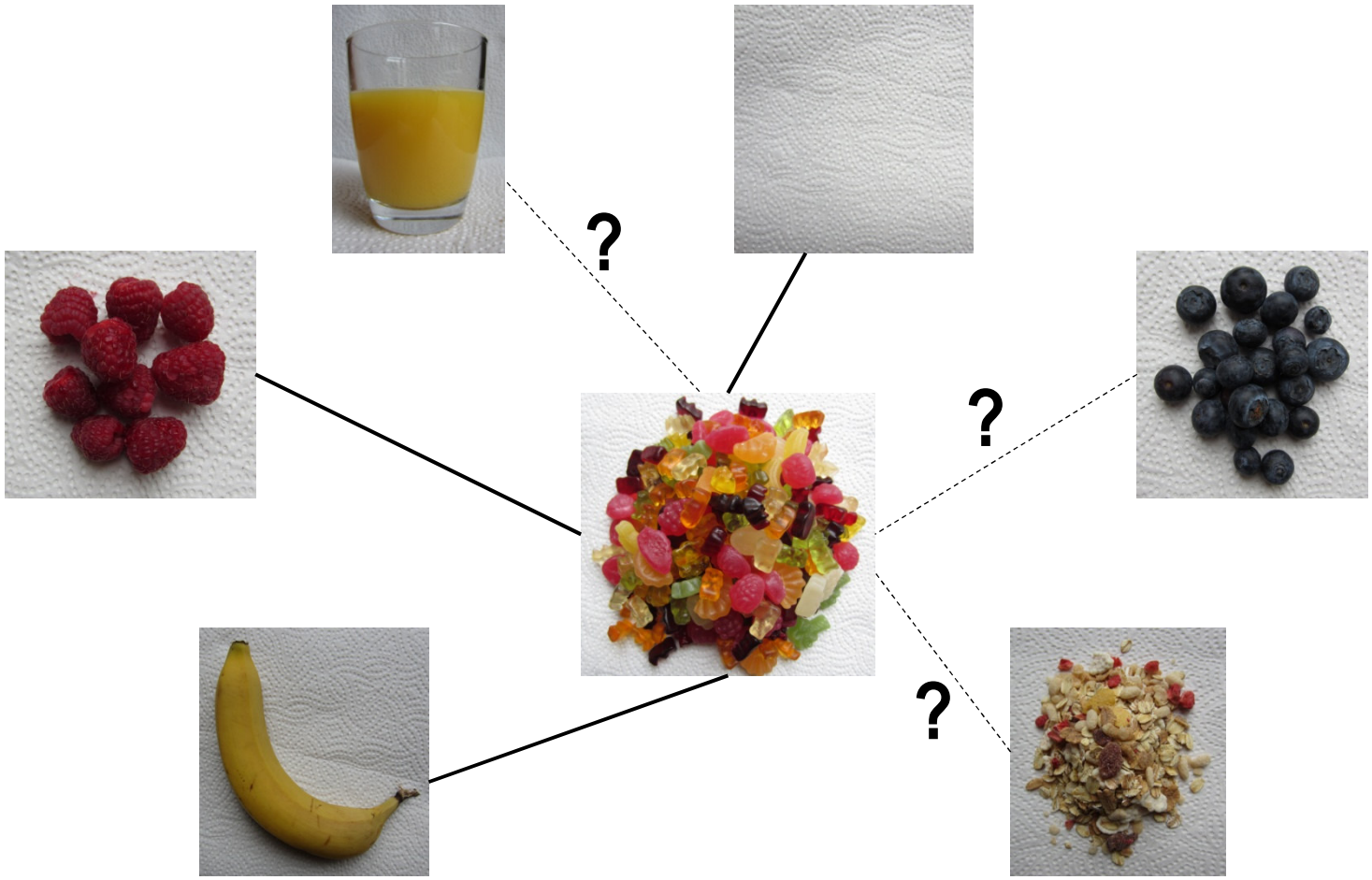
One of the key strengths of statisticians is understanding the data, being able to find inherent patterns, to investigate prognostic factors.
Another key strength is the knowledge of appropriate statistical methods, not only with regards to analyzing data, but also with respect to the designing of studies and investigating relevant endpoints

The different players in the HTA area (regulators, payers, prescribers, patients) have different questions and needs.
Hence, equally important to be able to understand data during the analysis, is the ability to set up clinical trials and other types of studies that enable us to address these different questions.

Own Data - Summary

- **Understand the different needs** of regulators, payers and patients
- **Translate these** into
  - optimized **study designs** and **analyses**
  - with **relevant endpoints**
  - enabling **maximal amount** of **relevant information**
- **Draw correct conclusions, provide interpretation**
- **Communicate** these to the various audiences
- **Anticipate** future needs

Comparator (Data)



Comparator (Data)

Again, the different needs and requirements of e.g. regulators and payers have to be taken into account.

Regulatory: Reflect standard of care and be aligned with clinical and regulatory guidelines; placebo controlled trials may be sufficient

Payers: Reflect standard of care in local clinical practice, want head to head active controlled trials.

Furthermore, there might be differences across payers/markets with regards to comparators they find appropriate.

Keywords: off-label, in-label, definition of standard of care

Comparator (Data) – Direct & indirect comparisons (I/II)

- Systematic literature review
  - important first step, needs time and cross-functional input,
  - make sure that the package of evidence is comprehensive (ie includes the relevant comparators) and follows the different requirements
- Analysis – theoretical aspects
  - respect/check key assumptions (Exchangeability, Homogeneity, Similarity, Consistency)
  - Strategy to find/defend optimal choice of analysis method
- Analysis – practical aspects
  - Critically assess the data (Clinical and statistical sources of heterogeneity), Investigate heterogeneity and inconsistent treatment effects, Conduct meta-regression analyses to explore important prognostic variables including (extensive) sensitivity analyses, Present results and provide interpretation, Describe extent of heterogeneity, Describe limitations and potential biases

Comparator (Data) – Direct & indirect comparisons (II/II)

- Communication
  - An IC/NMA is not an easy task to do with lots of inherent difficult topics. The communication of those topics, the assumptions taken, the results to a (in most cases) non-statistician audience is a challenge in itself.
- Future needs

  What might be the future needs?
  E.g.
  - Relative efficacy -> relative effectiveness
  - Combination of randomized and observational data
  - Combination of individual patient-level data and summary data
  - Impact of the EU Transparency initiative

Economic evaluation (I/II)

- Cost data, e.g.
  - understanding their structure and distribution (definitely not symmetrical)
  - understanding the needs from payers (mean, not median)
  - handle cost data with a lot of zeros (2-stage models)
  - handle cost data in the event of censoring
- Economic models - Modeling & Simulation, e.g.
  - Markov models
  - Discrete event simulation
  - Budget impact models

Economic evaluation (II/II)

- Input data to inform a model, e.g.
  - Clinical Trials (extrapolation of survival data, modeling of survival data, Resource Use, Quality of Life (QoL) & Other Outcomes)
  - Observational Studies (Compliance, Chart Reviews, QoL, Treatment Satisfaction)
  - Literature Reviews (Epidemiology, Resource Use, Unit Costs, Treatment Patterns)
- Probabilistic models
  - understanding distributions and the variance-covariance structure of input data
- Further use of economic models, e.g.
  - Using early health economic models to support drug development decisions

Bringing all aspects together: The „Cake“ Challenge (I/II)

This recipe is much too complicated. We would prefer a simpler cake…

This cake is too expensive – we can only allow this for patients allergic to apples…

We might choose this cake, but we first need to compare it with our own cakes…

This is dark chocolate! Is this safe enough for our patients?
We need more local data…

This cake looks local, but it was not baked according to our preferred recipe.
We don‘t like it…

Bringing all aspects together: The „Cake“ Challenge (II/II)

In summary, there will never be a „cake“ that satisfies the needs of Regulatory (EMA, FDA) and all local reimbursement agencies.
The best we can do here is to optimize it so that most of the needs (or the most important ones) are fullfilled, and at the same time stay consistent & scientifically sound;
In this context it is of extreme importance to be clear on what we do and what we don‘t do and the corresponding consequences (for everyone!).

Examples of challenges in the above figure, not necessarily specific or unique for a single country:

- trend to slicing to save cost
- safety questions, need for local real world data
- questioning study designs and variables used (-> surrogate parameters)
- need to go „down“ to regions within a country for further negotiations
- More complex vs simpler analysis approaches

Summary

- HTA has to be considered over the whole lifecycle of a product
- Regulators, payers and patients have different needs & requirements
- Statistical topics in HTA are manifold
- Lots of opportunities (& needs!) for technical and strategic input & influence
- Highly cross-functional work in a constantly changing environment
- Learn and adapt as you go

References & Links (I/II)

- Hans-Georg Eichler, Brigitte Bloechl-Daum, Eric Abadie, David Barnett, Franz König and Steven Pearson. **Relative efficacy of drugs: an emerging issue between regulatory agencies and third-party payers** NATure revIeWS | Drug Discovery; vOluMe 9 | AprIl 2010 | 277-291 www.nature.com/nrd/journal/v9/n4/pdf/nrd3079.pdf
- **HTA Special Interest Group** (EFSPI/PSI) www.psiweb.org/index.php?p=resources&fid=871 (HTA handbook for statisticians, publications, etc.)
- **Benefit-Risk Special Interest Group** (EFSPI) www.psiweb.org/index.php?p=resources&fid=1449
- International Society of Pharmacoeconomics and Outcomes Research (**ISPOR**)
  www. ispor.org
  ISPOR Special Interest Groups: www.ispor.org/sigs/sigsindex.asp
  ISPOR Task Forces: www.ispor.org/taskForces/TFindex.asp
  ISPOR Good Practices: www.ispor.org/workpaper/practices_index.asp

References & Links (II/II)

- **EFPIA** – A Comparative Analysis of the Role and Impact of Health Technology Assessment:
  http://www.efpia.eu/documents/21/100/A-comparative-analysis-of-the-role-and-impact-of-Health-Technology-Assessment
- **EMA Transparency Initiative**:
  www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000556.jsp&mid=WC0b01ac0580614159
- **IMI** Innovative Medicines Initiative: www.imi.europa.eu
- **EUnetHTA**: www.eunethta.eu
- **NICE Decision Support Unit** & Technical Support Documents : http://www.nicedsu.org.uk/
- **HTAi** (Health Technology Assessment International): www.htai.org
- **iHEA** (International Health Economics Association): www.healtheconomics.org