

Evidence table UV 2

Research question: Which patient, socio-economic and care characteristics are associated with high healthcare utilisation in countries with a high-income economy?

Study reference	Study characteristics	Patient characteristics	Prognostic factor(s)	Outcome and follow-up	Estimates of prognostic effect	Comments
<b>Entire population 18+</b>						
Hull, 2018	<p>Type of study: Cohort study</p> <p>Setting and country: Linked primary care and ED attendance data in the three geographically contiguous East London CCGs of Newham, Tower Hamlets and City &amp; Hackney, UK</p> <p>Funding and conflicts of interest: No funding given; The authors have declared no competing interests.</p>	<p>Inclusion criteria: All patients registered at the 141 practices on or before 1 July 2013. Primary and secondary care usage data were extracted for each patient for the 2-year study period from 1 January 2014 through 31 December 2015</p> <p>Exclusion criteria: None specified N= 819.590 (626.395 adults (aged 18&lt;))</p> <p>Mean age ± SD: not reported; Age groups were reported, we report only data from adults: 18–34 289 383 (46.2) 35–44 137 402 (21.9) 45–54 91 132 (14.5) 55–64 53 979 (8.6) 65–74 30 071 (4.8) ≥75 24 428 (3.9)</p> <p>Sex: 51.7 % M / 48.3 % F</p> <p>Potential confounders or effect modifiers:</p>	<p>Prognostic factor(s) and method of measurement: - <u>Sex</u>: extracted from North and East London Commissioning Support Unit (NELCSU) - <u>Age</u>: extracted from North and East London Commissioning Support Unit (NELCSU) - <u>Ethnicity</u>: self-reported during registration or routine consultation: extracted from North and East London Commissioning Support Unit (NELCSU) - <u>Deprivation</u>: English indices of deprivation (IMD) 2015 score as a measure of social deprivation - <u>Residential status</u>: extraction not reported - <u>Nr of long-term conditions</u>: extraction and total count of presence of 16 (Quality Outcomes Framework(QOF)) long-term conditions; including different exclusive clusters - <u>Nr of GP consultations per year, per patient</u>: extracted from North and East London Commissioning Support Unit (NELCSU)</p>	<p>Duration or endpoint of follow-up: - Emergency Department (ED) attendance within 2-year study from 1 January 2014 through 31 December 2015</p> <p>For how many participants were no complete outcome data available? N (%): 0 (0%)</p> <p>Reasons for incomplete outcome data described? N/A</p>	<p>(Adjusted) Factor-outcome associations (OR (95% CI); p= p-value): <i>ED attendance during study period</i> - <u>Sex (female)</u>: 0.92 (0.90-0.93); p= 0.00 - <u>Age (bands)</u>: 18-34 (ref): 1 35-44: 0.79 (0.78-0.81); p= 0.00 45-54: 0.72 (0.71-0.74); p= 0.00 55-64: 0.66 (0.64-0.67); p= 0.00 65-74: 0.69 (0.67-0.71); p= 0.00 ≥75: 0.98 (0.94-1.01); p= 0.18 - <u>Ethnicity</u>: White (ref): 1 South Asian: 0.90 (0.89-0.92); p= 0.00 Black: 1.08 (1.06-1.10); p=0.00 - <u>Deprivation</u>: 1 least deprived (ref): 1 2: 1.06 (1.04-1.09); p=0.00 3: 1.08 (1.05-1.10); p=0.00 4: 1.11 (1.09-1.14); p=0.00 5 most deprived: 1.15 (1.12-1.18); p=0.00 - <u>Residential status</u>: Independent (ref): 1 Housebound: 2.01 (1.86-2.18); p=0.00 Care home: 1.20 (1.02-1.41); p=0.03 - <u>Nr of long-term conditions</u>: 0 (ref): 1 1: 1.12 (1.10-1.13); p=0.00 2: 1.28 (1.25-1.31); p=0.00</p>	In univariate analyses age group ≥ 75 has an OR 3.21 (3.12-3.29). This effect disappears when corrected for the other variables in the multivariate model.

		Smoking and BMI.			3: 1.65 (1.59-1.71); p=0.00 ≥ 4: 2.55 (2.44-2.66); p=0.00 - <u>Nr of GP consultations per year, per patient</u> : 0.5-2 (ref): 1 0: 0.29 (0.28-0.29); p=0.00 ≥2.5: 2.44 (2.40-2.48); p=0.00  Incremental predictive value <sup>1</sup> : Not reported	
Agborsangaya, 2013	Type of study: Cross-sectional study  Setting and country: Data from the Health Quality Council of Alberta (HQCA) 2010 Patient Experience, Canada  Funding and conflicts of interest: No statement about funding or conflicts by authors	Inclusion criteria: Sample of adult Albertans aged 18 years or older on their experiences and satisfaction with the quality of health services they receive in the past year.  Exclusion criteria: None specified.  N= 4.946  Mean age ± SD: 46.6 (16.5)  Sex: 52.3 % M / 47.7 % F  Potential confounders or effect modifiers: age, sex, education, income and family structure (children and adults living in the same household)	Prognostic factor(s) and method of measurement: - <u>Morbidity status</u> : patient-reported of 14 listed chronic conditions and 2 additional chronic conditions from open-ended item. Multimorbidity was defined as 2 or more chronic conditions.	Duration or endpoint of follow-up: - Hospitalization (yes/no, self-reported) in the previous year - Emergency department visits (yes/no, self-reported) in the previous year  For how many participants were no complete outcome data available? N (%): 64 (1.3%) (of 5010 respondents)  Reasons for incomplete outcome data described? Not reported.	(Adjusted) Factor-outcome associations : <i>Hospitalization in previous year</i> - <u>Morbidity status</u> (OR (95% CI); no p-values reported): 0 conditions (ref): 1 1 condition: 1.2 (0.9-1.7) 2 conditions: 1.8 (1.2-2.7) 3 conditions: 2.3 (1.4-3.7) 4 conditions: 2.9 (1.7-5.0) ≥ 5 conditions: 3.2 (1.9-5.3) Multimorbidity: 2.2 (1.7-2.9)  <i>Emergency department visit in previous year</i> - <u>Morbidity status</u> (OR (95% CI); p-values not reported): 0 conditions (ref): 1 1 condition: 1.8 (1.4-2.3) 2 conditions: 1.6 (1.2-2.2) 3 conditions: 2.7 (1.8-4.0) 4 conditions: 1.9 (1.2-3.0) ≥ 5 conditions: 2.5 (1.6-3.9) Multimorbidity: 1.8 (1.4-2.2)  Incremental predictive value <sup>1</sup> : Not reported	
Milani, 2016	Type of study: Cross-sectional study  Setting and country: Members of HealthStreet, a community outreach	Inclusion criteria: participants 18 and over from Northeast and North Central Florida who completed the HealthStreet Intake Form from November	Describe prognostic factor(s) and method of measurement: - <u>Sex</u> : self-reported during in-person interview - <u>Nr of chronic diseases</u> : self-reported during in-person interview, from a list of 5 most	Duration or endpoint of follow-up: Frequent ED visits defined as 2 or more visits in the last 6 months  For how many participants were no complete outcome data available?	(Adjusted) Factor-outcome associations : <i>Frequent emergency department visits in previous six months</i> (OR (95% CI); p-values not reported) - <u>Males with 1-2 Chronic Diseases Compared to None</u>	

	<p>engagement program at the University of Florida, from Northeast and North Central Florida, USA</p> <p>Funding and conflicts of interest: Co-author L.B. Cottler is the Founder and Director of HealthStreet, from which the data were obtained. Co-author C.W. Striley is Co-Director of HealthStreet. Sadaf Milani is funded by the Graduate School Fellowship at the University of Florida.</p>	<p>2011 to July 2016 were included</p> <p>Exclusion criteria: None specified.</p> <p>N= 7.143 (table 1 reports only 7.136 participants)</p> <p>Mean age ± SD: <i>Males</i> No frequent ED use: 43.7 (15.6) Frequent ED use: 45.7 (13.7) <i>Females</i> No frequent ED use: 44.2 (16.2) Frequent ED use: 40.8 (14.3)</p> <p>Sex: 42.0 % M / 58.0 % F</p> <p>Potential confounders or effect modifiers: age, depression, marital status, employment status and food insecurity</p>	<p>common chronic diseases: asthma, COPD, coronary artery disease, hypertension, and diabetes</p>	<p>N (%): not reported</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>1.58 (1.2, 2.0) <u>- Males with 3-5 Chronic Diseases Compared to None</u> 4.98 (2.9, 8.6) <u>- Females with 1-2 Chronic Diseases Compared to None</u> 1.61 (1.3, 1.9) <u>- Females with 3-5 Chronic Diseases Compared to None</u> 2.49 (1.7, 3.6)</p> <p>Incremental predictive value<sup>1</sup>: Not reported</p>	
<b>Entire population 50+</b>						
<p>Ilinca 2015</p> <p>(Study with SHARE data, also used in Palladino, 2016, but with different aim and analyses and unclear (possible) overlap)</p>	<p>Type of study: Longitudinal cohort study</p> <p>Setting and country: Telephone based questionnaire, in 3 waves (biennial) collected (baseline and follow-ups), Survey of Health, Ageing and Retirement in</p>	<p>Inclusion criteria: The target population for the baseline samples consists of all persons born 1960 or earlier having their regular domicile in the respective country, together with their current partners/ spouses, independent of age.</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Frailty</u> (phenotype definition by Fried et al. 2001), consisting of assessing five dimensions: grip strength, energy, walking speed, physical activity, and unintentional weight loss. An individual is frail if three or more of the above dimensions are compromised, whereas s/he is robust when none of these</p>	<p>Duration or endpoint of follow-up: the number of doctor visits and hospitalization in the 12 months prior to the study</p> <p>For how many participants were no complete outcome data available? N (%): no missing values</p> <p>Reasons for incomplete outcome data described? The sample consisted of 83.019</p>	<p>(Adjusted) Factor-outcome associations : <i>Number of doctor visits in the 12 months prior to the study (Incidence Rate Ratios (fixed effects), No CIs reported)</i> <u>Frailty</u> - Robust (ref): 1 - Prefrail: 1.168, p-value &lt;0.001 - Frail: 1.452, p-value &lt;0.001</p> <p><u>Multimorbidity</u> 1.228, p-value &lt;0.001</p>	<p>Number of general practitioner (GP) visits in the 12 months prior to the study was also an endpoint, but not included in this review because it was outside of the scope</p>

	<p>Europe (SHARE), in 10 European countries: Denmark, Sweden, the Netherlands, Germany, France, Belgium, Switzerland, Austria, Spain, and Italy, from the three regular panel waves of SHARE, as published in releases 2.5.0 and 1.1.1</p> <p>Funding and conflicts of interest: None reported</p>	<p>Exclusion criteria: none specified</p> <p>N= 50.967</p> <p>Age bands (N): 50–59: 26.095 60–69: 28.005 70–79: 19.282 80+: 9.618</p> <p>Sex: not reported for total group</p> <p>Potential confounders or effect modifiers: psychological factors, financial distress</p>	<p>deficits are present. Intermediate situations are defined as prefrailty. Santos-Eggimann et al. (2009) adapted this operationalization to the SHARE dataset and Romero-Ortuno et al. (2010) validated it.</p> <p><u>Multimorbidity</u> Method of measurement and definition not reported (other information collected through questionnaire. In Palladino 2016 multimorbidity was defined as the presence of two or more chronic diseases.)</p> <p><u>ADL limitations</u> KATZ ADL-6</p> <p>Other variables, self-reported by respondent in telephone based questionnaire: <u>Long-term illness</u> <u>Age category</u> <u>Male</u> <u>Living with partner</u> <u>Children</u> <u>Education</u> <u>Household Wealth</u> <u>Smoker (has ever smoked)</u></p>	<p>observations from 50.967 individuals. The resulting panel was unbalanced: 10.159 and 11.734 individuals had been observed in all the three waves and in two waves, respectively. To ensure attrition did not affect their estimates, the authors ran variable addition tests (Verbeek and Nijman 1996). Results rejected the hypothesis of significant correlation between the pattern of missing values and our health utilization variables. The authors also ran the estimation on pooled data and on individual waves, and verified the robustness of our results. Finally, the authors decided against using the balanced longitudinal subsample because death and incapacity were likely to be important sources of nonresponse in the SHARE data. Therefore, such a restriction would introduce bias by eliminating the more frail individuals from the analysis ( Jones et al. 2007).</p>	<p>Interaction effects: - Prefrail x multimorbidity: 0.947 (p-value not significant) - Frail x multimorbidity: 0.727, p-value&lt;0.001</p> <p><u>ADL limitations</u> 1.037, p-value&lt;0.05</p> <p><u>Long-term illness</u> 1.172, p-value&lt;0.001</p> <p><u>Age category</u> -50-59: reference - 60-69: 0.972, p-value not significant - 70-79: 0.936, p-value not significant - 80+: 0.916, p-value not significant</p> <p><u>Sex (male)</u> Pooled effects (no fixed effects available): 0.991, p-value not significant</p> <p><u>Living with partner</u> 1.034, p-value not significant</p> <p><u>Children</u> 1.173, p-value not significant</p> <p><u>Education</u> - Primary: reference - Secondary 0.949, p-value not significant - Tertiary 0.930, p-value not significant</p> <p><u>Household wealth</u> - 1<sup>st</sup> quartile (reference) - 2<sup>nd</sup> quartile: 1.009, p-value not significant - 3<sup>rd</sup> quartile: 0.983, p-value not significant - 4<sup>th</sup> quartile 1.011, p-value not significant</p>	
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					<p>Incremental predictive value<sup>1</sup>: not reported</p> <p><i>Hospitalization in the 12 months prior to the study (Odds Ratios (conditional logit) no CIs reported)</i></p> <p><u>Frailty</u></p> <ul style="list-style-type: none"> <li>- Robust (ref): 1</li> <li>- Prefrail: 1.234 p-value &lt;0.001</li> <li>- Frail: 1.895, p-values &lt;0.001</li> </ul> <p>No CIs reported</p> <p><u>Multimorbidity</u></p> <p>1.434, p-value &lt;0.001</p> <p>Interaction effects</p> <p>Prefrail x multimorbidity: 1.023, p-value not significant</p> <p>Frail x multimorbidity: 0.737, p-value &lt;0.05</p> <p><u>ADL limitations</u></p> <p>1.087, p-value &lt; 0.01</p> <p><u>Long-term illness</u></p> <p>1.172, p-value &lt;0.01</p> <p><u>Age category</u></p> <ul style="list-style-type: none"> <li>-50-59: reference</li> <li>-60-69: 1.059, p-value not significant</li> <li>-70-79: 1.220, p-value not significant</li> <li>- 80+: 1.296, p-value not significant</li> </ul> <p><u>Sex (male)</u></p> <p>Pooled effect (no conditional logit available): 1.282, p-value&lt;0.001</p> <p><u>Living with partner</u></p> <p>1.240, p-value not significant</p> <p><u>Children</u></p> <p>0.861, p-value not significant</p> <p><u>Education</u></p> <ul style="list-style-type: none"> <li>- Primary: reference</li> <li>- Secondary: 1.015, p-value not</li> </ul>	
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					<p>significant - Tertiary: 0.986, p-value not significant</p> <p><u>Household wealth</u> - 1<sup>st</sup> quartile: reference - 2<sup>nd</sup> quartile: 1.053, p-value not significant - 3<sup>rd</sup> quartile: 0.971, p-value not significant - 4<sup>th</sup> quartile: 1.153, p-value not significant</p> <p>Incremental predictive value<sup>1</sup>: Not reported</p>	
<p>Palladino, 2016</p> <p>(Study with SHARE data, also used in Ilinca, 2015, but with different aim and analyses and unclear (possible) overlap)</p>	<p>Type of study: Longitudinal cohort study</p> <p>Setting and country: Telephone based questionnaire, in 1 wave (biennial) collected (baseline and follow-ups), Survey of Health, Ageing and Retirement in Europe (SHARE), in 16 European countries: Austria, Belgium, Switzerland, Germany, Denmark, Spain, France, Italy, Netherlands, Sweden, Czech Republic, Poland, Estonia, Hungary, Portugal and Slovenia, from wave 4 (2011-12)</p>	<p>Inclusion criteria: The target population for the baseline samples consists of all persons born 1960 or earlier having their regular domicile in the respective country, together with their current partners/spouses, independent of age.</p> <p>Exclusion criteria: none specified</p> <p>N= 56.427</p> <p>Median age ± IQR: 66 (58-73) years</p> <p>Sex: 44.1 % M / 55.9 % F</p> <p>Potential confounders or effect modifiers: age, sex, number of people living in the same household, residence, educational</p>	<p>Describe prognostic factor(s) and method of measurement: Number of coexistent chronic diseases reported by each respondent. Multimorbidity was defined as the presence of two or more chronic diseases.</p>	<p>Duration or endpoint of follow-up: Number of medical doctor visits (number of medical doctor visits, defined as the sum of general practitioner (GP), emergency room and outpatient visits during the last year) and being hospitalized, number of hospitalizations and length of hospital stay</p> <p>For how many participants were no complete outcome data available? N (%): not reported</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>(Adjusted) Factor-outcome associations :</p> <p><i>Number of medical doctor visits</i> <u>Increasing number of CDs</u> (negative binomial model Incidence Risk Ratio (IRR) (95%CI)): IRR 1.336, 95% CI = 1.310–1.350), p-value not reported</p> <p><i>Being hospitalized</i> <u>Increasing number of CDs</u> (multivariate logistic regression OR (95% CI), p-values not reported): 1.49 (1.42–1.55)</p> <p><i>Number of hospitalizations</i> <u>Increasing number of CDs</u> (negative binomial model Incidence Risk Ratio (IRR) (95%CI)): IRR 1.419, 95% CI = 1.363–1.492), p-value not reported</p> <p><i>Length of hospital stay</i> <u>Increasing number of CDs</u> (negative binomial model Incidence Risk Ratio (IRR) (95%CI)): IRR 1.632, 95% CI = 1.537–1.733), p-value not</p>	

	Funding and conflicts of interest:	level and employment status.			reported	
					Incremental predictive value <sup>1</sup> : Not reported	
Glynn, 2011	<p>Type of study: Cross-sectional study</p> <p>Setting and country: All patients from three family practices (10 primary care physicians) from a mixed urban/rural setting in the West of Ireland.</p> <p>Funding and conflicts of interest: Study was supported by a grant from the Irish College of General Practitioners Research and Education Foundation. AWM has received funding from Pfizer to support educational meetings for GPs who teach medical students from the Department of General Practice at NUI, Galway. LG has received an honorarium from Roche laboratories for contribution to the development of chronic kidney disease guidelines</p>	<p>Inclusion criteria: All active (two or more consultations in the previous 2 years) patients &gt;50 years of age</p> <p>Exclusion criteria: visitors, patients who had moved away or practice inter-referrals were excluded (by the specific inclusion criteria)</p> <p>N= 3309</p> <p>Age groups: 50-59 years: 39.6% 60-59 years: 29.5% 70-79 years: 19.0% ≥ 80 years: 12.0%</p> <p>Sex: 49.1% M / 51.9% F</p> <p>Potential confounders or effect modifiers: Age, sex and free medical care eligibility</p>	<p>Describe prognostic factor(s) and method of measurement: Multimorbidity: count of chronic conditions according to the World Health Organization definition (health problems that require ongoing management over a period of years or decades). Multimorbidity was defined as two or more chronic medical conditions occurring simultaneously.</p>	<p>Duration or endpoint of follow-up: Health care utilization: hospital out-patient visits and hospital admissions in the previous 12 months.</p> <p>Healthcare costs: Unit cost data for primary care consultations, hospital out-patient visits and hospital admissions were obtained from national data sources and applied to each component of health care utilization to estimate the total cost of care. Total health care cost = primary care consultations + hospital outpatient visits + hospital admissions</p> <p>For how many participants were no complete outcome data available? N (%): Not specified</p> <p>Reasons for incomplete outcome data described? Not specified</p>	<p>(Adjusted) Factor-outcome associations: <i>Hospital out-patient visits in the previous 12 months</i> Adjusted mean difference (95% CI), 0 chronic conditions: 0.63 (0.52–0.73) (reference) 1 chronic conditions: 1.17 (1.04–1.30) (p &lt; 0.001 compared to baseline) 2 chronic conditions: 1.43 (1.29–1.57) (p &lt; 0.001 compared to baseline) 3 chronic conditions: 1.92 (1.71–2.12) (p &lt; 0.001 compared to baseline) 4 chronic conditions: 2.42 (2.10–2.75) (p &lt; 0.001 compared to baseline) &gt;4 chronic conditions: 3.58 (3.11–4.06) (p &lt; 0.001 compared to baseline)</p> <p><i>Hospital admissions in the previous 12 months</i> Odds ratio (95% CI) 0 chronic conditions: Reference group 1 chronic conditions: 1.16 (0.71–1.89) (p-value=0.55) 2 chronic conditions: 1.86 (1.18–2.94) (p-value &lt; 0.01) 3 chronic conditions: 2.12 (1.33–3.38) (p-value &lt; 0.01) 4 chronic conditions: 3.80 (2.35–6.12) (p-value &lt; 0.01) &gt;4 chronic conditions: 4.51 (2.79–7.29) (p-value &lt; 0.01)</p> <p>The statistical models used were adjusted for explanatory variables</p>	

	for primary care. Other authors declare no conflict of interest.				<p>(sex, free medical care eligibility) and were fixed at an age covariate value of 65 years.</p> <p><i>Healthcare costs</i> Adjusted mean cost estimate for total healthcare cost (mean cost estimate, € (95% CI), p-value of pairwise comparison with 0 chronic conditions) 0 chronic conditions: 562.07 (549.33-574.81) (reference) 1 chronic conditions: 888.22 (871.82-904.61) (p-value =0.026 compared to baseline) 2 chronic conditions: 1320.14 (1296.62-1343.66) (p-value =0.002 compared to baseline) 3 chronic conditions: 1631.82 (1600.03-1663.62) (p-value =0.001 compared to baseline) 4 chronic conditions: 2339.01 (2283.36-2394.65) (p-value =0.000 compared to baseline) &gt;4 chronic conditions: 3029.11 (2970.95-3087.27) (p-value =0.000 compared to baseline) The statistical model (Generalized Linear Model, assuming Gamma variance log link) used in the above analysis was adjusted for explanatory variables (sex, free medical care eligibility and practice cluster) and is fixed at an age covariate value of 65 years.</p> <p>Incremental predictive value<sup>1</sup>: Not reported</p>	
Kennedy, 2017	<p>Type of study: Cohort study</p> <p>Setting and country: population-representative cohort</p>	<p>Inclusion criteria: Adults aged 50 years or over</p> <p>Exclusion criteria: None specified</p> <p>N= 8.170 (authors</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Sex</u> Recorded by interviewer</p> <p><u>Education</u> primary/elementary,</p>	<p>Duration or endpoint of follow-up: Having an outpatient visit in the last 12 months (self-reported, asked and recorded by interviewer)</p> <p>For how many participants were</p>	<p>(Adjusted) Factor-outcome associations : <i>Having an outpatient visit in the last 12 months (Odds ratio (95% CI), p-value)</i> <u>Sex</u> Male: reference group</p>	Age not included in model because of strong correlation with number of chronic conditions



<p>study of community living (not in a long-term care institution) older adults resident in the Republic of Ireland.</p> <p>Funding and conflicts of interest: None declared.</p>	<p>report 8171 in abstract</p> <p>Mean age ± SD: Not reported, all participants aged over 50 years. Age groups for different pain profiles were reported.</p> <p>Overall (calculated) age groups: 50-64: 59.9% 65-74: 21.5% &gt;75: 18.6%</p> <p>Sex: 48.1% M / 51.9% F</p> <p>Potential confounders or effect modifiers: age not included in model because of strong correlation with number of chronic conditions</p>	<p>secondary/high school and third level/university, recorded by interviewer</p> <p><u>Private health insurance/free government funded medical care (GMS eligible) or free visits to GP (doctor visit card -DVC)</u> Self-reported, asked and recorded by interviewer</p> <p><u>Pain, self-reported.</u> Participants were asked if they are often troubled with pain (yes/no). Four pain profiles were created and one 'no pain profile; Pain profile 1 was the largest of the pain profiles (n = 980, 12% of the cohort) and was characterised by those reporting pain at only one site (100%), whose pain did not impact on daily activities (100%) and the majority of whom (65%) did not take analgesic medications. Those in pain profile 2 (n = 488, 6%) all had a single site of pain were all impacted in daily activities, but did not (0%) take medication. Pain profile 3 was characterised by multi-site pain (100%), with most people impacted in daily activities (66%) and taking medication (65%). All those in pain profile 4 reported single-site pain that impacted on their daily activities and all took medication.</p> <p><u>Number of chronic conditions</u> Self-reported chronic illness in eight areas ((hypertension, diabetes, heart disease, cancer, lung disease, osteoporosis, stroke and arthritis)</p>	<p>no complete outcome data available? N (%): not specified, but at least 1 participant (numbers in table 1 do not add up)</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>Female: 0.96 (0.96-0.97), p-value&lt;0.001</p> <p><u>Education</u> Primary: reference group Secondary: 1.11 (1.10-1.12), p-value &lt;0.001 Tertiary: 1.31 (1.29-1.32), p-value &lt;0.001</p> <p><u>Private Health insurance/GMS or DVC eligible</u> No: reference group Yes: Private Health: 1.15 (1.14-1.16), p-value &lt;0.001 GMS/DVC: 1.02 (1.01-1.03), p-value&lt;0.001</p> <p><u>Pain, self-reported</u> No pain: reference group Profile 1: 1.18 (1.17-1.20), p-value &lt;0.001 Profile 2: 1.47 (1.44-1.49), p-value &lt;0.001 Profile 3: 1.64 (1.62-1.67), p-value &lt;0.001 Profile 4: 1.75 (1.73-1.78), p-value &lt;0.001</p> <p><u>Number of chronic conditions</u> None: reference group One: 1.98 (1.96-2.00), p-value &lt;0.001 Two or more: 2.97 (2.93-3.00), p-value &lt;0.001</p> <p><u>Polypharmacy (5 of more medications)</u> No: reference group Yes: 2.11 (2.09-2.14), p-value &lt;0.001</p> <p>Incremental predictive value<sup>1</sup>: not reported</p>	
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			<p><u>Polypharmacy</u> Respondents were asked to show the packaging of the medications to the interviewer, who recorded the names into a computer-based medication inventory</p>			
<b>Entire population 65 + or 85+ (and 3 studies with subgroup based on sex or ethnicity)</b>						
Bussche, van den, 2011	<p>Type of study: Cross-sectional study</p> <p>Setting and country: unselected primary care population consisting of all members aged 65 and over (n = 123,224) of a statutory health insurance company operating nationwide in Germany, the Gmünder ErsatzKasse (GEK) in 2004</p> <p>Funding and conflicts of interest: GG received funding from statutory health insurance companies for scientific analyses, among them from the GEK.</p>	<p>Inclusion criteria: all members aged 65 and over of a statutory health insurance company operating nationwide in Germany, the Gmünder ErsatzKasse (GEK)</p> <p>Exclusion criteria: none specified</p> <p>N= 123.224</p> <p>Mean age ± SD: 72.0 ± 6.1</p> <p>Sex: 57.6% M / 42.4% F</p> <p>Potential confounders or effect modifiers: no other confounders or effect modifiers.</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Age</u> From the database</p> <p><u>Sex</u> From the database</p> <p><u>Nursing dependency (yes/no)</u> Statutory nursing dependency is given when a patient receives services from a statutory nursing insurance fund, a parallel agency to the statutory health services insurance scheme. Receiving services from the statutory nursing insurance is used as a proxy for disability in this study</p> <p><u>Number of chronic conditions</u> Chronically ill patient had at least one of the 46 chronic conditions from a list defined by the authors in at least three quarters within the one-year observation period 2004. Multimorbidity was defined as 3 or more chronic conditions from the list.</p>	<p>Duration or endpoint of follow-up: number of contacts with ambulatory care physician practices per year and number of different physicians contacted within the year.</p> <p>For how many participants were no complete outcome data available? N (%): not specified</p> <p>Reasons for incomplete outcome data described? Not specified</p>	<p>(Adjusted) Factor-outcome associations :</p> <p><i>Number of contacts with ambulatory care physician (regression coefficient (95% CI), p-value)</i> <u>Age</u> -0.03 (-0.01-0.05), p-value=0.0031</p> <p><u>Sex (female)</u> 0.05 (-0.17-0.28), p-value=0.6317</p> <p><u>Nursing dependency (yes)</u> 10.37 (10.01-10.72), p-value &lt;0.0001</p> <p><u>Number of chronic conditions</u> 2.33 (2.28-2.38), p-value &lt;0.0001 Log scale: 1.62 (1.57-1.67), p-value&lt;0.0001</p> <p>Incremental predictive value<sup>1</sup>: not reported R<sup>2</sup> : 0.30</p> <p><i>Number of different physicians contacted within the year(regression coefficient (95% CI). p-value)</i> <u>Age</u> -0.05 (-0.05 - -0.05), p-value&lt;0.0001</p> <p><u>Sex (female)</u> 0.16 (0.12-0.19), p-value&lt;0.0001</p> <p><u>Nursing dependency (yes)</u> -0.20 (-0.28 - -0.14), p-value&lt;0.0001</p> <p><u>Number of chronic conditions</u> 0.24 (0.23-0.24), p-value&lt;0.0001 Log scale: 0.25 (0.24-0.26), p-</p>	

					value<0.0001	
					Incremental predictive value <sup>1</sup> : not reported R <sup>2</sup> : 0.195	
Ensrud, 2018	<p>Type of study: Prospective cohort study</p> <p>Setting and country: Participants enrolled in Osteoporotic Fractures in Men (MrOS) Study in United States fro 2000-2002</p> <p>Funding and conflicts of interest: The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provided support: the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Center for Advancing Translational Sciences (NCATS), and NIH Roadmap for Medical Research under the following grant numbers: U01 AG027810,</p>	<p>Inclusion criteria: Men aged 65 years or over, with successful matches to Medicare data and enrolled in the Medicare Fee-For-Service(FFS) Program part A and B during the year 7 exam, who were active and survived 7 years (2007-2008),</p> <p>Exclusion criteria: None specified</p> <p>N= 1.701</p> <p>Mean age ± SD: 79.3 ± 5.3</p> <p>Sex: 100 % M / 0 % F</p> <p>Potential confounders or effect modifiers: age, site, health status, marital status, multimorbidity, mobility, depressive symptoms, physical activity, hospitalization in the last year, and cognitive function.</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Mobility</u> Mobility at Y7 was ascertained from the average usual gait speed in two trials over a 6-m course. Mobility was categorized as poor (gait speed &lt; 0.8 m/s), intermediate (gait speed 0.8 to &lt;1.0 m/s), or good (gait speed ≥ 1.0 m/s)</p> <p><u>Multimorbidity</u> Participant multimorbidity burden was ascertained with the Elixhauser method (15–17) that took into account the presence or absence of 31 specific medical conditions using ICD9 codes in Medicare inpatient and outpatient claims data for the 12 months prior to the date of the Y7 MrOS examination. Multimorbidity was categorized as none (0–1 conditions), mild–moderate (2–4 conditions), or high (≥5 conditions)</p>	<p>Duration or endpoint of follow-up: <u>Hospitalization</u> Data on hospital stays and inpatient facility days for the 12-month period following the date of the Y7 exam were obtained from the Medicare Provider Analysis and Review (MedPAR) file</p> <p><u>Inpatient and Post-Acute Care (PAC) facility days among those hospitalized</u> Data on hospital stays and inpatient facility days for the 12-month period following the date of the Y7 exam were obtained from the Medicare Provider Analysis and Review (MedPAR) file. Among men hospitalized, PAC facility days during this same time period were calculated using a modified version of the Wei algorithm (18); dates for stays in skilled nursing or inpatient rehabilitation or nursing facility were identified using dates in the MedPAR file and the Minimum Data Set (version 2.0)</p> <p>For how many participants were no complete outcome data available? N (%): not reported</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>(Adjusted) Factor-outcome associations :</p> <p><u>Mobility</u> <u>Hospitalization (OR (95% CI) p-value not reported)</u> Good (≥1.0 m/s) 1.00 (referent) Intermediate (0.8 to &lt;1.0 m/s) 1.31 (0.93–1.86) Poor (&lt;0.8 m/s) 1.61 (1.05–2.47)</p> <p><u>Inpatient and Post-Acute Care (PAC) facility days among those hospitalized (RR (95% CI), p-value not reported)</u> Good (≥1.0 m/s) 1.00 (referent) Intermediate (0.8 to &lt;1.0 m/s) 0.98 (0.58–1.60) Poor (&lt;0.8 m/s) 1.46 (0.79–2.44)</p> <p><u>Multimorbidity</u> <u>Hospitalization (OR (95% CI) p-value not reported)</u> None (0–1 conditions) 1.00 (referent) Mild–moderate (2–4 conditions) 1.62 (1.16–2.27) High (≥5 conditions) 2.86 (1.92–4.26)</p> <p><u>Inpatient and Post-Acute Care (PAC) facility days among those hospitalized (RR (95% CI), p-value not reported)</u> None (0–1 conditions) 1.00 (referent) Mild–moderate (2–4 conditions) 1.51 (0.92–2.34)</p>	

	<p>U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, and UL1 TR000128. This manuscript is the result of work supported with resources and use of facilities of the Minneapolis VA Health Care System.</p> <p>No conflicts of interest reported.</p>				<p>High (≥5 conditions) 1.71 (1.02–2.77)</p> <p>Incremental predictive value<sup>1</sup>: Not reported</p>	
<p>Bazargan, 2019</p>	<p>Type of study: Cross-sectional study</p> <p>Setting and country: 11 senior housing units, 16 predominantly African-American churches, and one public housing project located in SPA6 in Los Angeles County.</p> <p>Funding and conflicts of interest: This study was supported by the Center for Medicare and Medicaid Services (CMS) grant 1HOCMS331621 to Charles R. Drew University of Medicine and Science (PI: M.</p>	<p>Inclusion criteria: Participants who were African American, 65 years or older, and who were able to complete an interview in English</p> <p>Exclusion criteria: participation in any other clinical trials, being institutionalized in a health care setting, and considerable cognitive impairment</p> <p>N= 609</p> <p>Age group: 65-75: 355 (58%) ≥ 75: 255 (42%)</p> <p>Sex: 35% M / 65% F</p> <p>Potential confounders or effect modifiers: continuity of medical</p>	<p>Describe prognostic factor(s) and method of measurement:</p> <p><u>Age and sex</u> Age (interval variable) and sex (dichotomous variable) were the demographic factors.</p> <p><u>Education</u> Method of measurement not explicitly reported (interview)</p> <p><u>Marital status</u> Method of measurement not explicitly reported (interview)</p> <p><u>Financial Difficulty</u> Financial difficulty was measured using a five-item measure with items that were on a five-point Likert scale (1 = always to 5 = never). Participants were asked in the last 12 months how frequently they were unable to: (1) buy the amount of food their family should have; (2) buy the clothes they feel their family</p>	<p>Duration or endpoint of follow-up: Emergency department visits (Participants were asked how many times they had utilized ED in the last 12 months. Responses were coded as 0, 1, or 2+)</p> <p>For how many participants were no complete outcome data available? N (%): not reported</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>(Adjusted) Factor-outcome associations :</p> <p><i>Emergency department visits (OR (95% CI), p-values only reported as significant or not significant</i></p> <p><u>Sex (Male)</u> Female: 1 (reference) no visit (vs 2+visits): 0.50 (0.29-0.85), p-value significant 1 visit(vs 2+ visits): 0.45 (0.25-0.82), p-value significant</p> <p><u>Age (65-75 years)</u> ≥ 75 years: 1 (reference) no visit (vs 2+visits): 1.18 (0.68-2.04), p-value not significant 1 visit(vs 2+ visits): 0.92 (0.51-1.66), p-value not significant</p> <p><u>Education (&lt; high school diploma or high school diploma)</u> ≥ some college: 1 reference High school diploma: no visit (vs 2+visits): 0.77 (0.38-1.54), p-value not significant 1 visit(vs 2+ visits): 0.85 (0.40-1.81), p-value not significant</p>	

	<p>Bazargan). Additionally, Dr. Bazargan is supported by the NIH under award #4MD008149 and R25 MD007610 (PI: M. Bazargan), 2U54MD007598 (PI: J. Vadgama), and U54 TR001627 (PIs: S. Dubinett, and R. Jenders). Dr. Sharon Cobb, Lisa Barkley, and Cheryl Wisseh are scholars supported by the Clinical Research Education and Career Development (CRECD), II grant 5R25 MD007610, NIH-NIMHD. Shervin Assari is partly supported by the CMC grant 1HOCMS331621 (PI: M. Bazargan), National Institute on Drug Abuse (NIDA) grant DA035811-05 (PI = M. Zimmerman), National Institute on Minority Health and Health Disparities (NIMHD) grant 4P60MD006923-05 (PI = V. Mays), the National Institute of Child Health and Human Development (NICHD) grant D084526-03, and the National Cancer</p>	<p>care, accessibility of medical care, pain, depressive symptoms, self-rated health, satisfaction with medical care</p>	<p>should have; (3) pay their rent/mortgage; (4) pay their monthly bills; and (5) make ends meet. A higher score was indicative of less financial difficulty within the last 12 months (alfa = 0.934).</p> <p><u>Number of chronic Medical Conditions (CMCs)</u> Number of CMCs was measured by asking whether participants have been diagnosed with the following conditions: (1) asthma or bronchitis; (2) arthritis; (3) high blood pressure; (4) heart problems; (5) diabetes mellitus; (6) back pain/injury; (7) depression; (8) cancer; (9) thyroid problems; (10) sleeping/insomnia; (11) stroke; (12) migraine headache; and (13) stomach or intestinal problems.</p> <p><u>Disability Status</u> Method of measurement not explicitly reported (interview)</p>		<p>&lt; High school diploma: no visit (vs 2+visits): 0.65 (0.35-1.21), p-value not significant 1 visit(vs 2+ visits): 0.73 (0.38-1.43), p-value not significant</p> <p><u>Marital status (married or living with companion)</u> Not married: 1 (reference) no visit (vs 2+visits): 0.66 (0.32-1.39), p-value not significant 1 visit(vs 2+ visits): 1.00 (0.43-2.28), p-value not significant</p> <p><u>Financial Difficulty</u> no visit (vs 2+visits): 0.89 (0.67-1.18), p-value not significant 1 visit(vs 2+ visits): 0.97 (0.71-1.33), p-value not significant</p> <p><u>Number of chronic Medical Conditions (CMCs) (0-2 and 3-5 chronic conditions)</u> ≥ 6 chronic medical conditions: 1 (reference) 3-5 chronic medical conditions: no visit (vs 2+visits): 1.70 (0.92-3.13), p-value not significant 1 visit(vs 2+ visits): 1.51 (0.78-2.94), p-value not significant 0-2 chronic medical conditions: no visit (vs 2+visits): 2.61 (1.03-6.59), p-value significant 1 visit(vs 2+ visits): 1.87 (0.68-5.13), p-value not significant</p> <p><u>Disability Status (No)</u> Yes: 1 (reference) no visit (vs 2+visits): 0.90 (0.52-1.58), p-value not significant 1 visit(vs 2+ visits): 0.96 (0.52-1.76), p-value not significant</p> <p>Incremental predictive value<sup>1</sup>: not reported Nagelkerke R<sup>2</sup>: 14.0; -2log Likelihood</p>	
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	Institute (NCI) grant CA201415-02 (Co-PI = R. Mistry).  The authors declared no conflict of interest.				= 1049.8; df = 34; Sig: 0.0001.	
Teh, 2018	<p>Type of study: Longitudinal cohort study</p> <p>Setting and country: Te Puāwaitanga O Nga Tapuwae Kia ora Tonu: Life and Living in Advanced Age; a Cohort Study in NZ (LiLACS NZ) is a cohort study of Māori (indigenous people in New Zealand) and non-Māori octogenarians</p> <p>Funding and conflicts of interest: This work was supported by the Health Research Council of New Zealand (HRC 09/068B; UoA ref: 3624940) and Ministry of Health New Zealand (MOH ref: 345426/00; UoA ref 3703221) which funded the project management and data collection work; Ngā Pae o te Māramatanga (UoA ref: 3624946) which funded the Māori engagement and</p>	<p>Inclusion criteria: Individuals living within defined NZ Central North Island regional boundaries of the Bay of Plenty and Lakes District Health Boards (excluding the Taupo region of the Lakes District Health Board); Māori with a birth date between 1 January 1920 and 31 December 1930 (aged 80–90 years in 2010); and non-Māori with a birth date between 1 January 1925 and 31 December 1925 (turning 85 years in 2010)</p> <p>Exclusion criteria: Not specified</p> <p>N= 888 (657 had medications data, 501 were non-Maori)</p> <p>Mean age ± SD: Non-Maori 84.6 ± 0.6</p> <p>Sex: Maori 43 % M / 57 % F 46 % M / 54 % F</p> <p>Potential confounders or effect modifiers: sex, education status</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Specific clusters</u> First step of the method was hierarchical cluster analysis, identifying 6 disease clusters: Non-Maori (n=501) Cluster 1 'Well' n= 89 Cluster 2 'CHF and AF' n= 66 Cluster 3 'Depression and arthritis' n= 83 Cluster 4 'Cancer' n=63 Cluster 5 'Respiratory and diabetes' n=111 Cluster 6 'Stroke' n=89</p> <p><u>Multimorbidity (≥3 conditions) (only for 48-month any hospitalisation)</u> Fourteen pre-specified medical conditions prevalent in older adults were identified from self-report ('Have you ever been told by a doctor that you have had [condition]?'), General Practice (GP) records (list of conditions), hospitalisation records, physical assessments (Figure 1). Only participants having a record of presence/absence of respective conditions in one of the five sources were included in analyses</p>	<p>Duration or endpoint of follow-up: Pre 12 month admission and 48 month any hospitalisation</p> <p>For how many participants were no complete outcome data available? N (%): Non-Maori: Number for prescribed medications, PIMs, PPOs: 100/501 (20%); hospital admission: 3/501 (1%).</p> <p>Reasons for incomplete outcome data described? Questionnaire: 5 participants did not complete questionnaire. GP medical records: • No consent, n = 41. • Consented but review was not completed (n = 59), Consented but participants changed their mind (n = 24), Consented but GP refused to give out information (n = 2). NZHIS: 60 participants refused consent.</p>	<p>(Adjusted) Factor-outcome associations : Non-Maori <i>Pre 12-month admission (OR (95% CI), p-value)</i> <u>Specific clusters</u> Cluster 1 'Well' : reference Cluster 2 'CHF and AF' : 1.98 (1.13-3.47), p&lt;0.05 Cluster 3 'Depression and Arthritis' : 1.68 (0.95-2.96), p-value not significant (p&gt;0.05) Cluster 4 'Cancer' : 1.59 (0.87-2.91), reported p&lt;0.05, possibly an error Cluster 5 'Respiratory and Diabetes' : 1.82 (1.06-3.11), p-value &lt;0.05 Cluster 6 'Stroke' : 2.72 (1.63-4.53), p-value&lt;0.01</p> <p><i>48-month any hospitalisation (HR (95%CI), p-value)</i> <u>Specific clusters</u> Cluster 1 'Well' : reference Cluster 2 'CHF and AF' : 1.32 (0.90-1.94), p-value not significant (p&gt;0.05) Cluster 3 'Depression and Arthritis' : 1.48 (1.03-2.12), p-value &lt;0.05 Cluster 4 'Cancer' : 1.11 (0.75-1.65), p-value not significant (p&gt;0.05) Cluster 5 'Respiratory and Diabetes' : 1.30 (0.92-1.83), p-value not significant (p&gt;0.05) Cluster 6 'Stroke' : 1.34 (0.94-1.92), p-value not significant (p&gt;0.05)</p> <p><u>Multimorbidity (≥3 conditions)</u> &lt;3 conditions: reference ≥3 conditions: 1.10 (0.88-1.36), p-value not significant (p&gt;0.05)</p>	All non-Maori participants turned 85 years in the study year

	<p>project management; New Zealand Heart Foundation project grant for investigating cardiac markers (UoA Ref: 3625921) and a Heart Foundation Research Fellowship (UoA ref: 3702288). We thank the sponsors.</p> <p>The authors declared no conflicts of interest.</p>	and deprivation index.			Incremental predictive value <sup>1</sup> : Not reported	
Nägga 2012	<p>Type of study: Cross-sectional study</p> <p>Setting and country: population-based survey of 85-year old individuals residing in Linköping municipality, Sweden.</p> <p>Funding and conflicts of interest: grants from The Health Research Council of the South-East of Sweden (FORSS-8888, FORSS-11636, FORSS-31811), the County of Ostergotland (LIO-11877, LIO-31321, LIO-79951) and the Janne Elgqvist Family Foundation. The authors have no conflict of interest</p>	<p>Inclusion criteria: All residents in the municipality of Linköping born in 1922 (n = 650) were identified through the local authority's register and invited by letter to participate in the study</p> <p>Exclusion criteria: Not specified.</p> <p>N= 496</p> <p>Mean age ± SD: 85 (no mean age and SD reported, but all participants were born in 1922)</p> <p>Sex: 38% M / 62% F</p> <p>Potential confounders or effect modifiers: not specified</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Community assistance</u> Postal questionnaire</p> <p><u>Number of assistive technology devices</u> Postal questionnaire</p> <p><u>Number of visits to GP</u> Data on the number of visits to the GP were collected from the local healthcare utilization database which comprises statistics for all inhabitants regarding all types of visits to health care and costs</p> <p><u>Multimorbidity (2 or more chronic diseases)</u> Data on the presence of disease were collected from the information provided by patients and their relatives in the questionnaire and from documentation on diseases and drugs in the patients' electronic case reports. Chronic disease was registered if the disease fulfilled</p>	<p>Duration or endpoint of follow-up: Hospitalization (extracted from the local health care utilization database, number and duration of in-patient care episodes (hospitalization was defined as &gt;24h in-patient care in preceding 12 months))</p> <p>For how many participants were no complete outcome data available? N (%): Missing data were excluded from the analysis and calculated percentages obtained from the number of valid responses.</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>(Adjusted) Factor-outcome associations : <i>Hospitalization in preceding 12 months (OR (95% CI), p-values not reported)</i> <u>Community assistance</u> 1.9 (1.1-3.2)</p> <p><u>Number of assistive technology devices (</u> 1.2 (1.1-1.4)</p> <p><u>Number of visits to GP</u> 1.3 (1.2-1.5)</p> <p><u>Multimorbidity</u> 1.9 (1-3.5)</p> <p>Incremental predictive value<sup>1</sup>: not reported Cox and Snell R2: 0.118 Nagelkerke R2: 0.178</p>	<p>Predictors excluded in model: type of housing, physical exercises, transportation service, personal alarms, SES, feelings of loneliness, having worries, EQ-5D VAS.</p>

	with the sponsors.		one or more of the following criteria: permanently present; caused by an irreversible pathological condition; or requiring rehabilitation or a long period of care.			
<b>Specific population based on healthcare utilisation or chronic conditions (without specific index-condition)</b>						
Specific population based on > 2 primary care visits						
Abernathy, 2016  (* Moran 2017)	Type of study: Cross-sectional study  Setting and country: Medical University of South Carolina (MUSC) University Internal Medicine (UIM) primary care Clinic, USA  Funding and conflicts of interest: The author(s) received no financial support for the research, authorship, and/or publication of this article. The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.	Inclusion criteria: Adults ≥18 years of age were eligible for the study if they were seen at least twice in the Medical University of South Carolina (MUSC) University Internal Medicine (UIM) primary care clinic from October 1, 2010 through September 30, 2013  Exclusion criteria: Patients who died before September 30, 2013  N= 10.408  Mean age ± SD: Mental Health: 57.9 ± 15.6 Non-Mental Health: 58.1 ± 16.9  Sex: 36.9% M / 63.1% F  Potential confounders or effect modifiers: RES (primary care physician as a resident),	Describe prognostic factor(s) and method of measurement: Data were extracted from 4 local databases: Practice Partner Database (PPD) outpatient electronic medical record (EMR), EPIC outpatient EMR, Medical University Hospital Authority (MUHA) inpatient database, and IDX physician-scheduling database  <u>- Age</u> <u>- Ethnicity</u> <u>- Sex</u> <u>- Marital status</u> <u>- Insurance (uninsured or public insured)</u>  <u>Poverty</u> Researchers used patient residence zip code matched with the 2010 census to determine poverty status of the patient's area residence. The variable Poverty was given a value of 1 if that zip code has ≥25% of citizens below the federal poverty level (FPL)  <u>Mental health</u> Mental health diagnosis recorded.  <u>Clusters of diseases</u>	Duration or endpoint of follow-up: Count of any acute care use (hospital or emergency department [ED]) at the Medical University Hospital from October 1, 2010 through September 30, 2013. Patients admitted to the psychiatric inpatient unit were excluded. Utilization was coded as a count variable by the sum of all ED and inpatient hospitalizations from the administrative data. Patients who present to the ED and are then hospitalized are only counted as a hospitalization. For how many participants were no complete outcome data available?  N (%): 0 (0%)  Reasons for incomplete outcome data described? Not reported	(Adjusted) Factor-outcome associations: <i>Acute care use (Rate Ratio (95% CI), p-value)</i> <u>Age</u> 0.98 (0.98-0.98), p-value <0.0001  <u>Ethnicity (non-white)</u> 1.35 (1.30-1.40), p-value <0.0001  <u>Sex (male)</u> 1.12 (1.09-1.16), p-value <0.0001  <u>Marital Status (unmarried)</u> 1.12 (1.09-1.16), p-value <0.0001  <u>Insurance (uninsured or public insured)</u> Uninsured: 0.95 (0.86-1.05), p-value 0.3100 Public insured: 1.56 (1.49-1.64), p-value <0.0001  <u>Poverty</u> 1.13 (1.10-1.16), p-value <0.0001  <u>Mental Health</u> 1.41 (1.30-1.53), p-value <0.0001  <u>Multiple chronic conditions (MCC) cluster</u> 1.80 (1.70-1.90), p-value <0.0001  <u>Cancer cluster</u> 1.82 (1.63-2.03), p-value <0.0001	



		place of residence (rural versus urban), visit compliance, distance (distance from the patients' zip code center point to the MUSC healthcare campus)	Agglomerative hierarchical clustering was used to identify patient subgroups with similar comorbidities. Each patient was forced into only one particular cluster. A 10-cluster solution is presented as the most clinically relevant number of clusters, clusters 1, 2, 3, 5, 7, and 10 (Table 2) were combined together to serve as the reference cluster in the multivariate model. Mental health comorbidities were excluded from the clusters, but included in the multivariate analysis as a separate variable.  Clusters in multivariate analysis: - Multiple chronic conditions - Cancer - COPD - Renal disease		<p><u>COPD cluster</u> 1.50 (1.38-1.64), p-value&lt;0.0001</p> <p><u>Renal disease cluster</u> 2.57 (2.40-2.75), p-value&lt;0.0001</p> <p>Interaction effects: <u>MCC cluster + Mental Health</u> 1.34 (1.22-1.47), p-value&lt;0.0001</p> <p><u>Cancer cluster + Mental Health</u> 1.11 (0.94-1.31), p-value 0.2287</p> <p><u>COPD cluster + Mental Health</u> 1.2 (1.06-1.36), p-value &lt;0.0038</p> <p><u>Renal disease cluster + Mental Health</u> 1.27 (1.15-1.40), p-value&lt;0.0001</p> <p>Incremental predictive value<sup>1</sup>: not reported</p>	
Specific population based on decedents						
Wagner, 2019	<p>Type of study: Retrospective cohort study</p> <p>Setting and country: University of Washington, USA</p> <p>Funding and conflicts of interest: Funded by the Cambia Health Foundation and UW Medicine. The authors declared that no competing financial interests existed.</p>	<p>Inclusion criteria: decedents 18 years or older, identified from Washington State Death Certificates (2010–2015); who had an affiliation with UW Medicine. With a nonsurgical inpatient stay at an affiliated hospital in the two years before death or two or more outpatient visits from the same site in the last 32 months of life, with at least one occurring during the last 24 months and at least one chronic conditions</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Number of chronic conditions</u> Based on ICD9 codes recorded in the EHR during the decedent's last 24 months of life, eligible decedents had at least one of nine chronic conditions: malignant cancer/leukemia, chronic pulmonary disease, coronary artery disease (CAD), congestive heart failure (CHF), severe chronic liver disease, chronic renal disease, dementia, diabetes with end organ damage, and peripheral vascular disease</p>	<p>Duration or endpoint of follow-up: an inpatient hospital admission, an emergency department (ED) visit; or an ICU stay in the last 30 days of life.</p> <p>For how many participants were no complete outcome data available? N (%): 2.638(12.0%) (Missing data on race and education reduced the size of the analysis sample to 19.430 decedents.)</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p>(Adjusted) Factor-outcome associations :</p> <p><i>Any ED-visit in last 30 days(OR (95% CI), p-value)</i> <u>Number of chronic conditions</u> 1 chronic condition: reference 2 chronic conditions: 1.67 (1.36-2.05), p-value&lt;0.001 3+ chronic conditions: 2.15 (1.74-2.66), p-value&lt;0.001</p> <p><i>Any ICU care in last 30 days(OR (95% CI), p-value)</i> <u>Number of chronic conditions</u> 1 chronic condition: reference 2 chronic conditions: 1.81 (1.64-2.01), p-value &lt;0.001 3+ chronic conditions: 3.08 (2.78-3.41), p-value &lt;0.001</p> <p><i>Any inpatient care in last 30 days(OR</i></p>	

		<p>as defined by the authors</p> <p>Exclusion criteria: none specified</p> <p>N= 22.068 (but in analysis 19.430)</p> <p>Mean age ± SD: 65.8 ± 14.8</p> <p>Sex: 57.2% M / 42.8% F</p> <p>Potential confounders or effect modifiers: age at death, sex, race/ethnicity (white, non-Hispanic, or other), level of education (less than high school graduate or greater than high school graduate), the patient's last known insurance status (private, Medicare, Medicaid, military coverage, other, or uninsured), and the UW Medicine location with which the patient was affiliated.</p>			<p>(95% CI), p-value)</p> <p><u>Number of chronic conditions</u></p> <p>1 chronic condition: reference</p> <p>2 chronic conditions: 1.75 (1.61-1.90), p-value&lt;0.001</p> <p>3+ chronic conditions: 2.80 (2.57-3.05), p-value&lt;0.001</p> <p>Incremental predictive value<sup>1</sup>: not reported</p>	
Specific population based on (elderly) patients with chronic disease(s)						
Bock, 2014	<p>Type of study: Prospective cohort study</p> <p>Setting and country: Patient recruited from 158 GP practices in eight different cities in Germany</p> <p>Funding and</p>	<p>Inclusion criteria: patients aged 65 to 85 years suffering from multiple chronic conditions. Random selection of 24.862 patients.</p> <p>Exclusion criteria: Patients without multimorbidity, defined as co-occurrence of</p>	<p>Describe prognostic factor(s) and method of measurement:</p> <p><u>Age</u> Self-reported in questionnaire</p> <p><u>Sex</u> Self-reported in questionnaire</p> <p><u>Marital status</u> Self-reported in questionnaire</p> <p><u>Income</u> Self-reported in questionnaire</p>	<p>Duration or endpoint of follow-up: Six-month costs in Euro (total and per health care sector (Inpatient Physician, Non-Physician, Medical Supplies, Pharmaceuticals, Nursing Care and Informal Care)</p> <p>For how many participants were no complete outcome data available? N (%): Income data were missing in 12.7% of cases. The severity of</p>	<p>(Adjusted) Factor-outcome associations :</p> <p><i>Six months costs in Euro (B regression coefficient (SE), p-value (NS=not significant ≥0.05)</i></p> <p><u>Age</u> Total -10.30 (36.6), p-value NS</p> <p>Inpatient -17.6 (22.1), p-value NS Physician -1.0 (3.0), p-value NS Non-physician -3.3 (1.6), p-value &lt;0.05</p>	

	<p>conflicts of interest: The study was funded by the German Federal Ministry of Education and Research (grant numbers 01ET0725-31 and 01ET1006A-K). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors declared that no competing interests existed.</p>	<p>three or more chronic conditions from a list of 29 diseases; no regular patient of the participating practice; unable to participate in interviews (especially blindness and deafness); not able to speak and read German; residence in a nursing home; severe illness probably lethal within three months according to the GP; insufficient ability to consent (especially dementia) and participation in other studies. Retrospective exclusion because of diagnosis of dementia of death before the start of the study.</p> <p>N= 1.051 (randomly selected for collection of information on health care utilization)</p> <p>Mean age ± SD: 74.4 ± 5.2 years</p> <p>Sex: 41.3% M / 58.7% F</p> <p>Potential confounders or effect modifiers: Not specified</p>	<p><u>Educational level</u> Self-reported in questionnaire</p> <p><u>Comorbidity score</u> Illness level was assessed by GP's diagnoses of 46 selected different chronic conditions. The severity of each respective chronic condition was assessed by the GP by giving 1 to 4 points to each existing chronic condition. A weighted count score for multimorbidity was created, consisting of the amount of severity points. As 'depression' was one of the initial chronic diseases, the weighted count score for comorbidity (multimorbidity apart from depression) for the following analyses only consists of the remaining 45 diseases and the described count score of the respective severities</p> <p><u>Depression</u> Depressive symptoms were measured using a short form of the Geriatric Depression Screening Scale, the GDS-15 [27,28], a self-rating scale with a score ranging from 0 to 15 points. A score of six points or more on this scale was defined as being depressed, in the following also referred to as "depression".</p> <p><u>Functional status</u> Self-reported, using the Barthel index</p>	<p>the chronic illnesses could not be calculated in 4.5% of the total cases due to missing values. In all other categories the percentage of missing values did not exceed 0.5%.</p> <p>Reasons for incomplete outcome data described? Only for resource utilizations (when participant stated 'yes' but left out the corresponding quantity). For other missing values no reason was described.</p>	<p>Medical supplies 5.1 (2.4), p-value NS Pharmaceuticals -6.5 (4.6), p-value NS <b>Nursing care 10.9 (2.8), p-value&lt;0.001</b> Informal care 2.0 (27.9), p-value NS</p> <p><u>Sex (female, ref male)</u> Total -128.3 (374.5), p-value NS</p> <p>Inpatient -298.1 (255.7), p-value NS Physician 31.6 (35.0), p-value NS <b>Non-physician 69.9 (15.4) p&lt;0.001</b> Medical supplies 22.4 (29.0), p-value NS Pharmaceuticals -38.8 (44.7), p-value NS Nursing care 37.3 (28.6), p-value NS Informal care 47.4 (234.5), p-value NS</p> <p><u>Marital status (we chose only to report widowed compared to married (single and divorced did not show significant associations)</u> Total -141.4 (440.4), p-value NS</p> <p>Inpatient 197.4 (256.6), p-value NS Physician 51.3 (71.5), p-value NS Non-physician -12.3 (17.5), p-value NS Medical supplies -36.2 (27.1), p-value NS Pharmaceuticals -67.9 (42.9), p-value NS <b>Nursing care 120.2 (42.0), p-value &lt;0.01</b> Informal care -394.0 (321.5), p-value NS</p> <p><u>Income</u> Total -21.2 (212.21), p-value NS</p> <p>Inpatient 243.0 (166.2), p-value NS Physician -22.0 (39.4), p-value NS <b>Non-physician 32.3 (11.9), p-value</b></p>	
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					<p><b>&lt;0.01</b>  Medical supplies -10.3 (11.5), p-value NS  Pharmaceuticals 32.1 (49.8), p-value NS  Nursing care 30.1 (19.9), p-value NS  Informal care -326.5 (144.5), p-value NS</p> <p><u>Educational level (low is reference)</u>  Total middle -255.0 (329.0) , p-value NS; high -644.3 (443.8), p-value NS</p> <p>Inpatient middle -231.8 (189.8), p-value NS; high -317.8 (316.0), p-value NS  Physician middle 13.1 (33.4) , p-value NS; high -317.8 (316.0), p-value NS  <b>Non-physician middle 44.2 (17.5), p-value&lt;0.05</b>; high 15.8 (28.3), p-value NS  <b>Medical supplies</b> middle -30.0 (28.5), , p-value NS; <b>high -67.4 (33.6), p-value &lt;0.05</b>  Pharmaceuticals middle 15.8 (52.9), p-value NS; high -47.4 (75.1), p-value NS  Nursing care middle 6.8 (26.2), p-value NS; high 93.6 (65.0), p-value NS  Informal care middle -73.0 (250.9), p-value NS, -3538 (315.2), p-value NS</p> <p><u>Comorbidity score</u>  <b>Total 167.1 (64.3), p-value&lt;0.01</b></p> <p>Inpatient 109.1 (61.9), p-value NS  <b>Physician 14.7 (6.3), p-value&lt;0.05</b>  Non-physician 1.5 (1.2), p-value NS  Medical supplies -0.4 (2.7), p-value NS  <b>Pharmaceuticals 24.4 (3.9), p-value&lt;0.001</b>  Nursing care 4.8 (2.7), p-value NS  Informal care 13.1 (19.6), p-value NS</p> <p><u>Depression</u></p>	
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					<p><b>Total 2936.1 (976.3), p-value&lt;0.01</b></p> <p>Inpatient 884.4 (515.8), p-value NS  Physician 88.1 (93.4), p-value NS  Non-physician 38.0 (29.7), p-value NS  Medical supplies 46.0 (42.0), p-value NS</p> <p><b>Pharmaceuticals 327.4 (99.1), p-value&lt;0.001</b></p> <p>Nursing Care 132.2 (86.2), p-value NS  Informal Care 1420.1 (758.3), p-value NS</p> <p><u>Functional status</u></p> <p><b>Total -519.7 (68.9), p-value&lt;0.001</b></p> <p>Inpatient -63.4 (38.5), p-value NS  Physician -0.5 (3.2), p-value NS  <b>Non-physician -7.4 (2.1), p-value &lt; 0.001</b>  Medical supplies -3.8 (2.2), p-value NS</p> <p><b>Pharmaceuticals -11.4 (3.9), p-value&lt;0.01</b>  <b>Nursing care -15.9 (5.9), p-value&lt;0.01</b>  <b>Informal care -417.3 (62.0), p-value &lt;0.001</b></p> <p>Incremental predictive value<sup>1</sup>: not reported  R2 (adjusted):  Total 0.332</p> <p>Inpatient 0.035  Physician 0.001  Non-physician 0.090  Medical supplies 0.011  Pharmaceuticals 0.063  Nursing care 0.116  Informal care 0.404</p>	
Specific population based on ED visit						
Cunningham, 2017	Type of study: retrospective cohort study (combination	Inclusion criteria: Adult, English-speaking patients in the ED	Describe prognostic factor(s) and method of measurement: <u>Age</u>	Duration or endpoint of follow-up: Frequent ED visitor in the previous year (the 95th percentile (10 or	(Adjusted) Factor-outcome associations : <i>Frequent ED visitor in the previous</i>	

	<p>of data from 2 different cross-sectional studies</p> <p>Setting and country: Two urban emergency departments in Philadelphia, USA</p> <p>Funding and conflicts of interest: HRSA/HHS, Grant/Award Number: D55HP10334; there was no declaration of potential conflicts of interest</p>	<p>waiting rooms and exam rooms</p> <p>Exclusion criteria: Patients assigned to the most urgent group on the Emergency Severity Index were excluded.</p> <p>N= 1.113</p> <p>Mean age ± SD: Infrequent ED visitors: 48.34 ± 17.29 Frequent ED visitors: 43.24 ± 15.31</p> <p>Sex: 45,3% M / 54,7 % F</p> <p>Potential confounders or effect modifiers: Whether a participant reported that they could get what they need from their primary care physician.</p>	<p>Recorded from the Electronic Medical Record</p> <p><u>Race/ethnicity</u> Recorded from the Electronic Medical Record</p> <p><u>Number of chronic conditions</u> Recorded from the Electronic Medical Record</p> <p><u>Number of primary care physician visits in last 12 months</u> Self-reported by patient, through questionnaire</p>	<p>more ED visits in the previous year in the data) as the frequent ED visit cutoff)</p> <p>For how many participants were no complete outcome data available? N (%): not reported</p> <p>Reasons for incomplete outcome data described? Not reported</p>	<p><i>year (OR (95% CI), p-value)</i></p> <p><u>Age</u> 0.94 (0.92-0.97), p-value &lt;0.001</p> <p><u>Race/ethnicity</u> African American: 2.06 (1.17-3.63), p-value =0.013</p> <p><u>Number of chronic conditions</u> 1.43 (1.29-1.59), p-value &lt;0.001</p> <p><u>Number of PCP visits in last 12 months</u> 1.14 (1.05-1.22), p-value = 0.001</p> <p>Interaction Age + number of chronic conditions: 1.01 (1.00-1.01), p-value = 0.032</p> <p>Incremental predictive value<sup>1</sup>: not reported Nagelkerke R<sup>2</sup> = 0.286</p>	
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<sup>1</sup> Incremental predictive value is the predictive value beyond standard demographic factors and the established risk factors (e.g. smoking, blood pressure, lipid levels, diabetes, cancer stage, etc.), for example change in c-statistic

### Systematic Reviews

Specific population based on high-cost patients						
Wammes, 2018	<p>Type of study: Systematic review of observational studies</p> <p>Setting and country: studies from high-income countries— as defined by the World Bank</p> <p>Funding and conflicts of interest:</p>	<p>Inclusion criteria: - studies published in 2000 and later - the article reported characteristics and utilisation of the top-X% (eg, top-5% and top-10%) patients of costs of a given population</p> <p>Exclusion criteria: - Studies not written in English and conference</p>	<p>Describe prognostic factor(s) and method of measurement: <u>Predisposing characteristics</u>: characteristics that predispose people to use or not to use services, although such characteristics are not directly responsible for use (eg, age, sex, education, ethnicity and beliefs);</p> <p><u>Enabling characteristics</u> that facilitate or impede use of services (income/wealth/</p>	<p>Duration or endpoint of follow-up: High-cost patient (e.g. top-5% and top-10%)</p> <p>For how many participants were no complete outcome data available? N (%): N/A</p> <p>Reasons for incomplete outcome data described? N/A</p>	<p>(Adjusted) Factor-outcome associations : <u>Predisposing characteristics</u> Age (32 studies), sex (both male (9 studies) and female(16 studies) were reported), ethnicity(several, in total 10 studies), place of residence(8 studies), employment status: early retiree (1 study), education (less than high school degree, 1 study)</p> <p><u>Enabling characteristics</u> Type of health insurance (14 studies),</p>	<p>Most of the included studies were descriptive. The article does not differentiate between factors identified with descriptive factors and through (multivariate) models that adjust for confounders.</p>

	<p>The study was conducted as part of a research program funded through the Dutch Ministry of Health. No competing interest declared.</p>	<p>abstracts N= 55 articles Mean age ± SD: N/A Sex: N/A Potential confounders or effect modifiers: not reported</p>	<p>Insurance as ability to pay for services, organisation of service provision and health policy); <u>Need characteristics</u> needs or conditions that laypeople or healthcare providers recognise as requiring medical treatment. <u>Expenditure/healthcare utilisation categories</u> Not specified</p>		<p>Income (positive (3 studies), negative (5 studies) and no relation (3 studies)), proportion of physicians who are medical specialists (2 studies) <u>Need characteristics</u> Chronic illness (22 studies) Multimorbidity/comorbid illness (31 studies) Decedents/survival (14 studies) Activities daily living (7 studies) Health status (9 studies)  Specific disease groups: Certain infectious and parasitic diseases (9 studies), Neoplasms (21 studies), Diseases of the blood and bloodforming organs and certain disorders involving the immune mechanism (4 studies), endocrine, nutritional and metabolic diseases (32 studies), mental and behavioural disorders (32 studies), diseases of the nervous system (10 studies), diseases of the eye and adnexa (5 studies), diseases of the circulatory system (36 studies), diseases of the respiratory system (30 studies), diseases of the digestive system (9 studies), diseases of the skin and subcutaneous tissue (5 studies), diseases of the musculoskeletal system and connective tissue (15 studies), diseases of the genitourinary system (22 studies), pregnancy, childbirth and the puerperium (5 studies), congenital malformations, deformations and chromosomal abnormalities (1 study), Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (6 studies), Injury, poisoning and certain other consequences of external causes (9 studies), Factors</p>	
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					<p>influencing health status and contact with health services (3 studies)</p> <p><u>Expenditure/healthcare utilisation categories</u>  (Inpatient) hospital care (31 studies), subacute care/postacute care services rehabilitation (11 studies), hospitalisations/admission/ patient days/length of stay (17 studies), emergency department (12 studies), outpatient (physician) visits (13 studies), long-term care (11 studies), mental health (10 studies), physician services (13 studies), intensive care unit (2 studies), prescription drugs (16 studies), subsequent use (13 studies), prior use (5 studies), persistent users (21 studies)</p> <p>Incremental predictive value<sup>2</sup>: N/A</p>	
<b>Specific population based on (elderly) patients with chronic disease(s)</b>						
Lehnert, 2011	<p>Type of study: Systematic review of observational studies</p> <p>Setting and country: Only English and German language articles were included</p> <p>Funding and conflicts of interest: The authors disclosed receipt of the following financial support for the research and/or authorship of this article: This study is part of</p>	<p>Inclusion criteria:  - The relationship between MCCs and HCU/HCCs was examined for an elderly general population (not defined by sharing a particular index disease).  - Original cross-sectional or longitudinal study published in a peer-reviewed journal.  - A clearly described measure of MCCs was included as an explanatory variable.  - Primary study outcome was an</p>	<p>Describe prognostic factor(s) and method of measurement:  Multiple chronic conditions (MCC) measured with a clearly described measure</p>	<p>Duration or endpoint of follow-up:  <i>Healthcare utilisation</i>  - Hospital admissions (via ED/acute, planned or total)  - Early unplanned hospital readmission within 28 days  - Number of planned, acute and total healthcare admissions  - Emergency department use  - Number of prescriptions/medications taken  - Number of physician visits  - Home health visits  - Nights spend at the hospital</p> <p><i>Healthcare costs</i>  - Annual out-of-pocket expenditures  - Annual health care costs  - Annual prescription drug expenditures</p>	<p>(Adjusted) Factor-outcome associations :  <u>Multiple chronic conditions and number of studies reporting an association with endpoint (number of studies: multivariate/univariate (association) or unclear)</u></p> <p><i>Healthcare utilisation</i>  - Hospital admissions: ) ED/via acute (1 study: 1 multivariate), planned (1 study: 1 multivariate), total (7 studies: 2 multivariate, 1 reported both negative and positive association depending on age group and morbidity burden, 4 unclear)  - Early unplanned hospital readmission (2 studies: 1 multivariate, 1 unclear)  - Emergency department use (4 studies: 1 multivariate, 3 unclear)</p>	<p>It was not reported for every study whether the association was analysed with univariate or multivariate analyses. If the authors did not specify the type of analysis, it was counted as 'unclear'.</p>



	<p>Multicare I and Esther-Net and was funded by the German Federal Ministry for Education and Research (Grant Nos.: 01ET0728, Multicare I; 01ET0719, Esther-Net). The German Federal Ministry for Education and Research had no further role in the study design; in the collection, analyses, and interpretation of data; in writing the report; and in the decision to submit the article for publication. The publication of study results was not contingent on the sponsor's approval. The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.</p>	<p>aggregate measure of HCU (e.g., physician use, hospital use, use of pharmaceuticals) or HCCs.</p> <p>- The article was in English or German language.</p> <p>Exclusion criteria: Not specified</p> <p>N= 35 articles</p> <p>Mean age ± SD: N/A</p> <p>Sex: N/A</p> <p>Potential confounders or effect modifiers: not reported</p>		<p>For how many participants were no complete outcome data available? N (%): N/A</p> <p>Reasons for incomplete outcome data described? N/A</p>	<ul style="list-style-type: none"> <li>- Number of prescriptions/medications take (6 studies: 3 multivariate, 3 unclear)</li> <li>- Number of physician visits (6 studies: 2 multivariate, 4 unclear)</li> <li>- Home health visits (1 study: 1 unclear)</li> <li>- Nights spend at the hospital (3 studies: 3 unclear) (1 study reported patients with both types of physicians having more chronic conditions compared to patients with none or only one type of physician)</li> </ul> <p><i>Healthcare costs</i></p> <ul style="list-style-type: none"> <li>- Annual out-of-pocket expenditures (8 studies: 6 unclear, 1 adjusted analysis, 1 adjusted analysis for only prescription drug out-of-pocket expenditures)</li> <li>- Annual healthcare costs (9 studies: 8 unclear, 1 study reported a univariate but no multivariate association)</li> <li>- Annual prescription drug expenditures (5 studies: 1 adjusted analysis, 4 unclear)</li> </ul> <p>Incremental predictive value<sup>1</sup>: N/A</p>	
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