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海外のアウトカムバリデーション手法の紹介および日本に展開するにあたっての留意点

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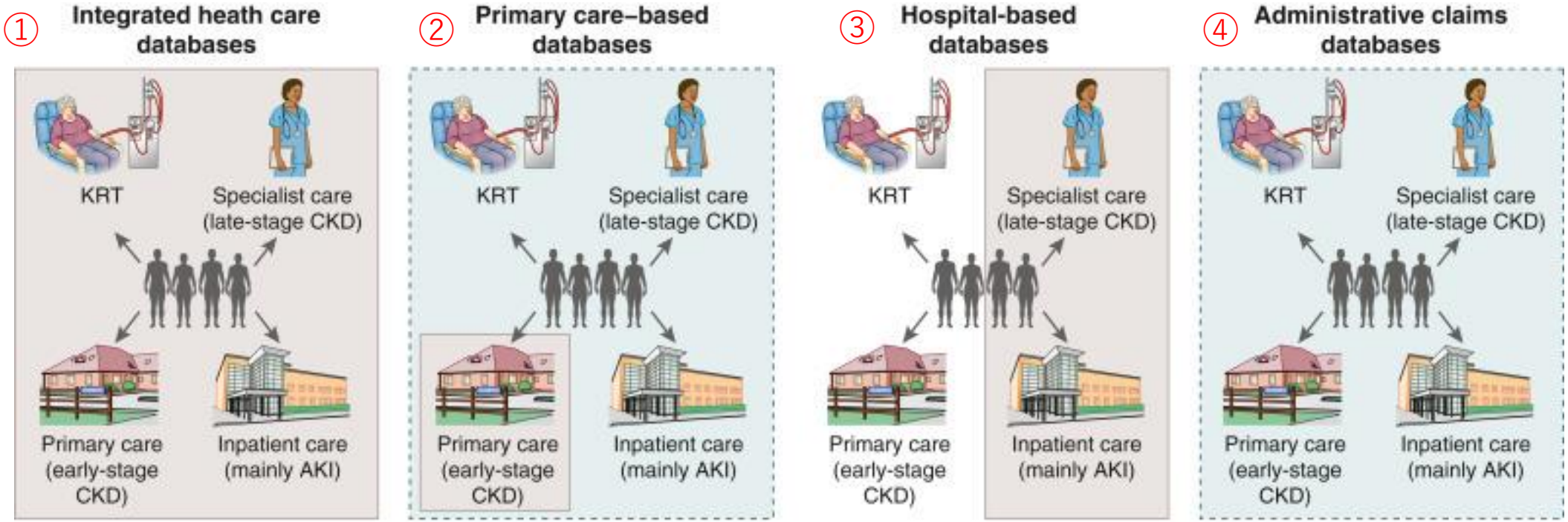
(1) 世界の医療データベースの種類

パターン①



For example:
- SCREAM
- Danish databases
- Canadian provincial databases
- US Veterans Affairs
- Kaiser Permanente databases
- Thailand electronic health records

For example:
- UK CPRD
- SIDIAP database
- Dutch primary care data

For example:
- Some HMO databases
- Some disease (e.g., diabetes) registries
- MIDNET in Japan

For example:
- US Medicare and commercial databases
- Taiwan NHI database
- Korean NHI databases
- NDB in Japan

Availability of laboratory test results and coded diagnoses

Availability of coded diagnoses for CKD, AKI, and KRT

(Carrero, Fu, Iwagami, Nitsch et al. Kidney Int, 2022).[4]

(1) 世界の医療データベースの種類：バリデーションの方法

パターン①

For example:
- SCREAM
- Danish databases
- Canadian provincial databases
- US Veterans Affairs
- Kaiser Permanente databases
- Thailand electronic health records

②

For example:
- UK CPRD
- SIDIAP database
- Dutch primary care data

③

For example:
- Some HMO databases
- Some disease (e.g., diabetes) registries
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④

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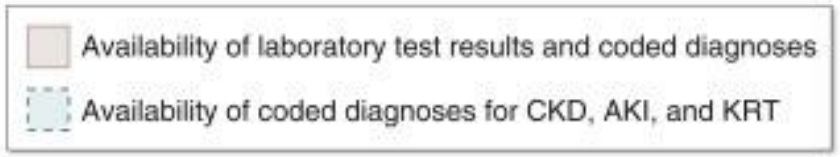
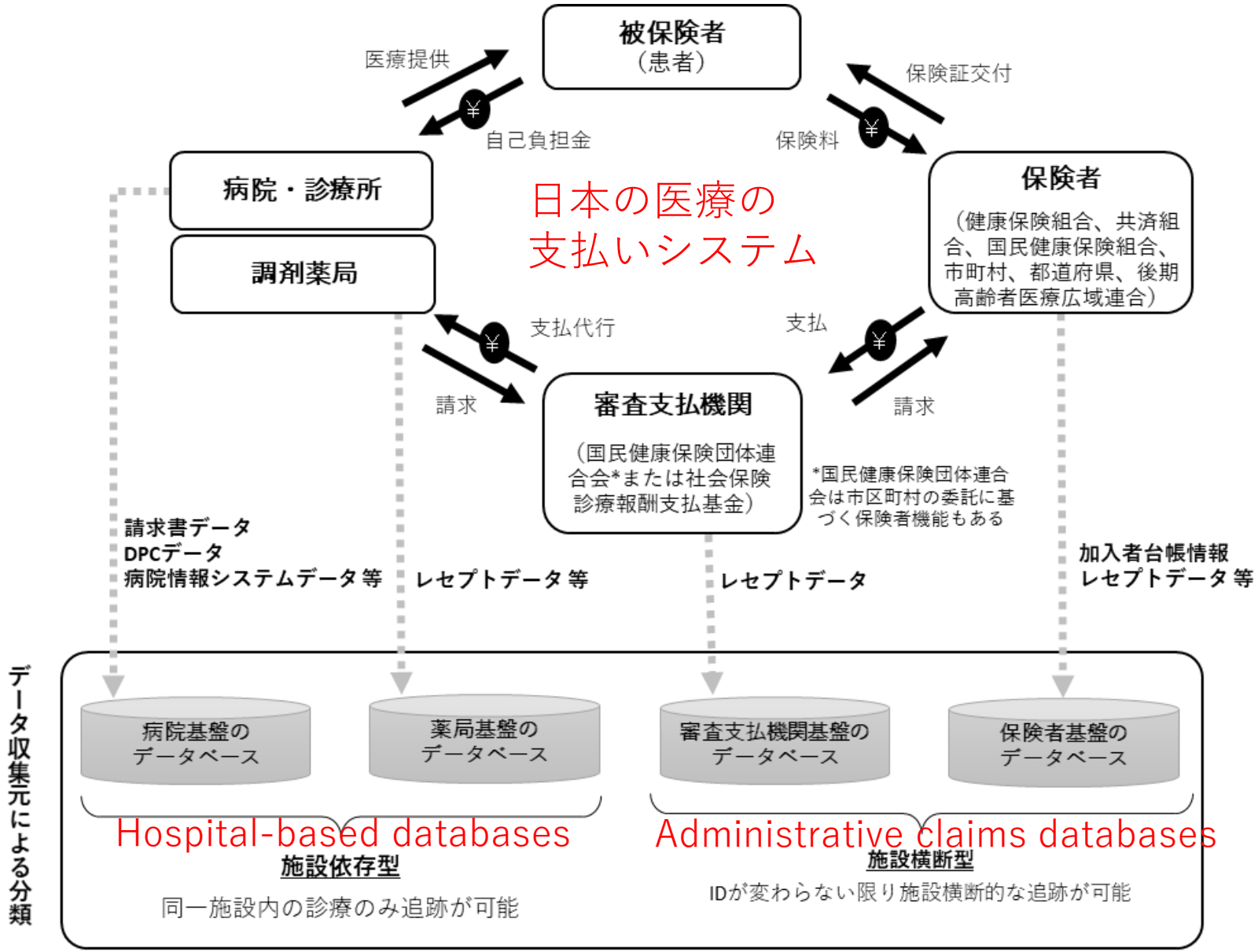


(Carrero, Fu, Iwagami, Nitsch et al. Kidney Int, 2022).

(2) 日本の医療データベースの種類



石黒智恵子氏より提供
(これからの薬剤疫学 p33)

(3) アウトカムバリデーション (特に陽性的中度) が重要な理由

例1: 完璧なアウトカム定義で研究を行えた場合 (感度100%、特異度100%、陽性的中度100%)

医薬品A群		真の上部消化管出血		
		Yes	No	合計
疾患定義	Yes	100	0	100
	No	0	900	900
	合計	100	900	1000

医薬品B群		真の上部消化管出血		
		Yes	No	合計
疾患定義	Yes	50	0	50
	No	0	950	950
	合計	50	950	1000

医薬品A群 1000人 → 上部消化管出血 100人

真の相対リスク2.0

医薬品B群 1000人 → 上部消化管出血 50人

例2: アウトカム定義の感度が高く、陽性的中度が低い場合 (感度100%、特異度80%、陽性的中度20.8~35.7%)

医薬品A群		真の上部消化管出血		
		Yes	No	合計
疾患定義	Yes	100	180	280
	No	0	720	720
	合計	100	900	1000

医薬品B群		真の上部消化管出血		
		Yes	No	合計
疾患定義	Yes	50	190	240
	No	0	760	760
	合計	50	950	1000

医薬品A群 1000人 → 上部消化管出血 280人

相対リスク1.17 (過小評価)

医薬品B群 1000人 → 上部消化管出血 240人

例3: アウトカム定義の感度が低く、陽性的中度が高い場合 (感度50%、特異度100%、陽性的中度100%)

医薬品A群		真の上部消化管出血		
		Yes	No	合計
疾患定義	Yes	50	0	50
	No	50	900	900
	合計	100	900	1000

医薬品B群		真の上部消化管出血		
		Yes	No	合計
疾患定義	Yes	25	0	25
	No	25	950	975
	合計	50	950	1000

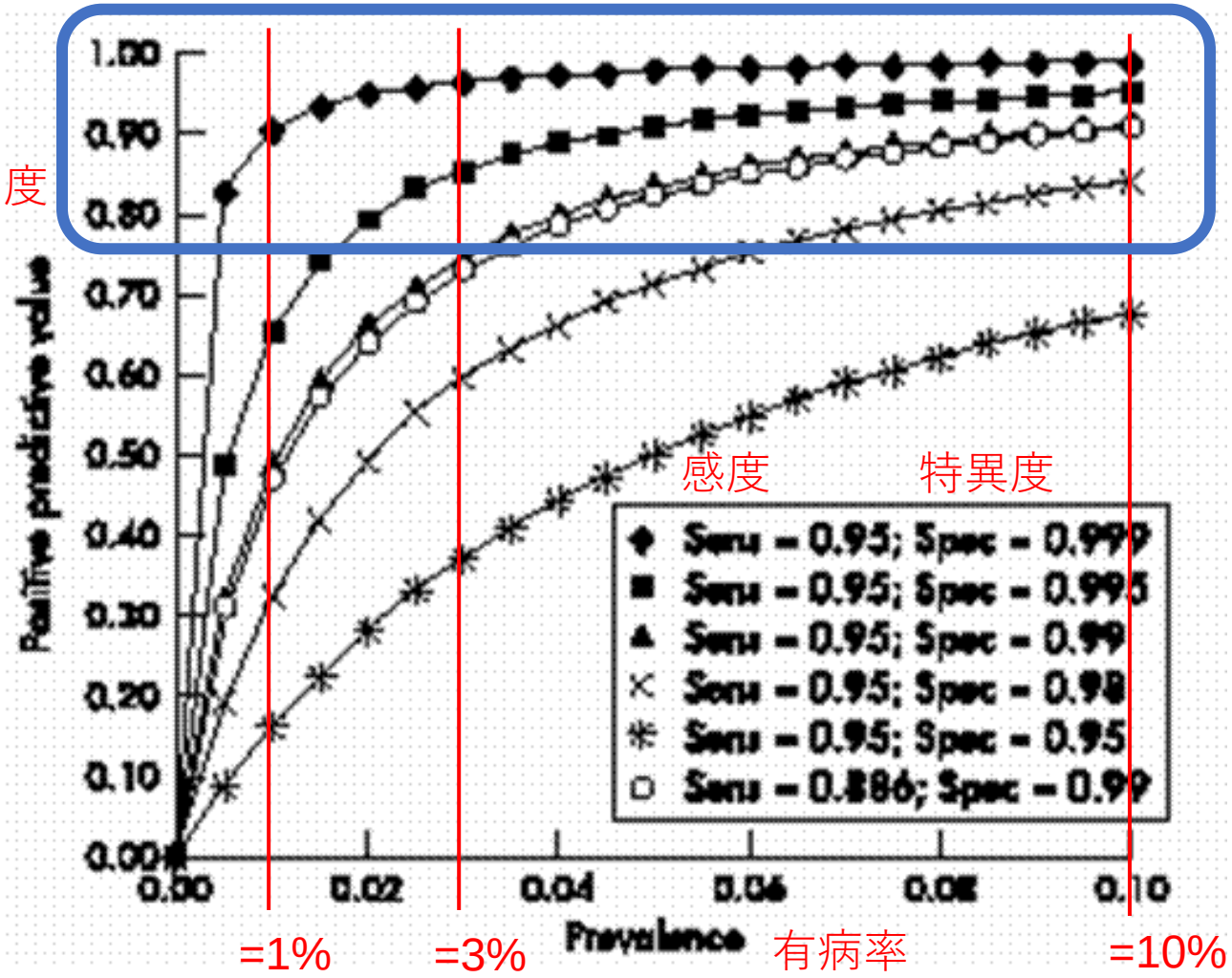
医薬品A群 1000人 → 上部消化管出血 50人

相対リスク2.0

医薬品B群 1000人 → 上部消化管出血 25人

(4) 陽性的中度と有病率・感度・特異度の関係

陽性的中度
(PPV)



高い陽性的中度の達成は(実は)なかなか厳しい

(Sex Transm Infect 2003; 79, 94-97のFigure 1、“BMJ Open Access” optionより取得)

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3. 日本に展開するにあたっての留意点

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2. 海外のアウトカムバリデーションの事例

(1) オーバービュー (国際薬剤疫学会のバリデーション特集号)

(2) 英国

(3) 米国

(4) 台湾

(1) オーバービュー (国際薬剤疫学会のバリデーション特集号)

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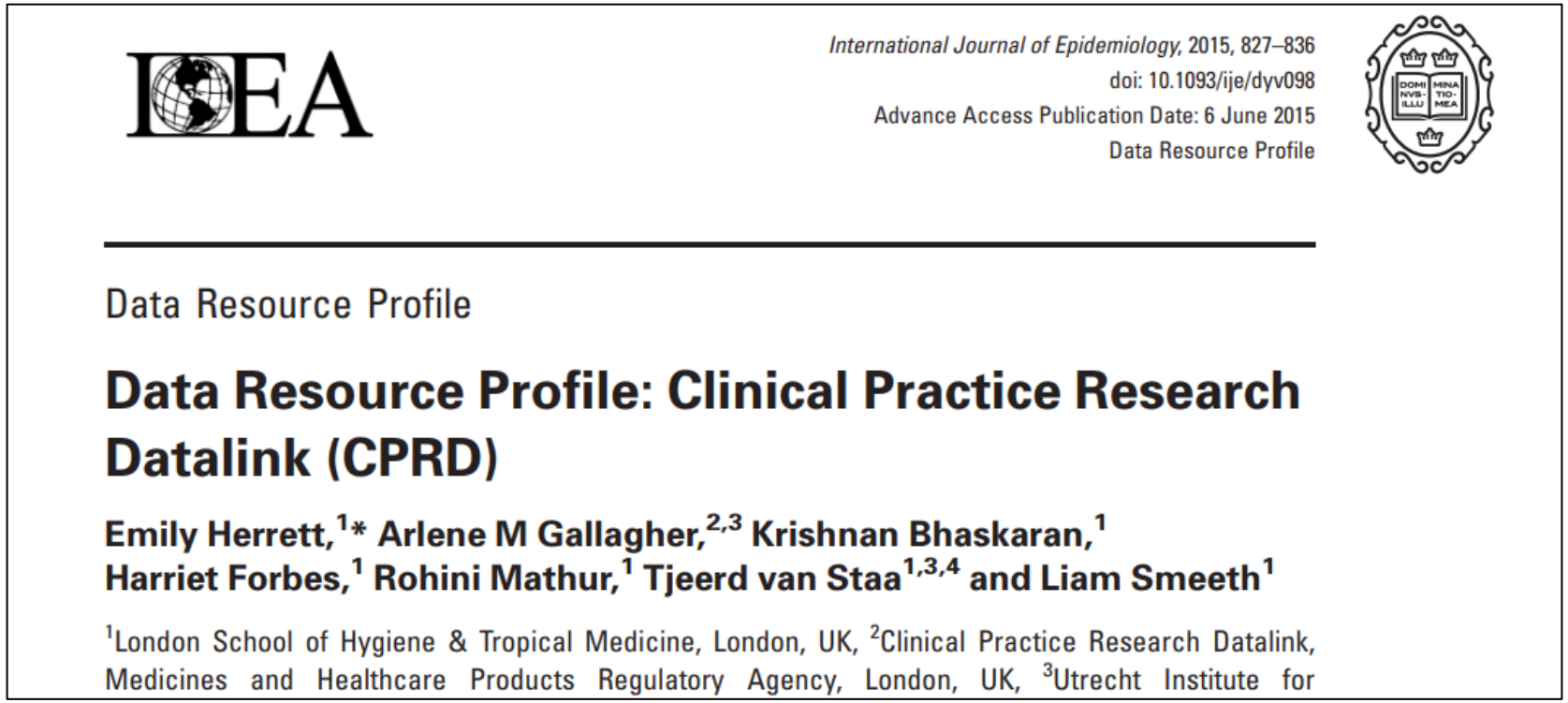
国（地域）	医療情報データベース（データ源）	対象疾患（状態）	方法
米国	Kaiser Permanente Colorado	1型糖尿病	カルテレビュー（220例）
米国	FDA Sentinel System	アナフィラキシー	カルテレビュー（62例）
米国	Centers for Medicare and Medicaid Services（CMS）hospitalization records	心筋梗塞	ARICコホート研究の心筋梗塞の記録をゴールドスタンダード
米国	Optum Integrated Claims-Clinical Database	肥満関連疾患（のICDコード）	電子カルテの肥満の記録をゴールドスタンダード
米国	Veterans Aging Cohort Study（の中のレセプト・電子カルテデータ）	COPD	コホート研究の中のスパイロメトリーに基づくCOPDの診断をゴールドスタンダード
米国	HealthCore Integrated Research Database	ER+/HER2- 乳がん	Anthem's Cancer Care Quality Programの中の診断をゴールドスタンダード
米国	United States Department of Defense health system	小児の1型・2型糖尿病	カルテレビュー（400例）
米国	United States Department of Defense health system および Optum Research Database	多発性骨髄腫	SEERがんレジストリーの診断をゴールドスタンダード
米国	Slone Birth Defects Study	母親の報告した出産時在胎週数と出生体重	カルテレビュー（それぞれ3122例、4760例）
米国・英国	Medicare 、 HealthCore Integrated Research Database、CPRD、THIN	感染による入院	カルテレビュー（それぞれ109例、82例、98例、56例）

国（地域）	医療情報データベース（データ源）	対象疾患（状態）	方法
英国	CPRD	経口ステロイド薬の処方	78人の関節リウマチ患者の自己申告をゴールドスタンダード
英国	CPRD	変形性股関節症	170例について担当プライマリケア医に質問票を送り、その回答をゴールドスタンダード
英国	THIN	脳出血（の発症日）	THINのフリーテキスト部分およびリンクされた入院データをゴールドスタンダード
英国	THIN	脳出血、消化管出血、泌尿生殖器系出血	THINのフリーテクスト部分のレビュー（それぞれ154例、462例、547例）
スペイン	BIFAP database	HPVワクチン接種	カルテレビュー(978人)
スペイン	BIFAP database	大腸がん	カルテレビュー(760例)
カナダ	Administrative data in Quebec, Canada	抗うつ剤を処方する際の適応病名	処方システムの医師記載の適応病名をゴールドスダンダード
デンマーク	Danish National Registries	自殺・自傷	カルテレビュー (357例)
スウェーデン	population-based twin cohort	親が報告した子の喘息	Swedish health care registersの中の医師の診断や処方をゴールドスタンダード
フランス	French hospital discharge diagnoses database	心不全入院	カルテレビュー（陽性的中度計算のために200例、感度計算のために229例)
台湾	National Health Insurance database	がん	がんレジストリとリンケージ

(2) 英国 ：オーバービュー



International Journal of Epidemiology, 2015, 827–836
doi: 10.1093/ije/dyv098
Advance Access Publication Date: 6 June 2015
Data Resource Profile

Data Resource Profile

Data Resource Profile: Clinical Practice Research Datalink (CPRD)

Emily Herrett,[1]* Arlene M Gallagher,[2,3] Krishnan Bhaskaran,[1] Harriet Forbes,[1] Rohini Mathur,[1] Tjeerd van Staa[1,3,4] and Liam Smeeth[1]

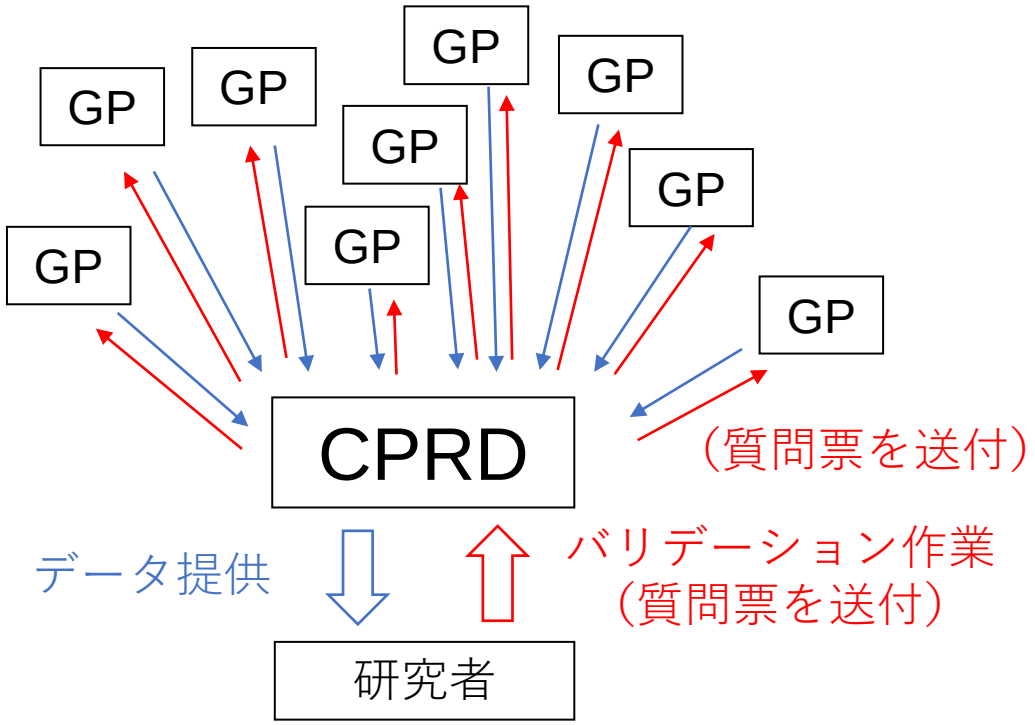
[1]London School of Hygiene & Tropical Medicine, London, UK, [2]Clinical Practice Research Datalink, Medicines and Healthcare Products Regulatory Agency, London, UK, [3]Utrecht Institute for

Validation of the CPRD has shown high positive predictive value of some diagnoses and, where evaluated, comparisons of incidence with other UK data sources are also broadly similar.[35–38] However, reporting of validation studies was often too poor to permit a clear interpretation, and the majority of studies focused on positive predictive value rather than sensitivity or specificity.[39]

(2) 英国：General practitioner (GP)に質問票を送付する方法

BMJ Open Validation of chronic obstructive pulmonary disease recording in the Clinical Practice Research Datalink

約700 General practitioner (GP)



結果（の一部）：119件送付した質問票のうち、89件の回答がGPから得られた。そのうち、77件が真のCOPD（ゴールドスタンダードを満たしている）と判断された。

→ PPV = 77/89 = 86.5 %
(95%CI 77.5-92.3%)

https://bmjopen.bmj.com/content/4/7/e005540.long（オープンアクセス）

(2) 英国：General practitioner (GP)に質問票を送付する方法

BMJ Open **Validation of chronic obstructive pulmonary disease recording in the Clinical Practice Research Datalink**

CPRD内で該当する人数（おそらく感度と比例）

n = 71,780 **1**

n = 76,325 **2**

n = 74,271 **3**

n = 79,759 **4**

n = 10,417 **5**

n = 13,951 **6**

n = 172,285 **7**

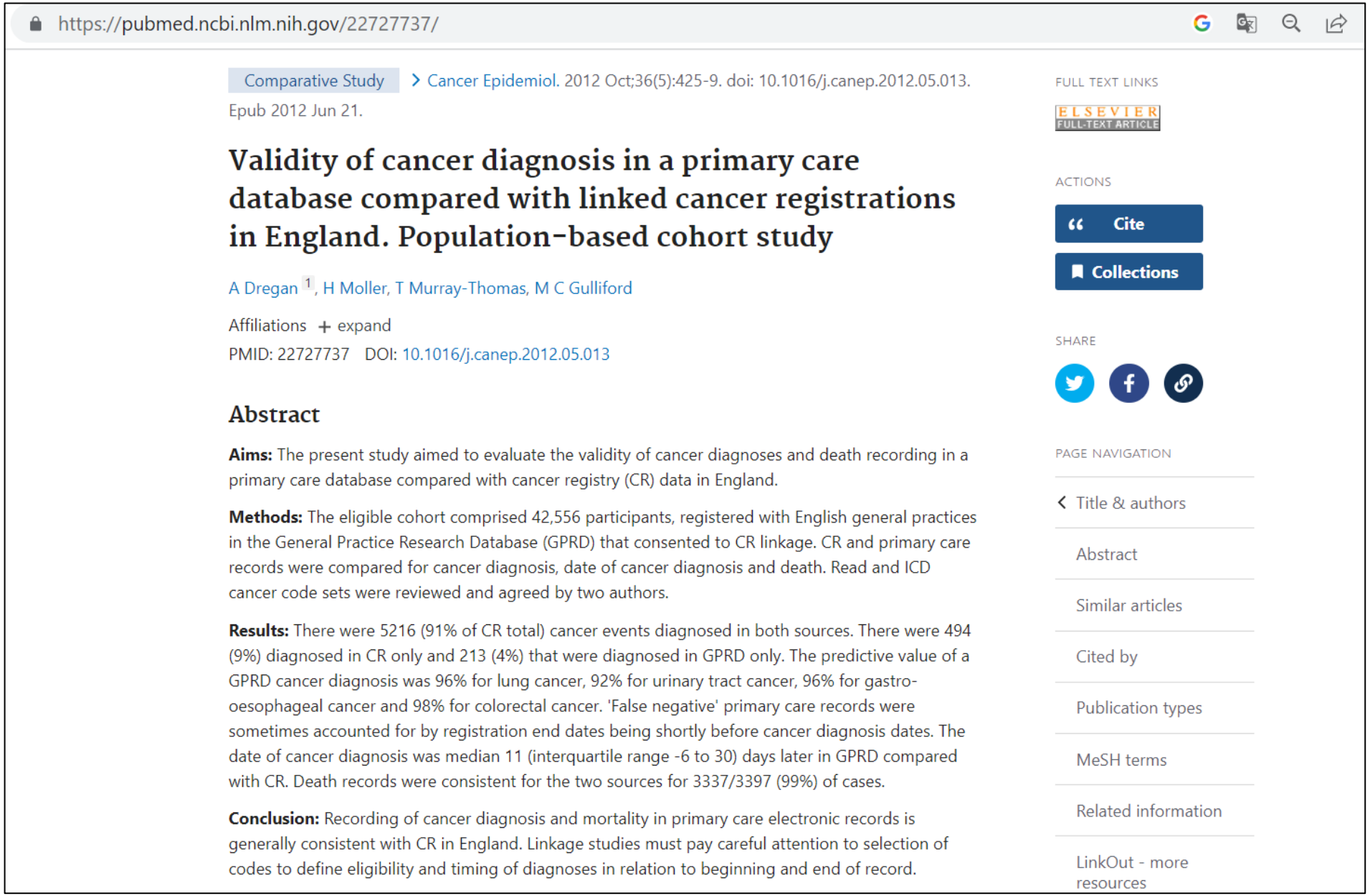
n = 620,905 **8**

Table 2 The positive predictive value (PPV) and proportion of patients diagnosed with chronic obstructive pulmonary disease (COPD) within each algorithm

Algorithm	Number of questionnaires sent out (n=951)	Number evaluable returned (n=696) (%)	Number with confirmed COPD	PPV and 95% CI
COPD Code+spirometry +COPD medication	119	85 (71.4)	76	89.4, 80.7 to 94.5
COPD Code+spirometry	119	79 (66.4)	67	83.8, 73.7 to 90.4
COPD Code+COPD medication	119	88 (73.9)	77	87.5, 78.6 to 93.0
COPD Code only	119	89 (74.8)	77	86.5, 77.5 to 92.3
Bronchitis+COPD medication	119	98 (82.4)	44	44.4, 34.8 to 54.5
Bronchitis only	119	84 (70.6)	26	29.5, 20.8 to 40.1
Symptoms+spirometry	119	83 (69.7)	37	43.5, 33.2 to 54.4
Symptoms only	118	90 (75.6)	11	12.2, 6.8 to 20.9

Conclusions: Patients with COPD can be accurately identified from UK primary care records using specific diagnostic codes. Requiring spirometry or COPD medications only marginally improved accuracy.

(2) 英国：他データベースとのリンケージによる方法



https://pubmed.ncbi.nlm.nih.gov/22727737/

Comparative Study > Cancer Epidemiol. 2012 Oct;36(5):425-9. doi: 10.1016/j.canep.2012.05.013. Epub 2012 Jun 21.

Validity of cancer diagnosis in a primary care database compared with linked cancer registrations in England. Population-based cohort study

A Dregan [1], H Moller, T Murray-Thomas, M C Gulliford

Affiliations + expand

PMID: 22727737 DOI: 10.1016/j.canep.2012.05.013

Abstract

Aims: The present study aimed to evaluate the validity of cancer diagnoses and death recording in a primary care database compared with cancer registry (CR) data in England.

Methods: The eligible cohort comprised 42,556 participants, registered with English general practices in the General Practice Research Database (GPRD) that consented to CR linkage. CR and primary care records were compared for cancer diagnosis, date of cancer diagnosis and death. Read and ICD cancer code sets were reviewed and agreed by two authors.

Results: There were 5216 (91% of CR total) cancer events diagnosed in both sources. There were 494 (9%) diagnosed in CR only and 213 (4%) that were diagnosed in GPRD only. The predictive value of a GPRD cancer diagnosis was 96% for lung cancer, 92% for urinary tract cancer, 96% for gastro-oesophageal cancer and 98% for colorectal cancer. 'False negative' primary care records were sometimes accounted for by registration end dates being shortly before cancer diagnosis dates. The date of cancer diagnosis was median 11 (interquartile range -6 to 30) days later in GPRD compared with CR. Death records were consistent for the two sources for 3337/3397 (99%) of cases.

Conclusion: Recording of cancer diagnosis and mortality in primary care electronic records is generally consistent with CR in England. Linkage studies must pay careful attention to selection of codes to define eligibility and timing of diagnoses in relation to beginning and end of record.

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(3) 米国：Medicare claims dataを用いた研究

https://pubmed.ncbi.nlm.nih.gov/35344378/

Ann Intern Med. 2022 May;175(5):656-664. doi: 10.7326/M21-4009. Epub 2022 Mar 29.

Risks for Anaphylaxis With Intravenous Iron Formulations : A Retrospective Cohort Study

Chintan V Dave [1], Gary M Brittenham [2], Jeffrey L Carson [3], Soko Setoguchi [4]

Affiliations + expand

PMID: 35344378 DOI: 10.7326/M21-4009

Abstract

Background: The risks for anaphylaxis among intravenous (IV) iron products currently in use have not been assessed.

Objective: To compare risks for anaphylaxis among 5 IV iron products that are used frequently.

Design: Retrospective cohort study using a target trial emulation framework.

Setting: Medicare fee-for-service data with Part D coverage between July 2013 and December 2018.

Participants: Older adults receiving their first administration of IV iron.

Measurements: The primary outcome was the occurrence of anaphylaxis within 1 day of IV iron administration, ascertained using a validated case definition. Analysis was adjusted for 40 baseline

(3) 米国：Medicare claims dataを用いた研究

Follow-up and Outcomes

The primary study end point was the occurrence of anaphylaxis, which was ascertained using a validated case definition based on the combination of International Classification of Diseases, CPT, and HCPCS codes (16). The algorithm has an overall positive predictive value (PPV) of 75% and comprises the following 3 components: 1) anaphylaxis resulting in hospitalization (PPV = 77%), 2) an outpatient or emergency department visit due to anaphylactic shock accompanied by codes relating to the administration of cardiopulmonary resuscitation or epinephrine or the occurrence of hypotension (PPV = 73%), and 3) 2 separate encounters for anaphylactic shock within the same day representing different encounter types (that is, inpatient, outpatient, or emergency department visit; PPV = 88%).

16. Walsh KE, Cutrona SL, Foy S, et al. Validation of anaphylaxis in the Food and Drug Administration's Mini-Sentinel. Pharmacoepidemiol Drug Saf. 2013;22:1205-13. [PMID: 24038742] doi:10.1002/pds.3505

(3) 米国：Medicare claims data 論文内に引用されていたバリデーション論文

https://pubmed.ncbi.nlm.nih.gov/24038742/

Pharmacoepidemiol Drug Saf. 2013 Nov;22(11):1205-13. doi: 10.1002/pds.3505. Epub 2013 Sep 5.

Validation of anaphylaxis in the Food and Drug Administration's Mini-Sentinel

Kathleen E Walsh [1], Sarah L Cutrona, Sarah Foy, Meghan A Baker, Susan Forrow, Azadeh Shoaibi, Pamala A Pawloski, Michelle Conroy, Andrew M Fine, Lise E Nigrovic, Nandini Selvam, Mano S Selvan, William O Cooper, Susan Andrade

Affiliations + expand

PMID: 24038742 PMCID: PMC4113322 DOI: 10.1002/pds.3505

Free PMC article

Abstract

Purpose: We aim to develop and validate the positive predictive value (PPV) of an algorithm to identify anaphylaxis using health plan administrative and claims data. Previously published PPVs for anaphylaxis using International Classification of Diseases, ninth revision, Clinical Modification (ICD-9-CM) codes range from 52% to 57%.

Methods: We conducted a retrospective study using administrative and claims data from eight health plans. Using diagnosis and procedure codes, we developed an algorithm to identify potential cases of anaphylaxis from the Mini-Sentinel Distributed Database between January 2009 and December 2010. A random sample of medical charts (n = 150) was identified for chart abstraction. Two physician adjudicators reviewed each potential case. Using physician adjudicator judgments on whether the case met diagnostic criteria for anaphylaxis, we calculated a PPV for the algorithm.

Results: Of the 122 patients for whom complete charts were received, 77 were judged by physician adjudicators to have anaphylaxis. The PPV for the algorithm was 63.1% (95%CI: 53.9-71.7%), using the clinical criteria by Sampson as the gold standard. The PPV was highest for inpatient encounters with ICD-9-CM codes of 995.0 or 999.4. By combining only the top performing ICD-9-CM codes, we identified an algorithm with a PPV of 75.0%, but only 66% of cases of anaphylaxis were identified using this modified algorithm.

Conclusions: The PPV for the ICD-9-CM-based algorithm for anaphylaxis was slightly higher than PPV estimates reported in prior studies, but remained low. We were able to identify an algorithm that optimized the PPV but demonstrated lower sensitivity for anaphylactic events.

(3) 米国：Medicare claims data 論文内に引用されていたバリデーション論文

Methods

This project was a collaboration among the FDA, the Mini-Sentinel Operations Center, and selected Mini-Sentinel Academic and Data Partners. Five Mini-Sentinel Data Partners participated in this project: (1) HealthCore, Inc.; (2) Humana; (3) three member health plans within the Kaiser Permanente Center for Effectiveness and Safety Research; (4) two member health plans within the HMO Research Network; and (5) Vanderbilt University.

Table 1

Final electronic claims-based algorithm for the identification of anaphylaxis

Criterion A: (995.0 [other anaphylactic shock] or 999.4 [anaphylactic shock due to serum]) inpatient or emergency department encounter

OR

Criterion B: (995.0 [other anaphylactic shock] or 999.4 [anaphylactic shock due to serum]) outpatient encounter **PLUS** a code for one of the following symptoms/procedures/treatments:

- **i.** bronchospasm (519.11) or
- **ii.** stridor (786.1) or
- **iii.** hypotension (458.9) or
- **iv.** epinephrine (J0170 or J0171) OR
- **v.** injection of diphenhydramine (J1200) or
- **vi.** CPR (92950 or 99.60)

OR

Criterion C: (995.3 [allergy unspecified] or 995.2 [other unspecified adverse effect of drug] or E930-E949 [drugs, medicinal and biological substances causing adverse effects in therapeutic use]) inpatient or emergency department encounter

vii. **PLUS** a code for one of the following symptoms/procedures/treatments:

1. bronchospasm (519.11) or
2. stridor (786.1) or
3. injection of diphenhydramine (J1200)

viii. **and ALSO** a code for one of the following symptoms/procedures/treatments

1. hypotension (458.9) or
2. epinephrine (J0170 or J0171) or
3. CPR (92950 or 99.60)

For inpatient and ED codes: all patients who met inclusion criteria were sampled.

For outpatient encounters: All patients who meet inclusion criteria, excluding patients with an encounter in the prior 30 days that documents an anaphylaxis code (995.0 or 999.4) were sampled.

(3) 米国：Medicare claims data 論文内に引用されていたバリデーション論文

先述のAnn Intern Med論文内の記載にどう対応するか？

The algorithm has an overall positive predictive value (PPV) of 75% and comprises the following 3 components:

1) anaphylaxis resulting in hospitalization (PPV = 77%)

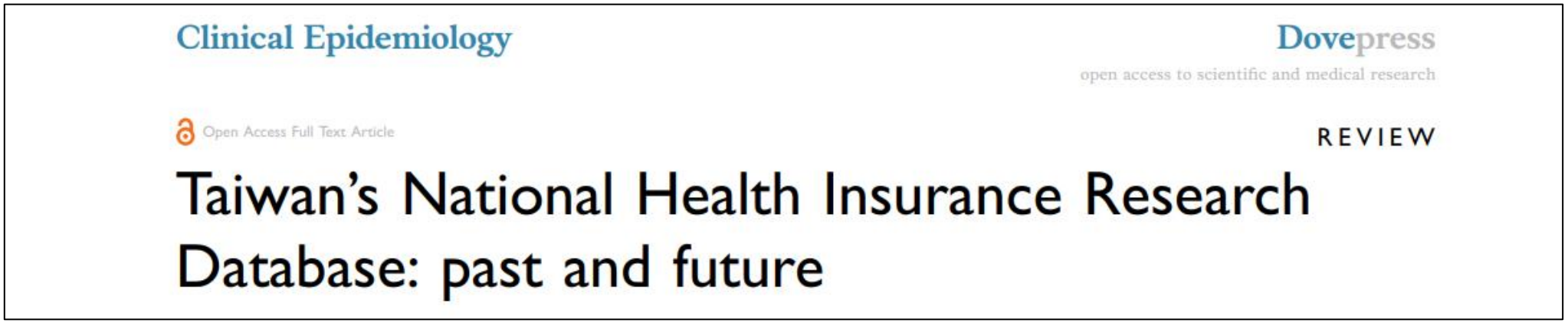
2) an outpatient or emergency department visit due to anaphylactic shock accompanied by codes relating to the administration of cardiopulmonary resuscitation or epinephrine or the occurrence of hypotension (PPV = 73%)
（どれ？著者達で独自に計算？）

3) 2 separate encounters for anaphylactic shock within the same day representing different encounter types (that is, inpatient, outpatient, or emergency department visit; PPV = 88%).

Table 3
Validation of diagnosis and procedure codes in health plan administrative databases among patients meeting criteria for identification of anaphylaxis*

	Number of charts reviewed	Number of cases confirmed	Positive predictive value (95% confidence interval)
Criterion A			
Other anaphylactic shock (ICD-9-CM 995.0)			
Overall	82	57	69.5% (58.4% - 79.2%)
Inpatient			
All inpatient encounters	30	23	76.7% (57.7% - 90.1%)
Concurrent treatment/symptom codes			
Injection adrenalin/epinephrine (HCPCS J0170, J0171)	2	2	100.0% (15.8% - 100.0%)
Injection diphenhydramine (HCPCS J1200)	2	1	50.0% (1.3% - 98.7%)
Cardiopulmonary Resuscitation (ICD-9 99.60, CPT 92950)	1	1	100.0% (2.5% - 100.0%)
Hypotension (ICD-9-CM 458.9)	4	4	100.0% (39.8% - 100.0%)
Emergency Department			
All emergency department encounters	56	38	67.9% (54.0% - 79.7%)
Concurrent treatment/symptom codes			
Injection adrenalin/epinephrine (HCPCS J0170, J0171)	16	12	75.0% (47.6% - 92.7%)
Injection diphenhydramine (HCPCS J1200)	19	13	68.4% (43.5% - 87.4%)
Cardiopulmonary Resuscitation (ICD-9 99.60, CPT 92950)	1	1	100.0% (2.5% - 100.0%)
Hypotension (ICD-9-CM 458.9)	1	1	100.0% (2.5% - 100.0%)
More than 1 encounter type (inpatient, emergency department, ambulatory) with a code for anaphylaxis	17	15	88.2% (63.6% - 98.5%)

(4) 台湾：オーバービュー



Several validation studies have been performed to evaluate the validity of diagnosis codes in the NHIRD (Table 2). Most of the validated diagnosis codes are for some common conditions or severe diseases, and with modest to high sensitivity and positive predictive values (eg, epilepsy,[24] ischemic stroke,[25] hypertension, diabetes, hyperlipidemia, fibrillation,[26] all cancer,[27] etc.). Notably, ICD-10 diagnosis codes adopted after the year 2015 in the NHIRD have not been validated yet. Furthermore, under the NHI program, patients with severe illnesses can apply for catastrophic illness certification, so as to be exempted from certain NHI payments and copayments for each health care encounter. All applications for catastrophic illness certification are reviewed by experts, and therefore the diagnosis can be considered highly accurate; hence, the catastrophic illness file has been used for case ascertainments in respective research.

(4) 台湾：オーバービュー

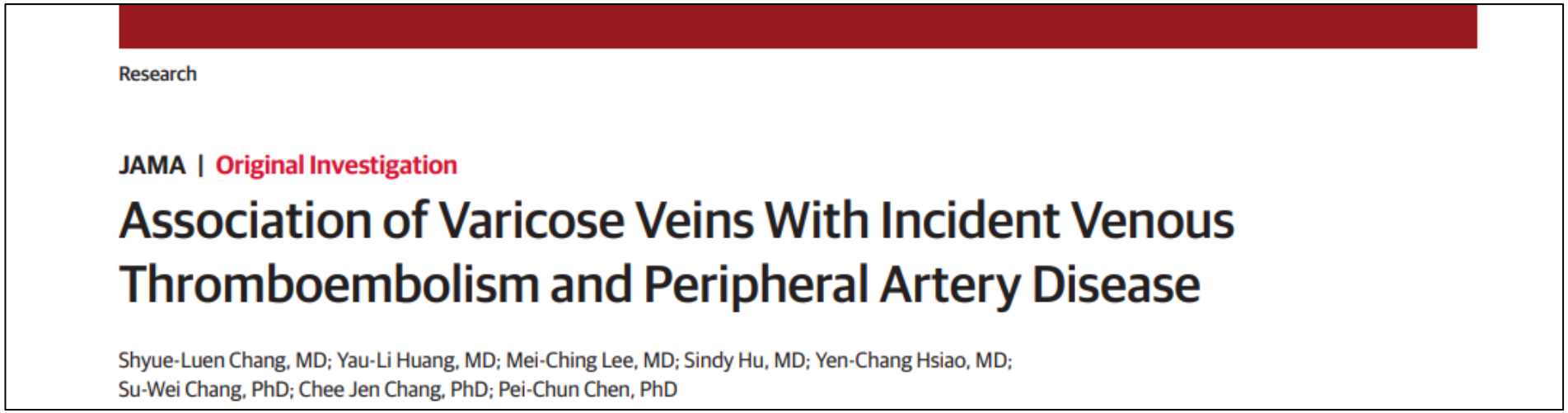
Table 2 Summary of validation studies regarding the validity of diagnosis codes in the NHIRD

Diseases/ conditions	ICD-9-CM code	Sensitivity, %	Positive predictive value, PPV %	Note	References
Acute ischemic stroke	433.xx, 434.xx	94.5	97.9	Chart review by neurologic specialist as reference standard	Pharmacoepidemiol Drug Saf 2011[47]
Epilepsy	345.xx	81.4	76.8	Chart review by neurologic specialist as reference standard; specificity: 99.8%	Epilepsia 2012[24]
Pneumonia	480.xx–486.xx	92.3–94.7	Not available	Chart review by medical doctors as reference standard	CMAJ 2014[48]
Coronary artery bypass graft post-operative surgical site infection	996.03, 996.61, 996.72, 998.5 038.0–038.4, 038.8, 038.9, 682.6, 682.9, 780.6, 790.7, 875.0, 875.1, 891.0, 891.1, 996.03, 996.61, 996.72, 998.3, and 998.5.	35.3	19.4	Health care-associated infection surveillance data and manually reviewed medical charts as reference standard; specificity: 97.0%	BMC Med Inform Decis Mak 2014[49]
Acute myocardial infarction	410.xx	88.0	92.0	Chart review by neurologic specialist as reference standard	J Epidemiol 2014[50]

(4) 台湾：オーバービュー

Renal dysfunction	250.4, 283.11, 403.x, 404.x, 580–589, 753.0, 753.1	38.4	76.0	Taiwan Stroke Registry as reference standard; only validated in stroke patients; specificity: 94.7%	Int J Stroke 2015[51]
Acute ischemic stroke	433.xx, 434.xx	97.3	88.4	Taiwan Stroke Registry as reference standard	J Formos Med Assoc 2015[25]
Tuberculosis contact	V01.1 with at least 1 chest radiographic examination or 795.5	98.3	Not available	Chart review by pulmonologists as reference standard	Medicine 2016[52]
Hypertension	401.x, 402.x, 403.x, 404.x, 405.x	92.4	88.5	Few conditions in patients with stroke. Taiwan Stroke Registry as reference standard	Int J Cardiol 2016[26]
Diabetes	250.x	90.9	92.0		
Hyperlipidemia	272.x	69.1	89.5		
Coronary artery disease	410.x, 411.x, 412.x, 413.x, 414.x	63.7	47.6		
Atrial fibrillation	427.31	72.8	71.1		
Tuberculosis	010–018 plus prescriptions of at least two anti-tuberculosis drugs	96.3	Not available	Chart review by pulmonologists as reference standard	Chest 2017[53]
Heart failure	428	Not available	97.6	Chart review by cardiologic specialist as reference standard	J Am Heart Assoc 2017[54]
Ischemic stroke	433–437	Not available	94.2		
All cancer	140–208	91.5	93.6	National Cancer Registry of Taiwan as reference standard	Pharmacoepidemiol Drug Saf 2018[27]
Varicose veins	454	Not available	98.0	Chart review as reference standard	JAMA 2018[55]

(4) 台湾：Varicose Veins (静脈瘤) の研究の事例



Research

JAMA | Original Investigation

Association of Varicose Veins With Incident Venous Thromboembolism and Peripheral Artery Disease

Shyue-Luen Chang, MD; Yau-Li Huang, MD; Mei-Ching Lee, MD; Sindy Hu, MD; Yen-Chang Hsiao, MD; Su-Wei Chang, PhD; Chee Jen Chang, PhD; Pei-Chun Chen, PhD

Identification of Study Patients and Validation of Varicose Veins Diagnosis

We identified patients diagnosed with varicose veins from January 1, 2001-December 31, 2013, according to the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 454.xx for an outpatient or inpatient claim….

To assess the validity of the 454 code corresponding to the diagnosis of varicose veins, we reviewed a random sample of outpatient medical records from 3 branches of Chang-Gung Memorial Hospital (Taipei, Linkou, and Taoyuan) that provide health care services to patients with diverse characteristics. There were 239 patients in this sample, which represented 1.5% of all patients (n=16028) diagnosed with varicose veins, of whom 39 could not be evaluated due to incomplete or unidentifiable medical records. The validation criterion was met in 196 of the remaining 200 patients, with a positive predictive value of 98% (95% CI, 0.95%-0.99%) (see eMethods in theSupplement).

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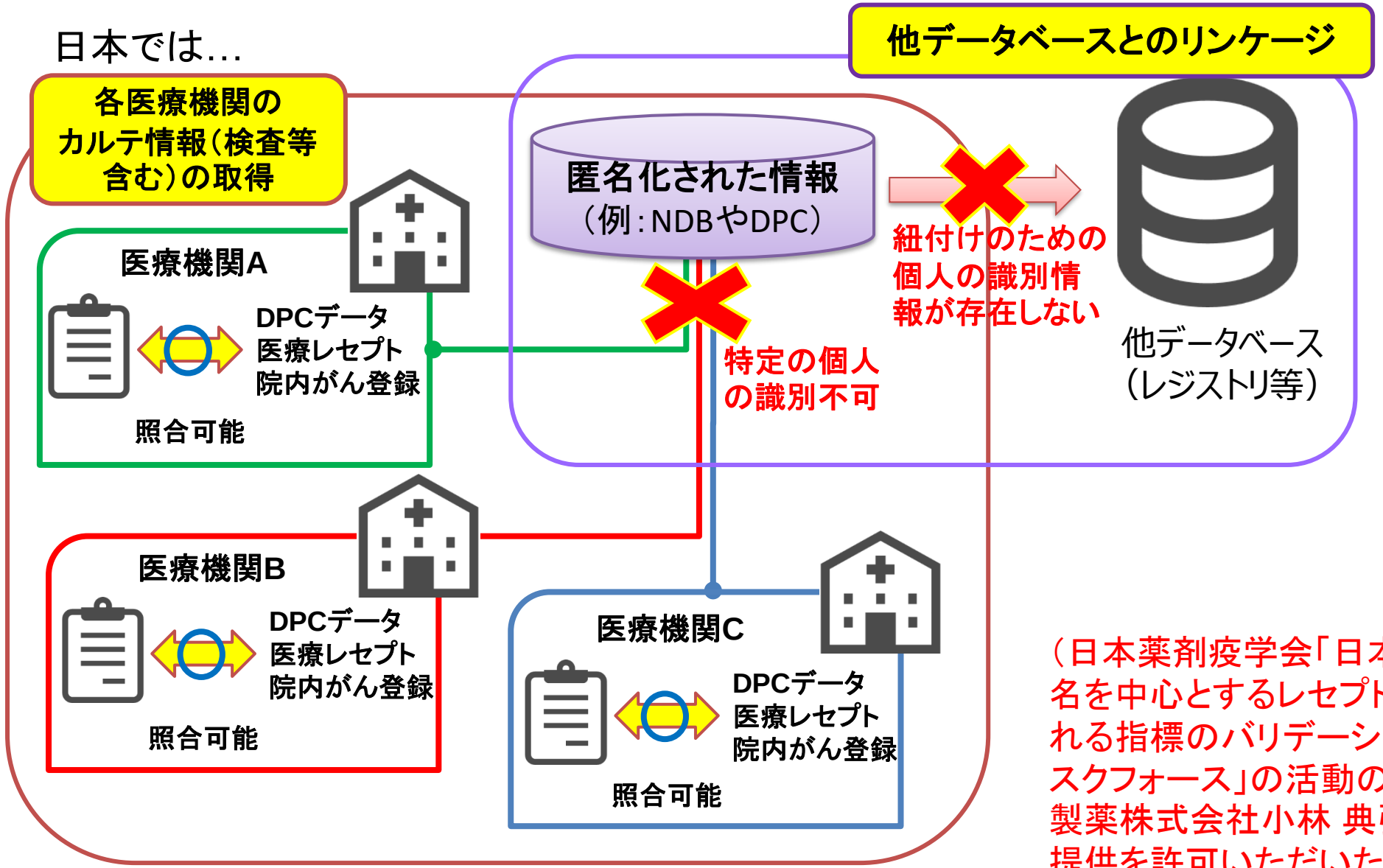
3. 日本に展開するにあたっての留意点（岩上の私見）

- 日本は病院数 (>**8000**)、診療所数 (>**100,000**)が非常に多い。
  (参考：人口が日本の約半分の英国は、病院数>**450**、診療所数>**7,000**)
- 日本の高齢患者は、複数の病院・診療所にかかっていることが多い。
- 一方、日本の患者は、同じ疾患（例：糖尿病、関節リウマチ、がん等）については、同じ病院にかかり続けることも多い。
- 日本は、入院における病名入力は、主に**DPC**システムのおかげで、海外と比しても標準化が進んでいると思われる。
- 一方、外来における病名入力は、主に診療報酬請求のために行われることが多く、病院・診療所間の入力方針のばらつきも大きいかもしれない。
- 日本では、いったん匿名加工した医療データから、患者**ID**や患者カルテ、担当医師に「さかのぼる」ことは現状無理である（匿名加工する前のデータであれば「さかのぼる」ことができる）。
- 日本では、いったん匿名加工した医療データと、他のデータベースをリンケージすることは現状無理である（各医療機関の中で、匿名加工前の異なるデータ (例**: DPC**と院内がん登録) を「照らし合わせる」ことはできる）。
- 以上を踏まえると結局、米国や台湾のように、単・少数の病院でバリデーションを行い、どこまでその結果 (**“better”**なアルゴリズム、感度、特異度、的中度) が各データベースに外挿可能か議論するのが現実的だろう。

3. 日本に展開するにあたっての留意点（岩上の私見）



（日本薬剤疫学会「日本における傷病名を中心とするレセプト情報から得られる指標のバリデーションに関するタスクフォース」の活動の際に、塩野義製薬株式会社小林 典弘氏より作成・提供を許可いただいた図）

まとめ（Take Home Message)

- 世界の医療データベースは主に、①統合的データベース、②プライマリケアデータベース、③病院データベース（日本のMID-NET®含む）、④診療報酬請求データベース（日本のNDB含む）に分かれ、それぞれのシステムの中でバリデーション研究もおこなわれている。
- 英国は、プライマリケアデータベースの中からバリデーションしたい疾患患者をランダムサンプリングしてgeneral practitioner (GP)に質問票を送付する方法や、他データベースとリンケージする方法でバリデーション研究を行っている。
- 米国は、単・複数の病院の中でバリデーション研究を行ったり、(Mini-) Sentinelプロジェクトの中で行ったバリデーション研究をもとに”better”なアルゴリズムを考えて（異なるデータベースであるが、データの発生源が似ていると思われる）データベース研究に用いたりしている。
- 台湾は、よく中を見てみると、単・複数の病院の中でバリデーション研究を行って、その結果を診療報酬請求データベース全体に外挿しようとしている。
- 日本でも、その限界をよく踏まえた上で、米国や台湾と同様のアプローチを取るのが現実的かもしれない。