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Registry-Based Studies in Psychiatry: Advantages, Challenges, Applications, and Future Directions a Narrative Review

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ABSTRACT

Psychiatric disorders contribute substantially to global morbidity and disability, while traditional randomized controlled trials (RCTs) often lack generalisability due to restrictive designs and limited follow-up. Registry-based studies have emerged as a complementary approach, leveraging real-world data to address these limitations. To synthesise the conceptual foundations, methodological approaches, applications, advantages, challenges, and future directions of registry-based studies in psychiatry, and to evaluate their role alongside conventional RCTs. A narrative (integrative) review was conducted following Sukhera (2022) guidelines. Literature from PubMed, Scopus, and Google Scholar (1990–March 2026) was systematically searched using terms related to registry-based research and psychiatry. Key methodological and application-focused studies were selected through iterative screening and citation chaining. Registry-based studies utilise routinely collected clinical and administrative data to enable large-scale, longitudinal, and population-level psychiatric research. They support diverse designs, including cohort studies, case-control analyses, and registry-based randomized controlled trials (rRCTs). Major advantages include high external validity, large sample sizes, cost-effectiveness, and long-term follow-up. Key challenges involve data quality, diagnostic validity, confounding, limited psychosocial variables, and ethical considerations. Applications span epidemiology, treatment outcomes, risk prediction, and health systems research. Registry-based studies are a powerful complement to traditional RCTs, bridging the gap between controlled evidence and real-world psychiatric practice. Advances in digital health, artificial intelligence, and global registry infrastructure are expected to enhance their impact, particularly in advancing precision psychiatry and equitable mental health research.

INTRODUCTION

Psychiatric disorders represent a major global public health challenge, affecting more than one billion people worldwide and ranking among the leading causes of years lived with disability, with annual economic costs exceeding US$1 trillion (World Health Organization, 2025 and Fan *et al.*, 2025). Traditional randomised controlled trials (RCTs), although the gold standard for establishing causality, frequently fail to reflect real-world psychiatric practice. Strict eligibility criteria exclude patients with comorbidities, substance use disorders, or complex psychosocial needs, while high costs, lengthy recruitment, and limited follow-up further restrict generalisability and feasibility (Mulder *et al.*, 2018, Andrade, 2025). In psychiatry, where multimorbidity, long-term outcomes, and rare adverse events are commonplace, these limitations create critical evidence gaps (Li *et al.*, 2016). Registry-based studies address these shortcomings by leveraging routinely collected clinical, administrative, and sociodemographic data for both observational and experimental research (Munk-Jørgensen & Østergaard, 2011). Unlike RCTs, which require prospective protocol-driven collection, registries utilise existing healthcare records electronic health records, hospital contacts, prescriptions, and vital statistics to enable large-scale, population-level analyses with minimal additional burden (Shiely *et al.*, 2024). A registry is defined as a systematic collection of unit-level data covering a complete target population according to precise rules, allowing unique identification and regular updates (Li *et al.*, 2016). In psychiatry, such systems have transformed entire nations into longitudinal cohorts. The Danish Psychiatric Central Research Register (DPCRR), operational electronically since 1969 with outpatient data from 1995, and the Ferrara Psychiatry (FEPSY) database in Italy exemplify this approach, demonstrating high diagnostic validity for severe disorders while highlighting coverage gaps for milder cases managed in primary care (Munk-Jørgensen & Østergaard, 2011, Mors *et al.*, 2011 and Ferrara *et al.*, 2023). This narrative review synthesises the conceptual foundations, methodological approaches, applications, advantages, limitations, and future directions of registry-based studies in psychiatry. Following Sukhera (2022), it adopts a subjectivist-interpretivist stance to integrate diverse evidence and provide critical, forward-looking perspectives for clinical, research, and policy audiences. The review is limited to psychiatric applications, noting linkages to non-mental-health registers only when directly relevant to mental health outcomes, and treats milder primary-care conditions as coverage gaps rather than primary focus.

MATERIALS AND METHODS

This narrative review addresses the research question:

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What are the conceptual foundations, methodological approaches, applications, advantages, challenges, and future directions of registry-based studies in psychiatry, and how do they complement traditional randomised controlled trials in generating real-world evidence. Following Sukhera (2022), a narrative (integrative) review approach was chosen to provide interpretive synthesis, critique, and forward-looking perspectives across heterogeneous literature, consistent with a subjectivist-interpretivist paradigm.

Literature was identified via iterative searches in PubMed, Scopus, and Google Scholar (January 1990–March 2026) using terms such as "registry-based" OR "register-based" OR "rRCT" combined with "psychiatry" OR "mental disorders." Seminal Nordic and non-Nordic papers (e.g., DPCRR, FEPSY) were prioritised, supplemented by citation chaining. English-language peer-reviewed articles, reviews, and methodological papers addressing psychiatric applications or generalisable registry methods were included. Purely non-psychiatric registries (unless linked to mental health outcomes), non-English publications, and purely descriptive abstracts were excluded. Selection was iterative, with emphasis on real-world relevance and equity. Sufficiency was reached when core themes were comprehensively covered by pivotal sources. Authors' expertise in real-world evidence and global mental health shaped the interpretive lens on pragmatic utility, diagnostic gaps, and LMIC scalability. This process aligns with narrative review standards, ensuring transparency while preserving flexibility (Sukhera, 2022).

Foundations and Historical Context

Registry research in psychiatry originated in the Nordic countries, where well-organised public registers have supported pioneering epidemiological studies for decades (Munk-Jørgensen & Østergaard, 2011). The Danish Psychiatric Central Research Register (DPCRR) is the cornerstone, recording every psychiatric contact nationwide since 1938, with outpatient data systematically included from 1995 (Mors *et al.*, 2011). Linked via unique personal identifiers to vital statistics, somatic care, socioeconomic data, and biobanks, the DPCRR has transformed the entire Danish population into a large-scale longitudinal cohort (Shiely *et al.*, 2024). Recent reviews confirm high diagnostic validity for severe mental disorders while highlighting persistent coverage gaps for milder conditions managed in primary care (Mors *et al.*, 2011). This linkage infrastructure enables inter-generational, sibling, and twin analyses with near-complete follow-up and minimal attrition (Shiely *et al.*, 2024).

In non-Nordic contexts, the Ferrara Psychiatry (FEPSY) database in Italy exemplifies scalable replication by applying an Extract-Transform-Load process to routine electronic health records (1991–2021), yielding 3,861,432 records on 46,222 patients (Ferrara *et al.*, 2023). Unsupervised cluster analysis within FEPSY has identified clinically meaningful subgroups, demonstrating that even non-research-oriented records can generate actionable epidemiological insights (Doherty *et al.*, 2023). These foundations illustrate the broader shift from prospectively designed research to secondary use of routinely collected data, aligning with subjectivist-interpretivist paradigms that emphasise contextual realities of mental health care. [10] Consequently, registry-based approaches complement traditional RCTs by addressing long-term outcomes, rare events, and real-world heterogeneity (Li *et al.*, 2016).

Types of Registry-Based Studies in Psychiatry

Registry-based studies in psychiatry are classified primarily by analytical approach rather than prospective design, as data collection is already ongoing and embedded in routine healthcare systems (Mathes & Pieper, 2018). Descriptive studies provide detailed characterisation of incidence, prevalence, treatment pathways, and patient trajectories using large-scale registry data (Munk-Jørgensen & Østergaard, 2011). Cross-sectional analyses examine exposure and outcome variables concurrently within registry records, delivering population-level snapshots of psychiatric morbidity at defined time points (Gliklich *et al.*, 2020). Case-control and nested case-control designs efficiently investigate rare psychiatric outcomes by comparing individuals with and without the outcome for prior exposures recorded in the registry (Andrade, 2022). Cohort studies follow exposed and unexposed groups longitudinally to assess outcomes, often applying target-trial emulation through covariate adjustment to approximate randomised conditions using observational data (Rohde *et al.*, 2024). Before-after and interrupted time-series designs evaluate the impact of policy changes or interventions on mental health metrics over time (Rohde *et al.*, 2024). Registry randomised controlled trials (rRCTs) represent the experimental end of the spectrum, embedding randomisation, recruitment, and follow-up directly within established registries for pragmatic comparative effectiveness research (Li *et al.*, 2016). A recent methodological review of 162 rRCTs documented broad utilisation of registries for patient identification, randomisation, endpoint collection, and long-term monitoring, highlighting their efficiency across diverse clinical settings (Urban *et al.*, 2025). These varied designs leverage the unique strengths of registries to address research questions that are infeasible or unethical in traditional RCTs while preserving methodological rigour (Shiely *et al.*, 2024).

Applications of Registry-Based Studies in Psychiatry

Registry-based studies in psychiatry are widely applied across epidemiology, clinical research, and health systems due to their ability to capture large, real-world populations over time (Prakash *et al.*, 2014). They enable accurate estimation of incidence, prevalence, and temporal trends of mental disorders at a population level, often over decades. Linkage with genetic, environmental, and socioeconomic data allows investigation of etiological

factors and complex risk pathways in psychiatric disorders (Munk-Jørgensen & Østergaard, 2011). Longitudinal registry data facilitate evaluation of clinical outcomes, including disease course, relapse, treatment response, and mortality (Ferrara *et al.*, 2023). They are also crucial for comparative effectiveness and safety studies in real-world populations often excluded from randomized trials (Doherty *et al.*, 2023). Additionally, registries support health services research by assessing healthcare utilization, quality of care, and system-level variations (Prakash *et al.*, 2014). Registry-based designs further enable policy evaluation and surveillance using methods such as interrupted time-series analyses, which are difficult to implement in conventional trials. (Prakash *et al.*, 2014, Doherty *et al.*, 2023) Overall, registry-based studies provide a comprehensive platform for advancing real-world psychiatric research and informing clinical and policy decisions (Sukhera, 2022). These applications are particularly powerful in psychiatry because they capture the dynamic, multimorbid trajectories that RCTs often exclude, thereby addressing the 'evidence-to-practice' gap highlighted by Mulder *et al.* (2018).

Advantages of Registry-Based Studies in Psychiatry

Registry-based studies offer substantial methodological advantages in psychiatric research by capturing large, representative populations that closely reflect real-world clinical practice (Munk-Jørgensen & Østergaard, 2011). Large sample sizes provide high statistical power, enabling robust investigation of rare psychiatric conditions and adverse events that are often infeasible in traditional trials (Shiely *et al.*, 2024). They demonstrate strong external validity through inclusion of heterogeneous patients with comorbidities, improving generalisability to routine care (Doherty *et al.*, 2023). The longitudinal design supports extended follow-up for assessing disease trajectories, treatment outcomes, and delayed effects (Ferrara *et al.*, 2023). These studies are also cost-effective and time-efficient, relying on routinely collected data with minimal recruitment needs (Doherty *et al.*, 2023). Additional strengths include seamless data linkage with genetic, socioeconomic, and other health databases for multidimensional analyses, near-complete follow-up via unique identifiers (Munk-Jørgensen & Østergaard, 2011) and support for pragmatic hybrid designs such as registry-based randomised controlled trials that combine methodological rigour with real-world applicability (Li *et al.*, 2016). Overall, they serve as a powerful complement to traditional research, strengthening real-world evidence in psychiatry (Shiely *et al.*, 2024)

Limitations and Challenges of Registry-Based Studies in Psychiatry

Despite their strengths, registry-based studies in psychiatry carry important methodological and practical limitations that require careful consideration (Doherty *et al.*, 2023). Primary concerns include data quality and completeness, as registries are collected for administrative or clinical rather than research purposes, resulting in missing variables, inconsistent coding, and limited clinical detail (Ferrara *et al.*, 2023). Diagnostic validity varies markedly: severe conditions are generally well recorded, whereas milder or subclinical cases managed in primary care remain underrepresented. (Munk-Jørgensen & Østergaard, 2011). This leads to misclassification and underestimation bias, especially for common disorders such as anxiety and depression (Beerten *et al.*, 2024). The designs are also vulnerable to confounding and lack of randomisation, restricting causal inference despite advanced methods such as propensity scoring or target-trial emulation (Li *et al.*, 2016). Additional limitations include restricted availability of key variables (psychosocial factors, symptom severity, and patient-reported outcomes) (Ferrara *et al.*, 2023), regional variability in registry design and coding that reduces comparability and generalisability, and ethical-legal barriers related to data privacy, consent, and governance (Doherty *et al.*, 2023). Registries further fail to capture treatment adherence, informal care, or community interventions (Doherty *et al.*, 2023). Overall, robust conclusions demand meticulous methodological design, validation, and interpretation (Shiely *et al.*, 2024). Such underrepresentation risks perpetuating inequities for marginalised populations; future registries must therefore prioritise primary-care linkage.

Future Directions and Innovations in Registry-Based Psychiatry

The future of registry-based studies in psychiatry is closely linked to advances in digital health, data science, and global health systems, which are expanding the scope and precision of real-world evidence generation (Ferrara *et al.*, 2023). Key developments include integration of artificial intelligence and machine learning for predictive modelling, phenotyping, and early identification of mental disorders using large-scale registry data (Ferrara *et al.*, 2023). Multi-source data linkage—incorporating genomics, wearable devices, and social determinants of health—will enable more comprehensive and personalised approaches to research and care (Munk-Jørgensen & Østergaard, 2011). Emerging registry-based randomised controlled trials (rRCTs) will strengthen pragmatic comparative-effectiveness and implementation studies, while standardisation of data elements, coding systems, and reporting frameworks such as CONSORT-ROUTINE will improve quality, transparency, and comparability (Shiely *et al.*, 2024). There is growing emphasis on expanding registry infrastructure in low- and middle-income countries (LMICs), where mental health burden is high but systems remain underdeveloped (Prakash *et al.*, 2014). Integration with digital platforms (mobile health and telepsychiatry) will support real-time monitoring, (Ferrara *et al.*, 2023) and ethical innovations in governance, dynamic consent, and privacy-preserving techniques will be essential (Doherty *et al.*, 2023). Overall, the evolution toward learning health systems positions registry-based research as a cornerstone of precision

psychiatry (Munk-Jørgensen & Østergaard, 2011). These advances must be pursued equitably to avoid widening the global mental health data divide.

RESULTS AND DISCUSSION

Registry-based studies have fundamentally reshaped psychiatric research by enabling the integration of large-scale, longitudinal, and real-world data into clinical and epidemiological inquiry (Munk-Jørgensen & Østergaard, 2011). This review highlights how registries bridge critical gaps left by traditional randomized controlled trials, particularly in addressing heterogeneity, long-term outcomes, and rare adverse events in psychiatric populations (Li *et al.*, 2016). The ability to link diverse data sources—including clinical, genetic, and socioeconomic datasets—has expanded the scope of psychiatric research from descriptive epidemiology to complex causal and systems-level analyses (Munk-Jørgensen & Østergaard, 2011). At the same time, the emergence of registry-based randomized controlled trials reflects an important methodological evolution toward pragmatic and implementation-focused research designs (Shiely *et al.*, 2024). However, the findings also underscore persistent challenges, particularly related to data quality, diagnostic validity, and incomplete capture of psychosocial variables, which are central to psychiatric assessment (Ferrara *et al.*, 2023). These limitations highlight the need for careful methodological approaches, including validation studies, advanced statistical techniques, and transparent reporting standards (Doherty *et al.*, 2023). Importantly, disparities in registry infrastructure between high-income countries and low- and middle-income settings remain a significant barrier to global applicability and equity in psychiatric research (Doherty *et al.*, 2023). Future progress will depend on improving data standardization, expanding digital health integration, and strengthening ethical governance frameworks to ensure responsible and inclusive use of registry data (Doherty *et al.*, 2023). Collectively, these findings underscore the evolving role of registry-based methodologies in strengthening evidence generation and informing real-world psychiatric practice (Munk-Jørgensen & Østergaard, 2011). The interrelationship between these domains is summarised in a conceptual framework (Figure 1), illustrating how registry-based studies integrate methodological foundations, applications, strengths, limitations, and future innovations.

The synthesis presented here is shaped by the authors' collective experience in clinical psychiatry and real-world evidence generation, which naturally emphasises pragmatic solutions and equity in data infrastructure. We acknowledge that different author teams or historical contexts might foreground alternative narratives (e.g., greater focus on privacy ethics or AI risks). This reflexivity is inherent to the narrative approach and strengthens, rather than detracts from, the interpretive value.

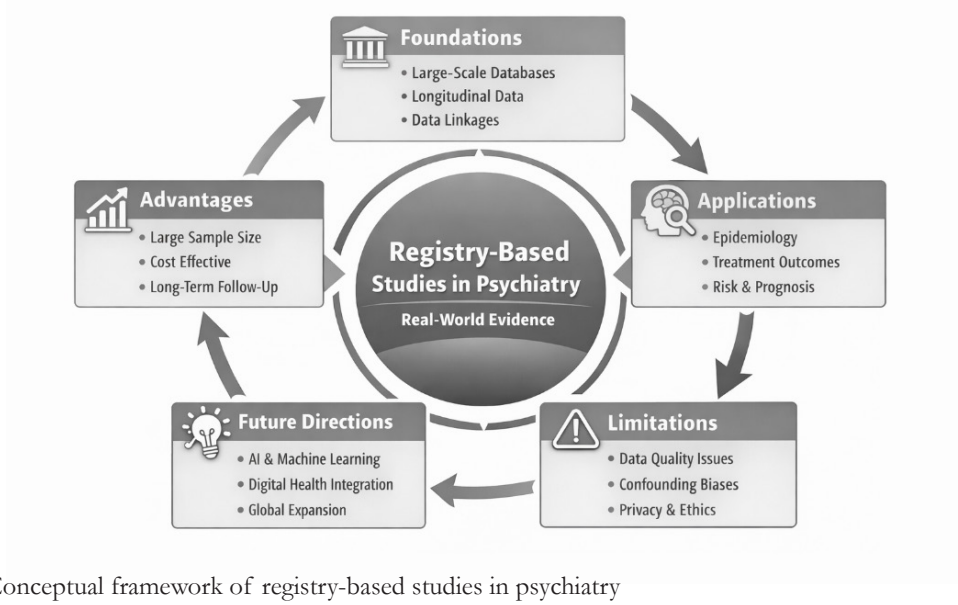

Figure 1: Conceptual framework of registry-based studies in psychiatry

The cyclical model integrates methodological foundations (data sources and linkage), applications (epidemiology, outcomes, risk prediction), advantages (large sample size, real-world validity, longitudinal follow-up), limitations (data quality, confounding, ethical concerns), and future directions (AI, digital health, global expansion). Arrows illustrate the iterative flow from evidence generation to clinical/policy impact and back to infrastructure refinement.

CONCLUSION

Registry-based studies have emerged as a powerful approach in psychiatric research, providing robust real-world evidence across epidemiology, treatment outcomes, and health systems. Their strengths, including large sample sizes, longitudinal follow-up, and real-world applicability, make them an important complement to traditional experimental designs. Despite methodological and ethical challenges, ongoing advances in data science,

digital health, and registry infrastructure are expected to enhance their impact. Strengthening registry ecosystems, particularly in resource-limited settings, will be essential to ensure equitable and comprehensive mental health research. Overall, registry-based approaches play a critical role in bridging the gap between controlled evidence and real-world psychiatric practice.

Strengths and Limitations of This Review

This integrative narrative review delivers a cohesive synthesis of registry-based studies in psychiatry by linking methodological foundations, applications, advantages, limitations, and future directions within a single conceptual framework, while following Narrative review guidelines by Sukhera (2022) standards for rigor and emphasising real-world utility, LMIC equity, and complementarity to RCTs. Limitations include its non-systematic narrative design, which reflects the authors' clinical and research perspectives, predominant reliance on high-income-country literature (making LMIC applicability aspirational), and a synthesis current only to March 2026 that may miss rapid advances in AI and digital health integration.

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