

Study Profile

National and Sub-national Prevalence, Trend, and Burden of Mental Disorders and Substance Abuse in Iran: 1990 – 2013, Study Protocol

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Abstract

Background: The measurement of population-based dimensions of mental disorders and their effects on the population health is one of the major public health concerns. There is some evidence on the trend and point estimations of mental disease and substance abuse for many specific groups of Iranian population but there is a progressive requirement to documents on their exposure distribution at sub-national level, information about their trends, and their effects on the population health.

Methods: The present protocol is aimed to provide the standards of data collection and methodology processes for estimating the trends of selected mental disorders and their attributed burden at national and sub-national levels. For nine categories of mental disorders, we will estimate 1990 to 2013 trends of prevalence, Years of Life Lost due to premature mortality (YLLs), and Years Lived with Disability (YLDs) and Disability-Adjusted Life Years DALYs by sex, age group, and province. We will also quantify the uncertainty intervals for the estimates of interest.

Conclusion: The study of National and sub-national prevalence, trend, and burden of mental disorders and substance abuse in Iran provides valuable convincing evidences for policy makers and other stakeholders for more evidence-based priority setting, resource allocation, interventions, service providing, and evaluation at both national and sub-national levels. The results also could be used for future complementary global, regional, national, and sub national studies.

Keywords: Burden, Iran, mental disorders, prevalence, trend

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Introduction

Estimating the burden of disease, injuries and risk factors is one of the most crucial elements for understanding the community health status and evidence-based policy decision making.¹⁻⁵ The measurement of such dimension seems to be more difficult for non-fatal diseases and disorders as like as mental disorders.⁶⁻⁷

However, due to the high worldwide prevalence of such disorders, it is important to evaluate the burden of mental disorders within the community. In a study conducted in 2001, it was found that 21 % of total worldwide disease burden was due to mental

illnesses.⁸⁻⁹

According to the findings of Global Burden of Diseases (GBD) project in 2010, mental disorders and substance abuse were among the leading causes of disease burden in the world; accordingly, 183.9 million DALYs and 7.4 % of all diseases' DALYs were attributable to mental and substance abuse disorders. The mentioned DALYs rate included 8.6 million YLL and 175.3 million YLD.¹⁰

In the study of disease burden in Iran in 2003, following general events and accidents, psychiatric disorders ranked second among all the causes of disease burden.¹¹ Among the top 20 causes of disease burden for men in Iran in 2003, drug abuse, depression disorder, and bipolar disorder ranked third, seventh, and ninth, respectively. While for women, major depressive disorder and bipolar disorder ranked second and ninth, respectively.¹¹ In addition, according to the World Health Organization's report in 2004, mono-polar depression was the third leading cause of the burden of disease.¹²

Although there are considerable studies on estimation of burden of diseases at global, regional, and country levels,^{1-5,13-14} there are little reliable information at sub-national level and no information about the trends and the effects of disease on the population health in Iran.¹¹

The study of National and Sub-national Burden of Diseases, Injuries, and Risk Factors (NASBOD) is the first comprehensive systematic effort to estimate the burden of diseases, Injuries, and

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Risk Factors for Iranian population.¹⁵

The study of burden of mental diseases is a part of NASBOD study which is aimed to estimate the trends and burden of mental diseases and substance abuse disorders at national and sub-national levels from 1990 to 2013.¹⁶ The diseases prevalence, YLLs, YLDs, and DALYs will be estimated by age, sex, and province.¹⁵ The diseases prevalence, YLLs, YLDs, and DALYs will be estimated by age, sex, and province.¹⁵

In this study, the burden of mental disorders will be studied for 9 categories including: mental disorders, depression, bipolar disorder, generalized anxiety disorder, obsessive disorder, PTSD disorder, schizophrenia, and ADHD; the substance abuse disorders include opioids and amphetamines abuse. This paper aims to explain the process of running this study; including definitions, organization, methodology of systematic review of literature for mental disease, data sources, and methods for calculating the burden of disease in Iran.

Methods and Materials

Overview

NASBOD is a comprehensive multidisciplinary study with participation of key stakeholders at national and sub-national levels and with the support of Ministry of Health and Medical Education of Iran.¹⁶

As a one of the sub groups of NASBOD “Mental health group” has benefited from local and international partners and consultants from different fields of psychiatry, public health, epidemiology, clinical psychology, health economics, epidemiology, and social medicine. Similar to other technical teams this specialized branch is responsible for providing the practical definition of related diseases and risk factors, contributing in accessing surveys datasets, conducting the studies, interpreting the results and preparing the reports. Under the supervision of main core team, Tehran Psychiatric Institute and Mental Health Research Center, National Research Center for Addiction and Mental Health, as collaborative partner of technical team with scientific consultant of the specialized sub groups, in each specific filed, would be responsible for providing advice on the selection and definition of diseases, identifying the data sources, contributing in designing and conducting the systematic search, estimation the attributed burden, and reporting and publishing the results. The team focuses on National and sub-national trend and burden of mental disorders and substance abuse in Iran (1990 – 2013).

Diseases Selection process

During the present study as the main reference of diseases selection, we used the list of Global Burden of Disease (GBD) 2010,³ and also the list of mental disorders which has developed in partnership with the National Mental Health Research Network. This list was adjusted with respect to the country's health profile. In order to include diseases in the list, we used the World Health Organization's report, the report on the global burden of mental illness in 2010; the list of high priority mental diseases in Iran (which has been formed based on epidemiologic studies conducted in Iran); and the study of burden of disease in 2003.¹¹

The initial list included 23 diseases which have been modified according to some selection criteria such as; intensity, prevalence, incidence, clinical judgment, and data availability. Finally, due to the high prevalence and availability of related data, some fields

such as anxiety disorder and obsessive-compulsive disorder were selected.¹⁶⁻¹⁷ The final list of selected diseases includes nine mental disorders that are presented in table 1. This table also contains the approved clinical and practical definition of diseases.

Definition of mental illnesses and disorders

The standard diagnostic criteria used in different studies are mainly based on DMS IV and structured clinical interviews or the diagnostic interviews using checklists.¹⁸ From a scientific point of view, the clinical psychiatric interview is also accepted as a diagnostic criterion. In addition, other diagnostic tools or methods, which are acceptably correlated with clinical interviews, can be considered as a diagnostic criterion, when necessary.¹⁹⁻²⁰ Moreover, interviews or reports that are based on the international classification of diseases (ICD-10) are also acceptable.²¹⁻²² The multiplicity and diversity of tools used for evaluation is a significant challenge found in different studies. Additionally, some of the studies use diagnostic tools while other studies utilize the tools which evaluate the severity of disease.²³ For instance, usually the conducted studies used Beck inventory or GHQ to evaluate depression and anxiety disorder and they reported the results based on those tools, while of the mentioned tools are not diagnostic tools and do not have enough validity as a diagnostic tool.²⁴⁻²⁶

Data sources

1) Systematic Literature Review

Based on the scientific panel, we chose Institute of Scientific Information (ISI), PubMed/Medline, and SCOPUS as the main international electronic data sources. IranMedex, Irandoc, and Scientific Information Database (SID) were chosen as comprehensive national electronic data sources.

The systematic review will be conducted according to PRISMA guideline.²⁷ Our search would be restricted to population-based studies related to our objectives, published from 1990 to 2013; however there is no language restriction.

While searching Iranian databases, we will search for all abstracts, conferences articles, theses, and reports published in Persian. The Persian keywords are equivalent to their English counterparts. In addition, to obtain and review the gray literature, which are not available in electronic databases, we will search in reports and booklets published by the Ministry of Health and we will contact the author (s) to obtain the further necessary information. Moreover, we will follow manual searches for reviewing unpublished data sources such as governmental reports, projects' reports, conferences, and reference lists. To access unpublished data, key informants and authors will be contact.

Study selection

The present study will include all national, provincial, district and community based related studies from Jan 1990 to Dec 2013. The inclusion criteria cover all cross-sectional studies, population-based studies, disease registry, hospital-based surveys, and all of the articles which discuss the prevalence and incidence of the diseases.

Our review only covers the studies conducted on the general population, and it excludes those studies which are conducted in clinical centers are patient care centers. In addition, we will exclude studies with response rate of less than 60 percent. Besides, the studies which only included a particular socioeconomic population group or class, a specific and limited age group, or those

Table1. Clinical and Practical Definitions of Selected Mental and Substance abuse disorders

NO	Disease	Clinical definition	Practical definition	ICD-10 Cods
1	Major Depression	A disease with these criteria: Depressed mood, lack of interest and pleasure in daily activities, Significant weight loss or gain, Insomnia or hypersomnia Psychomotor agitation or retardation, Fatigue or loss of energy, Feelings of worthlessness or excessive or inappropriate guilt, Diminished ability to think or concentrate, or indecisiveness, Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide.	Diagnostic interview based on DSM iv tr	F32
2	Bipolar disorder	A serious mental illness in which common emotions become intensely and often unpredictably magnified. Individuals with bipolar disorder can quickly swing from extremes of happiness, energy and clarity to sadness, fatigue and confusion. These shifts can be so devastating that individuals may commit suicide.	Diagnostic interview based on DSM iv tr	F31
3	post-traumatic stress disorder (PTSD)	An anxiety problem that develops in some people after extremely traumatic events, such as combat, crime, an accident or natural disaster. People with PTSD may relive the event via intrusive memories, flashbacks and nightmares; avoid anything that reminds them of the trauma; and have anxious feelings they didn't have before that are so intense their lives are disrupted.	Diagnostic interview based on DSM iv tr	F43.1
4	Generalized Anxiety Disorder (GAD)	Excessive anxiety and worry of events or activities. The person finds it difficult to control the worry. The focus of the anxiety and worry is not confined to features of an Axis I disorder. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. The disturbance is not due to the direct physiological effects of a substance or a general medical condition and does not occur exclusively during a Mood Disorder, a Psychotic Disorder, or a Pervasive Developmental Disorder.	Diagnostic interview based on DSM iv tr	F41.1
5	Obsessive-Compulsive Disorder (OCD)	Obsessions: recurrent and persistent thoughts, impulses, or images that are experienced, at some time during the disturbance, as intrusive and inappropriate and that cause marked anxiety or distress and not simply excessive worries about real-life problems The person attempts to ignore or suppress or neutralize them with some other thought or action. The person recognizes that they are a product of his or her own mind. Compulsions: Repetitive behaviors or mental acts that the person feels driven to perform in response to an obsession, or according to rules that must be applied rigidly. They are aimed at preventing or reducing distress or preventing some dreaded event or situation.	Diagnostic interview based on DSM iv tr	F42
6	Schizophrenia	Two or more symptoms, each present for a significant portion of time during a 1 month period Delusions Hallucinations Disorganized speech Grossly disorganized or catatonic behavior Negative symptoms Social/occupational dysfunction Continuous signs of disturbance persist for at least 6 months	Diagnostic interview based on DSM iv tr	F20 (F20–F29)
7	attention-deficit hyperactivity disorder (ADHD)	A behavioral condition that makes focusing on everyday requests and routines challenging. People with ADHD typically have trouble getting organized, staying focused, making realistic plans and thinking before acting. They may be fidgety, noisy and unable to adapt to changing situations. Children with ADHD can be defiant, socially inept or aggressive. Families considering treatment options should consult a qualified mental health professional for a complete review of their child's behavioral issues and a treatment plan.	Diagnostic interview based on DSM iv tr	F90
8	Amphetamine Dependence/ Abuse	A maladaptive pattern of substance use leading to clinically significant impairment or distress is manifested by one or more of the following, occurring within a 12-month period: • Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home • Recurrent substance use in situations in which it is physically hazardous • Recurrent substance-related legal problems • Continued substance use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance	Diagnostic interview based on DSM iv tr	F15–F15.2
9	Opioids Dependence/ Abuse	substance Abuse: Substance Dependence: A maladaptive pattern of substance use leading to clinically significant impairment or distress is manifested by three or more of the following, occurring at any time in the same 12-month period: • Tolerance, as defined by either of the following: • A need for markedly increased amounts of the substance to achieve intoxication or desired effect • Markedly diminished effect with continued use of the same amount of the substance • Withdrawal, as manifested by either of the following: • The characteristic withdrawal syndrome for the substance • Taking the same (or a closely related) substance to relieve or avoid withdrawal symptoms • Taking the substance often in larger amounts or over a longer period than was intended • Having a persistent desire or unsuccessful efforts to cut down or control substance use	Diagnostic interview based on DSM iv tr	F11

focused on a specific group or people with a special disease will be excluded from our study.

Our review is focused on mental disorders with special diagnostic criteria and it uses individual-based diagnostic tools (interview). Therefore, our study only includes those studies which used a structured or semi-structured interview for the assessment, and the assessment had been conducted either directly by an individual or a tool. The articles were selected for the review using PRISMA flowchart.²⁷ First, we will exclude duplicated articles and then the relevant articles will be selected for the next step. In the next step, two reviewers independently will evaluate all the titles, at the next step all the abstracts, and finally all the full-text articles. The selected full text articles will be then checked by two independent trained reviewers using a papers' quality assessment checklist. In case of disagreement between the two reviewers, a third reviewer will check and settle the case.

The burden of disease, in fact, is the estimation of disease prevalence, disease-related disability and mortality. The common existing information about the prevalence of mental disorders just involves one-year prevalence which is indeed a combination of lifetime prevalence and point prevalence. In this type of the measurement of prevalence, the history of illness in the year before the assessment is registered. The weight of a disability used in this study is based on the survey data collected in global burden of disease (GBD) 2010. In this study, disability weights were determined based on the consensus among experts. In our study, in case of the absence of disability weights related to each mental disease or disorder we will benefit from the "consensus of experts". In the burden of mental diseases study, using available data sources, the mental diseases will be assessed regarding the prevalence, incidence, and DALYs which are made up of two components of YLLs and YLDs.

Data extraction

In this stage, data from eligible full text articles will be extracted and entered into data extraction sheet independently by two researchers. Using standard format of GBD studies, assigned to specific selection criteria, data extraction sheet would be defined and approved by main researchers of every technical team.

In brief, the collected data will be categorized as follows: General information of study (title, citation, scope, publication year, coverage, study design, data source, measures, sample size, sampling method, sample weight, response rate, contact address of corresponding author), demographic information (age, sex), Outcomes (prevalence, incidence, relative risk, standard deviation (SD), confidence interval (CI) or standard error (SE)).

2) National Data Sources

National mental health survey, 1999

In Noorbala et al. study, a total of 35,014 people, aged 15 years and older, were selected via random cluster sampling. The participants filled out the 28-item General Health Questionnaire, as a tool to assess the mental health and screen the psychiatric disorders. In this study, the cutoff point was measured via following up and referring back for a subgroup of 879 patients and conducting a clinical psychiatric interview based on DSM-IV criteria.²⁸

National mental health survey, 2001

Mohammadi, et al. studied a total of 25180 people, who were selected via systematic random cluster sampling from among

people aged 18 years and older living in urban and rural areas of the country. The participants filled out the Affective Disorders and Schizophrenia questionnaire which contains 904 items.²⁹

National mental health survey in 2010 – 2011

The study was aimed to determine the prevalence of psychiatric disorders and the severity of mental disorders among the people aged 15 to 64 years living in the country in a period of 12 months, and also to determine the costs associated with mental disorders and how it is paid. It was a cross sectional study which was conducted on 7886 people aged 15 to 64 years, who were living in Iran; the participants were selected via a three-stage random sampling. The tools used in the interview included demographic and socioeconomic questionnaire, Composite international diagnostic inventory (CIDI), services utilization inventor, Sheehan Disability Scale Questionnaire, MDQ spectrum disorder screening questionnaire, and aggressiveness and suicide inventory. Half of the subjects were randomly assigned to the General Health Questionnaire (GHQ) and the other half to substance abuse and sexual disorders. The alleged psychosis patients, who were diagnosed by the initial screening, underwent structured diagnostic SCID interviews which were conducted by a psychiatrist via telephone. The data were collected between winter 2010 and spring 2011 through home visits, and the interviews were carried out by psychologist interviewers who were mainly working as mental health experts at national health network.³⁰

Epidemiological surveys of drug dependence in the country

From 2001 to 2011, four epidemiological surveys of drug dependence were conducted in Iran in the years 1999, 2003, 2006, and 2011. The first three studies were indeed the quick assessments of drug abuse which were performed by Welfare Organization and the National Drug Control Organization. In the study conducted in 2011, the mental health status of a sample of 7786 people living in the Islamic Republic of Iran was assessed.³¹

Death registry

Due to the importance of mortality information to estimate levels and trends on mortality and because of the low quality of death registry system in Iran, to estimate the plausible level of mortality for children and adult The NASBOD study will benefit from all possible data sources that help estimating prevalence and incidence of diseases, or premature deaths by cause and applying different methods.³²

Hospital data

To measure disability-adjusted life years (DALYs), we require to data about the comprehensive list of disease distribution by sex, age and region as well as deaths and major risk factors. Aim to that we will use the national survey on inpatient data on the representative valid data of all 863 hospitals (all existing hospitals) admissions from 1996 to 2011 (33).

Statistical methods and analysis plans

Despite of our extensive search and attempt to access to all national surveys, the gaps of data are predictable for many provinces or for some provincial representative data. Moreover, all age groups, both sexes, and/or both rural and urban areas of residency have not been included in some surveys.

One of the most important predictable challenges is the missing

data. Especially for sub-national levels data has not been reported for all of our data required data points for all of study years, each age group, both sex and all of provinces. Dealing to that, using advanced statistical methods or proxy covariates, we will try to impute missing data.^{34–35}

In order to estimate measures and their uncertainty interval by sex, age, year, and province, we will benefit from two distinct statistical models including multilevel autoregressive model and, spatio-temporal model. We will use two models to make sure that there is no model dependency in the results.^{34–35}

Bayesian multilevel autoregressive model

To overcome above limitation, This advanced model used when the data nested at more than one level includes districts, provinces, sub-regions, regions, and national levels respectively.³⁴ The hierarchical nature of this model enables us to borrow information from higher levels to the lower levels also units of each level depending to the degree of data availability give information from each other. Different components including linear time trends, nonlinear changes over time, covariate effects, and nonlinearity associated with age, heterogeneity of data sources, and age-by-study variability would be addressed by model.

Spatiotemporal model

One of the models to handle the data scarcity is Spatio-temporal Bayesian hierarchical modeling with conditional autoregressive (CAR) prior for spatial random effects.³⁵ The first assumption in this model is the nearby areas are more linked than farther away. This assumption allows model to improve estimations for the areas with non-completed or missing observations with borrowing information from the neighboring areas. Additionally, to combine incompatible areal units between data sources and/or over the years, spatio-temporal misalignment modeling will performed.

Ethical considerations

The study has been approved by the ethical committee of Tehran University of Medical Science.

All of the included studies will be cited in all reports and all publications. For more required information we will contact with the corresponding authors.

Discussion

The major part of the burden of mental disorders is due to the high prevalence of disorders and the associated disabilities, which extremely affect the quality of life of affected people or even their families. Lack of community-based services for these patients, has doubled the costs of health care services provided for these patients. Moreover, due to the restrictions in service for psychiatric patients and also because of the high prevalence of this type of disorders, the patients have a limited access to these services. The burden of mental disorders worldwide has increased to 37.6 % in a period between 1990 and 2010.^{36–40} These studies are following up again in 2013.⁴⁰

Mental disorders and substance abuse were accounted for 7.4 % of the global burden of disease in 2010.³⁹ The burden of mental disorders and substance abuse was ranked fifth in global DALY in 2010; in other words, it was higher than the burden of traffic accidents, unintentional injuries, diabetes, and HIV/AIDS.⁵ Among mental disorders, the highest level of DALY is associated with

depression and then anxiety disorder. The highest level of YLD is also attributable to the same two diseases.¹⁰ There are many efforts, with different methodological approaches, on sub-national level estimation in other country.^{10,41–51}

In the study conducted in Iran in 2003, based on ICD-10 classification, mental disorders were the second leading cause of DALY among all Iranian population. The highest DALY in this group was related to depression.¹¹ Comparing the burden of mental disorders in 1999 and 2010, major depressive disorder and anxiety disorder were among the five leading causes of YLD. These two diseases were also the major cause of the burden and increase in DALY in 2010.⁴⁰ It is also predicted that by 2030 depression will be the second leading cause of disease burden all over the world.⁵²

Mental disorders are also important because they are sometimes associated with physical illnesses or disorders. For instance, major depression is a risk factor for suicide, and some other diseases like coronary heart disease and stroke. Moreover, when accompanied with certain diseases including CHD, mental disorders increase the risk of death. It has also been observed that sometimes depression emerges following the treatment of some diseases such as tuberculosis and diabetes. Some special types of depression cause exceptional complications, for instance post-partum depression not only disrupts mothers' functions, but also due to improper care of the child, serious illness threaten the children.^{52–54}

The above-mentioned estimates, signifies the need for taking special actions including: policymaking, planning and management of health programs, prioritization, strategic research in the field of mental diseases, development and allocation of human and financial resources and development of organizational capabilities for design, implementation and evaluation of cost-effective interventions.

The conducted studies are mainly regional or even at national levels rather than provincial. Moreover, they were cross-sectional. Thus, there is a progressive need for reproducing a more comprehensive study.^{10,28,55–56}

In comparison with previous national studies, the present study will have several achievements. First; this study analyzes the trend of epidemiologic changes of mental and behavioral disorders at provincial and national levels. We will provide scientific evidences for the prevalence and attributable burden of mental disorders and substance abuse; inequality in their distribution and attributable burden; their trend from 1990 to 2013, and also prediction models for more evidence-based health policy.¹⁵ Aim to that, all available sources of data and advanced quantitative methods will be used in our estimations. As the other distinction, compared with previous studies,^{11,28,39,55} at national and sub-national levels, we will provide more data points led to higher quality of estimation. It is noticeable that, through the participatory process all of stakeholders would be enjoyed from capacity building and also from accessibility to high data sources. More over we developed a disease list which is consistent with the national profile of the diseases.

One of our problems in information sources, which are commonly observed, is to use of a variety of tools, sometimes non-diagnostic. We have no choice but to ignore many of them, cross walking methods or use the statistical modeling to solve such problems.

One of the limitations of present study is the uncertainty of data. This uncertainty arises from the sampling errors, heterogeneity of the different data sources, and differences in provincial registra-

tion systems. Using the developed modeling and statistical methods we will estimate and report the different source of uncertainty.

As another limitation, the misalignment between the sources of covariates and the source of outcomes of interest which is led from nature of these two sources of data would be deal with a number of new statistical models.

Another problems such as diverse categories of causes of death which makes problems in the use of mortality data, poor quality of some data sources, and probable data scarcity, would be addressed through advanced statistical modeling.³⁴⁻³⁵

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Another problems such as diverse categories of causes of death which makes problems in the use of mortality data, poor quality of some data sources, and probable data scarcity, would be addressed through advanced statistical modeling.^{15,32}

In conclusion, present study is the first comprehensive systematic attempt to response the existing important gaps in epidemiology information of main mental disorders in Iran. The achievements will help us to broaden the evidence on the geographic distributions of the selected mental diseases, and identifying mental health disparities across provinces. The results also will light the path of future related research at sub-national, national, regional, and even global levels. The practical finding and outcomes would be disseminated at various scales for all of stakeholders.

The study of national and sub-national prevalence, trend, and burden of mental disorders and substance abuse in Iran provides valuable data on the diseases prevalence, years of life lost due to premature mortality (YLLs), years of life lived with disability (YLD), and Disability Adjusted Life Years (DALY), by age, sex, and province from 1990 to 2013.

It provides convincing evidences for policy makers and other stakeholders for more evidence-based priority setting, recourse allocation, interventions, service providing, and evaluation at both national and sub-national levels.

Abbreviations

BMDs: Burden of Mental Disease Study; **DALY:** Disability-Adjusted Life Years; **GBD:** Global Burden of Disease; **NASBOD:** National and Sub-national Burden of Disease; **YLL:** Years of Life Lost due to premature mortality; **YLD:** Years of Life Lost due to Disability;

Competing interests

The authors declare that they have no competing interests.

Author's contributions

General designing of the paper was by the NASBOD core team. Shirin Djalalinia, had equal contribution as first author. All other co-authors had contribution in the designing of systematic review, primary draft preparation. All authors have given approval of the final version of the manuscript.

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