phuse·hybrid

Single Day Event

Rashmi G Jain, Lead Statistician,
Novo Nordisk

Utilize Real world Evidence (RWE) to coverage decisions in 10 different evidence types

Internal

Disclaimer

The view and opinions expressed in this presentation are the views, thoughts, and opinions belonging solely to the presenter, and not necessarily to the presenter's employer, organization, committee or other group or individual. This presentation is intended to exhibit, how to use RWE to verify different evidence categories with case studies. No data or confidential information belonging to Novo Nordisk has been used in this presentation.

Internal

Abstract

The use of electronic gadgets to gather and store huge amounts of health-related data has been speedily increasing. This real-world data (RWD) holds potential to allow us to better design and conduct Real World Evidence (RWE) studies in the health care settings to answer questions previously thought impracticable. Real world evidence will be helpful to investigate below mentioned 10 important questions like Adherence/persistence of treatment, Attitudinal/perceptions research, burden of disease, cost effectiveness, epidemiology, healthcare resource utilisation, patient profiles, quality of life, real world effectiveness and real-world safety. These analysis will be helpful for better healthcare decision making.

In this presentation will evaluate the use of RWE throughout the drug development process. Exploring different potentials of RWE with help of different case studies. I will also cover different stat analysis methods and possible outcomes of case studies. Will understand gaps in RWD Sources and limitations with RWE analysis.

Internal

Background: What is Real World Evidence (RWE)?

Real World Evidence measures healthcare outcomes, behaviour and resources associated with treatments **outside of a conventional clinical trial setting**, relevant for Industry, Regulatory, payers, HCPs and Patients*.

Real World Data (RWD)

Patient-level data not collected in conventional randomized controlled trials

Real World Insights (RWI)

Insights generated from RWD for scientific or commercial purposes

Real World Evidence (RWE)

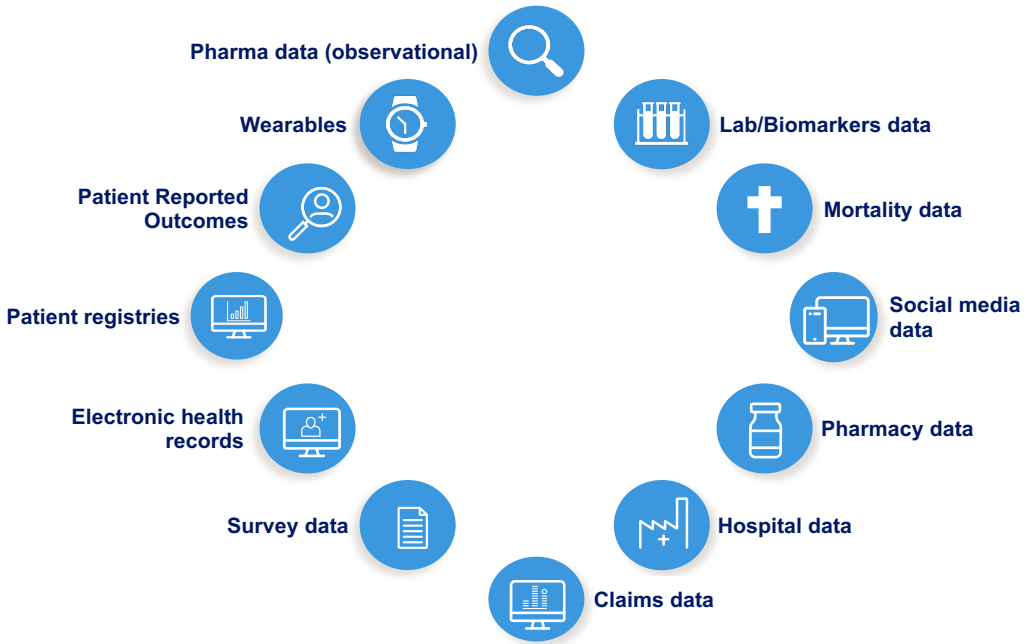
RWI used with the intention to support a claim or belief to produce evidence for multiple stakeholders

*The ISPOR real-world data task force report. Value Health 2007;10:326-35. ISPOR: International Society For Pharmacoeconomics and Outcomes Research Market Access, Novo Nordisk (2015) QuintilesIMS

RWD data sources

The traditional use of RWE

Choose a data source you have available and that is fit for purpose.



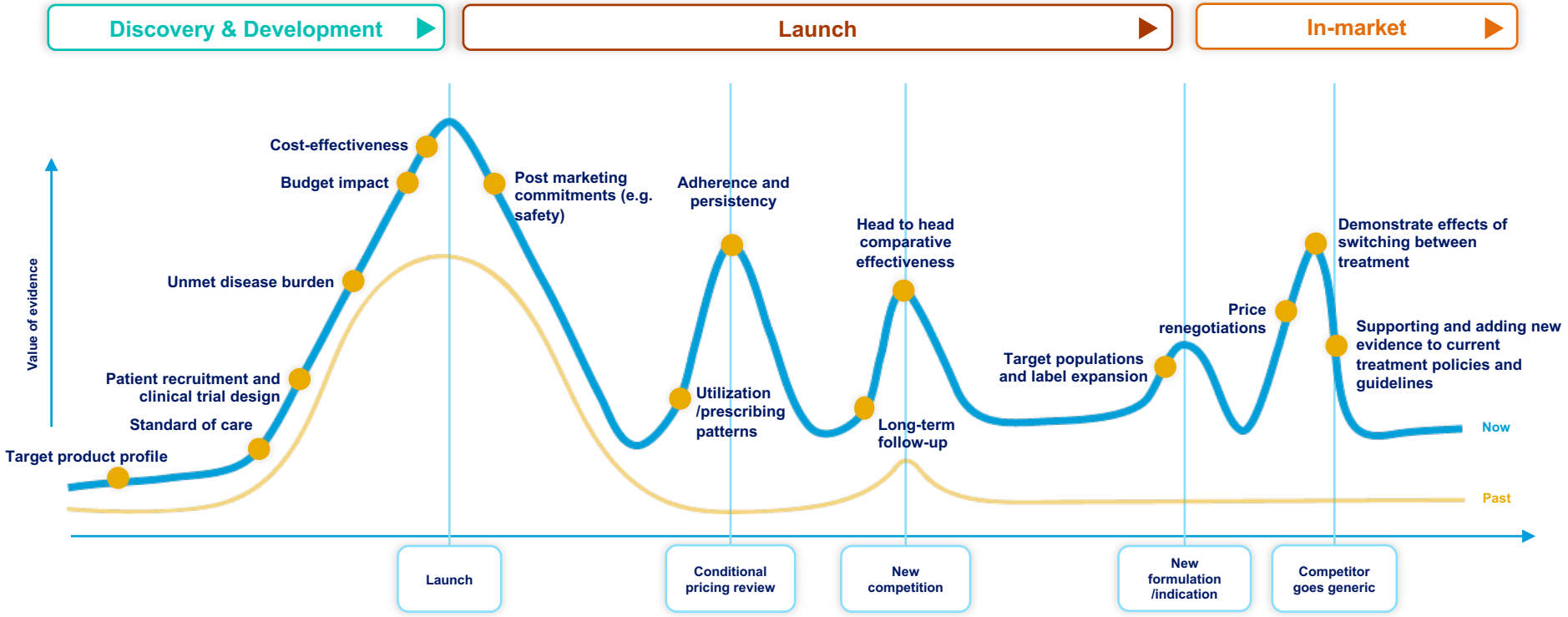
Understanding of the real world situation of a disease

Supplement to evidence from RCTs

Monitoring of adverse events

Long-term outcomes and effectiveness

RWE across the product lifecycle



Sources
1. Roberts & Ferguson 2020 Real-World Evidence: Bridging Gaps in Evidence to Guide Payer Decisions
2. Khosa et al 2018 Real world evidence (RWE) - a disruptive innovation or the quiet evolution of medical evidence generation?
3. Sax et al. 2016 Value-based pricing and drug development productivity
4. Hampson et al. 20018 Real World Evidence for coverage decisions: opportunities and challenges

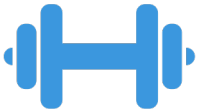
Now - Today: Additional evidence has to be generated to support access and market maintenance along the product`s life cycle.
Past - Total evidence of a drug was evaluated out of RCT.

RCT: Randomised controlled trial, RWD: Real world data

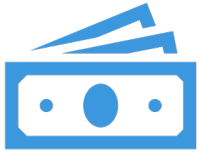
Evidence categories

Adherence/persistence of treatment

Attitudinal/perceptions research



Burden of disease



Cost effectiveness

Epidemiology

Healthcare resource utilisation

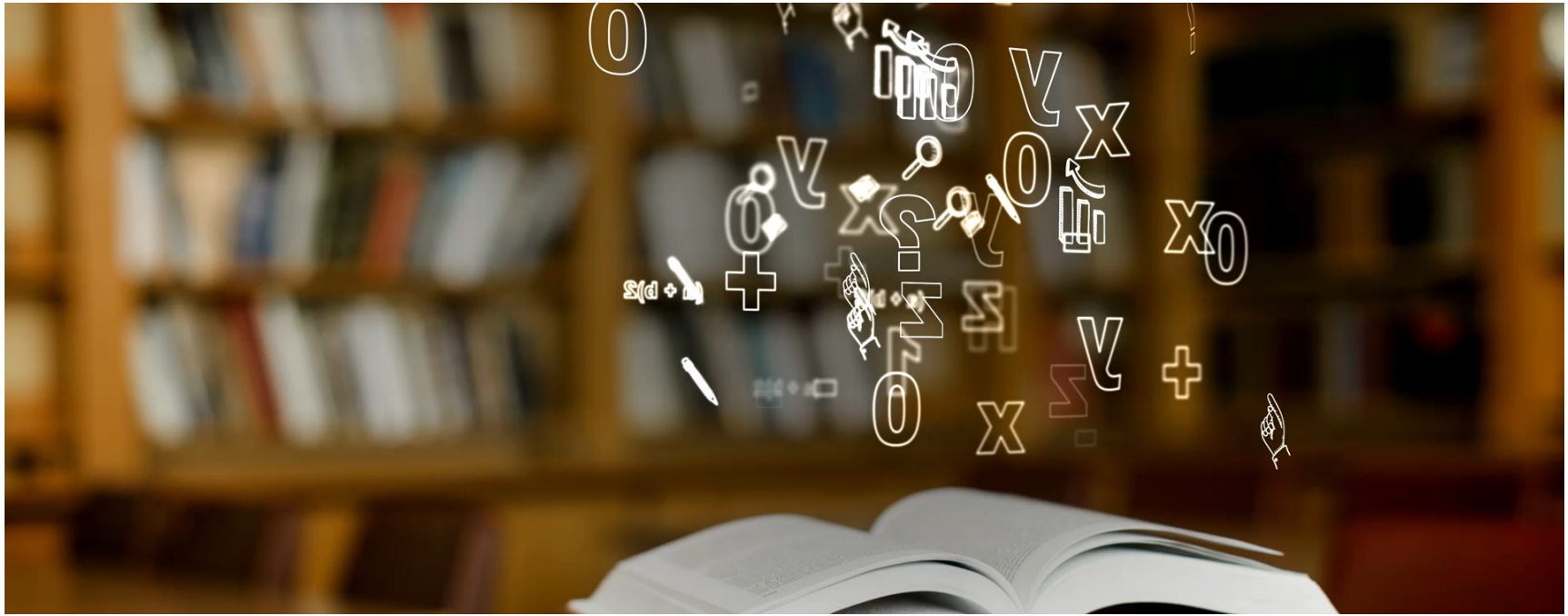
Patient profiles

Quality of life

Real world effectiveness

Real world safety

Case studies



	Evidence of adherence/persistence of treatment	Evidence of Attitudinal/perceptions research
Evidence gap	• Investigating if switching to new device improved treatment experience in pediatric patients.	• Explore physician experiences and treatment satisfaction with insulin in clinical practice.
Statistical methods	• Questainnair data : compared preference, self-reported adherence, satisfaction, perceived ease of use, and device subjective benefits was used. • Differences between participants who preferred newdevice and those who did not were tested using a t-test.	• Data based on survey with physicians treating people with type 1 or type 2 diabetes. General practitioners and specialists, was used. • To study the difference in responses between GPs and specialists, significance testing was done at a 95% confidence level. • For some questions, significance testing at a 95% confidence level was calculated between T1D and T2D to study the differences in physician responses for the two patient groups.
Study results	• Mean score shows significantly more patients preferred and were more satisfied with new device vs. previous device. • Participants reported greater perceived ease of use and fewer missed injections.	• The main prescription drivers for insulin, versus other treatment, were faster onset of action, improved postprandial glucose (PPG) control, and dosing flexibility. • Most physicians were more satisfied with insulin than other treatment.
Data impact	• Results suggest that improvements in device features could be associated with improved treatment experience.	• Physician experiences Using insulin have been positive, and better PPG control. More concerned about postprandial hyperglycemia with other treatment. • Difficulty in taking the dose at the right time was a concern many patients

Internal

	Evidence of Burden of disease	Evidence of Cost effectiveness
Evidence gap	• To identify patient and caregiver insights on the unique challenges of patients with haemophilia and obesity (PwHO).	• Explore the relationship between target joints and direct medical costs for persons with severe haemophilia.
Statistical methods	• Descriptive statistical analysis was performed for group surveyed (PwHO, SP and CG). Further analysis was performed for preidentified subpopulations. These included self-reported (SR) obesity (OB) or overweight (OW), cBMI, haemophilia severity, age, current treatment regimen, historical treatment, current relationship status, current employment, presence of haemophilia-related comorbidities and geographic region.	• Data collected from the 'Cost of Haemophilia across Europe - a Socioeconomic Survey' (CHESS) study. • The marginal effect of the presence of one or more target joints on NDDCs was assessed using a generalized linear model (GLM). • The log-link function in combination with a gamma distribution is used to estimate medical costs. A confirmatory analysis of the family and link functions was conducted using the modified Park test.
Study results	• PwHO, spouse/partners and caregivers showed awareness of general and haemophilia-specific consequences of excess body weight. • Most tried general approaches to improve eating, increase activity with little success and desire more education on weight management and more details on specific actionable recommendations distributed through existing haemophilia channels.	• Mean adjusted non-drug related direct costs (NDDCs) for persons with no target joints were less than for persons with one or more target joints is proven with statistically significance
Data impact	• These insights will better inform the creation of weight-loss programmes for PwHO community.	• Show that the presence of one or more target joints has a significant impact on non-drug related costs for patients with severe haemophilia.

Internal

	Evidence of Epidemiology	Evidence of Patient profiles
Evidence gap	• Cardiovascular disease and risk factor prevalence in Type 2 diabetes	• To understand the patient view and preference for an oral GLP-1 RA, when launched, compared to injectable GLP-1 RA products in the market.
Statistical methods	• Simple summary statistics used to describe the prevalence and distributions of disease and risk factors. • Counted risk factor thresholds each person had: HbA1c ≥ 7%, SBP > 130 mmHg, total cholesterol ≥ 5 mmol/l or BMI ≥ 30 kg/m2, or current smoking. • Logistic regression was used to quantify the differences in risk factors in those with and without prior CVD.	• Choice tasks tested preference between hypothetical profiles, preference between profiles with actual trial data, and willingness to initiate treatment. Relative importance of attributes was determined using conditional logit regression. • The analyses of hypothetical choice set results used a conditional logit regression model to regress stated preferences, in order to determine the crude relative preference for each attribute.
Study results	• Diabetes drugs used was highest in the 50-70-year age groups. • The number of diabetes drugs used was similar in those with and without CVD, but the use of insulin was higher in those with CVD compared with those without. Overall, very few of those with CVD and those without were on a GLP-1 agonist and SGLT2 inhibitor.	• Orally administered medication were preferred by more patients than injectable profiles. • Respondents were more willing to initiate treatment with an orally administered medication.
Data impact	• There continues to be a high prevalence of CVD among people with Type 2 diabetes and a high level of unmet need for risk factor control. • Substantial scope for reducing the excess risk of CVD in diabetes through improved management of known risk factors.	• Product launch in market by demonstrating the benefits of an oral GLP-1 RA showcasing patient preference for the formulation alongiside RCT data which shows product stronger effectiveness when compared to current oral alternatives.

Internal

	Evidence of Healthcare resource utilisation	Evidence of Quality of life
Evidence gap	• Understanding, the total and breakdown of excess costs due to obesity in detail will allow for a quantification of healthcare resource utilisation.	• To deepen understanding of impact of hemophilia B adults and children relationship with their families
Statistical methods	• Annual healthcare cost burden was estimated using a Clalit cost compendium, which is a summation of the reported total costs associated with the use of all inpatient and outpatient visits, procedures, diagnoses, medication purchases, and laboratory tests. • A linear model was used to assess the independent association of age and BMI group with annual healthcare cost burden. The log transform was used to make annual healthcare cost burden conform close to the normal distribution. Multivariate models included additional covariates. Individuals aged 25-29 with a healthy weight defined as the reference group.	• Data from survey, which was composed of 100+ multiple-choice and rating scale questions used. • No statistical comparisons between the groups were performed because they were convenience samples, and statistical tests would have been underpowered. • Data are presented as percentages of respondents
Study results	• Adjusted linear regression showed a significant relationship between age and BMI group with costs. • The annual cost increased as both age and BMI increased, with the highest cost among individuals aged ≥70 with class III obesity	• Mental health concerns were also substantial in Hemophilia B patients, with many reporting moderate to extreme anxiety or depression, experienced a negative response to disclosure or impact on relationships, Many were in relationships and looked toward having children in the future.
Data impact	• Total healthcare costs were significantly higher for people with obesity compared to people without obesity. • The average costs increased with higher age and higher BMI.	• The impact of severe hemophilia on relationships has been reported. Mild to moderate hemophilia B also significantly influences relationships of affected men/women and boys/girls, especially in disclosing their diagnosis, selecting a partner and feeling bullied by peers/colleagues.

Internal

	Evidence of Real-world effectiveness	Evidence of Real-world safety
Evidence gap	• With a growing portfolio of GLP-1 RA products entering the market it is important to understand how switching between GLP-1RAs impact outcomes, and what the switching patterns are.	• Analyze ability of new treatment to maintain glycaemic control whilst avoiding hypoglycaemia.
Statistical methods	• Data collected from EHR and prescription data. • Mean HbA1c and weight changes from baseline were estimated using an analysis of covariance model. Covariates used are demographic factors and clinical history (baseline HbA1c, baseline weight, CVD in the past 1 year, insurance type and Time from baseline assessments to index date and time from baseline assessments to index date squared were both included in the model to control for non-linearity in effect based on time.	• Data collected from prospective, non-interventional, open-label, single-arm study. • Non-severe hypoglycaemia was assessed in the 4-week period prior to initiating new treatment and in the 4-week period before EOS or discontinuation using negative binomial regression.
Study results	• Switching to once weekly GLP-1 RA from another GLP-1 RA led to significant improvement in both glycaemic control and weight loss. • The beneficial effect of switching to once weekly GLP-1 RA on glycaemic control was significant at 6 months and maintained at 12 months.	• Tendency towards less risk of hypoglycaemia. • No unexpected safety findings were observed..
Data impact	• Helpful for clinical decision making when patients are being switched between GLP-1 RA products	• Use locally for scientific exchange and for commercial promotion to the extent that local regulations allow.

Internal

Summary (1/2)

The traditional usage of RWE was considered only for:

- Understanding of the real-world situation of a disease
- Supplement to evidence from RCTs
- Monitoring of adverse events
- Long-term outcomes and effectiveness.

Currently RWE used and can be used in the future to drive value across the entire product cycle.

Internal

Summary (2/2)

Through case studies we learnt, RWE was helpful to investigate 10 important evidence categories:

- Adherence/persistence of treatment - to investigate switching to new treatment improve patient experience
- Attitudinal/perceptions research - exploring users experience and treatment satisfaction with treatment
- Burden of disease - identifying unique challenges of patients with different diseases
- Cost effectiveness - exploring relationship between sever disease conditions and medical costs
- Epidemiology - exploring risk factors associated with two diseases
- Healthcare resource utilisation - exploring patients' response to improved treatment compared with current treatment
- Patient profiles - understanding detailed cost break down to quantify health care resource utilisation
- Quality of life - Understanding disease impact on patients' relation with their family
- Real world effectiveness - to understand switching treatment patterns between treatments
- Real-world safety - analysing safety of new treatment

RWE analysis helps to take better healthcare decisions.

Internal

Reference

Full article: The role of growth hormone device optimization in patient-reported outcomes: real-world evidence from South Korea (tandfonline.com)

Full article: A survey of physician experience and treatment satisfaction using fast-acting insulin aspart in people with type 1 or type 2 diabetes (tandfonline.com)

Awareness, Care and Treatment In Obesity maNagement to inform Haemophilia Obesity Patient Empowerment (ACTION-TO-HOPE): Results of a survey of US patients with haemophilia and obesity (PwHO) and their partners and caregivers - Croteau - 2020 - Haemophilia - Wiley Online Library

The relationship between target joints and direct resource use in severe haemophilia | Health Economics Review | Full Text (biomedcentral.com)

Cardiovascular disease prevalence and risk factor prevalence in Type 2 diabetes: a contemporary analysis - McGurnaghan - 2019 - Diabetic Medicine - Wiley Online Library

A comprehensive descriptive assessment of obesity related chronic morbidity and estimated annual cost burden from a population-based electronic health record database | Israel Journal of Health Policy Research | Full Text (biomedcentral.com)

Preference for Oral and Injectable GLP-1 RA Therapy Profiles in Japanese Patients with Type 2 Diabetes: A Discrete Choice Experiment - PubMed (nih.gov)

Mild-severe hemophilia B impacts relationships of US adults and childr | PROM (dovepress.com)

Outcomes in GLP-1 RA-Experienced Patients Switching to Once-Weekly Semaglutide in a Real-World Setting: The Retrospective, Observational EXPERT Study | SpringerLink

A Real-World, Prospective, Non-interventional Study of Adults with T2D Switching to IDegAsp from Glargine U100 or U300 in Japan | SpringerLink