# Structured Expert Elicitation in Drug Development

Roel Straetemans, PhD
Distinguished Scientist, Statistical Modeling & Methodology (SMM)
June 9th, 2025 – PSI 2025 Annual Conference

Johnson&Johnson

# Disclaimer

"The opinions expressed in this presentation and on the following slides are solely those of the presenter and not necessarily those of Johnson & Johnson. Johnson & Johnson does not guarantee the accuracy or reliability of the information provided herein."

# Acknowledgements

Tobias Mielke, PhD (QS Consulting, J&J)

External authors on published papers of SEE in clinical development

# Overview

1. Why Structured Expert Elicitation in Clinical Development

2. Application examples of Prior Elicitation within clinical development
   - At J&J – SHELF
   - External
   - One case example

3. Conclusions

# The need for elicitation

Mt Everest Challenge in Scientific Leadership Training

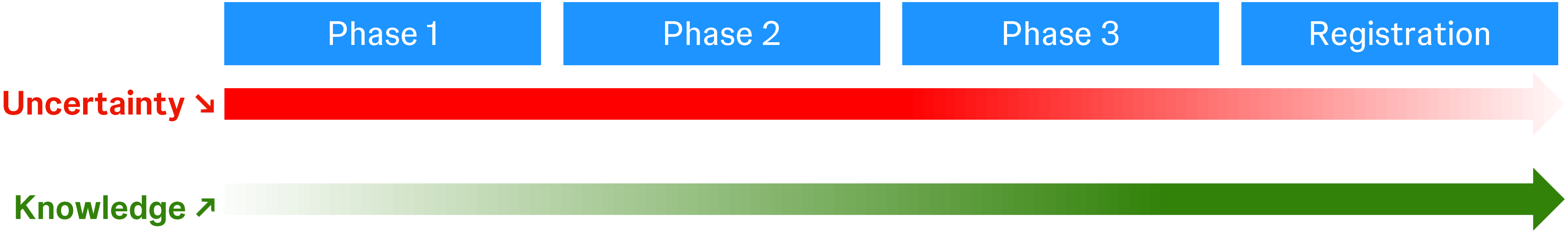
- We need to climb the mountain as a team
- Everyone gets some data.
- But everyone gets different data or might interpret data differently.

We have all biased perspectives.
Others **don't know** what we know.

Lack of this understanding results in failure.

# Why SEE in Clinical Development

- Clinical Development is accompanied with uncertainty and knowledge gaps




- High investments based on assumptions with large degree of uncertainty.
- SEE quantifies uncertainty and helps guiding study design and decision making

***For statisticians:** Not SEE or data – but SEE and data*

# SEE at J&J

- June 2022: an Expert Elicitation Workstream was formed

- Goal was to implement a framework that allows to:
  - Improve (formal) quantification of (un)certainty on quantities of interest using expert insights
  - Focus on addressing clearly defined research problems
  - Identify and bridge knowledge gaps
  - Optimize designs & Guide Decision Making

- SHELF process was chosen (more next slide) as basis for the framework

- Sub workstreams formed for milestones in the elicitation process

- End of 2022 the formal SEE process was implemented

# The Sheffield Elicitation Framework (SHELF)

Oakley J. E. and O'Hagan, A. (2016). SHELF: the Sheffield Elicitation Framework (version 3.0). School of Mathematics and Statistics, University of Sheffield, UK. (http://tonyohagan.co.uk/shelf)

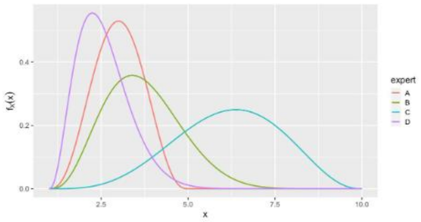
https://shelf.sites.sheffield.ac.uk/

University of Sheffield | Sheffield Elicitation Framework

Home | Download SHELF | E-learning course | Software | Survival extrapolation | Reading list

## The Sheffield Elicitation Framework (SHELF)

SHELF is a package of documents, templates and software to carry out elicitation of probability distributions for uncertain quantities from a group of experts. Elicitation is increasingly important for quantifying expert knowledge in situations where hard data are sparse. This is often the context in which difficult policy decisions are made.




It is generally important to elicit from a group of experts, rather than a single expert, in order to synthesise the range of knowledge and opinions of the expert community. However, SHELF may be used for a single expert with only trivial modification.

Despite this growing role for elicitation, there has been little in the way of training and support available to those who wish to conduct elicitations. SHELF is a response to this shortage. By reading and carefully following the SHELF documentation, it should be possible for an untrained facilitator to carry out competent elicitation.

**Jeremy Oakley**

Professor of Statistics, the University of Sheffield
j.oakley@sheffield.ac.uk

University staff profile | Google Scholar

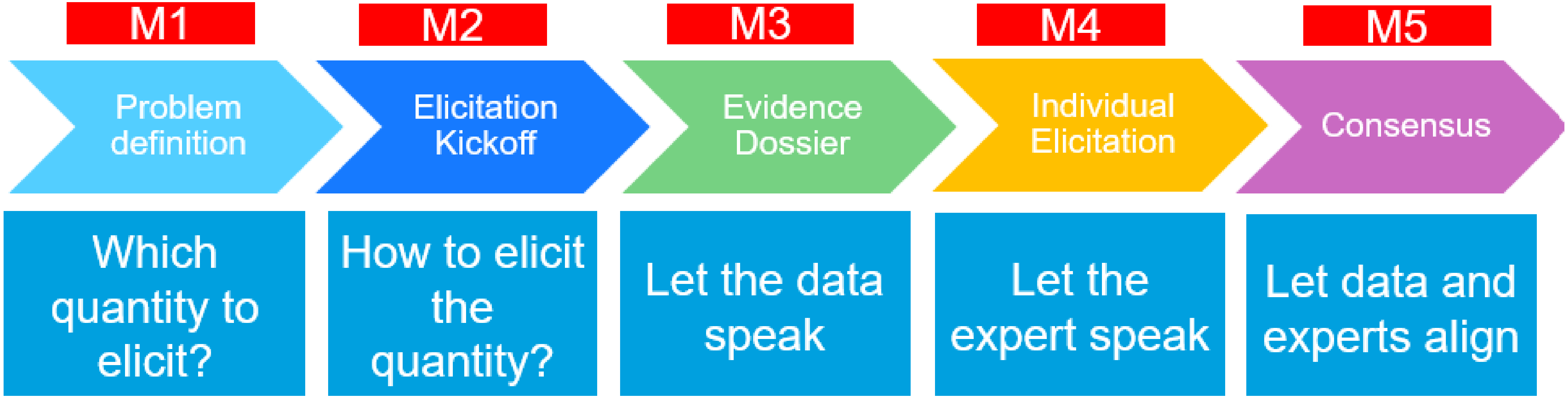
**Tony O'Hagan**

Emeritus Professor, the University of Sheffield
a.ohagan@sheffield.ac.uk

Google Scholar

# The Five Milestones in the Elicitation Process*

*: Dallow et al, 2018




- Sub workstreams:
  - Evidence Dossier
  - Elicitation Form
  - Training

# Elicitation Projects at J&J

- QoI:
  - Treatment Effect ➔ Assessing OC
  - Subgroup effects → Optimization of multiplicity strategy
  - Prior Distributions for Dose Response curve parameters ➔ Dose Selection Ph2b
  - Decision Rule for IA in FiH SAD study
  - Determination of clinically relevant effect for Go/No-Go

- Positive Experiences / Wins:
  - Consensus Meeting ➔ Gain in insight
  - Quantification and documentation of heterogeneity ➔ impact on Design & Decision Making

- Challenges:
  - Time: preparation – timeframe of project
  - Expert understanding of the statistical nature of the process
  - Technical aspects

# Elicitation Projects at J&J

- QoI:
  - Treatment Effect → Assessing OC
  - Subgroup effects → Optimization of multiplicity strategy
  - Prior Distributions for Dose Response curve parameters → Dose Selection Ph2b
  - Decision Rule for IA in FiH SAD study
  - Determinat

- Positive Experie
  - Consensus
  - Quantificat … Making

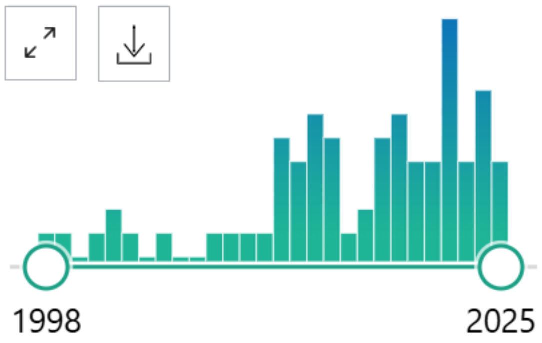
- Challenges:
  - Time: preparation – timeframe of project
  - Expert understanding of the statistical nature of the process
  - Technical aspects

Largest value for stakeholders:
**Deepened understanding of assumptions and their implications, due to scientific discussions (not immediately coupled to study design!)**

Prior distribution just a side product (and that’s ok!)

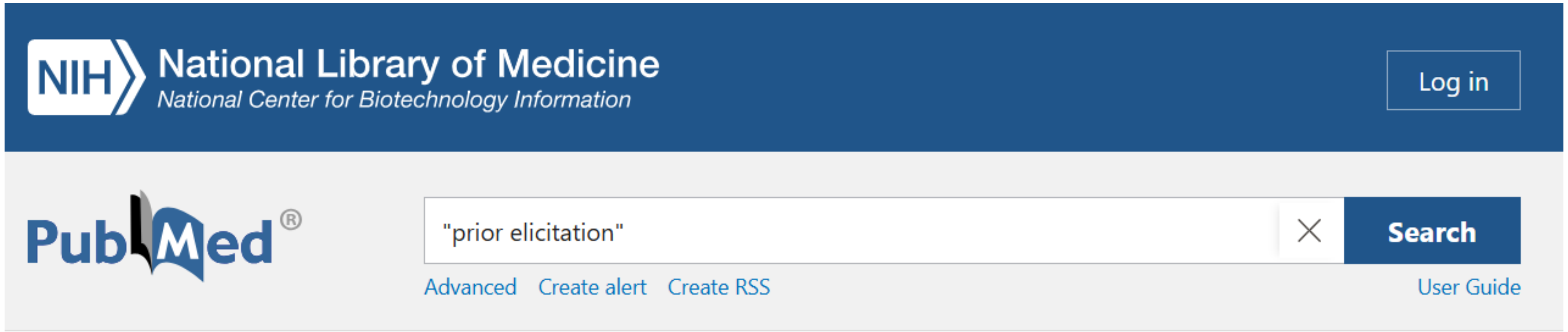
# Published Case Studies

RESULTS BY YEAR




| Year | Count | Clinical Trials |
|---|---|---|
| 2025 | 4 | 3 |
| 2024 | 7 | 5 |
| 2023 | 4 | 1 |
| 2022 | 10 | 6 |
| 2021 | 4 | 2 |
| 2020 | 4 | 2 |
| 2019 | 6 | 4 |
| 2018 | 5 | 1 |
| 2017 | 2 | 0 |
| 2016 | 1 | 1 |
| 2015 | 5 | 1 |
| 2014 | 6 | 3 |
| 2013 | 4 | 2 |
| 2012 | 5 | 4 |
| 2011 | 1 | 1 |
| 2010 | 1 | 0 |
| 2009 | 1 | 1 |
| 2008 | 1 | 0 |
| 2005 | 1 | 0 |
| 2003 | 1 | 0 |
| 2002 | 2 | 1 |
| 2001 | 1 | 1 |
| 1999 | 1 | 1 |
| 1998 | 1 | 1 |

Search query: "prior elicitation"




- Total of **65**


International Journal of Environmental Research and Public Health

MDPI

*Review*

**Prior Elicitation for Use in Clinical Trial Design and Analysis: A Literature Review**

**Danila Azzolina [1,2], Paola Berchialla [3], Dario Gregori [1] and Ileana Baldi [1,*]**

**Citation:** Azzolina, D.; Berchialla, P.; Gregori, D.; Baldi, I. Prior Elicitation for Use in Clinical Trial Design and Analysis: A Literature Review. *Int. J. Environ. Res. Public Health* **2021**, *18*, 1833. https://doi.org/10.3390/ijerph18041833

- "A total of 42 articles pertain to clinical trial and the majority of them (81%) reports parametric techniques as elicitation method."

- Total involving CT ≥ **57**

**Not widespread**

J&J

# Published Case Studies

International Journal of *Environmental Research and Public Health*

MDPI

*Review*

## Prior Elicitation for Use in Clinical Trial Design and Analysis: A Literature Review

**Danila Azzolina [1,2], Paola Berchialla [3], Dario Gregori [1] and Ileana Baldi [1,*]**

**Citation:** Azzolina, D.; Berchialla, P.; Gregori, D.; Baldi, I. Prior Elicitation for Use in Clinical Trial Design and Analysis: A Literature Review. *Int. J. Environ. Res. Public Health* **2021**, *18*, 1833. https://doi.org/10.3390/ijerph18041833

Received: 21 July 2017 | Revised: 26 January 2018 | Accepted: 8 February 2018

DOI: 10.1002/pst.1854

**SPECIAL ISSUE PAPER**

WILEY

## Better decision making in drug development through adoption of formal prior elicitation

Nigel Dallow[1] | Nicky Best[1] | Timothy H Montague[2]

# Published Case Studies

**QoI**

Treatment Effect – Study Design:
- SS – Assurance
- Rare disease
- New indication
- Multi-stage trials
- Clinical Relevance

Treatment Effect – Analysis:
- Bayesian (borrowing) analysis

Dose Response
- categorical -> model
- Parameters:
  - toxicity
  - efficacy

Ph1-3

**Gains**

Formal documentation

improved study designs
- Patient population
- Co-rescue medication
- Multiplicity and adaptations

**Strong scientific driven discussion**
- Collective understanding
- Allows identification of gaps
- Critical assessment of “evidence /assumptions”
- Most appreciated by experts

**Challenges**

Technical/statistical
- Experts - statistical quantities
- Bias due to aspiration
- Models/Software
- Elicitation AND Data

Pragmatic
- When/worthwhile to do
- Choice of experts
- Changing project plans/timing
- Reaching consensus
- Evidence Dossier (time – bias)

# Published Case Studies

**QoI**

Treatment Effect – Study Design:
- SS – Assurance
- Rare disease
- New indication
- Multi-stage trials
- Clinical Relevance

Treatment Effect – Analysis:
- Bayesian (borrowing) analysis

Dose Response
- categorical -> model
- Parameters:
  - toxicity
  - efficacy

Ph1-3

**Gains**

Formal documentation

improved study designs
- Patient population
- Co-rescue medication
- Multiplicity and adaptations

**Strong scientific driven discussion**
- Collective understanding
- Allows identification of gaps
- Critical assessment of "evidence /assumptions"
- Most appreciated by experts

**Challenges**

Technical/statistical
- Experts - statistical quantities
- Bias due to aspiration
- Models/Software
- Elicitation AND Data

Pragmatic
- When/worthwhile to do
- Choice of experts
- Changing project plans/timing
- Reaching consensus
- Evidence Dossier (time – bias)

# Published Case Studies

QoI

Treatment Effect – Study Design:
- SS – Assurance
- Rare disease
- New indication
- Multi-stage trials
- Clinical Relevance

Treatment Effect – Analysis:
- Bayesian (borrowing) analysis

Dose Response
- categorical -> model
- Parameters:
  - toxicity
  - efficacy

Ph1-3

Gains

Formal documentation

improved study designs
- Patient population
- Co-rescue medication
- Multiplicity and adaptations

**Strong scientific driven discussion**
- Collective understanding
- Allows identification of gaps
- Critical assessment of “evidence /assumptions”
- Most appreciated by experts

Challenges

Technical/statistical
- Experts - statistical quantities
- Bias due to aspiration
- Models/Software
- Elicitation AND Data

Pragmatic
- When/worthwhile to do
- Choice of experts
- Changing project plans/timing
- Reaching consensus
- Evidence Dossier (time – bias)

# Published Case Studies

QoI | Gains | Challenges

Treatment Effect – Study Design:
- SS – Assurance
- Rare disease
- New indication
- Multi-stage trials
- Clinical Relevance

Treatment Effect – Analysis:
- Bayesian (borrowing) analysis

Dose Response
- categorical -> model
- Parameters:
  - toxicity
  - efficacy

Ph1-3

Formal documentation

improved study designs
- Patient population
- Co-rescue medication
- Multiplicity and adaptations

**Strong scientific driven discussion**
- Collective understanding
- Allows identification of gaps
- Critical assessment of “evidence /assumptions”
- Most appreciated by experts

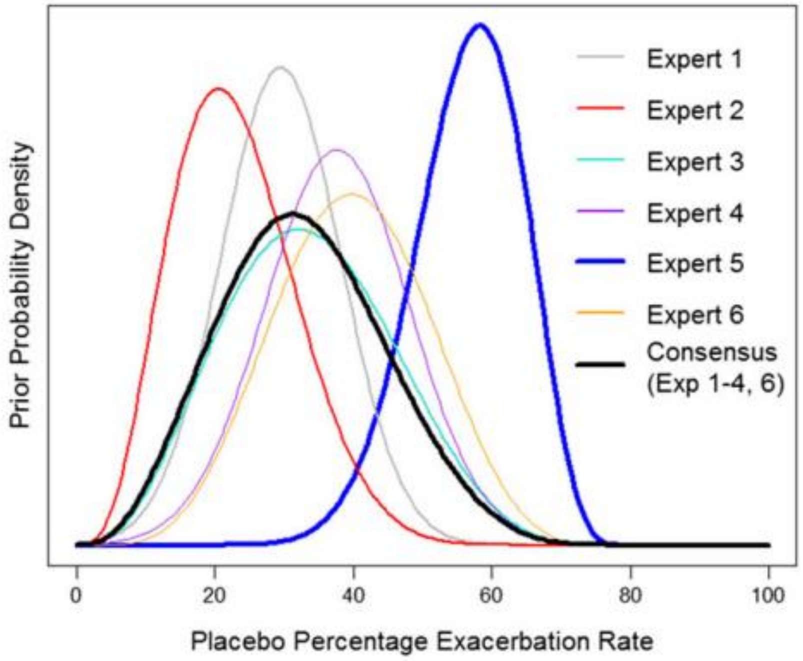
Technical/statistical
- Experts - statistical quantities
- Bias due to aspiration
- Models/Software
- Elicitation AND Data

Pragmatic
- When/worthwhile to do
- Choice of experts
- Changing project plans/timing
- Reaching consensus
- Evidence Dossier (time – bias)

# Published Case Studies – Example*

*: Dallow et al, 2017

- Case Study 2: rare diseas  - Ph3 – Internal & External experts
- QoI:  Proportions experiencing an exacerbation on Placebo and on Active Treatment
- Two experts very different opinion




- During Consensus origin of heterogeneity identified ➔ adaptation of inclusion/exclusion criteria
- “Failed” consensus – Very important insight into trial design

# Conclusion

- SEE does not appear to be consistently integrated in Clinical Development

- Gains :
  - ❑ Formal quantification of uncertainty and knowledge gaps
  - ❑ Thorough Scientific discussion
  - ❑ Increased study design & decision making

- Challenges:
  - ❑ Timing and time
  - ❑ Convince other stakeholders not familiar with the process to invest time/effort (including stats!)
  - ❑ Broader view on the challenges: see Mikkola et al*

- Recommendations:
  - ❑ Need for experienced facilitators – very early in start of project
  - ❑ Invest in training & tools
  - ❑ Broader set of recommendations: see Mikkola et al*



*:Mikkola et al 2024

# References


- Oakley J. E. and O'Hagan, A. (2016). SHELF: the Sheffield Elicitation Framework (version 3.0). School of Mathematics and Statistics, University of Sheffield, UK. (http://tonyohagan.co.uk/shelf)

- https://shelf.sites.sheffield.ac.uk/

- Dallow N, Best N, Montague TH. Better decision making in drug development through adoption of formal prior elicitation. Pharm Stat. 2018 Jul;17(4):301-316. doi: 10.1002/pst.1854. Epub 2018 Mar 30. PMID: 29603614.

- Azzolina D, Berchialla P, Gregori D, Baldi I. Prior Elicitation for Use in Clinical Trial Design and Analysis: A Literature Review. Int J Environ Res Public Health. 2021 Feb 13;18(4):1833. doi: 10.3390/ijerph18041833. PMID: 33668623; PMCID: PMC7917693.

- Mikkola P et al. Prior Knowledge Elicitation: The Past, Present and Future. Bayesian Analysis. 2024, 19(4),p1129-1161. DOI: 10.1214/23-BA1381