Applied Nursing Research 45 (2019) 1–5

Contents lists available at ScienceDirect

Applied Nursing Research

journal homepage: www.elsevier.com/locate/apnr

Original article

Comparing comorbidity measures and fatigue post myocardial infarction☆

Carolyn E. Horne (PhD, RN) (Assistant Professor)[a,*], Sharona Johnson (PhD, RN, FNP-BC) (Director of Advanced Clinical Practice)[b], Patricia B. Crane (PhD, RN, FNAP, FAHA) (Associate Dean for Research and Scholarship)[a]

[a] College of Nursing, East Carolina University, Greenville, NC 27858, United States of America
[b] Vidant Health, Greenville, NC 27858, United States of America

ARTICLE INFO

Keywords:
Fatigue
Comorbidities
Myocardial infarction

ABSTRACT

Purpose/Aims: The purpose of this study was to examine comorbidity measures that may relate to the symptom of fatigue post MI: self-reported comorbidities, medication-validated comorbidities, weighted comorbidities for fatigue, and number of comorbidities.

Design: Using a cross sectional design, we interviewed a convenience sample of 98 adults, 65 and older, who were 6 to 8 months post myocardial infarction.

Methods: Participants self-reported their comorbidities using a list of 23 comorbid conditions. All medications were visually inspected, and medications were reviewed by a geriatric pharmacist for a common side effect of fatigue. The Revised Piper Fatigue Scale was used to measure fatigue.

Results: The mean age of the participants was 76 (SD = 6.3), and most of the sample were White (84%). Neither medication-validated comorbidities nor those medications with fatigue as a common side effect explained fatigue. When controlling for age, sex, and marital status, self-reported comorbidities explained 10% of the variance in fatigue (F (4, 93) = 2.65; p = 0.04). Having 5 or more self-reported comorbidities explained 7% of variance in fatigue scores (F (1, 96) = 7.53; p = 0.007).

Conclusion: Comorbidities are associated with fatigue post MI. Adults post MI with 5 or more comorbidities should be screened for fatigue.

1. Introduction

Fatigue is a common symptom reported by older adults following myocardial infarction (MI) (Alsén, Brink, Brändström, Karlson, & Persson, 2010) with up to 73% (Crane, Abel, & McCoy, 2015) indicating post MI fatigue. The proportion of post MI fatigue is greater than fatigue in the general population (Cheng, Gurland, & Maurer, 2008; Ricci, Chee, Lorandeau, & Berger, 2007) (18 to 38%) and in community dwelling older adults (43%) (Hardy & Studenski, 2008). In fact, fatigue levels reported 6 to 8 months post MI (Crane et al., 2015) are similar to fatigue reported by breast cancer survivors (Stover, Reeve, Piper, et al., 2013). Fatigue experienced after a MI affects quality of life (Dueñas, Ramirez, Arana, & Failde, 2011) and participation in physical activity at recommended levels for prevention of a recurrent MI (Alsen & Brink, 2013; Crane et al., 2015). Because fatigue is one of the most frequent complaints in primary care (Stadje, Dornieden, Baum, et al., 2016) and the prevalence of fatigue is high in those post MI, understanding factors contributing to fatigue is important in developing a plan of care for secondary prevention of coronary heart disease.

Adults who are post MI typically have other comorbid conditions that may affect the symptom of fatigue, such as diabetes (30%) (Fritschi & Quinn, 2010) and obesity (38%) (Benjamin et al., 2018). Fatigue is also associated with non-cardiovascular conditions such as rheumatoid arthritis (Katz, 2017), cancer (Daniels, Oerlemans, Krol, Creutzberg, & van de Poll-Franse, 2014), and chronic obstructive pulmonary disease (Frei, Muggensturm, Putcha, et al., 2014). Thus, examining comorbidities after an MI may assist in identifying adults at highest risk for fatigue.

Comorbidity, also referred to as multimorbidity and coexisting disease, is the total burden of illness beyond the disease of specific interest (Valderas, Starfield, Sibbald, Salisbury, & Roland, 2009). In previous research investigators have primarily focused on the effect of comorbidities, not how comorbid conditions influence symptoms. For example, results of studies examining comorbidities centered on the

☆ No conflicts of interests noted by any of the authors.

* Corresponding author.
E-mail addresses: hornec@ecu.edu (C.E. Horne), shajohns@vidanthealth.com (S. Johnson), cranep14@ecu.edu (P.B. Crane).

https://doi.org/10.1016/j.apnr.2018.11.004
Received 5 June 2018; Received in revised form 15 October 2018; Accepted 5 November 2018
0897-1897/ © 2018 Elsevier Inc. All rights reserved.

relationship of comorbidities with prolonged hospitalizations, decreased quality of life, and increased healthcare costs (Marengoni, Angleman, Melis, et al., 2011; Valderas et al., 2009). Comorbidities have traditionally been measured using standardized instruments with strong validity and reliability to predict outcomes such as mortality or length of stay, such as Charlson Comorbidity Index, Cumulative Illness Rating Scale, Index of Coexistent Diseases, Kaplan–Feinstein Index, and Chronic Disease Score (Charlson, Pompei, Ales, & MacKenzie, 1987; de Groot, Beckerman, Lankhorst, & Bouter, 2003; Lash et al., 2007; Linn, Linn, & Gurel, 1968; Von Korff, Wagner, & Saunders, 1992). The vast majority of these instruments obtain information from the medical record.

Review of the medical record is time intensive as it requires consent of the individual, healthcare provider, and/or organization. Obtaining medical records in rural populations may not be feasible due to time and resources, and medical records have incomplete data (Davis, 2015). These issues are especially cogent for primary care providers in rural settings who may not have access or have limited access to electronic health records and rely on self-report. Further, comorbidity data in the acute inpatient setting medical record may differ from the primary care record data, requiring adjudication of record accuracy (Lash et al., 2007). Although the medical record may be the gold standard for determining comorbidities, researchers have demonstrated that self-report is highly correlated with medical records (Horton, Rudick, Hara-Cleaver, & Marrie, 2010; Olomu, Corser, Stommel, Xie, & Holmes-Rovner, 2012; Vigen et al., 2016). Thus, using self-report comorbidity data in community samples is an acceptable method of determining comorbidities.

Comorbid conditions and the medications associated with each add to the complexity in understanding the symptom of fatigue. Examining the current medications post MI is one method to validate self-reported comorbidities. However, a limitation to using only medication-validated comorbidities is that some comorbidities may be controlled by other means, such as diet, resulting in missing important comorbid conditions.

Although we know that certain disease states, like heart failure and chronic obstructive pulmonary disease, have an associated symptom of fatigue (Roversi, Fabbri, Sin, Hawkins, & Agustí, 2016), medications also contribute to fatigue. Beta-blockers (Kalra et al., 2013) and statins (Golomb, Evans, Dimsdale, & White, 2012) are medications frequently prescribed post MI, in which fatigue is a common side effect. Further, adults with coronary heart disease take an average of 7 medications per day (Moss & Crane, 2010). The summative or potentiating effects of medications may result in a greater feeling of fatigue post MI.

Understanding the best way to examine comorbidities and fatigue in primary care is important. Identification of adults post MI with fatigue is necessary to assist them in managing their fatigue and increasing their participation in physical activity. The purpose of this study was to examine comorbidity measures and the associations with the symptom of fatigue post MI: self-reported comorbidities, medication-validated comorbidities, weighted comorbidities for fatigue, and number of comorbidities. In this study fatigue was defined as a fatigue, tiredness, or exhaustion that was different than the fatigue experienced prior to their MI. Research questions were: a) Which comorbidity measure (self-report, medication validated, weighted medication) best explains fatigue in older adults 6 to 8 months post MI?; b) Do the numbers of comorbidities influence fatigue in older adults 6 to 8 months post MI?; and c) When controlling for age, sex, and marital status, do the number of comorbidities explain the variance in fatigue post MI?

2. Methods

2.1. Design

We used data from a cross-sectional, descriptive design to answer the research questions.

2.2. Setting and sample

A consecutive non-probability sampling strategy was used to obtain equal numbers of men ($n = 49$) and women ($n = 49$) who had been discharged with a diagnosis of MI within the last 6 to 8 months. The diagnosis of MI was classified using the International Classification of Disease 9 codes 410.0–410.9. A list of those discharged alive with an MI diagnosis was obtained, and a registered nurse from the tertiary care center contacted those meeting the inclusion criteria and conducted the initial screening. A list of older adults meeting inclusion criteria and agreeing to release their name and contact information was then provided to the research team. Each was contacted by telephone, provided more detailed information about the study, and determined a time and place to conduct data collection. Less than 10% of those contacted refused to participate in the study.

Data were collected in a setting of the participants choosing with the majority preferring their home. An a priori power analysis indicated a sample of 97 would detect a 0.15 effect with 80% power at 0.05 of significance with 6 predictors (age, sex, race, and three comorbidity measures). Exclusion criteria included non-English speaking, adults who were < 65 years of age, not 6 to 8 months posts MI, and anyone with mental or physical disability precluding informed consent. The time frame for data collection was chosen to allow for completion of Phase II cardiac rehabilitation, pharmacological optimization, and stabilization of depression post MI. Institutional review board approval and written informed consent were obtained prior to participation in the study. A total of 98 adults with equal numbers of men and women comprised the sample.

2.3. Measurement

To capture all comorbidities, a comprehensive list of comorbidities was designed by combining two comorbidity measures: The Chronic Disease Score and the Charlson Comorbidity Index Score. Both indices have been validated to predict outcomes such as mortality and hospitalization and used extensively in the literature (Charlson et al., 1987; Crooks, West, & Card, 2015; McGregor, Kim, Perencevich, et al., 2005; Putnam, Diana, Fishman, et al., 2002). The Chronic Disease Score was developed using medications from the pharmaceutical database instead of ICD codes to measure chronic disease status (Von Korff et al., 1992). The index includes 17 comorbid conditions that were validated against medical records and physician rating of disease severity (Von Korff et al., 1992; Yurkovich, Avina-Zubieta, Thomas, Gorenchtein, & Lacaille, 2015). The Chronic Disease Score is a valid predictor of disease status, self-rated health status, hospitalization, and mortality (Putnam et al., 2002; Von Korff et al., 1992). The Charlson Comorbidity Index ranks comorbidities to predict mortality from medical records and is a valid prognostic indicator of 1-year mortality (Bar & Hemphill, 2011; Crooks et al., 2015; D'Hoore, Bouckaert, & Tilquin, 1996; Sundararajan et al., 2004). A numeric score is calculated for each patient based on the sum of the weighted disease categories. The index includes 19 comorbid conditions that have been weighted by their strength of association with mortality (Charlson et al., 1987; de Groot et al., 2003).

The Chronic Disease Score Scale has 17 chronic (comorbid) conditions similar to the Charlson Comorbidity Index, but it did not include cardiovascular comorbidities, such as stroke and peripheral vascular disease. Therefore, the following five comorbidities from the Charlson Comorbidity Index were added to the Chronic Disease index: (a) peripheral vascular disease, (b) cerebrovascular disease, (c) liver disease, (d) hemiplegia, and (e) renal disease. Also, obesity, defined as a body mass index > 30, was added to our comorbidity measure totaling 23 possible comorbid conditions.

Participants were asked if a healthcare provider had ever told them they had a comorbid condition: self-reported comorbidity. A score of 1 was recorded for every positive response, and a summative score for self-reported comorbidity was tabulated. All medications were then

visually inspected and verified by the participant for each self-reported comorbidity. For example, participants may state their beta-blocker and their angiotensin converting enzyme as 'blood pressure' medication. Despite the number of medications for each comorbid condition, comorbidities that had at least one medication for the condition scored as 1 and summed: medication validated comorbidity. A geriatric pharmacist reviewed all medications recorded on the demographic health form. Medications with a common side effect of fatigue in the product information literature were identified by a geriatric pharmacist, and those comorbidities with medications with a major side effect of fatigue were summed: weighted comorbidity for fatigue.

The Revised Piper Fatigue Scale (RPFS) was used to measure fatigue (Piper et al., 1998). The RPFS is a 22 item instrument used to measure multidimensional fatigue. There are 4 subscales: (1) behavioral/severity (2) the affective meaning (3) the sensory subscale and (4) the cognitive/mood. Each self-reported response is rated on a Likert scale from 0 to 10. The total score for the RPFS ranges from 0 to 220. To place the score on a 10-point scale, the total fatigue score may be divided by 22. Higher scores indicate higher fatigue.

Demographic data were collected from each participant using an investigator developed health status questionnaire comprised of 22 items. This questionnaire obtained self-reported demographics, such as age, race, and income, and cardiovascular related health questions such as family history and modifiable cardiac risk factors. Each participant also had height and weight measured using standardized procedures and body mass index was calculated.

2.4. Data analyses

Descriptive statistics were used to describe the sample. To examine differences in comorbidities, nonparametric statistics, chi square, were used for categorical data and parametric statistics, independent *t* -tests, were used for continuous data. Multiple regression was used to answer the research questions. Data were analyzed using Statistical Package for the Social Science 22.0 (SPSS Inc., Chicago, IL, USA).

3. Results

Most participants ($N = 98$) were White (84%) with a mean age of 76 years ($SD = 6.3$) and had ejection fractions ≥40 (61%). Total fatigue scores were divided by 22 to place fatigue on a 1 to 10 scale. Mean fatigue was 3.96 ($SD = 2.2$) in adults reporting fatigue after their MI that differed from fatigue experienced prior to their MI. Using cut score models for PFS (Stover et al., 2013), 25% ($n = 24$) reported no fatigue, 34% ($n = 33$) mild, 32% ($n = 31$) moderate, and 10% ($n = 10$) severe (see Table 1).

Age was not significantly correlated with any of the measures of comorbidity. Participants reported 2 to 11 comorbid conditions ($M = 5.2$; $SD = 1.78$; $IQR = 2$). Over one-third of the sample (39.8%) and 75% of Black participants ($X^2 = 1.53$; $p = 0.22$) had 5 or more self-reported comorbidities (see Table 2). When examining the comorbidities that at least 10% of the sample reported, the highest mean fatigue scores were noted in those reporting asthma, rhinitis, ulcer, respiratory illness, and arthritis.

Participants with more comorbidities had higher BMI ($t = -2.49$ (96); $p = 0.02$) and higher fatigue scores ($t = -2.74$ (96); $p = 0.007$). The average self-reported comorbidity ($M = 5.20$; $SD = 1.78$) was higher than the medication validated comorbidity ($M = 3.91$; $SD = 1.2$) and the weighted comorbidity for fatigue ($M = 1.24$; $SD = 0.73$). The self-reported comorbidity and medication validated comorbidity were strongly correlated ($r = 0.683$; $p < 0.001$), but the self-reported comorbidity was weakly correlated with the weighted comorbidities for fatigue ($r = 0.269$; $p = 0.007$).

The self-reported comorbidity was the only significant predictor explaining 8% of the variance in fatigue (F (3, 94) = 2.86, $p = 0.014$; B = 10.82). Using simple regression, five or more comorbidities (self-reported comorbidity) explained 7% of the variance in fatigue (F (1, 96) = 7.53; $p = 0.007$). When controlling for age, sex, and marital status, self-reported comorbidities explained 10% of the variance in fatigue (F (4, 93) = 2.65; $p = 0.04$). Despite no difference in fatigue scores by sex, using simple regression, self-reported comorbidity explained 9% of fatigue in women (F (1, 47) = 4.67; $p = 0.03$) but not in men (F (1, 47) = 2.93; $p = 0.09$). Finally, we explored if the cardiovascular comorbidities of hypertension, diabetes, obesity, and high cholesterol influenced fatigue in this post-MI population. This model was not significant ($R^2 = 0.024$; F (4, 93) = 0.58; $p = 0.68$).

Table 1
Demographics by fatigue levels.

Variable	None to mild fatigue ($n = 57$) *N* (%) or mean (± SD)	Moderate to severe fatigue ($n = 41$) *N* (%) or mean (± SD)	*p* Value
Age in years	74.9 (± 5.55)	76.95 (± 7.27)	0.133
Sex, % male	17 (44.7)	32 (53.3)	0.31
Ethnicity			0.017
White	34 (90)	48 (80.0)	
Black other	5 (9)	11 (27)	
Marital status			0.98
Single	28 (49)	20 (49)	
Married	29 (51)	21 (51.2)	
Education			0.40
Less than high school	15 (26)	14 (34)	
High school graduate and above	42 (74)	27 (66)	
BMI	27.98 (± 4.62)	29.0 (± 5.03)	0.53
Comorbidities	4.93 (± 1.59)	5.6 (± 2.0)	0.07

Table 2
Proportion of participants with multiple comorbidities ($N = 98$).

Number of comorbidities	*N* (%)
2	3 (3)
3	14 (14)
4	21 (21)
5	21 (21)
6	17 (17)
7	11 (11)
8	7 (7)
9	3 (3)
11	1 (1)

4. Discussion

Comorbidities explained a small amount of the variance in fatigue scores. Yet, small changes in fatigue may be clinically significant. Researchers examining clinically meaningful cut scores for fatigue in breast cancer survivors ($N = 857$) when using the Piper Fatigue Scale found that every increase in level of fatigue had meaningful decreases in physical, mental, and sexual health quality of life scores (Piper et al., 1998).

The prevalence of fatigue in this study is similar to the 67% of adult women 6 to 12 months post MI ($N = 84$) (Crane, 2005) reporting fatigue, and the 48% reporting fatigue 2 years post MI (Alsen & Brink, 2013). Fatigue categories in this study were similar to fatigue in adults with multiple sclerosis. Comparing fatigue severity levels in this study with multiple sclerosis participants ($N = 949$), 21.8% reported no fatigue compared to 25% in post-MI, 24.1% mild fatigue compared to 34% post MI, 27.3% moderate fatigue compared to 32% post MI, and 26% severe fatigue compared to 10% post MI (Fiest, Fisk, Patten, et al., 2016).

Fatigue remains a subjective and prevalent symptom post MI. While interventions that decrease fatigue may not show statistical significance, further research is needed to understand changes in fatigue that yield clinical significance. Results from this study may assist clinical nurses in identifying adults at risk for fatigue post MI. Once identified, other factors associated with fatigue post MI, such as depression and sleep (Dickson, Buck, & Riegel, 2013), should be examined and addressed to affect clinically significant fatigue.

We found that self-reporting of comorbid conditions strongly correlated with medication validated comorbidities. These results are similar to other findings indicating that self-report is associated with the health record (Horton et al., 2010; Olomu et al., 2012; Vigen et al., 2016). However, only the self-reported scale significantly influenced the symptom of fatigue. It is unclear how comorbidities influence symptoms as these coexisting conditions may share a common pathophysiological pathway or share symptoms resulting in a synergistic symptom experience. Further studies are needed with larger samples to examine the summative and potentiating effects of comorbid conditions on symptoms or if certain clusters of symptoms affect fatigue post MI.

In this sample five or more comorbidities explained the variance in fatigue scores. Multiple comorbidities were also noted in a study of self-management in heart failure (Dickson et al., 2013). Researchers found that 4 or more comorbidities decreased health failure self-management due to blaming symptoms on one condition when in fact it was related to another condition. In another study (Frei et al., 2014) researchers also found a strong association for decreased quality of life in adults with chronic obstructive pulmonary disease who had 5 comorbidities. Despite not knowing how the cumulative effect of comorbidities influence fatigue, in this study multiple comorbid conditions were related to fatigue. Thus, assessing the number of comorbidities is warranted when assessing post MI fatigue.

No differences were noted in the number of comorbidities and increasing age in this sample. The results differ from a larger study noting comorbid conditions increasing with age (Ahluwalia et al., 2011). Differences may be related to the small sample size or including only those who had experienced an MI. While not significant, a greater proportion of Black participants had 5 or more comorbidities. These findings are consistent with a larger study noting that Black participants had greater comorbidity scores in non-safety-net systems of care (Balasubramanian, Garcia, Corley, et al., 2017). The cross-sectional nature of this study does not allow examination of the temporal relation of age and race to comorbidities. Clinicians should continue to examine comorbid conditions, especially in aging adults and Black patients.

Self-report of comorbidities may engage the patient and the clinician in collaborating on care. Bidirectional communication of patients and clinicians would allow the clinician to review the patient's perspectives and identify additional information to inform their plan of care. Many electronic healthcare formats are open to patients. For example MyChart, an Epic Systems product, allows patients to review most of their medical records virtually, including diagnoses, medications, allergies, test results, appointments, and demographics (Cahill, Gilbert, & Armstrong, 2014). Because self-reported comorbidity was associated with fatigue in this study, exploring integration of the patient's self-report of comorbidities into patient's electronic health record in addition to clinician's documentation is warranted. Valuing the patient's voice in their health is the hallmark of patient-centered care.

Measurement of comorbidities remains an area of concern for scientists and clinicians (Meghani et al., 2013). In research, understanding how comorbidities influence specific outcomes is essential in recognizing the heterogeneity of the populations served and developing interventions to affect the outcomes, such as mortality. Conversely, in practice, clinicians are focused on the outcome, such as the symptom of fatigue or quality of life and determining the plan of care directed to which condition most likely contributes to the outcome. Despite varied approaches to understanding comorbidities, the ultimate goal is to improve outcomes. This study did not examine which comorbid condition contributed to fatigue. Further studies with larger samples are needed to examine the contribution of specific comorbid conditions on fatigue.

Understanding the symptom experience of fatigue will assist in determining clinically appropriate measures in managing complex comorbidities. In patient-centered care, clinicians must be attuned to the influence of multiple comorbid diseases and symptoms affecting quality of life (Fulton, Lyon, & Goudreau, 2014). This is especially cogent for the cardiovascular population as the symptom of fatigue is a primary barrier to participating in physical activity (Ahacic, Kareholt, Thorslund, & Parker, 2007), one of the most effective secondary prevention behaviors for self-management of coronary heart disease.

5. Limitations

In this study there were limitations. This is a single study with a small convenience sample in a specified region of the eastern U.S., limiting generalizability. Because fatigue was measured at one point in time, we may not have captured the dynamic relationship of fatigue and its relationship to a comorbid measurement tool. The time frame of 6 to 8 months after MI may also affect the results.

We did not identify if the MI was STEMI or NSTEMI. This identification may be important in understanding comorbidities and fatigue post MI. Despite these limitations, this study noted that self-report of comorbid conditions is important when examining one of the most frequent symptoms reported post MI, fatigue.

6. Conclusion and implication for practice

Self-reported comorbidities explained the symptom of fatigue, and this relationship was noted even when we controlled for age. Because fatigue is one of the most frequent complaints post MI, nurses should assess for both primary and secondary reasons for fatigue. This is especially important when caring for complex aging cardiovascular clients as fatigue is a prodrome to an MI (McSweeney, Cleves, Zhao, Lefler, & Yang, 2010) and affects quality of life and participation in physical activity at levels for cardiovascular benefit.

Nurses must champion research focused on symptom management to improve quality of life in aging adults with heart disease. This focus will facilitate the mission of assisting clients to experience wellness in the midst of disease.

Acknowledgements

Funding from NINR (1R15NR009033-01A1).

References

Ahacic, K., Kareholt, I., Thorslund, M., & Parker, M. G. (2007). Relationships between symptoms, physical capacity and activity limitations in 1992 and 2002. *Aging Clinical and Experimental Research, 19*(3), 187–193.

Ahluwalia, S. C., Gross, C. P., Chaudhry, S. I., Leo-Summers, L., Van Ness, P. H., & Fried, T. R. (2011). Change in comorbidity prevalence with advancing age among persons with heart failure. *Journal of General Internal Medicine, 26*(10), 1145–1151.

Alsen, P., & Brink, E. (2013). Fatigue after myocardial infarction - A two-year follow-up study. *Journal of Clinical Nursing, 22*, 1647–1652.

Alsén, P., Brink, E., Brändström, Y., Karlson, B. W., & Persson, L. O. (2010). Fatigue after myocardial infarction: Relationships with indices of emotional distress, and socio-demographic and clinical variables. *International Journal of Nursing Practice, 16*(4), 326–334.

Balasubramanian, B. A., Garcia, M. P., Corley, D. A., et al. (2017). Racial/ethnic differences in obesity and comorbidities between safety-net- and non-safety-net integrated health systems. *Medicine, 96*(11), e6326.

Bar, B., & Hemphill, J. C. (2011). Charlson comorbidity index adjustment in intracerebral hemorrhage. *Stroke, 42*(10), 2944–2946.

Benjamin, E. J., Virani, S. S., Callaway, C. W., Chamberlain, A. M., Chang, A. R., Cheng, S., et al. (2018). Heart disease and stroke statistics—2018 update. A report from the American Heart Association. *Circulation, 137*, e67–e492. https://doi.org/10.1161/CIR.0000000000000558.

Cahill, J. E., Gilbert, M. R., & Armstrong, T. S. (2014). Personal health records as portal to the electronic medical record. *Journal of Neuro-Oncology, 117*(1), 1–6. https://doi.

org/10.1007/s11060-013-1333-x.
Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases, 40*(5), 373–383.
Cheng, H., Gurland, B. J., & Maurer, M. S. (2008). Self-reported lack of energy (anergia) among elders in a multiethnic community. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 63*(7), 707–714.
Crane, P. B. (2005). Fatigue and physical activity in older women after myocardial infarction. *Heart & Lung, 34*, 30–38.
Crane, P. B., Abel, W. M., & McCoy, T. P. (2015). Fatigue and physical activity after myocardial infarction. *Biological Research for Nursing, 17*(3), 276–284.
Crooks, C. J., West, J., & Card, T. R. (2015). A comparison of the recording of comorbidity in primary and secondary care by using the Charlson Index to predict short-term and long-term survival in a routine linked data cohort. *BMJ Open, 5*(6), e007974.
Daniels, L. A., Oerlemans, S., Krol, A. D., Creutzberg, C. L., & van de Poll-Franse, L. V. (2014). Chronic fatigue in Hodgkin lymphoma survivors and associations with anxiety, depression and comorbidity. *The British Journal of Cancer, 110*(4), 868–874.
Davis, L. L. (2015). Determining time of symptom onset in patients with acute coronary syndromes: Agreement between medical record and interview data. *Dimensions of Critical Care Nursing, 34*(4), 222–231.
D'Hoore, W., Bouckaert, A., & Tilquin, C. (1996). Practical considerations on the use of the charlson comorbidity index with administrative data bases. *Journal of Clinical Epidemiology, 49*(12), 1429–1433.
Dickson, V. V., Buck, H., & Riegel, B. (2013). Multiple comorbid conditions challenge heart failure self-care by decreasing self-efficacy. *Nursing Research, 62*(1), 2–9.
Dueñas, M., Ramirez, C., Arana, R., & Failde, I. (2011). Gender differences and determinants of health related quality of life in coronary patients: A follow-up study. *BMC Cardiovascular Disorders, 11*, 24. https://doi.org/10.1186/1471-2261-11-24.
Fiest, K. M., Fisk, J. D., Patten, S. B., et al. (2016). Fatigue and comorbidities in multiple sclerosis. *International Jjournal of MS Care, 18*(2), 96–104.
Frei, A., Muggensturm, P., Putcha, N., et al. (2014). Five comorbidities reflected the health status in patients with chronic obstructive pulmonary disease: The newly developed COMCOLD index. *Journal of Clinical Epidemiology, 67*(8), 904–911.
Fritschi, C., & Quinn, L. (2010). Fatigue in patients with diabetes: A review. *Journal of Psychosomatic Research, 69*(1), 33–41.
Fulton, J. S., Lyon, B. L., & Goudreau, K. A. (2014). *Foundations of clinical nurse specialist practice* (2nd ed.). New York, New York: Springer Publishing Company.
Golomb, B. A., Evans, M. A., Dimsdale, J. E., & White, H. L. (2012). Effects of statins on energy and fatigue with exertion: Results from a randomized controlled trial. *Archives of Internal Medicine, 172*(15), 1180–1182.
de Groot, V., Beckerman, H., Lankhorst, G. J., & Bouter, L. M. (2003). How to measure comorbidity. *Journal of Clinical Epidemiology, 56*(3), 221–229.
Hardy, S. E., & Studenski, S. A. (2008). Fatigue predicts mortality in older adults. *Journal of the American Geriatrics Society, 56*, 1910–1914.
Horton, M., Rudick, R. A., Hara-Cleaver, C., & Marrie, R. A. (2010). Validation of a self-report comorbidity questionnaire for multiple sclerosis. *Neuroepidemiology, 35*(2), 83–90.
Kalra, P. R., Morley, C., Barnes, S., Menown, I., Kassianos, G., Padmanabhan, S., et al. (2013). Discontinuation of beta-blockers in cardiovascular disease: UK primary care cohort study. *International Journal of Cardiology, 167*, 2695–2699. https://doi.org/10.1016/j.ijcard.2012.06.116.
Katz, P. (2017). Fatigue in rheumatoid arthritis. *Current Rheumatology Reports, 19*(25), 1.
Lash, T. L., Mor, V., Wieland, D., Ferrucci, L., Satariano, W., & Silliman, R. A. (2007). Methodology, design, and analytic techniques to address measurement of comorbid disease. *Journal of Gerontology: Medical Sciences, 62A*(3), 281–285.
Linn, B., Linn, M., & Gurel, L. (1968). Cumulative illness rating scale. *Journal of the American Geriatrics Society, 16*, 622–626.
Marengoni, A., Angleman, S., Melis, R., et al. (2011). Aging with multimorbidity: A systematic review of the literature. *Ageing Research Reviews, 10*(4), 430–439.
McGregor, J. C., Kim, P. W., Perencevich, E. N., et al. (2005). Utility of the chronic disease score and Charlson Comorbidity Index as comorbidity measures for use in epidemiologic studies of antibiotic-resistant organisms. *American Journal of Epidemiology, 161*(5), 483–493.
McSweeney, J. C., Cleves, M. A., Zhao, W., Lefler, L., & Yang, S. (2010). Cluster analysis of women's prodromal and acute myocardial infarction symptoms by race and other characteristics. *Journal of Cardiovascular Nursing, 25*(4), 311–322.
Meghani, S. H., Buck, H. G., Dickson, V. V., Hammer, M. J., Rabelo-Silva, E. R., Clark, R., & Naylor, M. D. (2013). The conceptualization and measurement of comorbidity: A review of the interprofessional discourse. *Nursing Research & Practice, 2013*.
Moss, L., & Crane, P. B. (2010). Exploring polypharmacy in elderly women after myocardial infarction. *Journal of Women & Aging, 22*(1), 22–33.
Olomu, A. B., Corser, W. D., Stommel, M., Xie, Y., & Holmes-Rovner, M. (2012). Do self-report and medical record comorbidity data predict longitudinal functional capacity and quality of life health outcomes similarly? *BMC Health Services Research, 12*(1), 398.
Piper, B. F., Dibble, S. L., Dodd, M. J., Weiss, M. C., Slaughter, R. E., & Paul, S. M. (1998). The revised Piper Fatigue Scale: Psychometric evaluation in women with breast cancer. *Oncology Nursing Forum, 25*(4), 677–684.
Putnam, K. G., Diana, S. M. B., Fishman, P., et al. (2002). Chronic disease score as a predictor of hospitalization. *Epidemiology, 13*(3), 340–346.
Ricci, J. A., Chee, E., Lorandeau, A. L., & Berger, J. (2007). Fatigue in the US workforce: Prevalence and implications for lost productive work time. *Journal of Occupational and Environmental Medicine, 49*(1), 1–10.
Roversi, S., Fabbri, L. M., Sin, D. D., Hawkins, N. M., & Agustí, A. (2016). Chronic obstructive pulmonary disease and cardiac diseases: An urgent need for integrated care. *American Journal of Respiratory and Critical Care Medicine, 194*(11), 1319–1336.
Stadje, R., Dornieden, K., Baum, E., et al. (2016). The differential diagnosis of tiredness: A systematic review. *BMC Family Practice, 17*(1), https://doi.org/10.1186/s12875-016-0545-5.
Stover, A. M., Reeve, B. B., Piper, B. F., et al. (2013). Deriving clinically meaningful cut-scores for fatigue in a cohort of breast cancer survivors: A Health, Eating, Activity, and Lifestyle (HEAL) study. *Quality of Life Research, 22*(9), 2279–2292.
Sundararajan, V., Henderson, T., Perry, C., Muggivan, A., Quan, H., & Ghali, W. A. (2004). New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *Journal of Clinical Epidemiology, 57*(12), 1288–1294.
Valderas, J., Starfield, B., Sibbald, B., Salisbury, C., & Roland, M. (2009). Defining comorbidity: Implications for understanding health and health services. *Annals of Family Medicine, 7*(4), 357–363.
Vigen, C., Kwan, M. L., John, E. M., Gomez, S. L., Keegan, T. H., Lu, Y., et al. (2016). Validation of self-reported co-morbidity status of breast cancer patients with medical records: The California breast cancer survivorship consortium (CBCSC). *Cancer Causes & Control, 27*(3), 391–401.
Von Korff, M., Wagner, E. H., & Saunders, K. (1992). A chronic disease score from automated pharmacy data. *Journal of Clinical Epidemiology, 45*(2), 197–203.
Yurkovich, M., Avina-Zubieta, J. A., Thomas, J., Gorenchtein, M., & Lacaille, D. (2015). A systematic review identifies valid comorbidity indices derived from administrative health data. *Journal of Clinical Epidemiology, 68*(1), 3–14.