Moderated Discussion:

The Future of Real-World Evidence: Promising Possibilities and Perils Ahead

*Moderated by Lisa LaVange*

*Panelists: John Buse, Cindy Girman, Til Stürmer, & Bryce Reeve*

May 7, 2019
Moderated Discussion: The Future of Real-World Evidence: Promising Possibilities and Perils Ahead

John B. Buse, MD, PhD
Verne S. Caviness Distinguished Professor
Chief, Division of Endocrinology
Director, NC Translational and Clinical Sciences Institute
Executive Associate Dean, Clinical Research
University of North Carolina School of Medicine
RWE is here and now for safety

- Virtually every class of diabetes medications has one or more safety warnings, many reflected in prescribing information from RWE.

Pioglitazone and bladder cancer – HR 0.86 to 4.3.

Need better methods and consensus on reporting
RWE for efficacy is evolving

Data are from the Association of British Clinical Diabetologists (ABCD) Nationwide Audit

Baseline BMI (kg/m²)

Mean change from baseline

HbA₁c (%)
Body weight (kg)

LEAD programme excluded patients with BMI >40 kg/m²

BMI, body mass index
Data are from the Association of British Clinical Diabetologists (ABCD) Nationwide Audit
Fit for Purpose

Tenet #1
No database can possibly answer all research questions, even within a specific disease area.
How is RWD Used in Drug Development?
Tenet #2

Whether RWD sources can be used to address a research question depends on:

- the key elements of the question
- ultimate use of the data

Research Question Elements

PICOTS Framework

- Population
- Intervention
- Comparator (if relevant)
- Outcomes
- Timing
- Setting (outpatient, inpatient, specialty clinic)

……and key confounders

Use of Results

- Internal planning of trials
- Natural history data for context for clinical data
- Historical or concurrent control group for a trial
- CER
- pRCT
- PASS

Regulatory decisions
Many paths ahead....
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Insights from Pharmacoepidemiology

Til Stürmer, MD, MPH, PhD
Nancy A. Dreyer Distinguished Professor and Chair
Department of Epidemiology
UNC Gillings School of Global Public Health
University of North Carolina at Chapel Hill
Sackett DL. How to read clinical journals: I. Why to read them and how to start reading them critically. CMAJ 1981

Miettinen Stat Med 1983: ”control of the indication … commonly infeasible”


EBM working group JAMA 1992: “The criteria should not be presented in such a way that fosters nihilism”
Active-Comparator New User Design

- **Non-Active Comparator New User Design:** Confounding by Indication (Obesity)
  - Obese → Insulin
  - Glargine → CRC
  - NPH → CRC

- **Active-Comparator New User Design:** No Confounding by Indication (Obesity)
  - T2 Diabetes
  - Normal weight → No insulin → CRC
### Table 4—Effect of BMI on channeling between initiating glargine versus initiating NPH: external validation studies

<table>
<thead>
<tr>
<th>MGH</th>
<th>Glargine</th>
<th>NPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>574</td>
<td>412</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD*</td>
<td>32.7 ± 7.53</td>
<td>32.4 ± 8.43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI (kg/m²), n (%)</th>
<th>Glargine</th>
<th>NPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;19</td>
<td>4 (0.7)</td>
<td>8 (1.9)</td>
</tr>
<tr>
<td>19 to &lt;25</td>
<td>77 (13.4)</td>
<td>67 (16.3)</td>
</tr>
<tr>
<td>25 to &lt;30</td>
<td>150 (26.1)</td>
<td>105 (25.5)</td>
</tr>
<tr>
<td>30 to &lt;35</td>
<td>146 (25.4)</td>
<td>104 (25.2)</td>
</tr>
<tr>
<td>35 to &lt;40</td>
<td>114 (19.9)</td>
<td>64 (15.5)</td>
</tr>
<tr>
<td>40 to &lt;45</td>
<td>45 (7.8)</td>
<td>36 (8.7)</td>
</tr>
<tr>
<td>≥45</td>
<td>38 (6.6)</td>
<td>28 (6.8)</td>
</tr>
</tbody>
</table>
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Bryce B. Reeve, PhD
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Professor, Population Health Sciences
Professor, Pediatrics
Duke University School of Medicine
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The Future of RWE: Promising Possibilities and Perils Ahead

1. Stakeholder-driven
   • Feasible Study Designs
   • Patient-Centered
   • Clinically-Relevant

2. Diverse Samples (enriched by those who are typically under-represented)
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3. Multi-Methods Approaches
   - Data from different sources (e.g., self-report, passively collected data)
   - Quantitative and Qualitative data

4. Longer Follow-up data
Questions & Discussion