SYSTEMATIC REVIEW

Biopsychosocial factors associated with depression in the elderly: A systematic literature review [version 1; peer review: awaiting peer review]

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Abstract

Background: One of the most common mental illnesses worldwide and that has significant negative effects on well-being and physical health, is depression. Many factors that affect the occurrence of depression are biopsychosocial. Elderly people have high risk factors for depression. This study aims to review and find a gap in current evidence of biopsychosocial factors affecting depression in the elderly.

Methods: We conducted an advanced search on PubMed database between October and November 2021. We screened the bibliographies of the articles from the database search using a set of inclusion criteria: studies with quantitative design; elderly population sample; exploration of at least one biopsychosocial factor; depression as the outcome or dependent variable; written in English; and published between 2011 and 2021.

Results: We found 54 studies that met the inclusion criteria. Of these, five papers discussed biopsychosocial factors, 18 discussed biological and psychological/social factors, five discussed psychosocial factors, and the rest of the studies discussed one component of biopsychosocial factors. Biological factors influencing elderly depression include being female, having health problems or low health status, older age, genetics, brain structure, and biomarkers, taking certain drugs, and lack of or inability to carry out daily activities. Psychosocial factors include lack of social support, low education level, financial problems, single/unmarried, lack of contact with family/friends, living alone, low self-perceived health, stressful life events, loneliness, and losing hobbies. From the literature search, it was also found that there are biopsychosocial factors that have not been studied and are expected to be able to make references for future research. From this literature review, we found gaps in the availability of evidence about biopsychosocial factors that require further research.

Conclusions: Knowing the biopsychosocial factors that affect them
can help to prevent depression in the elderly.

**Keywords**
elderly, depression, biopsychosocial, systematic review

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Introduction

Many developing countries are experiencing rapid growth in their older populations (Isdijoso et al., 2020). The elderly are predicted to become 25% of the global population, or 74 million people by 2050 (Isdijoso et al., 2020). In Indonesia, citizens 60 years old or older have reached about 25.7 million people (Isdijoso et al., 2020). The older population in the UK is projected to grow, with people aged 65 and over making up 24% of the population by 2043 (17.4 million people) (Lewis, 2021). The proportion of the population aged 75 and over is projected to rise from 8% in 2018 to 13% in 2043, while the proportion aged 85 and over is projected to rise from 2% to 4% (Lewis, 2021). The elderly can have specific physical and mental health issues, including decreased mobility and increased frailty, with some of them losing their independence due to such issues. In the USA, 20% of adults aged 55 and over suffered from a mental health disorder at the beginning of the millennium (World Federation for Mental Health, 2013).

In older people, mental health problems can affect their ability to carry out the basic activities of daily living, reducing their independence, autonomy, and quality of life. A common mental health problem that occurs in older people is depression (Carayanni, Stylianopoulou, Koulierakis, Babatsikou, & Koutis, 2012). Depression is related to distress and suffering and can cause impairment in mental, physical, and social functioning (World Federation for Mental Health, 2013).

Depression is one of the most common mental illnesses worldwide, with serious consequences for one’s well-being and physical health (Thipprakmas, 2021). The elderly may be particularly impacted by depression due to high levels of risk factors including illnesses, social isolation, and lack of emotional support. Depression is considered as a clinical syndrome. Low mood, anhedonia, and decreased energy levels are the three basic symptoms of depression, according to the International Classification of Diseases (ICD) diagnostic classification systems (Pocklington, 2017; Thipprakmas, 2021).

Other clinical findings which were listed include loss of confidence, impaired concentration, disturbances in sleep, suicidal ideation, and changes in appetite. If the above symptoms are present for at least in two weeks, then a diagnosis of depression can be established (Pocklington, 2017).

Major depression presents with all three core symptoms according to ICD criteria, and at least five other symptoms also present (Pocklington, 2017).

Depression consists of two types: early-onset and late-onset depression. In individuals over the age of 65, there is a new diagnosis for depression, namely late-onset depression in which more than half of cases of depression in older adults are newly emerged i.e., the person has never experienced depression. Late-type depression is related to structural changes in the brain, cognitive deficits, and vascular risk factors (Pocklington, 2017).

There are two principal points of view commonly used to explain depression, the bio-medical perspective, and the psychosocial perspective. These perspectives oftentimes conflict with each other. The biomedical perspective asserts that disturbances in the functioning of the brain manifest as psychopathological symptoms, whereas the psychosocial perspective maintains that mental issues are caused by disruptive life experiences (Garcia-Toro & Aguirre, 2007).

Frequently, this twofold viewpoint influences certainly the different affirmations that are made about mental problems, albeit expressly it is progressively perceived that organic and psychosocial angles are generally involved, interfacing in a complex way. Indeed, this is the explanation for why the term “biopsychosocial model” has flourished (Garcia-Toro & Aguirre, 2007).

Depression in older adults is related to cognitive, physical, and social functional impairment (Pocklington, 2017). It is also related to a variety of psychological, biological, and social factors causing it (Alexopoulos & Kelly, 2009; Blazer, 2003). It has a variety of biopsychosocial risk variables that interact to predict the onset of depressive symptoms in a single person. However, it is unclear how much each risk factor contributes to the onset of depressive symptoms. A greater understanding of the individual contributions of biological, psychological, and social risk factors can have a big impact on the adoption of preventive actions to lower the population’s risk of depression (Diniz, 2020). Several studies have investigated several biological, psychological, and social factors associated with depression in the elderly, so this systematic review aims to review and synthesize current evidence of biopsychosocial factors affecting depression in the elderly and can also contribute to future research on factors that affect depression which can eventually contribute to the decrease in the incidence of depression in the elderly.
Objectives
This systematic review aims to examine and find gaps or current evidence regarding biopsychosocial factors that influence depression in the elderly. The review is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. See Reporting guidelines (Hadiwiardjo and Damayanti, 2022c) for the completed checklist.

Methods
We conducted an advanced search on PubMed database using a set of keywords which consisted of population sample keywords (elderly OR geriatric OR late life OR older) combined with independent variable keywords (psychological factors OR social factors OR biological factors OR biopsychosocial), and the outcome (depression). After obtaining these search results, we downloaded the records into our reference manager software Mendeley and removed any duplication. From those search results, we gathered 728 records of studies. The data search on PubMed was conducted in October - November 2021. The last data search was carried out on November 18, 2021.

We applied a two-step screening process that involved two reviewers. Both reviewers worked independently, and any disagreements were resolved through discussion. First, we screened the title and abstract of the bibliography using a set of eligibility criteria. The inclusion criteria were original studies with a quantitative design, that were peer-reviewed, with elderly people (over 60 years) as the population sample, and that explored at least one biopsychosocial factor, with depression as the outcome or dependent variable. Articles also needed to be written in English and published between 2011 and 2021 to be included. Studies published as review articles, qualitative studies, brief reports, letters to the editor or editorial comments, and working papers published in a language other than English were all excluded. In the first stage of screening, we removed studies before 2011 and collected 470 records to be screened. After further screening, 99 studies are eligible for the next screening process.

Further screening of 99 eligible studies was conducted with Population, Intervention, Comparison Outcome and Study (PICOS) criteria where if not appropriate it would be excluded. We retrieved the full text of the potentially relevant studies and conducted a second screening process. The selection process can be seen in the flowchart presented in Figure 1, also available in Extended data (Hadiwiardjo and Damayanti, 2022b). The eligible studies were extracted for the design of the study, country of origin, number of samples, the instrument used to measure depression, and factors associated with depression. That information was extracted from each included study into a standardized spreadsheet and checked by two reviewers. The two reviewers worked independently and if there were any disagreements, these were resolved by discussion between the two reviewers. Any ambiguous material from an included paper was clarified after contacting the respective authors, or else only the available data was analyzed. Microsoft Excel was used to organize the identified papers. The results were described narratively and helped to identify the gaps in the literature that can be filled by future studies.

These studies included quantitative synthesis. After the two-step screening process was conducted, 54 papers were reviewed and extracted. We first described the number of articles based on the country of origin of the article, the type of research design, and the year. Next, we extracted the data based on the research design, the number of samples, the measuring instruments used to measure depression and factors related to depression. After that, the purpose of the content analysis was to identify and assess the primary research streams, reporting in an objective manner on the various domains while also addressing future research prospects and problems.

The 54 papers were then reassessed using the Joanna Briggs Institute (JBI) checklist which is a tool for critical appraisal of a paper. The risk of bias can occur if the quality of the data from the reviewed papers is mostly of low quality. To determine the quality of the data, the JBI critical appraisal tool was used (we accessed this JBI checklist here). This critical appraisal was carried out by two reviewers and if there was a disagreement, it was discussed. From the critical appraisal results it was determined that 53 papers were high quality, and one paper was low quality. The last articles obtained are all used in this systematic review.

Results and discussion
A total of 54 studies met the inclusion criteria after the full-text screening. Previously there were papers that were eventually excluded because there were discrepancies in terms of population and outcome (Pollock & Berge, 2018). The full list of the 54 studies are available in Underlying data (Hadiwiardjo and Damayanti, 2022a). The process using the PRISMA flowchart is shown in Figure 1. The majority of the 54 studies came from the United States, followed by China, as seen in Figure 2.
Twenty-two papers used a cohort study design, two studies used a combination of cohort and a cross-sectional design, and 24 studies used cross-sectional design. We also included experimental and case-control studies. An illustration of the number of types of study designs used in all studies can be seen in Figure 3. Figure 3 shows that most studies use cross-sectional research designs which are then followed by cohort research designs.

The graph of publication shows the number of studies during the last eleven years from 2011 to 2021 as shown in Figure 4. The total number of publications collected from PubMed database are shown in Figure 4. In 2012 there were nine studies related to biopsychosocial factors related to depression in the elderly but from 2013 to 2020 there were less. In 2021 there was an increase in the number of studies related to depression in the elderly. This can be attributed to an increase in the elderly population globally which was also followed by an increase in the incidence of depression, so it was necessary to conduct more research.

An overview of critical appraisal using JBI Checklist shows that there are 53 papers with high quality paper and one paper with low quality as illustrated in Figure 5.

The data extraction of each study can be seen in Table 1. Five papers discussed biopsychosocial factors, 18 papers discussed biological and psychological/social factors, five papers discussed psychosocial factors, and the rest of the studies discussed one component of biopsychosocial factors associated with depression. Now we outline the results for the biological, psychological, and social factors of depression (examples of determinants and consequences are shown below).
Figure 2. Origin of included studies.

Figure 3. Design of included studies.
Biological factors were frequently found to influence geriatric depression. Such factors mentioned included gender (Brinda et al., 2016; Carayanni et al., 2012; Glei, Goldman, Liu, & Weinstein, 2013; Gureje, Oladeji, & Abiona, 2011; Kuroda et al., 2017; Leggett, Zarit, Nguyen, Hoang, & Nguyen, 2012; Misawa & Kondo, 2019; Odlum et al., 2018; Piboon, Subgranon, Hengudomsub, Wongnam, & Louise Callen, 2012; Rzewuska, Mallen, Straus, Belcher, & Peat, 2015), health problems (Arve et al., 2012; Carayanni et al., 2012; Choi, Kim, Marti, & Chen, 2014; Horita et al., 2013; Jovanova et al., 2016; Karczewska & Młynarska, 2021; Leggett et al., 2012; Meesters et al., 2014; Nicolosi et al., 2011; Olsen, Schirmer, Wils gaard, Bonnaa, & Hanssen, 2018; Popescu et al., 2012; Pusswald et al., 2012; Rhee, Jang, Kim, & Chang, 2021; Rzewuska et al., 2015; Sadler, McLaren, & Jenkins, 2013; Sanders, Comijs, Bremmer, Deeg, & Beckman, 2015; Wang et al., 2016; Ylli et al., 2016), older age (Olsen et al., 2018; Rippon & Steptoe, 2018; Rzewuska et al., 2015), genetics (Klinedinst, Resnick, Yerges-Armstrong, & Dorsey, 2015; Stringa et al., 2020), brain anatomical (Laird et al., 2019; Wang et al., 2018), cytokine level (Derry et al., 2021), taking drugs (Bond et al., 2020), low activity (Davison, McCabe, Knight, & Mellor, 2012; Kobylańska et al., 2019; Leggett et al., 2012; Meesters et al., 2014; Piboon et al., 2012; Rzewuska et al., 2015), diet (Ferrand et al., 2018) and BMI (body mass index) status (Horita et al., 2013). One study has found that women showed a significant positive association with geriatric depression (Brinda et al., 2016). Other literature found that the prevalence of depression is higher in women than in men (Piboon et al., 2012; Ylli et al., 2016). In total, ten different kinds of studies have shown that women were more likely to have depression or higher depressive symptoms than men, indicating a relationship between gender and older age depression.

Eighteen studies in this review have found that the presence of depression is associated with health problems including pain, degenerative diseases, multimorbidity, poor respiratory indicators, cardiovascular morbidity, insomnia, and a falling incident. One of the literature obtained a p<0.001, showing the significant relationship between health problems and depression (Nicolosi et al., 2011).
Table 1. Data extracted from eligible studies.

| No. | Author                  | Method       | Country   | Sample size | Instrument                                      | Biological                                    | Psychological                                           | Social                                                        |
|-----|-------------------------|--------------|-----------|-------------|-------------------------------------------------|-----------------------------------------------|----------------------------------------------------------|--------------------------------------------------------------|
| 1   | (Nicolosi et al., 2011) | Cross-sectional | Brazil    | 303         | Geriatric Depression Scale (GDS)                  | Health problems                               | Poor self-perceived health                               | Lower education level                                      |
| 2   | (Gureje et al., 2011)   | Cohort       | Nigeria   | 1408        | Major Depressive Disorder based on DSM-IV Axis I Disorders | Female                                        | -                                                        | Rural residence and poor social network                     |
| 3   | (Piboon et al., 2012)   | Cross-sectional | Thailand | 317         | Thai Geriatric Depression Scale                   | Female, functional ability                     | Stressful life events, loneliness, problem-focused and emotional focused coping strategy | Lack of social support, income                              |
| 4   | (Arve et al., 2012)     | Cohort       | Finland   | 276         | Zung depression scale                            | Negative health status                        | Feeling sick, Loneliness                                | -                                                            |
| 5   | (Leggett et al., 2012)  | Cross-sectional | Vietnam  | 600         | Center for Epidemiologic Studies- Depression Scale | Female, Pain, ADL assistance need             | -                                                        | Low education level, low economic status, and lack of emotional support |
| 6   | (Petkus, Gum, & Wetherell, 2012) | Cross-sectional | US       | 142         | Brief Symptom Inventory-18 (BSI-18), Structured Clinical Interview for DSM-IV Diagnosis (SCID) | -                                           | Thought suppression                                         | -                                                            |
| 7   | (Popescu et al., 2012)  | Cross-sectional | Canada   | 315         | Geriatric Depression Scale Short Form (GDS-15)   | Age-related macular degeneration (AMD), glaucoma, or Fuchs corneal dystrophy | -                                                        | -                                                            |
| 8   | (Carayanni et al., 2012) | Cross-sectional | Greece   | 360         | 15-item geriatric depression scale (GDS)          | Female, multimorbidity                         | -                                                        | Unmarried, not meeting friends, childless, economic problems, not caring for a grandchild, lack of social participation |
| 9   | (Davison et al., 2012)  | Case-Control | Australia | 100         | Major Depressive Disorder based on DSM-IV Axis I Disorders, 15-item version of the Geriatric Depression Scale | Lower physical health and higher disability levels | Purpose in life, and autonomy                           | Time spent in the facility, environmental mastery            |
| No. | Author                  | Method                      | Country   | Sample size | Instrument                                                                 | Biological                              | Psychological                          | Social                                    |
|-----|-------------------------|-----------------------------|-----------|-------------|----------------------------------------------------------------------------|------------------------------------------|----------------------------------------|-------------------------------------------|
| 10  | (Chan et al., 2012)     | Cohort                      | China     | 2630        | 15-item version of the Geriatric Depression Scale                         | Losing hobby, stressful events          | Losing pets, economic problems          |                                            |
| 11  | (Pusswald et al., 2012) | Case-Control                | Vienna    | 110         | Geriatric Depression Scale                                                | Parkinson disease                       | -                                      |                                            |
| 12  | (Glei et al., 2013)     | Cohort                      | Taiwan    | 4049        | Center for Epidemiologic Studies Depression scale (CES-D)                 | Female                                   | -                                      | Live far from family, widow, losing a child |
| 13  | (Sjöberg et al., 2013)  | Cohort                      | Sweden    | 891         | DSM-IV-TR                                                                 | -                                       | Loneliness, losing hobby               | Lack of contact with family, unmarried/widowed, low education level |
| 14  | (Sadler et al., 2013)   | Cross-sectional             | Australia | 171         | Centre for Epidemiologic Studies Depression Scale (CES-D)                 | Insomnia                                 | Dysfunctional beliefs about sleep and hopelessness |                                            |
| 15  | (Horita et al., 2013)   | Cross-sectional             | Japan     | 84          | Geriatric Depression Scale Short Form (GDS-15)                            | Low BMI, dyspnea, exercise capacity, Oxygen level | -                                      |                                            |
| 16  | (Lewin, Jöbges, & Werheid, 2013) | Cross-sectional             | Germany   | 105         | Geriatric Depression Scale Short Form (GDS-15)                            | -                                       | Self-efficacy, history of pre-stroke depression | Lack of social support                  |
| 17  | (Meesters et al., 2014) | Cross-sectional             | Dutch     | 99          | Centre for Epidemiologic Studies Depression Scale (CES-D)                 | Higher functional limitation, more chronic physical disorder | -                                      | Lack of social support                  |
| 18  | (Choi et al., 2014)     | Cross-sectional and Cohort  | United States | 5414       | Patient Health Questionnaire-2 (PHQ-2)                                    | Cardiovascular disease                   | -                                      |                                            |
| 19  | (Wild et al., 2014)     | Cohort                      | Germany   | 3124        | Patient Health Questionnaire (PHQ-8) depression scale                    | -                                       | -                                      | Health care needs                       |
| No. | Author                          | Method               | Country             | Sample size | Instrument                                                                 | Biological                                                                 | Psychological                              | Social                      |
|-----|---------------------------------|----------------------|---------------------|-------------|----------------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------------|-----------------------------|
| 20  | (Nadimpalli, James, Yu, Cothran, & Barnes, 2015) | Cross-sectional and Cohort | United States       | 487         | Centre for Epidemiologic Studies Depression Scale (CESD)                   | -                                                                          | -                          | Discrimination              |
| 21  | (Rzewuska et al., 2015)         | Cohort               | UK                  | 501         | Hospital Anxiety and Depression Scale (HADS)                               | Female, older age, pain, low activity level                                 | -                          | Lack of support, routine work |
| 22  | (Park & Yu, 2015)               | Experimental         | South Korea         | 24          | Beck Depression Inventory (BDI)                                             | Nordic walking (negative)                                                  | -                          | -                          |
| 23  | (Sanders et al., 2015)          | Cohort               | Netherland          | 1528        | Centre for Epidemiologic Studies Depression Scale (CESD)                   | Pain                                                                       | -                          | -                          |
| 24  | (Klinedinst et al., 2015)       | Cross-sectional      | US                  | 114         | Useful Depression Screening Tool (UDST)                                     | Single nucleotide polymorphisms (SNPs) in the NTRK3 gene, pain, physical activity | Fear of falling            | -                          |
| 25  | (Ylli et al., 2016)             | Cross-sectional      | Canada, Albania, Colombia, Brazil | 1995        | Centre for Epidemiologic Studies Depression Scale (CESD)                   | Multiple chronic conditions, and poor physical performance                  | -                          | Low education and insufficient income |
| 26  | (Jovanova et al., 2016)         | Cohort               | Netherland          | 1823        | Centre for Epidemiologic Studies Depression Scale (CESD)                   | Recognized myocardial infarction (RMI)                                     | -                          | -                          |
| 27  | (Wang et al., 2016)             | Cohort               | China               | 608         | Post stroke depression based on ICD-10 criteria                            | Insomnia, neurological deficit, low Barthel Index                           | -                          | -                          |
| 28  | (Manaf et al., 2016)            | Cross Sectional      | Malaysia            | 230         | Depression, Anxiety, and Stress Scale (DASS-21)                            | Poor health status                                                         | -                          | Single, living with family   |
| 29  | (Kato, Zweig, Schechter, Barzilai, & Atzmon, 2016) | Cross Sectional | US                  | 357         | Geriatric Depression Scale Short Form (GDS-15)                             | Attitudes toward life, self-rated health                                   | High level of care            | -                          |
| No. | Author                  | Method                  | Country                        | Sample size | Instrument                                                                 | Biological                       | Psychological                                                                 | Social                                                                                     |
|-----|-------------------------|-------------------------|--------------------------------|-------------|----------------------------------------------------------------------------|-----------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| 30  | (Brinda et al., 2016)   | Cross-sectional         | China, Ghana, India, Mexico, South Africa, Russia | 34159       | International Classification of Diseases-10th revision Diagnostic Criteria for Research (ICD-10 DCR) | Female, angina, stroke           | Bereavement                                                                   | Illiteracy, poverty, indebtedness, past informal-sector occupation, pension support and health insurance |
| 31  | (Kuroda et al., 2017)   | Cohort                  | Japan                          | 438         | Basic Checklist                                                            | Female, gender, age, diabetes, cognitive disorder | -                                                                              | -                                                                                           |
| 32  | (Matthieu, Lawrence, & Robertson-Blackmore, 2017) | Cohort                  | US                             | 346         | Patient Health Questionnaire-2 (PHQ-2)                                      | -                                 | -                                                                              | Social activities                                                                    |
| 33  | (Ferrand et al., 2018)  | Cross Sectional         | French                         | 402         | 30-items Geriatric Depression Scale                                        | High fish-fruit-vegetable compared to ready meals | -                                                                              | -                                                                                           |
| 34  | (Rippon & Steptoe, 2018) | Cohort                  | England                        | 9886        | Centre for Epidemiologic Studies Depression Scale (CESD)                   | Older age                        | -                                                                              | -                                                                                           |
| 35  | (Olsen et al., 2018)    | Cohort                  | Norway                         | 7068        | Hospital Anxiety and Depression Scale (HADS)                               | Age, cardiovascular morbidity    | -                                                                              | Low education level                                              |
| 36  | (Odum et al., 2018)     | Cross Sectional         | US                             | 3377        | Centre for Epidemiologic Studies Depression Scale (CESD)                   | Female, incontinence             | -                                                                              | Demanding spouse, lack of time with spouse                                          |
| 37  | (Wang et al., 2018)     | Cross Sectional         | China                          | 47          | Depression based on ICD-10 criteria                                         | White matter hyperintensity     | -                                                                              | Religious beliefs, family harmony                                                       |
| 38  | (Kobylanska et al., 2018) | Quasi-experimental     | Poland                         | 120         | 30-items Geriatric Depression Scale                                        | Mobility and independence       | -                                                                              | Education level                                                             |
| 39  | (Akila et al., 2019)    | Cross Sectional         | India                          | 510         | Geriatric Depression Scale Short Form (GDS-15)                              | Perceived mental health          | -                                                                              | Rural area, illiteracy, social support, financial problems                         |
| No. | Author | Method | Country   | Sample size | Instrument                                      | Biological                                                                 | Psychologicalclasification | Socialclassification |
|-----|--------|--------|-----------|-------------|------------------------------------------------|-----------------------------------------------------------------------------|----------------------------|----------------------|
| 40  | (Sakurai et al., 2019) | Cohort | Japan     | 400         | Zung Self-Rating Depression Scale               | -                                                                          | -                        | Living alone, social support |
| 41  | (Laird et al., 2019)   | Cross Sectional | US    | 113         | Montgomery-Åsberg Depression Rating Scale (MADRS) | Lower Grey Matter Volume (GMV) bilaterally in the insula, lower Total Intracranial Volume (TIV) | -                        | -                     |
| 42  | (Misawa & Kondo, 2019) | Cohort | Japan     | 3464        | Geriatric Depression Scale Short Form (GDS-15)   | Female                                                                     | Life events, sense of coherence, hobby, self-rated health | Meeting with friends |
| 43  | (Bui, 2020)            | Cohort | US        | 2200        | Centre for Epidemiologic Studies Depression Scale (CESD) | -                                                                          | -                        | Social support, density |
| 44  | (Stringa et al., 2020) | Cohort | Netherland | 2276        | Centre for Epidemiologic Studies Depression Scale (CESD) | Higher PRS-D (genetic)                                                    | -                        | Single, network         |
| 45  | (Bond et al., 2020)    | Cohort | Ireland   | 291         | Glasgow Depression Scale for people with a Learning Disability (GDS-LD) | Mood stabilisers, anxiolytic medications, hypnotic/sedative medications | Had trouble sleeping, difficulties in carrying out ADLs, difficulties in keeping up enthusiasm to get things done, feeling lonely, aggression | -                     |
| 46  | (Hong et al., 2021)    | Cohort | US        | 12998       | Health and Retirement Study (HRS) Psychosocial and Lifestyle Questionnaire | -                                                                          | Sense of control            | -                     |
| 47  | (Woods et al., 2021)   | Experimental | US | 189         | Hamilton Depression Rating Scale (HAM-D)           | -                                                                          | -                        | Unmarried, lack of social support, interpersonal problems |
| 48  | (Rhee et al., 2021)    | Cross Sectional | South Korea | 8522        | Geriatric Depression Scale Short Form (GDS-15) | Incident of fall                                                              | -                        | Unmarried, living alone, lack of network |
| No. | Author | Method | Country | Sample size | Instrument | Biological | Psychological | Social |
|-----|---------|--------|---------|-------------|------------|-------------|---------------|--------|
| 49  | (Cordes, Zwingmann, Rudisch, Voelcker-Rehage, & Wollesen, 2021) | Experimental | Germany | 52 | Centre for Epidemiologic Studies Depression Scale (CESD) | Exercise | - | - |
| 50  | (Chen et al., 2021) | Cross sectional Cohort | China | 1764 | Geriatric Depression Scale Short Form (GDS-15) | - | - | Social frailty |
| 51  | (Koo et al., 2021) | Cohort | South Korea | 3011 | Centre for Epidemiologic Studies Depression Scale (CESD) | - | - | Live alone and the periods of living alone |
| 52  | (Derry et al., 2021) | Cross sectional | US | 161 | Centre for Epidemiologic Studies Depression Scale (CESD) | Higher composite cytokine levels | - | - |
| 53  | (Paralikas et al., 2021) | Cross sectional | Greece | 230 | General Health Questionnaire 28 (GHQ-28) | - | - | Unmarried, single, divorced, widowed |
| 54  | (Karczewska & Mlynarska, 2021) | Cohort | Poland | 158 | Hospital Anxiety and Depression Scale (HADS) | ICD discharged | - | - |
There were three studies in this review that have found that older age is associated with depression (Olsen et al., 2018; Rippon & Steptoe, 2018; Rzewuska et al., 2015). One of the literature showed that age of ≥70 year associated with depression disorder (Rzewuska et al., 2015). Another study showed with increase in the subject age, greater depressive symptoms were present (Rippon & Steptoe, 2018). Other factors mentioned concerning older age depression were genetic, brain anatomical, and cytokine levels (Derry et al., 2021; Klinedinst et al., 2015; Laird et al., 2019; Stringa et al., 2020; Wang et al., 2018).

One study, namely research conducted by Bond, revealed that taking drugs such as mood stabilizers, anxiolytics, and hypnotic or sedatives were associated with depression (Bond et al., 2020). They obtained a p=0.001 for mood stabilizers, p<0.001 for anxiolytic, and p=0.009 for hypnotic or sedatives, suggesting a significant relationship for this drug-taking factor.

Low activity or low activity tolerance and disability were also found to have a positive relationship with older age depression (Davison et al., 2012; Kobylańska et al., 2018; Leggett et al., 2012; Meesters et al., 2014; Piboon et al., 2012; Rzewuska et al., 2015). Lastly, diet and BMI status were explored as possible biological factors (Ferrand et al., 2018; Horita et al., 2013).

From one study, it was found that female gender was significantly associated with depression where p<0.001 was found (Piboon et al., 2012). Gender differences in depression can potentially be explained genetically, where genetic studies have found that female twins with a history of depression in the family were more likely to develop depression, and according to the psychological perspective, men and women have different personality features, which could explain the gender variations in depression. A study showed that females are more nurturing, non-aggressive, modest, and reliant than males, and they are more likely to have a relationship-oriented disposition (Piboon et al., 2012).

Individuals who had a chronic disease or health problems, particularly related to the musculoskeletal system such as arthritis and osteoporosis, are likely to have a weakened sense of self-efficacy, which can cause functional impairment and their presence has been associated with depression (Nicolosi et al., 2011). Health problems like pain were a predictive of depressive symptoms (Leggett et al., 2012). Some other studies showed that once pain and depression occurred, they will remain associated (Sanders et al., 2015). People with comorbidities are more likely to suffer from depression, indicating that it is another risk factor (Carayanni et al., 2012).

Psychological factors
The results of this research showed that seventeen studies discussed psychological factors that influence the occurrence of depression in the elderly. These factors were low self-perceived health, stressful life events, loneliness, and losing hobby/interest/purpose in life.

According to research conducted by Nicolosi et al. (2011), poorer self-perceived health leads to more depressive symptoms (Nicolosi et al., 2011).

One of three studies on stress in life, namely the study conducted by Chan (2012), found that there is a relationship between the number of stressful events in life and the incidence of depression (p=0.0020), with the number of stressful events associated with an increased risk of having depression (Chan et al., 2012). In both men and women, life events predicted the odds of depression among older people (Misawa & Kondo, 2019).

According to research conducted by Bond et al. (2020), there is a significant relationship between loneliness and the occurrence of depression, where p<0.05 (Bond et al., 2020). Piboon (2012) found that loneliness had a significantly positive impact on depression, with an obtained p<0.001. Chan et al. also found that loss of hobbies is related to an increased incidence of depression (Chan et al., 2012).

Loneliness had a significantly positive relationship and was a predictor of depression among older adults because they are more likely to experience losses and changes in later life, so those that may feel lonely are more likely to suffer from depression than younger adults who do not feel lonely (Piboon et al., 2012).

Social factors
In this literature study, there were 20 studies that discussed social factors that affect the occurrence of depression in the elderly. The social factors were social/emotional support, education level, financial problem, marital status, lack of contact with family/friends, living alone, dependency, environmental and religious beliefs. According to three from 12 that examined social support, social support was associated with depression. Research conducted by Bui (2020) found
that there was a reciprocal relationship between social support and depressive symptoms, with p<0.001 (Bui, 2020). Meanwhile, research by Piboon (2012) found that there was a positive relationship between social support and depression (Piboon et al., 2012). Chen et al. found in their research that social frailty may be a predictor of depression among community-dwelling older adults (Chen et al., 2021).

This study found seven papers that discussed the relationship between education levels and the incidence of depression. In research conducted by Brinda (2016), it was found that low education correlated with geriatric depression (Brinda et al., 2016). Other studies have also found that less educated people have higher depressive symptoms (Akila, Arvind, & Isaac, 2019; Kobylańska et al., 2018; Leggett et al., 2012; Nicolosi et al., 2011; Olsen et al., 2018; Sjöberg et al., 2013).

Education was the key indicator of social risk for depression. Individuals with lower education tend to feel more uncertain about the future and on a higher poverty level which makes greater prevalence of depression (Nicolosi et al., 2011). Individuals with lower education and income may have less access to health services, putting them at higher risk of getting depressive symptoms (Nicolosi et al., 2011).

Financial problems or poverty were also found to be factors that influence the incidence of depression. In this study we found seven papers that discusses financial problems or poverty as factors that influence the occurrence of depression. Brinda (2016) showed that poverty had a positive association with depression in the elderly (Brinda et al., 2016). Other literature studies have suggested that a significant lack of income is associated with the prevalence of depression (Ylli et al., 2016), furthermore showing that income has a negative effect on depression (Piboon et al., 2012). Income also had an indirect effect on depression in older adults. Some studies reported that elderly people living alone are single, divorced or lost a partner where they then unknowingly suffer from financial burdens and look at their health status negatively (Koo, Son, & Yoo, 2021). It is also reported that elderly people who are reluctant to live alone are prone to depression (Koo et al., 2021).

Eight literature studies discussed the relationship between marital status and (Koo et al., 2021) depression. According to Manaf (2016), marital status was a factor that was significantly associated with depression where they obtained a p=0.001. Single elderly people experienced depression three times more often compared to elderly who are married (Manaf, Mustafa, Rahman, Yusof, & Aziz, 2016). Other literature showed that single/divorced/widowed people had more depressive symptoms than those who are married (Paralikas et al., 2021; Sjöberg et al., 2013).

In this study, we found that people with poor social networks, especially those lacking contact with friends, had an elevated risk of an incident of depression (Gureje et al., 2011). The frequency of meetings with friends predicted reduced odds of depression in older men (Misawa & Kondo, 2019).

It was also found that living alone is a risk factor associated with depression, where p<0.001 was obtained (Carayanni et al., 2012). Additionally, Living with an unmarried son was linked to a higher risk of depression than living with a married son and daughter-in-law (Glei et al., 2013). A study conducted by Koo (2021) also stated that those living alone are at higher risk of suffering from depression compared to those living with others (Koo et al., 2021). Lastly we found one study that stated that religious beliefs were associated with depression (Wang et al., 2018).

The risk of bias in this systematic review is that depression is assessed as all depression that occurs in the elderly, whether they have a chronic disease and not. In this literature review, based on the JBI checklist, high-quality papers were obtained.

**Limitations**

The limitation of the results of this systematic literature review is that most papers do not clearly identify the confounding factor. Papers included in this review are varied, so they do not allow for quantitative synthesis. Therefore, we discuss the results narratively in order to provide the big picture of the topic.

**Conclusions**

The results confirmed that biopsychosocial factors were correlated with depression within a population of older individuals. Depression is a clinical condition that requires a holistic approach with biopsychosocial factors. From the results of this literature search, it was also found that there are biopsychosocial factors that have not been studied and are expected to be able to make references for future research. As for the variables that have not been discussed before such as in biological factors are the weakening that occurs in the elderly and psychological factors are a history of previous mental status and coping style. Understanding the biopsychosocial factors influencing them is paramount in developing the management programs to tackle depression in the elderly.
Data availability

Underlying data
Figsshare: Data Extraction_Depression in Elderly from 54 research papers.csv. https://doi.org/10.6084/m9.figshare.19661373.v1 (Hadiwiardjo and Damayanti, 2022a).

This project contains the following underlying data:

- Data Extraction_Depression in Elderly from 54 research papers.csv.

Extended data
Figsshare: Prisma flowchart depression in Elderly. https://doi.org/10.6084/m9.figshare.19991789.v1 (Hadiwiardjo and Damayanti, 2022b).

This project contains the following extended data:

- Prisma search figure_Depression in Elderly.jpg (PRISMA flowchart).

Reporting guidelines
Figsshare: PRISMA checklist for 'Biopsychosocial factors associated with depression in the elderly: A systematic literature review'. https://doi.org/10.6084/m9.figshare.20152346.v1 (Hadiwiardjo and Damayanti, 2022c).

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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