

Understanding the journey of patients with depression in Brazil: A systematic review I released a "Technical Memorandum" to ensure specialized care for patients with mental disorders [6,7]. However, these policies did not translate into the required change in the mental healthcare state in the country, especially at the primary healthcare level [6]. Brazil Mental Health Law 10.216 recognizes the right to mental healthcare for people with mental disorders, but its implementation is not consistent across the country [8]. Moreover, the law is not in sync with the updated technical and scientific recommendations [6]. Another lacuna is that the Brazilian health policy does not recommend any mechanism for the ongoing evaluation of mental health services [6,7]. This could be due to the gaps in the availability of real-world data in Brazil, which is generally expected from the drive(s) for mental healthcare, particularly depression care by the Brazilian Health Ministry [9]. Therefore, the diagnosis and treatment are delayed, and the patients often present at a late stage of the disease, which poses a huge burden on the health system in managing these patients. There is an emergent need to identify these and other challenges associated with the lack of awareness and socio-behavioral issues contributing to the challenges, for example, the stigma associated with mental disorders, which contributes to the gap in depression care. The current prevalent situation of depression care in Brazil inspired the authors to take a dipstick in published data to inform locally effective early interventions at the primary care level. The methodology adopted was based on a novel approach for Mapping the Patient Journey Towards Actionable Beyond Pill Solutions for Non-communicable Diseases (MAPS) to help generate country-specific data related to various stages of the patient journey including awareness, screening, diagnosis, treatment, adherence, and control [10]. The MAPS approach is useful in implementing effective solutions and proposing practical recommendations using local evidence, which are directly applicable to the patients and healthcare systems that will use them. The study aimed to identify the gaps and quantify the data across various stages of patient journey touchpoints, including awareness, screening, diagnosis, treatment, adherence, and control, for depression that can support better patient outcomes in Brazil.

Methods
Study design This study used evidence mapping and a semi-systematic data review approach based on a structured semi-systematic literature search combined with an unstructured search and anecdotal data in the local context. It was followed by validation, synthesis, and quantitative mapping of the data on the prevalence and different patient journey touchpoints in terms of disease awareness, screening, diagnosis, treatment, adherence, and control for depression in Brazil. The definitions of the terms used in the study are provided in Table 1. This current review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, with minor modifications in line with the scope of this study [11].

Table 1. Definitions used in the study for various terms.

Term	Definition
Depression	Depression is defined according to the criteria common to the Diagnostic and Statistical Manual (DSM)-III, DSM-IV and DSM-V: the presence of ≥ 5 symptoms in the last 2 weeks with >1 symptom being either depressed mood or the loss of interest or pleasure. Mild depression is diagnosed when the severity of the symptoms is distressing but manageable, there are few, if any, symptoms beyond those necessary for the diagnosis, and they only slightly impair social or occupational functioning. Whereas in severe depression, the severity of the symptoms is extremely upsetting and uncontrollable, the number of symptoms is far greater than that needed to make the diagnosis, and the

symptoms significantly impair social and occupational functioning [47] Awareness Self-reported knowledge or awareness of depression/depressive disorders Screening Use of assessment questionnaires to screen for depression/depressive symptoms/depressive disorders Diagnosis Diagnosis of depression/ depressive disorder by an HCP Treatment Use of pharmacotherapy or psychotherapy to treat depression/depressive disorders Adherence Self-reported adherence and/or compliance with prescribed pharmacotherapy or psychotherapy Control/Remission Improvement in depressive symptoms during treatment The following 6 steps were used to construct the hypothesis: (1) Developing a comprehensive search strategy, (2) Establishing the inclusion and exclusion criteria, (3) Screening, and (4) Supplementing with additional and/or local data by a local expert, (5) Data extraction, and (6) Data analysis.

Search strategy Structured search The structured search was conducted on 3 electronic databases, including Embase, MEDLINE, and BIOSIS, using Medical Subject Headings (MeSH) terms and keywords for depression combined with search terms related to the prevalence and patient journey touchpoints. The search was designed to include all the studies related to depression in Brazil. The studies published in English, Portuguese, and Spanish language from January 1, 2006, to July 31, 2021 were included, as it provides a balance between the availability and relevance of the data over a decade.

Unstructured search An unstructured search was also conducted in the Incidence and Prevalence Database (IPD), World Health Organization (WHO), Ministry of Health of Brazil, Google, and national clinical practice and treatment guidelines with no restrictions on date limits to avoid missing any relevant study. The following keywords were used: Depression OR Major Depressive Disorder (MDD) OR Depressive disorder OR major depression OR mood disorder OR persistent depressive disorder OR unspecified depressive disorder OR antidepressant AND National OR registry OR survey OR real world OR real-world OR Incidence OR Prevalence OR Epidemiolog* OR Screen* OR Treat* OR Therap* OR Aware* OR Knowledge OR Diagnos* OR Undiagnos* OR underdiagnos* OR Adheren* OR Complian* OR Control* OR uncontrol* Brazil* OR Brasil* OR Latin America*.

Inclusion and exclusion criteria Studies were included in the analysis if they meet the following criteria: (i) Peer-reviewed published systematic review, randomized controlled study, and observational study; (ii) Human data from adult populations aged ≥ 18 years with depression; (iii) Reporting quantitative epidemiologic data for the patient journey touchpoints, including awareness, screening, diagnosis, treatment, adherence, and control; (iv) Depression is defined according to the criteria common to the Diagnostic and Statistical Manual (DSM)–III, DSM–IV, and DSM–V: the presence of ≥ 5 symptoms in the last 2 weeks with >1 symptom being either depressed mood or the loss of interest or pleasure [12–14]. The studies published before January 1, 2006; languages other than English, Portuguese, and Spanish; editorials, letters to the editor, thesis abstracts, case studies, studies with specific patient subgroups, studies not related to depression, duplicate records, studies including specific patient subgroups such as patients with comorbidities and pregnant women, and data not from the representative country were excluded. This comprehensive search strategy was followed to minimize the risk of missing relevant literature and to avoid significant unrelated studies.

Study selection An independent reviewer conducted both structured and unstructured searches by screening the titles, abstracts, and full texts of each study for relevance. A second independent reviewer reviewed the search results based on the study title, article citation, author

names, year of publication, abstract, study design, study participants, and study setting for their inclusion based on the eligibility criteria. In case, the patient journey data were not available from the nationally representative study population, studies with a smaller sample size of 500, population subgroups, and single centers were also included. Any disagreements were reconciled by discussion among both the reviewers and other co-authors. Furthermore, any identified data gaps were supplemented with publications in local languages and anecdotal data from local clinical experts. A survey was conducted by sharing a standard set of questions prepared by the local clinical experts to get the opinion of the key opinion leaders.

Data extraction After the manual screening, relevant data from the included articles were exported to Microsoft Excel for data extraction and were validated by local experts, who are also the authors of this paper, to ensure consistency with the local prevalent conditions and expert opinion. The synthesized evidence was represented as an evidence map. The data extracted from the studies included (1) Title of the article, (2) Article citation, (3) Authors, (4) Year of publication, (5) Abstract, (6) Population characteristics, (7) Sample size, (8) Prevalence of each indication in the subpopulation, and (9) Quantitative categorization of each patient journey touchpoint for depression. To provide a perspective of the local situation, in case an article mentioned a low proportion of the patients completing a particular stage of the journey, the locally prevalent issues mentioned in the article, possibly contributed to the low proportion of a patient journey touchpoint and the suggested interventions were captured by the extraction of the qualitative descriptions.

Quality of studies and data analysis The quality of the studies was ensured by reviewing the reporting items of the studies based on the reporting guidelines for their respective design [12–16]. The data from the included studies with respect to the patient journeys touchpoints such as prevalence, awareness, screening, diagnosis, treatment, adherence, and control of depression were pooled. The weighted averages were calculated for the diagnosis and treatment of depression, and a summary of the outcomes is visually presented in the form of a tabular summary of the outcome results. A simple average was calculated for the anecdotal data for the screening stage. Although the random effects model could also be considered as it appropriately uses the variable parameters; however, in this study, considering one variable, a simple average was used.

Results

Review of retrieved studies Of the 3175 articles retrieved for depression, 3173 were from structured search and 2 were from unstructured search. Of these, 9 articles from structured (research papers [n = 8], web-content [n = 1]) and 1 article from an unstructured search were considered for the final analysis. All the included studies were cross-sectional in design (Fig. 1). Among the included articles, 2 papers used the data from Sao Paulo Megacity Mental Health Survey, 1 study used data from Pesquisa Nacional de Saude or National Health Survey (PNS) 2013, and another study used the data from National Health and Wellness Survey 2011, while 1 study was based on an epidemiologic survey as a part of the Gender, Alcohol, and Culture: An International Study (GENACIS project). Three studies were cross-sectional and based on household interviews. While 4 studies used the "Composite International Diagnostic Interview" tool, 3 used Patient Health Questionnaire (PHQ-9), and 1 used an indigenous questionnaire.

5,037 Prevalence (16.9%) 6 Prado et al. [25] 2012 An epidemiological survey using a stratified probability sample 2,083 Prevalence (21.8%) 7 Fujii et al. [26] 2012 A cross-sectional survey 12,000 Prevalence (10.2%), Awareness (42.4%), Diagnosis (65.9%), Treatment (54.5%) 8

Andrade et al. [27] 2012 A representative sample survey 5,037 Prevalence (9.4%) 9 Moreno et al. [20] 2010 A cross-sectional study 1464 Prevalence (9%) 10 Lopes et al. 2016 National Health Survey (PNS) 60202 Prevalence (7.9%) 11 KOL Opinion (Anecdotal data) NA Screening (25% to 50%) Abbreviations: GHO: Global Health Observatory (The Global Health Observatory is an initiative of the World Health Organization to share data on global health, including statistics by country and information about specific diseases and health measures); KOL: Key Opinion Leader; WHO: World Health Organization. The study aimed to quantitatively map and identify the deficiencies in patient journey touchpoints in terms of awareness, screening, diagnosis, treatment, adherence, and control for depression in Brazil using a semi-systematic approach highlighting the knowledge gaps in the existing literature. 49,025 Prevalence (9.7%), Diagnosis (7.2%) 3 Munhoz et al. [22] 2016 Survey (household-based interviews) conducted with random and cluster-based sampling (performed in three stages: census tracts, households and individuals). Synthesized evidence indicates that the pooled prevalence of depression in Brazil ranged from 4.1% to 21.8%; 42.4% of patients had awareness of depression, 37.5% underwent screening, 18.7% had a diagnosis, and 54.4% received treatment. Keywords: Awareness Brazil Depression Patient journey Full Text Introduction Depression is one of the most common psychological disorders and imposes a significant burden on society and individuals. S No Authors Year Study design Sample size (n) Patient journey data 1 Wang et al. [21] 2017 A cross-sectional multistage representative study (Sao Paulo Mental Health Survey) 540 Treatment (32.80%) 2 Barros et al. [19] 2017 A population-based cross-sectional study (using the database of the National Survey on Health). A structured search of Embase, MEDLINE, and BIOSIS databases was conducted to identify the relevant studies published in English, Portuguese, and Spanish from 2006 to 2021. The study findings highlight the need for more research to accurately estimate the common patient journey touchpoints for depression to achieve better clinical outcomes in Brazil. As revealed by the United States Preventive Services Task Force Evidence Review, 97.7% of ambulatory patients attending primary clinics are not screened for depression at all [3]. Sample selected using a two-stage probabilistic sampling and interviewed in their home 1,820 Treatment (60.4%) 5 Viana et 2012 A cross-sectional al. [24] population-based epidemiological study. Clinics Abstract Despite having an organized mental health law and policy, a majority of patients with depression remain underreported and undertreated in Brazil. IPD, Incidence and Prevalence Database; WHO, World Health Organization, MOH, Ministry of Health. An unstructured search was also conducted on Google or government websites with no restrictions. The estimates also show that >50% of the global population would not self-report depression and around 12% would not seek prescription medication for the treatment [2]. As a result, 89% of patients with depression fail to receive guideline-recommended depression care [4], and 83% of the patients remain undertreated in primary care [5]. Similarly, depression generally remains underreported in Brazil. 60,202 Prevalence (4.1%) 4 Galvao et al. [23] 2014 A cross-sectional population-based study. Pooled estimates The population of Brazil was estimated in 2020 to be 212,559,000 [17]. Of 3175 articles retrieved, 10 articles met the inclusion criteria. PRISMA diagram showing selection of studies for inclusion in the review. Weighted or simple means were calculated for the pooled data. An estimated 264 million people are affected by depression globally [1]. Characteristics of the included articles. To address the data gaps, anecdotal data were also

considered. Brazil has refurbished its mental health law and policy and, recently. No data on adherence and control were available. The study-wise details are presented in Table 2. Fig. 1. Table 2.