

# EXTERNAL CLINICAL DATA

Opportunities for NCI

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# Definitions Applied to External Clinical Data

## SOURCES

- **RESEARCH** – Includes *structured data* from ***past clinical trials***; includes single arm or RCT control arm datasets collected into trial databases (Dbases)
  - Actionable innovations possible for future plans, such as standard options for oncology/NCI trial designs, stat plans, CRF, consent
  - Few initiatives are ongoing to support working practices for oncology single-arm trials & Dbases, especially for rare indications & combinations
- **HEALTHCARE DELIVERY** – *Unstructured and/or curated **Real World Data** (RWD)* from EHRs, insurance claims, registries, case studies, literature.
  - Multiple initiatives and regulatory guidances are available or emerging, largely supporting RWE utilities *outside of Oncology*

Reference: S. Khozin, G. Blumenthal, R. Pazdur, Real World Data for Clinical Evidence Generation in Oncology. JNCI, Nov 1, 2017

# APPLICATIONS OF EXTERNAL CLINICAL DATA

Growing experiences to optimize utilities, efficiencies, clinical impact, access

1. **Control arm supplementation (or replacement)**
  - a. **Trials randomized 3:1, 4:1 etc. with reduced N**
  - b. **Accelerated protocol completion, esp. rare populations**
2. **Safety Signal interpretation/context**
3. **Precision powering**
4. **Inclusion/exclusion criteria**
5. **Disease modeling; prognostic covariates**
6. **Assessment of geographic differences**  
**Support international collaborations**
7. **Biomarker development**
8. **Confidence in RCT control arm performance**

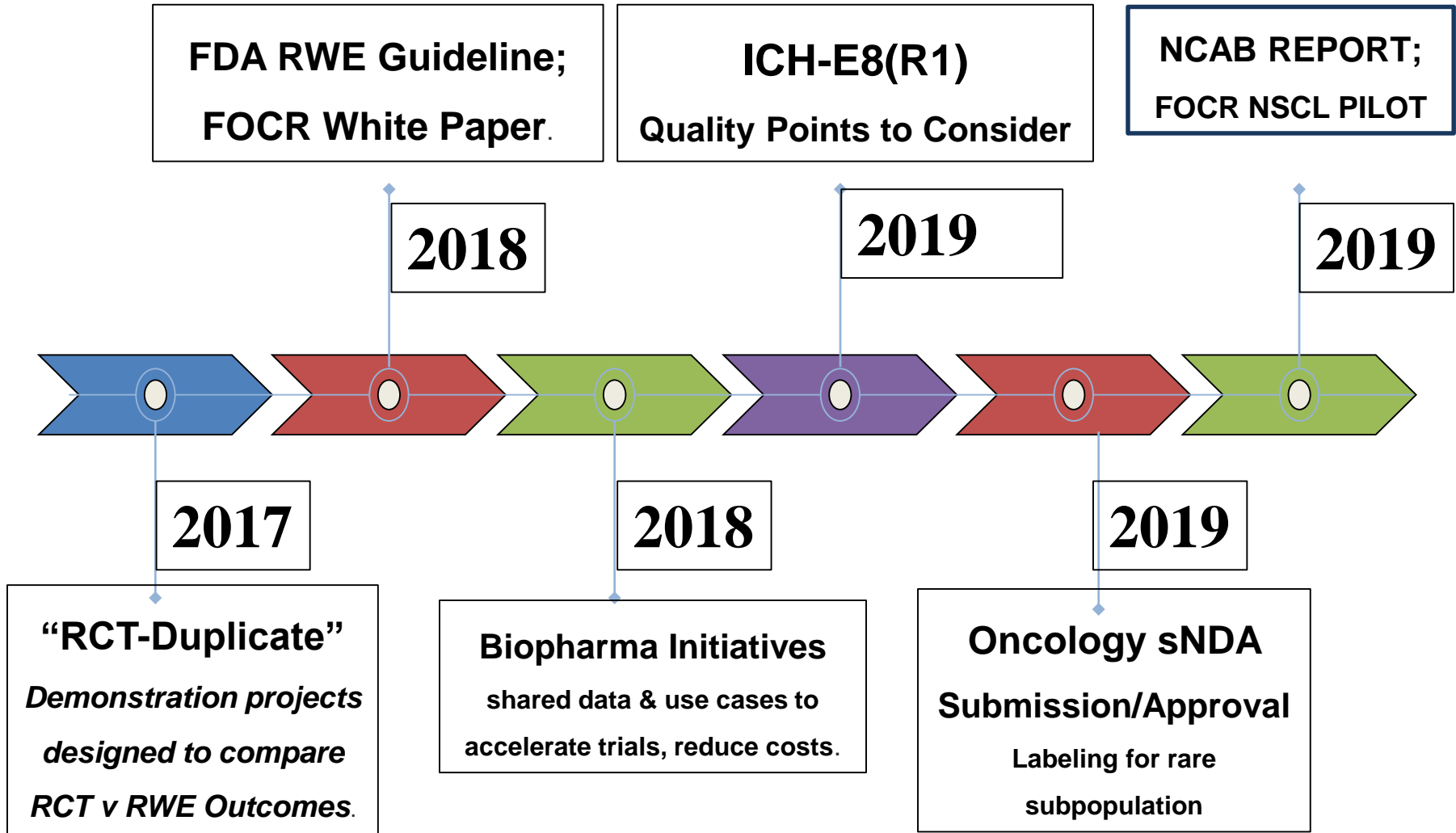
**“It may be possible for a single clinical study to use both internal and external control subjects...supplementing internal control group.”**

**- Source: ICH E8(R1) General Considerations for Clinical Trials**

# EMERGING EXPERIENCES

Top- Public Organizations

Bottom- Industry and NIH-Industry Partnerships

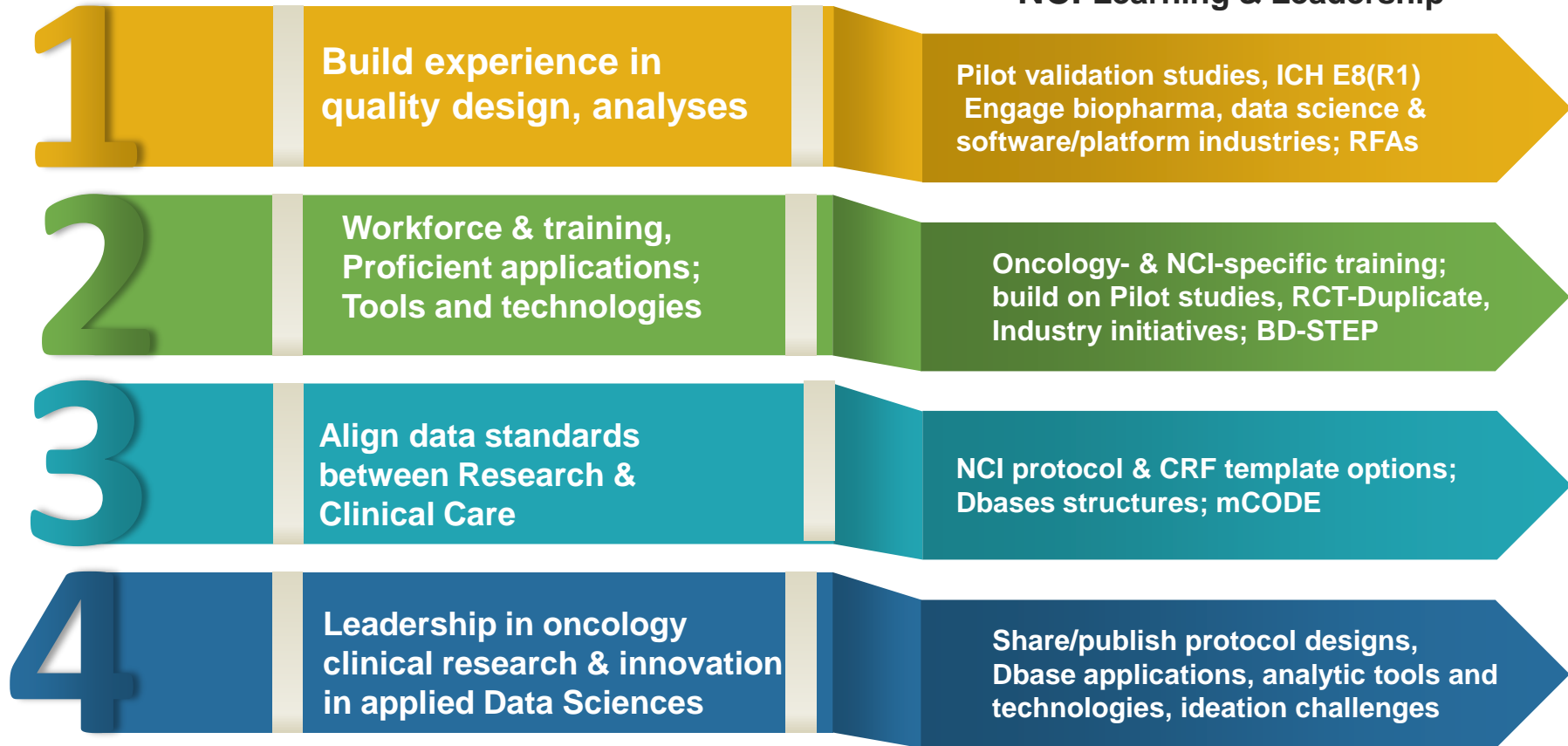


Excerpts represent multiple, recent initiatives

# NCAB Data Science Report & Opportunities for NCI

## NCAB Recommendations Data Sciences Report

## Actionable Opportunities NCI Learning & Leadership



# QUALITY OF DESIGN - POINTS TO CONSIDER

ICH-E8(R1) framework for quality, training, multi-regional harmonization

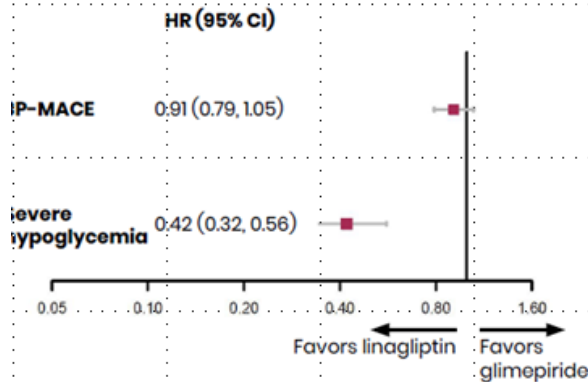
- **Pre-specified:**
  - **Data sources**
  - **Analytic platforms & plans**
- **Feasibility, appropriateness**
- **Propensity matching**
- **Relevant/justified values**
- **Transparency, audit-ready**
- **Bias assessment & reduction**



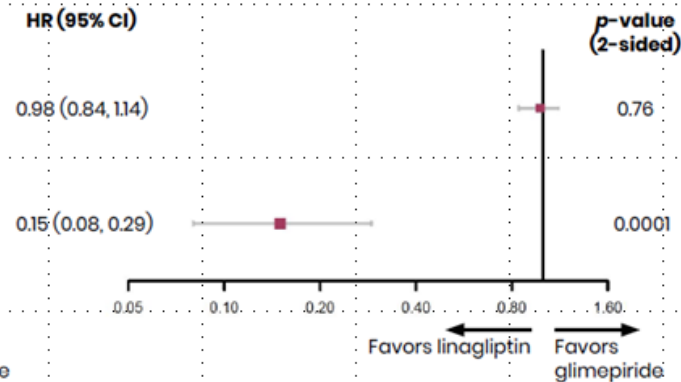
# LEARNING FROM NIH “RCT-DUPLICATE”

Quality Points to Consider, design, software application, analytic plan can support Oncology/NCI pilot studies, training, innovation

RCT DUPLICATE's RWE Prediction



The CAROLINA Trial



Source: As presented at ADA on June 10, 2019 in a session called "The CAROLINA Trial--First Results of the Cardiovascular Outcomes Trial Comparing Linagliptin vs. Glimepiride", moderated by Drs. Julio Rosenstock and Nikolaus Marx.

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SOURCE: RCT-DUPLICATE program in diabetes indications.  
Data presented at ADA meeting, June 10, 2019

# Summary - External Clinical Data

- **HEALTHCARE DELIVERY SOURCES**
  - Promising, rapid growth of validation/pilot studies, analytic technologies, quality guidances enabling international harmonized regulatory actions
  - Largely Real World Data outside of oncology rare indications/combinations
- **RESEARCH DATA SOURCES**
  - Few initiatives ongoing to support oncology-specific working practices
- **OPPORTUNITIES FOR NCI**
  - Aligns with NCAB recommendations to expand NCI data sciences, includes training, workforce development, applicable technologies
  - Supports international harmonization & partnership with global stakeholders



# Discussion Topics – External Clinical Data

- **Appropriate applications**
- **Quality considerations**
- **Pilot studies of external data & analytic platforms**
  - **employing research data from accessible dbases**
- **CTAC subgroup for further evaluation**