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ISPOR Clinical Outcome Assessment Special Interest Group: New Frontiers – Valuing COA Data And Guiding Principles For RWE

Monday, 4 November 2019: 12:30 – 13:45

AGENDA

- Introduction of COA SIG to new members (Katja Rudell)
- Update on Membership Engagement Project COA in RWE (Ana Maria Rodriguez and Angela Rylands)
  - Survey Development on COA in RWE and Results
  - 1st Virtual Roundtable on COA in RWE
- Update on Key Project 1 – Better Communication of COA language between different stakeholders (Bryan Bennett and Lynda Doward)
  - Update Book of Terms
  - Survey on Communication of COA – Launch on November 2nd

Welcome to the first official update of the COA SIG in 2019

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Milestones

- First Interest established in 2017
- First Business plan presented to ISPOR in 2018
- 2 Engagement meetings
  - Vote on Projects
- Business plan refined and approved in March 2019
- Kick of at ISPOR NOLA 2019
- First results at this meeting
- Membership: 202 Members
- 18 Members participate in Member Engagement Project – COA in RWE
- 20 Members Participate in Key Project 1 – Communication of COA

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Who We are

Chair
Katja
Rudell

ME Co-chair
Angela
Rylands

ME Co-Chair
Ana Maria
Rodriguez

KP Co Chair
Bryan
Bennett

KP Co Chair
Lynda
Doward

ISPOR Liaison
John
Guerino

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MEMBER ENGAGEMENT PROJECT

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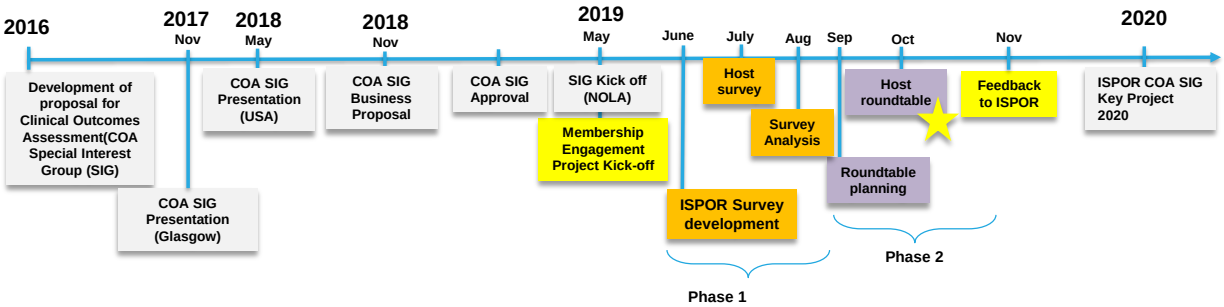
Feedback from ISPOR survey and a virtual roundtable meeting to investigate approaches to standardizing clinical outcome assessments (COAs) for real world studies

Angela Rylands, CPsychol, PhD, Kyowa Kirin

Ana Maria Rodriguez, PhD, MSc, Chartered PT IQVIA

Background to the virtual roundtable meeting – hosted 29th October 2019



Objective 1 to host a virtual roundtable meeting for industry colleagues to meet to discuss and ultimately agree upon how we should work together to develop guiding principles of COA in real world studies.

Objective 2 for outputs to input to finalising the next key project for 2020 and will help to shape the landscape of how COA data is collected robustly in real world studies.

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2019 Membership Engagement Workplan

SIG Member Engagement Project Plan	May/June
Development of survey and data platform preparation	June
Deployment of survey to gauge interest for virtual roundtable	
Survey data analysis and brief report	July
Preparation of virtual roundtable discussion points	August
Virtual roundtable invitations sent	
Conduct virtual roundtable	September
Data analysis	October
Results summary @ISPOR Europe 2019	November
Proposal for Key Project 2020	December

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Membership Engagement Work – The Team

Co-Chairs

- Angela Rylands, Senior International Outcomes Manager, Kyowa Kirin
- Ana Maria Rodriguez, Director, RWE Patient-Centered Endpoints, IQVIA

Working Group Contributors

- Laurie Batchelder, IQVIA
- Martha Bayliss, Optum
- Laurie Burke, LORA Group
- David Churchman, University of Oxford
- Helen Doll, Clinical Outcomes Solutions
- Coleen McHorney, Evidera
- Sara Nazha, McGill University
- HyeJin Park, Johnson & Johnson
- Vanessa Patel, Covance
- Jiat Ling Poon, Eli Lilly
- Ana Popielnicki, TransPerfect
- Justin Raymer, University of Oxford
- Tara Symonds, Clinical Outcomes Solutions
- Michelle Tarver, US Food & Drug Administration
- Robyn von Maltzahn, GSK
- Paul Williams, IQVIA

ISPOR · John Guerino, MHS, Manager, Scientific and Health Policy Initiatives

Chair of SIG · Katja Rudell, Director of Patient Centred Outcomes, Paraxel

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Survey topics

Topic 1: Identifying best practices for designing COAs for use in RW studies

- Identifying best practices for designing COAs for RW studies and designing RW studies where endpoints are measurable by COAs
- Best practices for analyzing COA data or results from RW studies

Topic 2: Operationalization of COA in RW studies

- Methods or standards adopted or adhered to for translation / cultural adaptations of COAs and bespoke surveys used in global RW studies
- Methods or standards adopted or adhered to for electronic migration /equivalence testing of COAs in RW
- How are missing COA data handled for RW studies

Topic 3: Regulatory Guidance surrounding COAs in RW studies

- How are decisions regarding COA documented for regulatory inspection?
- Availability and use of guidance documents (from FDA, EMA, other) to select endpoints measurable by COAs in RW studies

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Methods

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In the fall of 2019, the newly formed ISPOR Clinical Outcome Assessment Special Interest Group will be hosting a virtual roundtable meeting to examine ISPOR members' opinions on the key topics important for working together to develop guiding principles for the use of clinical outcome assessments (COAs) in real world (RW) studies .

As an ISPOR member, you are invited to take a 5-7 minute survey to provide input to the design of the upcoming virtual roundtable. The survey aims to identify key topics for the discussion of the upcoming virtual roundtable. Your input and perspective will shape the format and outputs of this roundtable meeting, as well as help to steer next year's key project for the ISPOR COA Special Interest Group which will aim to develop guiding principles for the use of COAs in RW studies.

Please complete the survey by **Friday, September 13th, 2019** and note that all responses are anonymous.

Click for the Survey

Thank you in advance for taking the time to share your insight and expertise. Your feedback is greatly appreciated. If you have any questions, please contact clinicaloutcomeSIG@ispor.org.

Sincerely,
The ISPOR Clinical Outcome Assessment Special Interest Group

- Participants received an email to complete 5-7 minute survey
- Asked about experience using or working with COA in RW
- Asked to indicate level of interest in topics and sub-topics for discussion at roundtable meeting
- Asked to indicate any areas of interest not covered by survey

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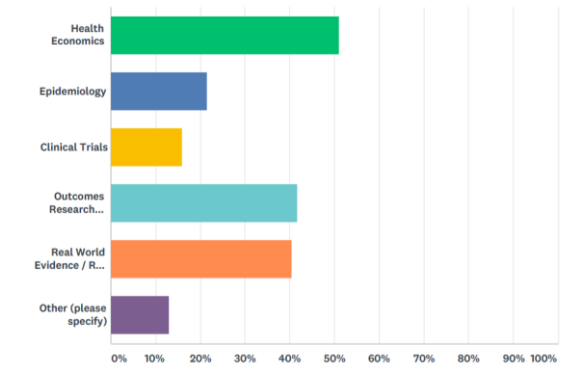
Survey Results - Demographics

Figure 1: Reported main field of work or expertise



Participants:

- N=368 ISPOR members
- Diverse mix of reported expertise in health economics (51%), epidemiology (22%), clinical trials (16%), outcomes research 42%, RWE (41%), other (13%)
- Over half coming from North America (51%) and just under half from Europe (43%) and less so from Asia (29%), Latin America (15%), Oceania (8%) and Africa (7%)

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Survey Results – Topic 1

Participants most interested in identifying *best practices for designing COAs* for use in RW Studies

Sub-Topic 1a: Identifying best practices for designing COAs for use in RW studies

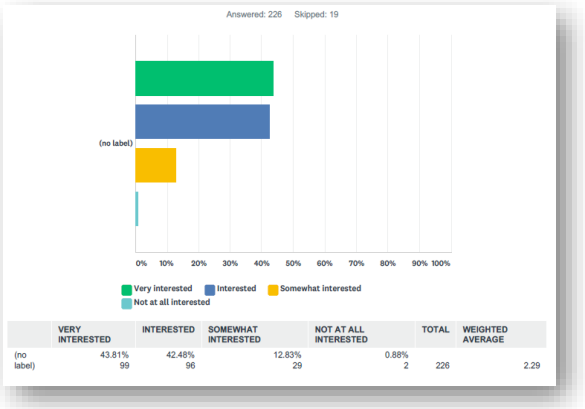
Very interested | Interested | Somewhat interested | Not at all interested

Sub-Topic 1b Identifying best practices for designing RW studies where endpoints are measurable by COAs (i.e. how to select the best COAs, developing bespoke survey questions, how to decide upon the frequency of data collection, how to minimize missing data etc.)

Very interested | Interested | Somewhat interested | Not at all interested

Sub-Topic 1c Discuss best practices for analyzing COA data or results from RW studies (e.g. analyses for meaningful interpretation of data, what constitutes the 'sensitivity to change' of a COA in RW setting, analyses for integration of COA data with data from other sources?)

Very interested | Interested | Somewhat interested | Not at all interested



	VERY INTERESTED	INTERESTED	SOMEWHAT INTERESTED	NOT AT ALL INTERESTED	TOTAL	WEIGHTED AVERAGE
(no label)	43.81% 99	42.48% 96	12.83% 29	0.88% 2	226	2.29

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Survey Results – Topic 1

Participants most interested in identifying *best practices for designing RW Studies* where endpoints are measurable by COAs

Sub-Topic 1a: Identifying best practices for designing COAs for use in RW studies

Very interested | Interested | Somewhat interested | Not at all interested

Sub-Topic 1b Identifying best practices for designing RW studies where endpoints are measurable by COAs (i.e. how to select the best COAs, developing bespoke survey questions, how to decide upon the frequency of data collection, how to minimize missing data etc.)

Very interested | Interested | Somewhat interested | Not at all interested

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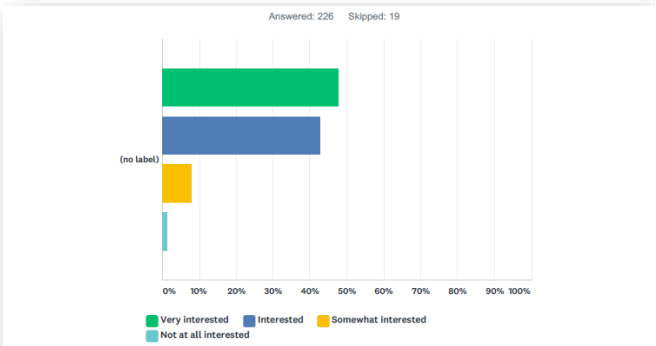
Very interested | Interested | Somewhat interested | Not at all interested



	VERY INTERESTED	INTERESTED	SOMEWHAT INTERESTED	NOT AT ALL INTERESTED	TOTAL	WEIGHTED AVERAGE
(no label)	47.79% 108	42.92% 97	7.96% 18	1.33% 3	226	2.37

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Survey Results – Topic 1

Participants most interested in discussing *best practices for analyzing COA data* or results from RW studies

Sub-Topic 1a: Identifying best practices for designing COAs for use in RW studies

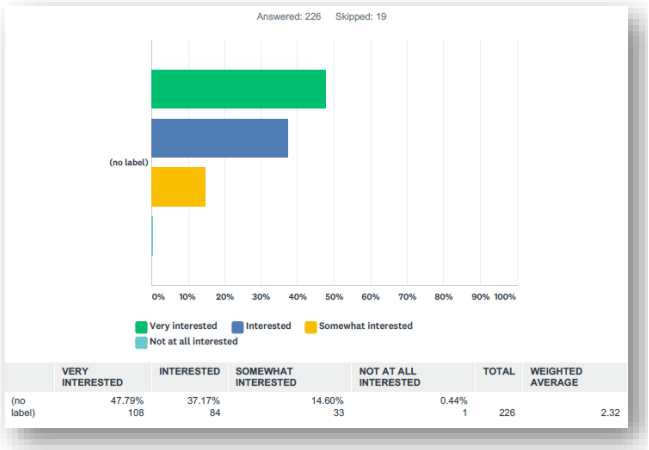
Very interested | Interested | Somewhat interested | Not at all interested

Sub-Topic 1b Identifying best practices for designing RW studies where endpoints are measurable by COAs (i.e. how to select the best COAs, developing bespoke survey questions, how to decide upon the frequency of data collection, how to minimize missing data etc.)

Very interested | Interested | Somewhat interested | Not at all interested

Sub-Topic 1c Discuss best practices for analyzing COA data or results from RW studies (e.g. analyses for meaningful interpretation of data, what constitutes the 'sensitivity to change' of a COA in RW setting, analyses for integration of COA data with data from other sources?)

Very interested | Interested | Somewhat interested | Not at all interested



	VERY INTERESTED	INTERESTED	SOMEWHAT INTERESTED	NOT AT ALL INTERESTED	TOTAL	WEIGHTED AVERAGE
(no label)	47.79% 108	37.17% 84	14.60% 33	0.44% 1	226	2.32

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Summary - Topic 1 – Participants demonstrated most interest in discussing further the sub-topics on design and analysis

- Identifying best practices for designing COAs for use in RW studies
- Discuss best practices for analyzing COA data or results from RW studies (e.g. analyses for meaningful interpretation of data, what constitutes the 'sensitivity to change' of a COA in RW setting, analyses for integration of COA data with data from other sources?)
- Identifying best practices for designing RW studies where endpoints are measurable by COAs (i.e. how to select the best COAs, developing bespoke survey questions, how to decide upon the frequency of data collection, how to minimize missing data etc.)

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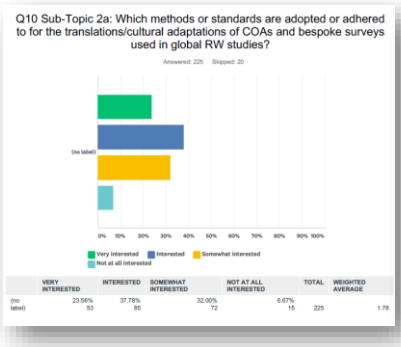
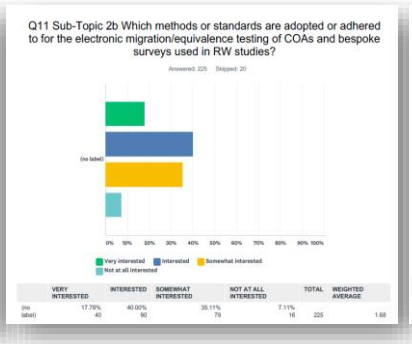
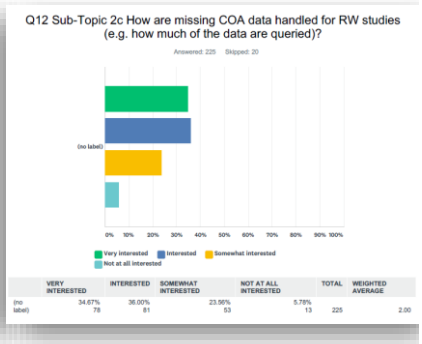
Survey Results – Topic 2

Participants not as interested in discussing Topic 2: Operationalization of COA in RW studies







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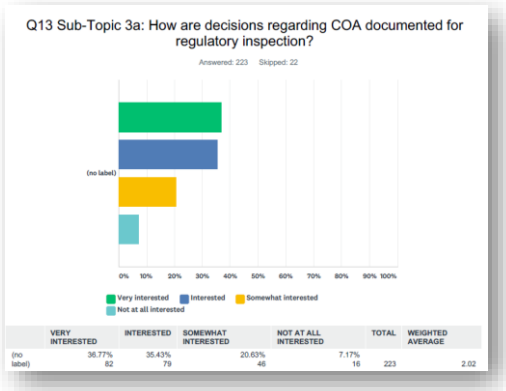
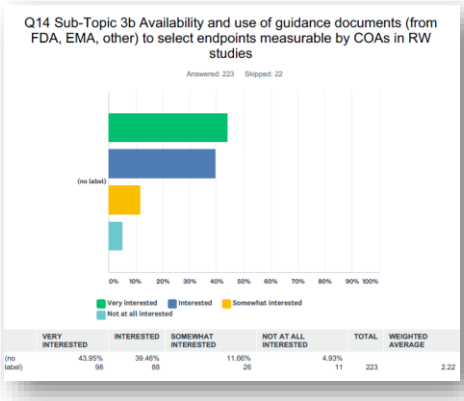
Survey Results – Topic 3

Participants also interested in having *Regulatory Guidance* surrounding COAs in RW studies





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- And an expressed interest in hearing the ***HTA / payer perspective as well as regulatory*** ….

Summary - Topic 3 – also interest in having *Regulatory Guidance* surrounding COAs in RW studies

- How are **decisions** regarding COA documented for regulatory inspection?
- Availability and use of **guidance documents** (from FDA, EMA, other) to select endpoints measurable by COAs in RW studies

- And expressed interest in perspective of HTAs

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Virtual Roundtable: Guiding Principles for Using COAs in Real World Studies

ISPOR COA Special Interest Group, Membership Engagement Project

October 29, 2019
11:00AM EDT

Roundtable Panelists

Tarry Ahuja, PhD
Canadian Agency for Drugs and Technologies in Health

Vishal Bhatnagar, PhD, MS
Oncology Center of Excellence, FDA

Martin Ho, PhD, MS
Center for Biologics Evaluation and Research, FDA

Lindsey Murray, PhD, MPH
Critical Path Institute

Daniel O'Connor, PhD, MsC
Medicines and Healthcare products Regulatory Agency

Paul Kluetz
FDA

Tara Symonds, PhD
Clinical Outcome Solutions

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Best practices for the use of COAs in RW studies

- What do you consider to be the **best practices** for designing RW studies where endpoints are measurable by COAs are commonly used?
- Do you consider that the **best practices** for **designing, selecting, analyzing, and interpreting** COA data or results from RW studies are generally followed?

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Best practices for the use of COAs in RW studies

1. Adherence to rigorous methodological, operational and epidemiological principles can be improved in RW studies:
   - Regulators require good scientific principles to be followed in clinical trials, but in RW these principles are not all followed.

2. Analytical Considerations:
   - Missing data may not be random
   - Importance of interpretation

3. Additional operational context:
   - License Costs
   - Plethora of Measures
   - Frequency of administration
   - Scheduled visits

Regulatory inspection and Guidance Documentation Available

- How are **decisions** on COAs documented for regulatory inspection in the context of RWE studies?
- What **guidance documents** (from FDA, EMA, HTA bodies) are consulted to select or develop/adapt COAs for the context of RW studies
- How will **newer initiatives** of considering RWE data for potential product label claims affect available COA recommendations in RWE?
- How do **HTA bodies**' current recommendations apply to the use COA data in RW studies?

Regulatory Context and Guidance Available

- Scientific principles used clinical trials should be applied to RW studies:
  - Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics, Draft Guidance (FDA, 2019)
  - ISPOR workshop on how to best implement COAs in RWE (2014)
  - Academy of Medical Sciences, UK (2015/2018)
  - ISPOR RWE transparency initiative (ISPE, NPC, Duke-Margolis)
  - SISAQOL exists for analysis discussions
  - 21st Century Cures Act: Patient-Focused Drug Development: Guidance 4 – Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making

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Regulatory Context and Guidance Available

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- Differences with Clinical Trials:
  - RWE data serving multiple purposes and for multiple stakeholder
  - Open label data: reticence to use such data in clinical trials
  - RWE data and its use needs to be better understood and initiatives are taken to acquire case studies where RWE COA data is used for regulatory purpose.
- In the context of the HTA, the more data the better, so COA data is encouraged to bring an added value to the clinical picture depicted.

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Next Steps

- Disease-specific COA recommendations in RW
- Recommendation of using well defined and reliable measures instead of developing new questionnaires / questions, e.g. PROMIS and PRO-CTCAE.
- Development of a repository of case studies of where RW has made a real impact in regulatory context
- White paper on best approaches and considerations to be made when selecting a COA for a RWE study

- What would you find would be a priority to assist RW studies for their COA strategies?

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Value of COA Data for all Stakeholders

ISPOR COA Special Interest Group, Key Project #1

October 29, 2019
11:00AM EDT

Key Project Team

Co-Chairs

- Lynda Doward, RTI-HS
- Bryan Bennett, BMS

Working Group Contributors

- Sarah Acaster, Acaster Lloyd Consulting Ltd
- Julia Braverman, Celgene
- Laurie Burke, LORA Group
- Helen Doll, Clinical Outcomes Solutions
- Cristina Ivanescu, IQVIA
- Ari Gnanasakthy, RTI-HS
- Helen Kitchen, DRG Abacus
- Jens Harald Kongsoe,
- Lori McLeod, RTI-HS
- Liz Moore, RWS
- Jayesh Patel, West Virginia University
- Chengetayi Pswarayi, Baxter
- Justin Raymer, University of Oxford
- Michelle Tarver, FDA
- Sue Vallow, Novartis
- Kate Williams, Acaster Lloyd Consulting Ltd
- Yogesh Vohra, University of Texas
- Emre Yucel, Amgen

ISPOR · John Guerino, MHS, Manager, Scientific and Health Policy Initiatives

Chair of SIG · Katja Rudell, Director of Patient Centred Outcomes, Paraxel

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Rationale

- COA data have value for many stakeholders including regulators, payers, healthcare providers and patients/patient advocates
- Regulators such as FDA and EMA have issued guidance providing clarity on COA nomenclature and what value COA data can offer in the regulatory drug evaluation environment
- However, there is a lack of clarity from other key stakeholders on both nomenclature and value of COA data
- This lack of clarity has the potential to limit the value of COA-based evidence for these stakeholder groups

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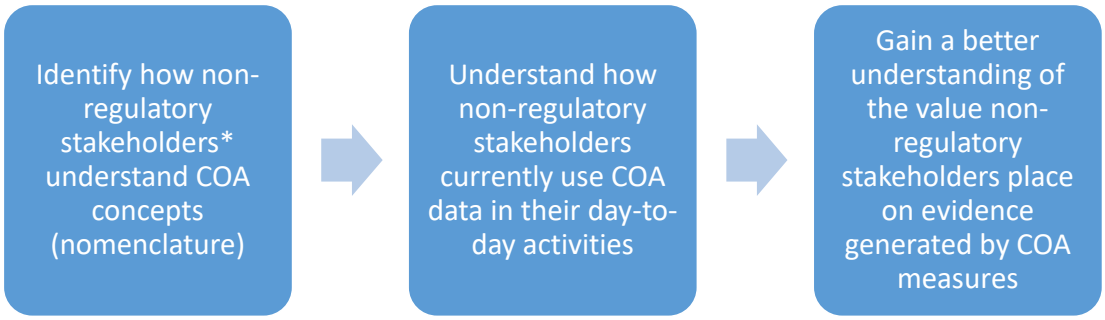
Key Project Aims



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Workplan

Review of the grey literature including regulatory websites/HTA websites	Initial planning conducted. To be completed Q1 2020
Review of COA definitions currently included in the ISPOR Book of Terms	Key terms for review identified Identification of authors / editors underway To be completed end-Q1 2020
Electronic survey conducted with ISPOR membership	Survey live on ISPOR Survey live through end-2019

Development of a strategy to harmonize COA nomenclature across all key stakeholders

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Grey Literature Review

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Search parameters

Key regulatory and HTA websites:
- UK (NICE/SMC)
- France
- Germany
- Spain
- Sweden
- Australia
- Canada
- US (ICER / Insurers)

Document Types:
- Technical appraisal documents
- Guidelines / guidance docs

Date Ranges:
- Previous 3 months

Published Reviews:
- Past 5 years

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Book of Terms

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Author / Review

- Identification of authors
- Editorial leads distribute terms to small teams.
- Each term reviewed / revised by max 2 people. Teams write terms and submit to section editors who harmonize and distribute to broader team for revision.

Task / Editorial Leads: Sarah Acaster, Helen Doll

Editorial Team: Sarah Acaster, Helen Doll, Lynda Doward, Bryan Bennett

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ISPOR COA Survey

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Survey Objectives

- To explore current understanding of specific COA terminologies by practitioners outside the COA field
- To determine how and where COA data are used in professional practice
- To understand the perceived value of COA data to non-COA practitioners

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ISPOR COA Survey

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Survey Overview

- Demographics and current role
- Understanding of COA terminology
- Use and value of COA data in current professional role
- Perceived value of COA data to decision making

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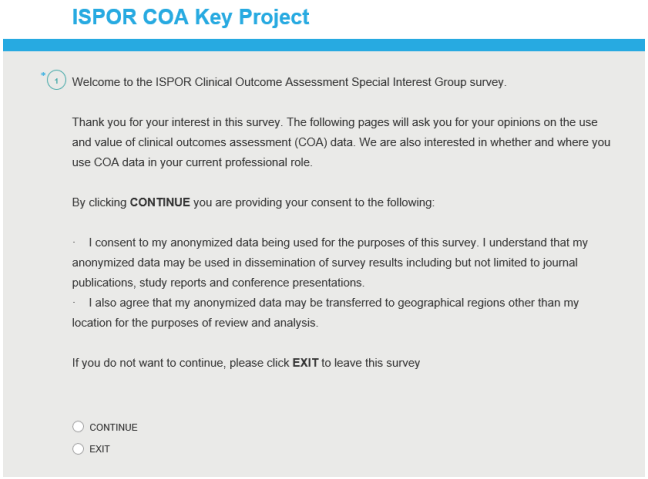
We are live!



https://www.surveymonkey.com/r/COAKEYPROJECT

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How you can help…

- Encourage colleagues and associates to complete survey
- Respondents do not have to be ISPOR members to complete
- Circulate the link!
- Survey will be live through end-December 2019

https://www.surveymonkey.com/r/COAKEYPROJECT

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Please Sign Up!

If you have any further questions, please direct them to clinicaloutcomeSIG@ispor.org