

## Decline in Estrogen Levels and Its Impact on Muscle Strength in Elderly Women: A Systematic Review

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### ABSTRACT

**Background:** In the musculoskeletal system, old age is closely related to a decline in muscle strength. Decreased muscle strength in women is caused by the influence of changes in estrogen hormone levels. Several studies were conducted to see how estrogen affects muscle mass, muscle function, muscle damage, muscle regeneration, inflammation in the body, mitochondrial function, and substrate metabolism. Therefore, the study was carried out with the aim of conducting further study focusing on estrogen on muscle strength in elderly women.

**Subjects and Method:** The study was conducted with a systematic review design. The study was carried out in accordance using PRISM guidelines with the PICO formula. Population: elderly women, Intervention: estrogen hormone, Outcome: muscle weakness. Article searches were carried out through several databases, namely PubMed, Cochrane Library, Scopus Database, and Physiotherapy Evidence Database (PEDro) with the keywords: estrogen OR "estrogen hormone" OR "muscle strength" OR "risk of falls" OR "menopause" OR "women elderly." Risk of bias assessment was carried out according to the study design of each article.

**Results:** There were 10 articles involved in this study. The article has a cross-sectional and longitudinal study design. Articles had a low and medium risk of bias assessment. 6 articles stated that there was a relationship between changes in estrogen hormone levels and muscle weakness. 4 articles stated that there was no relationship between changes in estrogen hormone levels and muscle weakness.

**Conclusion:** There is an inconsistent relationship between estrogen levels and muscle strength in elderly women.

**Keywords:** estrogen hormone, muscle weakness, elderly women, menopausal age.

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### BACKGROUND

The elderly population around the world continues to experience a significant increase. It is estimated that this proportion of individuals over the age of 60 will triple from 96.30 million in 2011 to 300.96 million by 2050. Increasing the number of

elderly populations is a challenge for every country in providing health services that meet the needs of the elderly. Old age is closely related to the decline in organ function which has an impact on the emergence of health disorders such as cardiovascular diseases such as hyper-

tension, metabolic diseases such as diabetes mellitus, depression, dementia, and an increased risk of osteoporosis (Ministry of Health and Family Welfare, 2011; Montesanto, 2017; Ferrucci et al., 2018).

In the musculoskeletal system, old age is closely related to the condition of decreased muscle strength. Decreased muscle strength results in decreased physical function, decreased independence, decreased quality of life, and increased risk of disability. The decline in muscle mass and muscle strength occurs much faster in women compared to men. Women have a greater prevalence of cases of decreased strength than men. The high prevalence of decreased muscle strength in women is caused by the influence of changes in hormone levels in elderly women, namely the hormone estrogen (Gariballa et al., 2017; Visser et al., 2005; Ian Janssen PhD., 2022; Cui et al., 2013).

The hormone estrogen not only plays a role in female reproduction but also plays a role in muscle tissue. Estrogen levels go up and down throughout a woman's life cycle. The level slowly rises when entering the age of 15 to 20 years and reaches its highest peak during pregnancy. Estrogen levels will decrease when entering menopause. This decrease in estrogen levels leads to an increased risk of decreased muscle strength. This statement is reinforced by another study that found that during menopause, there is an increase (Wiik et al., 2009) (Carcaillon et al., 2012) in levels of C-reactive protein (CRP), pro-inflammatory cytokines (Interleukin-6, IL-6), and Tumor Necrosis Factor-alpha (TNF- $\alpha$ ) which have a significant effect on the decrease in muscle strength (Chagas et al., 2017). Several studies say that decreased muscle strength in the elderly is closely

related to the incidence of fall risk. ( Fang, 2012, Tom et al., 2013)

Many studies have been conducted to determine the effects of changes in estrogen levels in elderly women. One of them is a study with a systematic review design, in a study focusing on how estrogen affects muscle mass, muscle function, muscle damage, muscle regeneration, inflammation in the body, mitochondrial function, and substrate metabolism (Critchlow et al., 2023). Therefore, the authors conducted a follow-up study focusing on whether there is a relationship between estrogen and muscle strength in elderly women.

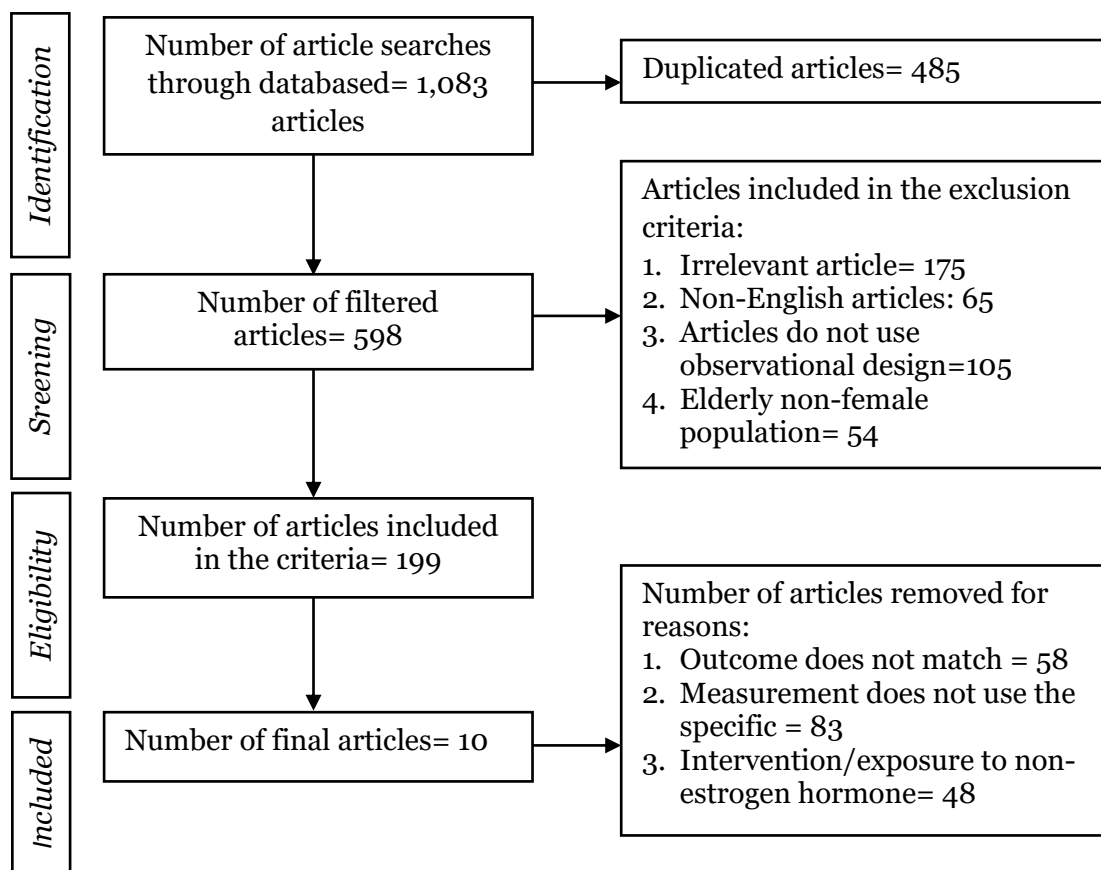
## SUBJECTS AND METHOD

### 1. Study Design

The study was conducted using a systematic study design review according to the PRISMA 2020 guidelines depicted in the flowchart (Figure 1).

### 2. Population and Sample

The study flow begins with the determination of PICO. P is the population i.e. Elderly women. I am an intervention i.e. the hormone estrogen. C is the comparison and O is the outcome or output, namely the decrease in muscle strength and the risk of falling. The second step is to search for articles. The search for articles was carried out through several data-based, namely PubMed, Cochrane Library, Scopus Database and Physiotherapy Evidence Database (PEDro) with the keywords "estrogen" OR "estrogen hormone" OR "muscle strength" OR "risk of falling" OR "menopause" OR "elderly women". The third step is screening and assessing the quality of each article. The fourth step is extraction and data synthesis. The fifth step is the presentation of results and discussion.



**Figure 1. PRISM Diagram**

### 3. Inclusion Criteria

The inclusion criteria of the articles included in the study were

- Articles with observational study type
- Population of elderly women, Menopausal women.
- Has external muscle weakness, decreased muscle strength
- Using specific measurements such as hand grip and fair index
- Indonesian and English articles
- Articles in full text and full access

### 4. Exclusion Criteria

The exclusion criteria of the articles included in the study were studies using unreliable muscle strength measurements, not using Indonesian or English language.

### 5. Operational Definitions

The operational definitions of populations, interventions, and outcomes are as follows:

- Elderly women are women who have entered the age of 60 years and above. At this time, women have entered menopause which begins at the age of 51 years (Andrea, 2023).
- Estrogen hormone is a hormone that plays a role in the menstrual cycle in women both in terms of development, maturation, and function. There are three main hormones namely Estradiol, Estrone, and Estriol. Not only does it play a role in the reproductive system, but the hormone estrogen plays a role in the endocrine system, Musculoskeletal, and immune system (Hamilton et al., 2017). Estrogen levels can be measured through blood tests. With a minimum level of 9.5 pmol/L (Carcaillon et al., 2012b).

c. A decrease in muscle strength is an ability that results from great speed or force over some time. Muscle strength is an important component for performing daily functional activities. Muscle strength is closely related to the risk of falls in people of older age (Frontera., 2014). To measure the presence of a decrease in muscle strength can use a handgrip dynamometer (Rantanen et al., 1999) and a fairly index (Garcia-Garcia., 2011).

**6. Instruments**

The assessment of article quality is carried out by checking according to the design of the article study, namely the cross-sectional study assessment and the longitudinal study assessment.

**RESULTS**

**1. Article search results**

The results of the article search conducted through 4 databases obtained a total of 1083 articles. There were 485 duplicate articles, 175 irrelevant articles, 65 non-English articles, 105 articles not using observational design, 54 articles had populations that were not elderly women, 58 articles had outputs that did not meet the inclusion criteria, 83 articles were not exposed to estrogen hormones and 48 articles did not use dynamometers, hand grips, and fairly indexes. Details of the articles involved in this study can be seen in Table 1.

**Table 1. Identity of the study article**

Author	Study design	Population	Intervention	Outcome
Cappola et al, (2009)	Longitudinal study	494 Women aged 70–79	IGF-1, DHEAS, and steroid, free testosterone (T)	Frailty status
Guligowska et al, (2021)	Cross-Sectional	61 Women aged 75 years	follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, testosterone, dehydroepiandrosterone sulfate (DHEAS), and cortisol	Handgrip strength
Kong, (2019)	Cross Sectional	1244 women aged 40-69 years	E2 (Estradiol 2)	Handgrip strength
Rolland, (2007)	Longitudinal study	49 Women aged 45-62 years	Estradiol	Maximum isometric knee extensor strength
Carcaillon, (2012)	Longitudinal study	137 Women >65 years old	Estradiol	Handgrip strength
Bochud, (2019)	Cross Sectional	172 Age women < 90 years	Estradiol	Handgrip strength
Baylis, (2012)	Longitudinal Study	101 women Age >60 years	dehydroepiandrosterone sulphate (DHEAS)	Handgrip strength
Yanagita, (2019)	Cross Sectional	108 women Age > 65 years	dehydroepiandrosterone sulphate (DHEAS)	Handgrip strength

Author	Study design	Population	Intervention	Outcome
Pesonen et al. (2021)	Cross Sectional	63 women aged >55 years	Estradiol	Maximal isometric knee extension strength
Rathnayake (2021)	Cross Sectional	350 women aged 55-60 years	Estradiol	Handgrip strength

**2. Assessment of article quality**

The assessment of the quality of the article study is carried out in accordance with the study design of each article. Six articles with study design cross sectional has a low risk of

bias. Four articles with study design longitudinal study have a moderate risk of bias. Details of the quality assessment of the article can be seen in tables 2 and 3.

**Table 2. Assessment of article quality with cross sectional study design**

No	Article	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	%Yes	Rob
1	Guligowska et al. (2021)	Y	Y	Y	Y	Y	N	Y	Y	75%	Low
2	Kong (2019)	N	N	Y	Y	Y	N	Y	Y	62.5%	Low
3	Bochud (2019)	Y	Y	N	N	Y	Y	Y	Y	75%	Low
4	Yanagita (2019)	Y	Y	Y	Y	N	N	Y	Y	75%	Low
5	Pesonen et al. (2021)	Y	Y	Y	Y	N	N	Y	Y	75%	Low
6	Rathnayake (2021)	Y	Y	Y	Y	N	N	Y	Y	75%	Low

Q1: Were the criteria for inclusion in the sample clearly defined? , Q2: Were the study subjects and the setting described in detail?, Q3: Was the exposure measured in a valid and reliable way?, Q4: Were objective, standard criteria used for measurement of the condition?, Q5: Were confounding variables identified?, Q6: Were strategies to deal with confounding variables stated?, Q7: Were the outcomes measured in a valid and reliable way?, Q8: Was appropriate statistical analysis used?, Y: Yes, N: No, Interpretation: ≤40% yes = high risk of bias, 50-69% yes = moderate risk of bias, ≥70% yes = low risk of bias.

**Table 3. Assessment of article quality with longitudinal study design**

No	Article	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	%Yes	Rob
1	Cappola et al. (2009)	Y	N	Y	Y	Y	N	Y	Y	N	N	Y	63.6	Moderate
2	Rolland (2007)	Y	N	N	Y	Y	N	Y	Y	Y	N	Y	63.6	Moderate
3	Carcaillon (2012)	N	Y	Y	Y	Y	Y	N	N	Y	N	Y	63.6	Moderate
4	Baylis (2012)	Y	N	Y	N	N	Y	Y	Y	Y	N	Y	63.6	Moderate

Q1: Were the two groups similar and recruited from the same population?, Q2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?, Q3: Was the exposure measured in a valid and reliable way?, Q4: Were confounding factors identified?, Q5: Were strategies to deal with confounding

factors stated?, Q6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?, Q7: Were the outcomes measured in a valid and reliable way?, Q8: Was the follow up time reported and sufficient to be long enough for outcomes to occur?, Q9: Was follow up complete, and if not, were the reasons to loss to follow up described and explored?, Q10: Were strategies to address incomplete follow up utilized?, Q11: Was appropriate statistical analysis used?, Y: Yes, N: No, Interpretation:  $\leq 49\%$  yes = high risk of bias, 50-69% yes = moderate risk of bias,  $\geq 70\%$  yes = low risk of bias

## DISCUSSION

Ten selected articles were analyzed in a systematic review. Of these ten articles, four stated that changes in estrogen levels during menopause are not associated with a decline in muscle strength. Meanwhile, six articles reported a relationship between a decrease in sexual hormone levels and a decline in muscle strength (Cappola et al., 2009; Rolland et al., 2007; Kong et al., 2019; Yanagita et al., 2019; Rathnayake et al., 2021; and Baylis et al., 2013). One study involved more than 300 elderly individuals aged 70–79 years, classified into Non-Frail, Pre-Frail, and Frail groups. The study results indicated that the lowest levels of Dehydroepiandrosterone Sulfate (DHEAS) were found in the Frail group, which also exhibited the lowest muscle strength. The second article involved a study of 77 postmenopausal women, using serum estrone as a parameter. The results showed that estradiol is associated with decreased muscle strength in postmenopausal women. The third and fourth studies used the same indicator, DHEAS. The third study involved 1,244 postmenopausal women, while the fourth involved 108 postmenopausal women. Both studies concluded that low DHEAS levels significantly contribute to muscle weakness in elderly women and are a risk factor for sarcopenia. The fifth study examined 350 elderly women over the age of 55. It found lower estradiol levels in postmenopausal women, which positively correlated with lower muscle strength measurements in this group. These findings were reinforced

by the sixth study, which involved 254 elderly women and reported that low DHEAS levels are a risk factor for muscle weakness and increased mortality rates.

DHEAS is a precursor for estrogen formation in postmenopausal women (Payne, 2004). Estrogen is divided into three types: estrone, estradiol, and estriol. Research indicates that estradiol plays a significant role in muscle contraction mechanisms. Estradiol enhances the intrinsic function of skeletal muscles, particularly actin and myosin, which form strong bonds during muscle contraction (Lowe, 2010). Consequently, a decline in DHEAS levels leads to a reduction in the intrinsic function of muscles.

Different results were demonstrated by studies conducted by Guligowska et al. (2021), Carcaillon et al. (2012c), Bochud et al. (2019), and Pesonen et al. (2021). Guligowska et al. (2021) aimed to examine the relationship between sex hormone levels and indicators of sarcopenia, one of which is muscle weakness (Cruz-Jentoft et al., 2019). The study found that sex hormone levels (gonadotropins and DHEAS) were strongly associated with sarcopenia in elderly men. However, in elderly women, no significant relationship was observed.

Interestingly, the decline in DHEAS in postmenopausal women was significantly associated with a reduction in muscle mass. This decrease in muscle mass is suspected to be related to elevated levels of Follicle Stimulating Hormone (FSH) found in postmenopausal women (Park et al., 2020). Another study suggested the possibility of

altered FSH receptor function in muscles as individuals age (Liu et al., 2017).

A study by Carcaillon et al. (2012) was conducted on two groups of postmenopausal women: those aged <79 years and those aged >79 years. The study aimed to examine the relationship between estradiol (E2) levels and muscle weakness in postmenopausal women. The results showed that E2 levels were higher in the <79 age group compared to the >79 age group.

According to previous theories, higher E2 levels are expected to lower the risk of muscle weakness. However, this study revealed contradictory results. Higher E2 levels were associated with an increased risk of muscle weakness. This finding was linked to elevated levels of high-sensitivity C-reactive protein (hs-CRP) in the <79 age group, which is associated with systemic inflammation. The interaction between higher E2 levels and inflammation may increase the risk of muscle weakness (Hubbard et al., 2009).

The study by Bochud et al. (2019) was conducted on elderly men and women to investigate the relationship between sex steroids, including estrogen, and muscle strength. The results indicated that there was no significant relationship between estrogen levels and muscle strength in elderly women. It remains unclear why this relationship was only observed in elderly men.

Similarly, the study by Pesonen et al. (2021) reported no association between low estradiol levels and decreased muscle strength. A potential explanation for this finding is that the study population consisted of elderly women who had only recently entered the premenopausal stage.

The relationship between estrogen hormones and muscle strength remains controversial. Further research is needed using various serum indicators to determine

the exact causes of muscle strength decline in elderly women.

This study has several strengths. First, it employed a longitudinal study design with a large population. Second, the risk of bias assessment for the research articles showed low to moderate values. Third, it utilized reliable tools for measuring muscle strength.

However, the study also has limitations. It relied solely on estrogen serum indicators, and future studies are encouraged to incorporate multiple serum indicators for a more comprehensive analysis.

The conclusion from the review of 10 articles with cross-sectional and longitudinal study designs indicates that there is a relationship between estrogen levels and muscle strength in elderly women. However, the decline in muscle strength in elderly women is not solely influenced by estrogen levels. Other factors, such as FSH levels and hs-CRP, also play a role in this process.

#### **AUTHOR CONTRIBUTION**

All authors have equal contributions.

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#### **CONFLICT OF INTEREST**

There is no conflict of interest in this study.

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