Real-world Data and Real-world Evidence in Support of Drug Development: Will China Soon be Leading the Way?

Prepared by:
Evidera

Prepared for:
ISPOR Asia Pacific Summit

21 September 2022 11:30 a.m. to 12:30 p.m. (KST/GMT+9)

Evidera | PPD

Conflict of Interest Statement

- Amanda Pulfer, Dimitra Lambrelli, and Lu Ban are paid employees of Evidera, a business unit of PPD, a Thermo Fisher Scientific company.

Content

01

Real-world Evidence and Regulatory Environment in China
Lu Ban, Evidera

- To provide an overview of the regulatory environment and use of RWE to support development of pharmaceutical products in China

02

Real-world Evidence Generation Ecosystem in China: An Innovator's Perspective
Sunil Garg, Astellas

- To provide an innovator's perspective on RWE generation in China

03

Challenges and Opportunities in Conducting Real-world Studies in China
Haijun Cao, Happy Life Technology

- To provide practical guidance on conducting studies using RWD in China from a local company perspective

04

Questions and Answers

Abbreviations: RWD = real-world data; RWE = real-world evidence

Evidera | PPD

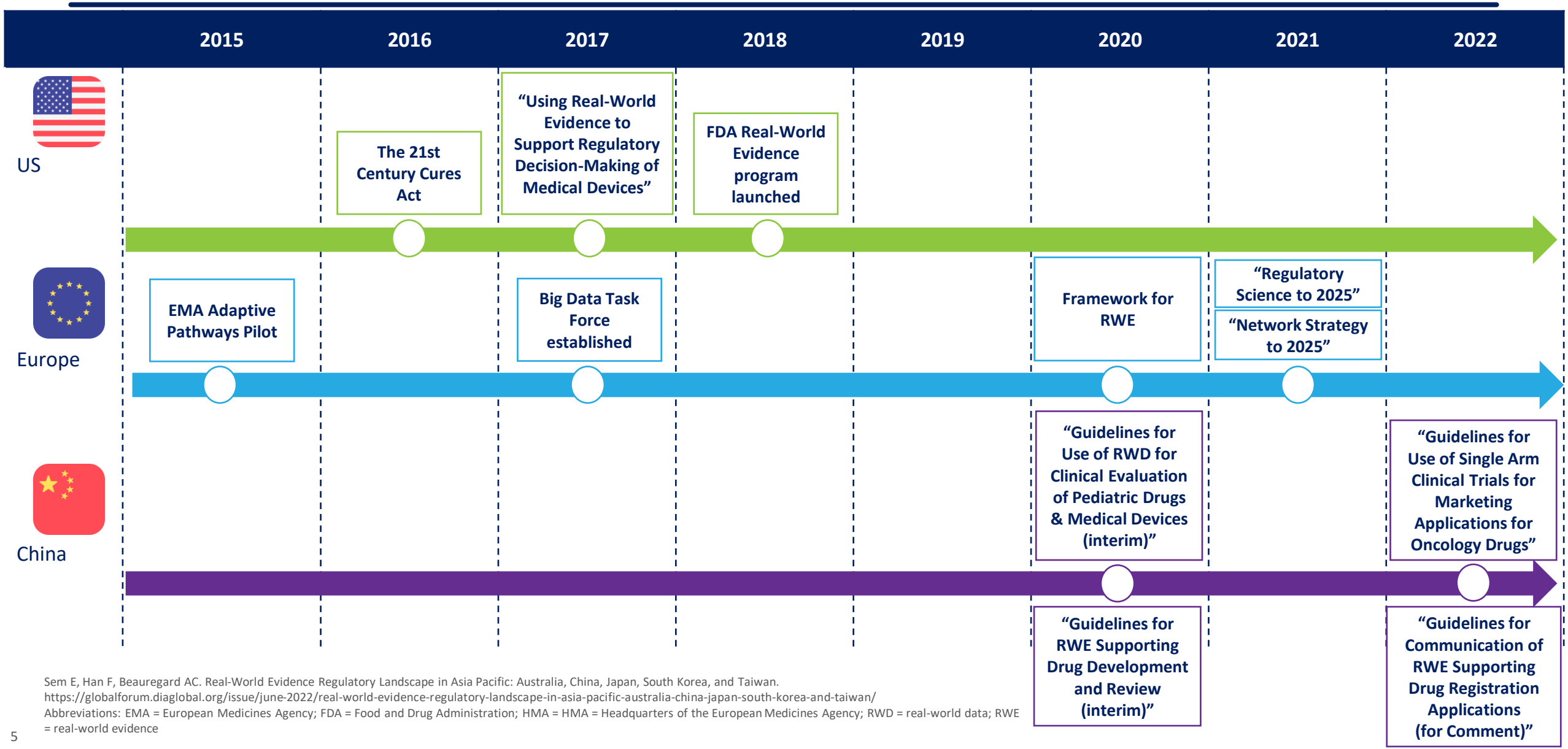
Real-world Evidence and Regulatory Environment in China

Lu Ban, PhD, Associate Director, RWE, Evidera

21 September 2022 11:30 a.m. to 12:30 p.m. (KST/GMT+9)

Evidera | PPD

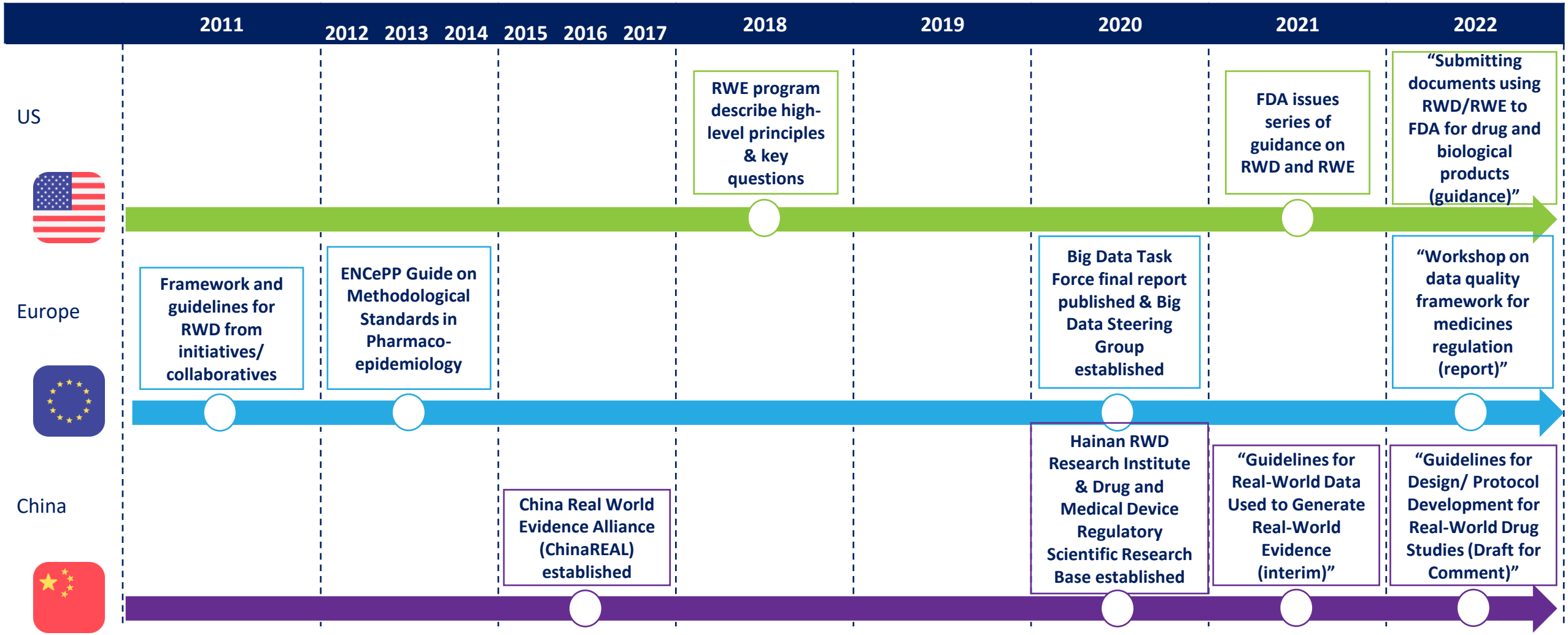
RWE Regulatory Frameworks and Policies



Sem E, Han F, Beauregard AC. Real-World Evidence Regulatory Landscape in Asia Pacific: Australia, China, Japan, South Korea, and Taiwan. https://globalforum.diaglobal.org/issue/june-2022/real-world-evidence-regulatory-landscape-in-asia-pacific-australia-china-japan-south-korea-and-taiwan/

Abbreviations: EMA = European Medicines Agency; FDA = Food and Drug Administration; HMA = HMA = Headquarters of the European Medicines Agency; RWD = real-world data; RWE = real-world evidence

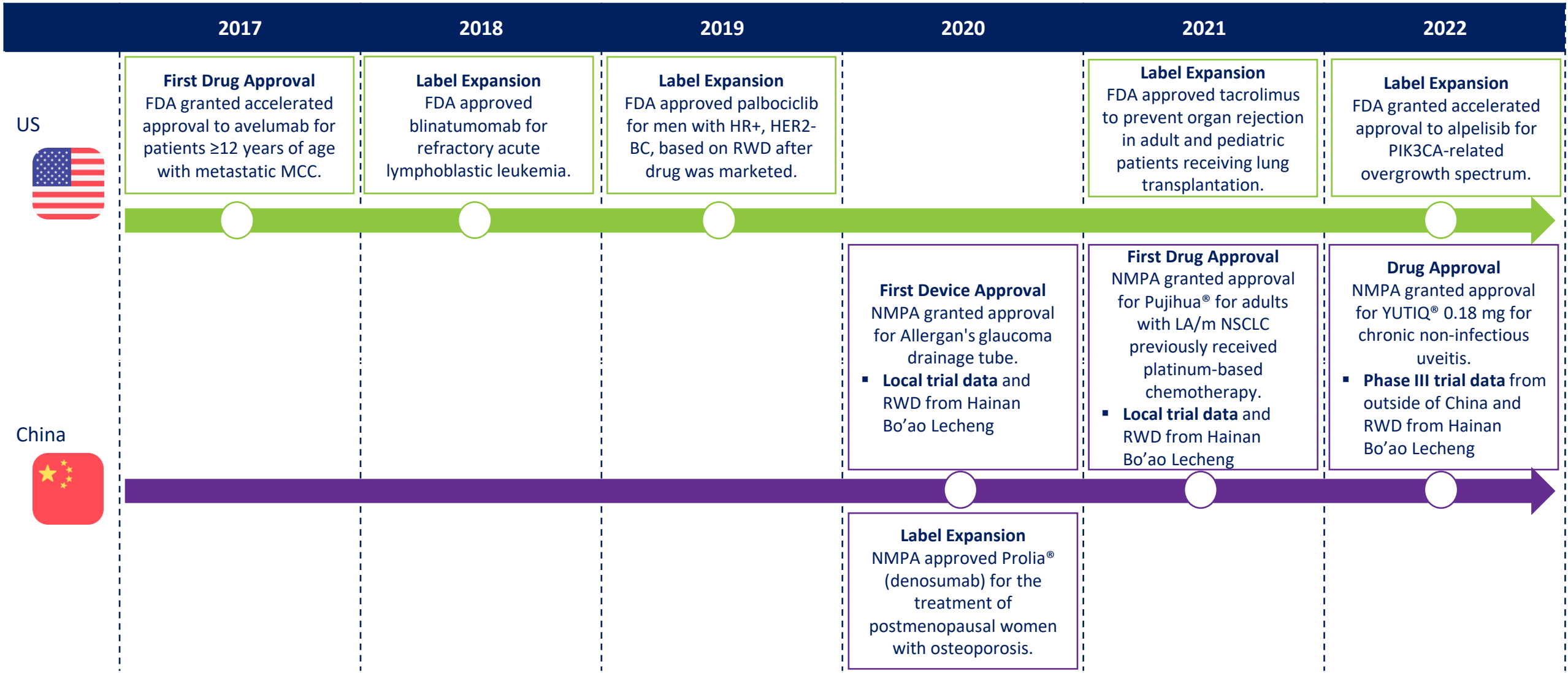
RWE Data Standards and Study Methods Recommendations



Sem E, Han F, Beauregard AC. Real-World Evidence Regulatory Landscape in Asia Pacific: Australia, China, Japan, South Korea, and Taiwan. https://globalforum.diaglobal.org/issue/june-2022/real-world-evidence-regulatory-landscape-in-asia-pacific-australia-china-japan-south-korea-and-taiwan/

Abbreviations: EMA = European Medicines Agency; FDA = Food and Drug Administration; HMA = Headquarters of the European Medicines Agency; NMPA = National Medical Products Administration; RWD = real-world data; RWE = real-world evidence; US = United States

RWE to Support Drug Approval in China and US



Abbreviations: BC = breast cancer; FDA = Food and Drug Administration; LA/m = locally advanced/metastatic; MCC = Merkel cell carcinoma; NMPA = National Medical Products Administration; NSCLC = non-small cell lung cancer; RWD = real-world data

RWE to Support Reimbursement through National Reimbursement Drug List (NRDL)

‘Golden ticket’- Major public reimbursement mechanism and essential for market access in China

- Covers 98% of the China population
- Includes high-value, high price drugs
- Listing essential to get into public hospitals

NRDL gets updated annually and there is an opportunity for RWE input

Preparation and Application
(formulate eligibility criteria and initial assessment)

Manufactures can submit applications
Clinical assessment will be based on efficacy, safety, economic impact, innovation, and equity

Review
(expert review and recommendations)

- Directly rejected
- Directly accepted

Negotiation
(formulate suitable price and include in the NRDL)

Manufacturers submit dossier, including health economics evaluations
Local RWD can be used for cost-effectiveness analysis and budget impact analysis

- For budget impact analysis, local RWD is a preferable data source
- For estimation of clinical effectiveness, RWE can be standalone or supplementary evidence

Liu GG, Wu J, He X, Jiang Y. Policy Updates on Access to and Affordability of Innovative Medicines in China. Value Health Reg Issues. 2022 Jul;30:59-66; National Health Commission of the People’s Republic of China. China adds 74 new drugs to medical insurance coverage list. http://en.nhc.gov.cn/2021-12/06/c_85285.htm.
Lou J, Kc S, Toh KY, et al. Real-world data for health technology assessment for reimbursement decisions in Asia: current landscape and a way forward. Int J Technol Assess Health Care. 2020 Oct;36(5):474-480.
China Pharmacoeconomic Evaluation Guidelines 2020

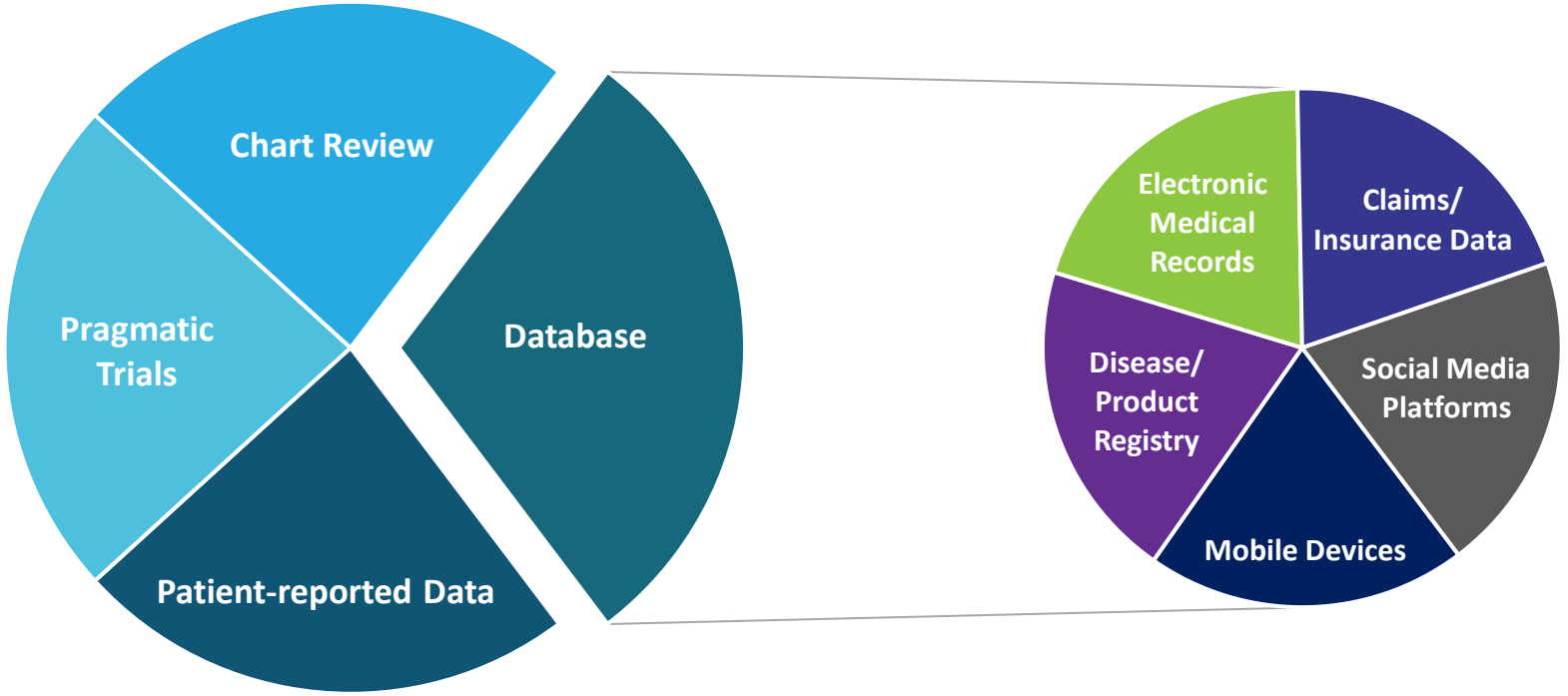
Evidera | PPD

Question. What types of data did you use/are thinking of using in China?

Different Types of RWD and Real-world Studies in China

Primary Data Collection

Secondary Use of Data



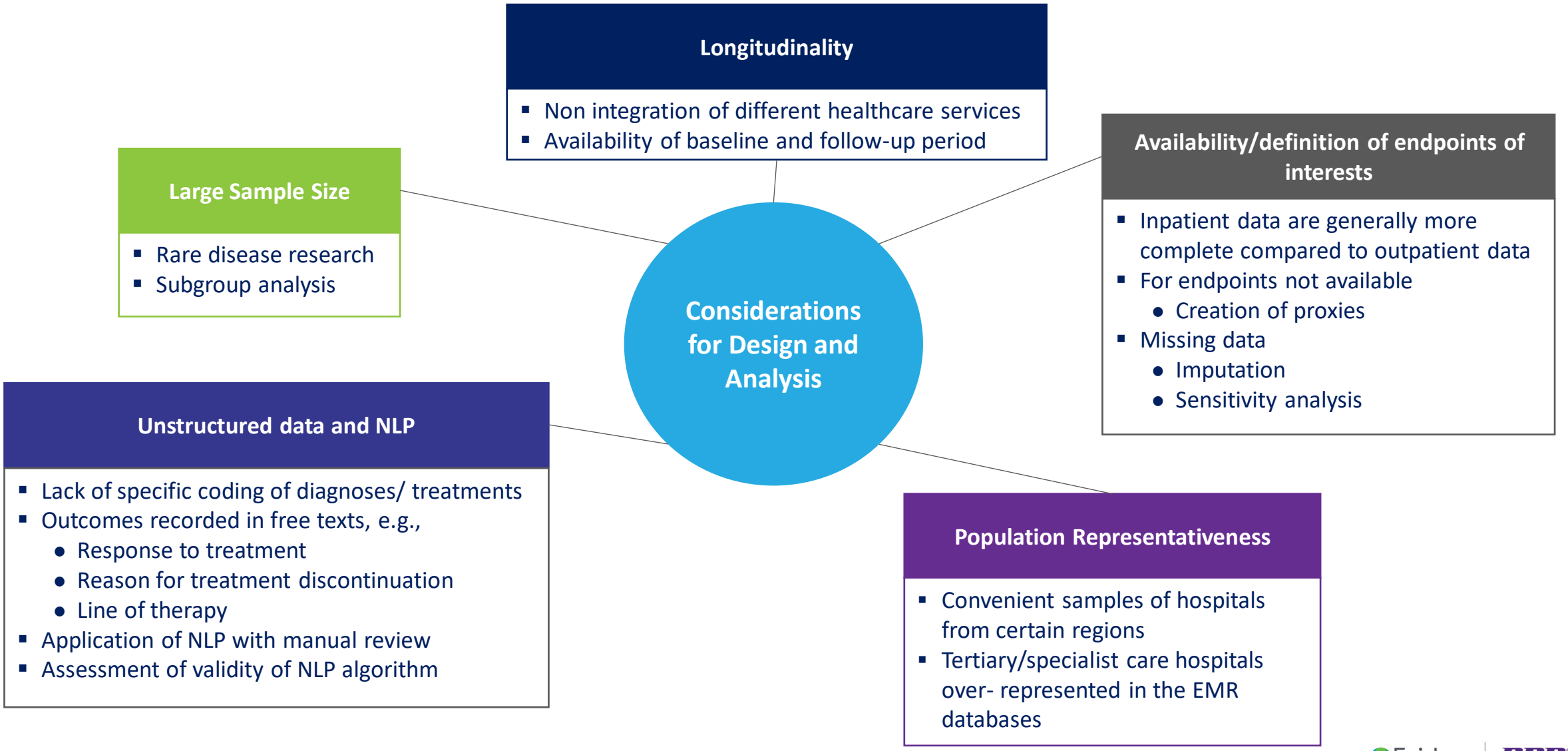
Organized data collection system not primarily used for research purposes/secondary re-usable data platform

Emerging Data Sources in China

Administrative Claims	▪ National Claims Database (from urban employee/resident medical insurance, e.g., Urban Employee Basic Medical Insurance [UEBMI]) ● Inpatient and outpatient claims ● Resampled annually ▪ Regional, e.g., Beijing, Tianjin, Guangzhou
EMRs	▪ Individual hospitals with various EMR systems ▪ Regional EMR data of multiple hospitals in a specific region ● e.g., Yinzhou District in Ningbo, Xiamen, Fuzhou, Shandong ▪ EMR data platforms covering multiple hospitals of different regions ● HLT, LinkDoc, Digital Health China ● Convenient samples ● EMR database ● National Anti-tumor Surveillance System (NATDSS), linked to death registry ● Linkage between different levels of hospitals is lacking ● Regional EMRs potentially can be linked to regional claims data, e.g., Yinzhou District in Ningbo and Xiamen EMRs.
Disease Registry	▪ Oncology ▪ Cardiovascular disease ▪ China National Rare Diseases Registry System

Xie J, Wu EQ, Wang S, et al. Real-World Data for Healthcare Research in China: Call for Actions. Value Health Reg Issues. 2022;27:72-81; Zhuo L, Cheng Y, Pan Y, et al. Prostate cancer with bone metastasis in Beijing: an observational study of prevalence, hospital visits and treatment costs using data from an administrative claims database. BMJ Open. 2019;9:e028214.
Abbreviations: EMR = electronic medical record; HLT = Happy Life Technology

Study Design and Analysis Considerations with Use of Secondary Data in China



Abbreviations: EMR = electronic medical record; NLP = natural language processing

Summary

- Indicators that China will be leading the way
  - Active promotion of use of RWE in regulatory and reimbursement decisions
  - Fast emerging data landscape with advancement of new technology
  - Great potential in oncology and rare disease research
  - Increased attention to patient privacy protection
- Potential considerations
  - Data quality and data accessibility
  - Proper study design and execution

Real-World Evidence Generation Ecosystem in China

An Innovator’s perspective

Sunil Garg
Senior Director, Lead of Evidence Generation Operations
Astellas Pharma, Singapore

September 21, 2022

DISCLAIMER

The speaker is a paid employee of Astellas. This presentation is intended for information purpose only and does not replace independent professional judgement. This presentation is not intended to be legal or medical advice. Statements of acts, position taken, and opinions expressed are those of the speaker individually and, unless expressly started to contrary, do not necessarily reflect the opinion or position of the speaker’s employer, Astellas, or any of its subsidiaries and/or related entities.

CHINA: CHANGING LANDSCAPE

1

National Reimbursement Drug List (NRDL)

- Volume-based centralized drug procurement policy; updated annually
- Pressure on drug prices cut will remain; local RWE to support cost effectiveness and budget impact will be key to NRDL negotiations
- Generic Quality Consistency Evaluation (GQCE) has put pressure on innovator's matured products

2

Shorter launch time for innovative and rare disease products/ stronger patent laws

- Accelerated approval pathways and breakthrough therapy designations
- New amendment (4th) to patent laws brings provision for patent term extension and patent linkages
- Legal provision to challenge patent violations

3

Increasing regulatory focus on RWE

- Release of relevant guidelines, i.e., Guiding principles of real-world evidence supporting drug development and review (trial)
- Development of networks, platforms and database, i.e., Establishment of Hainan Real World Data Research Institute.
- RWD for Clinical Evaluation of Medical Devices is one of the key projects in the Drug Regulatory Science Action Plan, i.e., market authorization of medical device for surgical management of refractory glaucoma with the submission of clinical RWE of racial differences

EXPERIENCES

- Different practice and understanding on patient privacy and informed consent requirements, i.e., informed consent requirements for chart review
- Data completeness: separate accessibility to different HIS/EMR modules, i.e., use of technology vendors to work with hospital IT for data access across HIS modules
- High legal and compliance risks: data ownership and commercial rights concerns multi-center EMR data
- Data technology vendors working practices and legality
- Inconsistent data variables with inconsistent vocabulary in different hospitals EMR – difficult data curation and analysis.

LESSONS LEARNED

- Feasibility assessment and review of data variable early on before conducting an RWE study; data source may include, e.g.,
  - Digital Health China & Linkdoc (National Oncology EMR)
  - National Cancer Center/1 Yong Cloud (National Anti-Tumor Drug Surveillance System)
  - Yidu Cloud (National Multi-disease EMR)
  - Ningbo, Gennlife (Multi EMR & Disease Claims)
  - Tianjin EHR (Regional Database)
- Use of data vendor/development of technology for a single window access to patient data spread across the HIS/EMR modules
- Work with site GCP/R&D in drafting a consistent and defined procedures to RWE data access to third parties

FUTURE DIRECTION

- Stakeholder collaborations and consortium to build RWE infrastructure by shaping RWE standards and sharing best practices
- Capacity building by investing in RWE education & infrastructure across stakeholders
- Provision of central Ethics committee to provide a single window clearance to RWE studies
- Simplify HGRAC regulations and requirements: a clear risk-based approach would be helpful
- Regulator to optimize the policy for RWD access, use and patient privacy protections, interoperability with overseas data, guidance on the use of new types of data (health mobile data, electronic wearable device data)
- Uncertainty in government polices: a value-based approach recommend in reimbursement assessments.
- Improvement in methodology and analytical technology by the CROs/data IT vendors
- Patient centric approach for a robust and meaningful RWD

Participation of Chinese patients in global studies for simultaneous development

Digitally and analytical enable environment with healthcare a strategic priority

Rise of domestic biotech R&D: leading chimeric antigen receptor T-cell (CAR-T) therapies

Rising China contribution to global pharma revenue

Changing regulatory landscape

Multinationals are at a crossroads – not just for the sales numbers but strategically it's too hard to miss the opportunity to ride the dragon. With broadening access to newer therapies and increasing evidence, China could lead the wave of an innovation-driven ecosystem.

Data quality

Patent protection mechanism

High attrition rates/talent crunch

Market access constrains and cost driven reimbursement negotiations

The Challenges and Opportunities in Conducting Real World Study in China

Prepared by:

Haijun Cao, M.D, PhD

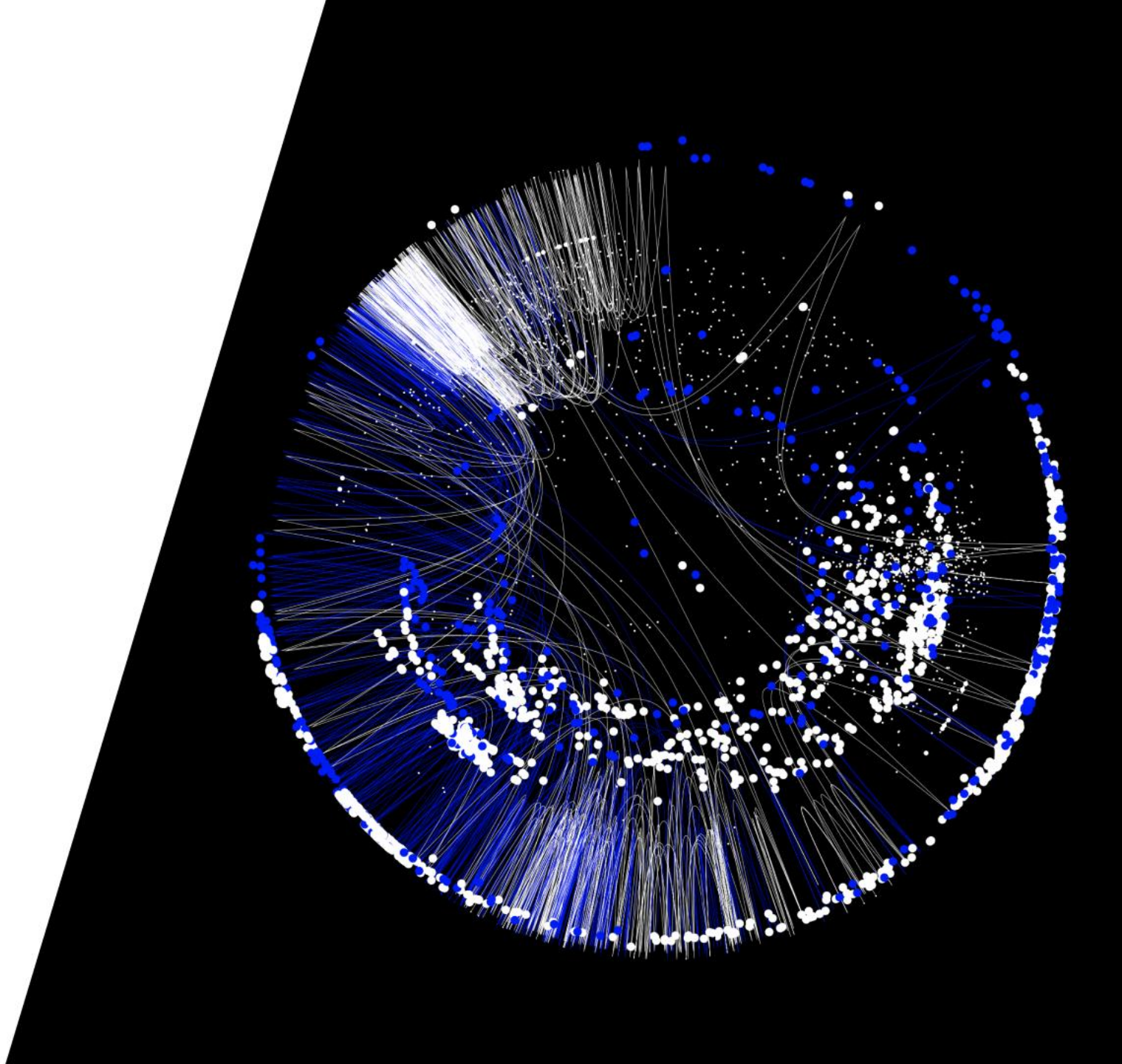
Prepared for:

ISPOR Asia Pacific Summit

21 Sept 11:30-12:30pm (Korean time) 2022

Happy Life Tech

Do Innovation

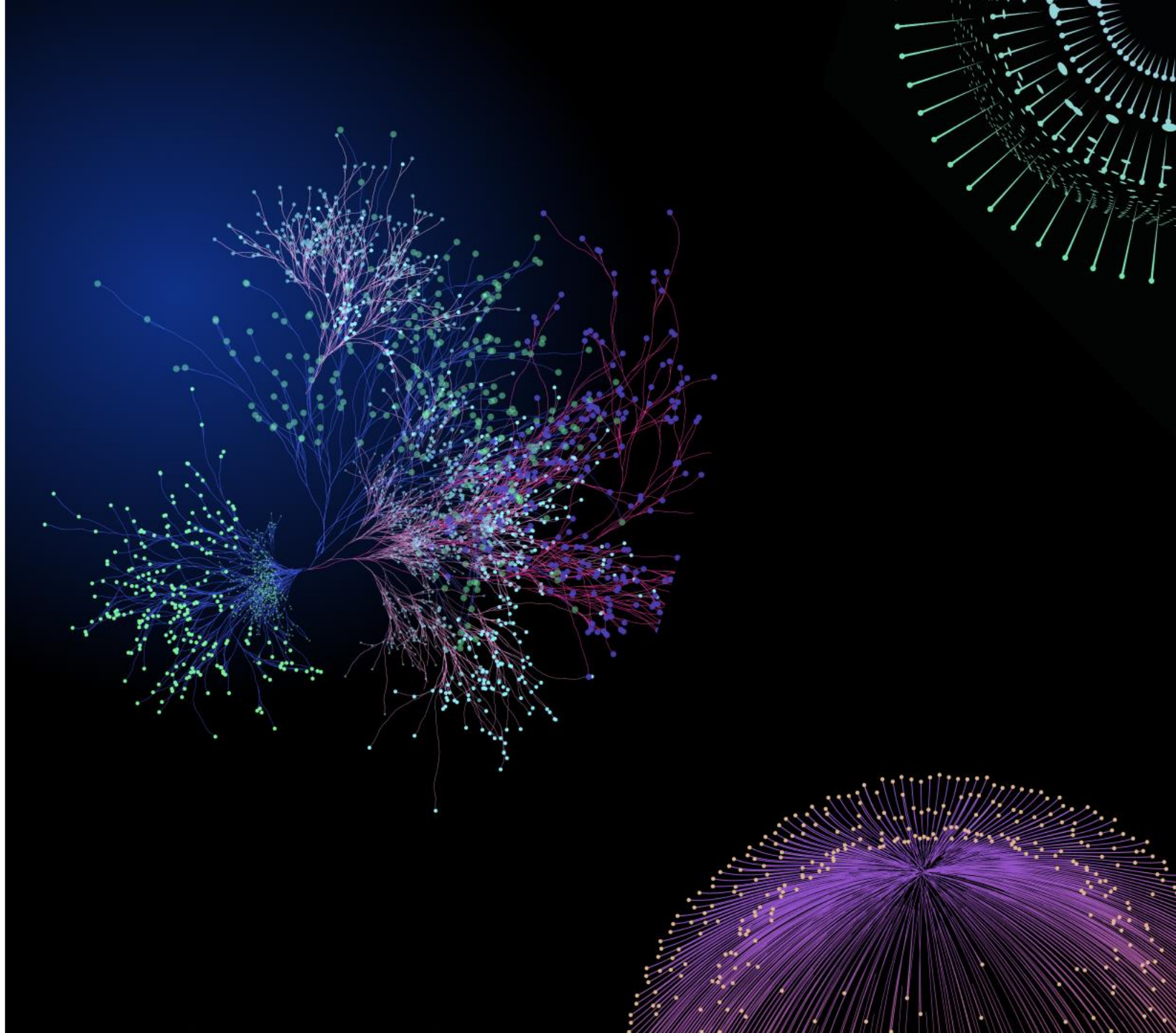


Disclaimer

This document is confidential and exclusively addressed to you for reference only. This document and any information contained herein shall not be disclosed or provided to any third party without our prior written consent. Any information contained in this document shall not be used by or relied upon by any person or institute in making any commercial decisions or as evidence.

Happy Life Tech

Do Innovation

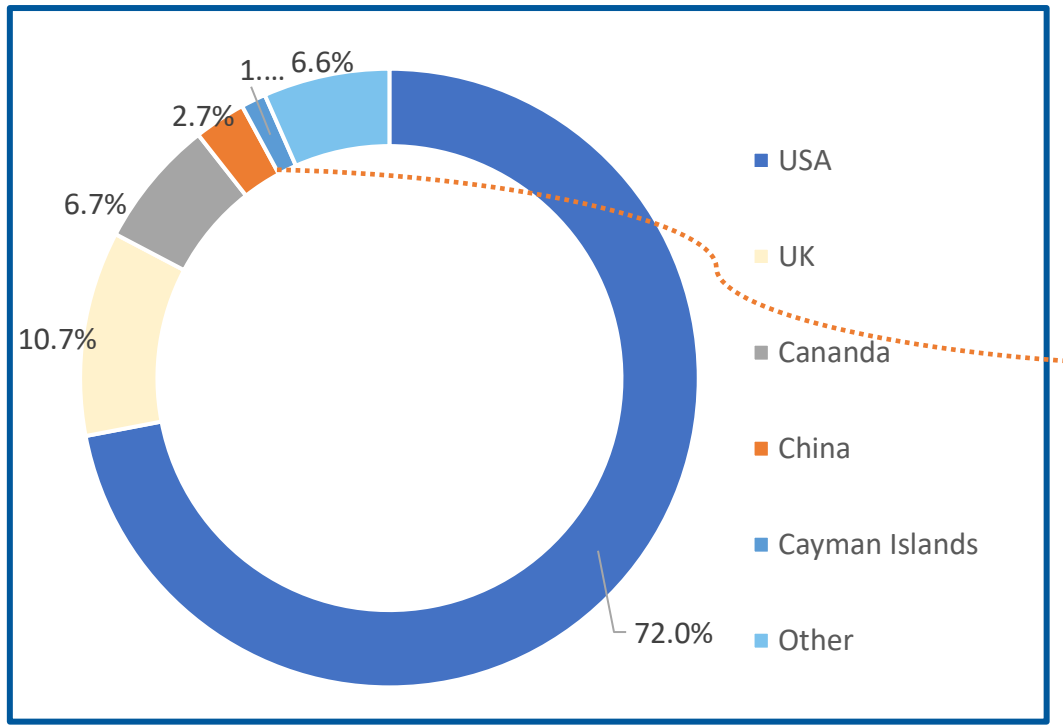


Question. What is your level of experience with conducting RWE studies in China?

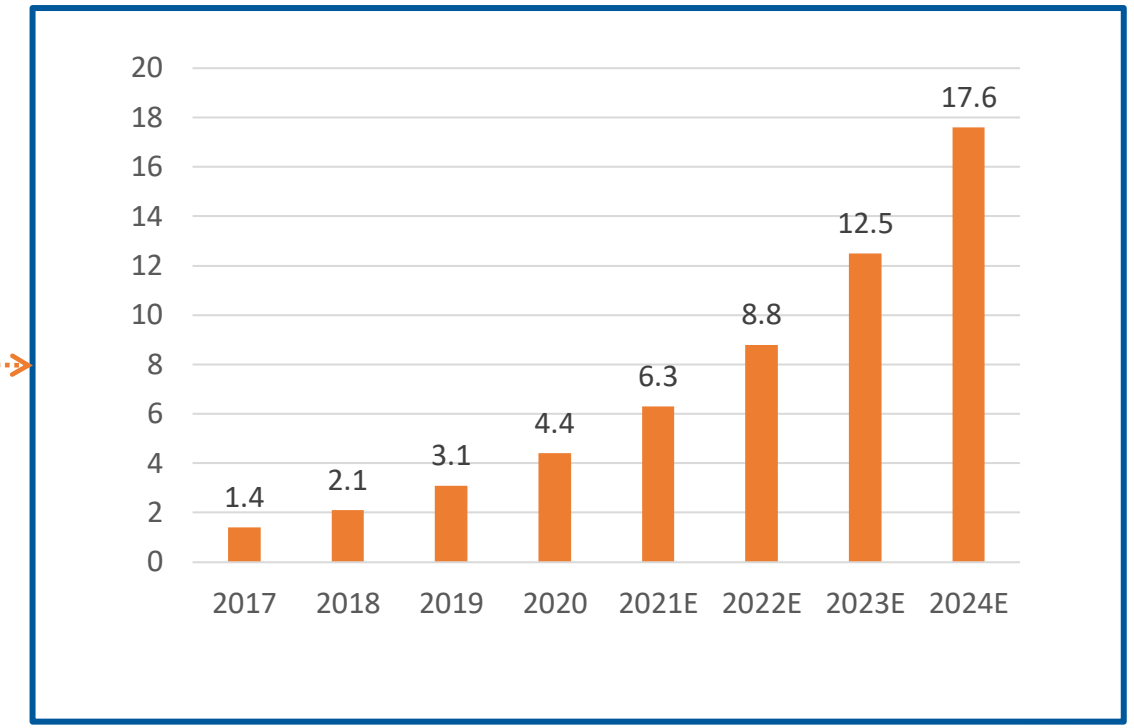
Happy Life Tech

Growing investment in healthcare data-related companies boost RWS development in China

Distribution of RWD companies in the world



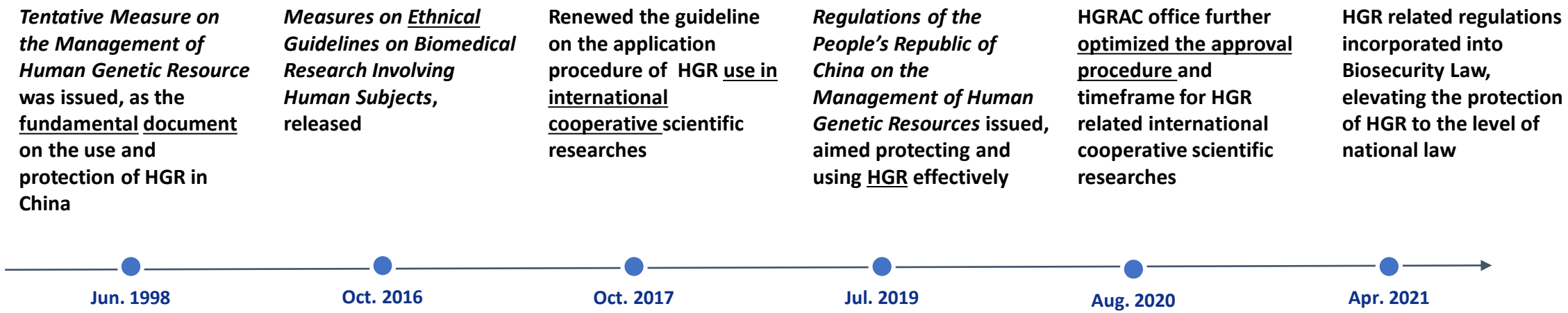
Total Investment of RWE in China (Billion Yuan)



Reference : CB Insights China.生物医药领域的真实世界数据行业报告2021

Cornerstone of RWS start-up: EC and HGRAC

EC and HGRAC Regulatory development in China



Ethnical committee (EC)

- Any institution conducting HGR related scientific studies is required to set ethnical committee, to guarantee the ethnic issues in studies
- Any studies involving HGR, including non-interventional retrospective studies, is required to pass the ethnical examination prior to the kickoff of the study
- Ethnical examination criteria includes the ethnic and scientific standard of the study design, the design of the consent form, fairness for the study subjects, etc.

Human Genetic Resource Administration of China (HGRAC)

- HGRAC operates under the Ministry of Science and Technology of PRC to regulate the use and protection of HGR in China

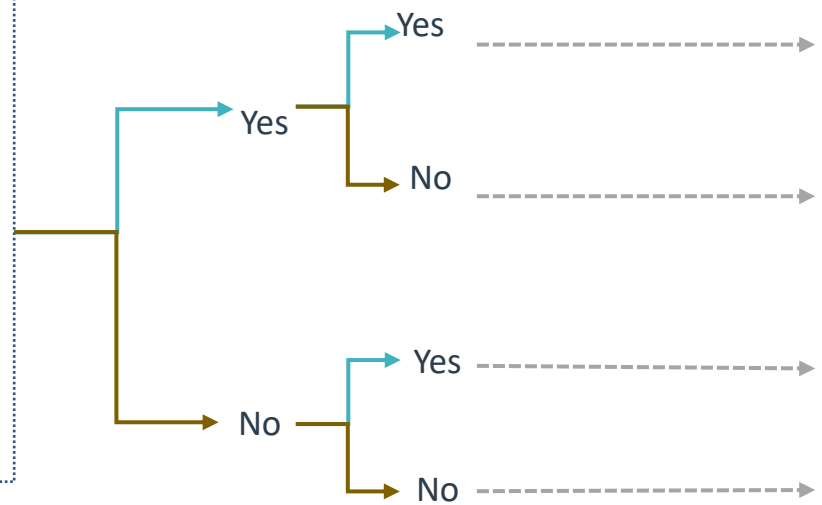
*All policy are available at 中国政府网_中央人民政府门户网站 (www.gov.cn)

HGRAC process for RWS projects in China

Starting

For research projects with international sponsorship

If meet any of the following:
1. Sample size is greater than 500
2. Rare diseases
3. Special locations, family, or ethnicity



Publish on international journals or make results public to international use

International collaboration review	Collection	External provision	Preservation
✓	✓	✓	✗
✓	✓	✗	✗
✓	✗	✓	✗
✓	✗	✗	✗

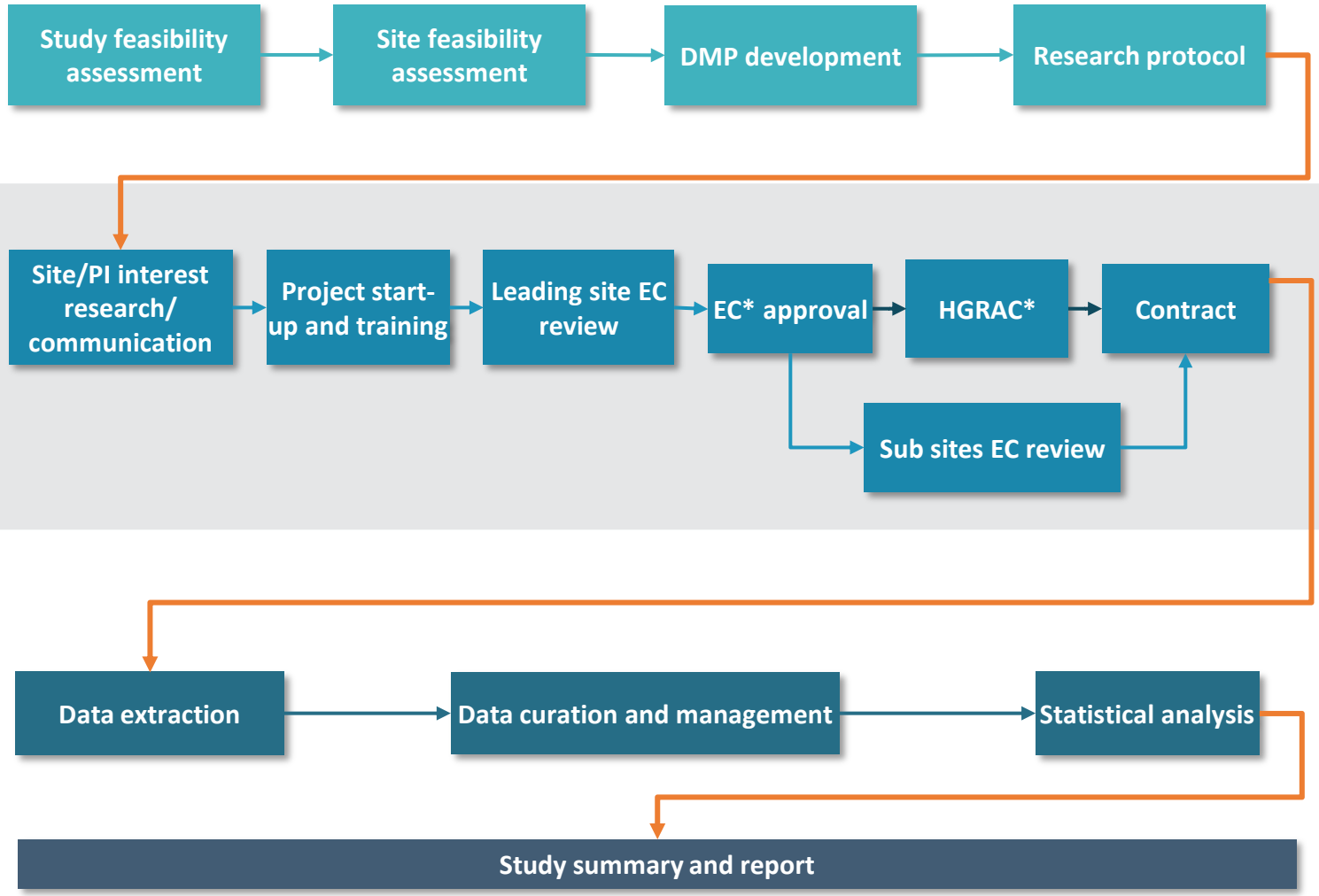
Site start-up and management to promote RWS execution in China

Phase 1 — Feasibility assessment and Study design

Phase 2 — Site start-up and management

Phase 3 — Data management and statistical analysis

Phase 4 — Study report and publication



EC: Ethics Committee;
HGRAC: Human Genetic Resources Administration of China

PI mapping and site selection

50%

Research project related

- Sample size
- Operation risk

35%

Principal Investigator

- Members of academic associations
- Authors of guidelines and consensus
- Publications
- Hospital titles

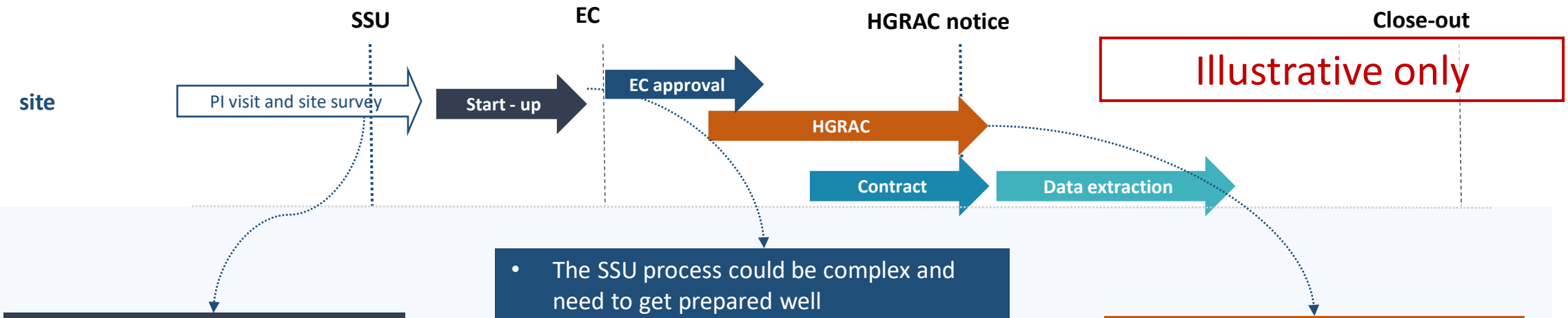
15%

Hospital and Department

- Overall rank of hospital
- Rank of oncology department
- Research capacity
- Oncology department capacity

	Source
Research	Authors of guidelines and consensus
	Members of academic associations
	Conference speakers
	PIs of key competitors

Rigorous SSU pre-planning to manage RWS operation

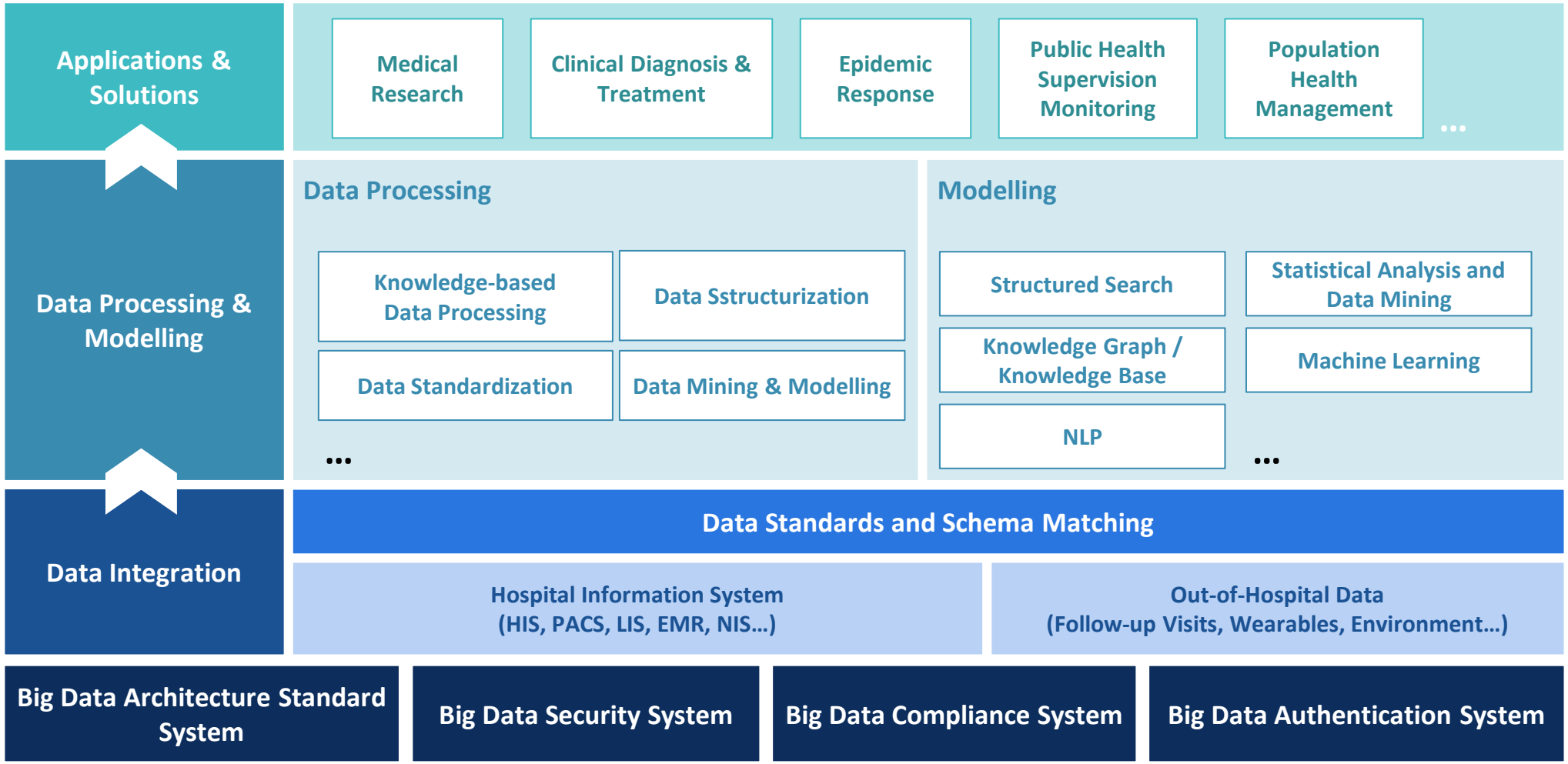


- Hospital checklist of documents for submission
- Sufficient time for hospitals to review site start-up materials.

- The SSU process could be complex and need to get prepared well
- Several weeks or several months for EC approval could be possible

- Upon contract finalization, the signing procedure can be completed within 1 month
- 2-4 months for HGRAC approval.

Solid and efficient technology provides opportunities for conducting RWS from different hospitals



Future considerations and actions to advance RWE in China

- Data authorization and compliance to obtain real world data is a huge challenge.
- Site start-up and management should follow the regulations of EC, HGRAC, and hospitals requirement, a big challenge for management of project timeline.
- Professionally qualified personnel and multi-background teams are required to manage hospital-based data and multi-source data collection and analysis.

Q&A