IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

RECAPITULATION OF GERONTOLOGY AND FRAILTY; DISCOVERING A CURRENT REVIEW

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ABSTRACT:

Gerontology is the study of the social, cultural, psychological, cognitive, and biological aspects of ageing. Due to the advancements in technology the studies concerning ageing has grown impressively. One of the most important fields of study under ageing is frailty, which is the main highlight of this article. Frailty is a dynamic syndrome which affects an individual not just physically but also mentally, socially and psychologically. Each of the mentioned domains has copious factors which lead to frailty. Finding out these factors in an individual can be helpful as it will aid in recognizing the correct interventions with the help of which frailty can be somewhat reversed and prevented. According to the several amount of research it has been found that the onset of frailty is not just because of ageing but also due to several environmental factors, chronic diseases and genetics, which further tells us that frailty is not just common to old adults but can be developed at a younger age as well. Some well-known models for instance, Phenotype and Cumulative deficit model and various other assessment tools have been developed in order to identify frailty in old individuals. Frailty also had a major impact on Covid-19 patients. Frail individuals were more severely harmed by the Corona Virus, similar rise in Cluster of Differentiation molecules can be observed in both frail and Covid-19 patients. Also, several biomarkers have been recognized that occur in an increased level in majority of frail individuals. According to a study it was found that not all old adults who are frail will identify themselves as frail, and for almost every

individual the definition of frailty was different. So, with the help of this article, a complete understanding of frailty which includes the domains of frailty, factors of frailty, models and tools for identifying frailty, developing interventions, types of important biomarkers, impact of Covid-19, perspective of old adults, etc., can be gained.

Keywords: Biomarkers, comorbidity, frailty, gerontology, multimorbidities.

Introduction

Gerontology is a comprehensive study of science that deals with the physical, mental, social, societal aspects of ageing and the diseases of the elderly. On the other side, geriatrics is more specifically concerned about the medical aspect of the old adults. Although gerontology and geriatrics have distinct interpretations, they both are simultaneously applied, in order to understand ageing. Over the years, there has been a gradual increment in the advancement of technology, which has further led to the development of gerontology as well as geriatrics. Gerontologists have involved themselves in this field of study, in order to improve old age and help the elderly stay independent for a longer period.

Ageing is a continuous process that begins from the time of birth or maybe even earlier. We are aware that Mortality rate and ageing are directly proportional to each other i.e with increasing age the rate of mortality increases. But the scenario is no longer the same. Through the years, life expectancy has increased dramatically, because of the improvements and developments of public health programs, which have led to a better lifestyle of people [1]. However, this decrease in mortality has come across as a huge limitation, since it has been causing a serious rise in chronic diseases and a concurrent decrease in physical and cognitive functions, which will lead to frailty and other health-related problems [2].

Health span and Lifespan are intimately related to each other. On the contrary, it is not obligatory that with the increase in lifespan, the health span will increase alongside [3]. Initially, it was surmised that the terms disability, comorbidity, ageing, and frailty could be used reciprocally, but due to the pursuit of research, it is now distinctly inferred that each of the mentioned terminologies are individualistic words and thus, have independent meanings [2]. Clinicians, researchers, and various other people have prioritized studying health span which is a concerning topic at the present moment. The void between life and health span is characterized by aggregation of several deficits, disabilities, comorbidities, etc., which is clinically denoted as Frailty [3].

The most problematic consequence of ageing in the population is the clinical syndrome frailty [4]. Frailty is an intricate terminology that can have a variety of different connotations, depending upon an individual's perspective. Although the term Frailty, was first coined in the geriatric field a few decades ago, its major understanding has come to light since 2000. It can be elucidated as a clinical and biological syndrome in which there is an increase in an individual’s vulnerability, to developing poor homeostasis, which will consequently, lead to deterioration of the immune system and cause hospitalizations, disabilities, comorbidities, fractures, stress, mortality and other clinical problems [5].

Frailty is a gradual age-related decline in physical, physiological, social, nutritive, psychological, and cognitive domains of the body [6]. Undoubtedly age increases the ubiquity of frailty, but there are certain susceptible groups of young adults, who are at a greater risk of becoming frail due to some persistent illness [7], hence now it has been validated that frailty can either be age-related or disease-related [8]. Several frailty assessment tools, for instance, the phenotype model, which categorizes individuals into frail, pre-frail, and robust [4,5], the cumulative deficit model [4,9] and various scales such as, Frail scale, Clinical frail scale, the Short Physical Performance Battery, Liver Frailty Index, the John Hopkins Frailty Indicator, the Edmonton scale, the Rockwood frailty index, the Carolina frailty index, etc. [7,1], have been developed in order to identify Frail individuals, which will further be helpful in discovering the right interventions and treatments. Treatments don't certainly mean medicaments; instead can also refer to a path to improve health. However, these tools do not completely provide a conclusive diagnosis, in lieu, identify impairments with respect to the domains aforementioned and can be advantageous for tracking down ways to mitigate and prohibit frailty. The field of frailty is still developing and will gradually progress with time.

In consonance with the biological level, a rise in oxidative indicators and pro-inflammatory cytokines can be observed in frail and pre-frail individuals, which concludes that there are some pertinent biomarkers associated with frailty that have been identified over the recent years, viz. oxidative stress and inflammation [10]. The inflammatory state is thought to be associated with immune-senescence which is additionally related to frailty [1]. Another aspect of how frailty is related immunologically can be understood by the outbreak of Covid-19. Both positive hospitalized Covid-19 patients and frail patients were intriguingly expressing an increase of similar Cluster of Differentiation molecules [11]. Therefore, frailty has been associated with a worse prognosis following Covid-19 infection [11, 12].

Various amount of studies and research conducted by researchers and clinicians have explained the development of frailty, several priorly mentioned models for finding frail individuals, biomarkers of frailty, their preventive measures, old adults perspective regarding frailty, etc. All of these topics will be accurately discussed in this article.

Frailty and Gerontology

Gerontologists are now focusing on a variety of topics one of which is Frailty. It is a concerning field of study which is meant to be explored in order to understand ageing, diseases, and mortality. Frailty is a reversible condition which not only affects physical functioning but others like cognitive, nutritive, physiological, and social factors [13]. Due to the decrease in mortality rates, the concern for frailty has grown. If on the basis of a mild disease we compare two old individuals one of whom is fit while the other is frail then it will be clearly observed that the fit will show less deterioration in health and after recovering will be back at the level of homeostasis while the frail individual will show a different result, the deterioration in health will be considerably high and even after recovering homeostasis will not be maintained, hence proved that frail individuals are under high risk of poor health [4]. Therefore, it is very important to find out a way with which we can identify frail individuals and help them.

Frailty Models

Two models were developed which would help identify frail individuals, the Phenotype model [4, 5] and the Cumulative Deficit Model [4, 9].

Phenotype Model

Phenotype model was developed by Fried et al. An observational study data of 5210 men and women aged over 65 years was collected from Cardiovascular Health Study (CHS) and were analyzed. Based on the analysis individuals were categorized into Frail, pre-frail, and robust which was identified by 5 components as mentioned in table 1. So, individuals having more or equal to 3 components were considered frail, those having 1-2 components were called pre-frail, while those having none of the components were categorized into robust. Hence, this study confirmed that frail individuals have higher mortality rates [4, 5].

Components used to identify frailty: The components like Weight loss, Tiredness, Slowness, Low physical activity, level Poor endurance and energy are used to identify frailty.

Cumulative Deficit Model: The second evaluated model was the Cumulative Deficit Model developed by Rockwood et al. using Canadian study of Health and Ageing (CSHA) a 5 year cohort study of 10,263 individuals whose mean age was 82 years was investigated. In comparison to the Phenotype model, this model consisted of 92 distinct parameters for instance, low mood, tremors, disabilities, etc. The Frailty Index (FI) was a simple calculation of 70 deficits which was used to measure the level of frailty in old adults. FI is equal to the number of deficits per total number of deficits. So, higher the FI value, it is more likely for an individual to be frail [4, 9].

Age and Disease related Frailty

Earlier it was believed that frailty can occur only due to increasing age. But by collecting the data from the Multidomain Alzheimer preventive trial Study (MAPT) and performing a 5 year preliminary study on the participants of 70 years who were either pre-frail or robust it was proven partially wrong. In a span of 60 months, continuous medical tests and assessments were conducted on the participants and the results were recorded [8]. Then, after observing all the collected data, the clinicians came to a conclusion that, frailty developed by three different reasons like Frailty developed due to age, Frailty developed due to some chronic illness, Frailty developed due to uncertain origin

Therefore, this analysis confirms that there is a relation between ageing, disease and frailty which furthermore explains that, frailty is a dynamic syndrome resulting from various physical, physiological, cognitive and social factors [8].

Development of Frailty

Earlier it was believed that Frailty is caused only due to Physical factors but with the help of Doetinchem cohort study (n= 4019) [6], it was understood that with increasing age not only our physical functioning degrades, but our social, physiological and cognitive functioning deteriorates as well. More the number of domains an individual accommodates into, more likely for he/she to be considered frail. In accordance to the mentioned domains individuals being active physically are less likely to be considered frail [6]. If individuals of

age 70-81 years were smoking, had a short duration of sleep along with other multimorbidities were considered physically frail [6]. An individual being psychologically frail was identified by the sex, smoking activity, sleep duration, low education level and other multimorbidities. One of the major factors for developing psychological frailty is personality.

Personality has a five factor model consisting of some major personality traits like [14], neuroticism, extraversion, openness to experience, agreeableness, conscientiousness. All the 5 traits have shown an interesting relationship between health and personality. Amongst the five, extraversion, neuroticism and conscientiousness are closely linked to Frailty [14].

Higher level of neuroticism, whereas, lower level of extraversion and conscientiousness, shows an increased frailty index value which is indicative of a frail individual [14]. Females are under a high risk of becoming psychologically frail. Old adults ranging from 70-81 years were susceptible to develop cognitive frailty [6]. In a panel study named English Longitudinal Study of Ageing (ELSA), several 50 year old participants were included [15]. In this study it was found that a variety of social factors influences the risk of frailty. Smoking, loneliness, low wealth, low education, obesity, high waist-hip ratio, being female, lower body strength, smoking, low level of physical activity, age are all some social factors that increase the chances of becoming frail of an individual no matter what the age is. Amongst all, age was the strongest predictor of frailty [15].

Table 1.

A four domain approach of frailty.

Domains of Frailty	**Factors**
Physical Frailty	Factors similar to the one mentioned in Table 1
Social Frailty	Loneliness, less social support
Psychological Frailty	Depression related symptoms, Personality
Cognitive Frailty	Memory Problems

So, if the mentioned factors in table 2 of different domains can be reversed by focusing on oneself, then Frailty as well can be reversed and lead to a healthy lifestyle. Hence, it is clear that people having low education are also exposed to becoming Frail. So, various assessment tools and models for estimating frailty should be used not only for old adults but also for other vulnerable groups [6]. Also, it has been understood that it is not only the physical factors that affects Frailty but there are several lifestyle factors that plays an important role in the development of frailty [6].

Frailty due to Malnutrition

Widely used frailty measure is the Phenotype model but because of its complexity its use is impractical. Hence, Short Physical Performance Battery (SPPB) can also be used as a frailty measuring tool [13]. SPPB has three tests included in it [16]:

- Gait Speed measured by observing the time taken to walk 4m distance.
- Lower Limb Strength measured by observing the time taken by an individual to rise 5 times from a chair.
- Balance (to stand up for 10 seconds, in 3 different positions, side by side, semi- tandem and tandem)

The complete scoring was out of 12, so according to the scores individuals were categorized into 4 groups as stated in table 3. SPPB has shown great results in identifying frail individuals, it is a reliable, valid and responsive frailty measuring tool, as it measures both, the physical activity and the physical performance of an individual [16].

Table 2.

Using SSPB tool to identify frail individuals.

SCORING out of 12	CATEGORIES
Less than 4 points	Dependent
4-6 points	Frail
7-9 points	Pre-frail
More than 9 points	Robust

As mentioned earlier, there are a variety of factors that influences the development of frailty in an individual. Using the SPPB measuring tool, it can be found that nutrient intake can also be an additional factor because of which frailty can be developed. In order to stay healthy one must have an adequate intake of nutrients because, being at risk of malnutrition increases the likelihood of becoming frail [13]. Differences in nutrient intake could be seen between Frail, Pre-frail and robust individuals. According to SPPB Frail and Pre-frail individuals showed less intake of Vitamin-D, Protein and PUFA n-3 [13]. All these nutrients play a vital role in our body. A low nutritional intake, mainly proteins and some micronutrients, favors the deterioration of the immune response [1], therefore there intake must be increased in frail individuals and also in malnutrition people in order to prevent frailty.

Frailty Assessment Tools

Due to advancement in technology there has been a significant drop in the mortality rates [2]. The cons of this advancement, is that the occurrence of chronic diseases has risen, whereas the cognitive functioning has degraded [2]. Therefore, identification of Frail individuals has become even more important. This identification process is supposed to be quick, reliable and easy. Hence, from this perspective, the two models mentioned above may be impractical. So, to overcome this obstacle, a new frailty tool was developed called the Frail Scale which simply consisted of 5 yes/no questions which further were related to Fatigue, resistance, inability to walk

a certain distance, weight loss and illness. This tool has proven to estimate frailty, mortality rates and various preventive measures among old adults [2].

There are several other assessment tools that have been developed which will help the clinicians to distinguish between beneficial and harmful interventions, for instance [1, 2, 7, 17, 18]

Clinical Frailty Scale, Edmonton Frail Scale, Frail Scale, Inter-Frail, Prisma-7, Sherbrooke Postal Questionnaire, Short Physical Performance Battery, Study of Osteoporotic Fractures Index, Liver Frailty Index, John Hopkins Frailty Indicator, Tilburg Frailty Indicator, Rockwood Frailty Index, and Carolina Frailty Index.

Comprehensive Geriatric Assessment (CGA) is one of the best ways to identify frailty [19]. It evaluates various domains like, medical, social, psychological and the body functions which help in providing the information regarding treatments and interventions for frail individuals. Since CGA identifies the impairments in an individual, the individual with higher number of impairments will be considered frail [19].

Although, various models and assessment tools for identifying frailty have been developed, but none of the tools, give a proper description regarding the cure or treatment. But according to the analysis of CGA, four treatments can be efficient for frail individuals, for instance [19]: Exercise, Caloric and Protein intake diet, Vitamin D intake &Reduction in Polypharmacy.

Still more research and study needs to be conducted on the topic Frailty, so that adequate amount of knowledge is gained for finding out the right treatments, which will help the old adults to have a healthy ageing and stay independent for a little longer [2].

Frailty measures for young adults

With age the prevalence of frailty increases, but there are several vulnerable groups whose mean age is approximately around 60 years and they, due to some chronic diseases are likely to become frail [7]. There are several tools and models developed in order to measure frailty in old adults, but these tools are quite challenging because of which clinicians face difficulty using them. Every developed frailty measure has its validity checked. So, the validity of a frailty measure is made sure by [7]: predictive validity& criterion validity,

Hence, according to all the developed measures of estimating frailty, there are no tools specifically designed to measure frailty in young adults of <60 years. However, some of the models and tools used for measuring frailty in old adults can be used to measure frailty in young adults as well. Some of the models and tools that meet the predictive and criterion validity are [7], the frailty index, phenotype measures, frail scale, Liver frailty Index and the Short Physical Performance Battery [7]. Still, more study and research needs to be done in order to prove that these tools are apt for measuring frailty in young individuals [7].

Biomarkers of Frailty

Inflammation is a defense mechanism taken up by the immune system of the body to fight unwanted antigens. However, in the later life, low level of inflammation begins even in the absence of a certain infection or disease which is referred to as inflamm-ageing [20]. With the help of the two models, namely phenotype and the cumulative deficit model, it has been assessed that frailty is closely linked to inflammation. Two important

inflammatory biomarkers identified are [20]: C reactive Protein (CRP) &Fibrinogen.

Both are blood based plasma proteins which increases in response to cytokines like IL-6 and systemic inflammation, respectively. Frail and pre- frail individuals showed higher quantity of these two biomarkers. According to the two models, FI score suggested that only fibrinogen maybe involved while for phenotype model both biomarkers were involved in developing frailty. Along with these biomarkers, blood lymphocyte level is also associated with frailty [1]. Immuno-senescence is thought to be involved in the development of chronic diseases which are related to frailty. Due to this immuno-senescence rise in inflammatory cells can be seen, i.e. excessive release of cytokines which further leads to less cell proliferation and resistance to apoptosis [1]. In old adults the number of Natural killer cells is increased while the CD4+ and CD8+ T lymphocyte is decreased. Hence, it was stated that, low level of T lymphocyte count is associated with high risk of frailty.

Frailty in Covid-19

Covid-19, a severe infectious disease caused by the most recently discovered corona virus. It emerged in December 2019 and caused a pandemic of respiratory illness. It has caused millions of deaths around the world along with various lasting health problems. Frail individuals have suffered an even extreme severity of Covid-19 [11]. Majorly, the frail individuals were more seriously harmed due to the cytokine storm, which reduces the immunological capability to function. Also, some similarity can be observed in Frail and Covid-19 diagnosed individuals, i.e. both the patients showed an increase in similar Cluster of Differentiation molecules, CD4, CD8, CD20, CD38 [11]. All the patients of Covid-19 showed frailty as common syndrome. Hence, frailty has been associated with worse prognosis following COVID-19 infection [12].

Old adults view on Frailty:

An interpretive descriptive qualitative study was conducted by Archibald and colleagues, in order to find out how old adults perceive of frailty. The participants were associated to the community and residential groups both belonging to very frail, frail, pre-frail and robust categories [21]. For the participants from the community group, a questionnaire was asked which consisted of 5 questions related to [21]: Aerobic Capacity, Weight loss, Resistance, Fatigue and Illness.

Based on this, the score 0 was indicative of robust individual, score of 1-2 indicates a pre-frail individual and a score of 3-5 is indicative of a frail individual [21].Degree of frailty for residential group was measured using the Frail-NH Scale, which consisted of 7 distinct components [21]: Fatigue, Resistance, Ambulation, Inconsistence, Weight Loss, and Nutritional Approach & Help with Dressing. The total scoring was out of 14; therefore, individuals with score of 2-5 were considered Frail whereas score of 7-9 indicates a very frail individual. Along with this analysis, the sample was also asked about describing frailty. As a result, the sample described Frailty in three different ways [21]:

1) **The old and Frail** - individuals who are skinny, slow moving, hunched over, dependent on others for mobility.
2) **Frailty at any age** - according to the sample, frailty does not occur at a particular age, instead people can be frail all their lives, due to a combination of mental and physical frailty.
3) **Frailty as a loss independence** - Frailty related to what a person's ability is without being dependent on others.

Also, several participants resisted from identifying themselves as Frail individuals [21]. By majority of the individuals, the term frailty was seen negatively, and little correlation was seen between frailty assessments and whether individuals identified themselves as frail [21].

Conclusion

In this modern era timeline, frailty has become very common not just for old individuals, but also for young adults and sometimes even children. Despite the development of various assessments, tools and interventions there still needs to be more research conducted on this field of gerontology to find proper interventions for different group of individuals. Separate tests should be developed to help in the prognosis of frailty in young group of individuals. It is not just ageing that leads to frailty, but several other factors have been discussed which can lead to the onset of frailty. The diagnosis of this dynamic syndrome can cause the development of various other secondary diseases which can be a reason of death or sometimes even loss of independency. It has shown adverse conditions on population that suffered from the Covid-19 pandemic. Hence, more study is required in order to understand the role of frailty in pandemics and various other diseases that can lead to worsening of the situation.

References

1. Navarro- Martínez, R., & Cauli, O. (2021). Lymphocytes as a Biomarker of Frailty Syndrome: A Scoping Review. Diseases, 9(3), 53.
2. Kojima, G., Liljas, A., & Iliffe, S. (2019). Frailty syndrome: implications and challenges for health care policy. Risk management and healthcare policy, 12, 23-30.
3. Sathyan, S., & Verghese, J. (2020). Genetics of frailty: A longevity perspective. Translational research: the journal of laboratory and clinical medicine, 221, 83-96.
4. Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. Lancet, 381(9868), 752-762.
5. Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W. J., Burke, G., & McBurnie, M. A. (2001). Frailty in Older Adults: evidence for a Phenotype. Journal of Gerontology: Medical Sciences, 56A(3), M146-M156.

6. van Oostrom, S. H., van der A, D. L., Rietman, M. L., Picavet, H., Lette, M., Verschuren, W., de Bruin, S. R., & Spijkerman, A. (2017). A four-domain approach of frailty explored in the Doetinchem Cohort Study. BMC geriatrics, 17(1), 196.
7. Spiers, G, F., Kunonga, T, P., Hall, A., et al. (2021). Measuring frailty in younger populations: a rapid review of evidence. BMJ Open, 11(3), e047051.
8. Angioni, D., Macaron, T., Takeda, C. et al. (2020). Can We Distinguish Age-Related Frailty from Frailty Related to Diseases? Data from the MAPT Study. The Journal of Nutrition, Health and Ageing, 24, 1144-1151.
9. Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D. B., McDowell, I., & Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. CMAJ: Canadian Medical Association journal = journal de l'Association medicale canadienne, 173(5), 489-495.
10. Álvarez-Satta, M., Berna-Erro, A., Carrasco-Garcia, E., Alberro, A., Saenz-Antoñanzas, A., Vergara, I., Otaegui, D., & Matheu, A. (2020). Relevance of oxidative stress and inflammation in frailty based on human studies and mouse models. Aging, 12(10), 9982-9999.
11. Hussien, H., Nastasa, A., Apetrii, M., Nistor, I., Petrovic, M., & Covic, A. (2021). Different aspects of frailty and COVID-19: points to consider in the current pandemic and future ones. BMC geriatrics, 21(5), 389.
12. Petermann-Rocha, F., Hanlon, P., Gray, S. R., Welsh, P., Gill, J., Foster, H., Katikireddi, S. V., Lyall, D., Mackay, D. F., O'Donnell, C. A., Sattar, N., Nicholl, B. I., Pell, J. P., Jani, B. D., Ho, F. K., Mair, F. S., & Celis-Morales, C. (2020). Comparison of two different frailty measurements and risk of hospitalisation or death from COVID-19: findings from UK Biobank. BMC medicine, 18(1), 355.
13. Moradell, A., Fernández-García, Á. I., Navarrete-Villanueva, D., Sagarra-Romero, L., Gesteiro, E., Pérez-Gómez, J., Rodríguez-Gómez, I., Ara, I., Casajús, J. A., Vicente-Rodríguez, G., & Gómez-Cabello, A. (2021). Functional Frailty, Dietary Intake, and Risk of Malnutrition. Are Nutrients Involved in Muscle Synthesis the Key for Frailty Prevention?. Nutrients, 13(4), 1231.
14. Gale, C. R., Mõttus, R., Deary, I. J., Cooper, C., & Sayer, A. A. (2017). Personality and Risk of Frailty: the English Longitudinal Study of Ageing. Annals of behavioral medicine: a publication of the Society of Behavioral Medicine, 51(1), 128-136.
15. Niederstrasser, N. G., Rogers, N. T., & Bandelow, S. (2019). Determinants of frailty development and progression using a multidimensional frailty index: Evidence from the English Longitudinal Study of Ageing. PloS one, 14(10), e0223799.
16. Treacy, D., & Hassett, L. (2018). The Short Physical Performance Battery. Journal of Physiotherapy, 64(1), 61.
17. Church, S., Rogers, E., Rockwood, K., Theou, O. (2020). A scoping review of the Clinical Frailty Scale. BMC geriatrics, 20(1), 393.

18. Kendhapedi, K. K., & Devasenapathy, N. (2019). Prevalence and factors associated with frailty among community-dwelling older people in rural Thanjavur district of South India: a cross-sectional study. BMJ Open, 9(10), e032904.
19. Lee, H., Lee, E., & Jang, I. Y. (2020). Frailty and Comprehensive Geriatric Assessment. Journal of Korean medical science, 35(3), e16.
20. Welstead, M., Muniz-Terrera, G., Russ, T. C., Corley, J., Taylor, A. M., Gale, C. R., & Luciano, M. (2020). Inflammation as a risk factor for the development of frailty in the Lothian Birth Cohort 1936. Experimental Gerontology, 139, 111055.
21. Archibald, M., Lawless, M., Ambagtsheer, R. C., et al. (2020). Older adults' understandings and perspectives on frailty in community and residential aged care: an interpretive description. BMJ Open, 10(3), e035339.