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Integrated Real-World Data Warehouses across Seven Evolving Asian Healthcare Systems: A Scoping Review

Wen-Yi Shau, Handoko Santoso, Vincent Jip, Sajita Setia

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Abstract

Background: Asia consists of diverse nations with extremely variable healthcare systems and socio-economic intricacies. Integrated real-world data (RWD) research warehouses provide vast interconnected datasets that uphold statistical rigor. However, their intricate details remain underexplored, restricting their broader application in healthcare research, policies and partnerships.

Objective: Building on our prior research that analyzed integrated RWD warehouses in India, Thailand and Taiwan, this study is an extension to seven distinct Asian healthcare systems: Hong Kong, Indonesia, Malaysia, Pakistan, the Philippines, Singapore, and Vietnam. We aimed to map the evolving landscape of RWD use, elucidate the current state of real-world evidence (RWE) generation from integrated databases, and understand evolving preferences for RWD methodologies and database(s) use.

Methods: A systematic scoping review methodology was employed, centering on contemporary English literature search on PubMed. Rigorous screening followed defined eligibility criteria to pinpoint studies utilizing integrated RWD from multiple healthcare facilities in at least one of the seven target Asian nations. Target nations were archetyped as 'Global Collaborators' or 'Solo Scholars' based on their publication count and extent of Cross-Country Collaboration Studies (CCCS) versus Single Country Studies (SCS) over the five-year study period.

Results: Out of the 1483 RWE research titles identified on May 9, 2023, 369 (24.9%) fulfilled the requirements for data extraction and subsequent analysis. Singapore, Hong Kong, and Malaysia contributed to ?100 publications, each marked by a higher proportion of SCS at 51% (80/157), 66.2% (86/130), and 50% (50/100), respectively, and were classified as Solo Scholars. Indonesia, Pakistan, Vietnam and the Philippines had fewer publications and a higher proportion of CCCS at 78.8% (26/33), 58.1% (18/31), 74.1% (20/27), and 86.4% (19/22), respectively and were classified as Global Collaborators. Collaboration with the countries outside the seven target nations appeared in 84.2%–97.7% of the CCCS of each nation. Among target nations, Singapore and Malaysia emerged as preferred research partners for other nations. From 2018 to 2023, most nations displayed an increasing trend in study numbers, with Vietnam (24.5%) and Pakistan (21.2%) leading the growth; the only exception was the Philippines, which declined by -14.5%. Clinical registry databases were predominant across all CCCS from every target nation. For SCS, Indonesia, Malaysia, and the Philippines favored clinical registries; Singapore had a balanced usage of clinical registries and EMR/EHR, while Hong Kong, Pakistan, and Vietnam leaned towards EMR/EHR. Over 90% of the studies took more than 2 years from completion to publication.

Conclusions: The observed variations in contemporary RWD publications across the 7 nations in Asia exemplify distinct research landscapes across nations that are partially explained by their diverse economic, clinical, and research settings. Nevertheless, recognizing these variations is pivotal for fostering tailored, synergistic strategies that amplify RWD's potential in guiding future healthcare research and policy decisions. Clinical Trial: RR2-10.2196/43741

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Methods: A systematic scoping review methodology was employed, centering on contemporary English literature search on PubMed (search date: May 9, 2023). Rigorous screening followed defined eligibility criteria to pinpoint studies utilizing integrated RWD from multiple healthcare facilities in at least one of the seven target Asian nations. No statistical hypotheses were established for the description of the results. Point estimates and their associated errors were determined for the data collected from eligible studies.

Results: Out of the 1483 RWE research titles identified on May 9, 2023, 369 (24.9%) fulfilled the requirements for data extraction and subsequent analysis. Singapore, Hong Kong, and Malaysia contributed to ≥100 publications, each marked by a higher proportion of SCS at 51% (80/157), 66.2% (86/130), and 50% (50/100), respectively, and were classified as Solo Scholars. Indonesia, Pakistan, Vietnam and the Philippines had fewer publications and a higher proportion of CCCS at 78.8% (26/33), 58.1% (18/31), 74.1%

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Introduction

Asia is a vast and diverse continent that also represents varied healthcare systems and socio-economic challenges. Multiple evidence-driven approaches tailored to each nation's unique healthcare and research context are required to draw essential data to support the ambitious goals for Universal Health Coverage in each country [1, 2]. The strength and necessity of Real-World Data (RWD) and its concrete data analytical interference in terms of Real-World Evidence (RWE) are integral to this evidence generation. RWE has the potential to inform health technology assessments (HTAs), guide evidence-driven policies, and streamline service delivery [3]. Yet, as crucial as RWE is, the Asian healthcare landscape lacks a cohesive framework to harness its full potential despite its promise in pharmacoeconomics, pharmacovigilance, and pharmacoepidemiology [3, 4].

The utility of RWD and RWE becomes even more apparent with large integrated research databases within health systems. The integrated warehouses offer vast connected datasets which sustain the statistical rigor and can assist in providing insights with minimal bias and confounding [5]. However, these data reservoirs have not been vastly studied across healthcare systems, which limits their broader utility in healthcare research, RWE data generation and, consequently, universal health coverage (UHC) [6].

Recognizing this potential, our previous research explored integrated RWD warehouses within the three diverse healthcare pilots for Taiwan, India, and Thailand [7]. Our systematic research identified some strong differences in the types of RWD and its warehouses in the three countries. Still, the results only partly reflected their divergent economic, social and clinical settings. Hence, we continued to conduct similar research in many other diverse Asian healthcare systems in line with our published protocol [8].

The literature on RWD practices and awareness about corresponding warehouses in certain Asian countries like China, Japan, and South Korea is significant [5, 9-17], partly because these countries also have recommendations on the utility of RWE by external regulators [3]. This study seeks to understand the evolving landscape of RWD utilization and its implications across Hong Kong, Indonesia, Malaysia, Pakistan, the Philippines, Singapore, and Vietnam, where RWD practices are emerging or undergoing significant development [4]. Our selection of countries for this scoping review was strategically based on selecting contrasting spectrum of HTA maturity across countries with evolving HTA systems, yet ranging from relatively mature systems in Singapore, Thailand, and Malaysia, to emerging frameworks in Indonesia, the Philippines, and Vietnam, and nascent stages in Pakistan [18, 19]. Each nation, with its individualistic healthcare challenges and unique research capabilities, underscores the need for understanding recent patterns in RWD research and usage of clinical research warehouses, especially in light of the marked underrepresentation of specific Asian demographics within traditional randomized clinical trials [20]. By systematically analyzing both Single country Studies (SCS) and Cross-country Collaborative Studies (CCCS), this research aims to delineate the current state of RWE generation and collaborative research initiatives for RWE from integrated databases across different nations in Asia. Our objectives also included a comprehensive understanding of the preference for RWD methodologies by contrasting the emphasis on Comparative Effectiveness Research (CER) with descriptive studies, and discerning the preferred and popular real-world research databases.

The cyclical interplay between a nation's economic strength, healthcare infrastructure, and research capacity perpetuates disparities in RWD generation. We hypothesized that Asian countries with less extensively documented RWD research trends could be effectively clustered based on systematic patterns in RWD generation. This will streamline our objective to evaluate trends in RWD generation and shed light on targeted

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capacity-building strategies essential for informed healthcare policymaking. Through this rigorous extended scoping research, we aim to present insights that resonate with clinical stakeholders, medical researchers, and health policymakers, thereby guiding the formulation of strategies attuned to each nation's healthcare challenges and research diversities and complexities.

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Methods

Research Approach

Our research approach was methodically aligned with the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) [21]. Our published protocol specified a preliminary focus on three countries, India, Thailand, and Taiwan, as a representative pilot to explore the diversity of healthcare systems and RWD utilization in Asia [8]. The outcomes from our initial study covering Taiwan, India, and Thailand have been previously published [7]. Relevant insights from this publication were incorporated into the archetyping of the nations wherever applicable. In this study, we expanded our protocol to seven other countries. However, we maintained consistency with the original protocol's methodological framework to ensure comparability across all countries studied. This expansion was aligned with our initial intent to potentially include more countries following the first research across three countries.

The search strategy is described in Table S1 in Multimedia Appendix 1. We filtered our search to include only English language publications from the last five years, aiming to highlight current and internationally relevant RWE or RWD. As the conversion of RWD to RWE emphasizes the stringent analytical processes necessary to yield valuable and credible findings, we intentionally chose to rely on PubMed as an exclusive source of relevant citations for screening. Our goal was to assess databases yielding robust RWD featured in esteemed, indexed, peer-reviewed journals while reducing potential duplicates. By focusing solely on PubMed, we tried to identify research representing this standard and offering evidence of the utmost scientific integrity. This strategy aligns with the specifications outlined in our protocol [8].

Screening Eligible Studies for Data Analysis

All retrieved study abstracts were directly imported into Covidence software for subsequent screening and data extraction. Studies were initially screened against predefined eligibility criteria to capture research from integrated RWD. The criteria encompassed four domains described in the original protocol: database type and requirement for research across >1 hospital/clinic, publication nature, RWD study type, and publication scope [8]. The scope of publication was adapted in this study to include citations with databases involving one of the target nations (Hong Kong, Indonesia, Malaysia, Pakistan, Philippines, Singapore or Vietnam). Inclusions also considered studies featuring non-target countries, as long as one of the seven target nations was involved. Table S2 in Multimedia Appendix 1 provides a snapshot of the eligibility criteria used in this research.

Duplicate removal and a two-step eligibility screening process was conducted in Covidence. The initial step (Phase 1) assessed titles and abstracts, with relevant studies advancing to full-text evaluation in the second phase. Given the study volume, the screening for both phases was divided between two reviewers. An independent reviewer examined a random 20% sample of the studies to maintain accuracy. Any ambiguities or discrepancies were collaboratively resolved and another reviewer was consulted, if needed. The final step involved data extraction and data analysis for eligible studies.

Data Extraction and Analysis

We utilized Covidence for data extraction by employing a custom template that covered:

- Basic study details: Covidence identifier (ID) based on the first author's last name & publication year, and title.
- Presence of cross-country collaboration in research (CCCS or SCS)
- Nature of publication (clinical study or protocol).

- Study categorization: Comparative Effectiveness Research (CER) vs. descriptive study (non-CER), with CER definitions adapted from Medical Subject Headings (MeSH). We expanded the criteria for CER to standardize its meaning in context of this research as the “studies comparing interventions and strategies (including the comparison between active and non-active interventions/strategies) to prevent, diagnose, treat, and monitor health conditions using validated methods for confounders elimination, e.g., matching, and statistical adjustments like stratification, weighting, regression, instrumental variable analysis etc.”

- Research source database classification involving medical records, health insurance claims, clinical registries, pharmacy claims, or composite databases.

- Disease specifics: name and area of the target disease under study (defined by primary diagnosis and pathophysiology; if intersecting, then by prime medical speciality in-charge). The disease categories encompassed cardiology & metabolic disorders (CVM), oncology, inflammatory & autoimmune disorders (IAD), infectious diseases & vaccines (IDV), and others. These categories represent major research fields in clinical medicine with notable disease burdens, selected to provide pertinent insights into RWD and RWE applications within these critical domains.

- Outcome types: clinical (treatment effect or safety), cost, or Patient-Reported Outcomes (PROs), with PROs capturing direct patient responses.

- Demographics (adults, children, or both), number of centres, study participants, length of study and duration between latest data collected to year of publication. The length or duration represented the span from the study's commencement to completion, as specified by the authors.

- The unique names for utilized databases. When provided, the specific database name utilized in each study was collected and organized by target nation, database type, and according to the disease area.

Two reviewers collaboratively managed data extraction, and all extractions underwent quality checks by another reviewer to ensure the accuracy and reliability of the extracted data. However, this process was not conducted independently or with blinding to the other reviewer's decisions. Disagreements between the two reviewers were settled through discussions, and an additional reviewer was involved whenever there was a need for a consensus.

The final search was conducted on May 9, 2023, covering the preceding five years; to account for partial yearly data in 2018 and 2023, we calculated equivalent of annual publication count using 365 multiplied to the average of daily publication number. We employed linear regression, using the year as a continuous predictor variable, to understand the annual trend in nation study counts. This provided insight into the average annual trend in study numbers throughout the study duration. In order to further even out year-to-year variations, a 2-year simple moving average (2y-SMA) was applied to enhance clarity of data trends. This SMA approach was consistent with our previous research methodologies [7]. Given the study's descriptive nature, there was no a priori statistical hypothesis. Statistical analyses were conducted to calculate point estimates and their associated errors. Categorical data was presented as frequencies and percentages, while continuous data was presented as mean and standard deviation (SD). We utilized Microsoft Excel for all data analyses. Adobe Illustrator was employed for crafting high-definition figures in the main manuscript. No generative artificial intelligence tools, whether independent or paired with PubMed or Covidence, were involved at any stage, be it ideation, search strategy, screening, data extraction, or data analysis for this research.

Results

Eligible Studies

The search was conducted on May 9, 2023, and yielded 1483 studies with one duplicate. Of these, 553 (37.3%) were included in phase 2 screening, and 369 (24.9%) studies were eligible for data extraction (Figure 1).

Figure 1. PRISMA chart for eligible studies.

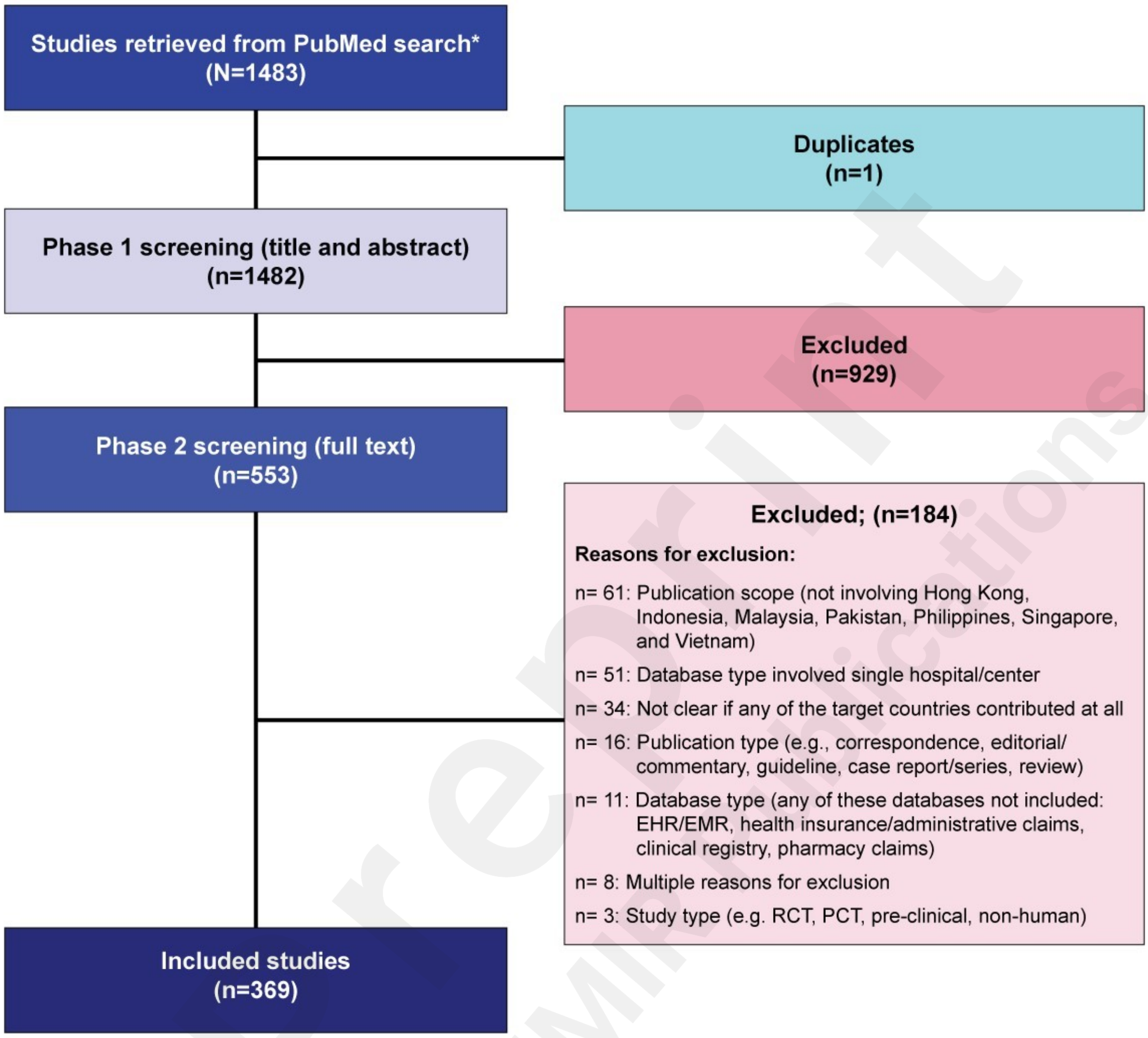

Figure legend: EHR: electronic health record; EMR: electronic medical record; PCT: pragmatic clinical trial; RCT: randomized clinical trials; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

The vast majority of the publications (361 or 97.8%) were original research, while the remaining 8 (or 2.2%) were study protocols. The country-wise distribution of SCS and CCCS is illustrated in Multimedia Appendix 2, Page 3.

Geographic Distribution and Collaboration Relationship

Among the 369 studies that qualified for data extraction, Singapore, Hong Kong, and Malaysia each contributed to ≥100 publications, with respective counts of 157, 130, and 100. The other four nations - Indonesia, Pakistan, Vietnam, and the Philippines - were involved in fewer publications, with 33, 31, 27, and 22, respectively, and each had over 50% of their studies classified as CCCS (refer to Table S3, Multimedia Appendix 1). Given their lower overall study numbers and the predominance of CCCS, these four nations were categorized as 'global collaborators' in certain subsequent analyses (Figure 2).

Figure 2. Archetype by number of publications and percentage of cross-country collaborative for real-world studies in last 5 years from ten nations in Asia

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Figure legend: Scatter plot archetyping countries based on two criteria: the total number of publications in the last five years and the percentage of those that were. Global Collaborators refers to the cluster, highlighted within the dashed lines, and includes countries with a relatively high percentage of cross-country collaboration studies but fewer total publications. Countries in this cluster include the Philippines, Indonesia, Vietnam, and Pakistan. They are characterized by engaging more in collaborative research with other countries and <100 RWD publications from integrated databases in last 5 years. Solo Scholars cluster includes other countries that have a lower percentage of CCCS (≤50%) and higher publications. Countries like Taiwan, which lie far to the right on the x-axis, indicate a high number of total publications with a relatively low percentage of CCCS, signifying a tendency to conduct independent research. The data for India, Taiwan, and Thailand were derived from our previous publication that employed the same methodology as this current research [7].

Collaborations involving countries beyond the seven target nations of this study were labelled as non-target countries (NTC). The cross-country collaboration network across the seven target nations and NTC is described in Table S4, Multimedia Appendix 1. The average number of collaborative countries (ANC) indicates the cross-country interconnection for research of a given nation. The ANC varied from 2.2 for Singapore to 4.1 for the Philippines. Despite the lowest ANC, Singapore was involved in 77 studies, making it the highest contributor to CCCS. On the other hand, Malaysia with a higher ANC of 3.1, participated in 50 CCCS, making it the most engaged collaborator within the Solo Scholars cluster. Notably, Malaysia participated in 55.6% of CCCS from Pakistan, 75% of CCCS from Vietnam, 80.8% of CCCS from Indonesia, and 84.2% of CCCS from Philippines.

NTC were common collaborators in CCCS across all seven target countries, with their involvement ranging from 84.2% to 97.7%.

Time trend

Figures 3 and 4 depict the yearly average counts and growth rates of SCS and CCCS across the seven target nations from Solo Scholars and Global Collaborators clusters, respectively.

Between 2018 and 2023, every target nation, except for the Philippines, which experienced a decline of -14.5%, exhibited an upward trend in the average number of studies published. Vietnam led with the steepest growth rate at 24.5%, trailed by Pakistan at 21.2%. For Solo Scholars, there were growing trends for all the 3 nations, with a growth rate of 6.2% with Hong Kong, 8.7% with Singapore, and 16.3 with Malaysia. Due to small in number of average studies by year in some of the individual Global Collaborators nations, growth trend is also presented collectively for Global Collaborators as a cluster in Figure 3b. Duplication studies within cluster were adjusted, thus the sum of CCCS from all 4 nations might be larger than the number of CCCS of cluster as whole. The growth rate was 21.2% in Global Collaborators Cluster after adjusting the duplicates.

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Figure 3. Annual trend of average publication number by geography distribution for Solo Scholars nations.

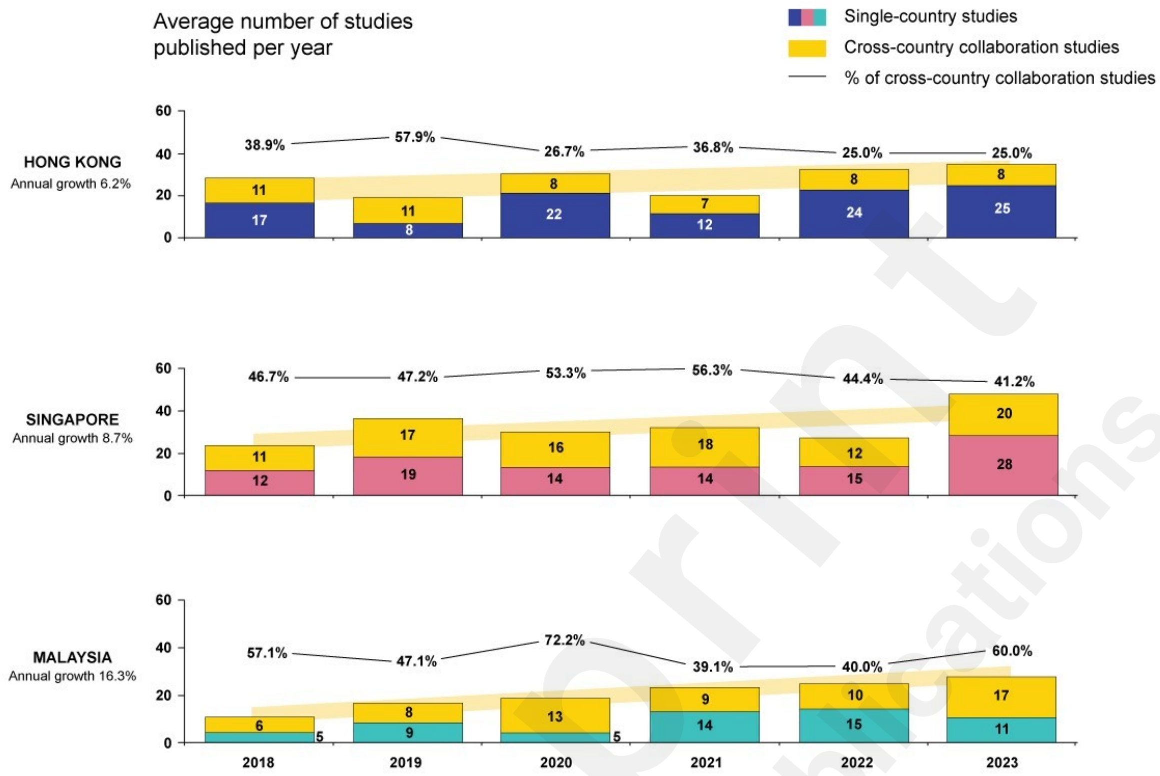

Figure legend: Malaysia displayed the highest annual growth rate of 16.3% followed by Singapore (8.7%) and Hong Kong (6.2%) among the Solo Scholars cluster.

Figure 4. Annual trend of average publication number by geography distribution for Global Collaborators nations.

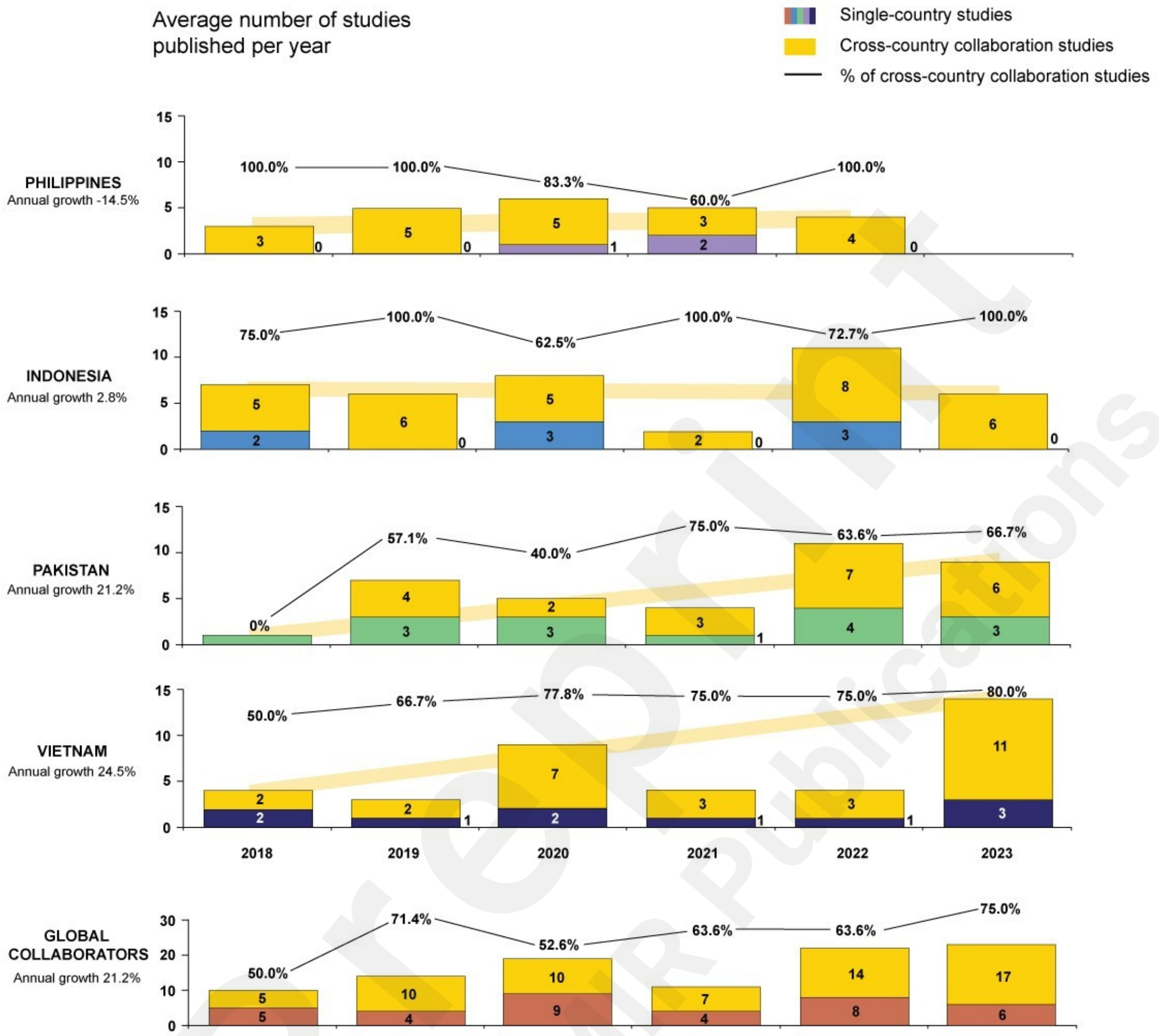

Figure legend: Vietnam exhibited the most significant increase in total studies among the seven target countries, followed by Pakistan and Malaysia. The Philippines was the only nation with a decline, while Indonesia and Hong Kong maintained a consistent study count with the slowest overall growth rates. Both Vietnam and, to a lesser degree, Indonesia and Pakistan demonstrated a rising participation in cross-country collaborative research. Due to small in number of average studies by year in some of the individual Global Collaborators nations, figures are also presented collectively for Global Collaborators as cluster in Figure 3b. Duplication studies within cluster were adjusted, thus the sum of CCCS from all 4 nations might be larger than the number of CCCS of cluster as whole. After adjusting for duplications, the overall growth rate of total studies was 21.2% among all Global Collaborators.

Overall attributes

Table 1 shows the primary attributes of the eligible studies from each of target nation by SCS and CCCS. Variable presented were study type, disease domain, data source, outcomes, participant demographics, length of study duration, time gap from last data available to publication, sample size, and number of research centers.

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Table 1. Study characteristics in seven target countries by SCS[a] and CCCS[b] (N=369)[c].

Table 1a. Study characteristics of Solo Scholars

	Singapore N= 157		Hong Kong N= 130		Malaysia N= 100	
	SCS	CCCS	SCS	CCCS	SCS	CCCS
	n=80	n=77	n=86	n=44	n=50	n=50
Study type (n, %)						
CER[d]	54 (67.5)	44 (57.1)	57 (66.3)	31 (70.5)	28 (56.0)	27 (54.0)
Non-CER (descriptive)	26 (32.5)	33 (42.9)	29 (33.7)	13 (29.5)	22 (44.0)	23 (46.0)
Disease Area (n, %)						
CVM[e]	33 (41.3)	32 (41.6)	36 (41.9)	20 (45.5)	13 (26.0)	25 (50.0)
IDV[f]	7 (8.8)	3 (3.9)	18 (20.9)	3 (6.8)	7 (14.0)	7 (14.0)
IAD[g]	2 (2.5)	3 (3.9)	6 (7.0)	1 (2.3)	6 (12.0)	2 (4.0)
Oncology	11 (13.8)	9 (11.7)	8 (9.3)	13 (29.5)	10 (20.0)	7 (14.0)
Others	27 (33.8)	30 (39.0)	18 (20.9)	7 (15.9)	14 (28.0)	9 (18.0)
Database type (n, %)						
EMR[h]/EHR[i]	43 (53.8)	19 (24.7)	69 (80.2)	12 (27.3)	11 (22.0)	12 (24.0)
Clinical registry	46 (57.5)	63 (81.8)	22 (25.6)	35 (79.5)	39 (78.0)	41 (82.0)
Health insurance/claims	4 (5.0)	1 (1.3)	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)
Pharmacy claims	1 (1.3)	0 (0.0)	0 (0.0)	1 (2.3)	2 (4.0)	0 (0.0)
Multiple databases	12 (15.0)	5 (6.5)	5 (5.8)	3 (6.8)	2 (4.0)	3 (6.0)
Study outcome (n, %)						
Clinical	78 (97.5)	76 (98.7)	86 (100.0)	44 (100.0)	49 (98.0)	48 (96.0)
Cost	4 (5.0)	0 (0.0)	2 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)
PROs[j]	0 (0.0)	5 (6.5)	1 (1.2)	2 (4.5)	1 (2.0)	7 (14.0)
Study population (n, %)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
Adults	63 (78.8)	61 (79.2)	67 (77.9)	37 (84.1)	32 (64.0)	37 (74.0)
Mixed	13 (16.3)	9 (11.7)	16 (18.6)	7 (15.9)	12 (24.0)	8 (16.0)
Pediatric	4 (5.0)	7 (9.1)	3 (3.5)	0 (0.0)	6 (12.0)	5 (10.0)
Study duration (years), mean (SD)	6.6 (4.8)	7.8 (7.4)	9.8 (7.3)	7.9 (6.7)	7.1 (4.2)	5.5 (7.4)
Lag period (years) from end of research to publication						
Overall mean (SD)	5.8 (3.0)	4.8 (2.5)	5.1 (2.9)	5.0 (2.6)	4.8 (1.6)	4.6 (2.5)
<2 years (n, %)	3 (3.8)	7 (9.1)	11 (12.8)	4 (9.1)	1 (2.0)	7 (14.0)
2 to 5 years (n, %)	39 (48.8)	47 (61.0)	46 (53.5)	23 (52.3)	33 (66.0)	24 (48.0)
>= 6 years (n, %)	34 (42.5)	16 (20.8)	26 (30.2)	10 (22.7)	16 (32.0)	9 (18.0)
Unknown (n, %)	4 (5.0)	7 (9.1)	3 (3.5)	7 (15.9)	0 (0.0)	10 (20.0)
Study size						
Sample size (in thousands), mean (SD)	56.0 (180.9)	813.4 (4383.2)	205.0 (607.8)	4187.1 (23979.1)	16.1 (30.7)	844.0 (4526.1)
Number of centers, mean (SD)	4.4 (5.1)	89.7 (215.0)	42.7 (60.2)	66.8 (147.8)	19.5 (15.4)	92.4 (156.9)

Table 1b. Study characteristics of Global Collaborators

	Indonesia N= 33		Pakistan N= 31		Vietnam N= 27		Philippines N= 22	
	SCS	CCCS	SCS	CCCS	SCS	CCCS	SCS	CCCS
	n=7	n=26	n=13	n=18	n=7	n=20	n=3	n=19
Study type (n, %)								
CER[d]	3 (42.9)	14 (53.8)	1 (7.7)	12 (66.7)	5 (71.4)	11 (55.0)	1 (33.3)	10 (52.6)
Non-CER (descriptive)	4 (57.1)	12 (46.2)	12 (92.3)	6 (33.3)	2 (28.6)	9 (45.0)	2 (66.7)	9 (47.4)
Disease Area (n, %)								
CVM[e]	1 (14.3)	13 (50.0)	2 (15.4)	5 (27.8)	2 (28.6)	9 (45.0)	1 (33.3)	8 (42.1)
IDV[f]	2 (28.6)	6 (23.1)	4 (30.8)	9 (50.0)	0 (0.0)	4 (20.0)	1 (33.3)	1 (5.3)
IAD[g]	2 (28.6)	2 (7.7)	0 (0.0)	1 (5.6)	3 (42.9)	1 (5.0)	0 (0.0)	2 (10.5)
Oncology	1 (14.3)	3 (11.5)	5 (38.5)	1 (5.6)	1 (14.3)	2 (10.0)	0 (0.0)	2 (10.5)
Others	1 (14.3)	2 (7.7)	2 (15.4)	2 (11.1)	1 (14.3)	4 (20.0)	1 (33.3)	6 (31.6)
Database type (n, %)								
EMR[h]/EHR[i]	2 (28.6)	12 (46.2)	9 (69.2)	9 (50.0)	4 (57.1)	10 (50.0)	1 (33.3)	7 (36.8)
Clinical Registry	4 (57.1)	18 (69.2)	3 (23.1)	13 (72.2)	1 (14.3)	12 (60.0)	2 (66.7)	14 (73.7)
Health insurance/claims	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)
Pharmacy claims	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Multiple databases	0 (0.0)	4 (15.4)	0 (0.0)	4 (22.2)	0 (0.0)	2 (10.0)	0 (0.0)	2 (10.5)
Study outcome (n, %)								
Clinical	7 (100.0)	26 (100.0)	13 (100.0)	16 (88.9)	6 (85.7)	20 (100.0)	2 (66.7)	19 (100.0)
Cost	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	1 (33.3)	0 (0.0)
PROs[j]	0 (0.0)	3 (11.5)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (15.8)
Study population (n, %)								
Adults	5 (71.4)	17 (65.4)	3 (23.1)	8 (44.4)	7 (100.0)	12 (60.0)	1 (33.3)	14 (73.7)
Mixed	2 (28.6)	6 (23.1)	9 (69.2)	8 (44.4)	0 (0.0)	5 (25.0)	2 (66.7)	4 (21.1)
Pediatric	0 (0.0)	3 (11.5)	1 (7.7)	2 (11.1)	0 (0.0)	3 (15.0)	0 (0.0)	1 (5.3)
Study duration (years), mean (SD)	3.1 (3.3)	7.1 (9.6)	2.1 (1.9)	9.1 (11.2)	4.8 (7.0)	8.2 (10.1)	12.0 (8.2)	8.4 (9.8)
Lag period (years) from end of research to publication								
Overall mean (SD)	4.3 (1.8)	4.2 (2.4)	3.8 (1.6)	3.3 (1.8)	4.6 (1.3)	4.7 (2.6)	4.0 (1.7)	3.9 (2.3)
<2 years (n, %)	1 (14.3)	5 (19.2)	2 (15.4)	6 (33.3)	0 (0.0)	3 (15.0)	0 (0.0)	4 (21.1)
2 to 5 years (n, %)	4 (57.1)	16 (61.5)	8 (61.5)	6 (33.3)	6 (85.7)	11 (55.0)	2 (66.7)	13 (68.4)
>= 6 years (n, %)	2 (28.6)	2 (7.7)	2 (15.4)	1 (5.6)	1 (14.3)	5 (25.0)	1 (33.3)	1 (5.3)
Unknown (n, %)	0 (0.0)	3 (11.5)	1 (7.7)	5 (27.8)	0 (0.0)	1 (5.0)	0 (0.0)	1 (5.3)
Study size								
Sample size (in thousands), mean (SD)	122.6 (304.2)	1513.4 (6235.5)	5.9 (9.8)	2226.8 (7525.4)	202.7 (525.9)	1982.8 (7132.4)	161.9 (280.2)	2094.2 (7322.2)
Number of centers, mean (SD)	5.0 (3.6)	88.9 (92.7)	19.9 (13.4)	35.7 (48.3)	11.7 (4.9)	181.9 (236.9)	3.0 (NA)	81.6 (96.7)

[a]SCS: single-country studies.
[b]CCCS: cross-country collaboration studies.
[c]Study numbers for database types and study outcomes may appear as duplicates; hence, the total percentage may not

account for 100%. Study numbers from CCCS may appear as duplicates for studies conducted in multiple target countries.The percentages may add up to less or more than 100 because of rounding.
[d]CER: comparative effectiveness research.
[e]CVM: cardiology and metabolic disorders.
[f]IAD: inflammatory and autoimmune disorders.
[g]IDV: infectious diseases and vaccines.
[h]EMR: electronic medical record.
[i]EHR: electronic health record.
[j]PRO: patient-reported outcome.

Study Type: Comparative Effectiveness Research (CER) or Non-CER (Descriptive)

Of the total 369 studies, 221 (59.9%) were CER studies, with the remaining 148 (40.1%) being non-CER or descriptive. The relative representation of CER vs non-CER for SCS and CCCS is illustrated in Multimedia Appendix 2, Page 4. Singapore, Hong Kong, Malaysia, and Vietnam had higher CER In both of their SCS and CCCS. Vietnam's SCS had the predominant CER representation at 5/7 (71.4%), followed by Singapore at 54/80 (67.5%) and Hong Kong at 57/86 (66.3%). For CCCS, Hong Kong led with 31/44 (70.5%) CER studies, followed by Pakistan with 12/18 (66.7%) and Singapore with 44/77 (57.1%). There were more descriptive non-CER studies in SCS from Pakistan, Philippines, and Indonesia; resulted in low CER counts and percentages being 1/13 (7.7%), 1/3 (33.3%), and 3/7 (42.9%), respectively.

Figure 5 shows the yearly trend of CER percentages from 2018 to 2023 break down by SCS and CCCS. The consistency in trends were more noticeable in SCS across the seven target nations compared to CCCS. An upward trend in CER% was observed in SCS for Hong Kong, and the Global Collaborators. Conversely, Malaysia’s SCS experienced a steady decrease in CER contribution over the same period.

Figure 5. Trend of comparative effectiveness research (CER) by single-country studies (SCS) and cross-country collaboration studies (CCCS*).

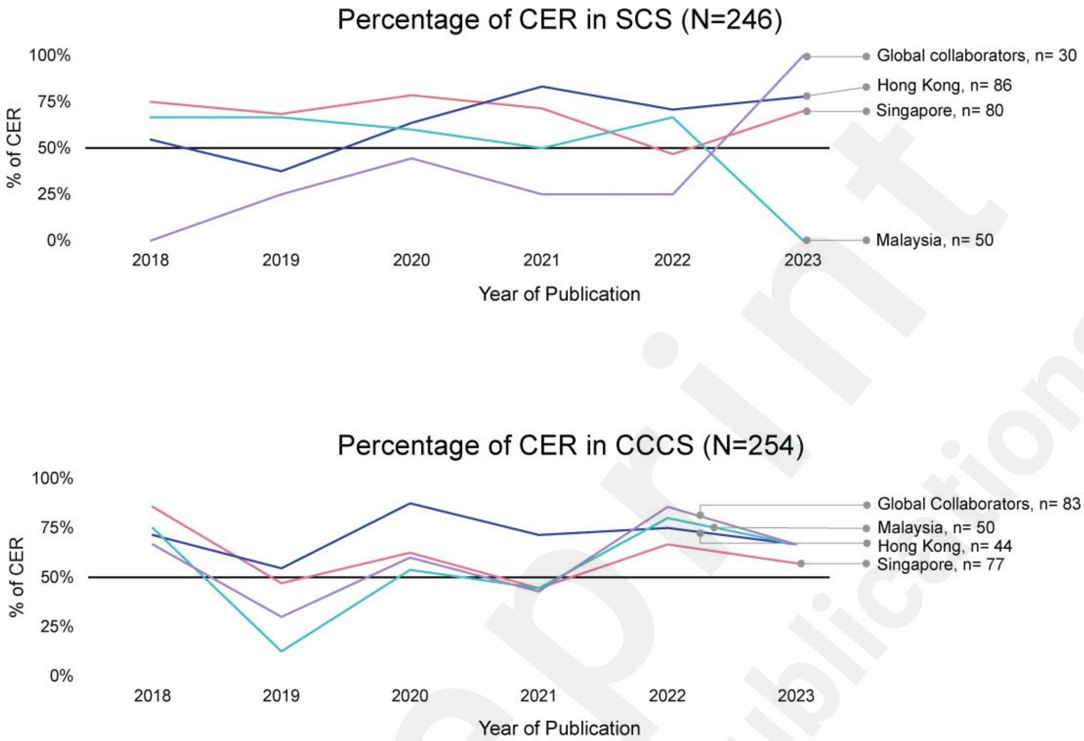

Figure legend: Trends in CCCS across the seven target countries showed more consistency compared to SCS. SCS of Hong Kong and Global Collaborators displaying a notable upward trend in CER percentages, while Malaysia's SCS consistently decreased in CER contribution.

***The count of CCCS represents the individual contributions of each country, leading to a total count across countries that exceeds the actual number of CCCS due to some studies involving multiple collaborators. Conversely, the total count of SCS matches the sum of SCS conducted by each country, as these studies are specific to individual nations without cross-country collaboration.**

The 2y-SMA trends for CER and descriptive studies are illustrated in Multimedia Appendix 2, pages 5-11 for the biennial average from 2018-2023. Hong Kong consistently elevated its CER contributions for both SCS and CCCS, increasing from 47.4% in 2018-2019 to 72.7% by 2022-2023 for SCS, and similarly for CCCS (61.1% in 2018-2019 to 72.7% in 2022-2023). Other notable rises in CER contributions for CCCS were witnessed in

Malaysia (33.3% in 2018-2019 to 75% in 2022-2023), Indonesia (33.3% to 70%), Pakistan (25% to 88.9%), and Vietnam (44.4% in 2019-2020 to 85.7% in 2022-2023). Conversely, Malaysia's SCS saw a consistent decline in CER contribution over the five years, dropping from 66.7% in 2018-2019 to 52.6% by 2022-2023. Furthermore, all of Pakistan's SCS were non-CER between 2018-2022, 12/12 (100%).

Database Type

Out of 369 studies, 341 (92.4%) utilized a singular database. Exclusive use of clinical registry database was most common at 188/369 (50.9%), followed by EMR/EHR at 145/369 (39.3%), health insurance/administrative claims at 5/369 (1.4%), and pharmacy claims at 3/369 (0.8%). Use of multiple databases was found in 28/369 (7.6%) of studies, primarily combining clinical registries and EMR/EHR (Multimedia Appendix 2, page 12). Usage of EMR/EHR database was more common for SCS studies accounting for its use in 120/246 (48.8%) of total SCS (Multimedia Appendix 2, page 13). On the other hand, the predominant exclusive database warehouse for CCCS studies was clinical registries, making up 90 out of 123 studies, or 73.2%. EMR/EHR's contribution to CCCS studies was notably lesser, representing only 25 out of 123, or 20.3%, which is considerably lower than its share in SCS studies (Table 1 and Multimedia Appendix 2, page 14).

Usage of the clinical registry database consistently dominated across all CCCS from all target nations, whether used on its own or in combination with other databases. For SCS:

- More clinical registries over EMR/EHR in Indonesia, Malaysia, and the Philippines, the figures were 4/7 (57.1%) vs. 2/7 (28.6%); 39/50 (78.0%) vs. 11/50 (22.0%); and 2/3 (66.7%) vs. 1/3 (33.3%), respectively.
- Singapore's usage was almost even with 46/80 (57.5%) with clinical registries and 43/80 (53.8%) with EMR/EHR.
- Conversely, Hong Kong, Pakistan, and Vietnam had more EMR/EHR over clinical registries: 69/86 (80.2%) vs. 22/86 (25.6%); 9/13 (69.2%) vs. 3/13 (23.1%); and 4/7 (57.1%) vs. 1/7 (14.3%), respectively.

Figure 6 reveals the evolution of EMR/EHR contributions, both exclusive and and in combination with other databases in the past five years. In SCS, Malaysia and the Global Collaborators experienced a consistent decline in EMR/EHR use, while Hong Kong exhibited an increase. Malaysia's EMR/EHR contribution in SCS remained consistently below 50% during this period. In contrast to SCS, where EMR/EHR use was predominant, CCCS from the target countries always had EMR/EHR contributions under 50% from 2018-2023 and no consistent time trend pattern was seen.

Figure 6. Trend of percentage of utilization of medical records by single-country studies (SCS) and cross-country collaboration studies (CCCS*).

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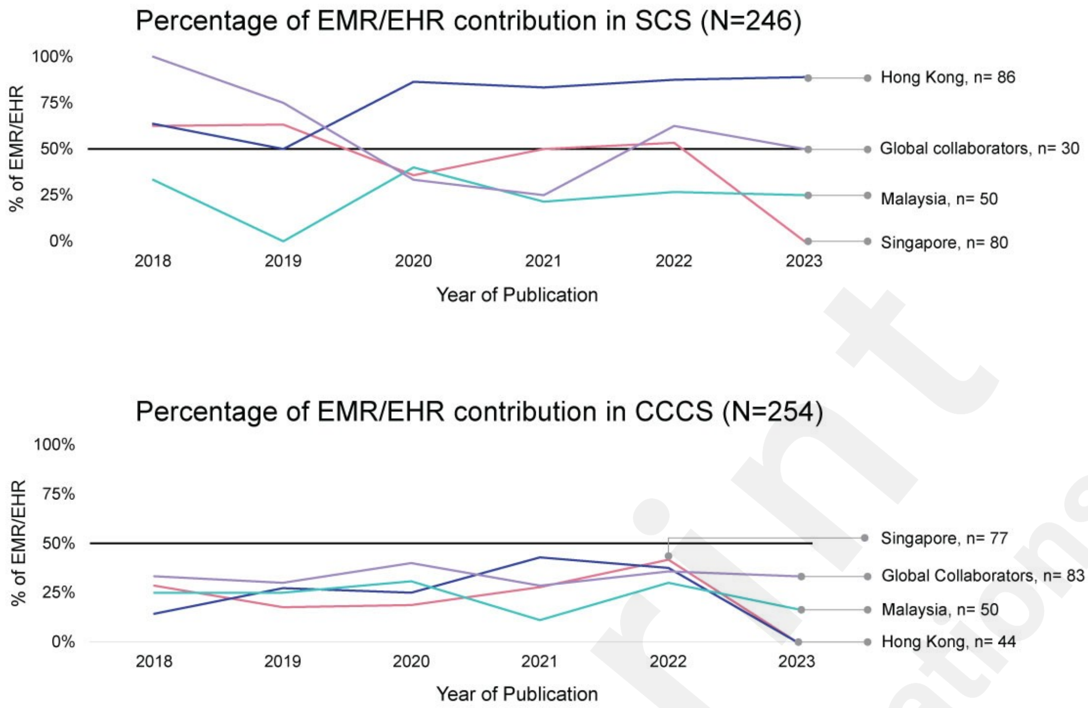

Figure legend: A decline in exclusive or combined use of EMR/EHR was observed for SCS in Malaysia and Global Collaborators, while Hong Kong saw an increase; in contrast, CCCS consistently reported EMR/EHR contributions below 50%, with no uniform trend emerging during this period.

*** The count of CCCS represents the individual contributions of each country, leading to a total count across countries that exceeds the actual number of CCCS due to some studies involving multiple collaborators. Conversely, the total count of SCS matches the sum of SCS conducted by each country, as these studies are specific to individual nations without cross-country collaboration.**

The 2y-SMA over the last five years indicated that the sole use of EMRs/EHRs in SCS from the seven target nations increased from 46.4% to 59.8%. Rather the reliance on clinical registry databases dipped from 50% to 37.8% (Multimedia Appendix 2, page 15). For CCCS, the distribution between clinical registries and EMR/EHR remained relatively steady where clinical registires was most common (Multimedia Appendix 2, page 16).

Disease Area

The leading research medical area was CVM, accounting for 136/369 (36.9%) of studies, trailed by oncology and IDV, each with 55/369 (14.9%). IAD was the least prevalent area, representing 23/369 (6.2%) of the research. The remaining 27.1% (100/369) of studies pertained to various other diseases. The proportion of CVM studies grew from 11/39 (28.2%) in 2018 to 14/36 (38.9%) in 2023, peaking in 2020 with 36/73 (49.3%). Conversely, IDV's share increased notably from 6/73 (8.2%) in 2020 to 21/84 (25.0%) in 2022 and 6/36 (16.7%) in 2023, surpassing oncology as the second primary therapeutic area in recent years (Multimedia Appendix 2, page 17).

Study Outcome(s)

Majority of 348 (94.3%) studies out of the total 369 presented clinical outcomes, whether in terms of treatment effect or safety. There were 21 (5.7%)

studies that discussed cost outcomes, PROs, or a combination of these with clinical results. In the SCS category, every study from Pakistan focused on clinical outcomes. While cost outcomes appeared in SCS from all countries except Malaysia and Pakistan. One study each from Hong Kong (1/86，1.2%) and Malaysia (1/50, 2.0%) included PROs outcomes. In the CCCS category, none of the selected nations presented studies focusing on cost outcomes (Table 1).

Study Population

Among the 369 studies obtained, 273 (74.0%) investigated adults, 24 (6.5%) focused on pediatric age group, and 72 (19.5%) encompassed both adult and pediatric participants. Notably, in the SCS category (Table 1b), Pakistan (in 9/13, 69.2%) and the Philippines (in 2/3, 66.7%) reported higher proportions of mixed populations than solely adult participants (Pakistan: 3/13, 23.1%; Philippines: 1/3, 33.3%).

Pediatric representation in the CCCS was 10 out of 123 (8.1%), slightly higher than in SCS (14/246, 5.7%). Within CCCS (Table 1b), Vietnam led in pediatric-focused research with 3 out of 20 studies (15.0%), followed by Indonesia (3/26, 11.5%), and Pakistan (2/18, 11.1%).

Study Duration

Information about study duration was reported for overall 349/369 (94.6%) studies. The average duration was 7.4 years with a standard deviation (SD) of 6.3 years, ranging from 0.01 to 35.8 years. In total, 13 studies had a duration of greater than 20 years. The mean for SCS was higher at 7.5 years (SD 6.0 years) compared to CCCS at 7.1 years (SD 6.8 years) (Multimedia Appendix 2, page 18).

Within the SCS, the Philippines (Table 1b) topped the list with the longest average study duration of 12.0 years (SD 8.2 years). As shown in Table 1a, Hong Kong followed closely with an average of 9.8 years (SD 7.3 years). Conversely, Pakistan and Indonesia registered the shortest mean study durations with 2.1 years (SD 1.9 years) and 3.1 years (SD 3.3 years), respectively. Over a 5-year span, based on a 2-year rolling average, the study duration in Indonesia showed an uptick, increasing from 0.6 years in 2018-2019 to 1.9 years in 2022-2023. Other target countries did not exhibit any consistent study duration trend patterns (Multimedia Appendix 2, pages 19-25).

For CCCS, Pakistan (Table 1b) led with the longest mean study duration of 9.1 years (SD 11.2 years), closely followed by the Philippines with 8.4 years (SD 9.8 years). Malaysia (Table 1a) recorded the shortest average study duration at 5.5 years (SD 7.4 years). The study duration in Indonesia's CCCS averaged 7.1 years (SD 9.6 years), which was notably longer than their SCS. Observing trends, there was a decline in the mean study duration for CCCS in Malaysia, Pakistan, the Philippines, and Vietnam. Conversely, the average study duration in Singapore's CCCS steadily rose, advancing from 5.6 years in 2018-2019 to 9.1 years in 2022-2023 (Multimedia Appendix 2, pages 19-25).

Lag Between the Research Period and Publication

Of the eligible studies, the majority of 205 out of total 369 (55.6%) were published between 2-5 years after the time of latest available data studied; 28.5% (105/369) were published later than 6 years; and 9.6% (35/369) were published within 2 years. The remaining 24 studies (6.5%) had unspecified year(s) of the research completion (Multimedia Appendix 2, page 26).

Eligible studies from all the target nations displayed a similar trend, with the majority being published within 2-5 years after the research period.However, in both Singapore and Hong Kong, the time taken from research completion to publication was notably longer for both SCS and CCCS, averaging 5.8 (SD 3.0) and 5.1 (SD 2.9) years for SCS, and 4.8 (SD 2.5) and 5.0 (SD 2.6) years for CCCS, respectively (Table 1a).

It is worth noting that 13.8% of CCCS were published within 2 years of research period but only 7.3% of SSC were published in this time frame. We observed upward trends in the time to publication within 2 years from 2018 to 2023. For SCS it was from 3.2% to 14.5%; and for CCCS was from 15.8% to 20.0% (Multimedia Appendix 2, pages 27-28).

The publication time lag also varied according to the RWD source (Multimedia Appendix 2, pages 29-30). In studies that relied on a single database, the EMR/EHR database consistently recorded the highest percentage of studies published within 2 years post-research. This trend held true for both SCS and CCCS, with EMR/EHR dominating the quick turnaround for publications. Specifically, in the SCS, 12.8% of studies using the EMR/EHR database were published within this 2-year timeframe, whereas only 2.1% of those using clinical registry databases met the same publishing speed. Consistent pattern for CCCS: 26.1% of studies used EMR/EHR were published within 2 years, in contrast to the 14.1% studies used clinical registry databases. Notably, neither the health insurance/medical claims database nor the pharmacy claims database saw any studies published within the 2-year window.

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Study Size: Sample Size and Number of Centers

The sample size was specified in 362 (98.1%) studies and varied considerably, ranging from as few as 16 to over 154,500,000. The average sample size (SD) was 672,352 (8,364,280). The average in CCCS was much higher at 1,824,035 (14,530,091) compared to 106,029 (397,049) in SCS (Multimedia Appendix 2, page 31). The 2y-SMA of sample size in SCS indicated an increasing trend from 51.7k to 178.7k during 2018 and 2023. In contrast, a sharp decline was observed in CCCS from 5,543.3k to 548.1k duing the same period (Multimedia Appendix 2, page 32). Hong Kong had the highest average sample size in SCS, 205.0k (607.8k) as well as in CCCS, 4,187.1k (23,979.1k) (Table 1).

The number of participating centers was only specified in 164 studies (44.4%). The mean (SD) number of centers was 44.3 (120.3), ranging from 2 to 1119. As noted in Table 1, Hong Kong reported the highest average of 42.7 (60.2) for SCS, followed by Pakistan 19.9 (13.4) and Malaysia at 19.5 (15.4). For CCCS Vietnam had the highest mean of study centers at 181.9 (236.9), which was higher than twice of overall CCCS mean of 78.4 (178.6).

The 2y-SMA for the number of study centers of SCS initially rose from 81.8 in 2018-2019 reaching a peak of 131.9 in 2019-2020 before declining to 99.1, 37.1 and finally 30.8 in the subsequent years. In CCCS, there was a downtrend starting from 16.1 in 2018-2019 to 10.7 centers at its lowest point in 2020-2021 before bounding back to 33.9 centers in 2022-2023 (Multimedia Appendix 2, page 33).

Table S5 in Multimedia Appendix 1 provides and overview of numbers of centres involved in RWD studies across various database types in target countries. The Philippines reported the highest average number of centers (197.0) in studies utilizing EMR/EHR databases, while Vietnam had a highest average (65.8) in studies associated with clinical registry databases. Information on the number of centers was not reported in many studies, particularly those utilizing health insurance/claims databases.

Database Names

Multimedia Appendix 3 provides the specific database name(s) utilized in each study, organized by target countries, database type, and disease area.

Discussion

This scoping review was built on our earlier research completed for Taiwan, India, and Thailand in Asia [7]; we have now expanded insights on integrated real-world study databases across seven additional diverse Asian healthcare systems in Hong Kong, Indonesia, Malaysia, Pakistan, the Philippines, Singapore, and Vietnam. This has enabled us to provide a comprehensive perspective on the current landscape of real-world evidence generation in these nations, thus aiding stakeholders in formulating informed research and policy decisions [22, 23].

The archetyping of the target nations into two country clusters, i.e., Solo Scholars and Global Collaborators, allowed us to uncover distinct patterns reflective of differing resources, priorities, and strategic objectives. Solo Scholars tend to conduct independent studies which exemplifies that these nations are equipped with robust research infrastructures. This autonomy allows for a deep dive into national health issues tailored to specific local contexts and country priorities [24]. On the other hand, Global Collaborators frequently engaged in international partnerships, a strategy that would be likely born out of necessity due to limited research funding and resources within the nation and, hence, a greater reliance on collaborative networks [25]. We found that over 90% of CCCS from Global Collaborators involving NTC also partnered with some of the 7 target nations. This collaborative pattern possibly indicated a stronger network of research collaboration within the neighboring regions of Asia. On the contrary, Solo Scholars like Singapore and Hongkong, despite the high CCCS involved NTC (>95%), there were about 40% of studies not partnered with other target nations. The emphasis on global or regional priorities could, however, overshadow the unique health challenges and priorities of these nations. This imbalance can lead to a scarcity of data and insights directly applicable to domestic healthcare [26].

Among Solo Scholars, Hong Kong, Malaysia, and Singapore emerged as significant contributors for domestic RWD publications, showcasing their robust research infrastructure and commitment to harnessing RWD. In contrast, Global Collaborators and especially the Philippines had fewer studies, which could be attributed to various reasons, from funding source to bureaucracies in research grant administration [27, 28]. Singapore emerged as the predominant contributor to the CCCS pool but on average Malaysia collaborated with more number of countries. It's also particularly noteworthy that, from 2018 to 2023, the majority of our target nations (except the Phillipines) manifested an increasing trend in the average number of studies published annually, with Vietnam leading in growth. Vietnam's healthcare system has been consistently advancing, and the nation is enhancing its research capabilities; this progress has been widely acknowledged in the literature [23, 29].

Diving deeper into the nature of these studies, there was an evident leaning towards CER over descriptive studies in several nations, such as Vietnam, Singapore, and Hong Kong. The proportion of CER to non-CER studies offers insights into the nature of the questions researchers in different regions were keen to address. Regions with a higher proportion of CER studies, like Vietnam's SCS, suggest an active interest in comparing the outcomes of different interventions / preventive and prognostic strategies, which can be crucial for policy decisions, including effective containment of COVID-19. Vietnam, along with Singapore and Hong Kong, have been extensively praised for effectively controlling the spread of COVID-19, especially during the early stages of the pandemic [30, 31]. While we cannot assert a direct link with certainty, the possibility of a connection through RWD from CER also playing a role in fostering better-informed public health decisions cannot be denied [32]. Moreover, Singapore's and Hong Kong’s well-established reputation as quality research hubs in Asia could further underscore the potential impact of robust research frameworks [33, 34].

The predilection for certain database types, be it clinical registries or EMR/EHR revealed a combination of availability, convenience, and hence the ease of use of these databases in different regions. The five-year trend showcased the evolving dynamics in RWD research. A clear preference for using the type of database warehouse, clinical registry versus medical records was apparent in individual nation. Nations leaning towards EMR/EHR databases, such as Hong Kong, might be signaling greater digitization of their health records or the perceived value in this data type [35, 36]. However, while nations like Indonesia, Malaysia, and the Philippines primarily leveraged clinical registries. Apart from Hong Kong, Pakistan and Vietnam also displayed a marked inclination towards EMR/EHR utilization.

The variance in research durations offers a window into the research efficiency and the possible administrative or infrastructural bottlenecks. Longer durations in nations like the Philippines could indicate complex, long-term studies or challenges in study execution and continuity [27]. Additionally, the expectation that RWD accelerates evidence generation is quite much in contrast with our findings, where there was an average lag of around 2–5 years from research completion to publication. Notably, over 90% of the studies extended beyond 2 years to reach publication, suggesting room for enhancing the efficiency of evidence generation, potentially through targeted support mechanisms. Interestingly, a comparatively higher proportion of CCCS in contrast with SCS (13.8 vs 7.3%) were published within 2 years, hinting at the efficiency benefits that international partnerships might offer in expediting research outputs. The larger study sample sizes and more number of centers, as observed in Hong Kong, reflect the ability to conduct expansive studies from territory-wide linked databases, indicating a propensity for large-scale, nationally representative research [37]. Similarly, the number of centers involved could also indicate the collaborative spirit within the research community or the need to pool resources.

The strategic application of RWE in healthcare research and policy formation is clearly evident on a global scale. Although there is an increasing reliance on HTA as a pivotal tool for informed healthcare decision-making, the nations categorized largely under the Global Collaborators Cluster face tremendous challenge in healthcare infrastructure and economic constraints to led independent RWE that could shape local healthcare policy and reimbursement decision-making [38, 39]. Hence, open data initiatives international collaborations, such as, Observational Health Data Sciences and Informatics and HTAAsiaLink, respectively, are crucial in this regard [40, 41]. There is also a potential for other international networks, e.g., the International Network of Agencies for Health Technology Assessment in facilitating the alignment of healthcare policies with benchmark evidence-based practices [42].

Limitations

In our efforts to comprehensively assess the landscape of research in the field, we encountered challenges in data extraction, mainly due to inconsistencies in how various studies reported certain characteristics, such as the number of centers or study periods. For instance, while some studies provided clear details on their duration, others only specified the enrollment phase, leaving us to speculate on the follow-up or observation period. Also, the screening and extraction process involved multiple reviewers working under tight schedules. We acknowledge that this approach diverges from the ideal practice of having at least two independent investigators screen each title, abstract, and full text and subsequently blindly extract data to each other's decisions. While we implemented quality checks, including spot assessments and team discussions, the constraints inevitably may have introduced occasional inaccuracies.

Moreover, in some nations, the limited number of studies could make percentage-based analyses less reflective of the true study landscape. Still, these analyses offer a preliminary understanding of research trends in those regions. We must also acknowledge that our analysis, with a search conducted in May 2023, assumes a linear distribution for studies in 2019 and 2023, which might slightly deviate from the actual figures due to approximations.

We might have inadvertently overlooked some relevant studies, especially if abstracts failed to mention key terms like RWD/RWE. Our decision to focus on

English publications and rely solely on PubMed for citations, while strategic, may have missed a handful of non-English studies or those from other databases. Nonetheless, the vast number of studies we analysed offers valuable insights into using RWD to produce RWE in our target countries. Also, we did not report study design and funding sources for included studies. While this information may have been valuable, we faced challenges in the extraction of study design and funding information due to lack of clear and inconsistent reporting across publications. This necessitated the exclusion of these variables to prevent any subjective interpretations.

Despite these challenges, our findings underscore a need in the research community: a call for clearer, more standardized reporting on the database used, study design, analysis methods and important time points. A particular area that warrants attention is the clarity in detailing study duration (which should encompass recruitment and observation periods), study design and funding sources. While we recognize the study's limitations, we believe it also paves the way for refining research methodologies in the future.

Conclusion - the Path Forward

Our comprehensive assessment of studies across the selected nations reveals intricate patterns that explain the diverse research landscape for RWD generation. Each nation's unique landscape for contemporary integrated RWD warehouses tells a narrative that is partially attributed to their economic, clinical, and research settings. Delving deeper into these patterns aids in formulating robust insights for future endeavors in healthcare research and policymaking, including prioritization for competency building based on a nation’s unique infrastructure, skill sets, research strengths and weaknesses [4]. As the healthcare landscape evolves, there is an undeniable value in understanding and leveraging RWD [43]. Recognizing the diverse approaches and challenges across countries can lead to more collaborative and informed strategies [4]. The goal should be to address the present gaps and pave the way for future synergistic, impactful, and patient-centric research [3].

In conclusion, the observed variations across nations reiterate the essence of context in healthcare research. Every nation's unique story, as told by their data, accentuates the need for a tailored approach in utilizing RWD – ensuring that it truly serves the multifaceted needs of healthcare research and decision-making.

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Authors' Contributions

All the authors were involved in the idea's conception, design, and interpretation of the facts and data. W-YS, and VJ were involved in data analyses. SS led the manuscript writing, and all authors were engaged in revising it for scientific content and final approval before submission for publication.

Conflicts of Interest

W-YS, and HS declare that while being employees of Pfizer, there is no conflict of interest in relation to the work presented in this article. The views and opinions expressed herein are solely those of the author(s) and do not reflect the views or positions of their employers.

Data availability

Multimedia Appendix 1: supplementary tables

Multimedia Appendix 2: supplementary figures

Multimedia Appendix 3: identified databases

Abbreviations

CCCS: cross-country collaboration studies
CER: comparative effectiveness research
CVM: cardiology and metabolic disorders
EHR: electronic health record
EMR: electronic medical record
HTA: health technology assessment
IAD: inflammatory and autoimmune disorders
ICU: intensive care unit
IDV: infectious diseases and vaccines
MeSH: Medical Subject Headings
NTC: non-target countries
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRO: patient-reported outcome
RCTs: randomized controlled trials
RWD: real-world data
RWE: real-world evidence
SCS: single-country studies
SMA: simple moving average
UHC: universal health coverage

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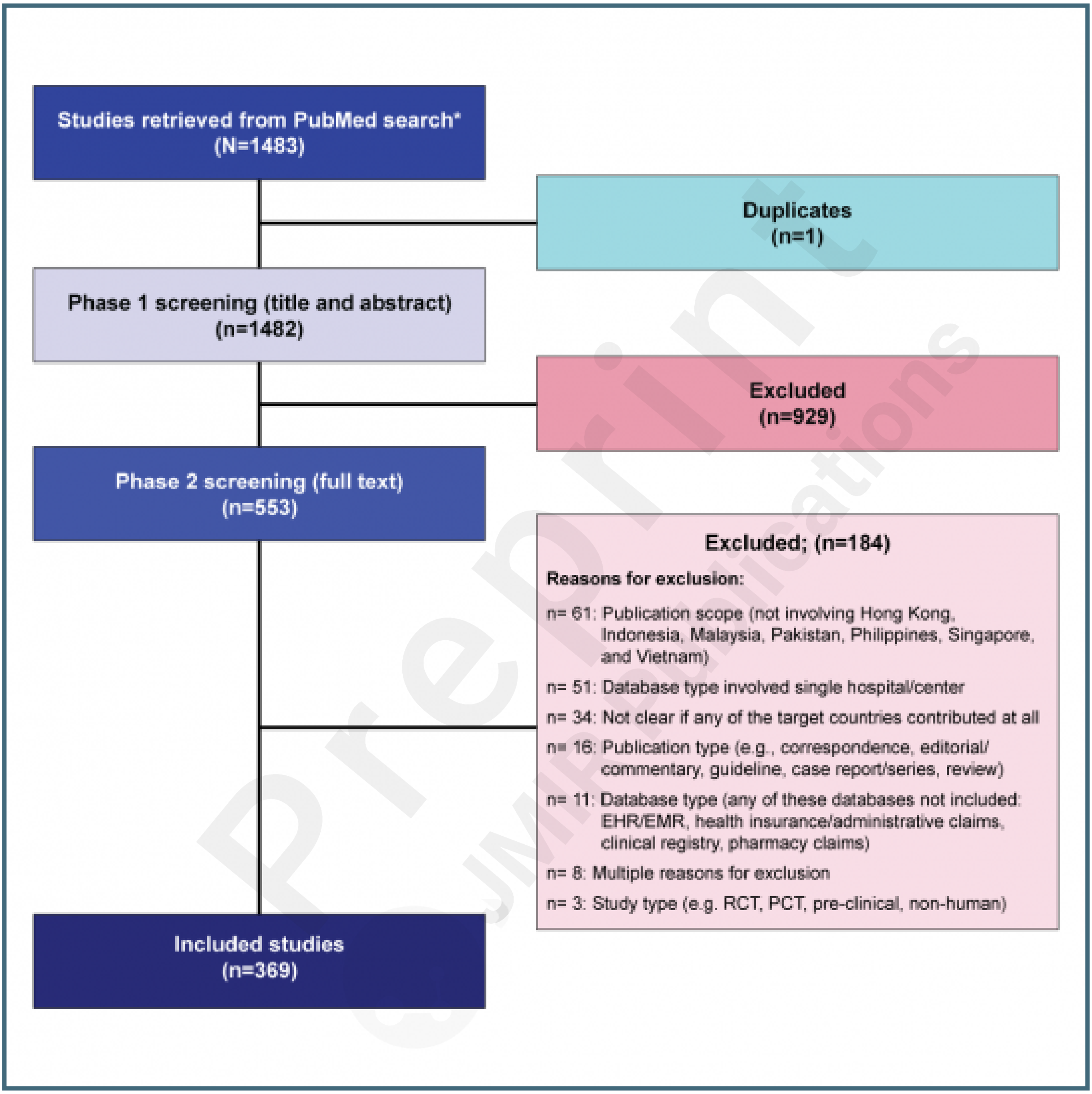
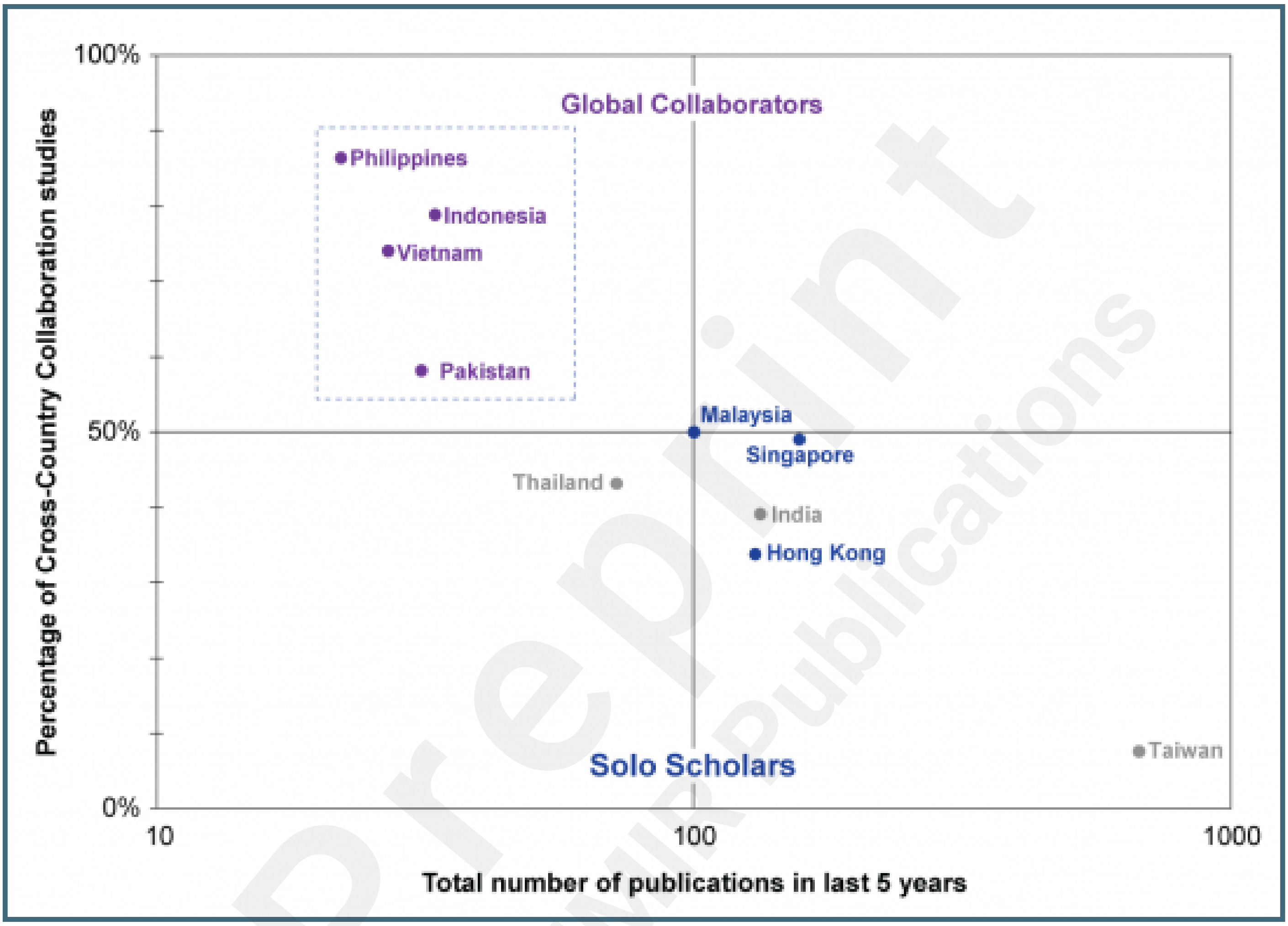
Supplementary Files

Figures

EHR: electronic health record; EMR: electronic medical record; PCT: pragmatic clinical trial; RCT: randomized clinical trials; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.




100%
50%
0%
10
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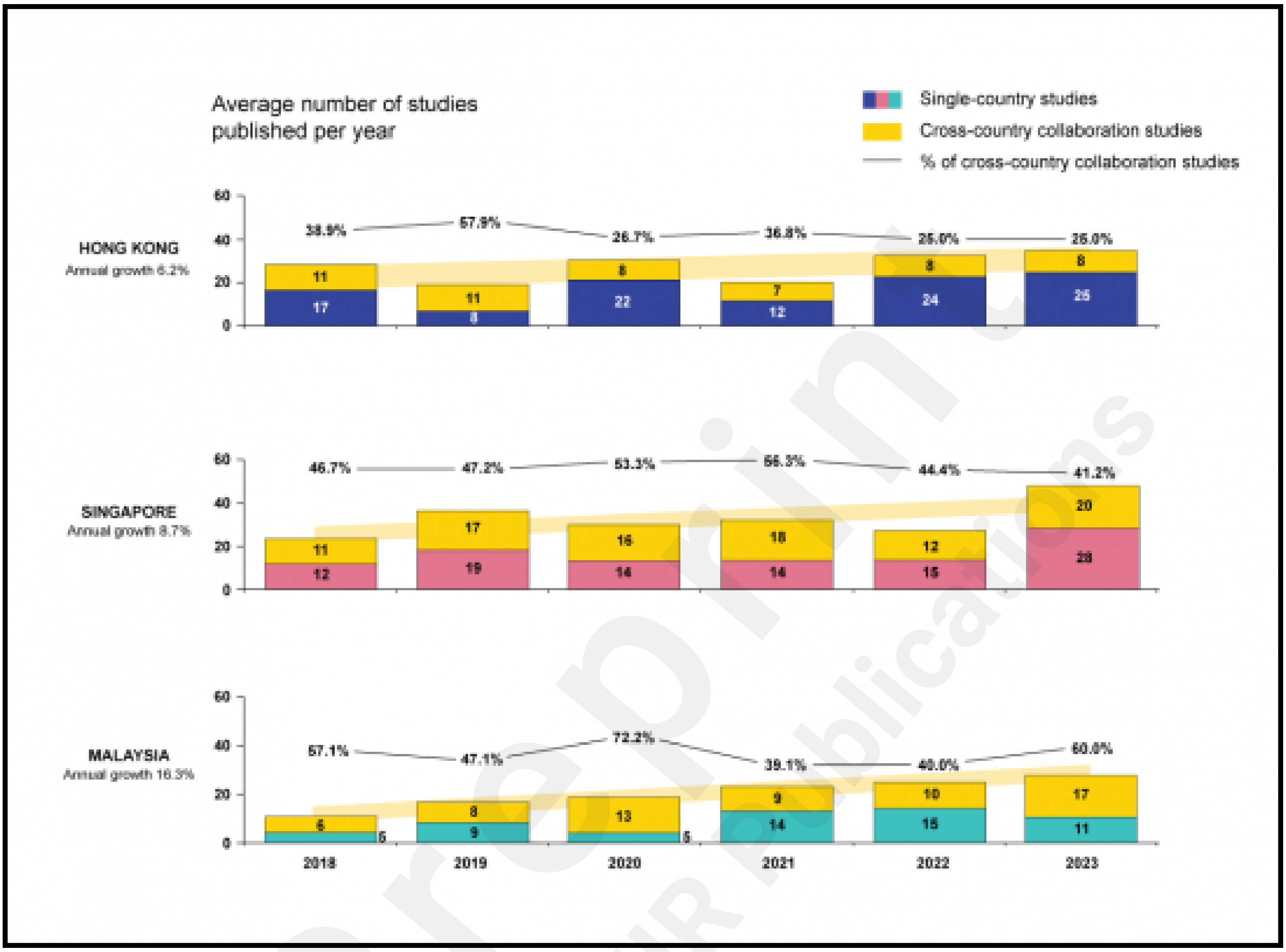
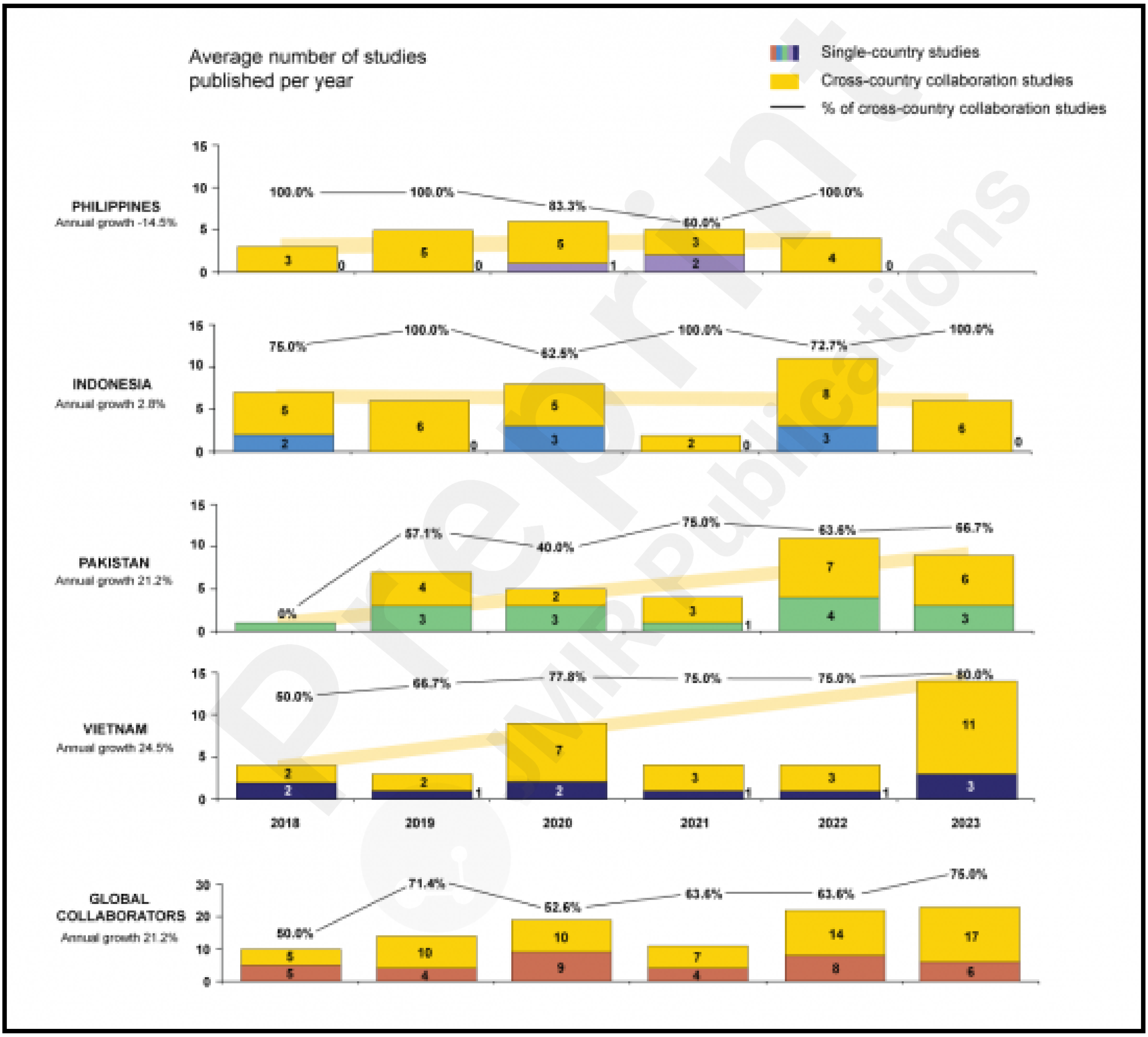
1000
Percentage of Cross-Country Collaboration studies
Total number of publications in last 5 years
Global Collaborators
Philippines
Indonesia
Vietnam
Pakistan
Malaysia
Singapore
Thailand
India
Hong Kong
Taiwan
Solo Scholars

Malaysia displayed the highest annual growth rate of 16.3% followed by Singapore (8.7%) and Hong Kong (6.2%) among the Solo Scholars cluster.



Vietnam exhibited the most significant increase in total studies among the seven target countries, followed by Pakistan and Malaysia. The Philippines was the only nation with a decline, while Indonesia and Hong Kong maintained a consistent study count with the slowest overall growth rates. Both Vietnam and, to a lesser degree, Indonesia and Pakistan demonstrated a rising participation in cross-country collaborative research. Due to small in number of average studies by year in some of the individual Global Collaborators nations, figures are also presented collectively for Global Collaborators as cluster in Figure 3b. Duplication studies within cluster were adjusted, thus the sum of CCCS from all 4 nations might be larger than the number of CCCS of cluster as whole. After adjusting for duplications, the overall growth rate of total studies was 21.2% among all Global Collaborators.



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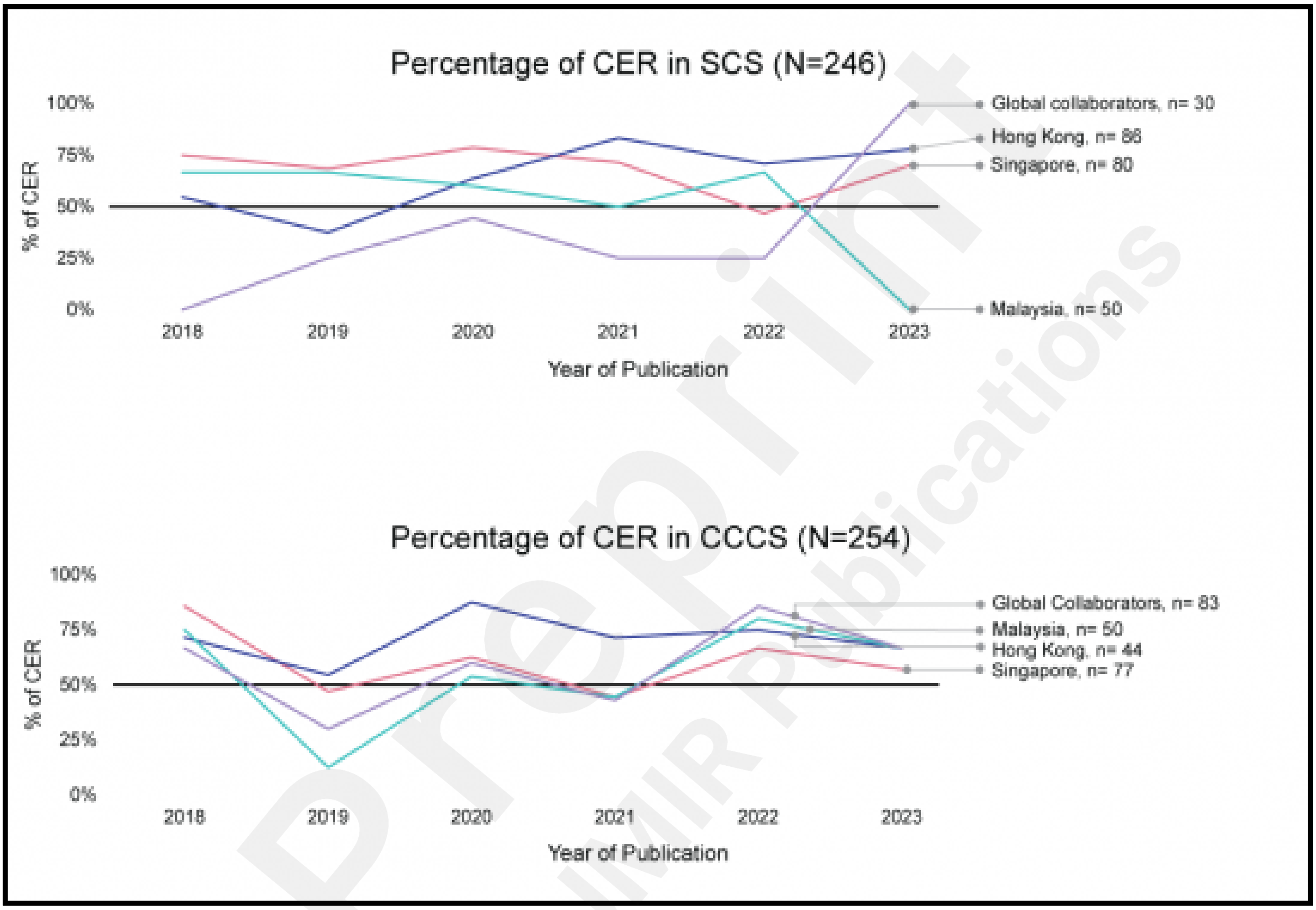
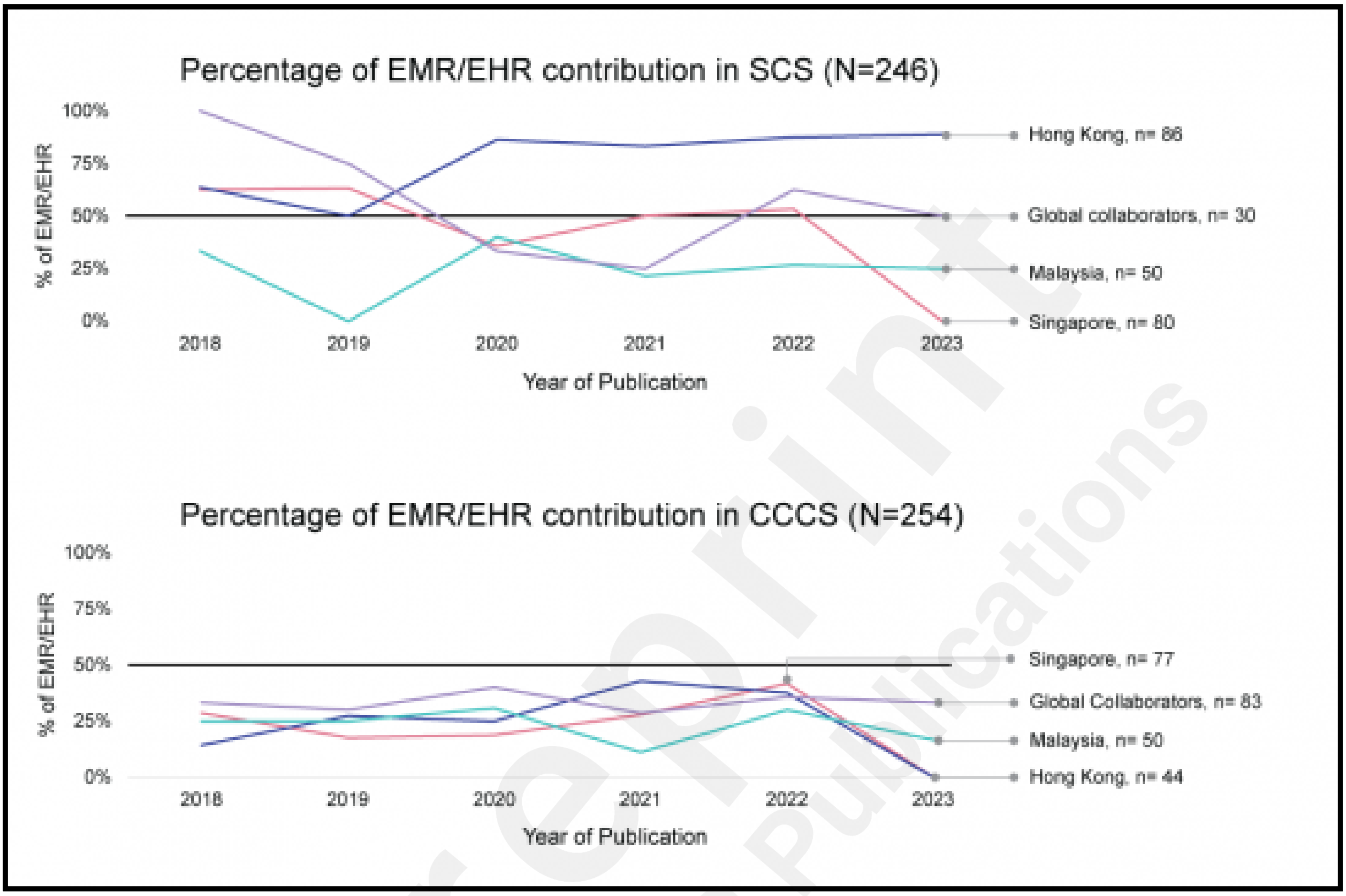
Trends in CCCS across the seven target countries showed more consistency compared to SCS. SCS of Hong Kong and Global Collaborators displaying a notable upward trend in CER percentages, while Malaysia's SCS consistently decreased in CER contribution. *The count of CCCS represents the individual contributions of each country, leading to a total count across countries that exceeds the actual number of CCCS due to some studies involving multiple collaborators. Conversely, the total count of SCS matches the sum of SCS conducted by each country, as these studies are specific to individual nations without cross-country collaboration. .



A decline in exclusive or combined use of EMR/EHR was observed for SCS in Malaysia and Global Collaborators, while Hong Kong saw an increase; in contrast, CCCS consistently reported EMR/EHR contributions below 50%, with no uniform trend emerging during this period.



Multimedia Appendixes

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Supplementary Tables.

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Supplementary Figures.

URL: http://asset.jmir.pub/assets/b5783797988f35e7d4a13da09d0d256a.pdf

Identified Databases.

URL: http://asset.jmir.pub/assets/2172a4bfac573853e1dff5a3d95fc6cd.pdf

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CONSORT (or other) checklists

PRISMA-ScR--Checklist - filled.

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