Correlates of In-Hospital Deaths among Hospitalizations with Pulmonary Embolism: Findings from the 2001—2008 National Hospital Discharge Survey

James Tsai*, Scott D. Grosse, Althea M. Grant, Nimia L. Reyes, W. Craig Hooper, Hani K. Atrash
Division of Blood Disorders, National Center on Birth Defects and Developmental Disabilities Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America

Abstract

Background: Deep vein thrombosis and pulmonary embolism (PE) are responsible for substantial mortality, morbidity, and impaired health-related quality of life. The aim of this study was to evaluate the correlates of in-hospital deaths among hospitalizations with a diagnosis of PE in the United States.

Methods: By using data from the 2001—2008 National Hospital Discharge Survey, we assessed the correlates of in-hospital deaths among 14,721 hospitalizations with a diagnosis of PE and among subgroups stratified by age, sex, race, days of hospital stay, type of admission, cancer, pneumonia, and fractures. We produced adjusted rate ratios (aRR) and 95% confidence intervals using log-linear multivariate regression models.

Results: Regardless of the listing position of diagnostic codes, we observed an increased likelihood of in-hospital death in subgroups of hospitalizations with ages 50 years and older (aRR = 1.82—8.48), less than 7 days of hospital stay (aRR = 1.43—1.57), pneumonia (aRR = 1.79—2.28), or fractures (aRR = 2.18) (except for first-listed PE), when compared to the reference groups with ages 1–49 years, 7 days or more of hospital stay, without cancer, pneumonia, or fractures while adjusting for covariates. In addition, we observed an increased likelihood of in-hospital death for first-listed PE in hospitalizations of women, when compared to those of men (aRR = 1.45).

Conclusions: The results of this study provide support for identifying, developing, and implementing effective, evidence-based clinical assessment and management strategies to reduce PE-related morbidity and mortality among hospitalized PE patients who may have concurrent health conditions including cancer, pneumonia, and fractures.

Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are part of a venous thromboembolism spectrum with a complex and multifaceted etiology involving the interactions of biological, behavioral, health, and environmental risk factors [1–4]. The 2008 Surgeon General’s Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism suggests that DVT and PE may contribute to as many as 100,000–180,000 deaths per year [5]. Furthermore, PE can result in substantial morbidities including recurrence, chronic pulmonary hypertension, disability, and impaired health-related quality of life [5–8]. Accumulating evidence suggests that hospitalized patients including those with cancer, pneumonia, and fractures may have a high risk of PE [14–17]. These health conditions were found among the leading diagnostic categories and linked to approximately 3.3 million hospitalizations in the United States in 2007 [12]. Recent data from the National Hospital Discharge Survey (NHDS) showed that the overall case-fatality rate of hospitalizations with a PE diagnosis declined from 11.4% to 7.1% during 2001–2008, even though a corresponding reduction in the estimated number of in-hospital deaths among such hospitalizations was not observed for the same period [13].

To date, numerous clinical and epidemiologic studies have assessed PE mortality by using data ascertained from death certificates, autopsy records, or participants of clinical investigations [14–17]. A number of studies have assessed the case-fatality rates of PE and the relationship between in-hospital death and risk factors among patients or hospitalizations with a PE diagnosis by using the national hospital discharge surveys [13,18–24]. However, few studies have examined the correlates of in-hospital death, encompassing diagnostic categories of cancer, pneumonia, and fractures, among a nationally representative sample of hospitalizations with a PE diagnosis in the United States. Such a study is valuable to identify risk factors for PE-related death and to provide observational evidence that can inform and improve clinical assessment and intervention strategies for hospitalized PE patients. Therefore, the aim of this study was to assess the correlates of in-hospital death, including demographic characteristics and clinical risk factors, among
hospitalizations with a PE diagnosis (i.e., first-listed and any-listed) in the United States by analyzing data from the 2001–2008 NHDS [25].

**Methods**

**Data Source**

The NHDS was conducted annually from 1965–2010 by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC) to collect demographic and medical information of a sample of hospitalizations from a national probability selection of hospitals in the 50 states and the District of Columbia [26]. The NHDS was designed to collect information on characteristics of inpatients discharged from non-Federal short-stay hospitals in the United States. The NHDS includes general or children’s general hospitals with an average length of stay of fewer than 30 days for all patients, Federal, military, and Department of Veterans Affairs hospitals were excluded, as were hospital units of institutions and hospitals with fewer than 6 beds staffed for patient use. Details about the survey methodology are available elsewhere [25]. The NHDS collects information of hospitalizations including age, race, sex, length of hospital stay, type of admission (e.g., emergency, urgent, and elective), discharge status (e.g., death), medical diagnosis and procedure codes. Data collection for the NHDS was approved by the NCHS Research Ethics Review Board (NCHS ERB #2011–12). Analysis of deidentified data from the survey is exempt from the federal regulations for the protection of human research participants.

**Hospitalization Records**

Because persons with multiple hospitalizations during the survey year may be sampled more than once, estimates from the NHDS are for hospitalizations, not for persons. Each sampled hospitalization has a maximum of seven diagnostic codes based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The first-listed code is a principal diagnosis. We limited our analysis to a sample of non-newborn hospitalizations with a first-listed PE (n = 8,990) or any-listed PE (n = 14,721). Table 1 lists the codes for identification of PE and selected diagnostic categories for the years 2001–2008. In addition to demographic variables (i.e., age, sex, and race), we also included covariates such as cancer, pneumonia, and fractures in the analysis. We included these covariates because they are well-established independent risk factors for PE and may represent important pathways for prevention.

**Statistical Analysis**

We combined 8 years of data to increase statistical reliability and to allow the analysis of some subpopulation groups that otherwise would have been too small to produce statistically reliable estimates [25,27]. We estimated the case-fatality rates in hospitalizations with a diagnosis of PE (i.e., first-listed and any-listed) and in subgroups stratified by age, sex, race, days of hospital stay, type of admission, and status of cancer, pneumonia, and fractures [28]. To examine the associations between in-hospital death and risk factors among hospitalizations with a PE diagnosis during the period 2001–2008, we produced unadjusted and adjusted rate ratios (aRRs) with 95% confidence intervals (CIs) by using demographic and medical risk factors as predictors; status of in-hospital death was used as an outcome variable in multivariate log-linear regression models.

To present all estimates that fully account for multiple stages of sampling, stratification, and clustering design of the NHDS, we accessed the restricted datasets through the Research Data Center (CDC, Atlanta, GA, 2011) [26]. We used SPSS 19 Complex Samples for Survey Analysis (IBM Corp., Armonk, NY, 2010) and STATA 11 (StataCorp LP, College Station, TX, 2009) to perform the data management and analyses to account for complex sample survey design [29].

**Results**

Except for a limited number of deaths in hospitalizations of fractures with first-listed PE, the case-fatality rates varied significantly by age, status of cancer, pneumonia, and fractures among hospitalizations with first-listed PE and any-listed PE (P<0.05 for Wald-F test). Specifically, the case-fatality rates were higher among hospitalizations with advanced ages, cancer, pneumonia, or fractures than among those with younger ages, without a diagnosis of cancer, pneumonia, or fractures (P<0.05 for Wald-F test) (Table 2). Of those hospitalizations with first-listed PE, we observed increased likelihoods of in-hospital death in subgroups with ages 50–79 years (aRR = 3.63; CI: 1.88–7.02), ages 80 years and older (aRR = 8.48; CI: 4.03–17.90), female (aRR = 1.45; CI: 1.09–1.93), less than 7 days of hospital stay (aRR = 1.37; CI: 1.12–2.21), cancer (aRR = 2.28; CI: 1.68–3.09), or pneumonia (aRR = 2.20; CI: 1.28–3.77), when compared to the reference groups with ages 1–49 years, male, 7 days or more of hospital stay, without cancer or pneumonia while adjusting for all covariates (Table 2). Similarly, of hospitalizations with any-listed PE diagnosis, we observed increased likelihoods of in-hospital death among subgroups with ages 50–79 years (aRR = 1.82; CI: 1.47–2.25), ages 80 years and older (aRR = 3.26; CI: 2.58–4.12), race/ethnicity listed under “other” (aRR = 1.36; CI: 1.15–1.76), less than 7 days of hospital stay (aRR = 1.43; CI: 1.15–1.76), cancer (aRR = 2.10; CI: 1.74–2.53), pneumonia (aRR = 1.79; CI: 1.48–2.17), or fractures (aRR = 2.32; CI: 1.68–3.20), when compared to the reference groups with ages 1–49 years, male, white, 7 days or more of hospital stay, without cancer or pneumonia.

**Table 1.** The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for identification of selected medical diagnoses, 2001–2008.

| Description          | ICD-9-CM codes* |
|----------------------|-----------------|
| Pulmonary embolism   | 415.1, 634.6, 635.6, 636.6, 637.6, 638.6, and 673.2 |
| Cancer (malignant neoplasm) | 140–208, 230–234 |
| Pneumonia           | 480–486         |
| Fractures            | 800–829         |

*Only three-digit category codes are listed for cancer, pneumonia, and fractures. doi:10.1371/journal.pone.0034048.t001
Table 2. Estimated case-fatality rates and rate ratios for in-hospital death among hospitalizations with a PE diagnosis, 2001—2008, NHDS, United States.

| Characteristics | In-hospital death | Any-listed PE (n = 14,721) |
|-----------------|-------------------|-----------------------------|
|                 | First-listed PE (n = 8,990) | Unadjusted RR (95% CI) | Adjusted RR (95% CI) | Case-fatality rate (%) (95% CI) | P-value | Unadjusted RR (95% CI) | Adjusted RR (95% CI) |
|                 |                   | P-value |                   |                   | Referrer |                   |                   |
| **Age**         |                   |         |                   |                   |         |                   |                   |
| 1—49           | 3,550             | 1.0 (0.5—1.9) | Referent | Referent | 4.0 (3.3—4.8) | Referent | Referent |
| 50—79          | 8,240             | 3.8 (3.2—4.5) | Referent | Referent | 8.1 (7.1—9.1) | Referent | Referent |
| ≥80            | 2,931             | 8.2 (5.8—11.3) | Referent | Referent | 13.6 (11.6—16.0) | Referent | Referent |
| **Sex**        |                   |         |                   |                   |         |                   |                   |
| Male           | 6,224             | 3.1 (2.5—3.7) | Referent | Referent | 8.3 (7.9—9.2) | Referent | Referent |
| Female         | 8,497             | 4.5 (3.5—5.6) | Referent | Referent | 8.2 (7.2—9.4) | Referent | Referent |
| **Race**       |                   |         |                   |                   |         |                   |                   |
| White          | 7,933             | 4.0 (3.2—4.9) | Referent | Referent | 8.5 (7.4—9.9) | Referent | Referent |
| Black          | 2,097             | 3.6 (2.9—4.6) | Referent | Referent | 7.9 (6.6—8.4) | Referent | Referent |
| Other          | 395               | 3.2 (3.0—5.6) | Referent | Referent | 10.6 (9.2—12.2) | Referent | Referent |
| Not stated     | 4,496             | 3.7 (2.4—5.6) | Referent | Referent | 7.7 (6.5—9.0) | Referent | Referent |
| **Days of hospital stay** |                   |         |                   |                   |         |                   |                   |
| ≥7 days        | 6,746             | 3.4 (2.6—4.3) | Referent | Referent | 7.6 (6.5—8.8) | Referent | Referent |
| <7 days        | 7,975             | 4.2 (3.4—5.1) | Referent | Referent | 8.8 (7.7—10.0) | Referent | Referent |
| **Type of Admission** |                   |         |                   |                   |         |                   |                   |
| Emergency      | 9,120             | 4.1 (3.4—5.1) | Referent | Referent | 8.4 (7.5—9.4) | Referent | Referent |
| Urgent         | 2,545             | 2.9 (2.1—4.1) | Referent | Referent | 7.4 (6.0—9.1) | Referent | Referent |
| Elective       | 1,643             | 2.9 (1.1—7.3) | Referent | Referent | 7.6 (5.2—10.9) | Referent | Referent |
| Not stated     | 1,413             | 5.4 (3.7—7.7) | Referent | Referent | 10.0 (8.1—12.3) | Referent | Referent |
| **Cancer**     |                   |         |                   |                   |         |                   |                   |
| No             | 12,233            | 3.3 (2.7—4.2) | Referent | Referent | 7.1 (6.3—8.1) | Referent | Referent |
| Yes            | 2,488             | 7.5 (6.1—9.2) | Referent | Referent | 14.1 (12.5—15.8) | Referent | Referent |
| **Pneumonia**  |                   |         |                   |                   |         |                   |                   |
| No             | 12,898            | 3.6 (3.0—4.3) | Referent | Referent | 7.5 (6.6—8.4) | Referent | Referent |
| Yes            | 1,823             | 7.1 (4.3—11.6) | Referent | Referent | 13.7 (11.5—16.3) | Referent | Referent |
| **Fractures**  |                   |         |                   |                   |         |                   |                   |
| No             | 14,354            | 3.9 (3.3—4.7) | Referent | Referent | 7.9 (7.2—8.8) | Referent | Referent |
| Yes            | 367               | 7.9 (3.3—4.7) | Referent | Referent | 17.8 (13.1—23.7) | Referent | Referent |

aMaximum subgroup sample size.
bConfidence interval.
cP-value for Wald-F test.
dRate ratio.
eRate ratio from log-linear regression model that adjusted for age, sex, race, days of stay, type of admission, cancer, pneumonia, and fractures.
fReferent rate ratio = 1.00.
gEstimate may not be reliable due to underreporting of race information.
hUnstable estimate due to small subgroup size.

Correlates of In-Hospital Deaths with PE

doi:10.1371/journal.pone.0034048.t002
hospital stay, without cancer, pneumonia, or fractures after adjustment of all covariates (Table 2).

Discussion

Previous studies have assessed many correlates of in-hospital death among PE patients in healthcare settings [21–24], our study expanded previous research by assessing in-hospital deaths with a PE diagnosis encompassing first-listed and any-listed ICD-9 diagnostic codes during 2001–2008. The associations of cancer, pneumonia, and fractures with in-hospital deaths among a nationally representative sample of hospitalizations with a first-listed and any-listed PE diagnosis in the United States during the study period have not been reported in the past. Such observational evidence is valuable for identifying risk factors that may place patients at an increased risk of death and for improving clinical assessment and management to prevent fatal PE. Regardless of the listing position, we observed an increased likelihood of in-hospital death in subgroups of hospitalizations with advanced ages, less than 7 days of hospital stay, cancer, pneumonia, or fractures (except for first-listed PE), when compared to the reference groups with ages 1–49 years, 7 days or more of hospital stay, without cancer, pneumonia, or fractures while adjusting for all covariates. In addition, we observed an increased likelihood of in-hospital death for first-listed PE in hospitalizations of women when compared to those of men. However, the exact reason for this increase remained unknown, additional research may be needed. Interestingly, regardless of the listing position, we did not find that type of admission (e.g., emergency admission) was a factor independently associated with in-hospital death with a PE diagnosis.

Some results of this study were consistent with evidence that mortality rates were high among patients with advanced ages or co-morbid conditions such as cancer. Recent data suggested that a decline in the overall case-fatality rate of US hospitalizations with a PE diagnosis could be attributable to a combination of an increased number of PE diagnoses resulting from the widely used computed tomography pulmonary angiography (e.g., detection of asymptomatic PE or small peripheral emboli) together with more effective treatment and fewer complications [13,20,30–32]. Regardless, the strength of associations between the correlates and in-hospital death remained essentially unchanged during the study period, when survey year was used as an additional stratification variable or as a covariate in the regression models (data not shown).

The results of our study provide support for enhancing efforts toward identifying and implementing appropriate preventive strategies among hospitalized patients, including those with co-morbid conditions such as cancer, pneumonia, and fractures in healthcare settings [33]. Because of the disease severity, fatal PE may occur early during a hospital stay and may be undiagnosed, clinicians must be attentive to identify PE patients. Because the case-fatality rate was higher among hospitalizations of a shorter hospital stay than those of a longer stay, our results suggest that fatal PE may occur early after a hospital admission [34,35]. As such, clinical assessment, diagnostic evaluation, and appropriate treatment for PE should be performed early and promptly among hospitalized patients [34,36,37].

Our study has some limitations. Cross-sectional surveys are not designed to evaluate a cause-effect relationship. The NHDS hospitalizations rates do not necessarily reflect rates per person, as hospitalizations of recurrent PE patients could be included. Because asymptomatic PE patients with other co-morbid conditions might be undiagnosed or misdiagnosed, or PE diagnosis might have not been made before death occurred, hospitalizations for these patients might not have been included in our study. Due to underreporting of race in the NHDS, extra caution is needed for making any statistical inference regarding race as such estimates may not be reliable [28]. Even though we adjusted for many covariates in the study, we were unable to control for potential anticoagulant therapies, medications, and other co-morbidities that may affect short-term mortality in PE patients, due to the constraints of administrative datasets.

The results from this analysis and earlier study suggest that a majority of in-hospital deaths with a PE diagnosis could be attributable to concurrent PE and other health conditions [13]. Presently, there is a paucity of information concerning the clustering of risk factors that may hinder timely diagnosis, obscure clinical assessment and management, and exacerbate the risk of morbidity, mortality, and impaired health-related quality of life in PE patients [38–42]. Given that PE is a continuing clinical and public health concern in the United States, additional research is needed to elucidate amenable or manageable risk factors that are associated with devastating health consequences including death among PE patients. As the US population is aging, the co-existence of two or more chronic health conditions is a growing public health problem and poses enormous challenges for clinicians, patients, and healthcare systems [43–45]. To effectively reduce PE-related mortality and to improve overall health and well-being among most PE patients, more epidemiologic research and multimorbidity intervention studies are needed in order to deliberate, investigate, inform, and advance evidence-based practice in healthcare settings where integrated interventions may be coordinated and delivered to patients with multiple health conditions including PE [46–48].

In conclusion, the results of this study provide support for identifying, developing, and implementing effective, evidence-based clinical assessment and management strategies to reduce PE-related morbidity and mortality among hospitalized PE patients who may have concurrent health conditions including cancer, pneumonia, and fractures.

Acknowledgments

The authors of this study sincerely thank Stephanie Robinson, MPH of the Research Data Center, National Center for Health Statistics, Centers for Disease Control and Prevention, for coordinating the review of our research proposal and providing administrative and technical support for accessing the data. Disclaimer: The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the Research Data Center, the National Center for Health Statistics, or the Centers for Disease Control and Prevention.

Author Contributions

Conceived and designed the experiments: JT SDG WCH. Performed the experiments: JT SDG AMG NLR WCH HKA. Analyzed the data: JT. Contributed reagents/materials/analysis tools: JT SDG AMG NLR WCH HKA. Wrote the paper: JT SDG. Critical revision of the paper for important intellectual content: JT SDG AMG NLR WCH HKA.

Administrative, technical, material support, and study supervision: AMG HKA.

References

1. Heit JA (2005) Venous thromboembolism: disease burden, outcomes and risk factors. J Thromb Haemost 3: 1611–7.

2. Rosendaal FR (2005) Venous Thrombosis: The Role of Genes, Environment, and Behavior. Hematology 2005: 1–12.
3. Goldhaber SZ (2010) Risk factors for venous thromboembolism. J Am Coll Cardiol 56: 1–7.
4. Stein PD, Matta F (2010) Epidemiology and incidence: the scope of the problem and risk factors for development of venous thromboembolism. Clin Chest Med 31: 611–20.
5. DHHS (2008) The Surgeon General’s Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism. Office of the Surgeon General. U.S. Department of Health & Human Services. Washington, DC. Available: http://www.surgeongeneral.gov/topics/deepvein/calltoaction/call-to-action-on-dvt-2008.pdf. Accessed 2011 Aug 8.
6. Zhu T, Martinez I, Emmerich J (2009) Venous thromboembolism: risk factors for recurrence. Arterioscler Thromb Vasc Biol 29: 298–310.
7. Klok F, van Kralingen K, van Dijk APJ, Heyning F, Vlegga H, et al. (2010) Quality of life in long-term survivors of acute pulmonary embolism. Chest 138: 1432–40.
8. Rubenfire M, Beyram M, Hector-Word Z (2007) Pulmonary hypertension in the critical care setting: classification, pathophysiology, diagnosis, and management. Crit Care Clin 23: 803–34, vi–viii.
9. Cohen AT, Alhkhan R, Arcelus JJ, Bergmann JF, Haas S, et al. (2005) Assessment of venous thromboembolism risk and the benefits of thromboprophylaxis in medical patients. Thromb Haemost 94: 750–9.
10. Geerts W (2009) Prevention of venous thromboembolism: a key patient safety priority. J Thromb Haemost 7 Suppl 1: 1–8.
11. Alhikhan R, Cohen AT, Combe S, Samama MM, Desjardins L, et al. (2004) Risk factors for venous thromboembolism in hospitalized patients with acute medical illness: analysis of the MEDENOX Study. Arch Intern Med 164: 963–8.
12. CDC (2010) National Hospital Discharge Survey: 2007 Summary. Available: http://www.cdc.gov/nchs/data/nhsr/nhsr029.pdf. National Health Statistics Reports 29. Accessed 2011 Aug 8.
13. Tsai J, Gross SD, Grant AM, Hooper WC, Atrash HK (2012) Trends in In-Hospital Deaths Among Hospitalizations With Pulmonary Embolism. Arch Intern Med. doi:10.1001/archinternmed.2012.198.
14. Alhikhan R, Peters F, Wilmott R, Cohen AT (2004) Fatal pulmonary embolism in hospitalised patients: a necropsy review. J Clin Pathol 57: 1254–7.
15. Hest JA (2008) The epidemiology of venous thromboembolism in the community. Arterioscler Thromb Vasc Biol 28: 570–2.
16. Stein PD, Beinath A, Meyers FA, Kayali F, Skaf E, et al. (2006) Pulmonary embolism as a cause of death in patients who died with cancer. Am J Med 119: 463–5.
17. Hordeker KT, Mannino DM, Leeper KV (2003) Pulmonary embolism mortality in the United States, 1979–1996: an analysis using multiple-cause mortality data. Arch Intern Med 163: 1711–7.
18. Stein PD, Kayali F, Olson RE (2004) Estimated case fatality rate of pulmonary embolism, 1979 to 1998. Am J Cardiol 93: 1197–9.
19. Stein PD, Kayali F, Olson RE (2004) Regional differences in rates of diagnosis and mortality of pulmonary thromboembolism. Am J Cardiol 93: 1194–7.
20. Wiener RS, Schwartz LM, Woloshin S (2011) Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. Arch Intern Med 171: 831–7.
21. Stein PD, Matta F (2012) Case fatality rate with pulmonary embolectomy for acute pulmonary embolism. Am J Med 125: 471–7.
22. Chughalhi HL, Janjua M, Matta F, Javeesh F, Stein PD (2011) Predictors of in-hospital mortality in patients receiving thrombolytic therapy for pulmonary embolism. Clin Appl Thromb Hemost 17: 656–8.
23. Stein PD, Matta F, Keyes DC, Willeyrd GL (2012) Impact of Vena Cava Filters on In-hospital Case Fatality Rate from Pulmonary Embolism. Am J Med 125: 478–84.
24. Ho KM, Burrell M, Rao S, Baker R (2010) Incidence and risk factors for fatal pulmonary embolism after major trauma: a nested cohort study. British journal of anaesthesi 105: 596–602.
25. Centers for Disease Control (2011) National Hospital Discharge Survey (NHDS). National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, Atlanta, Georgia. Available: http://www.cdc.gov/nchs/index.htm2011. Accessed 2011 Aug 8.
26. Centers for Disease Control (2011) Research Data Center (RDC), National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), U.S. Department of Health & Human Services. Washington, DC. Available: http://www.cdc.gov/rdc/2011. Accessed 2011 Aug 8.
27. Korn E, Graubard B (1999) Analysis of Health Surveys. New York: John Wiley and Sons, Inc.
28. Krousk L (1995) Underreporting of race in the National Hospital Discharge Survey. National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention. Report No.: Series 10, Number 225.
29. Brogan D (2005) Software for Sample Survey Data, Misuse of Standard Packages. Encyclopedia of Biostatistics. Bk-Sec: 5057–64.
30. DeMarco N, Dang Q, Kapoor W, Ragni M (2008) Pulmonary embolism incidence is increasing with use of spiral computed tomography. The American journal of medicine 121: 611–7.
31. Quality V, Rhee J, Cifu A (2012) The Diagnosis and Treatment of Pulmonary Embolism: A Metaphor for Medicine in the Evidence-Based Medicine Era. Arch Intern Med. doi:10.1001/archinternmed.2012.195.
32. Stein PD, Matta F (2012) Thrombolytic therapy in unstable patients with acute pulmonary embolism: saves lives but underused. Am J Med 125: 463–70.
33. Nicolaides A, Bredthin H, Farred J, Goldhaber S, Haas S, et al. (2006) Prevention and treatment of venous thromboembolism. International Consensus Statement (guidelines according to scientific evidence). Int Angiol 25: 101–61.
34. Agoli G, Becattini C (2010) Acute pulmonary embolism. N Engl J Med 363: 296–74.
35. Cushman M (2007) Epidemiology and risk factors for venous thrombosis. Semin Hematol 44: 62–9.
36. Tapon P (2008) Acute pulmonary embolism. N Engl J Med 359: 1037–52.
37. Stein PD, Sestman HD, Dalen JE, Bailey DL, Bajr M, et al. (2012) Controversies in diagnosis of pulmonary embolism. Clin Appl Thromb Hemost 17: 140–9.
38. Atuniaser J, Tejada J, Foley R (2012) The diagnosis and management of pulmonary embolism. Connecticut medicine 76: 5–14.
39. van Es J, Douma RA, Gerdes VEA, Kamphuisen PW, Buller HR (2010) Acute pulmonary embolism. Part 2: treatment. Nat Rev Cardiol 7: 613–22. doi:10.1038/nrcardio.2010.141.
40. Douma RA, Kamphuisen PW, Buller HR (2010) Acute pulmonary embolism. Part 1: epidemiology and diagnosis. Nat Rev Cardiol 7: 595–96. doi:10.1038/ nrcardio.2010.106.
41. Klok FA, Cohn DM, Middeldorp S, Schar Moo, Buller HR, et al. (2010) Quality of life after pulmonary embolism: validation of the PEmb-QoL Questionnaire. J Thromb Haemost 8: 525–32.
42. Smith SB, Geske JB, Morgenhalter TJ (2012) Risk Factors Associated with Delayed Diagnosis of Acute Pulmonary Embolism. The Journal of Emergency Medicine 42: 1–6.
43. Fortin M, Soubhi H, Hudon C, Bayls EA, van den Akker M (2007) Multimorbidity’s many challenges. BMJ [Editorial] 334: 1016–7.
44. Boyd CM, Darer J, Boulit C, Fried LP, Boult L, et al. (2005) Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA 294: 716–24.
45. Smith SM, O’Dowd T (2007) Chronic diseases: what happens when they come in multiples? The British Journal of General practice 57: 268–70.
46. Boyd CM, Fortin M (2010) Future of Multimorbidity Research: How Should Understanding of Multimorbidity Inform Health System Design? Public Health Reviews 32: 451–74.
47. Mercer SW, Smith SM, Wyke S, O’Dowd T, Watt GC (2009) Multimorbidity in primary care: developing the research agenda. Family practice [Editorial] 26: 79–80.
48. DHHS (2010) Multiple Chronic Conditions: A Strategic Framework. Optimum Health and Quality of Life for Individuals with Multiple Chronic Conditions. US Department of Health and Human Services (DHHS), Washington, DC.