ispe

REAL-WORLD EVIDENCE TASK FORCE

March 2021 ISSUE

THE EVIDENCE ACCELERATOR

The Evidence Accelerator (EA, COVID-19 Diagnostic and Treatment), a public-private partnership between the FDA, Reagan-Udall Foundation and Friends of Cancer Research, is planning an online textbook on RWE COVID-19 research. The RWE TF is invited to lead chapter 2 "Methods and Data Characterization". The RWE methods training subgroup (led by Christopher Rentsch and Joshua Gagne) will lead the project, in collaboration with others including COVID-19 and Statistic Methods subgroups. Please contact Josh and Christopher if you have any questions via the Methods Training Subgroup Exchange community.

ISPE STRATEGIC PLAN DISCUSSION

In January 2021's RWE TF co-leads meeting, Vin Lo Re, ISPE President-elect and Chair of the Strategic Planning Committee, shared the ISPE Strategic Plan with the group, and discussed the items related to the TF, including:

- Promote ISPE Externally
  - Prioritize (RWE) collaborations with other societies
  - Develop list of (RWE) collaborators/partners
  - Develop process to guide strategic collaboration with such groups
  - Contribute to presentation/publication of RWE content at non-ISPE venues and develop relevant ISPE-branded resource
- Advance Pharmacoepi Science
  - Develop priority list of (RWE) society/stakeholders
  - Establish ISPE presence (lead role) at data science conferences
  - Report of symposia and ISPE representation at such conferences

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TASK FORCE GENERAL UPDATE

The TF provided progress updates to the February 2021 Board meeting. The TF has submitted a symposium proposal to 2021 ICPE titled ""Enhancing Stakeholder Engagement for Real-World Evidence Collaborations", with invited speakers from a regulatory agency, a clinical journal, and data science societies. Additional workshop/symposium proposals from other subgroups have also been submitted.

ISPE RWE UPDATES

Ann McMahon and Christopher Rentsch will moderate the COVID-19 plenary and Rolf Groenwold and Jeremy Rassen will moderate the Methodological plenary during the 2021 Mid-Year Meeting.

Several subgroups have planned webinars in 2021 (before August) to provide more detailed updates on the progress to ISPE communities. Detailed plan and topics will be communicated later.

SUBGROUP UPDATES

FOR A LIST OF SUBGROUP MEMBERS VISIT THE RWE TASK FORCE WEBPAGE

SPOTLIGHT: WEBSITE CONTENTS SUBGROUP

- Completed Deliverables
  - Organized ISPE membership commenting on Draft Guidance from MHRA RWE in Clinical Trials –Guidance (completed, Dec. 2020)
  - Updated list of regulatory & other policies, guidelines & white papers regarding RWE on Website, include the recent Asian guidance; posted 3/9/2021 (https://www.pharmacoepi.org/strategic-initiatives/rwe-for-regulatory-decision-making/)
  - Developed draft process for updating/adding/refreshing the RWE website
- In Progress:
  - Initiated formal collaboration with Publications & Communications Cmte (PCC) regarding development of RWE Website Management Plan
  - Ongoing work to finalize a RWE Website Dissemination Plan
  - Ongoing work on project to optimize searchability of RWE Website, including materials contained in the Education Center
- Building Community
  - Monthly subgroup meetings (last meeting 3/4/21)

SPOTLIGHT: ISPE RWE MANUSCRIPT DEVELOPMENT SUBGROUP

- Completed/Published Manuscripts
  - Considerations in characterizing real-world data relevance and quality for regulatory purposes: A commentary*
    - Journal – Published in PDS
  - Use of real-world evidence in regulatory decisions for rare diseases in the United States-Current status and future directions*
    - Journal – Published in PDS
  - Real-world evidence to support regulatory decision-making for medicines: Considerations for external control arms
    - Journal – Published in PDS
  - The Certainty Framework for assessing real-world data in studies of medical product safety and effectiveness
    - Journal – Published in Clin Phar Ther
  - Methods for external control groups for single arm trials or long-term uncontrolled extensions to randomized clinical trials*
    - Journal – Published in PDS

  *Did not go through formal ISPE endorsement process
- 2021/Q1 Plans:
  - Real-world evidence to support regulatory decision making: New or expanded medical product indications
    - Status/Target – Accepted by PDS
  - Real-world evidence to support regulatory decision making in Oncology: Opportunities, challenges, and methodological consideration
    - Status/Target – Initiated ISPE endorsement, received member comments, under revision
  - Real-world evidence for treatments in Pediatrics: New opportunities and challenges
    - Status/Target – Initiated ISPE endorsement, received member comments, under revision
  - Conduct of observational studies in post-covid era
    - Status/Target – To initiate ISPE endorsement In February
  - A framework for extension studies using real-world data to examine long-term safety and effectiveness
    - Status/Target – To initiate ISPE endorsement

SPOTLIGHT: RWE AND REAL-WORLD DATA SOURCES

- Annie McNeill is stepping down from the co-chair role. Nancy Lin will be the new co-chair of the subgroup
- RWE activities with ISPE SIGs
  - Finished the landscape assessment within ISPE and interviewed 10 related SIGs. Discussed collaborative opportunities including joint webinars on data sources that are commonly used in their subject/geographical area
  - Formed a working group on how to conduct Multi-database studies (MDBS). Received ISPE funding on the manuscript titled “Guidance for the identification, collection and reporting of data source heterogeneity in multi-database pharmacoepidemiologic studies.”
  - Published a manuscript titled “Suitability of databases in the Asia-Pacific for collaborative monitoring of vaccine safety”; KM Duszynski, et al. PDS; 2021 Feb 26. doi: 10.1002/pds.5214.
- RWE activities with external groups
  - Conducted a database survey with collaborators in the NeuroGEN network (for details: Ilomäki J et al. Application of Healthcare 'Big Data' in CNS Drug Research: The Example of the Neurological and mental health Global Epidemiology Network (NeuroGEN). CNS Drugs. 2020 Sep;34(9):897-913.) to characterise databases within the network.

- Discussing with the Global Observational study in Medications Associated with Psychopharmacology (GOMAP) network to develop information package for available data sources that can be used in drug utilisation study
- Discussing with the EUropean NETwork for HYperkinetic DISorders (EUNETHYDIS) for RWE presentation at the upcoming EUNETHYDIS conference

RWE AND STATISTICAL METHODS

- Goal:
  - Develop resources for ISPE membership
- In Progress: Subgroup task members are developing a reference document with ~50 entries on established, emerging, and "cutting-edge" statistical methodologies. Each entry on a methodology includes:
  - The problem the method is trying to solve
  - 2-3 descriptive sentences on the method
  - Where the method is most appropriate
  - Key examples that could be used, eg, in a course
  - Canonical references, with a link to PubMed
  - Issues a design/method can have
  - Key criticisms
  - Key implementations
  - The subgroup will meet again in early 2021.
- Select Entry Examples:
  - Established PS methods including: two-way matched analyses, IPTW weighted analyses, SMR weighted analyses, PS balancing diagnostics, control calibration, balanced matching for 1:N matching
  - Emerging methods for innovative designs including: self-controlled designs, difference-in-difference analyses, interrupted time series, negative controls
  - Cutting-edge methods for missing values, including non-parametric imputation using random forests
- Next Steps:
  - Finish drafting and editing entries; Work with larger RWE Task Force to identify how such a resource could be most useful to ISPE membership (e.g. on the ISPE website).

RWE COVID-19 SUBGROUP

- Goals:
  - Coordinate and consolidate knowledge and expertise within ISPE with regards to the use of RWE addressing scientific questions on COVID-19 pandemic
  - Build collaborations with other societies, agencies, academic institutions, and patient advocacy groups with regards to RWE and COVID-19.
  - Core and Extended teams established Q4 2020
  - Monthly meetings with regular participation (15-20 persons) and active contributions
  - Representation from Academia, Regulatory Bodies, Industry
  - Interfaces with other RWE Task Force Workgroups (RWE for regulatory, RWE methods group, etc.)
- In Progress:
  - Submitted abstracts for two symposia ICPE 2021 on the use of RWD in the context of COVID-19 research and on pediatric COVID-19
  - Planned literature reviews/manuscripts on COVID-19 disease characterization, outcomes, impact on health care systems.
  - Planned literature reviews/manuscripts on COVID-19 vaccines and therapies (outcomes, methodological considerations)
  - Contributions to Duke-Margolis COVID-19 working groups under consideration
  - ISPE Webinar under consideration

RWE AND ONCOLOGY SUBGROUP

- In Progress:
  - Priority Outreach
    - Ongoing discussion on RWE curriculum with American Society of Clinical Oncology (Led by D Rivera)
    - Outreach beginning to AACR and ESMO
  - Manuscripts
    - Invitation for special article on improving paediatric drug safety (led by B. Carleton, December 2020)
    - Guidance on use of QBA to assess the direction and magnitude of bias when using RWD external comparators (Funded by ISPE call for manuscripts – multiple ISPE members: D Layton, T D Kou, G Liu, J Bosco, C Grey and D Rivera and non-members: T Lash, M Fox and E Ralphs) Kick off meeting held Feb 2021
  - Workshop Submissions
    - ICPE submission on External Comparators supported by Cancer SIG (led by L. Hester)
  - Webinars
    - Tentative Title: RWE and Oncology Task Force Subgroup: New data sources, designs, and collaborations to advance RWD
    - Planned for end June 2021
  - Meetings
    - Bimonthly core team member meetings to provide updates and discuss next steps, including collaborative research topics for new manuscript ideas. The next extended group meeting is planned for April 2021

ISPE – ISPOR SUBGROUP

- In Progress:
  - Manuscripts/Projects
    - Toward Rigorous Transparency - Harmonization of Protocol Templates for Design and Registration of Observational Hypothesis Evaluating Treatment Effectiveness (HETE) Studies
    - RWE study registration: https://osf.io/registries/rwe/discover
  - Webinars
    - ISPOR webinar Dec 17th, 2020
    - ISPE webinar TBD
- Next Steps:
  - Small group working on protocol template harmonization - “meat” of paper
  - Submit manuscript to ISPE and ISPOR for endorsement
  - Submit abstract/webinar/symposia proposals for 2022

RWE AND MEDICAL DEVICE

- In Progress:
  - Priority Outreach
    - MDEpiNet
    - ISPOR Medical Device SIG
    - NESTcc
    - IDEAL-D
    - AMIA device group
    - Regulators
    - Establish messaging (complete) and initial connections (complete)

        - Formal reach-out
    - Priority Manuscripts
        - Role of providers and methods to address safety/effectiveness of cardiac devices (e.g., LVAD) – Lead: Setoguchi
        - RWE of non-surgical ventilation – Lead: Ritchey
        - RWD of COVID diagnostics – abstract – Medical Device SIG
    - Other Efforts
        - Landscape review to establish baseline of RWE guidance for devices (completed)
        - Continued horizon scanning
            - Led to ISPE endorsed comments on IMDRF PMCF
- Next Steps (2021 Plans):
        - Integrate "extended team" into Medical Device SIG
        - Working through administrative and logistics matters for better engagement with priority organizations
        - Build ISPE RWE TF presence (as "ISPE") within MDEpiNet, NEST, IDEAL-D
            - Message: methodology experts who are keen to collaborate
        - Formal reach-out to device groups within ISPOR and AMIA
        - Complete priority manuscripts and begin/complete manuscripts in second tier priority areas
        - Planning and reach-out to second tier priority collaborators
        - Continued horizon scanning and contributing/commenting on device RWE topics

RWE AND REGULATORY DECISIONS MAKING SUBGROUP

- In Progress:
    - Workstreams (Lead/Co-Leads)
        - Map out timing: RWE guidance from regulatory authorities, HTAs - *Hisashi, Madlen*
        - Develop topics for abstract submissions - *Karolina, Helga, Jacinthe*
        - Identify ways to connect with EMA, ICH, and other groups developing guidelines, also HTAs - *Stella, Montse*
        - Coordinate & collaborate with RWE Duke-Margolis working group to try to integrate our team - *Ken, Shahed, Cindy*
- Manuscripts (Lead)
    - Parallels in process: RWE and PRO/COA fit-for-purpose for regulatory decisions –*Girman, in press*
    - Assessing whether a data source is fit-for-purpose for regulatory questions - *Cindy, Mary Beth*
    - What makes results 'believable' - *Cindy*
    - Regulatory decisions in a pandemic - *authors needed*
    - Increasing efficiency of RCTs for regulatory decisions post-approval *lead needed*
    - RWE needs for HTA bodies *(authors needed)*
    - White paper for clinical journals on confounding -*authors needed*
    - Design and methods that work well for specific regulatory decisions - *O'Mareen Spence, Cindy*
    - Data sharing beyond boundary and data protection policies - *Hisashi*
    - Patient-focused regulatory decision-marking paths and obstacles to realization - *Cathy Anne, Cindy*
    - To liaise with Manuscript Development subgroup:
        - Framework for data quality & representativeness for regulatory/HTA decision-making – *Karolina*
        - RWE endpoints for regulatory and HTA - *have 7 interested authors*
        - RWE to support regulatory decisions in vaccines - *O'Mareen Spence*
        - pRCTs and approaches to regulatory decisions – *Cindy*

        - Robustness and evaluation of novel designs for regulatory decisions - *Cindy*
        - Recommendations for international harmonization - *Jacinthe, Madlen*
- Workshops/Symposia
    - ISPOR virtual: Submitted abstract on what makes results 'believable'?
- Webinars to Target
    - Duke-Margolis-FDA

To view subgroup member lists, visit the RWE Task Force page on the ISPE website.

View our past December 2020 Newsletter