



Healthcare Decision-making in the Era of Real World Evidence

Presenters:

Prof. Muhammad Mamdani

Mo Amin

Topics Covered



1. What is RWE?
2. The Value of Real World Evidence (From Patient, Payer, Provider perspectives: Both Global & regional Perspectives)
3. Leveraging real world data to turn evidence into impact? (Global & Regional case studies)
4. Real-world evidence; A Snapshot of the Middle East
 1. ME Data Rich
 2. RWE & RCTs minimal contribution in ME
 3. Challenges in the Middle East
 4. Opportunities in the Middle East
5. Bridging the Evidence gap in the Middle East
6. Discussion points

Mo Amin

Prof.
Muhammad
Mamdani

Panel
Discussion

Panel Discussion

- Panel members are as follows:

- Prof. Muhammad Mamdani

- Director of Li Ka Shing Centre for Healthcare Analytics Research and Training (CHART), Toronto, Canada

- Dr. Mirna Matni

- Medical Control Department, National Social Security Fund, Beirut, Lebanon

- Dr. Fatma Maraiki

- Oncology Specialist Clinical Pharmacist, KFSH&RC, Riyadh, Saudi Arabia

Real World Evidence (RWE): Introduction

Mo Amin, PhD, MD

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Disclosures

- Amgen Inc. employee
- Owns Amgen stocks

What is RWE?

What is RWE?



Real-World Data (RWD) is defined as data on patients' health status, and/or healthcare delivery in real-world settings. They are derived from a number of sources and describe a heterogeneous patient population



Analysis of RWD generates Real-World Evidence (RWE)



RWE in turn, can generate meaningful insights into unmet needs, interventional pathways and the clinical and economic impact on patients and healthcare systems

Real-World Data

Real-World Evidence

Insights

Solutions Decisions

What is RWE?

01

RWE can supplement Randomized Control Trials (RCT) data

02

RWE impacts Healthcare Decision-Making

- Regulatory
- Disease Management

Types and Sources of RWD

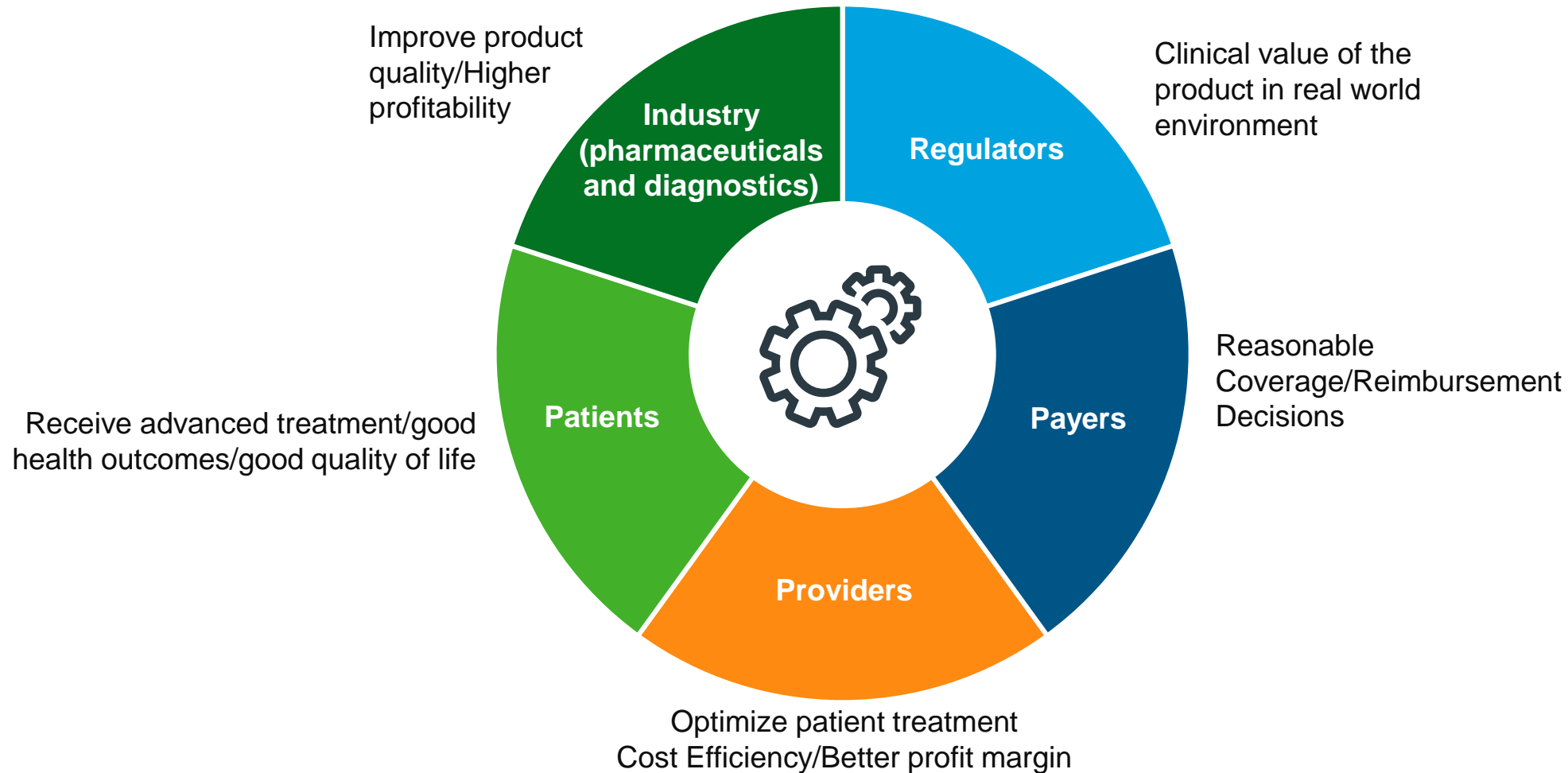


Real World Data (RWD) are derived/combined from several sources

- Pragmatic Clinical Trials
- Patient Registries
- Administrative Claims Database
- Surveys (patients/ providers)
- Medical Records
- Prescription Records

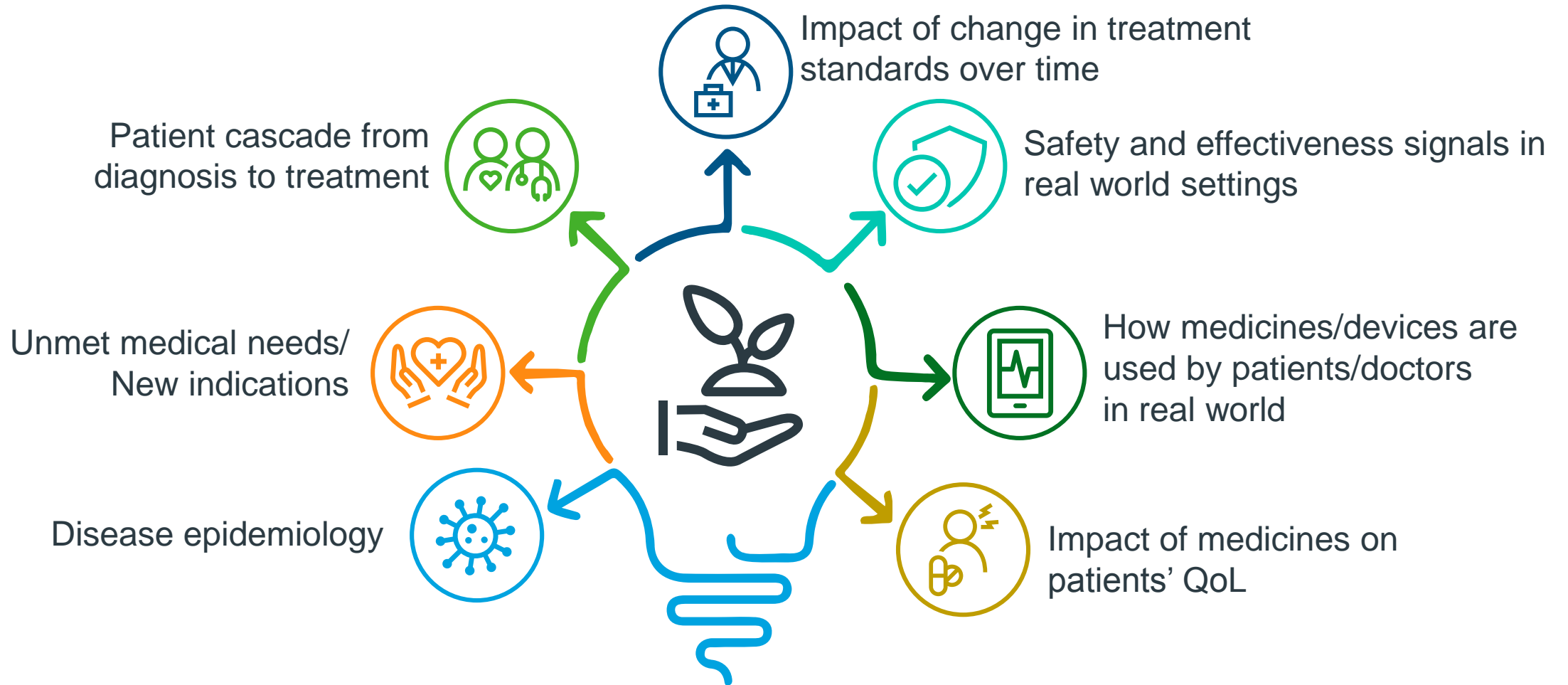
The Value of Real World Evidence

RWE is Valuable For All Stakeholders of a Healthcare System...

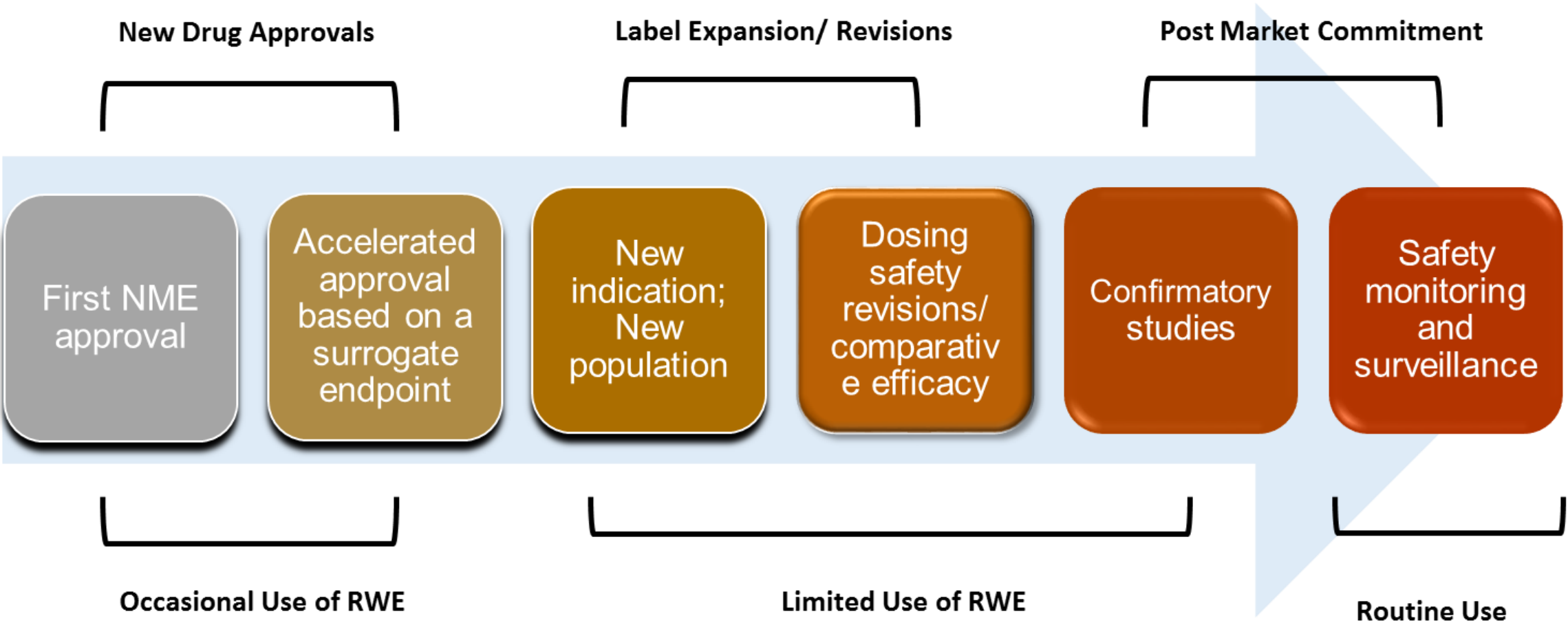


Value of Real World Evidence

RWE could be an enormously powerful source of information to understand



Overall Limited Use of RWE for Regulatory Purpose¹

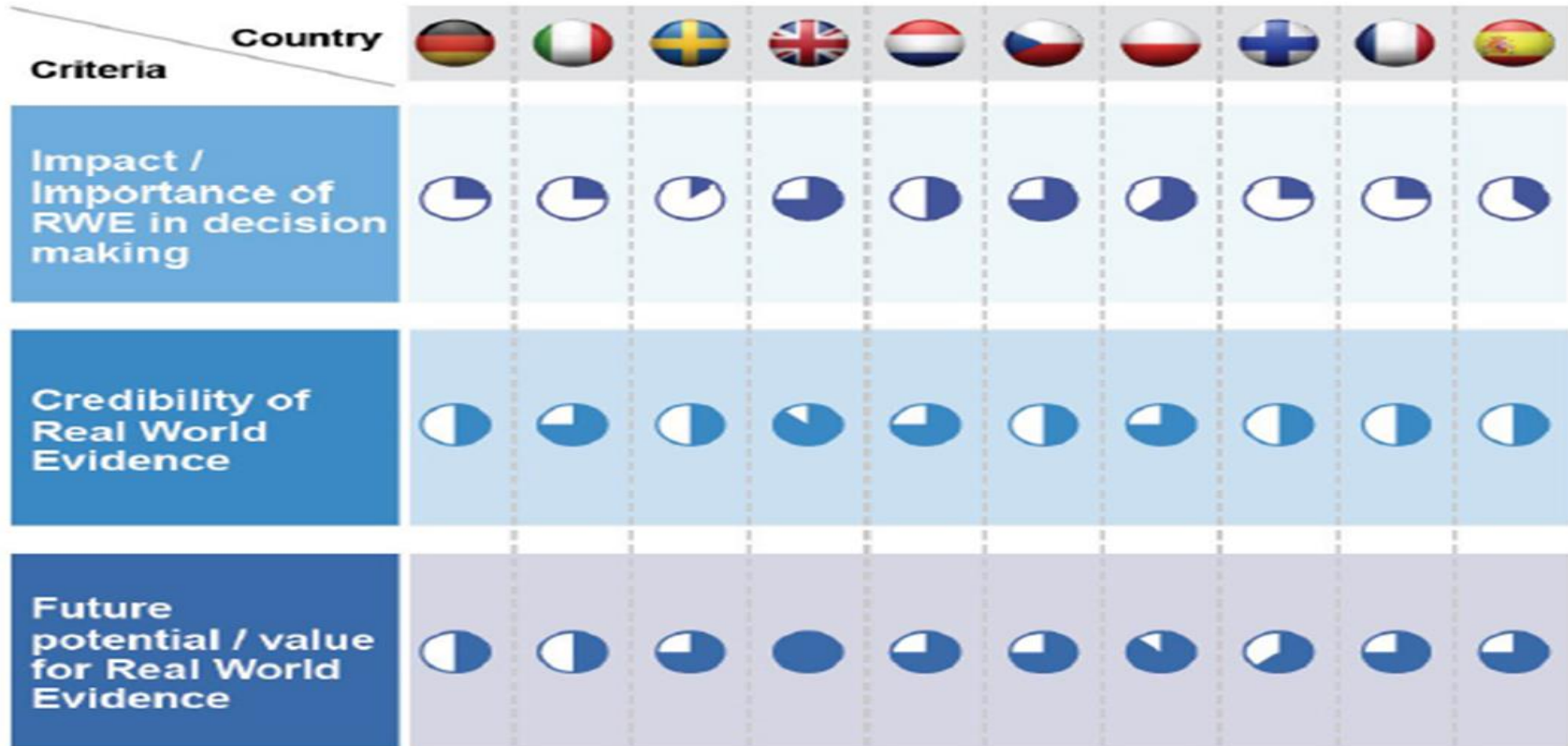


NME = New molecular entity

1. Duke Margolis Center for Health Policy. White paper: A framework for regulatory use of real-world evidence, 2017

Increasing Recognition for RWE from HTA Bodies

*Value and Importance of RWE Across Countries
(Payer RWE voice of the customer project 2015)*



A Multi-stakeholder Approach to Leverage the Potential of RWE



**Streamline the
regulatory/HTA/
payer environment**



**Establish scientific
partnership in data
design/analysis/
interpretation**



**Increase investment
and capabilities in data
collection, access and
analysis**

Real World Evidence Benefits



Thank You



RWE in Action: Driving Drug Policy

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Disclosure

- Presentation sponsored by Amgen

Leveraging Real World Data to Turn Evidence into Impact

How Do Randomized Trials Translate into Clinical Practice?

The New England Journal of Medicine

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VOLUME 341

SEPTEMBER 2, 1999

NUMBER 10



THE EFFECT OF SPIRONOLACTONE ON MORBIDITY AND MORTALITY IN PATIENTS WITH SEVERE HEART FAILURE

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ALFONSO PEREZ, M.D., JOLIE PALENSKY, M.S., AND JANET WITTES, PH.D.,
FOR THE RANDOMIZED ALDOSTERONE EVALUATION STUDY INVESTIGATORS*

ABSTRACT

Background and Methods Aldosterone is important in the pathophysiology of heart failure. In a double-blind study, we enrolled 1663 patients who had severe heart failure and a left ventricular ejection fraction of no more than 35 percent and who were being treated with an angiotensin-converting–enzyme inhibitor, a loop diuretic, and in most cases digoxin. A total of 822 patients were randomly assigned to receive 25 mg of spironolactone daily, and 841 to receive placebo. The primary end point was death from all causes.

Results The trial was discontinued early, after a mean follow-up period of 24 months, because an interim analysis determined that spironolactone was efficacious. There were 386 deaths in the placebo group (46 percent) and 284 in the spironolactone group (35 percent; relative risk of death, 0.70; 95 percent confidence interval, 0.60 to 0.82; $P < 0.001$). This 30 percent reduction in the risk of death among pa-

ALDOSTERONE has an important role in the pathophysiology of heart failure.¹⁻⁴ Aldosterone promotes the retention of sodium, the loss of magnesium and potassium, sympathetic activation, parasympathetic inhibition, myocardial and vascular fibrosis, baroreceptor dysfunction, and vascular damage and impairs arterial compliance.⁴⁻⁸ Many physicians have assumed that inhibition of the renin–angiotensin–aldosterone system by an angiotensin-converting–enzyme (ACE) inhibitor will suppress the formation of aldosterone. In addition, treatment with an aldosterone-receptor blocker in conjunction with an ACE inhibitor has been considered relatively contraindicated because of the potential for serious hyperkalemia.^{9,10}

Consequently, aldosterone-receptor blockers are used infrequently in patients with heart failure.^{11,12} There is increasing evidence to suggest, however,

- Spironolactone vs placebo in patients with heart failure
 - Inclusion / Exclusion
 - NYHA class III or IV at time of enrolment
 - LVEF < 35% within 6 months
 - Exclude patients with serum creatinine ≥ 2.5 mg/dL or serum potassium > 5 mmol/L
 - Follow-up
 - Lab and clinic follow-up at 4 weeks and 3 and 6 months
 - Appropriate use of ACE inhibitors and beta-blockers
 - D/c K-sparing diuretics and K⁺ supplements
 - Holding spironolactone for hyperkalemia or creatinine > 4 mg/dL
- ↓ Mortality by 30%
- ↓ HF Readmission by 35%
- ↔ Serious Hyperkalemia (NS)

How Do Randomized Trials Translate into Clinical Practice?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rates of Hyperkalemia after Publication of the Randomized Aldactone Evaluation Study

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ABSTRACT

BACKGROUND

The Randomized Aldactone Evaluation Study (RALES) demonstrated that spironolactone significantly improves outcomes in patients with severe heart failure. Use of angiotensin-converting-enzyme (ACE) inhibitors is also indicated in these patients. However, life-threatening hyperkalemia can occur when these drugs are used together.

METHODS

We conducted a population-based time-series analysis to examine trends in the rate of spironolactone prescriptions and the rate of hospitalization for hyperkalemia in ambulatory patients before and after the publication of RALES. We linked prescription-claims data and hospital-admission records for more than 1.3 million adults 66 years of age or older in Ontario, Canada, for the period from 1994 through 2001.

RESULTS

Among patients treated with ACE inhibitors who had recently been hospitalized for heart failure, the spironolactone-prescription rate was 34 per 1000 patients in 1994, and it increased immediately after the publication of RALES, to 149 per 1000 patients by late 2001 ($P < 0.001$). The rate of hospitalization for hyperkalemia rose from 2.4 per 1000 patients in 1994 to 11.0 per 1000 patients in 2001 ($P < 0.001$), and the associated mortality rose from 0.3 per 1000 to 2.0 per 1000 patients ($P < 0.001$). As compared with

- RWE study examining use of spironolactone and outcomes in > 30,000 elderly patients prior to and following publication of RALES RCT



Use of spironolactone by almost 500%



Incidence of hospitalization with hyperkalemia by 275%



Mortality – no change



HF Readmission – no change

RWE and Drug Policy – The Ontario Experience

The Ontario Drug Policy Research Network (ODPRN)

Infrastructure

Centralized data sources: ICES

Linked data on physician visits, hospitalizations, emergency department visits, drug use, etc at the population level

People

Network of scientists / clinicians

Highly skilled data analytics, statisticians, epidemiologists, health economists

Process

Questions driven by policy-makers

Standardized data extraction and analysis algorithms

Strict project management principles

Engagement

Regular, frequent meetings between analytics team, clinicians, and **policy-makers**

Academic Impact
Publications: > 150
Presentations: > 240

Impact
(over 10 years)

Drug Policy (> 20 drug policy changes)
Thiazolidinedione drugs for diabetes (2009): removed due to safety concerns
Blood glucose test strips (Aug 2013): > \$100 million cost reduction over 5 years
Hepatitis B drugs (2018): > 1,600 new patients gained access within 5 months

More RWE Examples



Use of Beta Blockers in Heart Attack Patients: An Early Application of Real World Evidence

- Well before the term “RWE” gained currency, observational data finding lent crucial support for use of beta blockers (BB) in patients who suffer heart attacks.
- 1990s: Medicare sponsored the Cooperative Cardiovascular Project (CCP), which examined medical records of over 200,000 heart attack patients.
- Project found substantial reductions in mortality among patients receiving BB, including previous counter-indicated cases
- The CCP bolstered previous evidence from RCTs and helped accelerate BB in heart attack patients as a standard practice.
- 2007, the National Committee for Quality Assurance ceased reporting use of BB in heart attack patients as a quality measure after finding use of the therapy had become widespread

The Salford Lung Studies: Prospective Real World Drug Trials Utilizing Community Resources

- World’s first Phase 3 pragmatic RCT of a novel drug therapy.
- Located in the UK study compared once-per-day inhaled corticosteroid against normal course of care for both COPD and asthma
- Patients are treated and monitored across encounters with physicians, physicians’ staff and pharmacists, through EMR
- The drug trial will test both the clinical effectiveness of treatments and their impact on patients’ ability to adhere and realize long-standing benefit.

The Transcatheter Valve Therapy Registry: Physicians Employ A Registry That Supports Post-Market Trials

- Transcatheter aortic valve replacement (TAVR) devices: new and innovative class of medical devices allow treatment of patients with diseased aortic valves ineligible/high a risk for conventional aortic valve replacement.
- 2011: American College of Cardiology and the Society of Thoracic Surgeons joined in a common strategy to “construct a new pathway for rollout” of TAVR procedures in the U.S
- The centerpiece of the strategy is a new TAVR registry that builds on the pre-existing registries administered by both societies.
- Developed common data formats and data collection methods that have expedited use of the registry to conduct prospective, randomized, post-market trials of different valve products.
- Evidence generated by the registry has already resulted in FDA approval of expanded indications for the Sapien Transcatheter Heart Valve

The HCA MRSA Studies: A Learning Health Care System uses RWE for Quality Improvement

- Hospital-acquired infections, including MRSA, are a growing threat to hospital patients and staff.
- There has been limited evidence to support adoption of competing infection control strategies for MRSA, leading at least nine states to simply mandate a screening and isolation strategy for hospitals
- A pragmatic, cluster-RCT trial conducted by Hospital Corporation of America (HCA) staff within the HCA system, and peer reviewed for publication in the New England Journal of Medicine, found strong evidence for a single approach.
- Trial cost <\$3 million – substantially less than a classic RCT, although an indication that “high-quality delivery science is not free.”

RWE In the Middle East

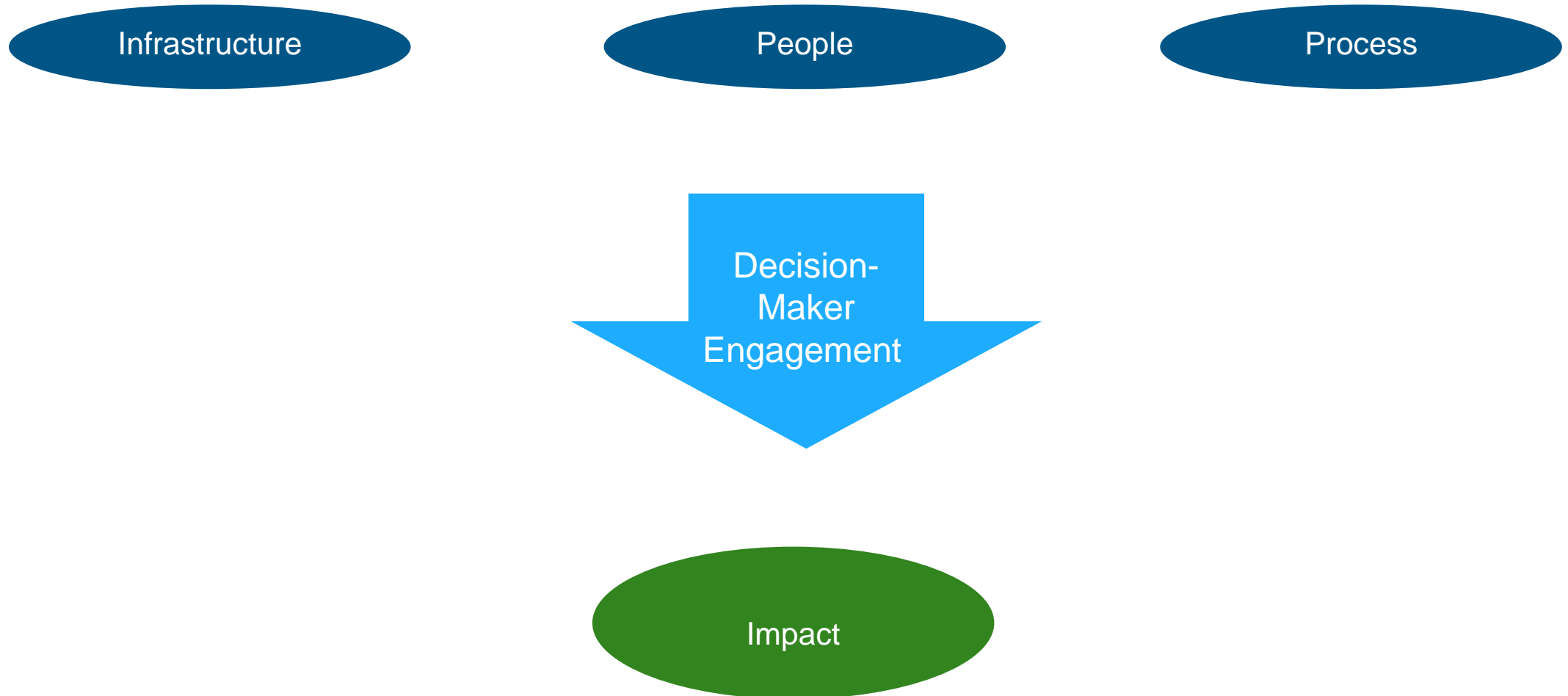
Middle East Population is Unique

- Population is 444,322,417 ~ 6% of world population (2017)
- A young and growing population, due to high fertility rate 2.8
- Life expectancy at birth has improved, but still at 74
- Culture plays an important role in fertility rates, access to healthcare, choice of physician gender, and the prevalence of some congenital conditions

... with Significant Disease Patterns

- Highest prevalence of Diabetes Mellitus globally, 13.7% in 2014
- Highest mortality rate of breast cancer (19 deaths per 100,000 women), about 42 thousand deaths in 2012
- Highest prevalence of HCV worldwide and the highest frequency of HCV-4 responsible for almost 80% of HCV infections
- ME has highest rate of rickets world wide
- High incidence of morbidity, infant death, child genetic diseases (e.g. Sickle Cell Disease, Thalassemia, and Down Syndrome)

RWE in the Middle East - Considerations



Examples of Data Sources in the Middle East

National Census Data

- Demographic data (age, gender)
- Socio-economic data (income)

National Registries

- National Cancer Registry (Oman, Saudi Arabia, Egypt)
- National MS Registry (Egypt)

Medical Records (institutional)

- King Saud Medical City
- Cairo University Hospital Medical Records

Health System Data

- Medical records
- Drug procurement records
- Staffing information
- Drug dispensing records

Private Health Insurance Claims Data

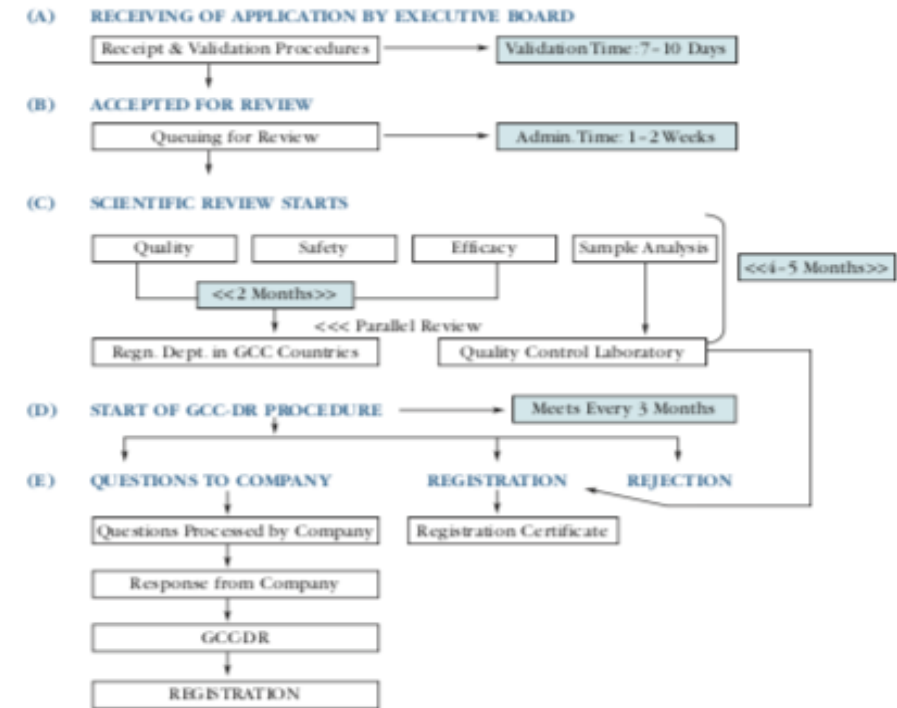
- Dubai (~ 9 million beneficiaries)
- Egypt (~ 4 million beneficiaries)

National Household and Health Expenditure Surveys (NHHS)

- Health System Financing
- Health spending
- Health conditions
- Health system utilization (physician visits)
- e.g. Egypt, Jordan













The Gulf Central Committee for Drug Registration (GCC-DR)

- GCC-DR is responsible for the centralized process for registration of pharmaceuticals
- The committee also reviews technical and post-marketing surveillance reports
- It includes members countries of Gulf Cooperation Council (GCC)
- Scientific Review is the most important step and contains review of product dossier on quality, safety, efficacy and conducting sample analysis
- It is not clear if RWE is acknowledged as a tool for drug/ device evaluation
- GCC states still have their own national registration authorities/ departments



Source: M. Al-Rubaie, S. Salek, S. Walker, Welsh School of Pharmacy, Cardiff University, UK and Centre for Innovation in Regulatory Science (CIRS), UK

Registration, Pricing & Procurement Stakeholders in MENA countries

Country	Registration	Pricing	Reimbursement	Generic purchasing
 Saudi	SFDA	SFDA	Different payer level (MoH, National Guard, MODA, etc)	Tender (NUPCO and SGH)
 UAE	UAE MoH	UAE MoH	DHA, MoH and HAAD	Tender through SGH, Direct purchase by HAAD, DHA
 Kuwait	MoH	MoH	MoH	Tender through CMS
 Qatar	MoH	Supreme council of health	HMC, NGOs, Private insurance	Tender Committee Secretariat (TCS)
 Oman	MOH (Directorate General of Pharmaceutical affairs and Drug Control)	MoH	MoH, CDC, Private Insurance, Patient	Tender by MoH/ Oman Tender Board
 Bahrain	National Health Regulatory Authority			MoH/ Tender Board/ Public hospitals
 Lebanon	MoH Drug Registration Tech Committee (DRTC)			Tender purchasing by MoH for public hospitals, direct purchase by private hospitals
 Jordan	JFDA			Tender purchasing by JPM
 Egypt	Egyptian Drug Authority (EDA)			Tender through MoH and semi-governmental entity
 Algeria	MoH & National Nomenclature Commission Future: ANPP	MoH Ministry of Labor Cross-pricing committee	Ministry of Labor, CNAS (National social insurance)	Tender through Pharmacie Centrale des Hopitaux (PCH)
 Morocco	MoH-Department of Drugs and Pharmacy) (DMP)	Pricing committee	National Agency of Insurance (ANAM), Committee for Economic and Financial Evaluation, Transparency commission	Purchasing through national & institutional tenders mainly MoH
 Tunisia	MoH DPM (Dept. of Medicine), Tech committee	Central Pharmacy of Tunisia (CPT), DPM	CNAM (Social welfare scheme)	Tender through CPT

Tunisia is the only country that has an independent HTA committee, the National Instance for Accreditation in Health Care (INASanté), which has a significant role in reimbursement decisions

Centralised Decentralised
 GCC countries include Qatar, Kuwait, UAE, KSA, Bahrain and Oman; Levant include Lebanon and Jordan; North Africa include Egypt, Algeria, Morocco and Tunisia

Source: Market Prognosis Q1 2018 through IQVIA team documents

Considerations for Using RWE in the Middle East



- **Data and Process**
 - **Centralized data infrastructure**
 - **Governance** and **stewardship**
 - **Accessing RWD** in time for decisions – e.g. registries
 - **Privacy** and **confidentiality** of patient data
- **People**
 - **IT infrastructure**
 - **Scientists / researchers**
 - **Analysts, epidemiologists, economists**
- **Engagement**
 - **Alignment** with HTA agencies
 - **Coordination** between different stakeholders
 - **Acknowledging RWE** as a valuable tool to support Healthcare decision-making

Discussion

The regional/ local need for RWE



- Do you see a need for more evidence generation in your region/country, and how do you feel those evidence could be leveraged?
- What is the influence of RWE on healthcare decision in your institution/country?
- Do you feel more local evidence would improve the current healthcare decision making process?

Current experience with RWE in the region (Strengths and weaknesses)



- Is there Real World Evidence (RWE) activities in your institution/Country? Please describe
- Who is responsible for RWE (if any)? is it institutional committee or national committee?
- What are the RWE challenges faced in your institution/country? and what would be the opportunities to build on?

How to improve the current situation and better partner



- Which institution/organization/entity support/fund RWE projects?
- Is there any regional/global model for RWE that you think could apply to your country/region?
- How do you see the future of RWE in your country/region, and what are the key success factors to develop evidence generation in the region?

Thank You



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