OMOP共通モデル データの活用経験

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Conflict of interest
利益相反

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Real-world data/ evidence for the product life cycle in pharmaceuticals
医薬品ライフサイクルにおけるリアルワールドデータ／エビデンスの創出

Pre-clinical → Phase I → POC → Phase IIb → Phase III → Filing → Launch → Post-launch

前臨床

- **Generate hypotheses**
  仮説の創出
- **Deepen disease understanding**
  対象疾患の理解
- **Select and prioritize indication**
  適応疾患の選択や優先順位付け

臨床試験

- **Inform study design & patient selection**
  試験デザインや患者選定
- **Define drivers of health economic benefit** by the analysis of healthcare cost and resource use
  医療経済的なベネフィットの定義づけ
  - Evaluate **feasibility of using synthetic control arms**
    臨床試験の合成対照群設定の実施妥当性評価
  - Systematically explore **novel trial designs**
    新たな臨床試験デザインの系統的探索
  - Leverage RWD to **inform PRO endpoints**
    患者報告アウトカムを用いたエンドポイント
  - **Inform Access discussions (pricing, reimbursement)**
    薬価や保険償還に関するディスカッション
- **Disease burden, natural course, treatment patterns, and unmet needs**
  疾患の疾病負荷や自然史、治療実態、アンメットニーズに関する調査

承認申請から市販後

- **Support filing and respond to questions from regulatory authority**
  承認申請の補助や照会事項対応
  - **Support LCM** with novel methods (e.g., pediatric development)
    新規手法によるライフサイクルマネジメントの支援
    - **Inform HTA**
      医療技術評価への利用
    - **Shape patient engagement & support programs**
      患者支援プログラムの検討
    - **Differentiate vs. competitors**
      他製品との差別化
    - Support **label expansion based on real-world evidence**
      適応拡大（対象疾患・用法用量等）
      - **Post-marketing surveillance**
        製造販売後調査

POC, Proof of Concept; PRO, Patient Reported Outcomes; LCM, Life Cycle Management; HTA, Health Technology Assessment

Hiramatsu K, Barrett A, Miyata Y et al. Current status, challenges, and future perspectives of real-world data and real-world evidence in Japan. *Drugs – Real World Outcomes.* 2021を参照の元に作成.

The Observational Medical Outcomes Partnership Common Data Model

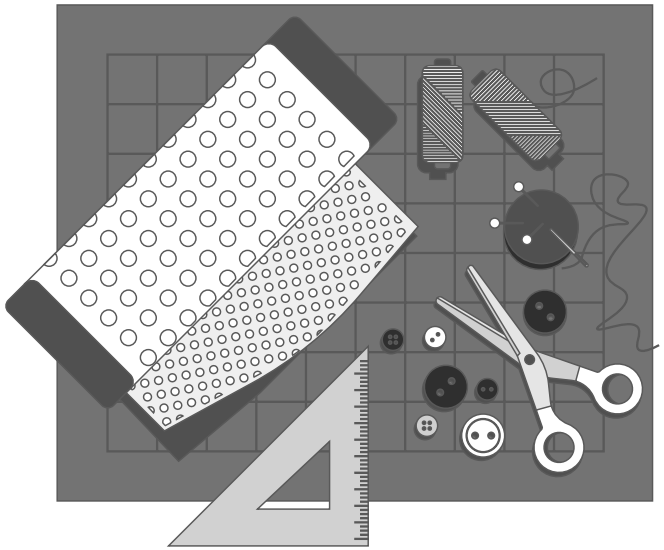
OMOP共通データモデル

Transform data contained within disparate databases into a common format (data model) as well as a common representation (terminologies, vocabularies, coding schemes), and then perform systematic analyses using a library of standard analytic routines that have been written based on the common format.

異なるデータベースを共通フォーマットかつ共通の表現（用語・語彙・コーディング方式）に変換. 共通フォーマットに基づく標準的分析ライブラリを用いた体系的分析.

Evidence can be generated using standardized analytics tools for data quality and characterization, medical product safety surveillance, comparative effectiveness, quality of care, and patient-level predictive modeling.

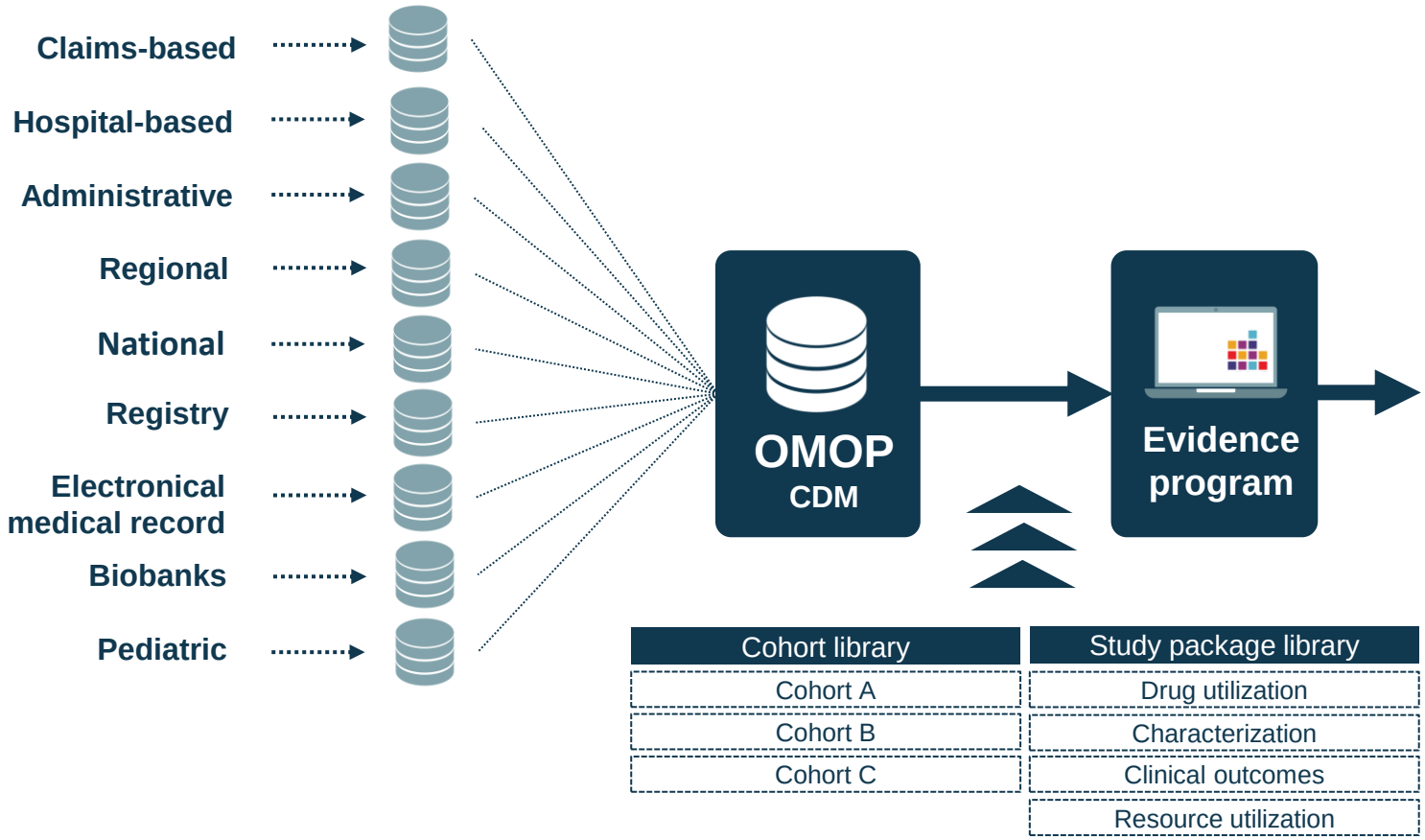
標準的な分析ツールを用いて種々の研究が実施できる.



Observational Health Data Science and Informatics (OHDSI), available at: https://www.ohdsi.org/data-standardization/ (Accessed on Jan 11, 2025).

Federated evidence generation program

連合型データネットワークによるエビデンス創出



- *Feasibility study*
- *Natural history*
- *Pharmacoepidemiology*
- *Pharmacovigilance*
- *Health economics*
- *Outcome research*

… and more

What are the merits of OMOP-CDM?

OMOP共通データモデルにどのようなメリットがある?

// Replicating studies across datasets

データセットを跨いで研究を再現できそう

// Increase international collaboration

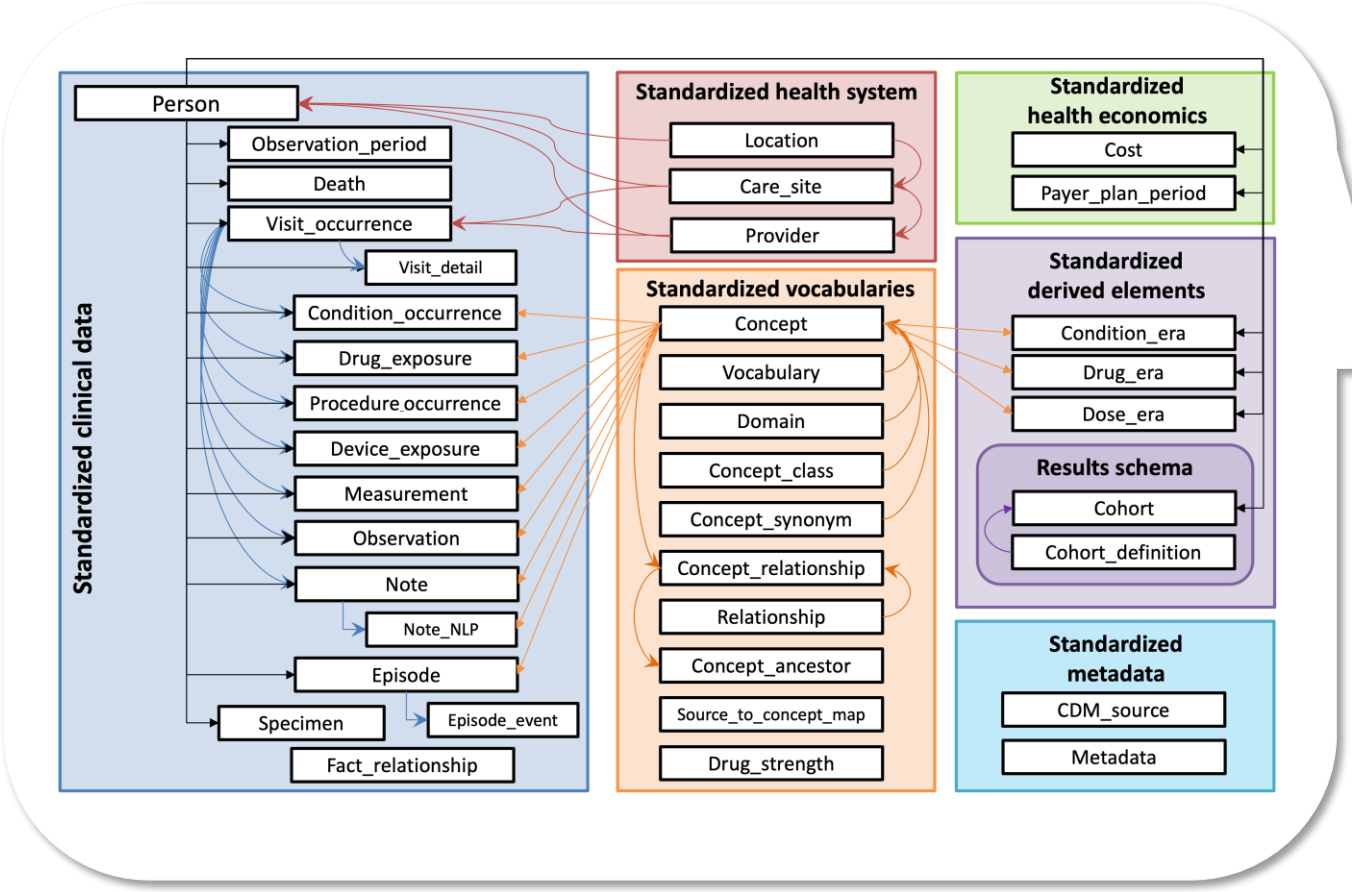
海外とのコラボレーションの機会が増えそう

// Ease data handling and analysis

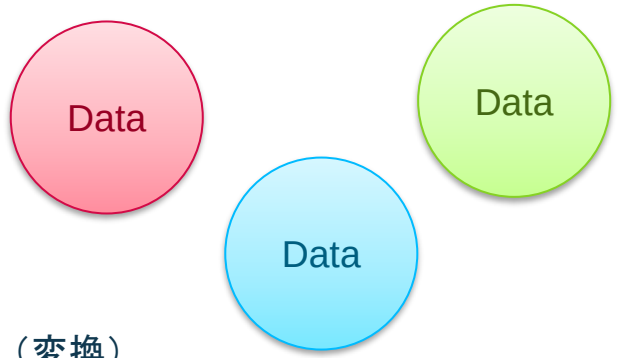
データハンドリングや解析が容易になりそう

Extract, Transform, Load process

E（抽出）T（変換）L（ロード）プロセス

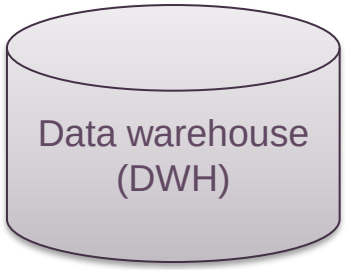


Extract （抽出）



Transform （変換）

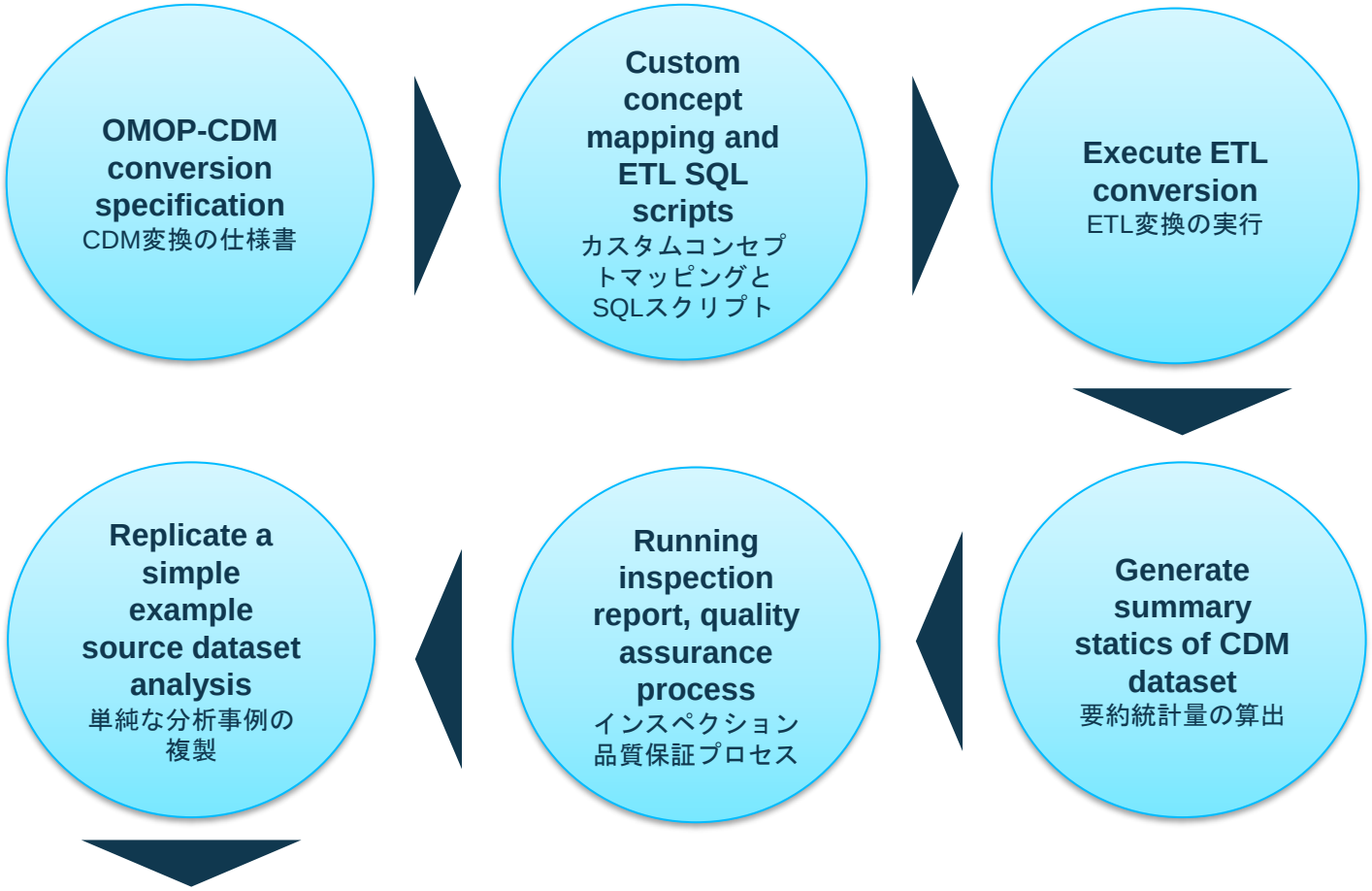
Load （ロード）



Observational Health Data Science and Informatics (OHDSI), available at: https://www.ohdsi.org/data-standardization/ (Accessed on Jan 11, 2025).

Process flow of OMOP-CDM conversion

OMOP-CDM変換の流れ



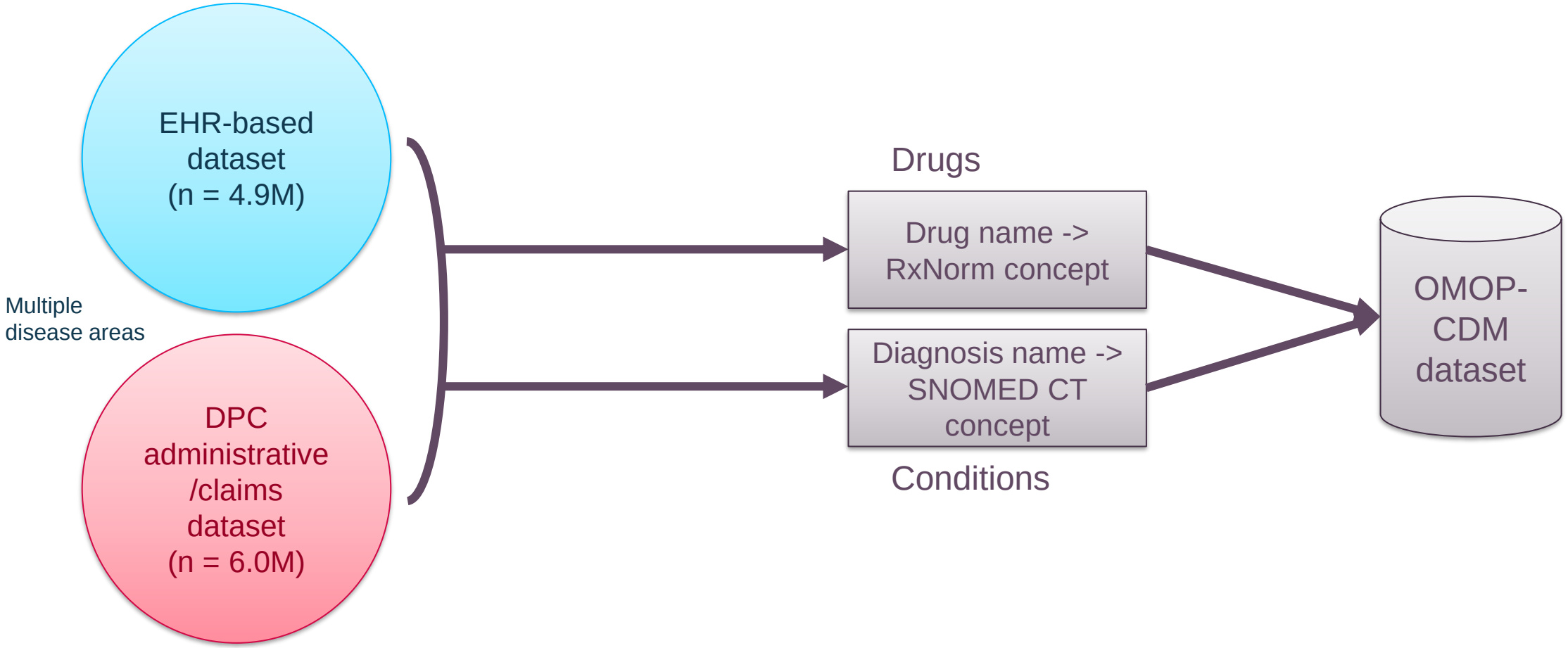
Load the new OMOP CDM datasets as new data sources in the ATLAS.

ATLASの新規データソースとしてLoad（ロード）

LOCATION
CARE_SITE
RROVIDER
PERSON
OBSERVATION_PERIOD
DEATH
LOCATION_HISTORY
VISIT_DETAIL
VISIT_OCCURRENCE
CONDITION_OCCURRENCE
CONDITION_ERA
PROCEDURE_OCCURRENCE
DRUG_EXPOSURE
DRUG_ERA
OBSERVATION
MEASUREMENT
DEVICE_EXPOSURE

Conversion of Japanese datasets into OMOP-CDM

日本データセットのOMOP共通モデルへの変換



Using standardized OMOP vocabularies
標準化されたOMOPのボキャブラリーを活用

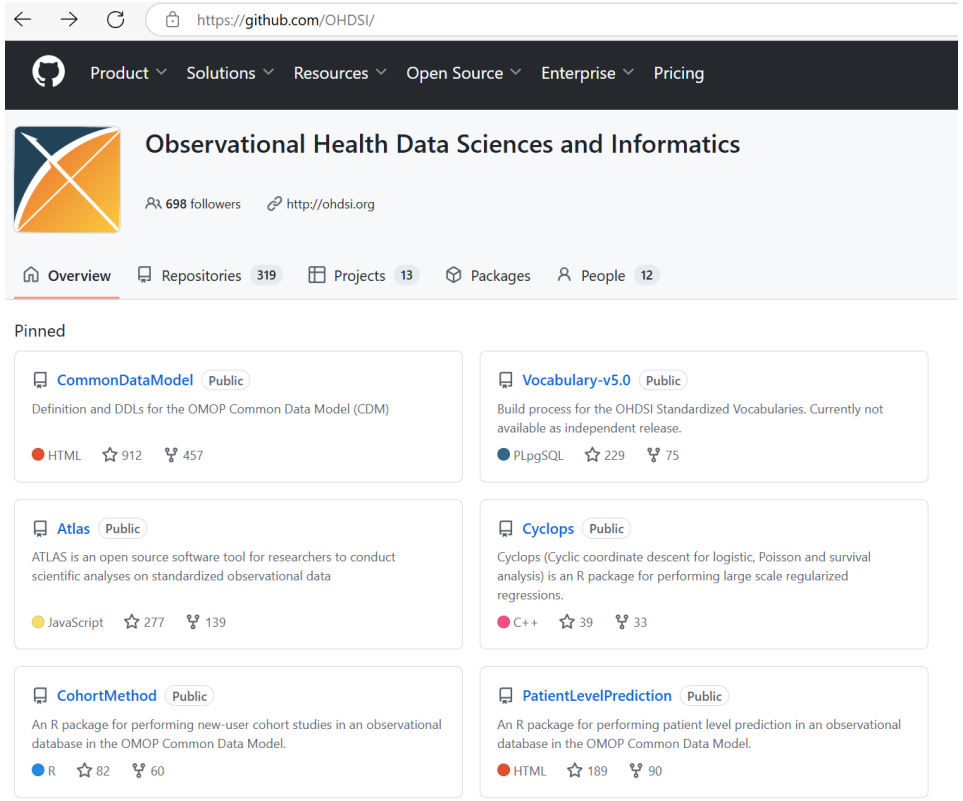
// Conditions コンディション
- // Prioritized subsets were custom-mapped (Condition)
- // Otherwise, ICD-10 4 condition category automated mapping was used

// Drugs/Device 薬剤/デバイス
- // Prioritized subsets were custom-mapped (Drug/Device)
- // Otherwise, ATC code to RxNorm automated mapping was used

// Labs 検査値
- // Custom-mapped (200+ labs)

// Procedures 処置
- // Custom map added to J&J JMDC data source Japan data source custom mapping (Procedure/Measurement/Observation)

// DPC FF1 DPC様式1
- // Custom-mapped (Measurement/Observation)



Observational Health Data Science and Informatics (OHDSI) Github, available at: https://github.com/OHDSI/ (Accessed on Jan 11, 2025).

Some unique nuances were kept through CDM conversion

共通モデル変換でも幾つかの独特なニュアンスを維持

Example 1

Standard Concept: Hemoglobin measurements

Adding attribute to find hemoglobin measurements before, after or during dialysis (for glanular measurement)

標準コンセプトに紐づける形でより詳細な測定時点の情報も含む検査値情報の属性を追加（例：ヘモグロビン値の測定）

Example 2

Diet expense during hospitalization from does not have a standard concept mapping.

Adding attribute to find diet expense to **include additional source concept**. (for glanular observation)

標準コンセプトがない観測項目を追加（例：入院中の食事費用）

Example 3

Standard concept: Abnormal results of cardiovascular function studies

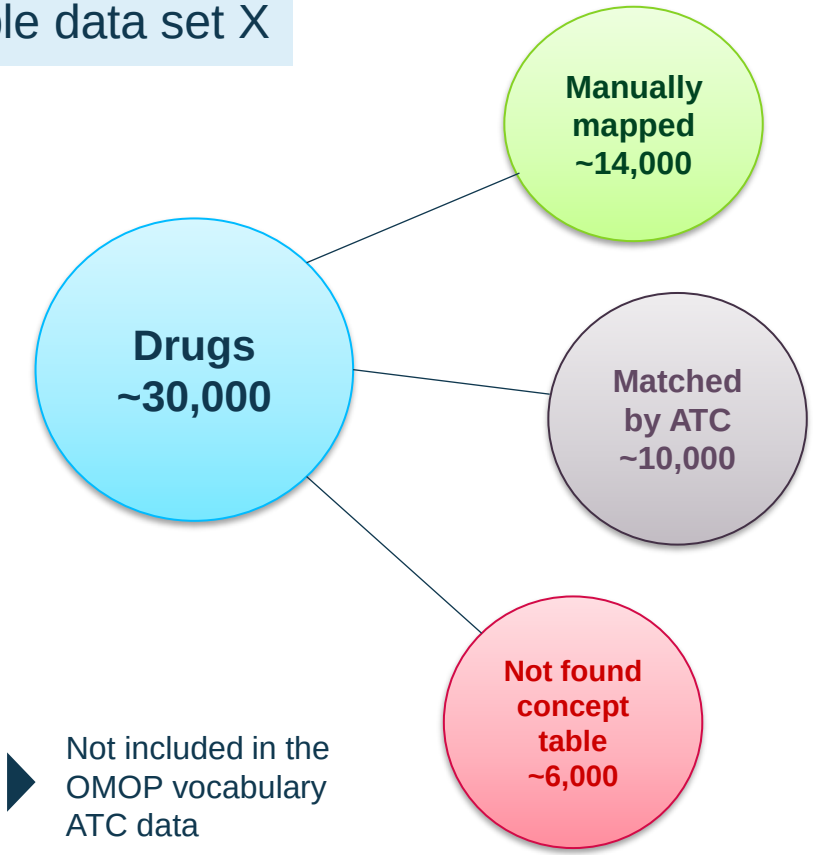
Adding attribute to find specific condition records e.g., vectorcardiography abnormal, electro cardiogram right axis deviation, early repolarization syndrome. (for glanular conditions)

標準コンセプトに紐づける形でより詳細な状態の属性情報を追加（例：心機能検査で特定された異常）

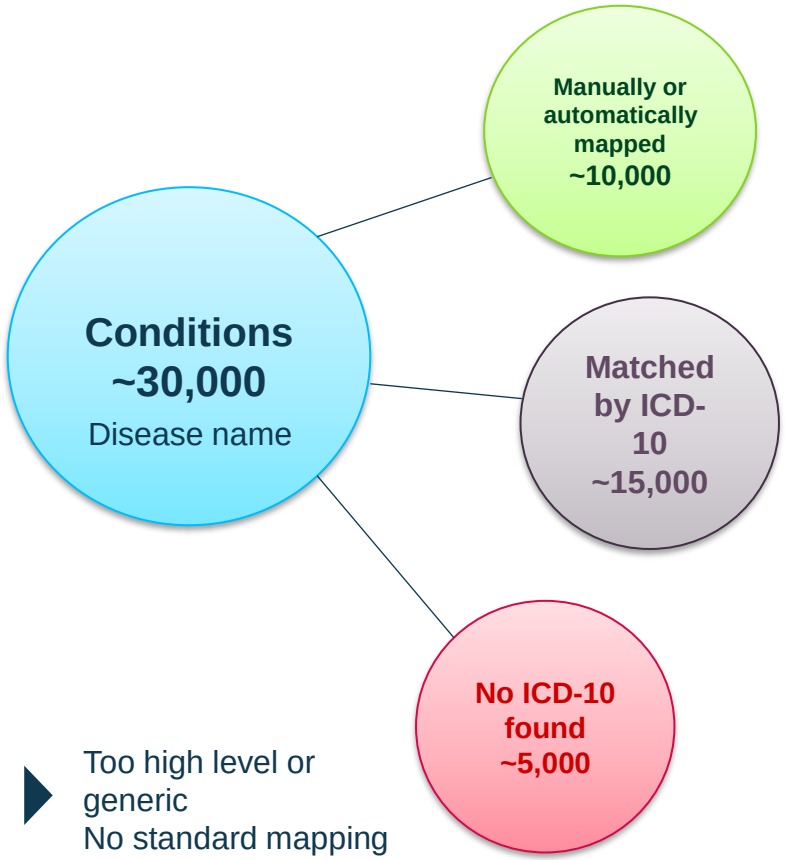
Not everything went well…

すべてが思った通りに進むわけでもなく…

Example data set X



Local drug
Latest drug
▶ Not included in the OMOP vocabulary ATC data



Using ICD-10 for mapping
▶ Too high level or generic
No standard mapping

OMOP'd data were used in an actual project
実際のプロジェクトでのOMOPデータの活用

Sato A, Molina-Rodoriguez D, Yoshikawa-Rayan K, et al. Early clinical experience of finerenone in people with chronic kidney disease and type 2 diabetes in Japan – a multi-cohort study from the FOUNTAIN (FinerenOne mUltidatabase NeTwork for evidence generAltioN). *J Clin Med.* 2024; **13**(14): 5107.

Journal of *Clinical Medicine*

MDPI

Article

Early Clinical Experience of Finerenone in People with Chronic Kidney Disease and Type 2 Diabetes in Japan—A Multi-Cohort Study from the FOUNTAIN (FinerenOne mUltidatabase NeTwork for Evidence generAtIoN) Platform

Atsuhisa Sato [1], Daloha Rodriguez-Molina [2], Kanae Yoshikawa-Ryan [3], Satoshi Yamashita [3], Suguru Okami [3,*], Fangfang Liu [2], Alfredo Farjat [2], Nikolaus G. Oberprieler [2], Csaba P. Kovesdy [4], Keizo Kanasaki [5,6] and David Vizcaya [2]

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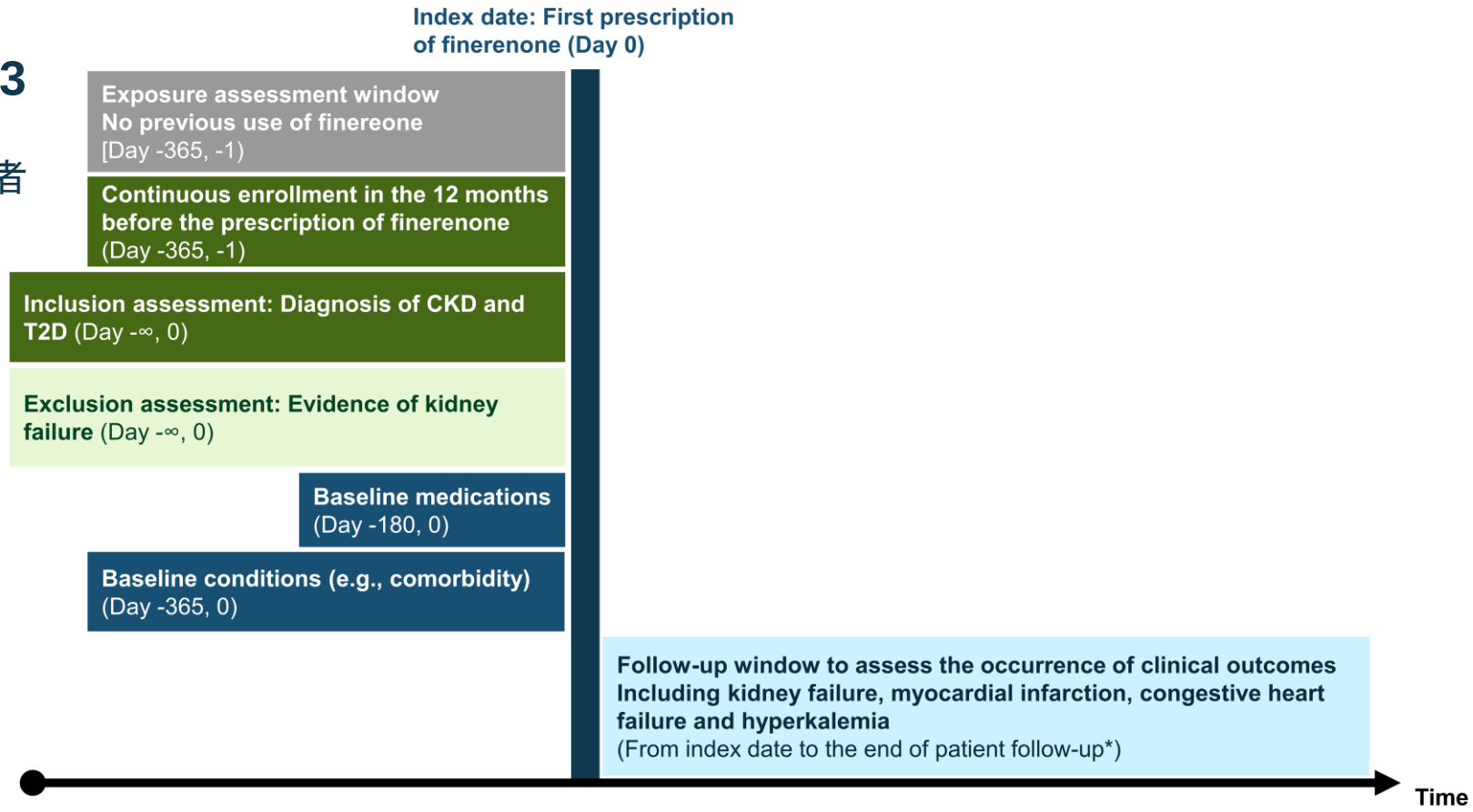
What are the baseline characteristics of patients with chronic kidney disease and type 2 diabetes who initiate finerenone?
フィネレノンを開始した2型糖尿病を伴う慢性腎臓病患者の背景はどのようになっているか?

Study outline
研究概要

// New user of finerenone from June 2022–Aug 2023
2022年6月から2023年8月の間に
フィネレノンの処方が開始された患者

// Patient characteristics and clinical outcomes
患者背景と臨床アウトカム



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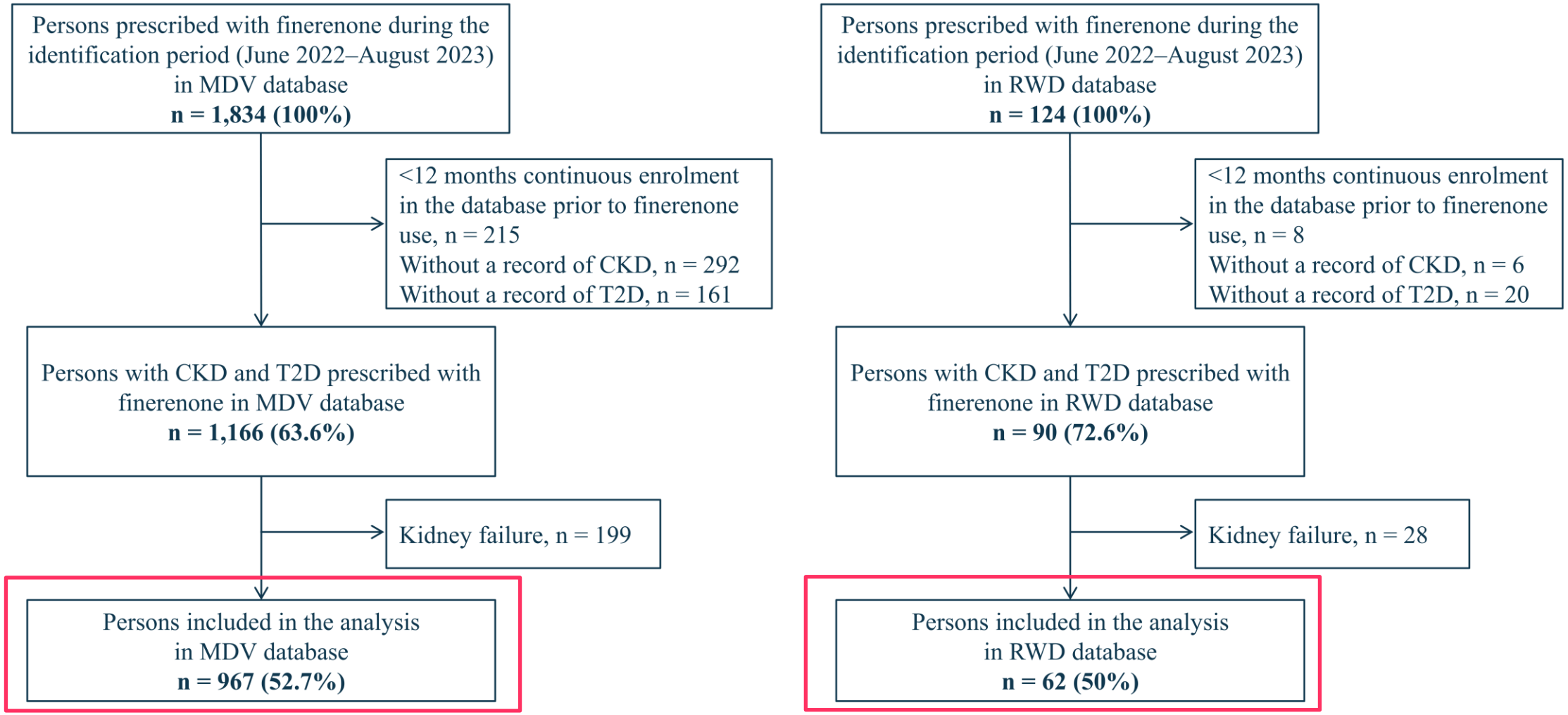
Flow diagrams of persons included in the study



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Characteristics of persons included in the study

	MDV (N = 967)	RWD Co. (N = 62)
Age (years)		
Mean ± SD	69.5 ± 12.4	72.4± 10.4
Median (Q1, Q3)	72 (62, 79)	74 (67, 80)
Gender, female, n (%)	264 (27.3)	17 (27.4)
Index year, n (%)		
2022	101 (10.4)	28 (45.2)
2023	866 (89.6)	34 (54.8)
Hemoglobin A1c, %		
Mean ± SD	7.4 ± 1.5	7.3 ± 1.1
Median (Q1, Q3)	7.0 (6.4, 8)	7.0 (6.5, 7.8)
Missing, n (%)	827 (85.5)	1 (1.6)
eGFR, mg/min/1.73 m^2		
Mean ± SD	–	43.4 ± 18.1
Category, n (%)		
Stage 2 60–89	–	2 (3.2)
Stage 3 30–59	–	33 (53.2)
Stage 4 15–29	–	27 (43.6)
Finerenone dose initiation, n (%)		
10 mg	854 (88.3)	58 (93.6)
20 mg	113 (11.7)	4 (6.5)
Comorbidity, n (%)		
Hypertension	894 (92.5)	59 (95.2)
Hyperlipidemia	568 (58.7)	44 (71.0)
Congestive heart failure	577 (59.7)	41 (66.1)
Prior hospitalization for heart failure	212 (21.9)	10 (16.1)
Coronary heart disease	372 (38.5)	23 (37.1)
Peripheral vascular disease	137 (14.2)	14 (22.6)
Atrial fibrillation	154 (15.9)	10 (16.1)
Acute coronary syndrome	177 (18.3)	16 (25.8)
Myocardial infarction	87 (9)	8 (12.9)
Cerebrovascular disease	215 (22.2)	15 (24.2)
Neuropathy	198 (20.5)	9 (14.5)
Retinopathy	149 (15.4)	9 (14.5)

	MDV (N = 967)	RWD Co. (N = 62)
Charlson Comorbidity Index		
Mean ± SD	8.2 ± 3.1	10.2 ± 3.5
Median (Q1, Q3)	8 (6, 10)	9 (8–12)
Diabetes Complication Severity Index		
Mean ± SD	5.2 ± 1.8	6.7 ± 2.1
Median (Q1, Q3)	5 (4, 6)	6 (5, 8)
Comedications, n (%)		
ACEi or ARB	776 (80.3)	50 (80.7)
ACEi	350 (36.2)	27 (43.6)
ARB	717 (74.2)	45 (72.6)
ARNI	208 (21.5)	10 (16.1)
Calcium-channel blockers	481 (49.7)	30 (48.4)
Beta-blockers	297 (30.7)	22(35.5)
Loop diuretics	218 (22.5)	17 (27.4)
Thiazide diuretics	45 (4.7)	2 (3.2)
Steroidal MRA	143 (14.8)	5 (8.1)
Non-steroidal MRA other than finerenone	64 (6.6)	1 (1.6)
Statins	571 (59.1)	44 (71.0)
Anticoagulants	153 (15.8)	11 (17.7)
Potassium binders	62 (6.4)	2 (3.2)
SGLT-2i	694 (71.8)	45 (72.6)
GLP-1 RA	268 (27.7)	19 (30.7)
SGLT-2i or GLP-1 RA	760 (78.6)	48 (77.4)
SGLT-2i and GLP-1 RA	202 (20.9)	16 (25.8)
Metformin	322 (33.3)	21 (33.9)
Dipeptidyl peptidase 4 inhibitors	480 (49.6)	40 (64.5)
Sulfonylureas	133 (13.8)	16 (25.8)
Meglitinides	122 (12.6)	13 (21)
Alpha-glucosidase inhibitors	113 (11.7)	4 (6.5)
Thiazolidinediones	30 (3.1)	1 (1.6)
Insulins	295 (30.5)	17 (27.4)

Sato A, Molina-Rodoriguez D, Yoshikawa-Rayan K, et al. Early clinical experience of finerenone in people with chronic kidney disease and type 2 diabetes in Japan – a multi-cohort study from the FOUNTAIN (FinerenOne mUltidatabase NeTwork for evidence generAltioN). *J Clin Med.* 2024; **13**(14): 5107.

Outcomes

	Number of Persons in Cohort	Number of Persons at Risk	Number of Events	Incidence Proportion (per 100 Persons)
MDV				
Hyperkalemia	967	832	18	2.16
Hospitalization associated with hyperkalemia	967	944	0	0
RWD Co.				
Hyperkalemia	62	37	1	2.70
Hospitalization associated with hyperkalemia	62	48	0	0

The median (Q1, Q3) durations of follow-up were 52 (27, 86) and 42 (15, 98) days in the MDV and RWD Co. databases, respectively.
Due to the short follow-up time, very few cases had cardiovascular or kidney failure outcomes.
短い追跡期間の為に十分なアウトカムの評価は出来なかった.

Sato A, Molina-Rodoriguez D, Yoshikawa-Rayan K, et al. Early clinical experience of finerenone in people with chronic kidney disease and type 2 diabetes in Japan – a multi-cohort study from the FOUNTAIN (FinerenOne mUltidatabase NeTwork for evidence generAItioN). *J Clin Med.* 2024; **13**(14): 5107.

Lessons learned

The relatively small sample size as well as the short follow-up times after finerenone initiation, due to the limited availability of data after the drug authorization of finerenone in Japan, restricted the robust estimation of the incidence of clinical outcomes.
比較的小規模なサンプルサイズや短い追跡期間による制約のあるデータセット

The common data structure based on the OMOP-CDM with the same analytical protocol ensures the reproducibility of the analyses conducted across different datasets. Consistent findings in the baseline characteristics and the incidence of clinical outcomes support the reliability of the findings from this study, despite the small-to-moderate sample size of the study population identified in each dataset.
OMOP-CDMに基づく共通のデータ構造と分析プロトコルによる再現性の担保.
一貫した結果は小規模なサンプルサイズながら、結果の信頼性を支持する.

Sato A, Molina-Rodoriguez D, Yoshikawa-Rayan K, et al. Early clinical experience of finerenone in people with chronic kidney disease and type 2 diabetes in Japan – a multi-cohort study from the FOUNTAIN (FinerenOne mUltidatabase NeTwork for evidence generAItioN). *J Clin Med.* 2024; **13**(14): 5107.

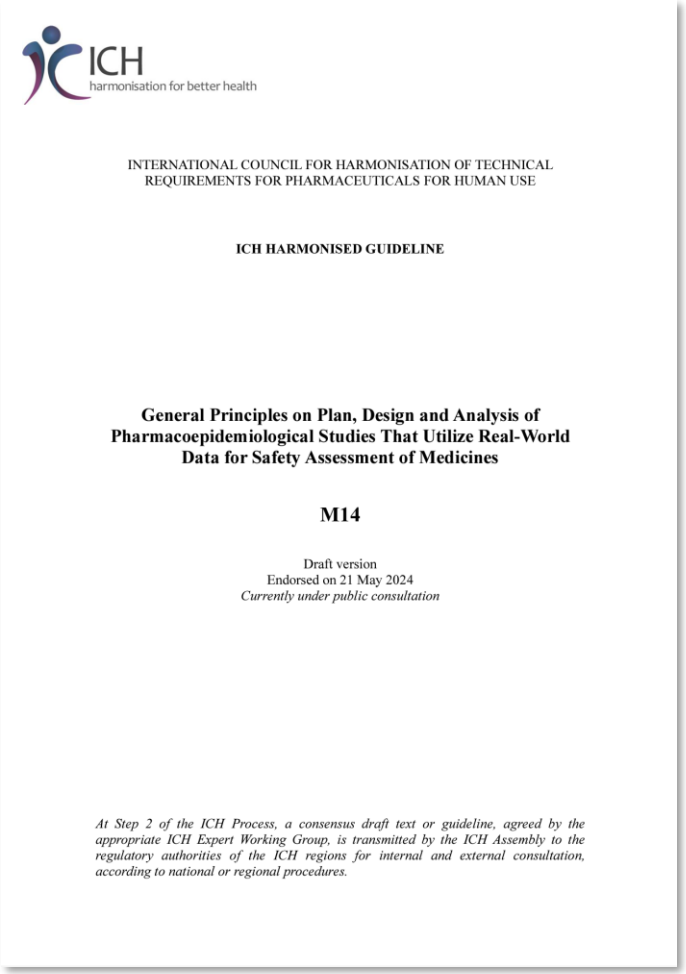
Federated Data Network (FDN)
連合型データネットワーク

// *Decreasing the time to conduct a study, either through pre-developed analyses, or by increasing the size of study populations as this shortens the time needed to obtain the desired sample size. Large sample sizes may facilitate research on rare events, rare diseases, and less common drug exposures;*
期待するサンプルサイズを得る為に要する時間を短縮することで調査の対象集団の規模を増大することによって、調査の実施にかかる期間を短縮する。サンプルサイズを大きくすることで、稀な有害事象、稀な疾患及びあまり一般的でない薬剤暴露に関する調査が促進される可能性がある。

// *Multi-database studies may provide additional knowledge on whether a drug safety issue exists in different populations or across countries and thereby may reveal causes of differential drug effects, inform the generalizability of results, the consistency of information and the impact of biases on estimates;*
複数のデータベースを用いた調査は、異なる集団又は国の間で医薬品の安全性上の問題が存在するか否かに関する追加の知見を提供しうる。また、追加の知見によって薬効に差が生じる原因が明らかにされる可能性があるだけでなく、結果の一般化可能性、情報の一貫性及び推定値へのバイアスが推定に及ぼす影響についての情報を提供する可能性もある。

// *Heterogeneity of treatment options and utilization patterns across institutions, communities or countries may allow for a more complete understanding of the effect of individual medicines; and*
治療選択肢及び医薬品の利用傾向が医療機関、地域または国の間で不均一であることによって、個々の医薬品の効果をより完全に理解することが出来る可能性がある。

// *Involvement of experts from various countries addressing terminologies, coding in databases and research practices provides opportunities to increase consistency of results of pharmacoepidemiological studies.*
様々な国の専門家が参加し、専門用語、データベースにおけるコード化、調査のプラクティスについて対処、議論することで、薬剤疫学調査の結果の一貫性を高められる可能性がある。



ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

General Principles on Plan, Design and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines

M14

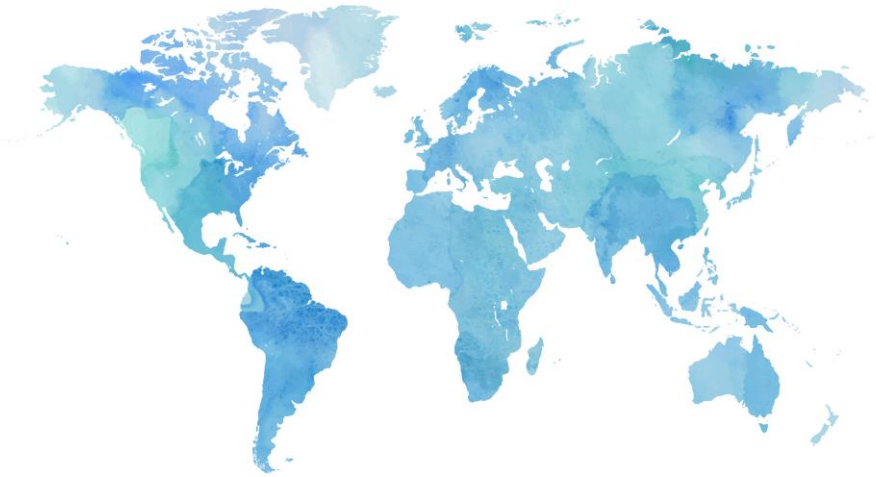
Draft version
Endorsed on 21 May 2024
Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

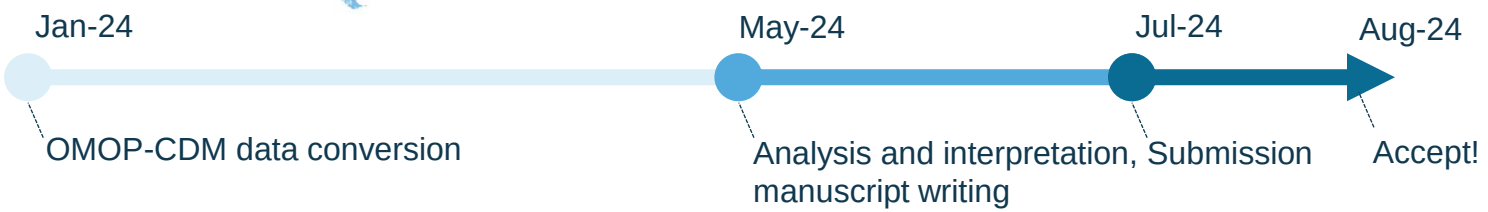
The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). General Principles on Plan, Design and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines. Available at: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://database.ich.org/sites/default/files/ICH_M14_Step3_DraftGuideline_2024_0521.pdf (accessed on January 16, 2025).

山川異域 風月同天

A Chinese ancient poems that read "山川異域 風月同天" is used for disaster aids between Japan and China.
It means no matter where we live, wind and moon connects us under the same sky.



Study package owner
OMOP data conversion expert
Epidemiologist
Project leader (initiator)



In this contemporary study, we report on the early clinical use of finerenone in real-world settings, just after drug authorization in Japan.
承認直後の早期の実臨床での使用実態を報告

This study provides new population-based insights, adding to the previously reported case series in persons with CKD stage 4 and treated with finerenone, with a broad range of individuals with CKD and T2D included in the study.
これまでに報告されていたケースシリーズに加えて広範な集団を含む新たな示唆を提供

Sato A, Molina-Rodoriguez D, Yoshikawa-Rayan K, et al. Early clinical experience of finerenone in people with chronic kidney disease and type 2 diabetes in Japan – a multi-cohort study from the FOUNTAIN (FinerenOne mUltidatabase NeTwork for evidence generAItioN). *J Clin Med.* 2024; **13**(14): 5107.

Bottom line
まとめ

// OMOP conversion takes a certain amount of time and effort.
OMOP変換にはある程度の時間もエフォートも要する.

// By putting into practice, we realized unique values of OMOP.
実践してみることでOMOPならではの価値にも気づくことがあった.

- // *Reproducibility* 再現性
- // *Federated data network* 連合型データネットワーク
- // *New ways of working and collaboration* 新たな働き方とコラボレーション

// It may be possible to create more value by utilizing a disease portfolio perspective rather than a project by itself.
プロジェクト個々よりも大きな疾患ポートフォリオの視点で活用することによってより価値を生み出すことができるかもしれない.

Health for all, Hunger for none

Thank you!

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