Real World Evidence
Collaboration and Convergence for Change

*Big Data, Digital and Tech—and Real World Applications and Implications for Industry*

Jennifer L. Wong
Senior Director, Real World Evidence Strategy & Alliances, Global Medical Affairs, AstraZeneca

48th Annual Conference (Vienna, Austria)

09 May 2019

The opinions and information presented in this document are my own and do not necessarily reflect the official views and policies of AstraZeneca.
Ambition of RWE

Higher quality and more comprehensive, efficient generation of evidence in order to make faster, better, earlier and more targeted discovery, access, and benefit-risk decisions

Create a holistic picture of the patient journey through the health care system through the collection, generation, utilization and analysis of real-world data to support RCTs

Build ecosystems and innovate through collaborations and strategic alliances to better serve patients, providers, payers, and partners for improved outcomes
Patient-Centered Science
Big Data to ‘N of 1’

- Pharma data
- Laboratory or biomarker data
- Mortality data
- Social media data
- Pharmacy data
- Hospital data
- Claims data
- Survey
- Electronic health and medical records
- Disease registries
- Consumer data
- Wearables
Complex, Converging Forces Changing Healthcare

The five disrupters

- Changes across entire ecosystem
- Disruption and convergence across people, process, data, technology
  - Data Science, Digital, AI/ML, Blockchain, Analytics, ‘Omics’, Value & Reimbursement
  - Educated and Empowered Patients!
- Need to understand various stakeholder needs, perspectives; generate evidence to improve outcomes, inform value, enable access, better lives
Growing Need to Generate Real-World Evidence

• Healthcare decision-makers are interested in clinical decisions and the evidence supporting those decisions

• Understanding stakeholders and decision-maker perspectives is key to generating the right evidence

- Is this the best treatment for my patients?
- How does this treatment affect mortality?
- Is this treatment cost-effective?
- What treatment is best for me?
- Does this treatment work? How safe is it?

Healthcare professional  Hospital  Payer  Regulator  Patient
Real-World Data vs Real-World Evidence

**RWD** are data relating to patient health status and/or to the delivery of health care collected from a variety of sources:

- Data from observational studies
- Electronic Health Record (EHR)
- Hospital/insurance claims/billing
- Patient-generated/reported information (PRO)
  (e.g. wearables, mobile, sensors)

**RWE** is the clinical evidence on the use and potential benefits or risks of a medical product derived from analyses of RWD:

- Early Access Programmes
- Post-Authorization safety study
- Pragmatic clinical trials
- Observational studies
- Non-interventional studies
- Registry studies
FDA Framework for RWE: Reliability and Relevance

Is the RWD selected fit for use to generate data for product effectiveness decisions?
- ✓ New or modified indications, expand labels for approved drugs
- ✓ Post-approval study requirements

Is the study design used to generate RWE able to provide robust scientific evidence to help address the regulatory question?
- ✓ Inform coverage decisions, develop guidelines and decision-support tools for use in clinical practice

Is the execution of the studies generating RWE able to meet FDA regulatory requirements?
- ✓ Support clinical trial designs and observational studies for innovative treatment approaches e.g. randomized designs using RWD, non-randomized, single-arm with RWD control, etc.

“As the breadth and reliability of RWE increases, so do the opportunities for FDA to make use of this information.”

Scott Gottlieb, FDA Commissioner
National Academies of Science, Engineering, and Medicine,
Examining the Impact of RWE on Medical Product Development, September 19, 2017
FDA’s Guidance on Use of Artificial Intelligence

Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

Discussion Paper and Request for Feedback
The healthcare environment in the US is changing, with increasing emphasis on value for the patient, provider and payers.

Oncology drugs often receive regulatory approval based on a limited number of patients and follow-up in registrational trials, making the need for RWE even more acute for specialty care portfolios.

Healthcare providers, patients and payors need to have high-quality data to inform treatment decisions relative to value. This will be critical to patient-centric value driven care in the future.
Validity, Generalizability, Reliability and Predictiveness

Only 3% of adult patients with cancer in the US enroll in oncology clinical trials\(^1\)

Cancer diagnosed in 1.7 million people in the US in 2015

97% of patient data locked away in unconnected files and servers

Patients enrolled in oncology clinical trials often are not representative of the real world population

- 25% of patients in clinical trials are aged ≥ 65 years
- 61% of patients in a real world setting are aged ≥ 65 years
- 40% of patients with kidney cancer were not healthy enough to qualify for the trials that supported the approval of their treatments
- 90% of patients in National Cancer Institute trials are white
- 77% of the USA population is white

A Call to Action to Modernize our Approaches

Reconstruction of His Majesty’s ship Salisbury. Credit: *Journal of the Royal society of Medicine*

https://www.vinceandassociates.com/blog/a-historical-timeline-of-clinical-trials
Big Data… Grows Bigger by the Day

About 3 quintillion bytes of data per day

How can RWE enrich RCT design?

**RCTs** provide evidence on efficacy and safety, and remain important for securing regulatory approval.

**RWE can complement RCTs** by assessing a wider range of outcomes representative of everyday clinical settings.

---

**How can RWE add value to clinical trials?**

- Identify diseases or indications that represent a substantial burden
- Characterize patient populations
- Use RWD as a synthetic control arm
- Target and design clinical trials (e.g. optimize inclusion/exclusion criteria)
Fit for Purpose: When and how to rely to RWE

- What is the clinical question of interest?
- When is it unethical to randomize patients with no other available treatments to placebo?
- Is it possible to do a single arm study?

<table>
<thead>
<tr>
<th>RCT</th>
<th>Database Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Randomization</td>
<td>No randomization</td>
</tr>
<tr>
<td>Controlled measurement</td>
<td>Non-standardized observations</td>
</tr>
<tr>
<td>Seeming simplicity of design</td>
<td>Seeming complexity of design</td>
</tr>
<tr>
<td>A priori confidence in causal conclusions</td>
<td>A-priori confidence in applicability to target population</td>
</tr>
</tbody>
</table>
RWE informs decisions across the product life cycle

- What is the disease epidemiology and unmet medical need?
- What is the patient pathway from diagnosis through treatment?
- What are the characteristics of the patient population?
- How feasible is the clinical protocol?
- What is the safety and effectiveness in the real world?
- Is this product cost-effective?
- How do we measure the value of this product?
- What is the overall outcome for the patient?
- How is the product used in the real world?

Adapted from Khosla S et al. F1000Res 2018;7:111
Real world applications for different stakeholder groups

Clinical Outcomes and Effectiveness
- Outcomes research
- Comparative effectiveness
- Subpopulation evaluation
- Patient-staging/decision trees
- Clinical trial recruitment and modelling

Adoption and Use
- Therapy adoption and diffusion
- Therapy and technology assessment
  - Biomarker testing
- Profiling for providers and patients

Value and Reimbursement
- Payer value proposition
- Pricing strategy
- Contracting strategy/evaluation
- Payer messaging
- Source of business

Clinical Trial Design and Execution
- Reduce clinical trial cycle time
- Screen patients and clinical trials based on predefined eligibility criteria
- Increase awareness of existing clinical trials to support patients’ road to health optimally
- Provide a list of patients for a trial and a list of trials for a patient
- Recruit new investigators
- Provide member ‘kits’ to support investigator activities, partnered with leading CROs
Sample of Real World Data, Digital & Tech Partnerships

- All of Us (NIH/Precision Medicine Initiative)
- Apple ResearchKit and Stanford (CVD)
- Verily and Sanofi (Diabetes)
- Amazon, JP Morgan, Berkshire Hathaway (“Haven”)
- Aetion, Harvard Medical School/Brigham Women’s Hospital and FDA (RWE platform)
- Science 37 and Novartis (NASH, site-less trials)
- IBM and Pfizer (Blockchain technology)
- Syapse and Amgen (Precision Oncology)
- Palantir and Merck (“Syntropy”) (Oncology)
- 23andMe and GSK (Genetics)
- Flatiron, Foundation Medicine, Roche (Oncology)
- AHA, Verily, AstraZeneca (CVD)
- HealthVerity marketplace/data exchange
- ASCO/CancerLinQ, Tempus, Concerto HealthAI and AstraZeneca (Oncology)
Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors

Convergence of Titans

Leading Companies - Advanced AI in Healthcare and Drug Discovery / 2019 Q1

AI-Companies

Pharma Corporations

Insilico

Tech Corporations

Numerate

Investors
Pharma-Tech Collaborations: Learning Healthcare Ecosystems, Platform-Based Approach

RWE platforms to serve cross-organizational needs at scale
“The goal is to get the right treatment to the right patient for the right reason, in order to get the right outcome for the right cost.

Andrew von Eschenbach, former FDA Commissioner