Real-world evidence data from drug registration to reimbursement

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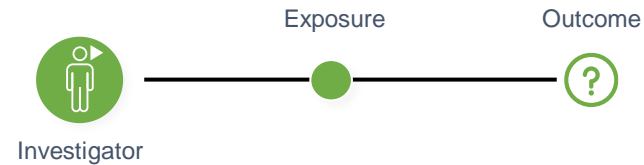- Please consider this disclosure as we proceed with the presentation.

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There are several potential sources of RWE

Retrospective
Data collected in the past.

Exposure   Outcome

Investigator
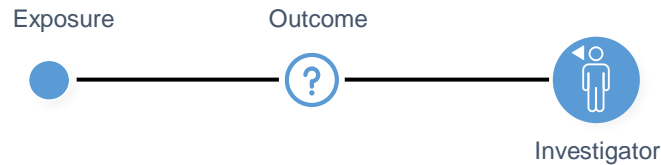
Prospective
Data collected into the future.

Exposure   Outcome

Investigator

Involves both retrospective and prospective data collection

Bidirectional
Data collected in the past and into future.

Exposure   Outcome

Investigator

Cross Sectional
Data collected to represent a single point in time.

Past   Future

Investigator

Neither retrospective or prospective

1. Grimes & Schulz. *The Lancet*. 2002; 359:57-61.   **2.** LaMorte. https://sphweb.bumc.bu.edu/otlt/mph-modules/ep/ep713_cohortstudies/ep713_cohortstudies2.html (Accessed Sept 2022).   **3.** Ranganathan & Aggarwal. *Perspect Clin Res.* 2018; 9:184-186.
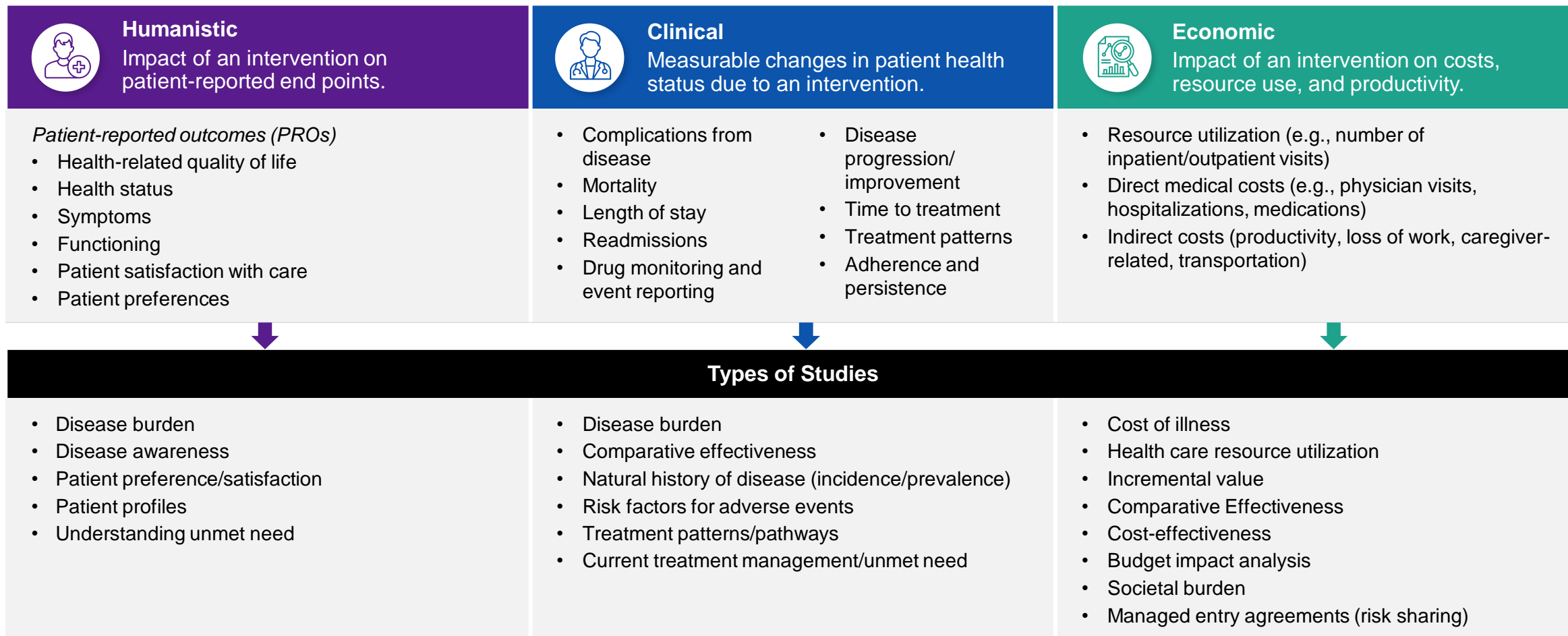
Coming from RWD sources very detailed

RWD source	Claims databases[1-3]	Electronic health record[4-7]	Hospital administrative data[8]	Patient registries[2,3,9-11]	Surveys and questionnaires[2,12,13]
Strengths	• Captures the continuum of care • Contains healthcare cost data • Large and well suited for rare outcomes	• Wide range of structured and unstructured information • May contain nuanced clinical data (e.g., line of therapy)	• Provides a detailed view into a patient's use of services in the hospital including financial data	• Useful for understanding quality of care, satisfaction, and resource utilization (long time frame) • Understanding rare diseases • May contain nuanced clinical data • Some registries capture HRQoL data	• Useful for evaluating functional status, quality of care, adherence, HRQoL, and preference
Limitations	• Patient disenrollment (longitudinal follow-up challenges) • Coding inaccuracies • Lacks in-hospital details and HRQoL data • Limited to services and drugs that are reimbursed	• Only captures the care provided by HCPs using the EHR • Lacks prescription details, HRQoL and financial data, • Curation required for unstructured data	• Typically lacking clinical depth and HRQoL data • Coding inaccuracies • Limited follow-up outside the hospital	• Risk of missing data • Data quality issues • Selection bias due to voluntary participation • Often no comparator treatment (or disease group) • Usually lacks financial data	• Reliability can be low due to differences in patients' abilities to recall, understand, and report • Patients may self-select for participation

Abbreviations: EHR = electronic health record; HCP = health care provider; HRQoL = health-related quality of life; RWD = real world data.
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4. Hansen et al. JAMA. 2007; 298:874-879.   5. Wilson & Bock. White Paper. 2012; 1-3.   6. Quek & Mardekian. J. Adv Ther. 2019; 36:708-720.   7. HealthIT.gov.
https://www.healthit.gov/faq/what-electronic-health-record-ehr (Accessed Sept 2022).   8. AAPC. https://www.aapc.com/medicalcodingglossary/administrative_data.aspx. (Accessed Sept 2022).   9. Siegler et al. Med Student Res J. 2013; 2:21-29.   10. Darden et al. Future Oncol. 2019; 15:141-150.   11. Weitzman et al. J Patient Rep Outcomes. 2018; 2:1. 12. Iversen et al. BMJ Open. 2012; 2:e001437. 13. Cella et al. RTI Press Book. 2015.

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Different health outcomes can be assessed using RWE

Humanistic	Clinical	Economic
Impact of an intervention on patient-reported end points.	Measurable changes in patient health status due to an intervention.	Impact of an intervention on costs, resource use, and productivity.
Patient-reported outcomes (PROs) • Health-related quality of life • Health status • Symptoms • Functioning • Patient satisfaction with care • Patient preferences	• Complications from disease • Mortality • Length of stay • Readmissions • Drug monitoring and event reporting • Disease progression/improvement • Time to treatment • Treatment patterns • Adherence and persistence	• Resource utilization (e.g., number of inpatient/outpatient visits) • Direct medical costs (e.g., physician visits, hospitalizations, medications) • Indirect costs (productivity, loss of work, caregiver-related, transportation)

Types of Studies

• Disease burden • Disease awareness • Patient preference/satisfaction • Patient profiles • Understanding unmet need	• Disease burden • Comparative effectiveness • Natural history of disease (incidence/prevalence) • Risk factors for adverse events • Treatment patterns/pathways • Current treatment management/unmet need	• Cost of illness • Health care resource utilization • Incremental value • Comparative Effectiveness • Cost-effectiveness • Budget impact analysis • Societal burden • Managed entry agreements (risk sharing)

Abbreviations: PRO = patient-reported outcome; RWE = real world evidence.

1. AHRQ. Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide. 2013. 2. AMCP. Outcomes Research Presentation. 2015. 3. Khosla et al. F1000Res. 2018; 7:111. 4.Venkataraman et al. PLoS One. 2014; 9:e113802. 5. Kalaiselvan et al. Indian J Anaesth. 2015; 59:715-20. 6. Rudrapatna & Butte. J Clin Invest. 2020; 130:565-74. 7. Centers for Disease Control and Prevention. https://www.cdc.gov/policy/polaris/economics/cost-illness/index.html (Accessed Sept 2022).

The value of RWE is recognized by many stakeholders

	Regulatory Agencies[1,2]	Payers / HTAs[3,4]	Providers[3-6]	Patients[2,6,7]
Key needs that RCTs & RWE may help to address	• Assess risk-benefit ratio when ethical, operational, or resource barriers may hinder the ability to conduct an RCT • Determine post-marketing requirements • Assess comparative effectiveness	• Increase budget predictability • Assess cost effectiveness • Assess comparative effectiveness	• Optimize care protocol • Stratify outcomes by subpopulations • Understand patient preferences	• Optimize personal health • Receive personalized treatment according to clinical characteristics and personal preferences
Evidence considered	• Effectiveness • Safety • Quality of life	• Effectiveness • Safety • Quality of life • Burden of illness • Costs and healthcare resource use • Cost-effectiveness and budget impact	• Effectiveness • Safety • Quality of life • Costs and healthcare resource use • Treatment sequence • Social determinants of health	• Effectiveness • Safety • Quality of life • Humanistic factors

Abbreviations: HTA = Health Technology Assessment; RCTs = randomized controlled trials.

1. Berger et al. *Value Health*. 2017; 20:1003-1008. 2. Duke-Margolis Center for Health Policy. https://healthpolicy.duke.edu/sites/default/files/2019-11/non internvetional_study_credibility_0.pdf (Accessed Sept 2022). 3. Khosla et al. *F1000Res*. 2018; 7:111. 4. Brooks & Field. (2020) https://www.optum.com/content/dam/optum3/optum/en/landing/ls/PJA/WF629798-PJA-ebook.pdf (Accessed Sept 2022). 5. Palacio et al. *Popul Health Manag*. 2018; 21:501-508. 6. American Academy of Family Physicians. (2017). https://www.aafp.org/family-physician/patient-care/clinical-recommendations/cpg-manual.html (Accessed Sept 2022). 7. Butler et al. *Biometrics*. 2018; 74: 18-26.

Thank you