

Adelphi

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Patient-Centered
Outcomes

Patient Focused Drug Development: Hot Topics

PSI Conference 2024

Monday 17th June 2024

Rachael Lawrance

What does patient focused drug development mean to you as a statistician?

We are a new SIG and we want to help you!



Patient-Focused Drug Development

The purpose of the PFDD SIG is to connect

and share information about patient-focused drug development

[Find out more](#)

PFDD SIG – who we are



Rachael Lawrance



Konstantina Skaltsa



Devin Peipert



Antoine Regnault



Piper Fromy



Evgenyia Reshetnyak



Cara Arizmendi



Alexandra Lauer

Why did we form?

- > COAs/PROs are now commonly included in clinical trials but, historically, PRO endpoints, analysis, interpretation and ultimately their value in drug development has not always been maximised
- > In 2017 the FDA introduced legislation describing increased focus on patients, and is developing a series of patient focused drug development guidance documents (PFDD) – of which the draft guidance 4 (draft April 2023) is of most interest to us as statisticians working in clinical trials
- > FDA guidance, as well as EMA guidance and key publications (e.g. SISAQoL) are still draft or evolving – and there are **still many challenges** – and **many statistical aspects are still unclear about good practice**
- > We are all really passionate about sharing knowledge, leading on best practice and excited about advancing statistical methodology in this area

PFDD SIG –purpose & objectives



The purpose of the PFDD SIG is to connect statisticians in pharmaceutical industry roles who work on progressing the inclusion of patient-reported outcomes (PROs) and clinical outcome assessments (COAs) across all phases of drug development process to share their knowledge and also lead statistical thinking and methods to solve common statistical challenges of use of COAs in drug development.

PFDD SIG –purpose & objectives



- > **Advance statistical methodology** for specific PFDD topics (topics to be shared later in this talk)
- > **Education for industry statistician & knowledge sharing:** sharing good practices and standards for PRO and COA based endpoints and are more widely disseminated to the PSI/EFSPI community and adopted in drug development across all therapy areas.
- > Interact with regulators, payers, patients and the broader clinical community to obtain a better understanding of their requirements relating to PFDD
- > Collaboratively partner with other SIGs in this area, either within PSI/EFSPI or in other groups, e.g., PSI/EFSPI HTA SIG, PSI/EFSPI Regulatory SIG, PSI/EFSPI Biomarkers SIG, ISOQoL Statistics SIG, SISAQoL etc.

Question 1

- > How familiar are you with FDA Guidance on patient focused drug development

Question 2

- > How useful is current guidance to you? Which statement fits you best?

FDA Guidance documents



ICH E9(R1) –estimands

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2021
ICH

Revision 1



PFDD Guidance 4 – still draft – lots of comments

Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints for Regulatory Decision-Making

APRIL 2023

Download the Draft Guidance Document

Read the Federal Register Notice

Draft



Submit
Docum
Assesse

PROs for symptomatic AEs

Project Optimus

Reforming the dose optimization and dose selection paradigm in oncology

Oncology: FDA/EMA/SISAQoL



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GUIDANCE DOCUMENT

Core Patient-Reported Outcomes in Cancer Clinical Trials

Draft Guidance for Industry

JUNE 2021

[Download the Draft Guidance Document](#)

[Read the Federal Register Notice](#)

Draft

FDA June 2021 (well used although draft)



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GUIDANCE DOCUMENT

Submitting Patient-Reported Outcome Data in Cancer Clinical Trials

NOVEMBER 2023

[Download the Final Guidance Document](#)

Final

Level 2 Guidance

Oncology – dataset structure, example completion rate tables/figures



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA 2016

1 April 2016

EMA/CHMP/292464/2014

Committee for Medicinal Products for Human Use (CHMP)

Appendix 2 to the guideline on the evaluation of anticancer medicinal products in man

The use of patient-reported outcome (PRO) measures in oncology studies

International standards for the analysis of quality-of-life and patient-reported outcome endpoints in cancer randomised controlled trials: recommendations of the SISAQOL Consortium



SISAQoL 2020

Corneel Coens*, Madeline Pe*, Amylou C Dueck, Jeff Sloan, Ethan Basch, Melanie Calvert, Alicyn Campbell, Charles Cleeland, Kim Cocks, Laurence Collette, Nancy Devlin, Lien Dorme, Hans-Henning Flechtner, Carolyn Gotay, Ingolf Griebsch, Mogens Groenvold, Madeleine King, Paul Kluetz, Michael Koller, Daniel C Malone, Francesca Martinelli, Sandra A Mitchell, Jammbe Z Musoro, Daniel O'Connor, Kathy Oliver, Elisabeth Piant-Louis, Martine Piccart, Chantal Quinten, Jaap C Reijneveld, Christoph Schürmann, Ashley Wilder Smith, Katherine M Soltys, Martin J B Taphoorn, Galina Velikova, Andrew Bottomley; for the Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints Data Consortium

Patient-reported outcomes (PROs), such as symptoms, function, and other health-related quality-of-life aspects, are increasingly evaluated in cancer randomised controlled trials (RCTs) to provide information about treatment risks, benefits, and tolerability. However, expert opinion and critical review of the literature showed no consensus on optimal methods of PRO analysis in cancer RCTs, hindering interpretation of results. The Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints Data Consortium was formed to establish PRO analysis recommendations. Four issues were prioritised: developing a taxonomy of research objectives that can be matched with appropriate statistical methods, identifying appropriate statistical methods for PRO analysis, standardising statistical terminology related to missing data, and determining appropriate ways to manage missing data. This Policy Review presents recommendations for PRO analysis developed through critical literature reviews and a structured collaborative process with diverse international stakeholders, which provides a foundation for endorsement; ongoing developments of these recommendations are also discussed.

Lancet Oncol 2020; 21: e83-96
*Joint first authors
European Organisation for Research and Treatment of Cancer, Brussels, Belgium
(C Coens MSc, M Pe PhD, L Collette PhD, L Dorme MSc, F Martinelli MSc, J Z Musoro PhD, A Bottomley PhD); Alliance Statistics and Data Center, Mayo Clinic, Scottsdale, AZ, USA (A C Dueck PhD); Alliance Statistics and Data Center, Mayo Clinic, Scottsdale, AZ, USA

PFDD Guidance 4

- Draft April 2023 – still under review!
- > COA Endpoint Considerations
 - Endpoint of interest
 - Estimation and missing data
- > Evaluating the Meaningfulness of Treatment Benefit
 - Interpretability of COA scores
 - Meaningful Score Differences & Meaningful Score Regions

Question 3: Knowledge sharing

- > Would a compiled resource area for statisticians relating to PFDD guidance's and key publications be useful to you?

Methods topics

- > Plenty of statistical challenges for us to collaborate on and share ideas
- > Any experts welcome to join us!

Question 4: Methods topics

> Topics/ideas – help us prioritise – what *is most useful to you in immediate future?*

- Pain estimands and estimators
- Use of PROs in early phase studies and their role in dose finding/optimization – practical stats points
- Methods for handling death – practical guidance
- Estimands and estimators for PROs assessing tolerability and safety
- Estimators: MMRM and plausibility of MAR
- Imputation methods and missing data – specific to PRO data in oncology studies - what is actually practical
- Diary data – endpoints
- Practical advice on presentation of MSRs (meaningful score regions as per FDA PFDD draft guidance 4)
- Use of PRO-CTCAE
- Other (please come and talk to us in person after the session!)

Topic Idea: Any experts interested to brainstorm on this?



**Patient-Focused Drug
Development**

- > PFDD SIG Methods Topic: – Response Shift Detection with Structural Equation Models (SEMs)
- **Promote utilization of SEMs in biostatistical research focused on questionnaire data.**
- Showcase ability to detect response shifts by application in one or several clinical studies with PRO data.
- **Discuss pros and cons of SEMs in the context of inferential statistics of clinical trial data.**



**Patient-Focused Drug
Development**

- > Thank you – please come and talk to us after the session!