Fit for Purpose Real World Data

Applying Decision Aids

The National Academies of Science, Engineering, and Medicine
Examining the Impact of Real-World Evidence on Medical Product Development:
A Three-Part Workshop Series
Workshop Three: Application
July 17 – 18, 2018

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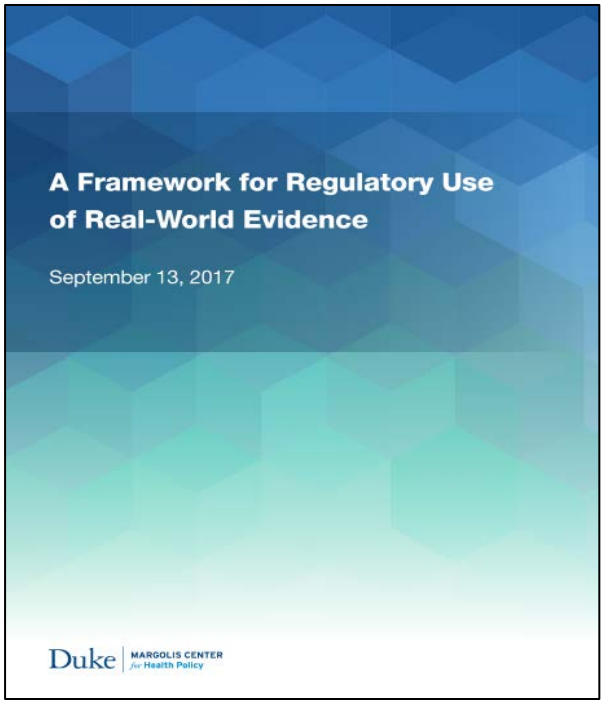
Duke-Margolis RWE Framework

- Released in September 2017
- Proposes a framework of considerations to guide sponsors and FDA in RWE discussions, and puts forward near-term steps on priority issues
- Intends to help clearly establish the current RWD/RWE landscape and the potential process that stakeholders should go through when assessing RWE approaches for regulatory use



Duke Margolis Real-World Evidence Collaborative

- White papers
  - Real-World Data Quality and Relevance: Characterizing Data for Regulatory Use *(working title)*
  - Improving the Credibility of Observational Studies for Regulatory Use *(working title)*
- Will be released in conjunction with Oct. 1, 2018 Public Meeting

Understanding the origin and anatomy of real world data

Perspective from a Pharmaceutical Company

Brande Yaist
Sr. Director- Global Patient Outcomes and Real World Evidence
Eli Lilly and Company

Real world evidence is defined by use of real world data

Real world evidence is the clinical **evidence** regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.

Real World Evidence (RWE) is one form of evidence (along with RCT, health economics studies, etc.) derived from primary or secondary real world data sources, with appropriate design/analyses, for the purpose of providing insights, on diseases, medicines, patient populations and healthcare practices, that will inform customer and internal decision making

Source: Eli Lilly and Company

There is no commonly accepted definition of real world data

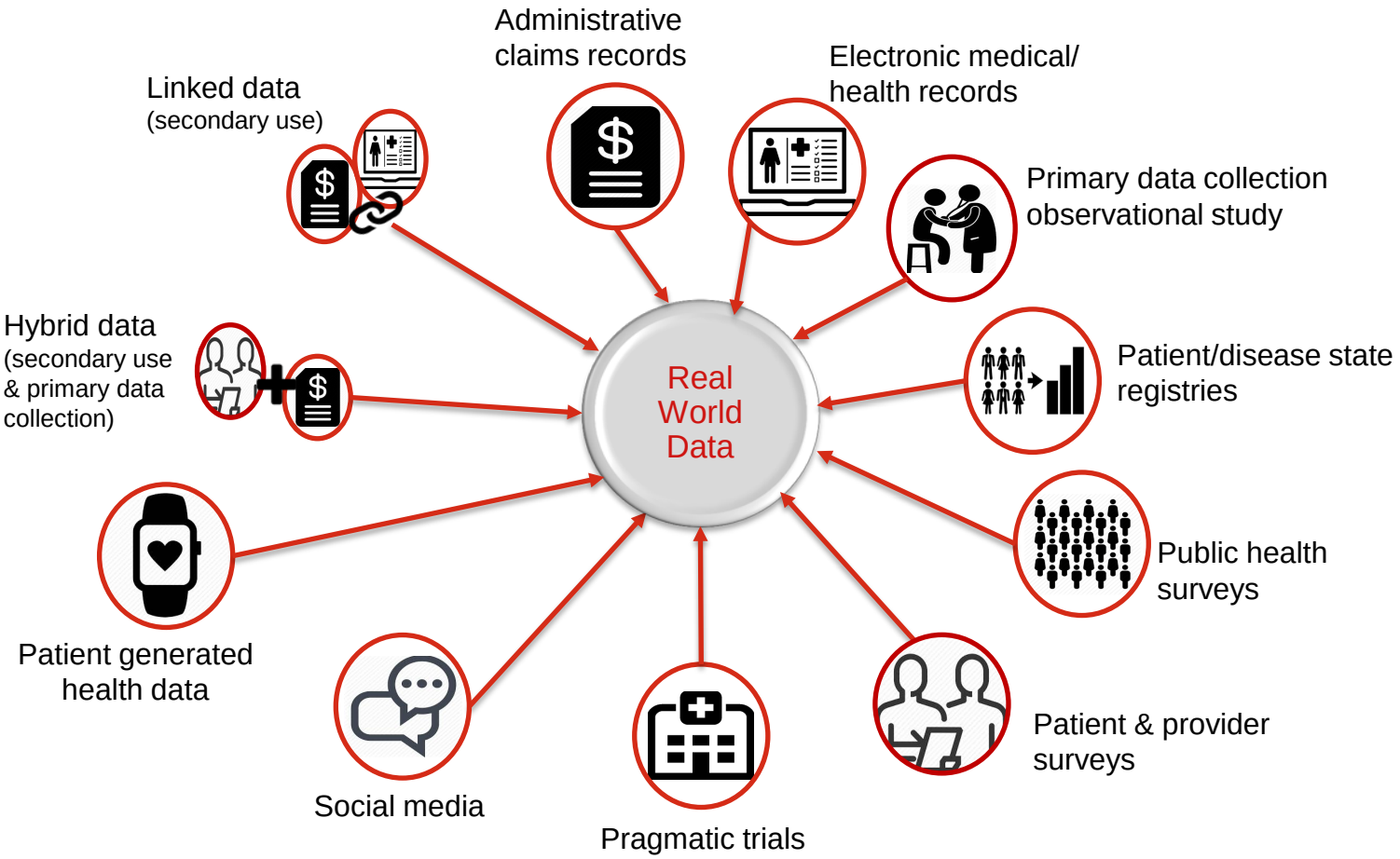
However, there are common themes…

Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources

Data used for clinical, coverage, and payment decision-making that are not collected in conventional randomized controlled trials

An umbrella term for data regarding the effects of health interventions (e.g., benefit, risk, and resource use) that are not collected in the context of conventional RCTs. Instead, RWD are collected both prospectively and retrospectively from observations of routine clinical practice. Data collected include, but are not limited to, clinical and economic outcomes, patient-reported outcomes, and health-related quality of life. RWD can be obtained from many sources including patient registries, electronic medical records, and observational studies.

There is a wide variety of possible RWD sources



Source: Eli Lilly and Company

Start with the question and context of the decision

1. State the RESEARCH QUESTION
2. LIST the DATA ELEMENTS of interest to answer the research question

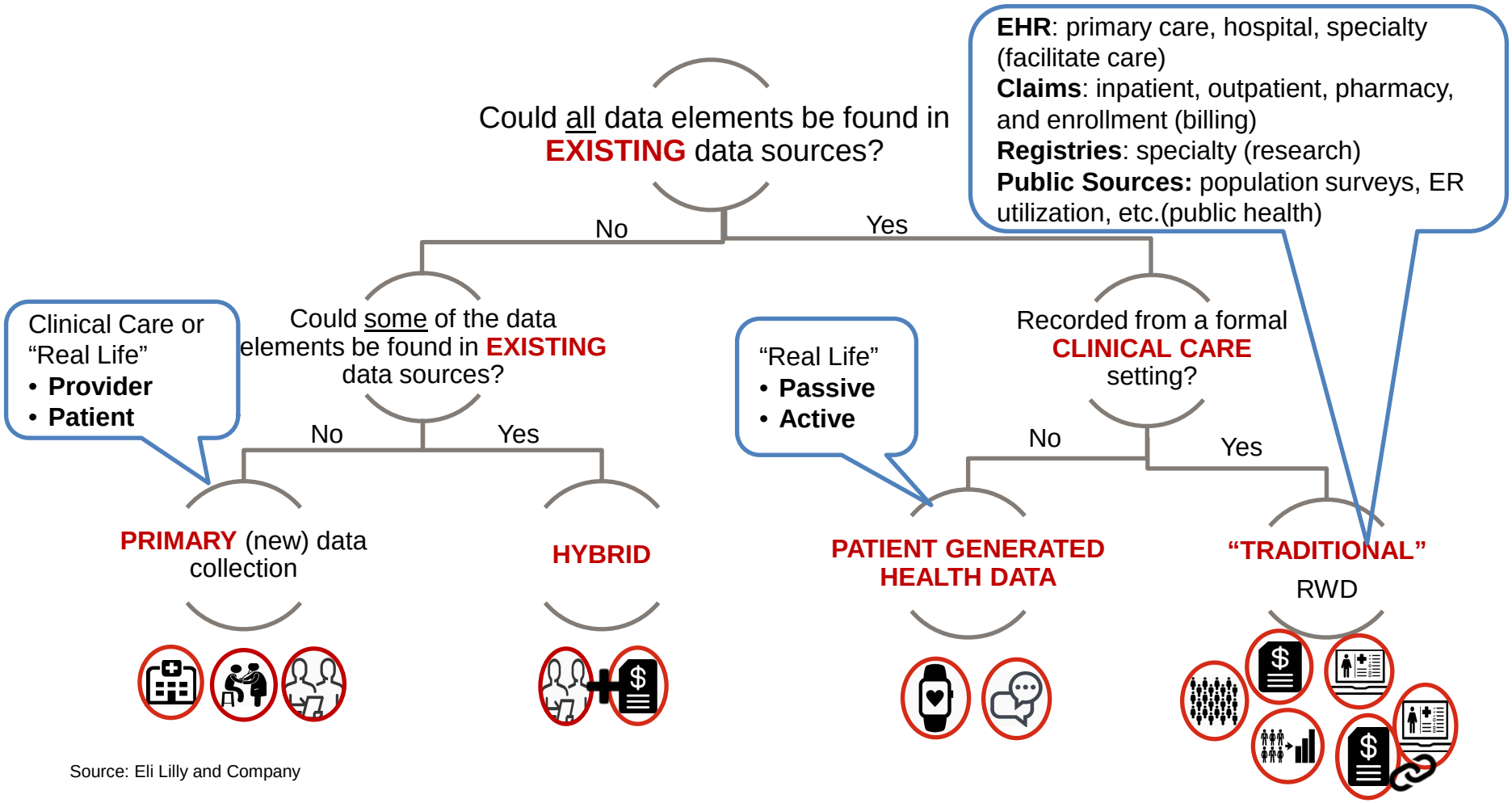
Is the drug safe and effective …
- in an expanded population?
- using different dose schedules or dosing?
- in a sub-population?
- in very small population unlikely to have RCT?
- in a new disease state?

Are there additional benefits/claims (e.g. functional measures, symptom improvement) in already approved indication?

Source: Eli Lilly and Company

Identify possible data sources

1. Do accepted standards exist? (e.g. MACE endpoints are well established for claims)
2. Key data elements (exposure, outcome, & covariate variables)



Source: Eli Lilly and Company

What is the comparative effectiveness of Carotid Artery Stenting versus Carotid Endarterectomy?

Could all data elements be found in **EXISTING** data sources?

- No
  - Could some of the data elements be found in **EXISTING** data sources?
    - No
      - **PRIMARY** (new) data collection
    - Yes
      - **HYBRID**
- Yes
  - Recorded from a formal **CLINICAL CARE** setting?
    - No
      - **PATIENT GENERATED HEALTH DATA**
    - Yes
      - **"TRADITIONAL"** RWD

Medicare + Registries + AHAA Survey + AMA Identifiers

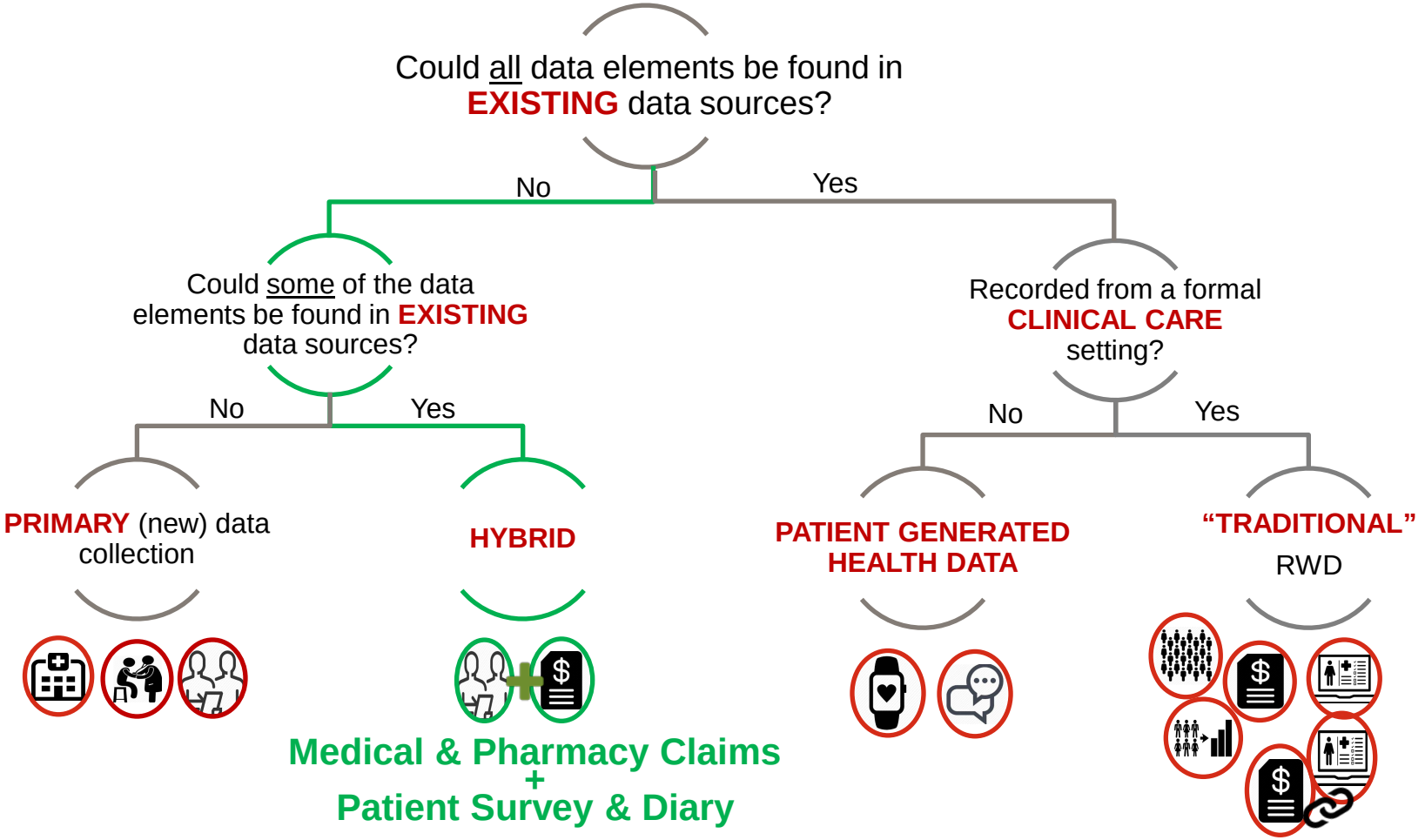
Jalbert JJ, Nguyen LL, Gerhard-Herman MD, et al. "Comparative effectiveness of carotid artery stenting versus carotid endarterectomy among Medicare beneficiaries." *Circ Cardiovasc Qual Outcomes* 2016; 9(3):275-85. [doi:10.1161/CIRCOUTCOMES.115.002336]

Stenting vs. Endatarectomy Considerations for data relevance

Availability of key data elements (exposure, outcome, & covariate variables)	• Exposure (CAS vs. CEA) • Outcomes (death, stroke/TIA, MI) • Covariates: patient demographics, comorbidities, degree of carotid stenosis, elective vs. emergent procedure status, surgeon characteristics
Representativeness	• All Medicare patients receiving CAS or CEA during study period
Sufficient subjects	• 1999 CAS and 3255 CEA patients treated by 337 physicians across 69 centers in the SVS-VR
Complete exposure window	• Yes, survival model
Longitudinality	• Medicare vital status file has date of death and Medicare claims capture stroke/TIA and MI.
Availability of elements for patient linking	• Medicare ⇔Surgical Vascular Registry ⇔ Cardiovascular Data Registry • Medicare ⇔American Hospital Association's Annual Survey Database • AMA Physician Masterfile ⇔ Medicare

Jalbert JJ, Nguyen LL, Gerhard-Herman MD, et al. Comparative effectiveness of carotid artery stenting versus carotid endarterectomy among Medicare beneficiaries. *Circ Cardiovasc Qual Outcomes* 2016; 9(3):275-85. [doi:10.1161/CIRCOUTCOMES.115.002336]

What are factors influencing treatment choice among patients with Chronic Idiopathic Constipation and Irritable Bowel Syndrome with constipation (CONTOR)



Breanna Essoi, Douglas C. A. Taylor, Jessica L. Abel, Robyn T. Carson, Alyssa Goolsby Hunter, Paul Buzinec, Carolyn Martin. "An Innovative Approach to Mixed-mode Longitudinal Data Collection: Methods and Response Rates from the Chronic Constipation and IBS-C Treatment and Outcomes Real-world Research Platform (CONTOR)." Poster presented at the International Society for Pharmacoeconomics and Outcomes Research 22nd Annual International Meeting, Boston, MA, USA, May 20–24, 2017)

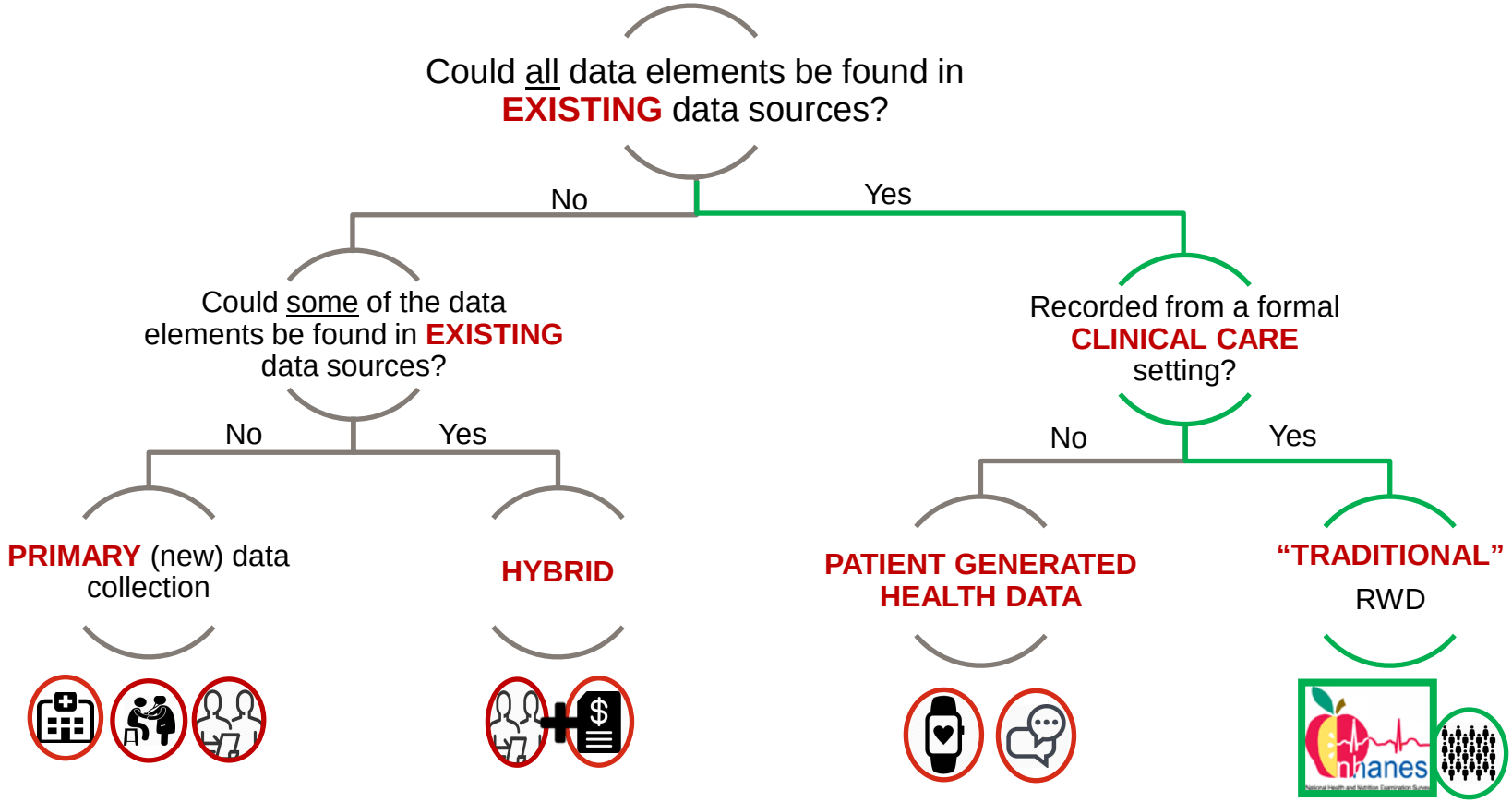
CONTOR: Considerations for data relevance

Availability of key data elements (exposure, outcome, & covariate variables)	• Claims: Diagnosis, drug exposure • Survey (168 questions) • Diary (77 questions)
Representativeness	• Medical and pharmacy claims and enrollment information • approximately 12 million patients annually from a • U.S. health plan with national coverage • Geographically diverse and broadly representative of the U.S. insured population.
Sufficient subjects	• 18,590 mailed, 2693 returned, 2052 complete/eligible
Complete exposure window	Yes
Longitudinality	December 2012 to June 2015
Availability of elements for patient linking	IRB approval + patient consent

Breanna Essoi, Douglas C. A. Taylor, Jessica L. Abel, Robyn T. Carson, Alyssa Goolsby Hunter, Paul Buzinec, Carolyn Martin. "An Innovative Approach to Mixed-mode Longitudinal Data Collection: Methods and Response Rates from the Chronic Constipation and IBS-C Treatment and Outcomes Real-world Research Platform (CONTOR)." Poster presented at the International Society for Pharmacoeconomics and Outcomes Research 22nd Annual International Meeting, Boston, MA, USA, May 20–24, 2017)

Additional Case Examples

What is the relationship between muscle mass and walking speed and quadriceps strength test?



Chen, Lei, David R. Nelson, Yang Zhao, Zhanglin Cui, and Joseph A. Johnston. "Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States." BMC geriatrics 13, no. 1 (2013): 74.

Muscle Mass: Considerations for data relevance

Availability of key data elements (exposure, outcome, & covariate variables)	• Quadriceps strength is not commonly done in patient care, BUT is done for NHANES
Representativeness	• Survey is weighted for representativeness of US Population
Sufficient subjects	• All survey subjects performed test
Complete exposure window	• Not applicable
Longitudinality	• Cross-sectional, assessing relationship at apoint in time
Availability of elements for patient linking	• Not applicable

Chen, Lei, David R. Nelson, Yang Zhao, Zhanglin Cui, and Joseph A. Johnston. "Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States." BMC geriatrics 13, no. 1 (2013): 74.

What are the patient-perceived treatment effectiveness, medication use, and healthcare resource utilization in psoriasis patients?

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MODERNIZING MEDICINE

Specialty Care eMR

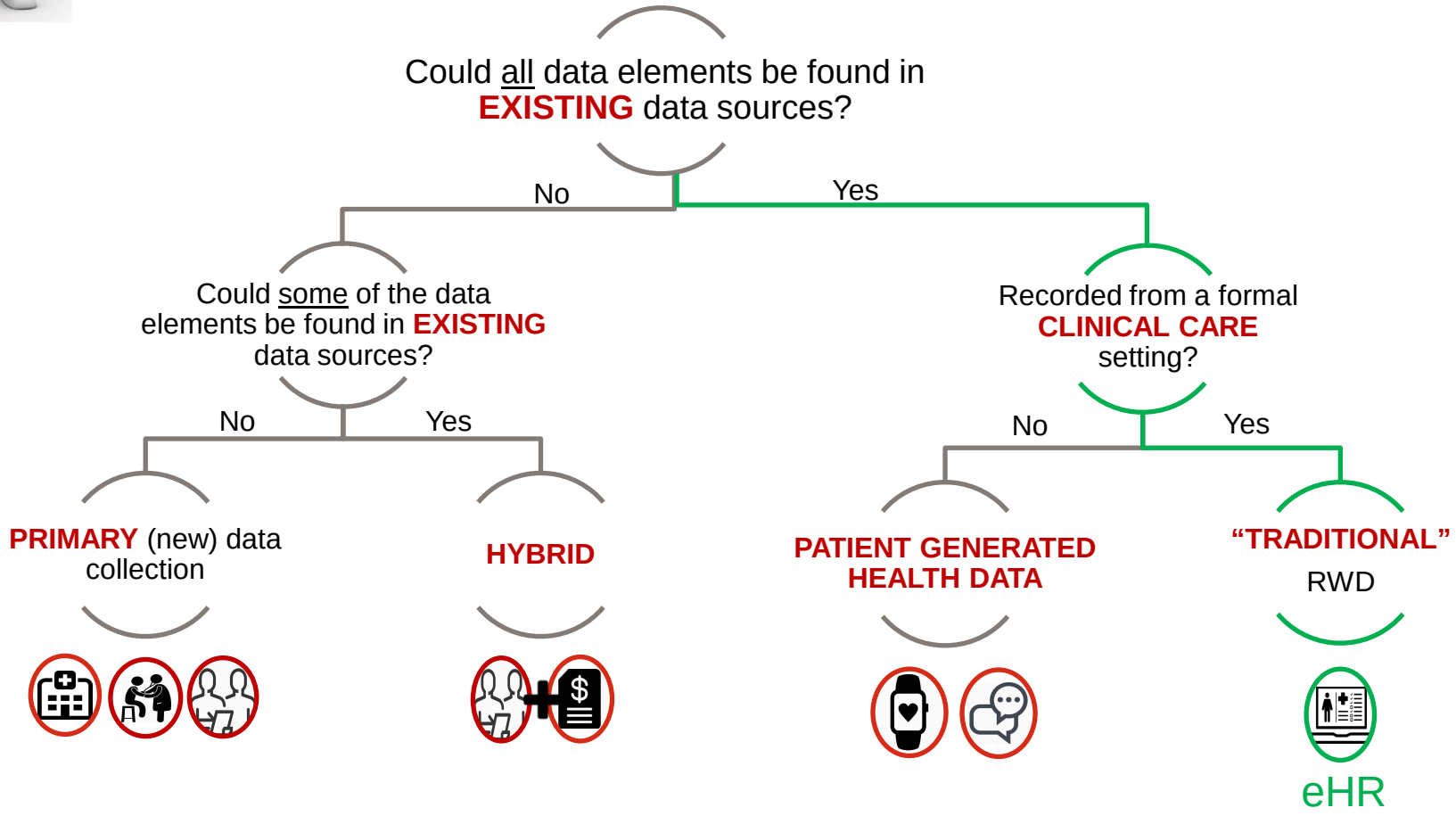
April W. Armstrong, Shonda A. Foster, Brian S. Comer, Chen-Yen Lin, William Malatestinic, Russel Burge and Orin Goldblum· "Real-world health outcomes in adults with moderate-to-severe psoriasis in the United States: a population study using electronic health records to examine patient-perceived treatment effectiveness, medication use, and healthcare resource utilization." BMC Dermatology 18:4 (June 2018)

Psoriasis: Considerations for data relevance

Availability of key data elements (exposure, outcome, & covariate variables)	• Physician's Global Assessment (PGA) and Body Surface Area (BSA) to determine disease severity (no proxy measurement required) • Patient assessment of treatment effectiveness • Treatment history, number of visits, and complexity of visits were available in coded fields.
Representativeness	• Dermatology-specific EHR platform used by over 4500 dermatology providers (30% of the market share across the US). This includes patients from 49 US states and 2 territories.
Sufficient subjects	• Over 500,000 psoriasis patients resulting in sufficient cohort after attrition
Complete exposure window	Yes
Longitudinality	September 2014- September 2015
Availability of elements for patient linking	NA

April W. Armstrong, Shonda A. Foster, Brian S. Comer, Chen-Yen Lin, William Malatestinic, Russel Burge and Orin Goldblum. "Real-world health outcomes in adults with moderate-to-severe psoriasis in the United States: a population study using electronic health records to examine patient-perceived treatment effectiveness, medication use, and healthcare resource utilization." BMC Dermatology 18:4 (June 2018)

Comparative effectiveness from a single-arm trial and real-world data: alectinib versus ceritinib



Jessica Davies, Michael Martinec, Paul Delmar, Mathieu Coudert, Walter Bordogna, Sophie Golding, Reynaldo Martin, & Gracy Crane. "Comparative effectiveness from a single-arm trial and real-world data: alectinib versus ceritinib." 26 Jun 2018https://doi.org/10.2217/cer-2018-0032

NSCLC Control Arm Considerations for data relevance

Availability of key data elements (exposure, outcome, & covariate variables)	• Exposure (certinib) • Outcomes (death) • Covariates: patient demographics, staging, prior treatments)
Representativeness	• ~15% of US cancer patients, geographically and demographically diverse
Sufficient subjects	• 67 patients from the Flatiron database (183 patients from 2 Phase 2 CTs)
Complete exposure window	• Yes, survival model
Longitudinality	• Jan 2011- Feb 2016
Availability of elements for patient linking	• NA

Jessica Davies, Michael Martinec, Paul Delmar, Mathieu Coudert, Walter Bordogna, Sophie Golding, Reynaldo Martin, & Gracy Crane. “Comparative effectiveness from a single-arm trial and real-world data: alectinib versus ceritinib.” 26 Jun 2018https://doi.org/10.2217/cer-2018-0032