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Masters Program in Public Health, Universitas Sebelas Maret

Meta-Analysis

Meta-Analysis the Effects of Social Isolation and Loneliness on Cardiovascular Disease and Death in Elderly

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ABSTRACT

Background: The impact of social isolation and loneliness on health and well-being is recognized globally as a public health problem. Social isolation can be experienced at any age, especially the elderly. This study aims to analyze and estimate the influence of social isolation and loneliness on cardiovascular disease and death in the elderly.
Subjects and Method: The meta-analysis was carried out according to the PRISMA flow chart and the PICO model. P: Elderly, I: Social isolation and loneliness, C: Not social isolation and not lonely, O: Cardiovascular disease and death. Search for articles in this study through databases that include PubMed, Google Scholar, Science Direct and Scopus with keywords "social isolation" AND "loneliness" AND "cardiovascular disease" AND "elderly". "Social isolation" AND "loneliness" AND "mortality" AND "elderly". Full paper article with cohort design, adjusted Hazard Ratio for effect size, research outcome are cardiovascular disease and death. Analysis was performed using Revman 5.3.
Results: There were 18 articles with cohort designs originating from America, Finland, Canada, Taiwan, Australia, the United States, Japan, Denmark, Amsterdam, England, Sweden, Jerusalem, Europe with a total of 1,375,816 research samples. A meta-analysis of 13 cohort studies concluded that seniors who were socially isolated had a 1.23 times the risk of developing cardiovascular disease compared to those who were not socially isolated, and the effect was statistically significant (aHR= 1.23; 95% CI= 1.10 to 1.38; p= 0.003). In addition, the elderly who are socially isolated have a risk of dying 1.16 times compared to those who are not socially isolated, and this effect is statistically significant (aHR= 1.16; 95% CI= 1.07 to 1.21; p= 0.003). A meta-analysis of 13 cohort studies concluded that lonely elderly people had a 1.10 times greater risk of developing cardiovascular disease compared to lonely people, and the effect was statistically significant (aHR= 1.10; 95% CI= 1.01 to 1.20; p= 0.003). In addition, lonely elderly people have a risk of dying 1.19 times compared to being lonely, and the effect is statistically significant (aHR= 1.19; 95% CI= 1.02 to 1.39; p= 0.002).
Conclusion: Social isolation and loneliness increase the risk of cardiovascular disease and death in elderly.

Keywords: social isolation, loneliness, cardiovascular, death, elderly.

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BACKGROUND

With the development of medical technology and the improvement of healthy lifestyles, the average human life span is increasing; therefore, the number of elderly people is also increasing (Lee et al., 2018). Elderly is the final stage of development in the human life cycle. The age limit according to Law

Number 13 of 1998, is someone who has reached the age of 60 years and over. Elderly people can be categorized based on their ability to earn a living which is divided into two types, namely potential elderly if they are able to do work or activities that can produce goods or services, and non-potential elderly if they are powerless to make a living so their lives depend on the help of others. (Kemenkes RI, 2019).

Globally the elderly population continues to increase, currently the population in 11 member countries of the World Health Organization (WHO), in the Southeast Asian region who are over 60 years old and over, is 142 million. Today in the largest ASEAN countries are Singapore 9%, Thailand 7%. In Indonesia, it is predicted to increase higher than the elderly population in the Asian region and globally after 2050. The results of the 2010 population census stated that Indonesia is currently one of the top 5 countries with the most elderly population in the world.

The elderly population in Indonesia has increased significantly over the last 30 years with a population of 5.30 million (about 4.48%) in 1970, and increased to 18.10 million in 2010, in 2014 the elderly population amounted to 20.7 million (approx. 8.2%) and it is predicted that the number of elderly people will increase to 27 million (9.9%) in 2020.

Indonesia will become a country with a very high acceleration of aging in the period 1990-2020, as well as an increase in life expectancy from 66.7 years to 70.5 years. Thus Indonesia will enter an aging population marked by the percentage of elderly reaching 10% by 2020 (Kemenkes RI, 2019).

The impact of social isolation and loneliness on health and well-being is recognized globally as a public health problem. Social isolation can be experienced at any age, although some circumstances relate more specifically to older age (Gilmour and Ramage-Morin, 2020).

Global estimates of the proportion of older people in society experiencing lonelyness and social isolation for different regions and countries. As many as 20-34% of the elderly in 25 European countries and 25-29% in the US reported experiencing loneliness. A 2021 study shows the prevalence of loneliness ranges from 25-32% in Latin America, 18% in India and 3.8% in China. Another estimate of the prevalence of loneliness among the elderly is 29.6% in China and 44% in India, this figure is higher than in the rest of the world. Some comparable estimates of the prevalence of social isolation are 24% in the US, 10%–43% in North America, and 20% in India (WHO, 2021).

According to research conducted by Holt-Lundstad for 7 years analyzing 70 studies with 3,407,134 participants, Holt-Lundstad places social isolation at number two out of three loneliness problems regardless of any motive. In the first place is occupied by loneliness, then social isolation and the last is living alone, with a mortality rate of 32% of participants who experience lonelyness, 29% of participants who experience social isolation, and 26% of participants who live alone (Campagne, 2019).

Social relations are central to human well-being and are critically involved in the maintenance of health. Social isolation is an objective and measurable reflection of reduced size of social networks and lack of social contact. Individuals who are socially isolated are at increased risk for developing cardiovascular disease, communicable disease, cognitive impairment, and death. Social isolation has also been associated with increased blood pressure, reactive protein, and fibrinogen and with increased inflammatory and metabolic responses to stress (Steptoe et al., 2013).

Loneliness is often seen as a psychological manifestation of social isolation, reflecting the dissatisfaction individuals experience with the frequency and closeness of their social contacts or the discrepancy between the relationships they have and the relationships they wish to have. Loneliness itself has been associated with an increased risk of cardiovascular disease and death. blood pressure and cortisol, increased inflammatory response to stress, and modification of transcriptional pathways related to glucocorticoids and inflammatory processes (Steptoe et al., 2013).

This study aims to analyze previous primary studies and assess the effect of social isolation and loneliness on cardiovascular disease and death in the elderly.

SUBJECTS AND METHOD

1. Study Design

Meta-analysis was performed using the PRISMA flowchart using PubMed, Google Scholar, Science Direct and Scopus databases. With keywords including: "social isolation" AND "loneliness" AND "cardiovascular disease" AND "elderly". “Social Isolation” AND “loneliness” AND “mortality” AND “elderly”.

2. Steps of Meta-Analysis

Meta-analysis is carried out through 5 steps as follows:

1) Formulate research questions using the PICO model (PICO as follows Population= population aged ≥18 years. Intervention= Vaccination. Comparison= Not vaccinated. Outcome= COVID-19 infection).
2) Search primary study research articles from electronic databases and libraries, such as PubMed, Science Direct, and Google Scholar.
3) Conduct screening and quality assessment of primary research articles.
4) Extracting and analyzing data into the RevMan 5.3 application.
5) Interpret results and draw conclusions.

3. Inclusion Criteria

Full paper article with cohort design study, research subject is elderly, effect size used is adjusted Hazard Ratio, research outcome is cardiovascular disease and death.

4. Exclusion Criteria

Statistical results are reported in the form of bivariate analysis, articles published in languages other than English.

5. Operational Definition of Variables

Articles in this study are adapted to PICO. There was a PICO in this study, the population was elderly, with social isolation and loneliness interventions, and cardiovascular disease and death as outcomes.

Social isolation is a condition where a person experiences a decrease or even disappearance of the ability to interact with people around him.

Loneliness is a negative feeling associated with a lack of social relationships.

Cardiovascular is a disease caused by impaired function of heart and blood vessels.

Death is a process of activity in an individual's biological body which is characterized by loss of brain function, cessation of heart rate, cessation of blood pressure and cessation of the breathing process.

6. Study Instruments

Quality assessment in this study used a critical assessment checklist from the Cohort Study Checklist published by CASP.

7. Data Analysis

The articles in this study were collected according to the PRISMA flowchart and analyzed using the Review Manager 5.3 application. The analysis was carried out by calculating the effect size and heterogeneity consistency value (I^2) of the selected research results. The results of data analysis are in forest plots and funnel plots.

RESULTS

The process of searching for articles is done through several journal databases which include PubMed, Google Scholar, Science Direct and Scopus. The process of reviewing related articles can be seen in the PRISMA flow diagram in Figure 1. Research related to the effect of social isolation and loneliness on cardiovascular disease and death in the elderly consists of 18 articles. The initial search process yielded 2,291 results, after the deletion process of published articles, 1,411 articles were obtained. with 161 of them meeting the requirements for further full text review, 18 articles that met the quality assessment were included in the quantitative synthesis using meta-analysis.

It can be seen in Figure 2. that research articles originating from the European continent include (Denmark, Finland, Amsterdam, Sweden, England), the Americas include (United States, Canada), Asia including (Japan, Tokyo, Taiwan), and 1 article is from the continent of Australia.

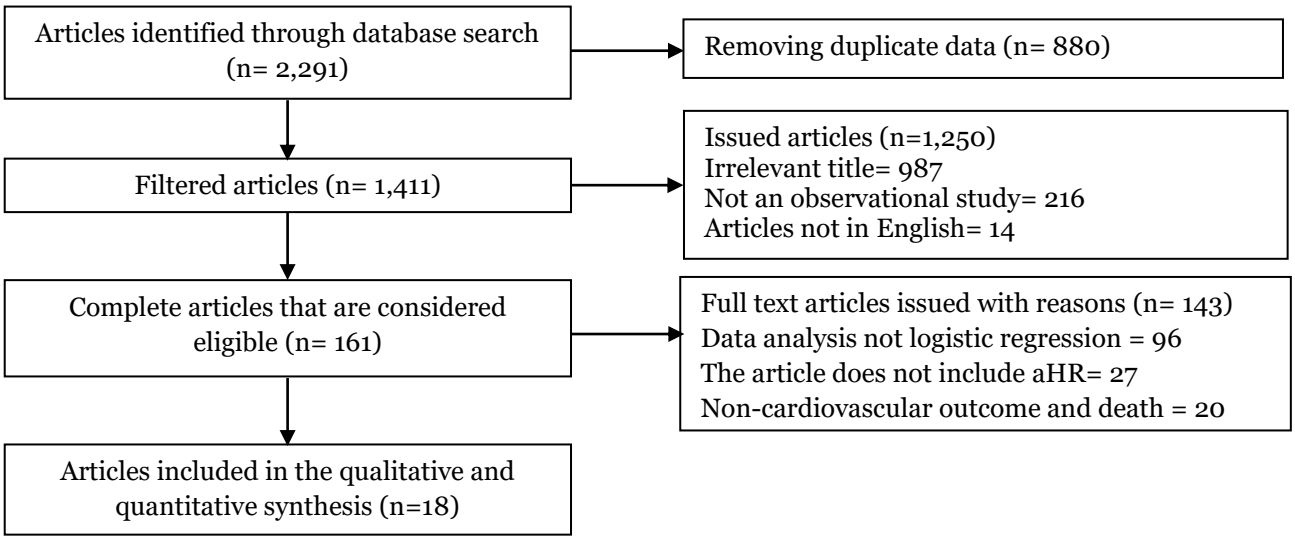

Figure 1. PRISMA diagram of the flow of social isolation and loneliness on cardiovascular disease and death

Figure 2. Map of the research area on the effect of social isolation and loneliness on cardiovascular disease and death

Table 1. Results of the quality assessment of the cohort study on the effect of social isolation on cardiovascular disease and death

Author (Year)	Criteria of Questions												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Luo et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Elovainio et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24
Gilmour et al. (2020)	2	2	2	2	1	2	2	2	2	2	2	2	23
Yu et al. (2019)	2	2	2	2	1	2	2	2	2	2	2	2	23
Hakulinen et al. (2018)	2	2	1	2	1	2	2	2	2	2	2	2	22
Poli et al. (2021)	2	2	2	2	1	2	2	2	2	2	2	2	23
Cene et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Sakurai et al. (2018)	2	2	2	2	1	2	2	2	2	2	2	2	23
Naito et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Tilvis et al. (2012)	2	2	2	2	1	2	2	2	2	2	2	2	23
Kotozaki et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Golaszewski et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Hoogendijk et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24

Description of the answer score:

0 = No
1 = Hesitant
2 = Yes

Table 2. Results of the quality assessment of the cohort study on the effect of loneliness on cardiovascular disease and death

Author (Year)	Criteria of Questions												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Elovainio et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24
Wang et al. (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24
Yu et al. (2020)	2	2	2	2	1	2	2	2	2	2	2	2	23
Christensen et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24
Hakulinen et al. (2018)	2	2	1	2	1	2	2	2	2	2	2	2	22
Novak et al. (2020)	2	2	2	2	1	2	2	2	2	2	2	2	23
Poli et al. (2021)	2	2	2	2	1	2	2	2	2	2	2	2	23
Henriksen et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24
Iecovich et al. (2011)	2	2	2	2	1	2	2	2	2	2	2	2	23
Tilvis et al. (2012)	2	2	2	2	1	2	2	2	2	2	2	2	23
Christiansen et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Conde sala et al. (2020)	2	2	2	2	1	2	2	2	2	2	2	2	23
Golaszewski et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Hoogendijk et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24

Description of the answer score:

0 = No
1 = Hesitant
2 = Yes

Description of the question criteria:

1 = Does the cohort study address the clinical problem clearly?
2 = Were the cohorts (study subjects in both exposed and non-exposed groups) selected in the right way?

3 = Are social isolation and loneliness accurately measured to minimize bias?
4 = Were the outcomes (cardiovascular disease status and death) accurately measured to minimize bias?
5 = Did the researcher identify all important confounding factors? Does the researcher account for confounding factors in the design and/or analysis?
6 = Does the research subject complete the research time in full? Were the research subjects followed up for a sufficiently long time?
7 = Are the results of this study reported in the aHR?
8 = How precise are the results?
9 = Can the results be trusted?
10 = Are the results applicable to the local (local) population?
11 = Are the results of this study compatible with the available evidence?
12 = What are the implications of this research for practice?

After assessing the quality of the research, a total of 18 articles were obtained with a cohort study design which will be used as a source of meta-analysis of the effects of social isolation and loneliness on cardiovascular disease and death. The article was then extracted and summarized according to the research PICO.

Table 3. Summary of primary cohort study articles in a meta-analysis of the effect of social isolation on cardiovascular disease and mortality

Author (Year)	Country	Sample	P	I	C	O
Luo et al. (2022)	America	15,000	Adult (60-89 years)	Social isolation	No Social Isolation	CVD, Mortality
Elovainio et al. (2017)	Finland	466,901	Elderly (65 years)	Social isolation	No Social Isolation	Mortality
Gilmour et al. (2020)	Canada	13,037	Elderly (65+ years)	Social isolation	No Social Isolation	Mortality
Yu et al. (2019)	Taiwan	24,726	Elderly (65 years)	Social isolation	No Social Isolation	Mortality
Hakulinen et al. (2018)	UK	502,632	Elderly (60-69 years)	Social isolation	No Social Isolation	CVD, Mortality
Poli et al. (2021)	Australia	11,486	Elderly (70+ years)	Social isolation	No Social Isolation	CVD
Cene et al. (2022)	US	44,174	Elderly 60-79 years	Social isolation	No Social Isolation	CVD
Naito et al. (2021)	Europe	119,894	60-70 years	Social isolation	No social isolation	CVD, Mortality
Tilvis et al. (2012)	Finland	3,858	Elderly (≥ 75 years)	Social isolation	No Social Isolation	Mortality
Kotozaki et al. (2022)	Japan	22,933	Elderly (65 years)	Social isolation	No Social Isolation	Mortality
Christiansen et al. (2021)	Denmark	24,687	60-79 years	Social isolation	No Social Isolation	CVD
Golaszewski et al. (2022)	US	57,825	Elderly (65-99 years)	Social isolation	No social isolation	CVD
Hoogendijk et al. (2020)	Amsterdam	1,427	Elderly (65+ years)	Social isolation	No social isolation	CVD

Based on Table 3, an overview of primary research on the effect of social isolation on cardiovascular disease and death, a meta-analysis of 13 articles was carried out with various locations, from America, Finland, Canada, Taiwan, England, Australia, Japan,

Denmark, and Amsterdam. Similarities were found in the study, namely the cohort study design, the research subjects were the elderly, the intervention was given social isolation and the comparison was not social isolation. In this study there were also differences in the number of samples, the smallest was 1,427, and the highest was 502,632.

Table 4. Adjusted Hazard Ratio (aHR) effect of social isolation on cardiovascular disease and death

Author (year)	aHR	CI 95%	
		Lower Limit	Upper Limit
Luo et al. (2022)	1.33	1.15	1.54
	1.28	1.01	1.62
Elovainio et al. (2017)	1.26	1.20	1.33
Gilmour et al. (2020)	0.90	0.80	1.20
Yu et al. (2019)	1.16	1.06	1.26
Hakulinen et al. (2018)	1.43	1.32	1.55
	1.25	1.03	1.51
Poli et al. (2021)	1.66	1.02	2.70
Cene et al. (2022)	1.23	1.08	1.41
Naito et al. (2021)	1.26	1.17	1.36
	1.15	1.05	1.25
Tilvis et al. (2012)	1.03	0.88	1.23
Kotozaki et al. (2022)	1.38	1.04	1.83
Christiansen et al. (2021)	1.16	0.93	1.46
Golaszewski et al. (2022)	1.08	1.03	1.12
Hoogendijk et al. (2020)	1.06	0.92	1.21

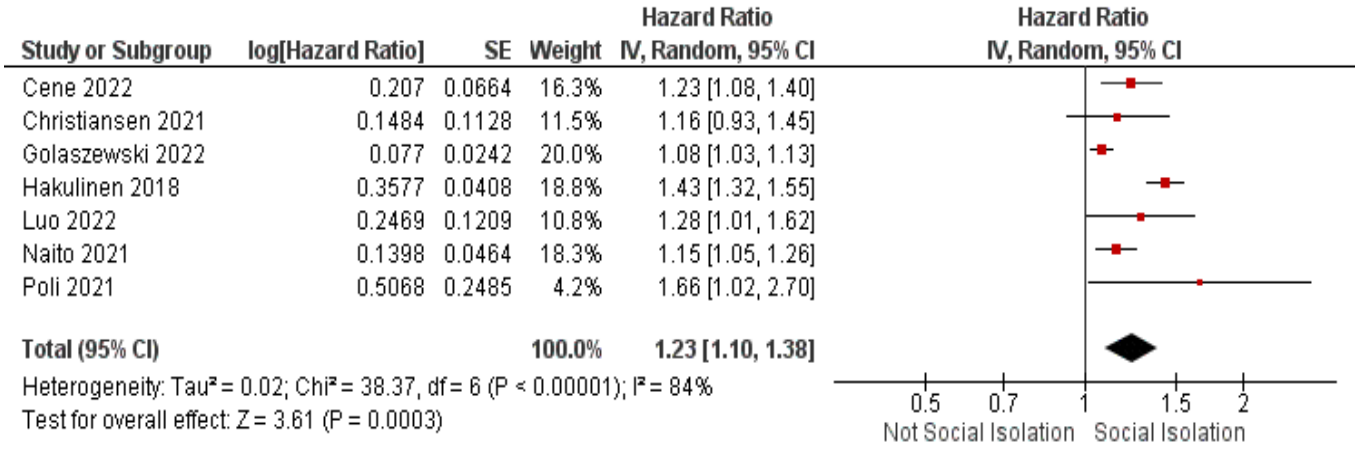

Figure 3. Forest plot of the effect of social isolation on cardiovascular disease

The forest plot in Figure 3 shows that there is an effect of social isolation on cardiovascular disease. Elderly people who are socially isolated have a risk of developing cardiovascular disease 1.23 times compared to those who are not socially isolated, and the effect was statistically significant (aHR= 1.23; 95% CI= 1.10 to 1.38; p= 0.003). The forest plots also show heterogeneous effect estimates (I^2 = 84%; p<0.001). Thus, the calculation of the average effect estimate uses the random effect model approach.

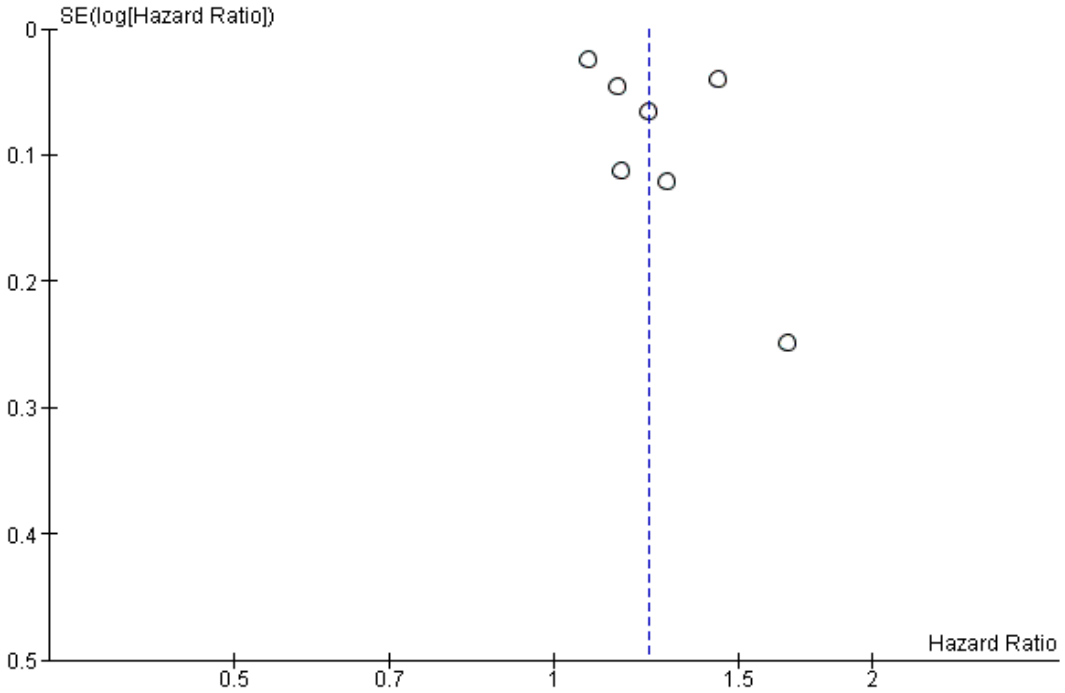

Figure 4. Funnel plot of the effect of social isolation on cardiovascular disease

The funnel plot in Figure 4. shows a symmetrical distribution of effects to the right and left of the estimated mean vertical line, it means there is no publication bias in this study.

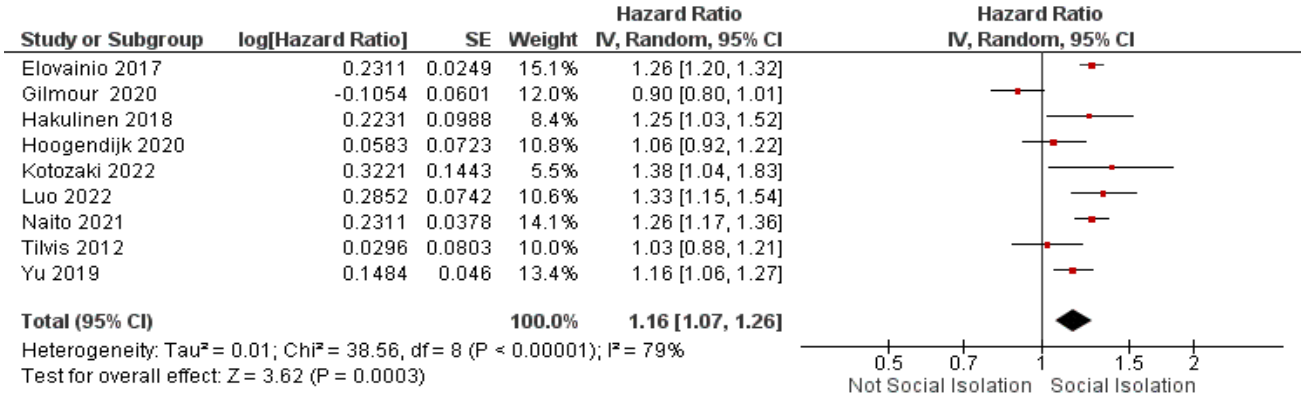

Figure 5. Forest plot of the effect of social isolation on mortality

Forest plot Figure 5 shows that there is an effect of social isolation on death. Elderly people who are socially isolated have a risk of dying 1.16 times compared to those who are not socially isolated, and the effect is statistically significant (aHR= 1.16; 95% CI= 1.07 to 1.21; p= 0.003). The forest plot also shows heterogeneous effect estimates (I^2= 79%; p<0.003). Thus, the calculation of the average effect estimate uses the random effect model approach.

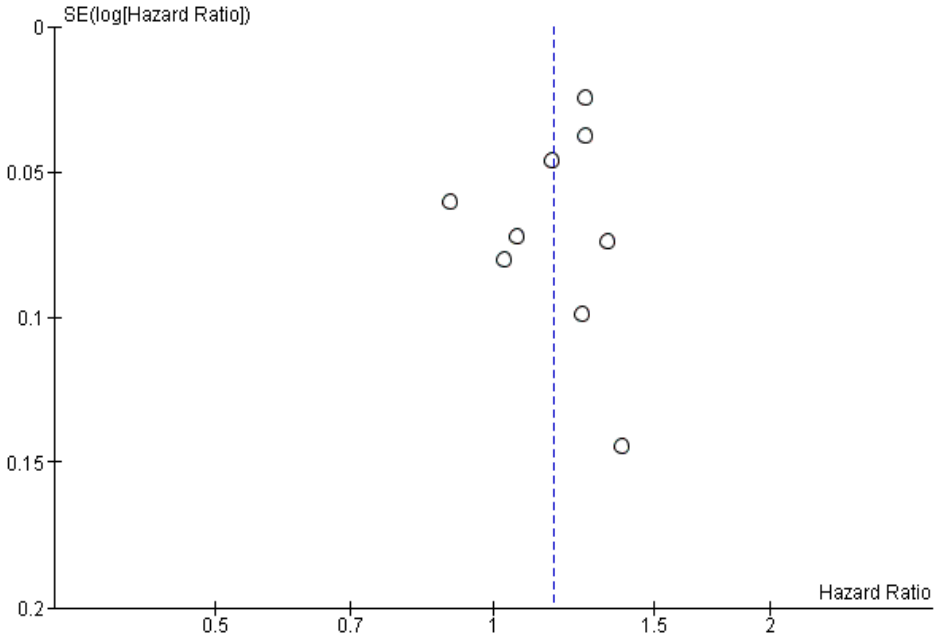

Figure 6. Funnel plot of the effect of social isolation on death

The funnel plot in Figure 6 shows an asymmetric distribution of effects. The effect estimates are more distributed to the right of the vertical line than to the left, this indicates publication bias. Because the distribution of effect estimates is mostly located to the right of the same vertical line as the location of the average effect estimate (diamond shape) which is also located to the right of the vertical line in the forest plot description, the publication bias tends to overstate the true effect (over estimates).

Table 5 Summary of primary cohort study articles in a meta-analysis of the effect of loneliness on cardiovascular disease and death

Author (year)	Sample	P	I	C	O
Elovainio et al. (2017)	466,901	Elderly (65 years)	Lonely	Not Lonely	Death
Wang et al. (2018)	2,610	Elderly (75+ years)	Lonely	Not Lonely	Death
Yu et al. (2019)	24,726	Elderly (65 years)	Lonely	Not Lonely	CVD, Death
Christensen et al. (2019)	13,443	Elderly (64 years)	Lonely	Not Lonely	Death
Hakulinen et al. (2018)	502,632	Elderly (60-69 years)	Lonely	Not Lonely	CVD
Novak et al. (2020)	524	Elderly (70 years)	Lonely	Not Lonely	Death
Henriksen et al. (2017)	1,363	Middle age (60+ years)	Lonely	Not Lonely	Death
Iecovich et al. (2011)	605	Elderly (70-85 years)	Lonely	Not Lonely	Death
Tilvis et al. (2012)	3,858	Elderly (≥ 75 years)	Lonely	Not Lonely	Death
Christiansen et al. (2021)	24,687	60-79 years	Lonely	Not Lonely	CVD
Conde sala et al. (2020)	48,691	Elderly 65+ years)	Lonely	Not Lonely	Death
Golaszewski et al. (2022)	57,825	Elderly (65-99 years)	Lonely	not lonely	CVD
Hoogendijk et al. (2020)	1,427	Elderly (65+ years)	Lonely	Not lonely	Death

Based on Table 5, the description of primary research on the effect of loneliness on cardiovascular disease and death was conducted through a meta-analysis of 13 articles with various research locations, namely from Finland, England, Taiwan, Denmark, England, Sweden, Jerusalem, Europe, the United States, and Amsterdam.

Similarities were found in the study, namely the cohort study design, the research subjects, namely the elderly, the intervention given was lonely with the comparison

not lonely. In this study there were also differences in the number of samples, the smallest was 524, and the highest was 466,901.

Table 6 Adjusted Hazard Ratio (aHR) the effect of social isolation on cardiovascular disease and death

Author (year)	aHR	CI 95%	
		Lower Limit	Upper Limit
Elovainio et al. (2017)	1.38	1.30	1.47
Wang et al. (2018)	1.20	1.00	1.60
Yu et al. (2019)	0.95	0.82	1.09
	1.39	1.05	1.85
Christensen et al. (2019)	2.14	1.43	3.22
Hakulinen et al. (2018)	1.06	0.96	1.19
Novak et al. (2020)	2.42	1.04	5.65
Poli et al. (2021)	2.55	1.34	4.83
Henriksen et al. (2017)	1.27	0.92	1.74
Iecovich et al. (2011)	0.02	0.61	1.04
Tilvis et al. (2012)	1.17	0.97	1.41
Christiansen et al. (2021)	1.24	1.02	1.51
Conde sala et al. (2020)	0.73	0.53	1.02
Golaszewski et al. (2022)	1.05	1.01	1.09
Hoogendijk et al. (2020)	1.06	0.92	1.22

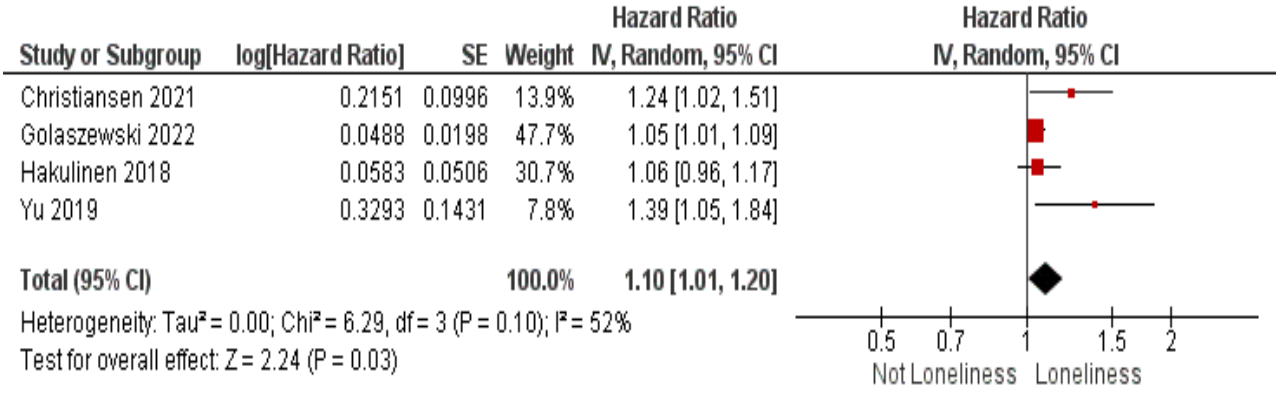

Figure 7 Forest plot of the effect of loneliness on cardiovascular disease

Forest plot Figure 7 shows that there is an effect of loneliness on cardiovascular disease. Lonely elderly had risk of developing cardiovascular disease 1.10 times compared to those who are not lonely, and the effect is statistical (aHR= 1.10; 95% CI= 1.01 to 1.20; p= 0.003). The forest plots show a rather heterogeneous effect estimation (I^2= 52%; p= 0.100). Thus, the calculation of the average effect estimate uses the random effect model approach.

The funnel plot in Figure 8 shows a symmetric distribution of effects to the right and left of the vertical mean estimation line, so there is no publication bias in this meta-analysis.

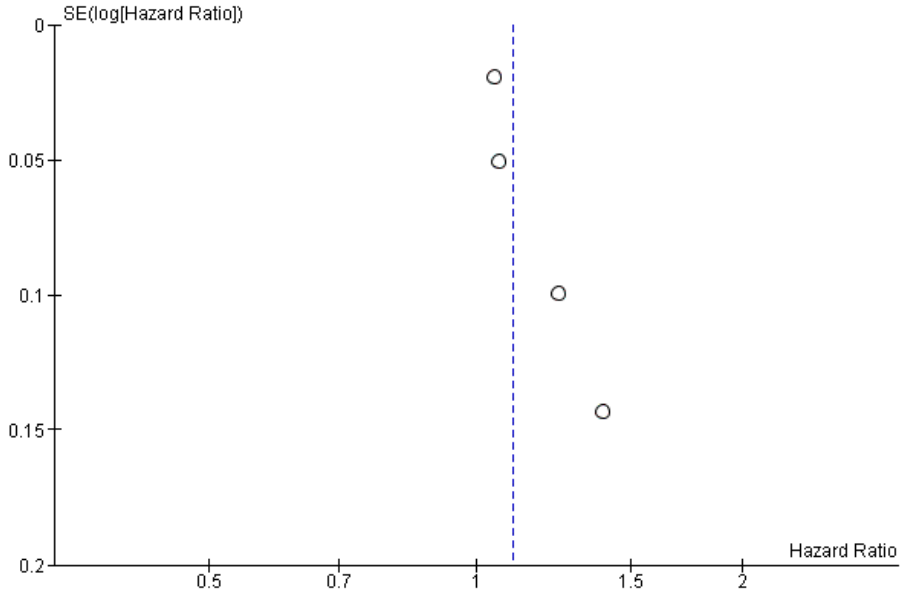

Figure 8. Funnel plot of the effect of loneliness on cardiovascular disease

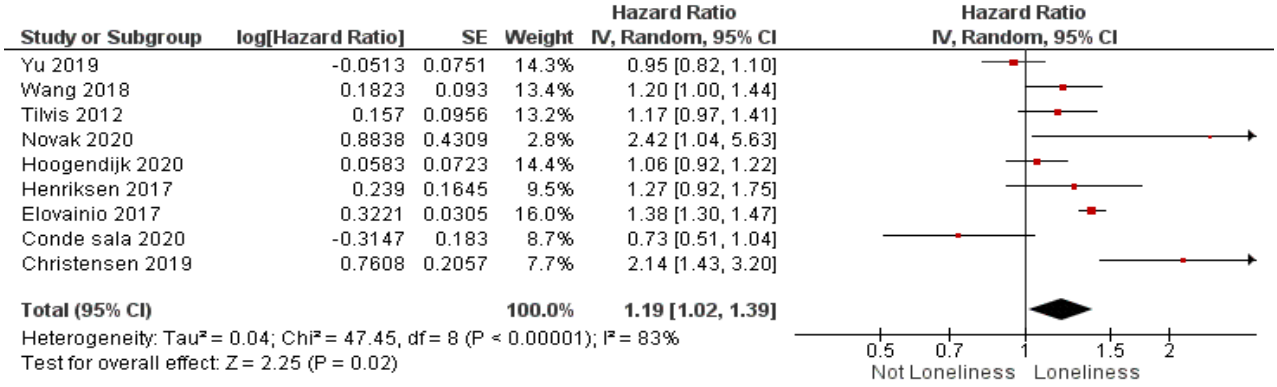

Figure 9. Forest plot of the effect of loneliness on death

Forest plot Figure 9 shows that there is an effect of loneliness on death. Lonely elderly have a risk of dying 1.19 times compared to those who are not lonely, and this effect is statistical (aHR= 1.19; 95% CI= 1.02 to 1.39; p<0.001). The forest plots show heterogeneity of effect estimates (I^2= 83%; p= 0.002). Thus, the calculation of the average effect estimate uses the random effect model approach.

The funnel plot in Figure 10 shows an asymmetric effect distribution to the right and left of the estimated mean vertical line. The effect estimates are more distributed to the right of the vertical line than to the left, indicating publication bias. Because the distribution of effect estimates is mostly located to the right of the same vertical line as the location of the average effect estimate (diamond shape) which is also located to the right of the vertical line in the forest plot description, the publication bias tends to overstate the true effect (over-estimated).

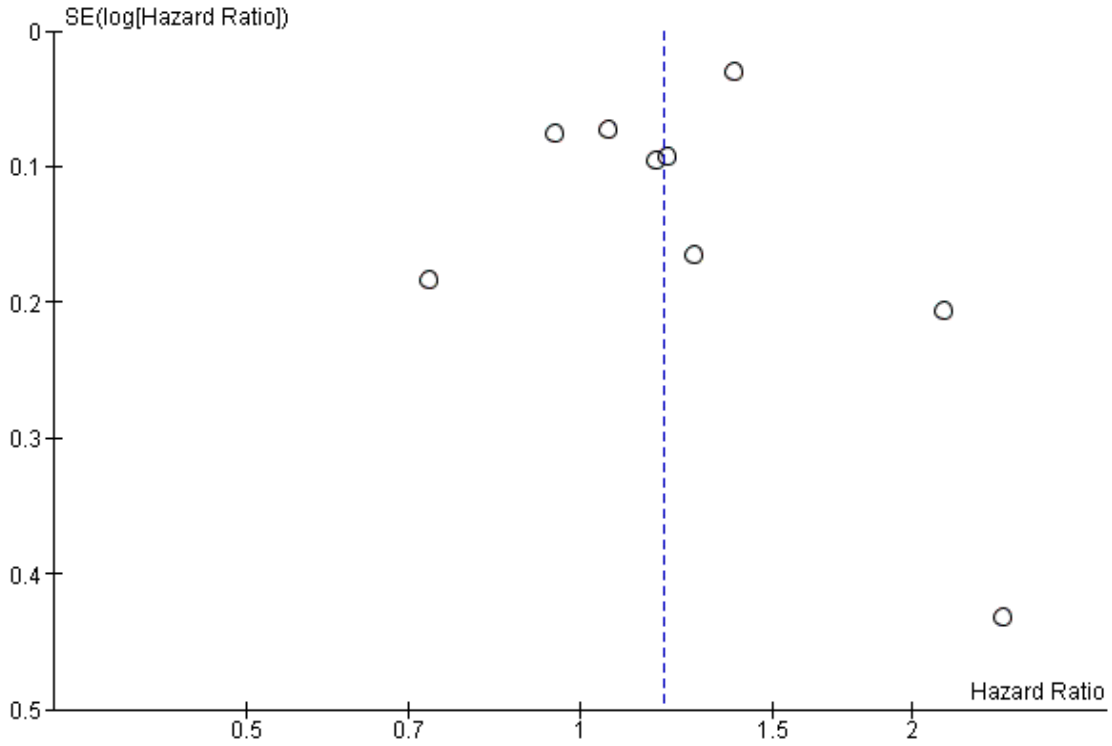

Figure 10. Funnel plot of the effect of loneliness on death

DISCUSSION

Disease burden related to non-communicable diseases had become a major public health problem. One third of all deaths in Indonesia are due to cardiovascular disease with stroke and coronary heart disease (CHD) being the main causes of mortality in the country. Similar to the situation in most other low and middle-income countries in the Asia-Pacific region, the prevalence of major cardiovascular risk factors, namely overweight, diabetes, and high blood pressure, has increased (Hussain et al., 2016).

Cardiovascular disease is the number one cause of death in the world. In 2012, an estimated 17.5 million people died from cardiovascular disease or around 31% of all deaths in the world (WHO, 2021). More than three quarters or around 80% of deaths from cardiovascular disease occur in low to middle income countries including Indonesia (WHO, 2016; AHA/ASA, 2013). The Indonesian Ministry of Health (2014) defines cardiovascular disease as a disease with disorders of the heart and blood vessels such as coronary heart disease, heart failure, hypertension and stroke (Jumayanti et al., 2020).

This systematic review and meta-analysis research raised the theme of the effect of social isolation and loneliness on cardiovascular disease and death in the elderly. The dependent variables analyzed were cardiovascular disease and death. The independent variables analyzed were social isolation and loneliness.

1. The Effect of Social Isolation on Cardiovascular Disease in the Elderly

A total of 7 cohort studies came from America, England, Australia, the United States, Denmark, and Amsterdam. The total sample is 788,611. This meta-analysis concluded that there is an effect of social isolation on cardiovascular disease. Socially isolated elderly have a risk of developing cardio-

vascular disease. Elderly people who are socially isolated have a risk of developing cardiovascular disease 1.23 times compared to those who are not socially isolated, and the effect is statistically significant (aHR= 1.23; 95% CI= 1.10 to 1.38; p= 0.003). The heterogeneity of the research data shows I^2 = 84% so that the spread of the data is stated to be heterogeneous (random effect model).

Social isolation increases cardiovascular disease in the elderly, this result is in accordance with the hypothesis. According to research by Cene et al. (2022) found that postmenopausal and socially isolated women had a higher risk of developing heart failure compared to women who did not experience social isolation (aHR= 1.23; 95% CI= 1.08 to 1.41).

This is supported by research (Luo and Hendrix, 2022), elderly who are socially isolated significantly increase the risk of cardiovascular disease (aHR= 1.33; 95% CI= 1.15 to 1.54). The results of the study were in line with those conducted by (Poli et al., 2021) which stated that individuals with poor social health were 42% more likely to develop cardiovascular disease. Elderly who experience social isolation can increase the risk of cardiovascular disease by 1.66 times compared to the elderly who do not experience social isolation.

2. The Effect of Social Isolation on Death in the Elderly

A total of 9 cohort studies came from America, Finland, Canada, Taiwan, England and Japan. The total sample is 1,168,981. This meta-analysis concludes that there is an effect of social isolation on death. Elderly who are socially isolated have a risk of experiencing death. Elderly people who are socially isolated have a risk of dying 1.16 times compared to those who are not socially isolated, and the effect is statistically significant (aHR= 1.16; 95% CI= 1.07 to 1.21; p= 0.003). The heterogeneity of the research data shows I^2 = 79% so that the spread of the data is stated to be heterogeneous.

In a meta-analysis study conducted by Roisin et al. (2022), Social isolation is associated with an increased risk of all causes of death (HR = 1.46, 95% CI = 1.08 to 2.04 I^2= 31%. This is in line with research from Kitakata et al., (2022), high risk for social Isolation is associated by risk-adjusted all-cause death at 180 days (HR= 7.89; 95% CI= 1.53 to 40.75).

Other research from Yang et al. (2013), high risk for social isolation associated with risk adjusted all causes mortality for 180 days HR= 7.89; 95% CI= 1.53 to 40.75). This is in line with research by Cacioppo et al., (2016) who argued that social isolation has been recognized as a major risk factor for morbidity and mortality in humans for more than a quarter of a century.

3. The Effect of Loneliness on Cardiovascular Disease in the Elderly

A total of 4 cohort studies came from England, Denmark and the United States. The total sample is 609,870. This meta-analysis concluded that there is an effect of loneliness on cardiovascular disease. Lonely elderlys are at risk of experiencing cardiovascular disease. Lonely elderly had a risk of developing cardiovascular disease 1.10 times compared to lonely, and the effect is statistically significant (aHR= 1.10; 95% CI= 1.01 to 1.20; p= 0.003). The heterogeneity of the research data shows I^2 = 52% so that the spread of the data is stated to be heterogeneous (random effect model).

According to research by Hegeman et al. (2018), elderly who experience loneliness have a risk of cardiovascular disease (aOR = 1.13 95% CI = 1.06 to 1.21; p <0.001). These results are in line with research conducted by Stokes et al. (2021), showing that lonelyness increases the risk of heart disease (HR= 1.49; 95% CI= 1.13 to 1.96).

Sharma et al. (2021), In his research one in three people in America reported experiencing loneliness in everyday life during the SARS-COV2 pandemic due to quarantine and social distancing. This loneliness is associated with higher cardiovascular incidents, and higher utilization of health services.

In their research, Foti et al. (2020) fcused on the relationship between loneliness and cardiovascular disease and diabetes mellitus (DM) in the United States. The results of this study showed that loneliness was significantly associated with cardiovascular events (OR= 1.10; 95% CI= 1.01 to 1.20) and Diabetes Mellitus (OR= 1.08; 95% CI= 1.00 to 1.16).

Julsing et al. (2016), this study found that elderly people who experience lonelyness increase the risk of cardiovascular disease (HR= 1.08; 95% CI= 1.00 to 1.17).

4. The Effect of Loneliness on Death in the Elderly

A total of 10 cohort studies came from Finland, England, Taiwan, Denmark, Sweden, Jerusalem, Europe and Amsterdam. The total sample is 564.148. This study concludes that there is an influence of loneliness on death. Lonely elderly had a risk of experiencing death. Lonely elderly had a risk of dying 1.19 times compared to being lonely, and the effect is statistically significant (aHR= 1.19; 95% CI= 1.02 to 1.39; p= 0.002). The heterogeneity of the research data shows I^2= 83% so that the spread of the data is stated to be heterogeneous (random effect model).

According to research by Kraav et al. (2021), stated that loneliness increases the risk of death from cardiovascular disease (HR= 1.14; 95% CI= 1.04 to 1.24; p= 0.003). O'Suilleabhain et al. (2019), found that the elderly who experienced emotional loneliness 18.6% increased the risk of all causes of death (HR= 1.18; p= 0.029).

Schutter et al. (2022), in a meta-analysis study showed that loneliness and social network size were less associated with the risk of death in the elderly (HR= 1.10; 95% CI= 1.06 to 1.14). Gao et al. (2021), The prevalence of loneliness varies between 25.3 and 32.4% in Latin America and 18.3% in India. China shows a low prevalence of loneliness (3.8%). In the meta-analysis pool, there is strong evidence supporting an association between loneliness and death in all Latin American countries (HR= 1.13; 95% CI= 1.01 to 1.26; I^2= 10.1% and China (HR= 1.58; 95% CI= 1.03 to 2.41), a study conducted by Beller (2022) in Germany showed that being alone significantly increased the risk of death (HR= 1.20; p= 0.290).

AUTHOR CONTRIBUTION

Ayu Novita Wulandari as a researcher who selects topics, searches for and collects research data. Bhisma Murti and Didik Tamtomo analyzed the data and reviewed research documents.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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