

Risk factors for the development and progression of frailty

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
Older age	Although the prevalence of frailty varies widely between studies depending on the definition of frailty used, the evidence shows that frailty increases steadily with age.	Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community dwelling older persons: a systematic review. <i>J Am Geriatr Soc.</i> 2012; 60(8):1487–92. [PubMed: 22881367].	
	The proportion of people living with frailty rises exponentially with increasing age, from 6.5% in those aged 60–69 years to 65% in those aged 90 or over.	Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. <i>Age & Ageing</i> 2015; 44(1): 162-165. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4311180/pdf/afu148.pdf	The English Longitudinal Study of Ageing (ELSA) provides high quality longitudinal data and was set up to document the experience of growing old in England in the 21st century. Gale et al defined physical frailty as the presence of three or more of the Fried Phenotype criteria. ⁱ
	According to a 2012 systematic review of studies in developed countries approximately one in 10 independently living adults aged 65 and older is frail. The prevalence of frailty by age group was estimated as follows: 65-69 years: 4%; 70-74 years: 7%; 75-79 years: 9%; 80-84 years: 16%; >85 years: 26%.	Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community dwelling older persons: a systematic review. <i>J Am Geriatr Soc.</i> 2012; 60(8):1487–92. [PubMed: 22881367].	This systematic review included studies from the UK, a number of other European countries, United States, Canada, Australia and Taiwan. These findings were calculated across 4 studies including 8,869 community-dwelling participants.
	Around 3% of the population aged 65+ in England live with severe frailty, 12% with	Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, Mohammed MA, Parry J, Marshall T. Development and validation of an electronic	This study used primary care electronic health record data on 931,541 patients aged 65–95, contained in the ResearchOne and The Health Improvement Network

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	<p>moderate frailty and 35% with mild frailty.</p>	<p>frailty index using routine primary care electronic health record data. Age Ageing. 2016 May;45(3):353-60. doi: 10.1093/ageing/afw039. Epub 2016 Mar 3. Erratum in: Age Ageing. 2017 Jan 17;; PMID: 26944937; PMCID: PMC4846793. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4846793/</p>	<p>(THIN) databases from 14 October 2008 to 14 October 2013 in order to develop and validate an electronic frailty index (eFI). Patients with an eFI score of 0–0.12 were defined as fit; >0.12–0.24 as having mild frailty; >0.24–0.36 as moderate frailty and >0.36 as severe frailty.</p>
	<p>Frailty is more prevalent in nursing home patients than in community-dwelling people in the same age groups.</p> <p>A systematic review of studies amongst nursing home patients aged 60 years or older estimated aggregated overall prevalence of frailty at 52.3% (95% CI: 37.9% - 66.5%) and prefrailty at 40.2% (28.9%- 52.1%).</p> <p>Overall prevalence of frailty by age group was estimated as follows: 60-69: 49.0% 70-79: 45.5% 80+: 61.8%</p>	<p>Kojima G. Prevalence of Frailty in Nursing Homes: A Systematic Review and Meta-Analysis. J Am Med Dir Assoc. 2015;16(11):940-945. doi:10.1016/j.jamda.2015.06.025</p> <p>Full text provided by author.</p>	<p>The studies, carried out in 7 different counties (but not UK), included relatively small numbers of participants.</p> <p>The overall prevalence of frailty was calculated based on 9 studies with a total of 1,373 nursing home patients.</p> <p>The overall prevalence of prefrailty was calculated based on 7 studies with a total of 1,163 nursing home patients.</p> <p>Only studies which used validated criteria or definitions of frailty were included in the Systematic Review, but the criteria/definition was not the same across all the included studies.</p>
Female Gender	<p>Frailty occurs more frequently in women than in men (16% versus 12%), according to one study based on data from the English Longitudinal Study of Ageing.</p> <p>A systematic review of studies amongst community-dwelling adults aged 65 and above reported a lower prevalence for both women (9.6%) and men (5.2%) but this review included data from a number of</p>	<p>Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. Age & Ageing 2015; 44(1): 162-165. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4311180/pdf/afu148.pdf</p> <p>Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community dwelling older persons: a systematic review. J Am Geriatr Soc. 2012; 60(8):1487–92. [PubMed: 22881367].</p>	<p>The data for this study was collected from 2002/3 to 2008/9 on 5,450 individuals aged 60 years and older participating in the English Longitudinal Study of Ageing.</p> <p>Gale et al defined physical frailty as the presence of three or more of the Fried Phenotype criteria.ⁱ</p> <p>This systematic review included studies from the UK, a number of other European countries, United States, Canada, Australia and Taiwan.</p> <p>This finding was calculated across 11 studies including 40,342 community-dwelling participants aged 65 and</p>

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	countries in addition to the UK.		older. The majority of the studies from which these estimates are derived defined frailty using the Fried Phenotype criteria ⁱ , although a small number used a definition that included social and psychological aspects.
	<p>Being female was reported to be a predictor of both frailty development and progression in another study which used data from the English Longitudinal Study of Ageing. Females were 28% more likely to develop frailty compared to males (Hazard Ratio (HR)=1.28, 95% Confidence Interval (CI): 1.17–1.40).</p> <p>Female participants were more frail than male participants at the end of the 12-year follow-up period, even after taking account of baseline frailty.</p>	<p>Niederstrasser NG, Rogers NT, 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. https://doi.org/10.1371/journal.pone.0223799</p>	<p>Data was collected from 2004/5 to 2016/17, on a representative sample of 7,240 people aged 50 and above in The English Longitudinal Study of Ageing (ELSA).</p> <p>Niederstrasser NG et al measured frailty using a 56-item Frailty Index comprised of self-reported health conditions, disabilities, cognitive function, hearing, eyesight, depressive symptoms and ability to carry out activities of daily living. Frailty progression was observed over a period of up to 12 years (2004/5 to 2016/17).</p>
	<p>A systematic review of studies amongst nursing home patients aged 60 years or older estimated the prevalence of frailty for men and women as follows:</p> <p>Women: 59.0% (95% CI: 41.4% - 75.4%) Men: 45.6% (95% CI: 34.1% - 57.4%)</p>	<p>Kojima G. Prevalence of Frailty in Nursing Homes: A Systematic Review and Meta-Analysis. J Am Med Dir Assoc. 2015;16(11):940-945. doi:10.1016/j.jamda.2015.06.025</p> <p>Full text provided by author.</p>	<p>The studies, carried out in 7 different countries (but not UK), included relatively small numbers of participants. The prevalence of frailty in women was calculated based on 8 studies with a total of 617 female nursing home patients. The prevalence in men was based on 9 studies with a total of 756 male nursing home patients.</p> <p>Only studies which used validated criteria or definitions of frailty were included in the systematic review, but the criteria/definition was not the same across all the included studies.</p>
Marital Status	The literature on the association between marital status and frailty seems to largely corroborate the extensive literature		

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	<p>demonstrating the association between longevity and better health with married status, particularly for men.</p>		
	<p>A very recent systematic review and meta-analyses showed that:</p> <ul style="list-style-type: none"> • Unmarried individuals were almost twice more likely to be frail than married individuals (pooled Odds Ratio (OR) =1.88, 95% CI: 1.70-2.07). • Widows and widowers were twice as likely to be frail compared with those who were married (12 studies: pooled Odds Ratio (OR)=2.17, 95% CI: 1.89-2.50); • Those who were divorced or separated were almost twice as likely to be frail compared with those who were married (10 studies: pooled OR=1.86, 95% CI: 1.47-2.35); • Those who never married were about a third more likely to be frail compared with those who were married (7 studies: pooled OR=1.37, 95% CI: 1.06-1.79). <p>Risks of frailty in the unmarried compared with the married were not statistically different between women and men.</p>	<p>Kojima G, Walters K, Iliffe S, Taniguchi Y, Tamiya N. Marital Status and Risk of Physical Frailty: A Systematic Review and Meta-analysis. <i>J Am Med Dir Assoc.</i> 2020;21(3):322-330. doi:10.1016/j.jamda.2019.09.017</p> <p>Full text obtained from lead author.</p>	<p>The 35 cross-sectional studies included in the review, undertaken across 21 different countries, included 80,754 community-dwelling older people with mean age ≥60 years.</p> <p>Frailty was defined using Fried phenotype criteria.¹</p>
	<p>An Italian study reported that marital status seems to significantly influence the onset of frailty, with some gender-specific differences. Unmarried and widowed men were at a higher risk of becoming frail, while widowed women were significantly less likely to become frail than married women.</p>	<p>Trevisan C, Veronese N, Maggi S, et al. Marital Status and Frailty in Older People: Gender Differences in the Progetto Veneto Anziani Longitudinal Study. <i>J Womens Health (Larchmt).</i> 2016;25(6):630-637. doi:10.1089/jwh.2015.5592</p> <p>Full text obtained from lead author.</p>	<p>The analysis included 1,887 people older than 65 years participating in the Progetto Veneto Anziani (Pro.V.A.) study and with no evidence of frailty at baseline.</p> <p>The incidence of frailty after 4.4 years was measured as the presence of at least three of the Fried criteria.¹</p>

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	<ul style="list-style-type: none"> Men who had never married were almost 4 times more likely to become frail (OR = 3.84, 95% CI: 2.76-5.35) compared to married men; however, there was no significant association between never having been married and frailty risk among women. Although men who were widowed were 43% more likely to develop frailty than married men (OR = 1.43, 95% CI: 1.06-1.95), women who were widowed were 33% less likely to develop frailty than married women (OR=0.77, 95% CI: 0.66-0.91). 		
Race / ethnicity	<p>A study which looked at the prevalence of frailty by ethnic groups in a sample of older people living in London reported that the highest prevalence of frailty was in South Asians, with Bangladeshis having the highest prevalence (32.9%), followed by Pakistanis (28.6%) and Indians (21.6%). The prevalence in the White population was 17.2% and in the Black ethnic group it was observed to be 14%.</p> <p>Some research points to higher rates of frailty among Black and Minority Ethnic populations being caused by socioeconomic factors, such as income or education (see study below – Szanton et al)</p>	<p>Pradhananga S, Regmi K, Razzaq N, Etefaghian A, Dey A, and Hewson D. (2019). Ethnic differences in the prevalence of frailty in the United Kingdom assessed using the electronic Frailty Index. AGING MEDICINE. 2. 10.1002/agm2.12083.</p> <p>https://www.researchgate.net/publication/335802452_Ethnic_differences_in_the_prevalence_of_frailty_in_the_United_Kingdom_assessed_using_the_electronic_Frailty_Index</p>	<p>Data on 13,510 people aged 65 years and over were extracted from the database of a network of general practitioners, covering 16 clinical commissioning groups in London.</p> <p>Frailty was determined using the electronic Frailty Index (eFI), which was automatically calculated using EHR data. Patients with moderate and severe frailty were categorised as frail.</p>
	Race was not associated with frailty after education was taken into account in a US study.	Szanton SL, Seplaki CL, Thorpe RJ Jr, Allen JK, Fried LP. Socioeconomic status is associated with frailty: the Women's Health and Aging Studies. J	Data was analysed on 727 women aged 70-79 years participating in the Women's Health and Aging Studies. Frailty was defined using Fried phenotype

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		<p>Epidemiol Community Health. 2010;64(1):63-67. doi:10.1136/jech.2008.078428 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2856660/pdf/nihms-183799.pdf</p>	<p>criteria¹ and participants were considered frail if they were positive for three or more of the criteria.</p>
<p>Low Income / socio-economic deprivation/ manual or blue collar occupations</p>	<p>The research evidence overwhelmingly points to frailty being most prevalent at a population level in individuals with low socioeconomic status and least prevalent in those with least socioeconomic disadvantage. The extent of the association varies between settings which is to be expected given the different ways in which frailty and socioeconomic status are measured in studies.</p> <p>The prevalence of frailty increased with increasing levels of deprivation in a study using data from the UK Biobank on nearly half a million middle-aged and older-aged people.</p> <ul style="list-style-type: none"> • A higher proportion of frail participants were relatively socioeconomically deprived (42% of frail participants in the most deprived quintile vs 16% in the non-frail group). • Compared to those in the least deprived fifth of areas (quintile), those in most deprived quintile had an almost 4-fold increase in odds of frailty (OR= 3.71, 95% CI: 3.49–3.94). <p>Findings from the Whitehall II study show a socioeconomic gradient in frailty at ages 55–85 years, defined on the basis of occupation at age 50 years.</p>	<p>Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. Lancet Public Health. 2018;3(7):e323-e332. doi:10.1016/S2468-2667(18)30091-4 https://www.thelancet.com/pdfs/journals/lanpub/PIIS2468-2667(18)30091-4.pdf</p> <p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. Lancet Public Health</p>	<p>The study included 493,737 participants aged 37–73 years from across England, Scotland, and Wales. Median follow-up duration was 7 years. Frailty was assessed using Fried’s frailty phenotype criteria.ⁱ</p> <p>Socioeconomic deprivation was assessed using Townsend scores which take into account percentage unemployment, percentage car ownership, percentage home ownership, and household overcrowding.</p> <p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, the</p>

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	<p>Low employment grade at age 50 years was associated with 2.60 times higher odds of later frailty (95% CI: 1.89–3.58). Intermediate employment grade was associated with 1.48 (95% CI: 1.16-1.88) times higher odds of later frailty.</p> <p>Participants who had long-term conditions or lifestyle risk factors for long-term conditions at the age of 50 years were more likely to develop frailty in later life, and these characteristics accounted for more than a third of the socioeconomic inequalities in frailty.</p> <p>The five most important contributing factors that individually accounted for 10% or more of the socioeconomic gradient in frailty were physical activity level, lung function measured by spirometry, body-mass index category, serum IL-6 and C-reactive protein concentrations.</p>	<p>2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>occupational class of each participant was based on the current or most recent Civil Service employment grade at age 45–55 years. Employment grade characterised classes of individuals with similar income, pension rights, job security, and work skills, and was divided into high, intermediate, and low groups.</p> <p>Frailty (defined according to the Fried phenotype ¹) was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>
	<p>Higher wealth was associated with lower frailty incidence and less frailty progression in a study that used data from The English Longitudinal Study of Ageing (ELSA). Compared to those in the lowest wealth quintile, those in the highest quintile had a 44% lower risk of developing frailty (HR=0.56, CI: 0.48–0.65). Participants in higher wealth quintiles were also significantly less frail compared to those in the lowest quintile at the end of the 12-year follow-up period.</p>	<p>Niederstrasser NG, Rogers NT, 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. https://doi.org/10.1371/journal.pone.0223799</p>	<p>The analysis was carried out on data collected from 2004/5 to 2016/17, on a representative sample of 7,240 people aged 50 and above participating in The English Longitudinal Study of Ageing (ELSA).</p> <p>Niederstrasser NG et al measured frailty using a 56-item Frailty Index comprised of self-reported health conditions, disabilities, cognitive function, hearing, eyesight, depressive symptoms and ability to carry out activities of daily living. Frailty progression was observed over a period of up to 12 years (2004/5 to 2016/17).</p> <p>Wealth was determined by dividing participants into quintiles based on their net wealth. Net wealth was</p>

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			<p>quantified as the net sums of housing wealth, physical wealth (including additional property wealth, wealth related to business and other physical assets) and financial wealth.</p>
	<p>A large study in adults aged 50-85 years across 14 higher income countries in Europe (excluding UK) and six lower income countries demonstrated a strong inverse gradient, with lower wealth showing higher levels of frailty and this pattern was consistent across the vast majority of higher and lower income countries in the study.</p>	<p>Harttgen K, Kowal P, Strulik H, Chatterji S, Vollmer S (2013) Patterns of Frailty in Older Adults: Comparing Results from Higher and Lower Income Countries Using the Survey of Health, Ageing and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE). PLoS ONE 8(10): e75847. doi:10.1371/journal.pone.0075847 https://pubmed.ncbi.nlm.nih.gov/24204581/</p>	<p>The two multi-country studies used were: the Study on Health, Ageing and Retirement in Europe (SHARE) and the World Health Organisation's Study on Global AGEing and Adult Health (SAGE). Data from nationally representative samples of community dwelling adults aged 50-85 years were analysed.</p> <p>A deficits count approach was used to construct a frailty index using 39 variables from SHARE and 40 variables from the SAGE dataset.</p>
	<p>A Systematic Review reported a likely association between occupational conditions and frailty and noted that intrinsically harder, manual, or blue-collar occupations are possible contributors to the development of frailty and its severity. The authors concluded that it seems quite complex to extrapolate whether the observed social gradient in frailty is related to the profession itself or to financial circumstances.</p>	<p>Iavicoli I, Leso V, Cesari M. The contribution of occupational factors on frailty. Arch Gerontol Geriatr. 2018;75:51-58. doi:10.1016/j.archger.2017.11.010 https://www.sciencedirect.com/science/article/pii/S0167494317303321?via%3Dihub</p>	<p>9 studies were included in the Systematic Review.</p>
	<p>There is a strong link between socioeconomic deprivation and multimorbidity. Multimorbidity seems to occur 10–15 years earlier in people living in the most deprived areas of the UK than it does in those living in the most affluent areas.</p>	<p>National Guideline Centre (UK). Multimorbidity: Assessment, Prioritisation and Management of Care for People with Commonly Occurring Multimorbidity. London: National Institute for Health and Care Excellence (UK); September 2016. https://pubmed.ncbi.nlm.nih.gov/27683922/</p>	
<p>Poor housing</p>	<p>Poor quality housing may be a risk factor for</p>		

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	<p>frailty, although the evidence appears to be very limited.</p> <p>A Spanish study demonstrated an association between poor housing conditions and frailty.</p> <ul style="list-style-type: none"> 65% of the frail, compared to 52% of the non-frail, lived in homes with ≥ 1 poor condition. Those who lived in homes with ≥ 1 poor condition had a 2-fold increased likelihood of being frail compared to those with no poor conditions (OR = 2.02, 95% CI: 1.09–3.75). <p>A study based on data collected in the English Longitudinal Study of Ageing, showed that adults aged ≥ 50 years who resided in cold homes had worse handgrip strength (a component of frailty) than their counterparts living in homes with measured temperatures $\geq 18^\circ\text{C}$.</p>	<p>Bibiana Pérez-Hernández, Esther Lopez-García, Auxiliadora Graciani, José Luis Ayuso-Mateos, Fernando Rodríguez-Artalejo, Esther García-Esquinas, Housing conditions and risk of physical function limitations: a prospective study of community-dwelling older adults, <i>Journal of Public Health</i>, Volume 40, Issue 3, September 2018, Pages e252–e259, https://doi.org/10.1093/pubmed/fdy004</p> <p>Shiue I. Cold homes are associated with poor biomarkers and less blood pressure check-up: English Longitudinal Study of Ageing, 2012-2013. <i>Environ Sci Pollut Res Int.</i> 2016;23(7):7055-7059. doi:10.1007/s11356-016-6235-y https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4820485/</p>	<p>Data were analysed on 1602 adults aged ≥ 60 years participating in the Seniors-ENRICA (Study on Nutrition and Cardiovascular Risk in Spain) cohort. Frailty was assessed with the Fried¹ frailty phenotype criteria and individuals were considered frail if they met ≥ 3 of the 5 criteria. To assess housing condition the following questions were asked: (i) Do you live in an apartment building with no elevator? (ii) Do you have piped hot water at home? (iii) Do you have a heating system at home? (iv) Do you frequently feel cold at home? (v) Do you have a bathtub or shower? (vi) Do you have a refrigerator? (vii) Do you have a washing machine? (viii) Do you have a landline at home? (ix) Do you have a room of your own? A score of 1 was assigned for the absence of each of these services or for feeling cold; and a scale ranging from 0 to 9 was constructed by summing the scores across the 9 items. Individuals were classified into two categories: those with no poor conditions and those with ≥ 1 poor condition.</p> <p>The study included 7,740 adults aged ≥ 50 years participating in the English Longitudinal Study of Ageing, 2012–2013. Cold homes were defined as a room temperature below 18°C, as recommended by the World Health Organization. Room temperature was measured once in the room when various biomarkers were being measured.</p>
Low level of education	Research shows an inverse relationship between education level and frailty		

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	incidence (i.e. lower levels of education associated with higher levels of frailty).		
	A large study in adults aged 50-85 years across 14 higher income countries in Europe (excluding UK) and six lower income countries demonstrated a strong inverse education gradient, with lower levels of education showing higher levels of frailty and this pattern was consistent across the vast majority of higher and lower income countries.	Harttgen K, Kowal P, Strulik H, Chatterji S, Vollmer S (2013) Patterns of Frailty in Older Adults: Comparing Results from Higher and Lower Income Countries Using the Survey of Health, Ageing and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE). PLoS ONE 8(10): e75847. doi:10.1371/journal.pone.0075847 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3812225/	The two multi-country studies used were: the Study on Health, Ageing and Retirement in Europe (SHARE) and the World Health Organisation's Study on Global AGEing and Adult Health (SAGE). Data from nationally representative samples of community dwelling adults aged 50-85 years were analysed. A deficits count approach was used to construct a frailty index using 39 variables from SHARE and 40 variables from the SAGE dataset.
	Women with less than 12 years of education had a 3-fold greater odds of frailty (OR=3.01, 95% CI 1.99 - 4.54) compared to their more educated counterparts (more than 12 years of education) in a US study.	Szanton SL, Seplaki CL, Thorpe RJ Jr, Allen JK, Fried LP. Socioeconomic status is associated with frailty: the Women's Health and Aging Studies. J Epidemiol Community Health. 2010;64(1):63-67. doi:10.1136/jech.2008.078428 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2856660/pdf/nihms-183799.pdf	This study analysed data from a US study - Women's Health and Aging Studies - on 727 community-dwelling women aged 70-79 years. Frailty status was assessed using the Fried phenotype definition. ⁱ
	Older adults with a low educational level had almost a 3-fold increased odds of being frail compared with those with a high educational level (OR 2.94; 95% CI 1.84-4.71) in a 13-year study in the Netherlands. At baseline 14.8% of those with a low level of education were frail, higher than the 8.8% with a medium level of education and the 7.3% with a high level of education.	Hoogendijk EO, van Hout HP, Heymans MW, et al. Explaining the association between educational level and frailty in older adults: results from a 13-year longitudinal study in the Netherlands [published correction appears in Ann Epidemiol. 2014 Aug;24(8):628]. Ann Epidemiol. 2014;24(7):538-44.e2. doi:10.1016/j.annepidem.2014.05.002	The data used for this study was collected between 1995-96 and 2008-09 in the Longitudinal Aging Study Amsterdam. It included 1,205 participants aged 65 years and above at baseline (1995-96). Frailty was assessed with the criteria based on the Fried frailty phenotype definition. ⁱ At baseline, respondents were asked to state their highest level of education on a nine-category scale and grouped as follows: <ul style="list-style-type: none"> • Low (elementary school or less); • Medium (lower vocational or general intermediate education); and • High (intermediate vocational education, general

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			<p>secondary school, higher vocational education, college, or university).</p> <ul style="list-style-type: none"> •
	<p>A large European Study reported that in all of the countries included, frailty worsening was more prevalent among lower as compared with higher educated persons over a 2-year follow-up period (24% of those with <=10 years of education vs 19.2% of those with >10 years).</p>	<p>Etman A, Kamphuis CB, van der Cammen TJ, Burdorf A, van Lenthe FJ. Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? Eur J Public Health. 2015;25(2):345–50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447813/</p>	<p>Longitudinal data of 14,082 European community-dwelling persons aged 55 years and older participating in the Survey on Health, Ageing, and Retirement in Europe (SHARE) in 2004 and 2006, were used in this study. Physical frailty was based on the Fried Phenotype criteria,ⁱ but self-reported.</p>
Loneliness / Social isolation/ poor social support	<p>Loneliness appears to be an important determinant of frailty. Loneliness and social isolation, although related, are distinct concepts. Social isolation can be defined objectively using criteria such as having few contacts, and little involvement in social activities whereas loneliness is a subjective feeling of dissatisfaction with one’s social relationships. Research appears to show loneliness to be a more important risk factor for frailty than social isolation.</p>		
	<p>A study which gathered the views of people aged 50+ for the Department for Health in 2017 found that the most commonly cited biggest issue for older people was loneliness (mentioned by 56%).</p>	<p>Health, Ageing and Support: survey of views of people aged 50 and over A study for the Department of Health, 2017. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/707582/Health_Ageing_and_Support_Survey_2017_-_Report.pdf</p>	
	<p>Older people who experience high levels of loneliness appear to be at increased risk of becoming physically frail, although the association may be bi-directional.</p>	<p>Catharine R Gale, Leo Westbury, Cyrus Cooper, Social isolation and loneliness as risk factors for the progression of frailty: the English Longitudinal Study of Ageing, Age and Ageing,</p>	<p>The analysis included 2,817 people aged ≥60 from the English Longitudinal Study of Ageing. Loneliness was assessed using the Revised UCLA</p>

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	<p>High levels of loneliness were associated with an increased likelihood of becoming physically frail or pre-frail in a study based on the English Longitudinal Study of Ageing (ELSA).</p> <p>Compared to people who had a low score for loneliness, those with a high score for loneliness were 74% (Relative Risk=1.74, 95% CI: 1.29-2.34) more likely to develop prefrailty and 85% (RR=1.85, 95% CI: 1.14-2.99) more likely to develop frailty around 4 years later. However, no association was observed between frailty as measured by the broader frailty index and loneliness.</p> <p>Men with high scores for social isolation had an increased risk of becoming physically frail that was of borderline significance, but no association between social isolation and frailty was found amongst women.</p>	<p>Volume 47, Issue 3, May 2018, Pages 392–397, https://doi.org/10.1093/ageing/afx188</p>	<p>loneliness scale which enquires about frequency of feeling left out, isolated, and lacking companionship. Scores range from 3 to 9 and were categorised as follows: low (3); average (4 or 5); and high (≥ 6).</p> <p>A social isolation score was derived from data on living alone, frequency of contact with friends, family and children, and participation in social organisations.</p> <p>Frailty was assessed using both the Fried phenotype of physical frailty and a frailty index.i</p>
	<p>Loneliness was found to be associated with a 19% higher risk of developing frailty (HR=1.19, CI: 1.16–1.22) in another study based on the English Longitudinal Study of Ageing (ELSA).</p> <p>Loneliness was also found to be a significant predictor of worsening frailty.</p> <p>Social isolation was not associated with the progression or development of frailty, perhaps confirming that loneliness and social isolation are distinct concepts.</p> <p>The researchers acknowledge that the</p>	<p>Niederstrasser NG, Rogers NT, 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. https://doi.org/10.1371/journal.pone.0223799</p>	<p>Niederstrasser NG et al measured frailty using a 56-item Frailty Index comprised of self-reported health conditions, disabilities, cognitive function, hearing, eyesight, depressive symptoms and ability to carry out activities of daily living. Frailty progression was observed over a period of up to 12 years (2004/5 to 2016/17).</p> <p>Loneliness was assessed using the Revised UCLA Loneliness Scale which yields scores between 3 and 9, with higher scores indicating greater loneliness. Social isolation was derived as follows: being unmarried or not living with a partner (scored as 1), less than monthly contact with other family, friends and children (each scored as 1), and non-participation</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	association between loneliness and frailty may be bi-directional, but state that it is more likely that loneliness precedes frailty.		in any social activities (scored as 1). Resultant scores ranged between 0 and 5, with higher scores indicating greater social isolation.
	A large European study showed that individuals that didn't participate in any social activities had a 18% increased odds of worsening frailty status (either from robust to prefrail/frail or from prefrail to frail), two years after baseline, compared to those that participated in one or more social activities (OR = 1.18, 95 % CI: 1.08–1.30).	Etman A, Kamphuis CB, van der Cammen TJ, Burdorf A, van Lenthe FJ. Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? Eur J Public Health. 2015;25(2):345–50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447813/	This study investigated associations between social participation ('none', 'one or more') at baseline and frailty status at two-year follow-up using a large cohort of 14,082 community-dwelling adults aged 55 years and older participating in the Survey on Health, Ageing, and Retirement in Europe (SHARE). Physical frailty was based on Fried Phenotype criteria, ⁱ but self-reported. Frailty states were based on the total number of criteria met: 'frail' (≥3 criteria), 'pre-frail' (1–2 criteria), 'non-frail' (0 criteria). Social participation was measured with participating in social activities over the last month, e.g. voluntary work, cared for a sick person, participation at sports club ('none', 'one or more').
	A very large US study - The Women's Health Initiative Observational Study - showed that living alone was associated with a 20% lower likelihood of becoming frail (OR=0.80, 95% CI: 0.72-0.88), and the authors concluded that this was presumably because the frailest lose the capability to live independently.	Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study [published correction appears in J Am Geriatr Soc. 2017 Jul;65(7):1631-1632]. J Am Geriatr Soc. 2005;53(8):1321-1330. doi:10.1111/j.1532-5415.2005.53405.x https://escholarship.org/uc/item/9rp764f5	The Women's Health Initiative Observational Study in the US followed 28,181 women aged 65–79 free of frailty at baseline for 3 years. Frailty was defined using Fried frailty phenotype criteria. ⁱ
	Another study, also using data from the English Longitudinal Study of Ageing, reported that poor social support (in terms of deficient emotional support and reflecting negative social interaction with family and friends) adversely influences the trajectory of physical frailty over time.	Ding, Y.Y., Kuha, J. & Murphy, M. Multidimensional predictors of physical frailty in older people: identifying how and for whom they exert their effects. Biogerontology 18, 237–252 (2017). https://doi.org/10.1007/s10522-017-9677-9	This study included 4,638 participants aged 65–89 years in 2004, and used data from 2004, 2008/9 and 2012/13.

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
Body weight / Waist-hip ratio	<p>In the majority of studies increased levels of frailty among those with high and very high BMIs have been observed. Abdominal adiposity seems to confer additional risk, with greater levels of frailty among those with high waist circumferences.</p> <p>The evidence for very low BMI being a risk factor for frailty is less convincing, although this has been reported in several studies.</p>		
	<p>Findings from the Whitehall II study show that both overweight and obesity at age 50, increase the risk of frailty in later life.</p> <p>Compared to those with normal weight, those who were overweight were 34% more likely to develop frailty (OR=1.34, 95% CI: 1.07–1.69) while the likelihood increased 3.5-fold for those who were obese (OR=3.52, 95% CI: 2.62-4.72).</p> <p>Being underweight was not found to be a predictor of frailty.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. <i>Lancet Public Health</i> 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, behavioural and biomedical risk factors were based on measurements at age 45–55 years. Frailty (defined according to the Fried phenotype)ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>
	<p>In a study using data from the UK Biobank on nearly half a million middle-aged and older-aged people, being underweight, overweight, or obese all appear to significantly increase the risk of frailty.</p> <p>52% of frail participants were obese vs 18% of non-frail participants.</p> <p>Compared to those with normal weight, individuals who were overweight had just over a 50% increase in odds of frailty (OR=1.51, 95% CI: 1.42-1.59), while those who were obese had over a 300% increase in</p>	<p>Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. <i>Lancet Public Health</i>. 2018;3(7):e323-e332. doi:10.1016/S2468-2667(18)30091-4 https://www.thelancet.com/pdfs/journals/lanpub/PIIS2468-2667(18)30091-4.pdf</p>	<p>The study included 493,737 participants aged 37–73 years from across England, Scotland, and Wales. Median follow-up duration was 7 years. Frailty was assessed using Fried Phenotype criteria.ⁱ</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	odds of frailty (OR= 4.10, 95% CI: 3.90-4.31). Being underweight increased the odds of frailty by almost 200% (OR=2.92, 95% CI: 2.41–3.53).		
	Being underweight, overweight, or obese were all reported to carry significantly higher odds of frailty than normal weight in a large US study. This study showed that underweight participants were at higher odds of developing frailty than those of normal weight (OR=1.65, 95% CI: 1.11-2.45), similar to the odds for overweight women (OR=1.92, 95% CI: 1.73-2.13). Obese women were almost 4 times as likely to become frail than those of normal weight (OR 3.95, 95% CI 3.50-4.47), a similar finding to the UK Biobank study, and only slightly above the effect observed in the Whitehall Study.	Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study [published correction appears in J Am Geriatr Soc. 2017 Jul;65(7):1631-1632]. J Am Geriatr Soc. 2005;53(8):1321-1330. doi:10.1111/j.1532-5415.2005.53405.x https://escholarship.org/uc/item/9rp764f5	The Women's Health Initiative Observational Study in the US followed 28,181 women aged 65–79 free of frailty at baseline for 3 years. Frailty was defined using Fried Phenotype criteria. ¹
	A US study found that the prevalence of obesity was significantly higher amongst those who were frail, compared to the non-frail (32.7% vs 22.8%).	Lee DR, Santo EC, Lo JC, Ritterman Weintraub ML, Patton M, Gordon NP. Understanding functional and social risk characteristics of frail older adults: a cross-sectional survey study. BMC Fam Pract. 2018;19(1):170. Published 2018 Oct 19. doi:10.1186/s12875-018-0851-1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6195739/	The analysis related to 4,551 adults ages 65–90 who responded to the 2014/2015 cycle of the Kaiser Permanente Northern California Member Health Survey. A frailty index, based on self-reported data, was used to classify respondents as frail or non-frail. BMI was calculated using self-reported height and weight information.
	A high waist-hip ratio increased the risk of developing frailty by 25% (HR=1.25, 95% CI: 1.13–1.38) compared to a healthy ratio and was also a predictor of worsening frailty over 12 years of follow-up in a study based on The English Longitudinal Study of Ageing.	Niederstrasser NG, Rogers NT, 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. https://doi.org/10.1371/journal.pone.0223799	The analysis was carried out on data collected from 2004/5 to 2016/17, on a representative sample of 7,240 people aged 50 and above participating in The English Longitudinal Study of Ageing (ELSA). Niederstrasser NG et al measured frailty using a 56-item Frailty Index comprised of self-reported health

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	Overweight and underweight were not predictors of frailty in this study.		conditions, disabilities, cognitive function, hearing, eyesight, depressive symptoms and ability to carry out activities of daily living. Frailty progression was observed over a period of up to 12 years (2004/5 to 2016/17).
	There is emerging evidence that the risk of frailty increases in the presence of obesity particularly in the context of other unhealthy behaviours such as inactivity, a poor diet and smoking.	British Geriatrics Society: Fit for Frailty Part 1 https://www.bgs.org.uk/sites/default/files/content/resources/files/2018-05-23/fff_full.pdf	
Malnutrition / Inadequate nutritional intake / Loss of appetite	Inadequate nutritional intake is an important modifiable risk factor for frailty. Nutrition is a crucial contributing factor to the development of frailty and its key component sarcopenia (age-related loss of skeletal muscle mass and strength).	Goisser, S., Guyonnet, S., & Volkert, D. (2016). The role of nutrition in frailty: An overview. <i>The Journal of Frailty & Aging</i> , 5(2), 74–77. https://doi.org/10.14283/jfa.2016.87	
	An Italian study found that daily energy intake ≤ 21 kcal/kg versus >21 kcal/kg was significantly associated with frailty, increasing the likelihood of frailty by 24% (OR=1.24, 95% CI: 1.02–1.5). The percentage of participants with frailty in the study increased with the number of nutrient deficiencies - 32.8% of those with low intake of >3 nutrients were frail compared to 13.4% of those with no low intakes (OR=2.12, 95% CI: 1.29–3.50).	Bartali B, Frongillo EA, Bandinelli S, et al. Low nutrient intake is an essential component of frailty in older persons. <i>J Gerontol A Biol Sci Med Sci</i> . 2006;61(6):589-593. doi:10.1093/gerona/61.6.589 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2645617/	Analysis was based on data for 802 persons aged 65 - 93 years participating in an Italian study - the InCHIANTI (Invecchiare in Chianti, aging in the Chianti area) study. Frailty was defined by having at least two of the Fried Phenotype criteria. ¹ The European Prospective Investigation into Cancer and nutrition (EPIC) questionnaire was used to estimate the daily intake of energy and nutrients. Low intake was defined using the value corresponding to the lowest sex-specific intake quintile of energy and specific nutrients.
	A US study of older women showed that compared with women in the upper three	Semba RD, Bartali B, Zhou J, Blaum C, Ko CW, Fried LP. Low serum micronutrient	Analysis was based on data for 766 women, aged 65 and older, from the Women’s Health and Aging Study

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>quartiles, women in the lowest quartile of serum carotenoids (biomarker for fruit and vegetable consumption) and α-tocopherol (Vitamin E) had a 30% (HR=1.30, 95% CI:1.01–1.92) and 39% (HR=1.39, 95% CI: 1.02–1.89) respectively, increased risk of becoming frail.</p> <p>The number of nutritional deficiencies was associated with an increased risk of frailty - each additional nutrient deficiency raised the risk of frailty by almost 10% (HR=1.10; 95% CI: 1.01–1.20).</p>	<p>concentrations predict frailty among older women living in the community. <i>J Gerontol A Biol Sci Med Sci.</i> 2006;61(6):594-599. doi:10.1093/gerona/61.6.594 https://academic.oup.com/biomedgerontology/article/61/6/594/589475</p>	<p>I, a population-based study of moderately to severely disabled community-dwelling women in Baltimore, Maryland.</p> <p>Frailty was defined by the Fried phenotype criteriaⁱ and women were defined as frail by the presence of at least three, and not frail if they had up to two of the five components.</p> <p>Frailty status was determined at baseline and annually for 3 years of follow-up.</p> <p>Nutritional status was assessed using non-fasting blood samples. The participants were categorized into quartiles based on nutrient concentration with poor nutritional status defined as the lowest quartile of the distribution.</p>
	<p>There are conflicting results from studies into the association between Vitamin D deficiency and the development of frailty (Bonney et al). However, a 2018 systematic review reported that serum 25OH Vitamin D levels are significantly and directly associated with the risk of frailty (Ju et al). A meta-analysis of data from more than 20,000 study participants demonstrates a statistically significant inverse association between serum 25OH Vitamin D levels and the risk of frailty. A 25-nmol/L increase in 25OHD levels was associated with 11%-12% decrease in the incidence of frailty.</p>	<p>Bonnefoy M, Berrut G, Lesourd B, et al. Frailty and nutrition: searching for evidence. <i>J Nutr Health Aging.</i> 2015;19(3):250-257. doi:10.1007/s12603-014-0568-3 https://www.researchgate.net/publication/273153887_Frailty_and_nutrition_Searching_for_evidence</p> <p>Ju SY, Lee JY, Kim DH. Low 25-hydroxyvitamin D levels and the risk of frailty syndrome: a systematic review and dose-response meta-analysis. <i>BMC Geriatr.</i> 2018;18(1):206. Published 2018 Sep 4. doi:10.1186/s12877-018-0904-2 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6124011/</p>	<p>The systematic review identified 8 papers including 10 studies from Europe and the United States. The mean age of the participants ranged from 62.2 to 79.2 years</p>
	<p>Several studies have established a link between insufficient dietary protein intake / low serum protein concentrations and frailty or frailty-related parameters of functionality in older people.</p>	<p>Kaiser M, Bandinelli S, Lunenfeld B. Frailty and the role of nutrition in older people. A review of the current literature. <i>Acta Biomed.</i> 2010;81 Suppl 1:37-45. https://www.semanticscholar.org/paper/Frailty-and-the-role-of-nutrition-in-older-people.-Kaiser-Bandinelli/2b0cf5c6539ef9f5a0c80498b9c31f318</p>	

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
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	<p>In Italy, the InCHIANTI study reported that the prevalence of frailty in older adults in the lowest quintile of protein intake was almost double that of those in the highest quintile (OR=1.98, 95% CI: 1.18–3.31).</p>	<p>Bartali B, Frongillo EA, Bandinelli S, et al. Low nutrient intake is an essential component of frailty in older persons. <i>J Gerontol A Biol Sci Med Sci.</i> 2006;61(6):589-593. doi:10.1093/gerona/61.6.589 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2645617/</p>	<p>Analysis was based on data for 802 persons aged 65 - 93 years participating in an Italian study - the InCHIANTI (Invecchiare in Chianti, aging in the Chianti area) study. Frailty was defined by having at least two of the Fried Phenotype criteria.¹ The European Prospective Investigation into Cancer and nutrition (EPIC) questionnaire was used to estimate the daily intake of energy and nutrients.</p>
	<p>A Spanish study found significant negative associations between frailty and protein consumption, i.e. higher protein intake associated with decreasing frailty. For example, those in the highest quartile of protein intake had a 59% reduced odds of frailty (OR=0.41, 95% CI: 0.23–0.72) compared to those with the lowest intake, while those in the second highest quartile had a 55% reduced odds of frailty (OR= 0.45, 95% CI: 0.26–0.78).</p>	<p>Helena Sandoval-Insausti, Raúl F. Pérez-Tasigchana, Esther López-García, Esther García-Esquinas, Fernando Rodríguez-Artalejo, Pilar Guallar-Castillón, Macronutrients Intake and Incident Frailty in Older Adults: A Prospective Cohort Study, <i>The Journals of Gerontology: Series A</i>, Volume 71, Issue 10, October 2016, Pages 1329-1334, https://doi.org/10.1093/gerona/glw033</p>	<p>Data on 1,822 community-dwelling individuals aged 60 and older participating in the Seniors-ENRICA (Study on Nutrition and Cardiovascular risk factors in Spain) cohort study was analysed. Food consumption was assessed with a validated, computerized face-to-face diet history. Frailty was defined using Fried frailty Phenotype criteria.ⁱ</p>
	<p>In a large US study, a 20% increase in protein intake was associated with a 32% (95% CI: 23% - 50%) lower risk of frailty over a 3-year period.</p>	<p>Beasley JM, LaCroix AZ, Neuhaus ML, et al. Protein intake and incident frailty in the Women's Health Initiative observational study. <i>J Am Geriatr Soc.</i> 2010;58(6):1063-1071. doi:10.1111/j.1532-5415.2010.02866.x https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2924946/</p>	
	<p>Protein supplementation may prevent or reverse sarcopenia and frailty.</p>	<p>Bonnefoy M, Berrut G, Lesourd B, et al. Frailty and nutrition: searching for evidence. <i>J Nutr Health Aging.</i> 2015;19(3):250-257. doi:10.1007/s12603-014-0568-3. https://www.researchgate.net/publication/273153887_Frailty_and_nutrition_Searching_for_evid</p>	

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
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	Higher fruit and vegetable consumption may be associated with a lower risk of frailty.	Gotaro Kojima, Modifiable Lifestyle Risk factors of Frailty among Community-Dwelling Older People (Thesis for: PhD (Medicine)), August 2019. Obtained from Author.	Based on the findings of a Systematic Review conducted as part of a PhD thesis.
	Low daily fruit and vegetable consumption appeared to be a risk factor for frailty in the Whitehall II study. Compared to those who consumed fruit and vegetables on a daily basis, individuals with a lower intake were 29% more likely to develop frailty (OR=1.29, 95% CI: 1.05–1.58).	Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. <i>Lancet Public Health</i> 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext	The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, behavioural risk factors were based on measurements at age 45–55 years. Frailty (defined according to the Fried phenotype) ¹ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.
	<p>Research which used data from French and Spanish studies reported that those who consumed higher amounts of fruit, vegetables and both combined had a significantly lower short-term risk of developing frailty (over 2.5 years) in a dose-response manner.</p> <ul style="list-style-type: none"> • Compared with those consuming <1 portion of fruit /day (1 portion=120g of fruits) the odds of frailty for those consuming 1, 2 or >3 portions, were reduced by 41% (OR=0.59, 95% CI: 0.27-0.90), 42% (OR=0.58, 95%CI: 0.29-0.86) and 52% (OR=0.48, 95%CI: 0.20-0.75) respectively. • Compared with those consuming <1 portion of vegetables /day (1 portion = 150g of vegetables) the odds of frailty for those consuming 1, 2 or >3 portions, 	García-Esquinas E, Rahi B, Peres K, et al. Consumption of fruit and vegetables and risk of frailty: a dose-response analysis of 3 prospective cohorts of community-dwelling older adults. <i>Am J Clin Nutr</i> . 2016;104(1):132-142. doi:10.3945/ajcn.115.125781 https://academic.oup.com/ajcn/article/104/1/132/4569666	<p>Risks of Incident frailty according to fruit and vegetable consumption at baseline were investigated in 2,926 non-frail older men and women from three different cohorts (Three-City Bordeaux cohort and the Integrated Multidisciplinary Approach cohort from France and Seniors-ENRICA cohort from Spain).</p> <p>Frailty was defined using modified Fried criteria¹ and consumption of fruit and vegetables was self-reported.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>were reduced by 31% (OR=0.69, 95% CI: 0.42-0.97), 44% (OR=0.56, 95%CI: 0.35-0.77) and 48% (OR=0.52, 95%CI: 0.13-0.92) respectively.</p>		
	<p>A study using data from the English Longitudinal Study of Ageing reported that consumption of 5-10 portions of fruit and vegetables a day was associated with reduced odds of pre-frailty and frailty combined compared to those with low consumption (0-2.5 portions); Older people consuming 5 - <7.5 portions and 7.5 - <10 portions had risk reductions of 44% (OR=0.56, 95%CI: 0.37-0.85) and 54% (OR=0.46, 95% CI: 0.27-0.77) respectively, compared with those consuming 0 - <2.5 portions.</p> <p>No potential protective effect for incident pre-frailty/frailty were observed among participants consuming 10 or more portions per day.</p>	<p>Gotaro Kojima, Modifiable Lifestyle Risk factors of Frailty among Community-Dwelling Older People (Thesis for: PhD (Medicine)), August 2019.</p> <p>Thesis obtained from author.</p>	<p>Data on 1,577 robust (neither frail nor pre-frail) participants at baseline in the English Longitudinal Study of Ageing (ELSA) who were aged 60 years or older was analysed.</p> <p>Frailty was defined by modified Fried Frailty Phenotype criteria ¹ and consumption of fruit and vegetables was self-reported.</p>
	<p>There is some evidence that that the risk of frailty can be reduced through a Mediterranean diet (characterized by high consumption of nutrient-dense foods such as fruits and vegetables, whole meal cereals and oily fish, but low intake of saturated fats (Branko Gabrovec et al).</p> <p>The strength of the association between Mediterranean diet adherence and frailty risk appears to be fairly consistent across studies.</p>	<p>Gabrovec B, Panagiotopoulos E, Jelenc M., et al. Management of Frailty at Individual Level: A Systematic Review (WP6). https://advantageja.eu/images/WP6-Managing-frailty-at-individual-level-a-Systematic-Review.pdf</p>	<p>.</p>
	<p>An Italian study reported showed a 70% risk</p>	<p>Talegawkar SA, Bandinelli S, Bandeen-Roche K, et</p>	<p>Data from 690 community-living persons aged 65 and</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	reduction in frailty among those having high adherence to a Mediterranean-style diet over six years of follow-up compared to those with low adherence (OR=0.30, 95% CI: 0.14, 0.66).	al. A higher adherence to a Mediterranean-style diet is inversely associated with the development of frailty in community-dwelling elderly men and women. <i>J Nutr.</i> 2012;142(12):2161-2166. doi:10.3945/jn.112.165498 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3497964/	over participating in the Invecchiare in Chianti (InCHIANTI; aging in the Chianti area) study of aging was analysed. Frailty was defined as having at least 2 of the Fried Frailty Phenotype criteria. ¹ Dietary intake data in the cohort were collected using a Food Frequency Questionnaire. Adherence to a Mediterranean-style diet was computed using the Mediterranean Diet Score (MDS), categorised as: low adherence (MDS <=3), medium adherence (MDS 4–5), and high adherence (MDS >=6).
	A French study found that those with the highest Mediterranean Diet adherence (score 6-9) had a 68% frailty risk reduction (OR= 0.32, 95% CI: 0.14-0.72) two years later compared to those in the lowest Mediterranean Diet category (score 0-3).	Rahi B, Ajana S, Tabue-Teguo M, Dartigues JF, Peres K, Feart C. High adherence to a Mediterranean diet and lower risk of frailty among French older adults community-dwellers: Results from the Three-City-Bordeaux Study. <i>Clin Nutr.</i> 2018;37(4):1293-1298. doi:10.1016/j.clnu.2017.05.020F Full text provided by the authors.	This study followed 560 non-frail French people aged ≥75 years participating in the Three-City Bordeaux study, for a period of 2 years. Frailty was defined according to modified Fried frailty criteria. ¹ Adherence to the Mediterranean diet was computed from a food frequency questionnaire (scored as 0-9).
	In a Spanish study of older people aged ≥60, an increasing adherence to the Mediterranean Diet (MD) was associated with decreasing risk of frailty over 3.5 years of follow-up, although other potentially major explanatory factors were not considered. The highest level of adherence to the Mediterranean Diet was associated with a 52% risk reduction (OR=0.48, 95% CI: 0.30–0.77). Compared to individuals with the least adherence, those with an intermediate level of adherence to the MD had a 41% risk reduction (OR=0.59, 95% CI: 0.37–0.95).	Leon-Munoz LM, Guallar-Castillon P, Lopez-Garcia E, Rodriguez-Artalejo F. Mediterranean diet and risk of frailty in community-dwelling older adults. <i>J Am Med Dir Assoc.</i> 2014; 15(12):899±903. PMID:25127502. https://doi.org/10.1016/j.jamda.2014.06.013	Over a mean of 3.5 years, 1,815 community-dwelling individuals aged ≥60 years in Spain and participating in the Seniors Enrica study were followed-up. Frailty was defined using Fried phenotype criteria. ¹
	A Systematic Review and Meta-Analysis	Kojima G, Avgerinou C, Iliffe S et al (2018)	In this Systematic Review studies were included if they

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>which pooled data from four studies confirms that an increasing adherence to the Mediterranean Diet (MD) appears to be associated with decreasing risk of frailty.</p> <p>Compared to those with poor adherence to the Mediterranean Diet (MDS 0–3), those with the greatest adherence (MDS 6–9) had a 56% risk reduction (pooled OR = 0.44, 95% CI:0.31–0.64) and those with an intermediate level of adherence (MDS 4–5) experienced a 38% reduction (pooled OR = 0.62, 95% CI:0.47–0.82) in risk of frailty.</p> <p>Evidence is currently lacking regarding whether adherence to a Mediterranean diet can reduce the risk of frailty in non-Mediterranean populations.</p>	<p>Adherence to Mediterranean Diet Reduces Incident Frailty Risk: Systematic Review and Meta-Analysis. J Am Geriatr Soc 66:783–788</p> <p>https://onlinelibrary.wiley.com/doi/full/10.1111/jgs.15251</p>	<p>involved community-dwelling older people with a mean age of 60 and older and examined risk of developing frailty using validated criteria.</p> <p>Four studies were included involving 5,789 older people with mean follow-up of 3.9 years. All measured adherence to a Mediterranean diet using the Mediterranean Diet Score (MDS).</p> <p>Mediterranean diet scores range from 0 to 9, with a higher score indicative of greater adherence.</p>
<p>Sedentary lifestyle / Low physical activity</p>	<p>The extent of the association between physical activity and frailty differs widely between studies partly because there is no single definition of frailty and the way in which physical activity is measured in studies varies enormously.</p> <p>Findings from the Whitehall II study show that low physical activity in mid-life is a risk factor for frailty in later life. Compared to those who were active, individuals classified as moderately active had a 52% (OR=1.52, 95% CI: 1.17–1.97) higher odds of developing frailty, whilst being inactive appeared to more than double (OR=2.63, 95% CI: 2.06-3.37) the odds.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. Lancet Public Health 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, behavioural risk factors were based on measurements at age 45–55 years. Participants were assigned to one of three physical activity groups:</p> <ol style="list-style-type: none"> 1. inactive; 2. moderately active; 3. Active: less than 1 h per week of moderate and vigorous activity, 2-5 h or more per week of

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
			<p>moderate activity, or 1 h or more of vigorous activity.</p> <p>Frailty (defined according to the Fried phenotype criteria)ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>
	<p>A study that used data from the English Longitudinal Study of Ageing reported that compared with those defined as sedentary, mild physical activity was insufficient to significantly slow the progression of frailty, moderate physical activity reduced the progression of frailty in some age groups (particularly ages 65 and above) and vigorous activity significantly reduced the trajectory of frailty progression in older adults.</p>	<p>Rogers NT, Marshall A, Roberts CH, Demakakos P, Steptoe A, Scholes S. Physical activity and trajectories of frailty among older adults: Evidence from the English Longitudinal Study of Ageing. PLoS One. 2017;12(2):e0170878. Published 2017 Feb 2. doi:10.1371/journal.pone.0170878 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0170878</p>	<p>Data on 8,649 non-frail participants aged 50 and over in the English Longitudinal Study of Ageing was used. Participants were followed up for an average of 10 years.</p> <p>Frailty was defined using a 56-item frailty index.</p> <p>Levels of physical activity were self-reported.</p>
	<p>A Brazilian study demonstrated that low physical activity combined with excessive time spent in sedentary behaviour was strongly associated with frailty. Compared to those with high physical activity (physical activity level ≥ 150 min/wk. and sedentary behaviour < 540 min/day) those with low physical activity (< 150 and ≥ 540) were almost 3 times more likely to be frail (Prevalence ratio=2.83, 95% CI: 1.23-6.52).</p>	<p>da Silva, V.D., Tribess, S., Meneguici, J. et al. Association between frailty and the combination of physical activity level and sedentary behavior in older adults. BMC Public Health 19, 709 (2019). https://doi.org/10.1186/s12889-019-7062-0</p>	<p>A cross-sectional analysis was undertaken on 457 older adults (age aged 60 to 97 years) participating in the Longitudinal Study of the Elderly Health of Alcobaca, Bahia, Brazil.</p> <p>Frailty was measured using a modified version of the Fried Frailty Phenotype criteria.ⁱ</p> <p>Physical activity level and time spent in sedentary behaviour were self-reported using the International Questionnaire of Physical Activity.</p>
Smoking	<p>Findings from research into the association between smoking and frailty show mixed results and in some studies, smoking is associated with being less frail. These findings may have resulted from the “survivor effect”; frail smokers having died</p>	<p>Kojima, Gotaro & Iliffe, Steve & Walters, Kate. (2015). Smoking as a predictor of frailty: A systematic review. BMC Geriatrics. 15. 10.1186/s12877-015-0134-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC</p>	

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>early or becoming too frail to smoke, therefore smoking habit as a contributor to frailty may diminish in the very old.</p> <p>In the main, the research shows that smoking appears to be significantly associated with the development and progression of frailty, and so smoking cessation may potentially be beneficial for preventing or reversing frailty.</p>	<p>4618730/</p>	
	<p>A very large US study - The Women's Health Initiative Observational Study - showed that current smokers over the age of 65 had an almost 3-fold increased odds of frailty after 3 years compared to never-smokers (OR= 2.90, 95% CI: 2.35 - 3.57) whilst past smokers had a 12% increased odds (OR=1.12, 95% CI: 1.02 -1.23).</p>	<p>Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study [published correction appears in J Am Geriatr Soc. 2017 Jul;65(7):1631-1632]. J Am Geriatr Soc. 2005;53(8):1321-1330. doi:10.1111/j.1532-5415.2005.53405.x https://escholarship.org/uc/item/9rp764f5</p>	<p>The Women's Health Initiative Observational Study in the US followed 28,181 women aged 65–79 free of frailty at baseline for 3 years.</p> <p>Frailty was defined as the presence of 3 or more of the Fried Frailty Phenotype criteriaⁱ</p> <p>Smoking behaviour was self-reported.</p>
	<p>In a study based on data from the UK Biobank on nearly half a million middle-aged and older-aged people, frailty was significantly associated with smoking. 20% of frail participants were current smokers vs 9% of non-frail participants.</p> <p>Compared to those who had never smoked, current smokers had a 2.5-fold increase in odds of frailty (OR= 2.47, 95% CI 2.36–2.60) after an average of 7 years of follow-up.</p>	<p>Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. Lancet Public Health. 2018;3(7):e323-e332. doi:10.1016/S2468-2667(18)30091-4 https://www.thelancet.com/pdfs/journals/lanpub/PIIS2468-2667(18)30091-4.pdf</p>	<p>The study included 493,737 participants aged 37–73 years from across England, Scotland, and Wales.</p> <p>Median follow-up duration was 7 years.</p> <p>Frailty was assessed using Fried Frailty Phenotype criteria.ⁱ</p>
	<p>Smoking in midlife is a risk factor for frailty in later life, according to the findings from the Whitehall II study.</p> <p>Compared to those who had never smoked, current smokers had a 1.7-fold increased</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. Lancet Public Health 2018; published online June 13 https://www.thelancet.com/journals/lanpub/arti</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, behavioural risk factors were based on measurements at age 45–55 years. Frailty (defined according to the</p>

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	likelihood of developing frailty (OR=1.69, 95% CI: 1.27–2.25).	cle/PIIS2468-2667(18)30079-3/fulltext	Fried phenotype ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.
	<p>A study that used data from The English Longitudinal Study of Ageing reported that, amongst older adults aged 60 years or above, current smokers were 1.6 times more likely to develop frailty than non-smokers over the 4 years of follow-up, controlling for a wide range of potential confounders including age, gender, alcohol use, education, wealth, cognitive function and loneliness (OR=1.60, 95% CI: 1.02–2.51).</p> <p>These researchers suggest that the association between smoking and incident frailty can partially be explained by socioeconomic status.</p>	<p>Gotaro Kojima, Steve Iliffe, Stephen Jivraj, Ann Liljas, Kate Walters, Does current smoking predict future frailty? The English longitudinal study of ageing, Age and Ageing, Volume 47, Issue 1, January 2018, Pages 126- 131.</p> <p>https://doi.org/10.1093/ageing/afx136</p>	<p>The analysis was carried out on data for 2,542 community-dwelling adults aged 60 years or older participating in the English Longitudinal Study of Ageing (ELSA). Participants were free of frailty at baseline (2004-2005) and followed up over a 4-year period.</p> <p>Kojima et al defined frailty using the Fried Frailty Phenotype criteria.ⁱ</p> <p>Participants were classified as ‘current smoker’ or ‘non-smoker’ based on answers to the question ‘Do you smoke cigarettes at all nowadays?’</p>
	<p>Another study based on The English Longitudinal Study of Ageing (ELSA) showed that being a smoker or having a history of smoking is a predictor of both frailty development and worsening frailty.</p> <p>This study showed that a person with an average age of 67 who is overweight or obese and smokes or has a smoking history has a 37% chance of becoming frail, whereas a person with a healthy weight that has never smoked has a 19% chance of developing frailty.</p>	<p>Niederstrasser NG, Rogers NT, 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.</p> <p>https://doi.org/10.1371/journal.pone.0223799</p>	<p>The analysis was carried out on data collected from 2004/5 to 2016/17, on a representative sample of 7,240 people aged 50 and above participating in The English Longitudinal Study of Ageing (ELSA).</p> <p>Niederstrasser NG et al measured frailty using a 56-item Frailty Index comprised of self-reported health conditions, disabilities, cognitive function, hearing, eyesight, depressive symptoms and ability to carry out activities of daily living. Frailty progression was observed over a period of up to 12 years (2004/5 to 2016/17).</p> <p>Smoking status was self-reported.</p>
	A large multinational study (the Survey on Health, Ageing, and Retirement in Europe (SHARE)) from 11 European countries showed that current smokers aged 55 and	Etman A, Kamphuis CB, van der Cammen TJ, Burdorf A, van Lenthe FJ. Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? Eur J Public	This study involved nationally representative samples (14,082) of community-dwelling adults aged 55 and older from 11 European countries. It examined associations between smoking status (never, former

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	<p>older had a 16% increased odds of worsening frailty status (either from robust to prefrail/frail or from prefrail to frail) two years after baseline, compared to those who never smoked (OR=1.16, 95 % CI: 1.02–1.32).</p>	<p>Health. 2015;25(2):345–50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447813/</p>	<p>and current) at baseline and frailty status at two-year follow-up.</p> <p>Physical frailty was based on Fried’s phenotype criteria, ⁱ but self-reported. Frailty states were based on the total number of criteria met: ‘frail’ (≥3 criteria), ‘pre-frail’ (1–2 criteria), ‘non-frail’ (0 criteria).</p>
	<p>Smoking accelerates the rate of decline of bone density, muscular strength and respiratory function.</p>	<p>Age UK. Healthy Ageing evidence review. https://www.ageuk.org.uk/globalassets/age-uk/documents/reports-and-publications/reports-and-briefings/health--wellbeing/rb_april11_evidence_review_healthy_ageing.pdf</p>	
	<p>Since it affects bone health, smoking is also a risk factor for falls.</p>	<p>Public Health England (2017). Falls and fracture consensus statement: Supporting commission for prevention. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/586382/falls_and_fractures_consensus_statement.pdf</p>	
<p>Alcohol consumption / drinking patterns</p>	<p>Most research has suggested a paradox in the link between alcohol consumption and frailty over the life course (BGS).</p>	<p>British Geriatrics Society, Healthier for longer https://www.bgs.org.uk/sites/default/files/content/resources/files/2019-11-04/BGS%20Healthier%20for%20Longer.pdf</p>	
	<p>Several studies have shown alcohol’s beneficial effects against frailty, but this apparent protective effect is controversial, and it has been argued that it may be explained by methodological problems concerning biases and other possible</p>		

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	<p>explanatory factors that may not have been taken into account in studies. One possible explanation is a 'sick quitters' effect: sick individuals who stop drinking are sometimes classified in studies as non-drinkers and non-frail drinkers who continue to consume alcohol are classified as current drinkers, leading to an apparent lower risk of frailty among drinkers. Another potential issue with some studies is short follow-up periods (often less than 4 years) which may be too short to enable the relationship between alcohol intake and frailty to be robustly evaluated.</p>		
	<p>Findings from the Whitehall II study which had a follow-up period of 18 years on average show that both zero and high alcohol consumption in midlife appear to be risk factors for frailty in later life. Compared to those classified as moderate drinkers (women: ≤ 14 units per week; men: ≤ 21 units per week), individuals with a high intake were just over 50% more likely to become frailty (OR=1.54, 95% CI: 1.17–2.04), whereas those who abstained from alcohol has an almost 2-fold increased risk of frailty (OR=1.85, 95% CI: 1.43-2.38).</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. <i>Lancet Public Health</i> 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, behavioural risk factors were based on measurements at age 45–55 years. Frailty (defined according to the Fried phenotype)ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>
	<p>A study of male businessmen in Finland with a long follow-up period of almost 30 years found that high alcohol consumption in midlife predicted both frailty and prefrailty while moderate and zero consumption in midlife was not found to impact the risk of frailty. Compared with light intake (1-98g/week),</p>	<p>Strandberg AY, Trygg T, Pitkälä KH, Strandberg TE. Alcohol consumption in midlife and old age and risk of frailty: Alcohol paradox in a 30-year follow-up study. <i>Age Ageing</i>. 2018;47(2):248-254. doi:10.1093/ageing/afx165 https://academic.oup.com/ageing/article/47/2/248/4568700</p>	<p>The analysis included a sample of 2,360 men participating in the Helsinki Businessmen Study.</p> <p>Frailty and prefrailty were defined according to Fried's phenotypic definition of frailty,ⁱ which was modified into four criteria (shrinking, exhaustion, weakness, and physical inactivity). The participant was classified to be frail, prefrail, or not-frail if 3–4, 1–2, or zero criteria were met, respectively.</p>

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	<p>people with high consumption (>196g/week) in mid-life (mean age 49 years) were 1.6 times more likely to develop frailty (OR 1.61, 95% CI 1.01–2.56) and a 1.4 times more likely to develop pre-frailty (OR 1.42; 95% CI 1.06–1.92) 26 years later.</p>		<p>Alcohol consumption was self-reported and divided into zero, light (1–98g/week), moderate (99–196g/week), and high consumption (>196g/week).</p>
	<p>A systematic review and meta-analysis suggested that heavier alcohol consumption (at least 24 g of alcohol/day for men, 12g of alcohol/day for women or ≥5 days of drinking/week) is associated with lower incident frailty compared with no alcohol consumption among middle-aged and older people (pooled OR=0.61, 95%CI: 0.49–0.77). However, the authors reflect that the 39% decreased risk of incident frailty with heavier consumption may be due to methodological issues - their estimate was unable to take account of other possible explanatory factors, such as education, socio-economic status, smoking. Another possibility is the 'sick quitters' effect. They also noted that binge drinkers, who may be at high risk of incident frailty and likely to be in the highest alcohol consumption categories, were not identified separately in any of the included studies. Also, the follow-up periods of the included studies were short, between 2 to 3.3 years.</p>	<p>Kojima G, Liljas A, Iliffe S, Jivraj S, Walters K. A systematic review and meta-analysis of prospective associations between alcohol consumption and incident frailty. <i>Age Ageing</i>. 2018;47(1):26-34. doi:10.1093/ageing/afx086 https://academic.oup.com/ageing/article/47/1/26/3854659</p>	<p>The systematic review included 4 studies with 44,051 community-dwelling participants aged at 55 years and above.</p> <p>Three studies were from European countries and one was from the United States.</p>
	<p>In an English study there was no association between zero alcohol consumption and frailty risk over a 4-year period once other factors such as self-reported general health status and comorbidities were taken into account, which perhaps supports the 'sick</p>	<p>Kojima G, Jivraj S, Iliffe S, Falcaro M, Liljas A, Walters K. Alcohol Consumption and Risk of Incident Frailty: The English Longitudinal Study of Aging. <i>J Am Med Dir Assoc</i>. 2019;20(6):725-729. doi:10.1016/j.jamda.2018.10.011 https://discovery.ucl.ac.uk/id/eprint/10058512/1</p>	<p>This study analysed data on a nationally representative sample of 2,544 community-dwelling adults aged > 60 years participating in The English Longitudinal Study of Ageing (ELSA). Frailty status defined by Fried Frailty Phenotype criteria¹ was measured at baseline (2004) and 4 years</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	quitters' theory.	/Kojima Alcohol%20consumption%20and%20risk%20of%20incident%20frailty.%20The%20English%20Longitudinal%20Study%20of%20Ageing_AAM.pdf	later.
	A Spanish study suggests that certain drinking patterns, in particular drinking only with meals and the Mediterranean drinking pattern (MDP), may be associated with a lower risk of frailty in older adults. Compared with non-drinkers, those adhering to the MDP (defined as moderate alcohol intake, with wine preference and drinking only with meals) had a 32% reduced risk of developing frailty (OR=0.68, 95% CI: 0.47–0.99).	Ortolá R, García-Esquinas E, León-Muñoz LM, et al. Patterns of Alcohol Consumption and Risk of Frailty in Community-dwelling Older Adults. J Gerontol A Biol Sci Med Sci. 2016;71(2):251-258. doi:10.1093/gerona/glv125	This study used data on a nationally representative sample of 2,086 community-dwelling adults aged 60 and older recruited in 2008-2010 and followed through 2012. Incident frailty was defined as ≥ 2 of the following 4 Fried ⁱ criteria: exhaustion, muscle weakness, low physical activity, and slow walking speed. Alcohol consumption was self-reported at baseline (2008-2010).
	Moderate alcohol consumption may have a protective effect on developing frailty according to a very large US study - The Women's Health Initiative Observational Study. Women who consumed less than 1 drink per week had a 13% lower risk (OR= 0.87, 95% CI: 0.77-0.97) of frailty than non-drinkers, while moderate drinkers (1-14 drinks per week) had a 31% lower risk (OR= 0.69, 95% CI: 0.61-0.77).	Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study [published correction appears in J Am Geriatr Soc. 2017 Jul;65(7):1631-1632]. J Am Geriatr Soc. 2005;53(8):1321-1330. doi:10.1111/j.1532-5415.2005.53405.x https://escholarship.org/uc/item/9rp764f5	The Women's Health Initiative Observational Study in the US followed 28,181 women aged 65–79 free of frailty at baseline for 3 years. Frailty was defined as the presence of 3 or more of the Fried Frailty Phenotype criteria. ⁱ Alcohol consumption was self-reported.
Polypharmacy	23% of all over 75 year olds are taking inappropriate medications.	British Geriatrics Society. https://www.bgs.org.uk/resources/frailty-what's-it-all-about	
	The association of frailty and polypharmacy may be complex and bi-directional. On the one hand, frailty is linked to certain chronic diseases and multimorbidity which can consequently lead to polypharmacy. On the	Gutiérrez-Valencia M, Izquierdo M, Cesari M, Casas-Herrero Á, Inzitari M, Martínez-Velilla N. The relationship between frailty and polypharmacy in older people: A systematic review. Br J Clin Pharmacol. 2018; 84(7):1432-	

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	<p>other hand, there are plausible mechanisms by which drugs may affect the development of frailty. Several elements that are characteristic of frailty have been directly linked in research studies with number of drugs taken, including weight loss, balance disorders, poor nutritional status, and functional deterioration.</p>	<p>1444. doi:10.1111/bcp.13590</p>	
	<p>A Systematic Review report which acknowledged that the relationship between polypharmacy and frailty may be bi-directional reported that individuals who are frail appear to be between 1.8 and 2.5 times more likely to be exposed to polypharmacy and between 4.5 and 5.8 times more likely to be exposed to hyperpolypharmacy.</p> <p>The likelihood of being frail appears to increase by 13% with every medication added to the treatment (OR=1.13–1.20).</p>	<p>Gutiérrez-Valencia M, Izquierdo M, Cesari M, Casas-Herrero Á, Inzitari M, Martínez-Velilla N. The relationship between frailty and polypharmacy in older people: A systematic review. <i>Br J Clin Pharmacol.</i> 2018;84(7):1432-1444. doi:10.1111/bcp.13590 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6005607/</p>	<p>Definitions of polypharmacy varied between the studies included in the Review, from more than three to more than six medications, but the most repeated definition was the use of five or more drugs. Some studies also defined a third category among polypharmacy groups, when 10 or more drugs were consumed: hyperpolypharmacy or excessive polypharmacy.</p> <p>13 studies included community-dwelling individuals, five studies included hospitalized patients in acute units and the rest included outpatients, care home residents or mixed populations.</p>
	<p>A 8-year follow-up study to investigate whether polypharmacy is linked with a higher incidence of frailty in a large cohort of 4,402 North Americans at high risk of, or having, knee osteoarthritis, found that the incidence of frailty was significant in those taking 4–6 medications (15% versus 8% for 0-3 medications) and 6 times higher (46%) in people taking 7 or more medications.</p> <p>Compared to those taking 0-3 medications, participants using 4–6 medications had a 55% higher risk of frailty (HR = 1.55, 95% CI: 1.22–1.96), whereas those using 7 or more drugs had almost a 150% increased risk of frailty (HR = 2.47, 95% CI: 1.78–3.43), after</p>	<p>Veronese N, Stubbs B, Noale M, et al. Polypharmacy Is Associated With Higher Frailty Risk in Older People: An 8-Year Longitudinal Cohort Study. <i>J Am Med Dir Assoc.</i> 2017;18(7):624-628. doi:10.1016/j.jamda.2017.02.009 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5484754/</p>	<p>Frailty was defined using the Study of Osteoporotic Fracture index.</p>

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	<p>adjustment for other potential explanatory factors.</p> <p>Each drug used at the baseline increased the risk of frailty at the follow-up by 11% (HR = 1.11, 95% CI: 1.07–1.15).</p>		
	<p>An Australian study found that the use of 6.5 medications daily was associated with an increased risk of frailty and that the risk of being frail increases by 27% when the number of medications increases by one.</p>	<p>Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. <i>J Clin Epidemiol</i> 2012; 65: 989–95.</p>	<p>The study included 1,705 community-dwelling men aged ≥70 years enrolled in the Concord Health and Aging in Men Project in Sydney, Australia.</p>
<p>Multi-morbidity / Chronic disease</p>	<p>A certain amount of overlap between frailty and multi-morbidity is biologically plausible, and a bi-directional causal relationship between them is probable. Frailty may predispose persons to the development of multiple chronic diseases, but frailty may also stem from the coexistence of multiple diseases.</p>	<p>Vetrano D, Palmer K, Marengoni A, Marzetti E, Lattanzio F, Roller R, Samaniego L, Rodríguez-Mañas L, Bernabei R & Onder G. (2018). Frailty and Multimorbidity: A Systematic Review and Meta-analysis. <i>The Journals of Gerontology: Series A</i>. 74. 10.1093/gerona/gly110. https://academic.oup.com/biomedgerontology/article/74/5/659/4991880</p>	
	<p>Multiple morbidity is strongly associated with frailty in the UK Biobank. A study using data on nearly half a million middle-aged and older-aged people, demonstrated how the prevalence of frailty increased with increasing multimorbidity. 72% of frail participants were multimorbid compared with 25% of the non-frail.</p> <p>The proportion with at least four long-term conditions was 27% in the frail group versus 2.5% in the non-frail group (OR=27.1, 95% CI: 25.3–29.1).</p> <p>Compared to those with no long-term conditions, the odds of frailty in those with</p>	<p>Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. <i>Lancet Public Health</i>. 2018;3(7):e323-e332. doi:10.1016/S2468-2667(18)30091-4 https://www.thelancet.com/pdfs/journals/lanpub/PIIS2468-2667(18)30091-4.pdf</p>	<p>The study included 493,737 participants aged 37–73 years from across England, Scotland, and Wales. Median follow-up duration was 7 years. Frailty was assessed using Fried Frailty Phenotype criteria.ⁱ Long-term conditions were self-reported.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>one long-term condition was more than 2-fold higher (OR=2.27, 95% CI:2.12-2.42). For those with 2 long-term conditions the odds were 5 times higher (OR=5.12, 95% CI: 4.80-5.47), and for those with three, 10 times higher (OR=10.4, 95% CI: 9.69-11.1). Those with four or more long-term conditions were 27 times more likely to be frail than those with no long-term conditions (OR= 27.1, 95% CI: 25.3-29.1).</p> <p>The top five long-term conditions associated with frailty were:</p> <ol style="list-style-type: none"> 1. multiple sclerosis (OR=15.3, 99.75% CI: 12.8–18.2); 2. chronic fatigue syndrome (OR=12.9, CI: 11.1–15.0); 3. chronic obstructive pulmonary disease (OR=5.6, CI: 5.2–6.1); 4. connective tissue disease (OR=5.4, CI: 5.0–5.8); and 5. diabetes (OR=5.0; CI: 4.7–5.2). 6. 		
	<p>In a Systematic Review and meta-analyses, the prevalence of multimorbidity in frail individuals was 72% (95% CI: 63%–81%) and the prevalence of frailty among multimorbid individuals was 16% (95% CI: 12%–21%).</p> <p>Multimorbidity (defined as the presence of 2+ diseases) was associated with a twofold increased likelihood of being frail (pooled OR=2.27; 95% CI: 1.97–2.62).</p> <p>The three longitudinal studies included in the Review suggest a bi-directional association between multimorbidity and frailty.</p>	<p>Vetrano D, Palmer K, Marengoni A, Marzetti E, Lattanzio F, Roller R, Samaniego L, Rodríguez-Mañas L, Bernabei R & Onder G. (2018). Frailty and Multimorbidity: A Systematic Review and Meta-analysis. <i>The Journals of Gerontology: Series A</i>. 74. 10.1093/gerona/gly110. https://academic.oup.com/biomedgerontology/article/74/5/659/4991880</p>	<p>48 studies involving 78,122 participants aged 18 years or older were included in the Systematic Review, regardless of the study setting, study design, or definition of multimorbidity and frailty. 25 studies were included in one or more meta-analyses. 45 studies were cross-sectional and 3 longitudinal, with the majority of them including community-dwelling participants.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>A large European study showed that individuals with one or more chronic diseases had a 43% increased odds of worsening frailty status (either from robust to prefrail/frail or from prefrail to frail) two years after baseline, compared to those with no chronic disease (OR=1.43, 95 % CI: 1.28–1.60).</p>	<p>Etman A, Kamphuis CB, van der Cammen TJ, Burdorf A, van Lenthe FJ. Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? <i>Eur J Public Health</i>. 2015;25(2):345–50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447813/</p>	<p>The analysis was undertaken on a large cohort of 14,082 community-dwelling adults aged 55 years and older participating in the Survey on Health, Ageing, and Retirement in Europe (SHARE). Physical frailty was based on Fried Frailty Phenotype criteria, ⁱ but self-reported. Frailty states were based on the total number of criteria met: ‘frail’ (≥3 criteria), ‘pre-frail’ (1–2 criteria), ‘non-frail’ (0 criteria). Chronic diseases were measured by questioning ‘Has a doctor ever told you that you have any of the following conditions?’, followed by a list of 14 chronic conditions, e.g. hypertension, arthritis, osteoporosis).</p>
	<p>An American study found that frail people were over five times more likely than non-frail people to report that they have three or more chronic diseases (55.9% versus 10.1%).</p>	<p>Lee DR, Santo EC, Lo JC, Ritterman Weintraub ML, Patton M, Gordon NP. Understanding functional and social risk characteristics of frail older adults: a cross-sectional survey study. <i>BMC Fam Pract</i>. 2018;19(1):170. Published 2018 Oct 19. doi:10.1186/s12875-018-0851-1 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6195739/</p>	<p>The analysis related to 4,551 community-dwelling adults ages 65–90 who responded to the 2014/2015 cycle of the Kaiser Permanente Northern California Member Health Survey. A frailty index, based on self-reported data, was used to classify respondents as frail or non-frail.</p>
Pain	<p>Pain appears to be associated with an increased risk of frailty development and progression in older men and women, as evidence from a nationally representative study (The English Longitudinal Study of Ageing) shows.</p> <p>Compared to participants reporting no pain in 2004-2005, those reporting moderate or severe pain were 3 (OR=3.08, 95% CI:2.28-4.16) and almost 4 times (OR=3.78, 95% CI: 2.51-5.71) respectively, more likely to have become frail 8 years later.</p> <p>Pain, and the adverse aspects of the pain</p>	<p>Wade, K. F., Marshall, A., Vanhoutte, B., Wu, F. C., O'Neill, T. W., & Lee, D. M. (2017). Does Pain Predict Frailty in Older Men and Women? Findings from the English Longitudinal Study of Ageing (ELSA). <i>Journals of Gerontology – Series A Biological Sciences and Medical Sciences</i>, 72(3), 403–409. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5861874/</p>	<p>This study examined the association between the occurrence and severity of pain and subsequent frailty development after 8 years of follow-up among 5,316 men and women living in private households in England, with a mean age 64.5 years, participating in The English Longitudinal Study of Ageing. A frailty index (FI) was generated, with the presence of frailty defined as an FI >0.35. At baseline, participants were asked whether they were “often troubled with pain” and for those who reported “yes”, further information regarding the intensity of their pain (mild, moderate, or severe) was collected.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>experience may create a state of vulnerability to stressors which could explain why people with pain are at increased risk of developing, or experiencing worsening, frailty. Older adults experiencing pain are also less physically active, experience more comorbidities, and worse functional mobility, than older adults without pain and these adverse consequences of pain may be responsible for the increase in risk of developing frailty.</p>		
Hypertension	<p>Having hypertension in midlife increased the odds of frailty in later life by 39% (OR=1.39, 95% CI 1.10-1.76) in the Whitehall II study.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. Lancet Public Health 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, biomedical risk factors were based on measurements at age 45–55 years. Disease status was identified at age 45–55 years. Frailty (defined according to the Fried phenotype) ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p> <p>Hypertension was defined as at least 140 mm Hg systolic or at least 90 mm Hg diastolic blood pressure or on antihypertensive treatment.</p>
Cardiovascular disease	<p>Findings from the Whitehall II study show that cardiovascular disease (CVD) appears to be a risk factor for frailty.</p> <p>Compared to those free of CVD at age 50, individuals with the CVD had a 2-fold increased risk of frailty (OR=2.11, 95% CI: 1.18-3.79) in later life.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. Lancet Public Health 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, disease status was identified at age 45–55 years. Frailty (defined according to the Fried phenotype) ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
Poor Lung Function	<p>Findings from the Whitehall II study show that poor lung function (as measured by FEV) appears to be a risk factor for frailty.</p> <p>Compared to those in the highest one-third (tertile) of FEV scores, people in the middle and lowest tertile had significantly higher risks (54% and 90% higher respectively) of developing frailty.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. <i>Lancet Public Health</i> 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, biomedical risk factors were based on measurements at age 45–55 years. Frailty (defined according to the Fried phenotype) ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p> <p>Lung function was measured by using the largest forced expiratory volume (FEV) in 1 s (measured in L) value of three attempts, corrected for height. Participants were divided into 3 groups (tertiles) based on their FEV values as follows: Highest: (>3.58 L) Middle: 2.91–3.58 L) Lowest: (<2.91 L)</p>
Cognitive impairment	<p>There is substantial evidence than frailty and cognitive decline are associated, and the direction of the association may be bi-directional.</p>		
	<p>A number of epidemiological studies have reported a reciprocal relationship between cognitive decline and frailty in that frailty appears to increase the risk of future cognitive decline and cognitive impairment appears to increase the risk of frailty suggesting that cognition and frailty interact within a cycle of decline associated with ageing.</p>	<p>Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment--a review of the evidence and causal mechanisms. <i>Ageing Res Rev.</i> 2013;12(4):840-851. doi:10.1016/j.arr.2013.06.004</p>	
	<p>A Finnish showed that frail persons were</p>	<p>Kulmala J, Nykänen I, Mänty M, Hartikainen S.</p>	<p>Analysis was based on data from the Geriatric</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>almost 8 times more likely to have cognitive impairment (OR=7.8, 95% CI: 4.0–15.0), 8 times more likely to have some kind of dementia (OR=8.0, 95% CI: 4.0–15.9), almost 6 times more likely to have vascular dementia (OR=5.6, 95% CI: 1.2–25.8) and over 4 times more likely to have Alzheimer’s disease (OR=4.5, 95% CI: 2.1–9.6) than persons who were fit.</p>	<p>Association between frailty and dementia: a population-based study. <i>Gerontology</i>. 2014;60(1):16-21. doi:10.1159/000353859</p>	<p>Multidisciplinary Strategy for the Good Care of the Elderly (GeMS) study, a population-based intervention study in the City of Kuopio, Finland. The study included 654 persons aged 76–100 years. Frailty status was assessed using the Fried Frailty Phenotype definition.ⁱ Cognitive function was assessed with the Mini-Mental State Examination (MMSE). Clinically diagnosed dementia was assessed by specialists using diagnostic criteria.</p>
<p>Poor or Impaired psychological wellbeing / Depression/ Antidepressant Use</p>	<p>A Systematic Review and meta-analysis points to a reciprocal interaction between depression and frailty in older adults. Specifically, each condition is associated with an increased prevalence and incidence of the other and may be a risk factor for the development of the other.</p> <p>This meta-analysis suggests that frail older people are four times more likely to have depression than non-frail people. A similar increased odds for frailty was observed in older people with depression versus those without depression.</p> <ul style="list-style-type: none"> • Across eleven studies, frail people were 4 times more likely to have comorbid depression (OR=4.42, 95% CI: 2.66–7.35) compared to people without frailty. • Across 8 studies people with depression were 4 times more likely to have frailty (OR=4.07, 95%CI: 1.93-8.55) compared to those without depression. 	<p>Soysal P, Veronese N, Thompson T, Kahl K, Fernandes B, Prina M, Solmi M, Schofield P, Koyanagi A, Tseng P, Lin P, Chu C, Cosco T, Cesari M, Carvalho A and Stubbs B. (2017). Relationship between depression and frailty in older adults: A systematic review and meta-analysis. <i>Ageing Research Reviews</i>. 36. 10.1016/j.arr.2017.03.005. https://www.researchgate.net/publication/315723626_Relationship_between_depression_and_frailty_in_older_adults_A_systematic_review_and_meta-analysis</p>	<p>This Systematic Review included 24 studies in older adults with a mean age of 60 years or older. Included studies captured frailty using recognised criteria (e.g. Fried’s criteria)ⁱ and captured depression according to structured interview diagnostic criteria or depressive symptoms with a validated depression screening measure.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>Findings from the Whitehall II study show that depression at age 50 appears to be a risk factor for frailty in later life.</p> <p>Compared to those without depressive symptoms, individuals with depressive symptoms at age 50 had a 65% increased risk of frailty (OR=1.65, 95% CI: 1.33-2.03) in later life.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. <i>Lancet Public Health</i> 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, disease status was identified at age 45–55 years. Depressive symptoms were defined according to general health questionnaire caseness (GHQ-30, score ≥5). Frailty (defined according to the Fried phenotype) ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>
	<p>Another Systematic Review also recognised the bi-directional relationship. While it found that the relationship between depressive symptomatology and increased risk of incident frailty was robust, it reported that the opposite relationship was less conclusive.</p>	<p>Vaughan L, Corbin AL, Goveas JS. Depression and frailty in later life: a systematic review. <i>Clin Interv Aging</i>. 2015;10:1947-1958. Published 2015 Dec 15. doi:10.2147/CIA.S696 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687619/</p>	<p>This Systematic Review included 14 studies published from 2000 to 2015. Participants of included studies were aged 55 years or older and community dwelling. Included studies used an explicit biological definition of frailty based on Fried frailty phenotype criteria ⁱ and a screening measure to identify depressive symptomatology.</p>
	<p>In a large American study, depression and the use of antidepressants at baseline was associated with a higher incidence of frailty three years later.</p> <p>Women with high depressive symptom scores had more than a 2-fold higher risk of developing frailty (OR=2.19, 95% CI:1.86-2.59), and those with intermediate depressive symptoms had a 31% increased risk (OR=1.31, 95% CI: 1.14-1.50) compared to women without depressive symptoms.</p> <p>Antidepressant users exhibiting depressive symptoms were 3.63 times as likely to develop frailty as those without depression and not using antidepressants (95% CI = 2.37-5.55).</p> <p>Even amongst those for whom</p>	<p>Lahey SL, LaCroix AZ, Gray SL, et al. Antidepressant use, depressive symptoms, and incident frailty in women aged 65 and older from the Women's Health Initiative Observational Study. <i>J Am Geriatr Soc</i>. 2012;60(5):854-861. doi:10.1111/j.1532-5415.2012.03940.x https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3354009/</p>	<p>This study included 27,652 women aged 65-79 participating in the Women's Health Initiative Observational Study (WHI-OS). Antidepressant use was assessed through medication container inspection at baseline. Depressive symptoms were assessed at baseline using the Burnam depression screening instrument.</p> <p>Individuals were grouped into 4 categories:</p> <ol style="list-style-type: none"> 1. Antidepressant non-users who were not depressed; 2. Antidepressant users who were not depressed; 3. Antidepressant non-users who were depressed; and 4. Antidepressant users who were depressed.

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>antidepressants had been prescribed for conditions other than depression, antidepressant use was associated with an increased risk of becoming frail. This group were 1.73 times as likely to develop frailty compared to women without depression and not using antidepressants (OR=1.73, 95% CI: 1.41-2.12).</p>		
Vision impairment	<p>Poor vision may be associated with the onset of prefrailty and frailty. Research using data from the English Longitudinal Study of Ageing showed that non-frail older adults with self-reported poor vision have increased risks of becoming prefrail or frail compared with non-frail older adults with good vision. Among non-frail older adults at baseline, those who reported poor vision had an almost 2-fold increased risk of becoming prefrail or frail at 4-year follow-up compared to those with good vision (OR=1.86, 95% CI: 1.17-2.95).</p>	<p>Liljas AEM, Carvalho LA, Papachristou E, et al. Self-reported vision impairment and incident prefrailty and frailty in English community-dwelling older adults: findings from a 4-year follow-up study. <i>J Epidemiol Community Health</i> 2017;71:1053-1058. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5847099/</p>	<p>Data from the English Longitudinal Study of Ageing (ELSA) was used in this study which included 2,836 English community dwellers aged ≥60 years who were followed-up over a 4-year period. A score of 0 out of the 5 Friedⁱ phenotype components was defined as non-frail, 1–2 prefrail and ≥3 as frail. Vision impairment was assessed using a self-reported, validated question previously demonstrated to be accurate when compared with objectively measured eyesight by asking participants whether their eyesight was excellent, very good, good, fair or poor using glasses or corrective lens if they normally do so. Good vision was defined as reporting excellent, very good or good eyesight. Reporting fair or poor eyesight was classified as poor vision.</p>
Hearing impairment	<p>Hearing impairment is common in later life and is estimated to affect 20% of adults in Great Britain aged 60 and older.</p>	<p>Liljas AEM, Carvalho LA, Papachristou E, et al. (2016). Self-Reported Hearing Impairment and Incident Frailty in English Community-Dwelling Older Adults: A 4-Year Follow-Up Study. <i>Journal of the American Geriatrics Society</i>. 65. 10.1111/jgs.14687. https://www.researchgate.net/publication/311750236_Self-Reported_Hearing_Impairment_and_Incident_Fr</p>	

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>The association between hearing loss and frailty may be less straightforward than for vision loss.</p> <p>A Study using data from the English Longitudinal Study of Ageing showed that prefrail older adults with self-reported poor hearing appear to be at greater risk of becoming frail than prefrail older adults with good hearing. Among prefrail participants at baseline, those with hearing impairment had a 64% greater likelihood of being frail at 4-year follow-up (OR=1.57, 95% CI: 1.01-2.44) than those with good hearing. However, among participants who were not frail at baseline, there was no association between poor hearing and risk of frailty 4 years later, after wealth was taken into account.</p>	<p>ailty in English Community-Dwelling Older Adults A 4-Year Follow-Up Study</p> <p>Liljas AEM, Carvalho LA, Papachristou E, et al. (2016). Self-Reported Hearing Impairment and Incident Frailty in English Community-Dwelling Older Adults: A 4-Year Follow-Up Study. Journal of the American Geriatrics Society. 65. 10.1111/jgs.14687. https://www.researchgate.net/publication/311750236_Self-Reported_Hearing_Impairment_and_Incident_Frailty_in_English_Community-Dwelling_Older_Adults_A_4-Year_Follow-Up_Study</p>	<p>Data from the English Longitudinal Study of Ageing (ELSA) was used in this study which included 2,836 English community dwellers aged ≥60 years who were followed-up over a 4-year period. Having none of the five Fried frailty phenotype components¹ was defined as not frail, having one or two as prefrail, and having three or more as frail. Hearing impairment was measured using a self-reported, validated question previously demonstrated to be accurate when compared with objectively measured hearing asking participants to rate their hearing (using a hearing aid if they used one) as excellent, very good, good, fair, or poor. Reporting excellent, very good, or good hearing was classified as having good hearing. Experiencing fair or poor hearing was considered poor hearing.</p>
Hospital admission	<p>Hospital admissions are not only a consequence of frailty, they can be a cause of it. For example, there is evidence that hospital admission itself in a previously independent older person, is a risk factor for increasing dependency in all four activities of daily living (bathing, dressing, walking, and getting in and out of bed/chair).</p>	<p>Gill T, Gahbauer E, Han L & Allore H. (2015). The role of intervening hospital admissions on trajectories of disability in the last year of life: Prospective cohort study of older people. BMJ 2015;350:h2361 doi: 10.1136/bmj.h2361 https://www.researchgate.net/publication/277082859_The_role_of_intervening_hospital_admissions_on_trajectories_of_disability_in_the_last_year_of_life_Prospective_cohort_study_of_older_people</p>	<p>This study was carried out in Connecticut, United States, with 552 community-dwelling adults, aged 70 years or older, who were initially non-disabled in 4 essential activities of daily living: bathing, dressing, walking and getting in and out of bed/chair.</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>Frail patients with acute care needs are especially vulnerable to harm from delays in diagnosis and to 'deconditioning' while in hospital.</p> <p>A US study found that 12% of patients aged 70 and over saw a decline in their ability to undertake key daily activities (bathing, dressing, eating, moving around and toileting) between admission and discharge from hospital, and the extent of decline increased with age.</p>	<p>NHS England and NHS Improvement. Same-day acute frailty services: May 2019. https://improvement.nhs.uk/documents/6111/SDEC_guide_frailty_May_2019_update.pdf</p> <p>Covinsky KE, Palmer RM, Fortinsky RH, et al. Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: increased vulnerability with age. J Am Geriatr Soc. 2003;51(4):451-458. doi:10.1046/j.1532-5415.2003.51152.x https://www.researchgate.net/publication/7838440_Loss_of_Independence_in_Activities_of_Daily_Living_in_Older_Adults_Hospitalized_with_Medical_Illnesses_Increased_Vulnerability_with_Age</p>	<p>This US study was carried out on 2,293 patients aged 70 and older (mean age 80) hospitalised with medical illness.</p>
Hormone therapy use	<p>A very large US study - The Women's Health Initiative Observational Study - showed that compared to women who had never used hormone therapy, those who were current users had a 29% increased three-year odds of frailty (OR=1.29, 95% CI: 1.16-1.42) while past users had a 15% increased odds (OR=1.15, 95% CI:1.02 -1.30).</p>	<p>Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study [published correction appears in J Am Geriatr Soc. 2017 Jul;65(7):1631-1632]. J Am Geriatr Soc. 2005;53(8):1321-1330. doi:10.1111/j.1532-5415.2005.53405.x https://escholarship.org/uc/item/9rp764f5</p>	<p>The Women's Health Initiative Observational Study in the US followed 28,181 women aged 65–79 free of frailty at baseline for 3 years. Frailty was defined according to the Fried phenotype definition.¹ Hormone use was self-reported.</p>
Testosterone	<p>Research findings are not consistent as to the association between testosterone and frailty.</p> <p>A positive association between (lower free) testosterone and frailty was reported in one study (Hyde et al) but no significant association between level of testosterone was found in another other study (Baylis et al, Cawthon et al).</p>	<p>Hyde Z, Flicker L, Almeida OP, Hankey GJ, McCaul KA, Chubb SA, et al. Low free testosterone predicts frailty in older men: the health in men study. J Clin Endocrinol Metab. 2010; 95(7):3165±72. PMID: 20410223. https://doi.org/10.1210/jc.2009-2754</p> <p>Baylis D, Bartlett DB, Syddall HE, Ntani G, Gale CR, Cooper C, et al. Immune-endocrine biomarkers as predictors of frailty and mortality:</p>	

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
		<p>a 10-year longitudinal study in community-dwelling older people. Age (Dordr). 2013; 35(3):963±71. PMID: 22388931.</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3636387/</p>	
Biomarkers	<p>Findings from the Newcastle 85+ Study reported an association between inflammatory markers and frailty in the very old. Limited evidence was found for the role of immunosenescence in frailty in the over 85s in the study.</p> <p><u>Inflammation</u> Compared to the combined middle quartiles, being in the bottom quartile for basal Interleukin 6 (IL-6) or Tumour Necrosis Factor alpha (TNF-alpha) was associated with a lower risk of frailty (applies to both definitions of frailty).</p> <p>A greater risk of frailty was associated with high levels of C-reactive protein (CRP) (applies to both definitions of frailty).</p> <p>Low albumin levels were associated with a greater risk of frailty (applies to both definitions of frailty)</p> <p>Those with high neutrophils were significantly frailer (applies only to the Rockwood Frailty Index definition)</p> <p><u>Immunosenescence</u> For lymphocytes and memory/naïve CD8 T cell ratio, high levels were associated with a lower risk of frailty (applies only to the Fried Frailty phenotype definition).</p>	<p>Collerton J, Martin-Ruiz C, Davies K, et al. Frailty and the role of inflammation, immunosenescence and cellular ageing in the very old: cross-sectional findings from the Newcastle 85+ Study. Mech Ageing Dev. 2012;133(6):456-466.</p> <p>doi:10.1016/j.mad.2012.05.005</p>	<p>Analysis was carried out on data from the Newcastle 85+ Study - a population-based study of a large representative cohort of people aged over 85.</p> <p>Frailty was defined using both Fried's frailty phenotype criteria and the Rockwood Frailty Index.ⁱ</p>

Risk Factor	Impact on frailty	References	Contextual Information/ Notes
	<p>For memory/naïve B cell Ratio, those with low levels were significantly frailer (applies only to the Rockwood Frailty Index definition).ⁱ</p> <p><u>Cellular ageing</u></p> <p>No frailty associations were found with cellular ageing markers.</p>		
	<p>In the Whitehall II study blood biomarker risk factors for frailty were low HDL cholesterol, low ratio of total to HDL cholesterol, and high concentrations of Interleukin-6 and C-reactive protein.</p>	<p>Brunner EJ, Shipley MJ, Ahmadi-Abhari S, et al. Midlife contributors to socioeconomic differences in frailty during later life: a prospective cohort study. <i>Lancet Public Health</i> 2018; published online June 13 https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30079-3/fulltext</p>	<p>The Whitehall II study is a longitudinal cohort study of British civil servants which began in 1985 in participants aged 35–55 years, with repeated data collection every 2–3 years. For this analysis, biomedical risk factors were based on measurements at age 45–55 years. Frailty (defined according to the Fried phenotype)ⁱ was assessed at baseline and at one or more of three clinic visits during a median follow-up period of 18 years.</p>
<p>¹ A number of instruments are available to assess frailty but to-date there have been two main established methods for the evaluation of frailty in research settings.</p> <ul style="list-style-type: none"> • Fried’s criteria defines a clinical syndrome or phenotype, including unintentional weight loss, exhaustion, weak grip strength, slow walking speed and low physical activity and is the most widely used; and • the Frailty Index, first developed in Canada by Rockwood and colleagues, counts accumulated deficits of measures such as symptoms, signs, diseases and disabilities with the hypothesis that the more deficits a person has, the more likely that person is to be frail. 			

Consequences / Outcomes of frailty

Consequences / Outcomes	Impact of frailty	References	Contextual Information / Notes
Outcomes	<p>The consequence of frailty is an increased susceptibility to adverse health outcomes, including disability, falls, hospitalisation, long-term care, dementia, poor quality of life, and mortality.</p>	<p>Kojima G. Frailty as a Predictor of Nursing Home Placement Among Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. <i>J Geriatr Phys Ther.</i> 2018;41(1):42-48. doi:10.1519/JPT.0000000000000097</p> <p>Full text obtained from author.</p>	

Consequences / Outcomes	Impact of frailty	References	Contextual Information / Notes
Perceptions of Frailty	Despite widespread perceptions that frailty is an inevitable part of ageing (D'Avanzo et al), frailty is not a foregone conclusion and is in fact, potentially reversible (Puts et al).	D'Avanzo B, Shaw R, Riva S, Aposolo J, Bobrowicz-Campos E, Kurpas D. Stakeholders views and experiences of care and interventions for addressing frailty and pre-frailty: A meta-synthesis of qualitative evidence. PLOS One 12(7):e0180127 https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0180127&type=printable Puts MTE, Toubasi S, Andrew MK, Ashe MC, Ploeg J, Atkinsons E, Ayala AP, Roy A, Monforte MR, Bergman H, McGilton K. Interventions to prevent or reduce the level of frailty in community dwelling adults: a scoping review of the literature and international policies. Age and Ageing 2017: 46; 383-392. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5405756/pdf/afw247.pdf	
Frailty trajectory	Frailty takes five to ten years to develop and there is often a trajectory of slow functional deterioration.	NHS England/LTC Team, Toolkit for general practice in supporting older people living with frailty. https://www.england.nhs.uk/wp-content/uploads/2017/03/toolkit-general-practice-frailty-1.pdf	
CGA	Comprehensive Geriatric Assessment (CGA) is estimated to avoid one long-term care placement for every 20 people with a CGA.	Safe, compassionate care for frail older people using an integrated care pathway: Practical guidance for commissioners, providers and nursing, medical and allied health professional leaders. NHS England, February 2014. https://www.england.nhs.uk/wp-content/uploads/2014/02/safe-comp-care.pdf	
Attitudes	In terms of care for people who are frail,	D'Avanzo B, Shaw R, Riva S, Aposolo J,	45 papers were included in this synthesis of qualitative

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	<p>the literature shows that frail older people prioritise autonomy and protection; family members prioritise safety, finances, and the value of living at home; and health professionals prioritise safety, autonomy and personal care.</p>	<p>Bobrowicz-Campos E, Kurpas D. Stakeholders views and experiences of care and interventions for addressing frailty and pre-frailty: A meta-synthesis of qualitative evidence. PLOS One 12(7):e0180127 https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0180127&type=printable</p>	<p>evidence which focuses on experiences, understanding, and attitudes towards screening, care, intervention and prevention for frailty across frail and healthy older persons, caregivers, health and social care practitioners.</p> <p>The majority of included studies were conducted in a limited number of Western countries, with a focus on Northern Europe.</p>
<p>Relationship between older people and care providers</p>	<p>The quality of the relationship between older adults and care providers is significant in maintaining older adults' sense of control over their decision-making, and the sense of their personal value. Older people describe the encounter with health and social care as being largely concerned with the struggle for such control, and how this has implications for the frail older persons' satisfaction with care, but also for their self-esteem, with frustration expressed when choices are made according to preferences and standpoints determined by other people or by the care system.</p>	<p>D'Avanzo B, Shaw R, Riva S, Aposolo J, Bobrowicz-Campos E, Kurpas D. Stakeholders views and experiences of care and interventions for addressing frailty and pre-frailty: A meta-synthesis of qualitative evidence. PLOS One 12(7):e0180127 https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0180127&type=printable</p>	<p>45 papers were included in this synthesis of qualitative evidence which focuses on experiences, understanding, and attitudes towards screening, care, intervention and prevention for frailty across frail and healthy older persons, caregivers, health and social care practitioners.</p> <p>The majority of included studies were conducted in a limited number of Western countries, with a focus on Northern Europe.</p>
<p>Mobility difficulties / disability</p>	<p>Mobility difficulties are very common among people living with frailty (93% have difficulties vs only 58% of non-frail individuals) as evidenced by a study based on data from the English Longitudinal Study of Ageing. 57.1% of frail individuals have difficulties in performing activities of daily living (e.g. eating, bathing, dressing, mobility,</p>	<p>Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. Age & Ageing 2015; 44(1): 162-165. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4311180/pdf/afu148.pdf</p>	<p>The data analysed in this study was collected from 2002/3 to 2008/9 on 5,450 individuals aged 60 years and older participating in the English Longitudinal Study of Ageing.</p> <p>Gale et al defined physical frailty as the presence of three or more of the following conditions: unintentional weight loss, weakness, self-reported exhaustion, slow walking speed and low physical</p>

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	<p>toileting) versus 13.7% among non-frail individuals.</p> <p>Among those with difficulties with mobility or other daily activities, 63% of frail individuals and 20% of non-frail individuals use a walking stick.</p>		<p>activity.</p>
	<p>Frailty is a significant predictor of Activities of Daily Living (ADL) and Instrumental Activities of Daily living (IADL) disability among community-dwelling older people, according to a 2017 Systematic Review.</p> <ul style="list-style-type: none"> • Those who were classified as frail were between two and three times (2.23 and 2.76 depending on the measure reported in the included studies) more likely to develop or have worsening disability in relation to ADL compared with those who were classified as non-frail. • In relation to IADL, frail older people were about 4 times (3.62 and 4.24 depending on the measure reported in the included studies) more likely to develop or have worsening disability compared with those who were classified as non-frail. • These disability risks were observed in prefrail individuals to a lesser degree. 	<p>Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. <i>Disability and Rehabilitation</i> 2017;39:1897-1908.</p> <p>https://discovery.ucl.ac.uk/id/eprint/1520943/1/Kojima_MA%20ADL%20manuscript%20for%20UCL.pdf</p>	<p>This Systematic Review included 20 studies. Nine studies were from the USA, five from Europe (none from UK), two from Mexico, one each from Australia and Korea, and two studies used cohorts from multiple countries. Follow-up periods ranged from one year to 11 years.</p> <p>Studies which assessed the association between Frailty and ADL included some or all of the following to define disability: bathing, dressing, going to the toilet, getting into or out of a bed or chair, continence, feeding, walking, grooming and cutting up food.</p> <p>Studies which assessed the association between Frailty and IADL included some or all of the following to define disability: using the telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, and ability to handle finances grooming and using a map.</p>

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Falls	Weakness, impaired balance, and abnormal gait are major components of physical frailty and are likely to increase the risk of falling in older people.	Kojima G. Frailty as a Predictor of Future Falls Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. <i>J Am Med Dir Assoc.</i> 2015;16(12):1027-1033. doi:10.1016/j.jamda.2015.06.018 Full-text obtained from author.	
	Frailty has been demonstrated to be a significant predictor of future falls among community dwelling older people despite various criteria used to define frailty. Frailty was associated with a 24% - 84% (depending on how effect size was reported) increased risk of falls in a 2015 Systematic Review and Meta-Analysis.	Kojima G. Frailty as a Predictor of Future Falls Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. <i>J Am Med Dir Assoc.</i> 2015;16(12):1027-1033. doi:10.1016/j.jamda.2015.06.018 Full-text obtained from author.	11 studies incorporating 68,723 community dwelling individuals aged 60 years or older or mean age of 70 years or older were included in the Systematic Review and meta-analysis. To be included studies had to have measured frailty using validated criteria. More than half of the included studies were from the United States, 3 were from Europe (not UK), 1 was from Taiwan, and 1 included cohorts from multiple countries. Follow-up periods ranged from 1 year to 4 years.
	Around 1 in 3 adults over 65 who live at home will have at least one fall a year, and about half of these will have more frequent falls. In the UK, falls are the most common cause of injury related deaths in people over the age of 75.	https://www.nhs.uk/conditions/falls/	
Fractures	A 2016 Systematic Review and meta-analysis, which pooled data from a number of studies, suggests that both frailty and prefrailty are significant predictors of fractures. Frailty was associated with a 57% - 70% (depending on how effect size was reported)	Kojima G. Frailty as a predictor of fractures among community-dwelling older people: A systematic review and meta-analysis. <i>Bone</i> 2016;90:116-122. https://www.researchgate.net/publication/301552908_Frailty_as_a_Predictor_of_Fractures_among_Community-Dwelling_Older_People	Six studies involving 96,564 older people in the community were included in this review. The mean or median age was approximately 75 to 76 years old. Three studies were conducted in the United States, one study each was from the Netherlands and Italy and one study was from multiple countries. Various types of fractures were monitored as

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	increased risk of fractures and prefrailty with about 30% increased risk of fractures (pooled OR = 1.31, 95% CI: 1.18–1.46).	ng Community-dwelling Older People A Systematic Review and Meta-analysis	outcomes, including any, hip, and non-spine fractures. Follow-up periods varied from one year to 9 years.
Cognitive impairment / dementia	<p>A Systematic Review and Meta-Analysis suggests that frailty may be a significant predictor of Alzheimer disease, vascular dementia, and all dementia among community-dwelling older people.</p> <p>The results show that frailty at baseline increased the risk of developing Alzheimer disease by 28% (4 studies: pooled HR=1.28, 95% CI:1.00-1.63), vascular dementia by 170% (2 studies: pooled HR=2.70, 95% CI: 1.40-5.23) and all dementia by 33% (pooled HR=1.33, 95% CI: 1.07-1.67).</p>	<p>Kojima G , Taniguchi Y , Iliffe S , et al. Frailty as a predictor of Alzheimer’s disease, vascular dementia, and all dementia among community-dwelling older people: a systematic review and meta-analysis . J Am Med Dir Assoc. 2016</p> <p>https://discovery.ucl.ac.uk/id/eprint/1496819/1/Kojima%20et%20al%20Frailty%20as%20a%20Predictor%20of%20Alzheimer’s%20Disease%2C%20Vascular%20Dementia%2C%20and%20All%20Dementia%20among%20Community-Dwelling%20Older%20People%20-%20A%20Systematic%20Review%20and%20Meta-analysis%20AAM.pdf</p>	Seven studies were included in this review. Studies were eligible for inclusion if they were carried out among community-dwelling older adults aged 65 or older and assessed frailty using validated criteria. Follow-up period ranged from 3 to 10 years.
Lower health-related quality of life	<p>A systematic review and meta-analysis provides evidence of a consistent inverse association between frailty/prefrailty and quality of life among community-dwelling older people. Those classified as frail and prefrail had significantly lower mental and physical quality-of-life scores than those classified as non-frail.</p> <p>Interventions targeted at reducing frailty may have the additional benefit of improving corresponding quality of life.</p>	<p>Kojima G, Iliffe S, Jivraj S, Walters K. Association between frailty and quality of life among community-dwelling older people: a systematic review and meta-analysis. Journal of epidemiology and community health 2016;70:716-721.</p> <p>https://www.researchgate.net/publication/291186966_Association_between_frailty_and_quality_of_life_among_community-dwelling_older_people_A_systematic_review_and_meta-analysis</p>	<p>13 studies were included in this Systematic Review but only 4 were included in the Meta-analysis.</p> <p>Frailty was assessed using the Fried phenotype criteria.¹ Quality of Life was assessed using the 36-Item Short Form Health Survey which measures the physical functioning, role limitations due to physical problems, bodily pain, general perception of health, vitality, social functioning, role limitations due to emotional problems, and mental health.</p>

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	The association between frailty and quality of life may possibly be bi-directional. Those who are frail, or become frail, may experience a decline in their quality of life, which in turn is likely to worsen rather than improve their physical and mental health.		
Surgical complications	A US study found that an intermediate level of frailty in patients aged ≥ 65 years undergoing elective surgery was associated with a 2-fold higher odds of 30-day postoperative complications (OR=2.06; 95% CI: 1.18–3.60) while frail patients had a 2.5 times higher odds of complications (OR=2.54, 95% CI: 1.12-5.77) when compared with non-frail patients.	Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. <i>J Am Coll Surg.</i> 2010;210(6):901-908. https://www.journalacs.org/action/showPdf?pii=S1072-7515%2810%2900059-1	This Study followed 594 patients (age 65 years or older) presenting to the Johns Hopkins University Hospital for elective surgery between July 2005 and July 2006. Frailty was measured using Fried Frailty Phenotype criteria. ⁱ Patients scoring 4 to 5 were classified as frail, 2 to 3 were intermediately frail, and 0 to 1 were non-frail.
Greater health service utilisation / increased costs	Between 5% and 10% of all those attending Emergency Departments and 30% of patients in acute medical units (AMUs) are older and frail.	NHS England and NHS Improvement. Same-day acute frailty services: May 2019. https://improvement.nhs.uk/documents/6111/SDEC_guide_frailty_May_2019_update.pdf	
	Among a sample of patients aged 70 and above attending an NHS hospital, 29% were assessed as frail.	Conroy S, Dowsing T. The ability of frailty to predict outcomes in older people attending an acute medical unit. <i>Acute Med.</i> 2013;12(2):74-76.	Over a two-month period in 2011, patients attending the Acute Medical Unit (Monday to Friday) at the Leicester Royal Infirmary, aged 70 or over, were assessed for frailty using Canadian Study on Health and Aging Clinical Frailty Scale.
	Both frailty and prefrailty appear to be significant predictors of Emergency	Kojima G. Frailty as a Predictor of Emergency Department Utilization among Community-Dwelling Older People: A Systematic Review and	4 studies were included in this Review with a total of 2,112 community-dwelling older adults with a mean age of >60 years. The mean follow-up period was 1.4

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	<p>Department (ED) visits.</p> <p>In a Systematic review and meta-analysis frail older adults were approximately twice (pooled OR=2.14, 95% CI: 1.58-2.91) as likely to attend ED compared with those who are non-frail.</p> <p>Prefrailty increased the risk of an ED visit by 46% (pooled OR=1.46, 95% CI: 1.17-1.82).</p> <p>There was a dose-response relationship between the degree of frailty and ED visit risk.</p>	<p>Meta-Analysis. <i>J Am Med Dir Assoc.</i> 2019;20(1):103-105. doi:10.1016/j.jamda.2018.10.004</p> <p>Full text provided by author.</p>	<p>years.</p> <p>To be included studies had to have defined frailty according to validated frailty criteria.</p>
	<p>Frailty, assessed using the electronic Frailty Index (eFI), appears to be a robust predictor of emergency hospital admission.</p> <p>In a study involving almost a million older patients in the UK, emergency admission rates per 1,000 person-years at risk increased from 90.1 (95% CI: 90.0–91.1) for those identified as fit to 211.3 (95% CI: 209.5–213.1) for those with mild frailty, to 407.3 (95% CI: 403.3–411.4) for those with moderate frailty and to 706.7 (95% CI: 696.1–717.3) for those with severe frailty.</p> <p>Compared to those not classified as frail, patients classified as mildly frail were twice as likely (HR=1.93, 95% CI: 1.86–</p>	<p>Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, Mohammed MA, Parry J, Marshall T. Development and validation of an electronic frailty index using routine primary care electronic health record data. <i>Age Ageing.</i> 2016 May;45(3):353-60. doi: 10.1093/ageing/afw039. Epub 2016 Mar 3. Erratum in: <i>Age Ageing.</i> 2017 Jan 17;; PMID: 26944937; PMCID: PMC4846793. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4846793/</p>	<p>This study used primary care electronic health record data on 931,541 patients aged 65–95, contained in the ResearchOne and The Health Improvement Network (THIN) databases from 14 October 2008 to 14 October 2013).</p> <p>Patients with an eFI score of 0–0.12 were defined as fit; >0.12–0.24 as having mild frailty; >0.24–0.36 as moderate frailty and >0.36 as severe frailty.</p>

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	<p>2.01) to have an unplanned hospital admission within a year, while those with moderate frailty were 3 times more likely (HR= 3.04, 95% CI: 2.90–3.19) to be hospitalised and the severely frail 5 times more likely (HR = 4.73, 95% CI 4.43–5.06) to be hospitalised, after adjustment for age and sex.</p> <p>The mean number of bed-days per emergency admission increased from 9.0 for those identified as fit to 9.6 for those with mild frailty, to 10.3 for those with moderate frailty and to 11.1 for those with severe frailty.</p>		
	<p>A 2-year study conducted on 2 cohorts (a female inpatient cohort and an ‘ambulatory’ cohort) of NHS patients in England, found that individuals with frailty who are discharged from hospital appear to experience increased resource use even after short ‘ambulatory’ admission (<72 hours), compared to their non-frail peers.</p> <p>Frail patients in the ambulatory cohort were more likely to have emergency department attendances and emergency admissions than the non-frail patients in the ambulatory cohort.</p> <p>Individuals classified as frail in the ambulatory cohort had between 1.5 and 2.1 times more bed-days than those classified as non-frail, depending on how frailty was defined.</p>	<p>Keeble E, Roberts HC, Williams CD, Van Oppen J, Conroy SP. Outcomes of hospital admissions among frail older people: a 2-year cohort study. <i>Br J Gen Pract.</i> 2019;69(685):e555-e560. doi:10.3399/bjgp19X704621</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6650131/</p>	<p>This study was conducted in two populations aged ≥70 years discharged from NHS hospital units: those following short ‘ambulatory’ admissions (<72 hours) and those following longer inpatient stays. The ambulatory cohort was recruited in large teaching hospitals in Leicester and Nottingham between January 2009 and November 2010. The inpatient cohort was female patients admitted for inpatient care in Medicine for Older People wards in Southampton between November 2009 and February 2012.</p>

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	<p>This study demonstrates poor outcomes even among frail older people discharged from hospital after brief (<72 hours) stays.</p>		
	<p>In England, emergency admissions are particularly high in residential care homes (0.77 admissions per resident per year) compared with nursing care homes (0.63 admissions per resident per year). The average across both settings is 0.70 compared to 0.25 for the general population aged 65 years or older (based on data for 2016/17).</p> <p>In 2016/17, 41% of emergency admissions from care homes were for conditions that are potentially manageable, treatable or preventable outside of a hospital setting, or could have been caused by poor care or neglect. The equivalent figure for the general population aged 65 or older was 27%.</p> <p>People aged 65 and over in care homes attended A&E on average 0.98 times in the year 2016/7, compared with 0.43 times for the general population aged 65 or older. The figures for residential care homes and nursing care homes were 1.12 and 0.85 respectively. One possible explanation for the higher rate in residential care homes is that staff in these homes may have less support in</p>	<p>Wolters A, Santos F, Lloyd T, Lilburne C, Steventon A. Emergency admissions to hospital from care homes: how often and what for? Health Foundation. July 2019. www.health.org.uk/publications/reports/emergency-admissions-to-hospital-from-care-homes</p>	<p>The conditions that we deemed to be potentially manageable, treatable or preventable outside a hospital setting were as follows:</p> <ul style="list-style-type: none"> • acute lower respiratory tract infections, such as acute bronchitis; • chronic lower respiratory tract infections, such as emphysema; • diabetes; • food and drink issues, such as abnormal weight loss and poor intake of food and water, possibly due to neglect; • fractures and sprains; • intestinal infections; • pneumonia; • pneumonitis (inflammation of lung tissue) caused by inhaled food or liquid; • pressure sores; • urinary tract infections.

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	managing health needs within the home, and therefore rely more on emergency services. Also, health needs may not be detected as early in residential homes as in nursing homes.		
	Both prefrailty and frailty are associated with significantly higher healthcare costs when compared with robustness, according to a 2019 Systematic Review. The higher the degree of frailty, the higher the level of expenditure on healthcare.	Kojima G. Increased healthcare costs associated with frailty among community-dwelling older people: A systematic review and meta-analysis. <i>Arch Gerontol Geriatr.</i> 2019;84:103898. doi:10.1016/j.archger.2019.06.003 Full text provided by lead author.	5 studies involving 3,742,362 community-dwelling older people with a mean age of 60 years or higher were included in this Systematic Review.
	In a Canadian study frailty was associated with a substantially increased risk of early readmission or death after discharge from medical wards. Patients with moderate or severe frailty were more likely than non-frail patients to be readmitted or to die within 30 days after discharge (31.0% vs. 13.8%). Frail patients were more likely than non-frail patients to present to an emergency department during the 30-day follow-up period (32.7% v. 23.4%).	Kahlon S, Pederson J, Majumdar SR, et al. Association between frailty and 30-day outcomes after discharge from hospital. <i>CMAJ.</i> 2015;187(11):799-804. doi:10.1503/cmaj.150100 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4527901/	The study included 495 patients discharged from seven medical wards at two teaching hospitals in Edmonton between October 2013 and November 2014. Frailty was defined by means of the Clinical Frailty Scale.
Institutionalisation in long-term care	It has been estimated that just over half (52.3%) of people in Nursing Homes are frail, and about 40% are prefrail.	Kojima G. Prevalence of Frailty in Nursing Homes: A Systematic Review and Meta-Analysis. <i>J Am Med Dir Assoc.</i> 2015;16(11):940-945. doi:10.1016/j.jamda.2015.06.025 Full text provided by author.	Nine studies with a total of 1,373 nursing home patients were included in this Systematic Review and Meta-analysis. Four were from Brazil and Spain and one each from Taiwan, Lebanon, Egypt, The Netherlands, and Poland. To be included in the Review studies had to include nursing home participants aged 60 years or older and use validated criteria or definitions to define frailty.

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	<p>In a study involving almost a million older patients in the UK, frailty, assessed using the electronic Frailty Index (eFI), was a robust predictor of nursing home admission at 1,3 and 5 years. Compared to people without frailty, mild frailty almost doubled the 1 year nursing home admission rate (HR=1.89, 95% CI 1.63–2.15) while moderate frailty trebled the rate (HR=3.19, 95% CI: 2.73–3.73) and in those with severe frailty the admission rate was almost 5 times higher (HR=4.76, 95% CI: 3.92–5.77) compared to patients without frailty.</p>	<p>Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, Mohammed MA, Parry J, Marshall T. Development and validation of an electronic frailty index using routine primary care electronic health record data. <i>Age Ageing</i>. 2016 May;45(3):353-60. doi: 10.1093/ageing/afw039. Epub 2016 Mar 3. Erratum in: <i>Age Ageing</i>. 2017 Jan 17;; PMID: 26944937; PMCID: PMC4846793. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4846793/</p>	<p>This study used primary care electronic health record data on 931,541 patients aged 65–95, contained in the ResearchOne and The Health Improvement Network (THIN) databases from 14 October 2008 to 14 October 2013.</p> <p>Patients with an eFI score of 0–0.12 were defined as fit; >0.12–0.24 as having mild frailty; >0.24–0.36 as moderate frailty and >0.36 as severe frailty.</p>
	<p>A Systematic Review and meta-analysis suggests that frailty may be a significant predictor of nursing home placement among community-dwelling older adults. Frail and prefrail older adults were approximately 5 times (pooled OR=5.58, 95% CI: 2.94-10.60) and 3 times (pooled OR=3.26, 95% CI:1.21-8.78) more likely to be institutionalized, respectively, compared with those who are non-frail.</p>	<p>Kojima G. Frailty as a Predictor of Nursing Home Placement Among Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. <i>J Geriatr Phys Ther</i>. 2018;41(1):42-48. doi:10.1519/JPT.0000000000000097</p> <p>Full text obtained from author.</p>	<p>5 studies including 3,528 community-dwelling older adults were included in this review. Four studies were from Europe (Italy, Portugal, and Netherlands) and one from the United States.</p> <p>A range of criteria were used to define frailty. Follow-up periods ranged from 10 months up to 4 years, with the mean of 2.2 years.</p> <p>It should be noted that the numbers of participants who were admitted to nursing homes were fairly small in all of the included studies.</p>
	<p>The estimated average number of frailty related comorbidities (e.g. incontinence, mobility problems and pressure ulcers) is 1.72 in Residential homes and 1.98 in Nursing homes in England (based on data for 2016/17).</p>	<p>Wolters A, Santos F, Lloyd T, Lilburne C, Steventon A. Emergency admissions to hospital from care homes: how often and what for? Health Foundation. July 2019. www.health.org.uk/publications/reports/emergency-admissions-to-hospital-from-care-homes</p>	

Consequences / Outcomes	Impact of frailty	References	Contextual Information / Notes
Death	<p>In a study involving almost a million older patients in the UK, frailty, assessed using the electronic Frailty Index (eFI), was a robust predictor of mortality at 1,3 and 5 years. Mild frailty almost doubled the 1 year death rate (HR=1.92, 95% CI 1.81–2.04) while moderate frailty trebled the rate (HR=3.10, 95% CI: 2.91–3.31) and in those with severe frailty the death rate was 4-fold higher (HR=4.52, 95% CI: 4.16–4.91) compared to patients without frailty.</p>	<p>Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, Mohammed MA, Parry J, Marshall T. Development and validation of an electronic frailty index using routine primary care electronic health record data. <i>Age Ageing</i>. 2016 May;45(3):353-60. doi: 10.1093/ageing/afw039. Epub 2016 Mar 3. Erratum in: <i>Age Ageing</i>. 2017 Jan 17;; PMID: 26944937; PMCID: PMC4846793.</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4846793/</p>	<p>This study used primary care electronic health record data on 931,541 patients aged 65–95, contained in the ResearchOne and The Health Improvement Network (THIN) databases from 14 October 2008 to 14 October 2013.</p> <p>Patients with an eFI score of 0–0.12 were defined as fit; >0.12–0.24 as having mild frailty; >0.24–0.36 as moderate frailty and >0.36 as severe frailty.</p>
	<p>A 2-year study conducted on 2 cohorts (a female inpatient cohort and an ‘ambulatory’ cohort) of NHS patients in England, found that individuals with frailty who are discharged from hospital appear to experience increased mortality even after short ‘ambulatory’ admission (<72 hours), compared to their non-frail peers.</p> <p>Dependent on the measure used to define frailty, 32.2–36.8% of individuals classified as frail in the ambulatory cohort died during the 2-year follow-up period compared with 42.4–52.7% in the inpatient cohort.</p> <p>Frail patients in the ambulatory cohort were around twice as likely to die within 2 years compared with the non-frail. Frail patients in the inpatient cohort were between 1.6 and 2.3 times more likely to die within the 2 years than the</p>	<p>Keeble E, Roberts HC, Williams CD, Van Oppen J, Conroy SP. Outcomes of hospital admissions among frail older people: a 2-year cohort study. <i>Br J Gen Pract</i>. 2019;69(685):e555-e560. doi:10.3399/bjgp19X704621</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6650131/</p>	<p>This study was conducted in two populations aged ≥70 years discharged from NHS hospital units: those following short ‘ambulatory’ admissions (<72 hours) and those following longer inpatient stays. The ambulatory cohort was recruited in large teaching hospitals in Leicester and Nottingham between January 2009 and November 2010. The inpatient cohort was female patients admitted for inpatient care in Medicine for Older People wards in Southampton between November 2009 and February 2012.</p>

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	non-frail, dependent on whether the measure used to define frailty was the Fried frailty phenotype criteria or the Frailty Index. ⁱ		
	A US study found that those who were frail before a life-event (the death of a close relative or friend) had 2.6-fold (95% CI=1.6–4.0) increase in mortality risk compared to those becoming frail after the life event.	FRAILTY, BEREAVEMENT, AND MORTALITY, <i>The Gerontologist</i> , Volume 56, Issue Suppl_3, 1 November 2016, Page 286. https://doi.org/10.1093/geront/gnw162.1158	This study included 516 individuals who were non-frail at baseline but became frail and experienced the death of a close relative or friend during the 10-year follow-up.

ⁱ A number of instruments are available to assess frailty but to-date there have been two main established methods for the evaluation of frailty in research settings.

- Fried’s criteria defines a clinical syndrome or phenotype, including unintentional weight loss, exhaustion, weak grip strength, slow walking speed and low physical activity and is the most widely used; and
- the Frailty Index, first developed in Canada by Rockwood and colleagues, counts accumulated deficits of measures such as symptoms, signs, diseases and disabilities with the hypothesis that the more deficits a person has, the more likely that person is to be frail.