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# Depression and Risk for Hospitalizations and Rehospitalizations for Ambulatory Care-Sensitive Conditions in Denmark: a Population-Based Cohort Study

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**Guarantor:** Dr. Vestergaard has had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Data Sharing:** Requests for analyses of de-identified data from this study should be directed to Mogens Vestergaard (email: mv@ph.au.dk).

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ABSTRACT

**Objective:** Hospitalizations for ambulatory care-sensitive conditions (ACSCs) and early rehospitalizations are common and costly. We sought to determine whether individuals with depression are at increased risk for hospitalizations for ACSCs, and rehospitalization for the same or another ACSC, within 30 days.

Design: National, population-based cohort study.

Setting: Denmark.

**Participants:** 5,049,353 individuals  $\geq$  18 years old between January 1, 2005 and December 31, 2013.

**Measurements:** Depression was ascertained via psychiatrist diagnoses in the Danish Psychiatric Central Register or antidepressant prescription redemption from the Danish National Prescription Registry. Hospitalizations for ACSCs and rehospitalizations within 30 days were identified using the Danish National Patient Register.

**Results:** Overall, individuals with depression were 2.35-times more likely to be hospitalized for an ACSC (95% Confidence Interval [95%CI]: 2.32, 2.37) versus those without depression after adjusting for age, sex, and calendar period, and 1.45-times more likely after adjusting for socioeconomic factors, comorbidities, and primary care utilization (95%CI: 1.43, 1.46). After adjusting for ACSC-predisposing comorbidity, depression was associated with significantly greater risk for hospitalizations for all chronic (e.g., angina, diabetes complications, congestive heart failure exacerbation) and acute ACSCs (e.g., pneumonia) compared to those without depression. Compared to those without depression, persons with depression were 1.21-times more likely to be rehospitalized within 30 days for the same ACSC (95%CI: 1.18, 1.24) and

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1.19-times more likely to be rehospitalized within 30 days for a different ACSC (95%CI: 1.15,

1.23).

**Conclusions:** Individuals with depression are at increased risk for hospitalizations for ACSCs, and once discharged are at elevated risk for rehospitalizations within 30 days for ACSCs.

# ARTICLE SUMMARY

- A strength of our study is that we followed a nationwide, population-based cohort with nearly no loss to follow-up.
- Our use of data from a country with a national healthcare system with universal access to health care and a relatively homogeneous population may impact generalizability to other countries with more ethnically diverse populations and different healthcare settings.
- Although we lack data on potential mediators of an association between depression and ambulatory care-sensitive condition (ACSC)-related hospitalizations such as health-risk behaviors (e.g., smoking, sedentary lifestyle), previous studies that controlled for health-risk behaviors found that the association between depression and greater risk for ACSC-related hospitalizations was independent of these factors.
- Our data lacks the degree of detail required to determine if adequate treatment for depression could moderate the adverse outcomes seen here.

#### **INTRODUCTION**

Hospitalizations for chronic illnesses and their sequelae are a major contributor to rising healthcare costs in Western societies.<sup>1</sup> In the U.S., an estimated 10% of all hospitalizations may be preventable,<sup>2</sup> such as those for ambulatory care-sensitive conditions (ACSCs), a set of chronic and acute illnesses considered not to require inpatient treatment if patients receive timely and appropriate ambulatory care.<sup>3</sup> Hospitalizations for ACSCs have been estimated to cost the U.S. \$31.9 billion and £1.4 billion in the U.K. annually.<sup>4,5</sup> Moreover, early rehospitalizations, some of which may be due to ACSCs, are common and costly to health systems.<sup>6</sup> With the advent of accountable care organizations in the U.S. and other efforts to improve healthcare delivery worldwide, health systems are increasingly trying to prevent hospitalizations for ACSCs and early rehospitalizations in an effort to reduce healthcare spending.<sup>7-9</sup>

Depression is highly prevalent worldwide,<sup>10</sup> and is independently associated with more chronic disease sequelae,<sup>11</sup> greater healthcare costs,<sup>12</sup> and increased mortality.<sup>13</sup> Importantly, depression is amenable to treatment and could be a potentially modifiable risk factor for ACSC-related hospitalizations. Depression may increase hospitalizations for ACSCs through factors such as reduced adherence to chronic disease treatments and reduced self-care.<sup>14</sup> While prior studies have found higher risk of hospitalizations for ACSCs and/or early rehospitalizations among persons with depression, they have been limited to single centers,<sup>15,16</sup> specific chronic disease populations,<sup>17</sup> geographically-defined health systems,<sup>16,17</sup> and older adults.<sup>18</sup> Furthermore, previous research on depression and risk of rehospitalizations within 30 days has not focused on potentially preventable rehospitalizations,<sup>15,16,18,19</sup> such as rehospitalizations within 30 days for an ACSC, an outcome that is arguably of particular importance to health systems and health policy makers. Also, it remains unknown whether depressed individuals are

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at greater risk of ACSC-related hospitalizations and rehospitalizations simply because they are more likely to have underlying chronic diseases.<sup>20,21</sup>

Utilizing data from a population-based cohort of five million Danish adults, we sought to determine if individuals with depression are at increased risk for hospitalizations for ACSCs after adjusting for demographics, socioeconomic factors, comorbidity (ACSC-predisposing and non-ACSC-predisposing comorbidity), and primary care utilization. Further, we examined whether persons with depression who have been hospitalized for an ACSC are at greater risk for rehospitalization for the same, or another ACSC, within 30 days. We hypothesized that depression would be independently associated with increased risk for hospitalizations for ACSCs as well as rehospitalizations within 30 days for either the same or a different ACSC.

## **METHODS**

#### Population

We conducted a population-based cohort study of all adults  $\geq$  18 years old, alive and residing in Denmark at least one day between January 1, 2005 and December 31, 2013. The cohort was constructed using data from the Danish Civil Registration System,<sup>22</sup> which includes data on sex, date of birth, vital status, and emigration since January 1, 1968. In the register, Danish residents are each assigned a unique personal identification number which links to person-level data.<sup>22</sup>

The Danish Data Protection Agency and the Danish Health and Medicine Authority approved the study protocol, and requirement for informed consent was waived. *Primary Independent Variable* 

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Our primary independent variable of interest was depression as identified by either psychiatric diagnosis or filling at least one antidepressant prescription. Depression was treated as a time-dependent variable (i.e., an individual without a recorded depression diagnosis or antidepressant prescription redemption at baseline could be diagnosed with depression or redeem an antidepressant prescription during the follow-up period, moving from the "unexposed" to the "exposed" group). Information on psychiatric diagnoses was obtained from the Danish Psychiatric Central Register<sup>23</sup> (see Appendix 1), which includes diagnostic information on all psychiatric hospitalizations from 1969 onwards and outpatient specialty mental health visits from 1995 onwards.<sup>23</sup> Prescription fills for antidepressant prescriptions (i.e. selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and other non-tricyclic (TCA) antidepressants, see Appendix 1) were identified using the Danish National Prescription Registry.<sup>24</sup> This register includes data on all prescriptions dispensed at Danish pharmacies since 1995, including purchase date and classification of drugs according to the Anatomical Therapeutic Chemical Classification.<sup>25</sup> We excluded TCA prescriptions from our depression definition because of their frequent use for insomnia and/or pain. We also excluded bupropion or trazodone prescriptions since neither was approved for treating depression in Denmark during the study period. Individuals with schizophrenia, schizoaffective disorders or bipolar disorder were censored at date of diagnosis (see Appendix 2) and excluded from analyses.

#### **Outcomes of Interest**

Our primary outcome of interest was hospitalization for one of 12 ACSCs as defined by the Agency for Healthcare Research and Quality (AHRQ) (see Appendix 3).<sup>2</sup> Prior to December 31, 1993, register-based diagnoses were based on the Danish version of the International Classification of Diseases, 8th Revision (ICD-8).<sup>26</sup> From January 1, 1994 forward, the Danish BMJ Open: first published as 10.1136/bmjopen-2015-009878 on 2 December 2015. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by copyright

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version of the ICD-10<sup>27</sup> was used. Since the AHRO-defined ACSCs were originally derived using ICD-9 diagnoses, we included eight AHRQ-defined ACSCs (i.e., angina without concomitant cardiovascular procedures, chronic obstructive pulmonary disease (COPD) exacerbation, congestive heart failure (CHF) exacerbation, diabetes with short-term complications, diabetes with long-term complications, uncontrolled diabetes, hypertension (HTN), and appendicitis with perforation) that were translated into ICD-10 diagnosis codes and validated in a previous study.<sup>28</sup> We also included four AHRQ-defined ACSCs (i.e., bacterial pneumonia, diabetes-related lower extremity amputations, urinary tract infections (UTIs), and adult asthma exacerbations) based on ICD-10 codes used in prior Danish register-based studies.<sup>29-32</sup> We further divided ACSCs into five "chronic" ACSCs (i.e., angina, CHF exacerbation, HTN, diabetes-related, COPD/adult asthma exacerbation) and three "acute" ACSCs (i.e., appendicitis with perforation, pneumonia, and UTI). We used the Danish National Patient Register,<sup>33</sup> which contains information on all medical hospitalizations since January 1, 1977 and outpatient visits since January 1, 1995,<sup>33</sup> to obtain information on hospitalizations with principal discharge diagnoses for ACSCs occurring between January 1, 2005 and December 31, 2013. If a discharge was followed by an admission within one day, it was considered a transfer and counted as one admission only. We excluded hospitalizations with secondary obstetric diagnoses (ICD-10 codes: O00.0-O99.9).

Our secondary outcome of interest was rehospitalization for an ACSC within 30 days of discharge from the initial ACSC-related hospitalization. We counted rehospitalizations that were for the same ACSC, or for a different ACSC, using data from the Danish National Patient Register.

Socioeconomic Factors, Comorbid Medical Conditions, and Substance Abuse Disorders

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Information on marital/partnered status and education was obtained from Statistics Denmark and the Danish Educational Registers, respectively (see Appendix 4).<sup>34,35</sup> We categorized marital/partnered status as living with a partner (i.e., married, registered partnership, or cohabitation) or living alone (i.e., living without a partner, including widows/widowers). We classified maximum educational level attained into the following three categories based on the United Nations Educational, Scientific and Cultural Organization's International Standard Classification of Education: low (<10 years), middle (10–15 years), and high (>15 years).<sup>36</sup>

For the five chronic ACSCs, we defined ACSC-predisposing medical comorbidity specific for each ACSC in question (see Appendix 5). Information on ACSC-predisposing medical comorbidity and non-ACSC predisposing medical comorbidity was obtained from the Danish National Patient Register and based on Charlson Comorbidity Index (CCI) categories<sup>37</sup> (see Appendix 6) (e.g., myocardial infarction as ACSC-predisposing medical comorbidity for angina hospitalization, etc.), with two exceptions. Diabetes diagnoses were obtained from the Danish National Diabetes Register between January 1, 1990 and December 31, 2013 (see Appendix 7).<sup>38</sup> Chronic pulmonary disease was identified as either a diagnosis based on the CCI category obtained from the Danish National Patient Register or  $\geq$  two prescription redemptions within a six month period for medications treating obstructive airway diseases (see Appendix 8) as obtained from the Danish National Prescription Registry. Non-ACSC predisposing medical comorbidity included all remaining CCI diagnostic categories. We did not define ACSCpredisposing medical comorbidity for the three acute ACSCs.

Data on substance abuse (excluding tobacco abuse) was obtained from the Danish Psychiatric Central Register or the Danish National Patient Register (see Appendix 9). *Primary Care Utilization*  BMJ Open: first published as 10.1136/bmjopen-2015-009878 on 2 December 2015. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by copyright

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We obtained information on day-time face-to-face visits with primary care physicians (PCPs) or other primary care staff from the Danish National Health Service Register,<sup>39</sup> which has been collecting primary care administrative data since January 1, 1990. To reduce the chances of including a primary care visit that directly resulted in an ACSC-related hospitalization, we constructed a time-dependent variable counting the number of primary care visits from 10-375 days before any given day. We categorized primary care visits into three equally-sized categories of low, medium, or high utilization based on observed frequencies (i.e., 0-2, 3-9 or  $\geq$ 10 visits). *Statistical Analysis* 

We compared individuals with depression to those without depression using Poisson regression models in order to estimate incidence rate ratios (IRRs) for hospitalizations for ACSCs and subsequent rehospitalization within 30 days for an ACSC. We estimated corresponding 95% Confidence Intervals (95%CIs) using cluster robust variance estimation to account for interperson correlation and dichotomy of rehospitalizations. In these analyses, our outcomes of interest were a count of the number of hospitalizations for ACSCs. Age and calendar period were adjusted for using two-year and one-year age and time bands, respectively. All variables (including depression status), except sex, were treated as time-dependent. Individuals contributed at-risk time from January 1, 2005 or from their 18<sup>th</sup> birthday, whichever came last, and were censored at date of death, emigration, date of bipolar disorder or schizophrenia diagnosis, or on December 31, 2013, whichever came first.

For each ACSC-related hospitalization outcome, we fitted five risk models, adjusting sequentially for demographics (i.e., age, sex and calendar period), socioeconomic factors (i.e., marital/partnered status and education), ACSC-predisposing medical comorbidity (with each comorbid condition entered individually), other comorbidity (i.e., non-ACSC-predisposing

medical comorbidity entered individually and substance abuse), and primary care utilization. All model covariates were chosen *a priori* based on prior studies identifying their potential associations with both depression and healthcare utilization outcomes.<sup>12,16,17,40</sup> To address missing data on education, we conducted multiple imputation using five imputed data sets according to methods developed by Rubin.<sup>41</sup>

We performed two pre-specified sub-analyses. First, we examined whether the association between depression and risk for ACSC-related hospitalizations was modified by age. To do so, we repeated our Poisson regressions stratified by three age categories:  $\leq$  40 years old, 41-64 years old, and  $\geq$  65 years old. Second, we examined the associated risk for hospitalizations for chronic and acute ACSCs based on time since depression diagnosis in models adjusted for demographics.

In order to determine if an association between depression and risk for hospitalizations for ACSCs was impacted by our depression definition, we performed a pre-specified sensitivity analysis in which we repeated our regressions using three different depression definitions: antidepressant prescription alone, outpatient psychiatric visit-based diagnosis alone or psychiatric hospitalization for depression.

We fitted three models examining risk for rehospitalization within 30 days for an ACSC. The first model adjusted for demographics, the second included adjustment for socioeconomic factors and the third for medical and substance abuse comorbidities. Our outcome of interest in these models was time to rehospitalization for an ACSC within 30 days of discharge from the initial ACSC-related hospitalization. Individuals were at risk for the outcome on the day of discharge from their ACSC-related hospitalization. All variables in these analyses excluding sex were treated as time-dependent.

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We used two-sided significance tests for all analyses with statistical significance set at P < 0.05. Analyses were performed using STATA 13 (Stata Corporation, College Station, TX).

#### RESULTS

We followed a cohort of 5,049,353 individuals for a total of 38,674,363 person-years at risk, including 1,319,896 (26.1%) persons diagnosed with depression or who had redeemed an antidepressant prescription during the study period. Of those with depression, 1,182,495 (89.6%) cases were from antidepressant prescription fills while 137,401 (10.4%) cases were diagnosed by mental health specialists in outpatient or inpatient contacts. The mean age at initially registered depression diagnosis was 49.1 (standard deviation: 19.2) years old.

Table 1 displays the characteristics of our cohort by depression status. During the nine year follow-up period, we identified 1,255,640 hospitalizations for ACSCs, including 542,184 (43.2%) among persons with depression. There were 71.4 ACSC-related hospitalizations per 1,000 person-years among those with depression versus 23.0 per 1,000 person-years among those with depression versus 23.0 per 1,000 person-years among the study period.

[Please insert Table 1 here]

Compared to those without depression, the IRR for having any ACSC-related hospitalization was 2.35 (95% CI: 2.32, 2.37) for individuals with depression after adjusting for demographics. This association remained robust after adjusting for socioeconomic factors, and decreased though remained significant after adjusting for possible mediators including comorbidities and PCP visits during the previous year (Table 2).

In comparison to persons without depression, depression was associated with increased risk for hospitalizations for all of the chronic ACSCs even after adjusting for specific chronic

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ACSC-predisposing medical comorbidity (Table 2), particularly for hospitalizations for angina (IRR: 1.77; 95%CI: 1.73, 1.81), COPD/asthma exacerbations (IRR: 1.88; 95%CI: 1.84, 1.93), and diabetes-related hospitalizations (IRR: 1.83; 95%CI: 1.77, 1.89). Although these results were attenuated by adjusting for additional comorbidity and PCP visits during the previous year, depression remained independently associated with increased risk for hospitalizations for all chronic ACSCs, especially for hospitalizations for COPD/asthma exacerbations (IRR: 1.61; 95%CI: 1.57, 1.65), and diabetes-related hospitalizations (IRR: 1.69; 95%CI: 1.63, 1.75) (Table 2).

Similarly, depression was associated with increased risk for hospitalizations for all three acute ACSCs even after adjusting for medical and substance abuse comorbidity (appendicitis with perforation: IRR: 1.26; 95%CI: 1.21, 1.33; pneumonia: IRR: 1.55; 95%CI: 1.53, 1.56; UTI: 1.74; 95%CI: 1.71, 1.77). These associations remained significant after adjusting for PCP visits during the preceding year.

[Please insert Table 2 here]

When we stratified by age categories, we found that the association between depression and risk for hospitalizations for ACSCs was especially potent for individuals 40 years old or younger (IRR: 2.06; 1.98, 2.13). Depression was also independently associated with increased risk for hospitalizations for ACSCs among middle-aged and older adults (Table 3).

[Please insert Table 3 here]

In the first year after depression diagnosis, the associated risk for hospitalization for a chronic ACSC was nearly 3-times greater than those without depression (IRR: 2.89; 95%CI: 2.83, 2.96) (Figure 1). The associated risk remained nearly 2.4-times greater than for those without depression (IRR: 2.39, 95%CI: 2.34, 2.43) 10 or more years after depression diagnosis.

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During the first year after depression diagnosis, the associated risk for hospitalization for an acute ACSC was 3 1/3-times greater than for those without depression (IRR: 3.33, 95%CI: 3.27, 3.40), and the associated risk remained 2 <sup>1</sup>/<sub>4</sub>-times higher at  $\geq$  10 years after depression diagnosis (IRR: 2.25; 95%CI: 2.22, 2.29) (Figure 2).

[Please insert Figure 1 here]

[Please insert Figure 2 here]

In our sensitivity analysis in which we examined whether our results regarding risk for hospitalization for any ACSC were impacted by depression definition, we found that depression defined by antidepressant prescription alone (IRR: 2.31; 95%CI: 2.28, 2.33), outpatient psychiatric visit-based diagnosis alone (IRR: 2.66; 95%CI: 2.56, 2.77) or psychiatric hospitalization for depression (IRR: 2.69; 95%CI: 2.62, 2.77) were all associated increased risk for hospitalization for an ACSC after adjusting for demographics. These associations remained significant after adjusting for socioeconomic factors, comorbidities, and PCP visits in the previous year (antidepressant prescription alone: IRR: 1.44; 95%CI: 1.43, 1.45; outpatient psychiatric visit-based diagnosis: IRR: 1.54; 95%CI: 1.48, 1.60; psychiatric hospitalization for depression: IRR: 1.50; 95%CI: 1.46, 1.54).

Approximately 6.8% of all ACSC-related hospitalizations during the follow-up period were followed by an ACSC-related rehospitalization within 30 days, of which 73.0% were for the same ACSC and 27.0% were for a different ACSC. Of the 85,046 ACSC-related rehospitalizations within 30 days, 42,791 (50.3%) were among those with depression. Compared to those without depression, depression was associated with 1.36-times greater risk for rehospitalization within 30 days for the same ACSC (95%CI: 1.32, 1.39) and 1.44-times greater risk for rehospitalization within 30 days for a different ACSC (95%CI: 1.39, 1.49) after adjusting

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for age, sex, and calendar period (Table 4). After adjusting for socioeconomic factors and comorbidities, while attenuated, depression remained independently associated with greater risk for rehospitalization within 30 days for the same ACSC (IRR: 1.21; 95%CI: 1.18, 1.24) or another ACSC (IRR: 1.19; 95%CI: 1.15, 1.23).

[Please insert Table 4 here]

#### DISCUSSION

In this nationwide, population-based longitudinal study of over 5 million individuals, we found that depression was independently associated with higher risk for hospitalizations for both chronic and acute ACSCs and that the associated risk remained high for at least 10 years. To our knowledge, the present study is the first to show that depression was associated with higher risk of rehospitalization for the same or another ACSC within 30 days of an ACSC-related hospitalization. Importantly, we identified that the associated risk of hospitalizations for ACSCs was greater among persons with depression even when we adjusted for the higher prevalence of predisposing chronic diseases in this population.

An increased risk of hospitalization and subsequent rehospitalization for an ACSC among depressed individuals is troubling in light of evidence that some ACSC-related hospitalizations may have negative effects on long-term functioning, cognition and mental health.<sup>42</sup> Depression in-and-of-itself is known to increase the risk of cognitive decline and functional impairment,<sup>43,44</sup> both of which increase risk of ACSC-related hospitalizations.<sup>18,45</sup> Therefore, depressed individuals could be especially at risk for a vicious cycle of hospitalizations, rehospitalizations, and rapid decline.

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This study has important implications for development of interventions to prevent costly ACSC-related hospitalizations and rehospitalizations. A potential explanation for our findings is that depressed individuals may not receive timely and/or appropriate ambulatory care for chronic diseases such as diabetes or cardiovascular disease as well as acute diseases such as pneumonia or UTIs. Yet, we found that depression was independently associated with increased risk for hospitalizations for these conditions even in a country, Denmark, with universal access to primary care. Therefore, it could be reasonable to conclude that simply increasing access to primary care may not ameliorate these problems. This interpretation is supported by recent studies evaluating the impact of health care reform in Massachusetts that found improving access to care was not associated with reductions in ACSC-related hospitalizations or rehospitalizations within 30 days among high-risk populations.<sup>46,47</sup>

If expanding access to primary care by itself is insufficient to prevent hospitalizations for ACSCs among at-risk populations such as those with depression, then additional research is needed to identify cost-effective interventions that could reduce these potentially preventable events. One possibility is through ongoing efforts to integrate psychiatric care into primary care and other ambulatory care medical settings. Collaborative care for depression and comorbid conditions in primary care settings has been proven effective and cost-effective,<sup>48-53</sup> and its cost-effectiveness is in part due to reductions in hospitalizations for comorbid medical conditions.<sup>54</sup> Further studies of sufficient duration and size are needed to determine if collaborative care could prevent ACSC-related hospitalizations among individuals with depression. More research is also needed to ascertain if integrating aspects of collaborative care into existing interventions focusing on improving transitional care from the hospital back to primary care<sup>55,56</sup> could prevent early rehospitalizations for ACSCs. Such research would be of particular interest to accountable

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care organizations and health policy makers aiming to reduce healthcare costs while simultaneously improving patient outcomes and overall quality of care.

Our study has several strengths and limitations. We followed a nationwide, populationbased cohort with nearly no loss to follow-up. However, our use of data from a country with a national healthcare system with universal access to health care and a relatively homogeneous population may impact generalizability. Yet, these factors may enhance internal validity by decreasing the degree socioeconomic factors play in healthcare-seeking behavior, and potentially suggest that our estimates may be overly conservative. Further, our depression definition was based on a combination of psychiatric diagnoses and antidepressant prescription records, potentially introducing selection bias since patients with more severe depression are more likely to be prescribed antidepressants and/or referred to psychiatrists,<sup>57,58</sup> and is further exacerbated by inability to capture depressed individuals who have not sought treatment.<sup>59</sup> However, our sensitivity analysis examining different depression definitions did not yield differing results, and our primary depression definition has been used in prior related research.<sup>43</sup>

While we lack data on potential mediators of an association between depression and ACSC-related hospitalizations such as health-risk behaviors (e.g., smoking, sedentary lifestyle), previous studies in this area that controlled for health-risk behaviors found that the association between depression and greater risk for ACSC-related hospitalizations was independent of these factors.<sup>17,18</sup> Our data lacks the degree of detail required to determine if adequate treatment for depression could moderate the adverse outcomes seen here. Also, the registers lack detail to sufficiently ascertain illness severity, so we cannot fully exclude the possibility that our findings reflect that when compared to the general population, depressed individuals may present with

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higher acuity of medical illnesses and a greater burden of comorbidity, necessitating hospitalization for optimal treatment.

In conclusion, in a nationwide study in Denmark, we found that compared to individuals without depression, depression was associated with increased risk for hospitalizations for ACSCs. Furthermore, once hospitalized for an ACSC, depression was associated with greater risk for rehospitalization within 30 days for the same, or another, ACSC. Further research that clarifies the mechanisms linking depression and ACSC-related hospitalizations, and that JSC nt hospitalizats. develops interventions that prevent ACSC-related hospitalizations in persons with depression, is needed given the burden that recurrent hospitalizations places on individuals and society.

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## Table 1. Study cohort characteristics

	<b>Depression (n = 1,319,896)</b>			Without Depression (n = 3,782,713)		
Measure	Number of Hospitalizations for ACSCs	Person-Years at Risk	Percentage risk time spent in category (%)	Number of Hospitalizations for ACSCs	Person-Years at Risk	Percentage risk time spent in category (%)
Total	542,184	7,596,536	100.0	713,456	31,077,828	100.0
Age (years)						
$\leq 40$	28,434	1,771,769	23.3	69,350	11,940,484	38.4
41-64	158,633	3,697,843	48.7	197,925	13,201,867	42.5
$\geq$ 65	355,117	2,126,924	28.0	446,181	5,935,477	19.1
Sex						
Male	231,216	2,884,303	38.0	393,065	16,114,603	51.8
Female	310,968	4,712,233	62.0	320,391	14,963,225	48.2
Calendar period						
2005	47,853	661,461	8.7	79,756	3,564,097	11.5
2006	57,932	711,984	9.4	90,186	3,523,904	11.3
2007	46,477	761,231	10.0	67,588	3,494,327	11.2
2008	51,896	805,396	10.6	71,465	3,475,920	11.2
2009	63,150	848,956	11.2	83,274	3,452,336	11.1
2010	51,567	895,574	11.8	64,832	3,425,594	11.0
2011	74,991	938,720	12.4	89,372	3,405,029	11.0
2012	74,535	972,971	12.8	85,424	3,378,860	10.9
2013	73,783	1,000,243	13.2	81,559	3,358,761	10.8
Marital status						
Living with partner	226,573	3,585,166	47.2	348,530	15,922,753	51.2
Living alone	315,611	4,011,370	52.8	364,926	15,155,075	48.8
Education (years)						
< 10	265,781	2,751,794	36.2	312,769	8,845,177	28.5

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10-15	178,680	3,182,588	41.9	249,363	14,267,047	45.9
$\geq 16$	47,039	1,284,597	16.9	75,866	6,318,611	20.3
Missing	50,684	377,558	5.0	75,458	1,646,993	5.3
Comorbidity						
MI	89,475	261,404	3.4	109,123	556,446	1.8
CHF	118,101	212,889	2.8	137,507	367,223	1.2
Diabetes	155,739	761,878	10.0	165,161	1,567,720	5.0
Cerebrovascular	126,796	615,389	8.1	98,828	834,803	2.7
disease	120,150	010,000	011	,020		,
Peripheral vascular	79,566	283,055	3.7	70,493	443,853	1.4
disease	,			, , , , , , ,	,	
Chronic pulmonary	229,594	674,995	8.9	208,423	1,339,308	4.3
disease	- )				<u> </u>	
Dementia	44,638	217,259	2.9	19,519	110,040	0.3
Connective tissue	42,814	269,168	3.5	39,087	514,840	1.7
disease	<b>y</b> -				- ,	
Peptic ulcer disease	69,733	327,298	4.3	53,974	464,831	1.5
Renal disease	45,769	123,767	1.6	50,315	245,853	0.8
Mild liver disease	19,437	129,645	1.7	11,845	159,553	0.5
Moderate/severe	5,287	27,978	0.4	3,516	34,556	0.1
liver disease	- ,	- <u>)</u>			- ,	
Paraplegia	7,123	31,836	0.4	4,893	46,060	0.1
Cancer	102,324	608,120	8.0	118,072	1,430,995	4.6
Metastatic carcinoma	12,338	58,013	0.8	13,715	116,930	0.4
HIV/AIDS	1,011	10,673	0.1	998	22,685	0.1
Substance abuse disorders	87,977	792,810	10.4	42,932	881,074	2.8
Primary care visits in prior						
year						
0-2	119,055	2,487,888	32.7	196,845	17,355,110	55.8
3-9	223,859	3,739,020	49.2	317,381	11,687,211	37.6
$\geq 10$	199,270	1,369,628	18.0	199,230	2,035,670	6.5

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.SC = ambulatory care-sensitive . .IV = Human Immunodeficiency Virus; MI = . Abbreviations (in alphabetical order): ACSC = ambulatory care-sensitive condition; AIDS = Acquired Immunodeficiency Syndrome; CHF = congestive heart failure; HIV = Human Immunodeficiency Virus; MI = myocardial infarction.

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## Table 2. The risk of hospitalizations for ambulatory care-sensitive conditions associated with depression compared to

## individuals without depression

Outcome	<u>Model 1</u> Adjusted for demographics <sup>a</sup>	<u>Model 2</u> Adjusted for variables in Model 1 and socioeconomic factors <sup>b</sup>	<u>Model 3</u> Adjusted for variables in Model 2 and ACSC- predisposing comorbidity	Model 4 Adjusted for variables in Model 3 and non-ACSC- predisposing comorbidity <sup>h</sup> and substance abuse disorders	<u>Model 5</u> Adjusted for variables in Model 4 and PCP visits in the previous year
		<b>Incidence</b> Rate	e Ratio (95% Confid	ence Interval)	
Any ACSC	$2.35(2.32, 2.37)^{\dagger}$	$2.27 (2.25, 2.29)^{\dagger}$		$1.53 (1.51, 1.54)^{\dagger}$	$1.45(1.43, 1.46)^{\dagger}$
<b>Type of ACSC</b> <i>Chronic ACSCs</i> Angina COPD/Asthma exacerbation CHF exacerbation Diabetes-related HTN	$\begin{array}{c} 2.03 \ (1.99, \ 2.08)^{\dagger} \\ 3.17 \ (3.09, \ 3.24)^{\dagger} \\ 1.72 \ (1.67, \ 1.76)^{\dagger} \\ 2.88 \ (2.79, \ 2.98)^{\dagger} \\ 1.52 \ (1.48, \ 1.57)^{\dagger} \end{array}$	$\begin{array}{c} 2.00 \ (1.96, \ 2.05)^{\dagger} \\ 2.97 \ (2.90, \ 3.04)^{\dagger} \\ 1.67 \ (1.62, \ 1.71)^{\dagger} \\ 2.66 \ (2.57, \ 2.75)^{\dagger} \\ 1.48 \ (1.44, \ 1.53)^{\dagger} \end{array}$	$1.77 (1.73, 1.81)^{c^{\ddagger}}$ $1.88 (1.84, 1.93)^{d^{\ddagger}}$ $1.22 (1.19, 1.25)^{e^{\ddagger}}$ $1.83 (1.77, 1.89)^{f^{\ddagger}}$ $1.37 (1.33, 1.41)^{g^{\ddagger}}$	$\begin{array}{c} 1.52 \ (1.49,  1.56)^{\dagger} \\ 1.66 \ (1.62,  1.70)^{\dagger} \\ 1.09 \ (1.06,  1.12)^{\dagger} \\ 1.86 \ (1.80,  1.93)^{\dagger} \\ 1.30 \ (1.26,  1.34)^{\dagger} \end{array}$	$\begin{array}{l} 1.35 \left( 1.32,  1.38 \right)^{\dagger} \\ 1.61 \left( 1.57,  1.65 \right)^{\dagger} \\ 1.06 \left( 1.03,  1.09 \right)^{\dagger} \\ 1.69 \left( 1.63,  1.75 \right)^{\dagger} \\ 1.18 \left( 1.14,  1.21 \right)^{\dagger} \end{array}$
Acute ACSCs Appendicitis with perforation Pneumonia UTI	$1.31 (1.25, 1.37)^{\ddagger}$ $2.35 (2.33, 2.38)^{\ddagger}$ $2.38 (2.34, 2.42)^{\ddagger}$	$\begin{array}{c} 1.31 \ (1.25, \ 1.37)^{\ddagger} \\ 2.29 \ (2.27, \ 2.32)^{\ddagger} \\ 2.34 \ (2.31, \ 2.38)^{\ddagger} \end{array}$	. ( , ,	$1.26 (1.21, 1.33)^{\dagger}$ $1.55 (1.53, 1.56)^{\dagger}$ $1.74 (1.71, 1.77)^{\dagger}$	$1.21 (1.16, 1.27)^{\ddagger}$ $1.50 (1.48, 1.52)^{\ddagger}$ $1.63 (1.60, 1.66)^{\ddagger}$

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<u>Abbreviations (in alphabetical order)</u>: ACSC = ambulatory care-sensitive condition; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HTN = hypertension; PCP = primary care physician; UTI = urinary tract infection.

<sup>a</sup> Age, sex and calendar period.

<sup>b</sup> Educational level and marital status.

<sup>c</sup> Adjusted for myocardial infarction.

<sup>d</sup>Adjusted for chronic pulmonary disease.

<sup>e</sup> Adjusted for CHF.

<sup>f</sup>Adjusted for diabetes mellitus.

<sup>g</sup> Adjusted for myocardial infarction, CHF, cerebrovascular disease and peripheral vascular disease.

<sup>h</sup> Charlson Comorbidity Index diagnoses not previously adjusted for.

 $^{+}P < 0.001$ 

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# Table 3. The effect of age on the association of depression with risk of hospitalization for an

## ambulatory care-sensitive condition

Age categories	Adjusted for demographics	Adjusted for socioeconomic factors	Adjusted for comorbidities	Adjusted for PCP visits
	uemographies	<b>Incidence Rate Ratio</b>	comorbiunces	
		(95% Confidence Interval)		
$\leq$ 40 years old	2.88 (2.78, 3.00) <sup>‡</sup>	$2.83 (2.72, 2.93)^{\dagger}$	$2.34(2.25, 2.43)^{\dagger}$	$2.06(1.98, 2.13)^{\dagger}$
41 – 64 years old	2.93 (2.88, 2.98) <sup>‡</sup>	2.74 (2.69, 2.78)‡	1.94 (1.91, 1.97) <sup>‡</sup>	1.73 (1.70, 1.76) <sup>†</sup>
Age≥65 years old	$2.30(2.28, 2.32)^{\dagger}$	2.18 (2.15, 2.20) <sup>‡</sup>	1.34 (1.33, 1.36) <sup>‡</sup>	1.31 (1.30, 1.32) <sup>‡</sup>
	PCP = primary care	ohysician.		
<sup>+</sup> P < 0.001				

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in Model 2,

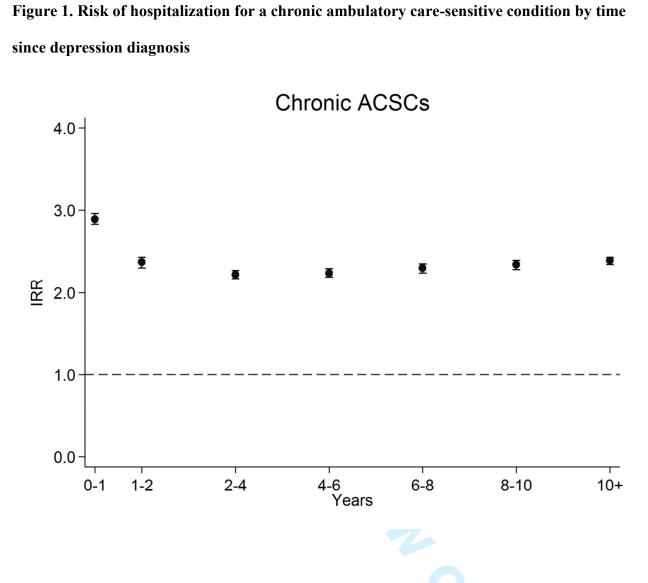
Table 4. The risk of rehospitalization within 30 days for the same or another ambulatory

care-sensitive	condition am	ong those with depre	ssion compared to inc	lividuals without
depression				
		Model 1	Model 2	<u>Model 3</u> Adjusted for variables

Model 1

Outcome	Adjusted for demographics	in Model 1 and socioeconomic factors	comorbidity and substance abuse disorders
		e Rate Ratio	
		dence Interval)	1
Same ACSC	1.36 (1.32, 1.39) <sup>‡</sup>	$1.34(1.31, 1.38)^{\dagger}$	$1.21 (1.18, 1.24)^{\dagger}$
Another ACSC	$1.44(1.39, 1.49)^{\dagger}$	$1.42 (1.37, 1.47)^{\dagger}$	1.19 (1.15, 1.23)‡
<u>Abbreviation</u> : $ACSC = a$	ambulatory care-sensitive	condition.	
<sup>+</sup> <i>P</i> < 0.001			

Adjusted for variables



<u>Abbreviations (in alphabetical order)</u>: ACSCs = ambulatory care-sensitive conditions; IRR =

incidence rate ratio.

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Figure 2. Risk of hospitalization for an acute ambulatory care-sensitive condition by time

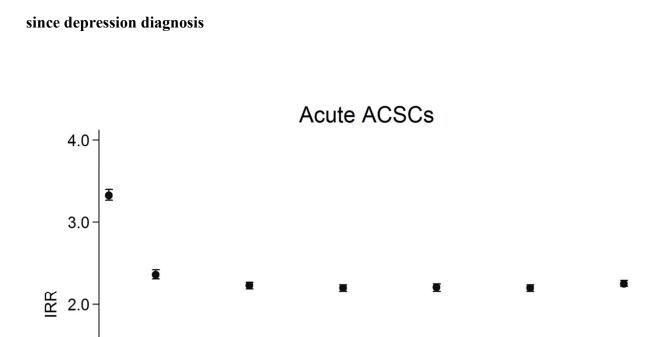
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<u>Abbreviations (in alphabetical order)</u>: ACSCs = ambulatory care-sensitive conditions; IRR = incidence rate ratio.

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Years

6-8

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10 +

2-4

### **Supplementary Online Material**

### <u>APPENDIX 1</u>: Information on depression obtained from the Danish Psychiatric Central Register and the Danish National Prescription Registry

### A diagnosis of depression was identified if at least one of the following criteria applied:

- 1. Registration of a diagnosis of depression in the Danish Psychiatric Central Register. And/or
- 2. Registration of at least one prescription of antidepressants redeemed in the Danish National Prescription Registry

#### Diagnosis according to a record of depression in the Danish Psychiatric Central Register:

296.09, 296.29, 296.99, 298.09,	F32, F33
300.49, and 300.19	

# Diagnosis according to a record of prescriptions for antidepressants in the Danish National Prescription Registry:

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Name	Drug	ATC-codes
SSRI (Selective serotonin re-uptake inhibitors)	Fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, and escitalopram	N06AB
MAOIs (Monoamine oxidase inhibitors)	Isocarboxazid and moclobemide	N06AF <i>,</i> N06AG
Other antidepressants	Mianserin, nefazodone, mirtazapine, venlafaxine, reboxetine, duloxetine, and agomelatine	N06AX

# <u>APPENDIX 2</u>: Information on severe mental illness obtained from the Danish Psychiatric Central Register.

	ICD-8	ICD-10
Schizophrenia	295 (excluding 295.79)	F20
Schizoaffective disorders	295.79, 296.8	F25

oolar affective disorders	296.19, 296.39	F30, F31

Hospitalizations for 12 of the conditions identified by the Agency for Healthcare Research and Quality as ACSCs in their report of prevention quality indicator			
Disease	Description in the AHRQ list	ICD-10	
Angina	<ul> <li>Angina Without Procedure Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for angina (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Discharges with a surgical procedure in any field (010-8699). Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS</li> <li>Denominator: Population in MSA or county, age 18 years and older.</li> </ul>	I20.0, I20.1, I20.8, I20.9, I24.0, I24.1, I24.8, I24.9 EXCLUSIONS: All surgical procedures (startin with a K in the Danish version of the NCSP, which means surgica	
COPD (Chronic obstructive pulmonary disorder) exacerbation	Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).	J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43.8, J43.9, J44.0-J44.9, J47.0-J47.9	

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	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	*qualify only if accompanied by secondary diagnosis of any of the other codes listed under COPD
	ICD-9-CM diagnosis codes: 4660 AC BRONCHITIS* 4920 EMPHYSEMATOUS BLEB 490 BRONCHITIS NOS* 4928 EMPHYSEMA NEC 4910 SIMPLE CHR BRONCHITIS 494 BRONCHIECTASIS -OCT00 4911 MUCOPURUL CHR BRONCHITIS 4940 BRONCHIECTAS W/O AC EXAC 49120 OBS CHR BRNC W/O ACT EXA OCT00- 49121 OBS CHR BRNC W ACT EXA 4941 BRONCHIECTASIS W AC EXAC 4918 CHRONIC BRONCHITIS NEC OCT00- 4919 CHRONIC BRONCHITIS NOS 496 CHR ADWAY ODSTRUCT NEC	
	AIRWAY OBSTRUCT NEC * Qualifies only if accompanied by secondary diagnosis of 491.xx, 492.x, or 496 (i.e., any other code on this list). Denominator: Population in MSA or county, age	
	18 years and older.	0.
CHF (Congestive heart failure) exacerbation	Congestive Heart Failure (CHF) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for CHF (see below).	I09.0-I09.9 I11.0, I13.0, I13.2, I13.9, I50.0, I50.1, I50.9, I46.9
	All discharges of age 18 years and older. <b>Exclude:</b> Discharges with cardiac procedure codes (see below) in any field. Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	<u>EXCLUSION:</u> Cardiac procedures: KFNG02, KFNG05, KFNA, KFNC, KFT, KFW, KFQ, BFCA01-BFCA07

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	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
Diabetes (with short-term complications)	Diabetes Short-term Complications AdmissionRateNumerator:Discharges with ICD-9-CM principal diagnosiscode for short-term complications (ketoacidosis,hyperosmolarity, coma) (see below).All discharges of age 18 years and older.	E10.0, E10.1, E11.0, E11.1,
	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	
	ICD-9-CM diagnosis codes: 25010 DM KETO T2, DM CONT 25022 DM W/ HYPROSM T2, DM UNCNT 25011 DM KETO T1, DM CONT 25023 DM W/ HYPROSM T1, DM UNCNT 25012 DM KETO T2, DM UNCONT 25030 DM COMA NEC T2, DM CONT 25013 DM KETO T1, DM UNCONT 25031 DM COMA NEC T1, DM CONT 25020 DM W/ HYPROSM T2, DM CONT 25032 DM COMA NEC T2, DM UNCONT 25021 DM W/ HYPROSM T1, DM CONT 25033 DM COMA NEC T1, DM UNCONT	
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
Diabetes (uncontrolled (without short- term or long-term complications))	Uncontrolled Diabetes Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for uncontrolled diabetes, without mention of a short-term or long-term complication (see below).	E10.9, E11.9

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	All discharges of age 18 years and older.
	Exclude:
	Transfers <sup>1</sup> .
	MDC 14 (pregnancy, childbirth, and puerperium) $^{2}$
	ICD-9-CM diagnosis codes:
	25002 DM, T2, UNCONT
	25003 DM, T1, UNCONT
	<b>Denominator:</b> Population in MSA or county, age
	18 years and older. May be combined with diabetes short-term
	complications as a single indicator.
Diabetes (with long-term	Diabetes Long-term Complications Admission E10.2-E10.8, E11.2-E11.8
omplications)	Rate
	Numerator:
	Discharges with ICD-9-CM principal diagnosis code for long-term complications (renal, eye,
	neurological, circulatory, or complications not
	All discharges of age 18 years and older.
	Exclude:
	Transfers <sup>1</sup> .
	MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>
	otherwise specified) (see below). All discharges of age 18 years and older. <b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>
	ICD-9-Civi diagnosis coues.
	25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT
	25041 DM RENAL COMP T1 CONT 25071 DM
	CIRCU DIS T1 CONT
	25042 DM RENAL COMP T2 UNCNT 25072 DM
	CIRCU DIS T2 UNCNT
	25043 DM RENAL COMP T1 UNCNT 25073 DM

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HTN (Hypertension)	COMP NEC T1 UNCNT 25060 DM NEURO COMP T2 CONT 25090 DM W COMPL NOS T2 CONT 25061 DM NEURO COMP T1 CONT 25091 DM W COMPL NOS T1 CONT 25062 DM NEURO COMP T2 UNCNT 25092 DM W COMPL NOS T2 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT Denominator: Population in MSA or county, age 18 years and older. Hypertension Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for hypertension (see below). All discharges of age 18 years and older.	110.0-110.9, 111.9, 112.9, 113.9 <u>EXCLUSION:</u> Cardiac procedures: KFNG02, KFNG05, KFNA, KFNC, KFT, KFW, KFQ, DECAME DECAME
	<ul> <li>Exclude: Discharges with cardiac procedure codes (see below) in any field. Transfers<sup>1</sup>. MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 4010 MALIGNANT HYPERTENSION 40310 BENIGN HYP HRT DIS W/OUT RF 4019 HYPERTENSION NOS 40390 HYPERTEN</li> </ul>	BFCA01-BFCA07

	Discharges with ICD-9-CM diagnosis code for perforations or abscesses of appendix (see below)	
Perforated appendicitis	Perforated Appendix Admission Rate Numerator:	K35.0, K35.1, K35.2, K35.3
	To years and older.	
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
	REVIS OR RELOCATE POCKET	
	3617 ABD-CORON ART BYPASS OCT96- 3779	
	INSER TEMP PACEMAKER SYS	
	REMOVAL OF LEAD W/O REPL 3616 2 INT MAM-COR ART BYPASS 3778	
	3615 1 INT MAM-COR ART BYPASS 3777	
	REPL TV ATRI-VENT LEAD	
	3614 AORTCOR BYPAS-4+ COR ART 3776	
	REVISION OF LEAD	
	2612 AODTOCOD BVDAS 2 COD ADT 2775	
	OR REPL LEAD EPICAR	
	3612 AORTOCOR BYPAS-2 COR ART 3774 INT	
	INSER LEAD IN ATRIUM	
	INT INSER LEAD ATRI-VENT 3611 AORTOCOR BYPAS-1 COR ART 3773 INT	
	3610 AORTOCORONARY BYPASS NOS 3772	
	3771 INT INSERT LEAD IN VENT	
	3606 INSERT CORONARY ART STENT OCT95-	
	INSERT PACEMAK LEAD	
	3605 PTCA-MULTIPLE VESSEL 3770 INT	
	TRANSPLANTATION	
	3602 PTCA-1 VESSEL WITH AGNT 375 HEART	
	REVAS BYPS ANAS NEC	
	3601 PTCA-1 VESSEL W/O AGENT 3619 HRT	
	Exclude ICD-9-CM procedure codes:	
	40490 MAL HYPERT HRT DIS W/OUT CHF/KF	
	40290 HYPERTENSIVE HRT DIS W/OUT CHF/ 40490 HYPER HRT/REN NOS W/OUT CHF/RF	
	40410 BEN HYPER HRT/REN W/OUT CHF/RF 40290 HYPERTENSIVE HRT DIS W/OUT CHF	
	40210 BEN HYPERTEN HRT DIS W/OUT CHF	
	40400 MAL HYPER HRT/REN W/OUT CHF/RF	

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	in any field.	
	All discharges of age 18 years and older.	
	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	
	<b>ICD-9-CM diagnosis codes (outcome of interest):</b> 5400 AC APPEND W PERITONITIS 5401 ABSCESS OF APPENDIX	
	<b>ICD-9-CM diagnosis codes (population at risk):</b> 5400 AC APPEND W PERITONITIS 5409 ACUTE APPENDICITIS NOS 5401 ABSCESS OF APPENDIX 541 APPENDICITIS NOS	
	<b>Denominator:</b> Number of discharges with diagnosis code for appendicitis in any field in MSA or county.	
Pneumonia	<ul> <li>Bacterial Pneumonia Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for bacterial pneumonia (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Discharges with diagnosis code for sickle cell anemia or HB-S disease (see below) in any field. Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> </ul>	J13-J14.9, J15.3-J15.4, J15.7-J15.9, J16.0-J16.9, J18.0-J18.9 EXCLUSION: Sickle cell disorders D57.0-D57.9
	ICD-9-CM diagnosis codes: 481 PNEUMOCOCCAL PNEUMONIA 48230 STREP PNEUMONIA UNSPEC	

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	4822 H.INFLUENZAE PNEUMONIA 48231 GRP A STREP PNEUMONIA 4829 BACTERIAL PNEUMONIA NOS 48232 GRP B STREP PNEUMONIA 4830 MYCOPLASMA PNEUMONIA 48239 OTH STREP PNEUMONIA 4831 CHLAMYDIA PNEUMONIA OCT96- 485 BRONCOPNEUMONIA ORG NOS 4838 OTH SPEC ORG PNEUMONIA 486 PNEUMONIA, ORGANISM NOS <b>Exclude ICD-9-CM diagnosis codes:</b> 28260 SICKLE-CELL ANEMIA NOS 28263 SICKLE-CELL/HB-C DISEASE 28261 HB-S DISEASE W/O CRISIS 28269 SICKLE-CELL ANEMIA NEC 28262 HB-S DISEASE WITH CRISIS	
UTIs (urinary tract infections)	Urinary Tract Infection Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code of urinary tract infection (see below). Exclude:	N10.0-N12.9, N15.1-15.9, N30.0- N30.9, N34.0-N34.9, N39.0
	Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:	1
	59000 CHR PYELONEPHRITIS NOS 59080 PYELONEPHRITIS NOS 59001 CHR PYELONEPH W MED NECR 59081 PYELONEPHRIT IN OTH DIS 59010 AC PYELONEPHRITIS NOS 5909	0
	INFECTION OF KIDNEY NOS 59011 AC PYELONEPHR W MED NECR 5950 AC CYSTITIS 5902 RENAL/PERIRENAL ABSCESS 5959 CYSTITIS NOS 5903 PYELOURETERITIS CYSTICA 5990 URIN TRACT INFECTION NOS	

	<b>Denominator:</b> Population in MSA or county.	
Adult Asthma exacerbation	Adult Asthma Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code of asthma (see below).All discharges of age 18 years and older.Exclude: Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 49300 EXT ASTHMA W/O STAT ASTH 49320 CH OB ASTH W/O STAT ASTH 49301 EXT ASTHMA W STATUS ASTH 49321 CH OB ASTHMA W STATUS ASTH 49321 CH OB ASTHMA W STATUS ACEX OCT00- 49322 CH OB ASTHMA W STAT ASTH 49301 INT ASTHMA W/O STAT ASTH 0CT00- 49311 INT ASTHMA W STATUS ASTH 49390 ASTHMA W/O STAT ASTHM 49312 INT ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ACEX OCT00- 49392 ASTHMA W STATUS ACEX OCT00- 49393 ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ACEX OCT00- 49393 ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ACEX OCT00-Denominator: Population in MSA or county, age 18 years and older.	J45, J46
Amputations (diabetes-related)	Rate of Lower-extremity Amputation among Patients with Diabetes Numerator: Discharges with ICD-9-CM procedure code for lower-extremity amputation (see below) in any field and diagnosis code of diabetes in any field (see below).All discharges of age 18 years and older.	Z89.4-Z89.7 *qualify only if registered with diabetes in the Danish National Diabetes Register or if registered with a diagnosis of diabetes (ICD-10:E10- 14, H36.0, O24, excluding O24.4) at the same admission as the ACSC

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Exclude:
Trauma (see below).
Transfers <sup>1</sup> .
MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>EXCLUSION:</b>
Traumatic amputations of lower
limb
ICD-9-CM procedure codes:
8410 LOWER LIMB AMPUTAT NOS 8415
BELOW KNEE AMPUTAT NEC S78.0-S78.9, S88.0-S88.9, S98.0-
8411 TOE AMPUTATION 8416 \$98.4, T05.3-T05.5
DISARTICULATION OF KNEE
8412 AMPUTATION THROUGH FOOT 8417
ABOVE KNEE AMPUTATION
8413 DISARTICULATION OF ANKLE 8418
DISARTICULATION OF HIP
8414 AMPUTAT THROUGH MALLEOLI 8419
HINDQUARTER AMPUTATION
ICD-9-CM diagnosis codes for diabetes:
25000 DMII WO CMP NT ST UNCNTR 25050
DMII OPHTH NT ST UNCNTRL
25001 DMI WO CMP NT ST UNCNTRL 25051
DMI OPHTH NT ST UNCNTRLD
25002 DMII WO CMP UNCNTRLD 25052 DMII
25001 DMI WO CMP NT ST UNCNTRL 25051 DMI OPHTH NT ST UNCNTRLD 25002 DMII WO CMP UNCNTRLD 25052 DMII OPHTH UNCNTRLD 25003 DMI WO CMP UNCNTRLD 25053 DMI OPHTH UNCNTRLD 25010 DMII KETO NT ST UNCNTRLD 25060 DMII NEURO NT ST UNCNTRLD 25011 DMI KETO NT ST UNCNTRLD 25061 DMI NEURO NT ST UNCNTRLD 25012 DMII KETOACD UNCONTROLD 25062 DMU NEURO UNCNTRLD
25003 DMI WO CMP UNCNTRLD 25053 DMI
OPHTH UNCNTRLD
25010 DMII KETO NT ST UNCNTRLD 25060
DMII NEURO NT ST UNCNTRL
25011 DMI KETO NT ST UNCNTRLD 25061
DMI NEURO NT ST UNCNTRLD
25012 DMII KETOACD UNCONTROLD 25062
DIMIT NEURO UNCNTRED
25013 DMI KETOACD UNCONTROLD 25063
DMI NEURO UNCNTRLD
25020 DMII HPRSM NT ST UNCNTRL 25070
DMII CIRC NT ST UNCNTRLD
25021 DMI HPRSM NT ST UNCNTRLD 25071
DMI CIRC NT ST UNCNTRLD

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25022 DMILLINDOGMED LINCONTROLD 25072	
25022 DMII HPROSMLR UNCONTROLD 25072	
DMII CIRC UNCNTRLD	
25023 DMI HPROSMLR UNCONTROLD 25073	
DMI CIRC UNCNTRLD	
25030 DMII O CM NT ST UNCNTRLD 25080	
DMII OTH NT ST UNCNTRLD	
25031 DMI O CM NT ST UNCNTRL 25081 DMI	
OTH NT ST UNCNTRLD	
25032 DMII OTH COMA UNCONTROLD 25082	
DMII OTH UNCNTRLD	
25033 DMI OTH COMA UNCONTROLD 25083	
DMI OTH UNCNTRLD	
25040 DMII RENL NT ST UNCNTRLD 25090	
DMII UNSPF NT ST UNCNTRL	
25041 DMI RENL NT ST UNCNTRLD 25091	
DMI UNSPF NT ST UNCNTRLD	
25042 DMII RENAL UNCNTRLD 25092 DMII	
UNSPF UNCNTRLD	
25043 DMI RENAL UNCNTRLD 25093 DMI	
UNSPF UNCNTRLD	
UNSIT UNENTIKED	
Exclude: Trauma	
ICD-9-CM diagnosis codes:	
8950 AMPUTATION TOE 8971 AMPUTAT BK,	
UNILAT-COMPL	
8951 AMPUTATION TOE-COMPLICAT 8972	
AMPUT ABOVE KNEE, UNILAT	
8960 AMPUTATION FOOT, UNILAT 8973	
AMPUT ABV KN, UNIL-COMPL	
8961 AMPUT FOOT, UNILAT-COMPL 8974	
AMPUTAT LEG, UNILAT NOS	071
8962 AMPUTATION FOOT, BILAT 8975	
AMPUT LEG, UNIL NOS-COMP	
8963 AMPUTAT FOOT, BILAT-COMP 8976	
AMPUTATION LEG, BILAT	
8970 AMPUT BELOW KNEE, UNILAT 8977	
AMPUTAT LEG, BILAT-COMPL	
<b>Denominator:</b> Population in MSA or county, age	
18 years and older.	

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	dmissions was performed if any ric diagnostic codes included: (		the diagnoses were present as t	secondary diagnosis at the s		
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1	<b>Appendix 4: Inform</b>	nation on socioec	conomic position (S	<b>EP) obtained from</b>	n	
	Statistics Denmark	, 				
1	Education level					
<	< 10 years					
	10-15 years					
	>15 years					
	Civil status					
	Living alone/single					
	Cohabitation					
	Partners					
1	Married					

ACSC Outcome	ACSC-predisposing medical comorbidity
Chronic conditions	
Angina	Myocardial infarction <sup>1</sup>
CHF exacerbation	CHF <sup>1</sup>
HTN	Myocardial infarction <sup>1</sup> CHF <sup>1</sup>
	Cerebrovascular disease <sup>1</sup> Peripheral vascular disease <sup>1</sup>
Diabetes-related ACSCs	Diabetes <sup>2</sup>
COPD exacerbation	Chronic pulmonary disease <sup>1</sup>
	or
	Redemption of at least 2 prescriptions of drugs for obstructive airway diseases within 6 months <sup>3</sup>
Adult asthma exacerbation	Chronic pulmonary disease <sup>1</sup>
	or
	Redemption of at least 2 prescriptions of drugs for obstructive airway diseases within 6 months <sup>3</sup>
Acute conditions	
Perforated appendicitis	-
Pneumonia	

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<sup>1</sup> Obtained from the Danish National Patient Register using the algorithm defined in the Charlson Comorbidity
Index (see appendix 6).
<sup>2</sup> Obtained from the Danish National Diabetes Register (see appendix 7)
<sup>3</sup> Obtained from the Danish National Prescriptions Registry (see appendix 8).

Appendix 6: Information on cl obtained from the Danish Nati	ronic diseases included in the C onal Patient Register	Charlson Comorbidity Index
	ICD-8	ICD-10
Myocardial infarction	410	121;122;123
Congestive heart failure	427.09, 427.10, 427.11,	150; 111.0; 113.0; 113.2
-	427.19, 428.99, 782.49	
Peripheral vascular disease	440, 441, 442, 443, 444,	170; 171; 172; 173; 174; 177
-	445,	
Cerebrovascular disease	430-438	I60-I69; G45; G46
Dementia	290.09-290.19, 293.09	F00-F03; F05.1; G30
Chronic pulmonary disease	490-493, 515-518	J40-J47; J60-J67; J68.4; J70.1;
		J70.3; J84.1; J92.0; J96.1; J98.2;
		J98.3
Connective tissue disease	712, 716, 734, 446, 135.99	M05; M06; M08; M09;M30;M31
	,,,,,,,	M32; M33; M34; M35; M36; D8
Ulcer disease	530.91, 530.98, 531-534,	K22.1; K25-K28
Mild liver disease	571, 573.01, 573.04	B18; K70.0-K70.3; K70.9; K71;
	, ,	K73; K74; K76.0
Diabetes mellitus	249.00, 249.06, 249.07,	E10.0, E10.1; E10.9; E11.0;
	249.09, 250.00, 250.06,	E11.1; E11.9

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	250.07, 250.09	
Hemiplegia	344	G81; G82
Moderate/severe renal	403,404,580-583, 584,	I12; I13; N00-N05; N07; N11;
Disease	590.09, 593.19, 753.10- 753.19, 792	N14; N17-N19; Q61
Diabetes mellitus with	249.01-249.05, 249.08,	E10.2-E10.8; E11.2-E11.8
chronic complications	250.01-250.05, 250.08	
Any tumour	140-194	C00-C75
Leukaemia	204-207	C91-C95
Lymphoma	200-203, 275.59	C81-C85; C88; C90; C96
Moderate/severe liver	070.00, 070.02, 070.04,	B15.0; B16.0; B16.2; B19.0;
Disease	070.06, 070.08, 573.00, 456.00-456.09	K70.4; K72; K76.6; I85
Metastatic solid tumour	195-198, 199	C76-C80
AIDS	079.83	B21-B24
		QL:

pendix 7: Information on diabetes obtained from the Danish National Diabetes Register.
gorithm: Individuals were classified as having diabetes on the day where at least one of the
lowing six criteria was met:
A diagnosis of diabetes made at any Danish hospital as registered in the Danish National Patient
Register (ICD-8:249, 250; ICD-10:E10-14, H36.0, O24, excluding O24.4).
A referral to chiropody of diabetic patients as registered in the Danish National Health Service
Register.(Andersen <i>et al.</i> 2011)
Five blood glucose measurements within one year as registered in the Danish National Health
Service Register.
Two blood glucose measurements per year for five consecutive years as registered in the Danish
National Health Service Register.
Two redemptions of oral anti-diabetic drugs within six months as registered in the Danish National
Prescription Registry.
Two redemptions of prescribed insulin as registered in the Danish National Prescription Registry.

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Appendix 8: ATC codes for drugs for obstructive airway disease obtained from the Danish National Prescription Registry.		
ATC codes	Type of drug	
R03	Drugs for obstructive airway diseases	
R03A	Adrenergics, inhalants	
R03B	Other drugs for obstructive airway diseases, inhalants	
R03C	Adrenergics for systemic use	
R03D	Other systemic drugs for obstructive airway diseases	

Appendix 9: Information on substance abuse disorders obtained from the Danish National
Patient Register and the Danish Psychiatric Central Register.

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ICD-10
F11.0–F11.9
F12.0–F12.9
F13.0-F13.9
F14.0-F14.9
F15.0–15.9
F16.0-F16.9
F18.0-F19.9
F10.0-F10.9
K70.0-K70.9
185.0–185.9

# The risk of ACSCs and rehospitalizations for ACSCs among persons with depression

		Considerations	
Study population:	<ul> <li>Depression study</li> <li>All persons born in Denmark, alive and minimum 18 years of age and still living in Denmark at some time between January 1, 1999 and December 31, 2013.</li> <li>Sub-analysis: Stratified by age categories: ≤ 40, 41-65, ≥ 65 (i.e., adult, middle-aged, older adults)</li> </ul>	000, 00, 0	
Follow-up:	January 1, 2005-December 31,2013	This enables us to make sure who has a mental disorder between 1995 and 2005	N O
Censor-in	18 years of birthday or study start, whichever comes last.	We do not want to include children. And also, this definition is a part of the AHRQ list. No age maximum.	
Censor-out	Emigration, death, SMI diagnosis or study end whichever comes first.	We will censor out persons with SMI!	
Dropping individuals	Out-censored before in- censored (children and young persons dying before their 18th years birthday, or emigration, SMI diagnosis or death before study start).		

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Exposure			
	Depression	Time-dependent variable (see Appendix 1):	
		• <u>All cases</u> of depression between 1969	
		and 2013 (diagnoses-in and outpatient	
		contacts) and between 1995 and 2013	
		(prescriptions). Remember that depression	
		identified by redemptions need at least 2	
		prescriptions within 6 months.	
		<u>Sub-analysis</u>	
		Risk of ACSC-related hospitalizations by	
		depression diagnosis-type (i.e., our rough	
		proxy for depression severity):	
		1) Psychiatric hospitalization for	
		depression	
		2) Outpatient depression diagnosis	
		only	
		3) Antidepressant prescriptions only	
	Dual diagnosis	If a person has a primary care determined	
		depression it is overruled by a diagnosis	
		from the registers (the secondary health	
		care).	
Outcome			
	1. The number of hospitalizations	1) <u>The algorithm</u> :	
	for ACSCs (Ambulatory care	We have modified this outcome measure	
	sensitive conditions) during follow-	because it is classified according to ICD-9	
	up	(and diagnoses in Denmark are according to	
	= hospitalization rates for the	ICD-8 before 1994 and ICD-10 since 1995).	071
	following categories:		
		We have used a <u>validated algorithm</u> from a	
	Using codes from the Danish ACSC	Danish 'translated versions' in a Danish	
	validation paper(Schiotz et al.	article (Schiotz et al. 2011). However, as this	
	<u>2011)</u> :	version does not include all of the categories	
	-Angina	of ACSCs from the AHRQ list, we have	
	-COPD exacerbation	additionally included for all practical	
	-Congestive heart failure	purposes, the rest of the categories	
	exacerbation	(pneumonia, amputations, urinary tract	
	-Diabetes-short term compl.	infections, and asthma)	
	-Diabetes long-term compl.	(and a translation of the codes from ICD-9 to	
	-Diabetes- uncontrolled	10 have been conducted with inspiration	

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-Hypertension -Appendicitis	from algorithms from previous Danish papers).	
Using codes with inspiration from Danish register-based studies (or own algorithms):         -Bacterial Pneumonia(Nielsen et al 2012)         -Lower extremities amputations (Jorgensen et al. 2014)         -Urinary tract infections         -Adult asthma exacerbation (Andersen et al. 2013)         combine COPD exacerbation and adult asthma exacerbation into a single category for analyses         2. The number of rehospitalization within 30 days after the index ACS hospitalization for the same ACSC or for a different ACSC	<ol> <li><u>Inpatient contacts only:</u> Per definition ACSCs includes ONLY inpatient.</li> <li><u>Principal discharge diagnosis</u> (see Danish article or Davydow 2013)</li> <li><u>Appendicitis with perforation</u></li> <li><u>Epidemiological considerations</u> One of the major epidemiological considerations for this study is the fact that</li> </ol>	

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		<ul> <li>of angina cases who has had ANY surgical procedures (NCSP surgical codes) at the SAME admission.</li> <li>Specific exclusions concerning diabetic amputations and concerning pneumonia</li> </ul>
Covariates		
Demographic	Age, gender, calendar period.	We are adjusting for age as a time- dependent variable divided into 2 years age- bands. We are adjusting for calendar period as a time-dependent variable divided into 1 year- time-bands.
Socio- economic position (SEP)	Depression paper Marital status (married, registered partners, cohabitant or single). Income (OECD-adjusted household income) Educational level	
Comorbidity		
Medical comorbidity (See Appendices 6- 8)	Diagnoses included in the Charlson Comorbidity index except for diabetes, which will come from the Diabetes Register, COPD/asthma exacerbations which will come from the combination of the CCI chronic pulmonary disease category and prescriptions.	Time-dependent We will identify hospital contacts for the chronic somatic diseases included in the CCI. Each diagnosis will be entered into the models as a time-dependent covariate. From 1995 onwards, outpatient contacts are also included. Adjusting for each category of disease from the CCI (instead of using an index).

	Substance abuse	See appendix 10	
Health care utilization	Primary care visits         (Face-to-Face-contacts=0101 contacts)         In the analyses, we will categorize according to the interquartile range of PCP visits in the cohort         We will count PCP visits from 10-225 days before any sizes days	<ul> <li># of GP visits during the follow-up period for each individual</li> <li>Time-dependent</li> <li>This could be confounded by indication, but reduced contacts to GP and hospitals could also be an intermediate variable between mental illness and ACSC.</li> </ul>	
Statistical Analyses	375 days before any given day.	20	
	Poisson regression with variance adjusted for clustering. <u>Outcome measures</u> : -number of hospitalizations per person years (rate measure). -rate ratios, RR	<ul> <li>I. The outcome will be the number of these events since we will be using Poisson regression models. The outcome measure is rate ratio which approximates the relative risks.</li> <li>-We make the analysis for any ACSC and subsequently the analyses for each category , dividing into "chronic" ACSCs and "acute" ACSCs.</li> <li><u>a) Sub-analyses for the time since analyses</u></li> <li><u>b) Analyses with adjustments</u></li> <li><u>For depression study</u></li> <li>Adjustment: Models 1-5: 1) age, gender and calendar period, 2)SEP, 3) ACSC-predisposing comorbidity for chronic ACSCs, 4) non-ACSC-predisposing comorbidity and substance abuse, 5) GP contacts</li> <li>a) Sub-analysis: Stratified by age categories: ≤ 40, 41-65, ≥ 65 (i.e., adult, middle-aged, older adults),</li> </ul>	

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		<ul> <li>adjusted in sequence of Models 1- 5</li> <li>b) Sensitivity analysis: depression diagnosis type analysis (hospitalization for depression vs. outpatient depression vs. prescription alone), adjusted in sequence of Models 1-5</li> <li>c) Time since depression diagnosis (adjusted for age, sex and calendar period)</li> <li>II. 30-day rehospitalizations for the same or another ACSC adjusted for demographics, then SES and comorbidity</li> </ul>
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Regarding transfers		
	Second a	dmission
First admission	ACSC	Non-ACSC
ACSC	Count the second ASCS*	Count the ACSC-admission
Non-ACSC	Count the ACSC-admission	Count as 0

\*This means that if the ACSC diagnoses are two different that it will be the second admission that counts.

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# Appendices

# **EXPOSURES (Appendices 1-3)**

# <u>APPENDIX 1</u>: Information on depression obtained from the Danish Psychiatric Central Register and the Danish National Prescription Registry

A diagnosis of depression was identified if at least one of the following criteria applied:

- 1. Registration of a diagnosis of depression in the Danish Psychiatric Central Register. And/or
- 2. Registration of at least one prescription of antidepressants redeemed in the Danish National Prescription Registry

Diagnosis according to a record of depression in the Danish Psychiatric Central Register:

ICD-8	ICD-10
296.09, 296.29, 296.99, 298.09,	F32, F33
300.49, and 300.19	

Diagnosis according to a record of prescriptions for antidepressants in the Danish National Prescription Registry:

Name	Drug	ATC-codes
SSRI (Selective serotonin re-uptake inhibitors)	Fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, and escitalopram	N06AB
MAOIs (Monoamine oxidase inhibitors)	Isocarboxazid and moclobemide	N06AF,

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		N06AG
Other antidepressants	Mianserin, nefazodone, mirtazapine,	N06AX
	venlafaxine, reboxetine, duloxetine,	
	and agomelatine	

### APPENDIX 2: Information on severe mental illness obtained from the Danish Psychiatric Central Register.

	ICD-8	ICD-10
Schizophrenia	295 (excluding 295.79)	F20
Schizoaffective disorders	295.79, 296.8	F25
Bipolar affective disorders	296.19, 296.39	F30, F31
Outcome		

### Outcome

	Categories	
Any ACSC	Any of the categories	
Type of ACSC		
Angina		
COPD/adult asthma		
exacerbation		
CHF exacerbation		
Diabetes-related ACSC	The 3 diabetes categories + amputations	
HTN		
Perforated appendicitis		
Pneumonia		
UTI		

Appendix 4: Information on Ambulatory Care Sensitive Conditions (ACSCs) obtained from the Danish National Patient

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Disease	Description in the AHRQ list	ICD-10
Angina	<ul> <li>Angina Without Procedure Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for angina (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Discharges with a surgical procedure in any field (010-8699). Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS</li> <li>Denominator: Population in MSA or county, age 18 years and older.</li> </ul>	I20.0, I20.1, I20.8, I20.9, I24.0, I24.1, I24.8, I24.9 EXCLUSIONS: All surgical procedures (starting with a K in the Danish version of the NCSP, which means surgical
COPD (Chronic obstructive pulm disorder) exacerbation	IonaryChronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).All discharges of age 18 years and older.Exclude:	J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43.8, J43.9, J44.0-J44.9, J47.0-J47.9 *qualify only if accompanied by

	Transfers <sup>1</sup> .	secondary diagnosis of any of the
	MDC 14 (pregnancy, childbirth, and puerperium) $^2$	other codes listed under COPD
	ICD-9-CM diagnosis codes:	
	4660 AC BRONCHITIS* 4920	
	EMPHYSEMATOUS BLEB	
	490 BRONCHITIS NOS* 4928 EMPHYSEMA	
	NEC	
	4910 SIMPLE CHR BRONCHITIS 494	
	BRONCHIECTASIS -OCT00	
	4911 MUCOPURUL CHR BRONCHITIS 4940	
	BRONCHIECTAS W/O AC EXAC	
	49120 OBS CHR BRNC W/O ACT EXA OCT00-	
	49121 OBS CHR BRNC W ACT EXA 4941 BRONCHIECTASIS W AC EXAC	
	4918 CHRONIC BRONCHITIS NEC OCT00-	
	4919 CHRONIC BRONCHITIS NOS 496 CHR	
	AIRWAY OBSTRUCT NEC	
	* Qualifies only if accompanied by secondary	
	diagnosis of 491.xx, 492.x, or 496 (i.e., any other	
	code	
	on this list).	
	<b>Denominator:</b> Population in MSA or county, age	
	18 years and older.	
CHF (Congestive heart failure)	Congestive Heart Failure (CHF) Admission Rate	109.0-109.9
exacerbation	<b>Numerator:</b> Discharges with ICD-9-CM principal diagnosis	111.0, 113.0, 113.2, 113.9, 150.0,
	code for CHF (see below).	150.1, 150.9, 146.9
	code for CHF (see below).	
	All discharges of age 18 years and older.	
	The discharges of age to years and order.	EXCLUSION:
	Exclude:	Cardiac procedures:
	Discharges with cardiac procedure codes (see	KFNG02, KFNG05, KFNA,
	below) in any field.	KFNC, KFT, KFW, KFQ,
	Transfers <sup>1</sup> .	BFCA01-BFCA07
	MDC 14 (pregnancy, childbirth, and puerperium) $^2$	

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ICD-9-CM diagnosis codes:	
39891 RHEUMATIC HEART FAILURE 40413	
BEN HYP HRT/REN W CHF&RF	
40201 MAL HYPERT HRT DIS W CHF 40491	
HYPER HRT/REN NOS W CHF	
40211 BENIGN HYP HRT DIS W CHF 40493	
HYP HT/REN NOS W CHF&RF	
40291 HYPERTEN HEART DIS W CHF 4280	
CONGESTIVE HEART FAILURE	
40401 MAL HYPER HRT/REN W CHF 4281	
LEFT HEART FAILURE	
40403 MAL HYP HRT/REN W CHF&RF 4289	
HEART FAILURE NOS	
40411 BEN HYPER HRT/REN W CHF	
Exclude ICD-9-CM procedure codes:	
3601 PTCA-1 VESSEL W/O AGENT 3619 HRT	
REVAS BYPS ANAS NEC	
3602 PTCA-1 VESSEL WITH AGNT 375 HEART	
TRANSPLANTATION	
3605 PTCA-MULTIPLE VESSEL 3770 INT	
INSERT PACEMAK LEAD	
3606 INSERT CORONARY ART STENT OCT95-	
3771 INT INSERT LEAD IN VENT	
3610 AORTOCORONARY BYPASS NOS 3772	
INT INSER LEAD ATRI-VENT	
3611 AORTOCOR BYPAS-1 COR ART 3773 INT	
INSER LEAD IN ATRIUM	
3612 AORTOCOR BYPAS-2 COR ART 3774 INT	
OR REPL LEAD EPICAR	
3613 AORTOCOR BYPAS-3 COR ART 3775	
REVISION OF LEAD	
3614 AORTCOR BYPAS-4+ COR ART 3776	
REPL TV ATRI-VENT LEAD	
3615 1 INT MAM-COR ART BYPASS 3777	
REMOVAL OF LEAD W/O REPL	
3616 2 INT MAM-COR ART BYPASS 3778	
INSER TEMP PACEMAKER SYS	
3617 ABD-CORON ART BYPASS OCT96- 3779	
REVIS OR RELOCATE POCKET	

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	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
Diabetes (with short-term complications)	Diabetes Short-term Complications Admission         Rate         Numerator:         Discharges with ICD-9-CM principal diagnosis         code for short-term complications (ketoacidosis,         hyperosmolarity, coma) (see below).         All discharges of age 18 years and older.         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	E10.0, E10.1, E11.0, E11.1,
	ICD-9-CM diagnosis codes: 25010 DM KETO T2, DM CONT 25022 DM W/ HYPROSM T2, DM UNCNT 25011 DM KETO T1, DM CONT 25023 DM W/ HYPROSM T1, DM UNCNT 25012 DM KETO T2, DM UNCONT 25030 DM COMA NEC T2, DM CONT 25013 DM KETO T1, DM UNCONT 25031 DM COMA NEC T1, DM CONT 25020 DM W/ HYPROSM T2, DM CONT 25032 DM COMA NEC T2, DM UNCONT 25021 DM W/ HYPROSM T1, DM CONT 25033 DM COMA NEC T1, DM UNCONT	1 0 1 1
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
Diabetes (uncontrolled (without short- term or long-term complications))	Uncontrolled Diabetes Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for uncontrolled diabetes, without mention of a short-term or long-term complication (see below).	E10.9, E11.9

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	All discharges of age 18 years and older.	
	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	
	ICD-9-CM diagnosis codes: 25002 DM, T2, UNCONT 25003 DM, T1, UNCONT	
	<b>Denominator:</b> Population in MSA or county, age 18 years and older. May be combined with diabetes short-term complications as a single indicator.	
Diabetes (with long-term complications)	Diabetes Long-term Complications Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below). All discharges of age 18 years and older. Exclude: Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	E10.2-E10.8, E11.2-E11.8
	ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT 25041 DM RENAL COMP T1 CONT 25071 DM CIRCU DIS T1 CONT 25042 DM RENAL COMP T2 UNCNT 25072 DM CIRCU DIS T2 UNCNT 25043 DM RENAL COMP T1 UNCNT 25073 DM CIRCU DIS T1 UNCNT	

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N (Hypertension)	I10.0-I10.9, I11.9, I12.9, I13.9 EXCLUSION: Cardiac procedures: KFNG02, KFNG05, KFNA, KFNC, KFT, KFW, KFQ, BFCA01-BFCA07
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Perforated appendicitis	Perforated Appendix Admission Rate Numerator: Discharges with ICD-9-CM diagnosis code for perforations or abscesses of appendix (see below) in any field.	K35.0, K35.1, K35.2, K35.3
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
		07/2
	REVIS OR RELOCATE POCKET	
	INSER TEMP PACEMAKER SYS 3617 ABD-CORON ART BYPASS OCT96- 3779	
	3616 2 INT MAM-COR ART BYPASS 3778	
	REMOVAL OF LEAD W/O REPL	
	3615 1 INT MAM-COR ART BYPASS 3777	
	REPL TV ATRI-VENT LEAD	
	3614 AORTCOR BYPAS-4+ COR ART 3776	
	3613 AORTOCOR BYPAS-3 COR ART 3775 REVISION OF LEAD	
	OR REPL LEAD EPICAR	
	3612 AORTOCOR BYPAS-2 COR ART 3774 INT	
	INSER LEAD IN ATRIUM	
	3611 AORTOCOR BYPAS-1 COR ART 3773 INT	
	INT INSER LEAD ATRI-VENT	
	3610 AORTOCORONARY BYPASS NOS 3772	
	3771 INT INSERT LEAD IN VENT	
	3606 INSERT CORONARY ART STENT OCT95-	
	INSERT PACEMAK LEAD	
	3605 PTCA-MULTIPLE VESSEL 3770 INT	
	TRANSPLANTATION	
	3602 PTCA-1 VESSEL WITH AGNT 375 HEART	
	3601 PTCA-1 VESSEL W/O AGENT 3619 HRT REVAS BYPS ANAS NEC	
	Exclude ICD-9-CM procedure codes:	
	40300 MAL HYPERT HRT DIS W/OUT RF	
	40490 HYPER HRT/REN NOS W/OUT CHF/RF	
	40290 HYPERTENSIVE HRT DIS W/OUT CHF	
	40410 BEN HYPER HRT/REN W/OUT CHF/RF	
	40210 BEN HYPERTEN HRT DIS W/OUT CHF	
	40400 MAL HYPER HRT/REN W/OUT CHF/RF	

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	All discharges of age 18 years and older.
	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>
	ICD-9-CM diagnosis codes (outcome of interest): 5400 AC APPEND W PERITONITIS 5401 ABSCESS OF APPENDIX
	ICD-9-CM diagnosis codes (population at risk): 5400 AC APPEND W PERITONITIS 5409 ACUTE APPENDICITIS NOS 5401 ABSCESS OF APPENDIX 541 APPENDICITIS NOS
	<b>Denominator:</b> Number of discharges with diagnosis code for appendicitis in any field in MSA or county.
neumonia	Bacterial Pneumonia Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for bacterial pneumonia (see below).J13-J14.9, J15.3-J15.4, J15.7-J15.4, J16.0-J16.9, J18.0-J18.9All discharges of age 18 years and older.EXCLUSION: Sickle cell disorders D57.0-D57.9Exclude: Discharges with diagnosis code for sickle cell anemia or HB-S disease (see below) in any field. Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> EXCLUSION: Sickle cell disorders D57.0-D57.9ICD-9-CM diagnosis codes: 491 DUFUMODICA 49220All 2020
	481 PNEUMOCOCCAL PNEUMONIA 48230 STREP PNEUMONIA UNSPEC 4822 H.INFLUENZAE PNEUMONIA 48231 GRP

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UTIs (urinary tract infections)	A STREP PNEUMONIA 4829 BACTERIAL PNEUMONIA NOS 48232 GRP B STREP PNEUMONIA 4830 MYCOPLASMA PNEUMONIA 48239 OTH STREP PNEUMONIA 4831 CHLAMYDIA PNEUMONIA OCT96- 485 BRONCOPNEUMONIA ORG NOS 4838 OTH SPEC ORG PNEUMONIA 486 PNEUMONIA, ORGANISM NOS <b>Exclude ICD-9-CM diagnosis codes:</b> 28260 SICKLE-CELL ANEMIA NOS 28263 SICKLE-CELL/HB-C DISEASE 28261 HB-S DISEASE W/O CRISIS 28269 SICKLE-CELL ANEMIA NEC 28262 HB-S DISEASE WITH CRISIS <b>Urinary Tract Infection Admission Rate</b> <b>Numerator:</b> Discharges with ICD-9-CM principal diagnosis code of urinary tract infection (see below). <b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	N10.0-N12.9, N15.1-15.9, N30.0- N30.9, N34.0-N34.9, N39.0
	ICD-9-CM diagnosis codes: 59000 CHR PYELONEPHRITIS NOS 59080 PYELONEPHRITIS NOS 59001 CHR PYELONEPH W MED NECR 59081 PYELONEPHRIT IN OTH DIS 59010 AC PYELONEPHRITIS NOS 5909 INFECTION OF KIDNEY NOS 59011 AC PYELONEPHR W MED NECR 5950 AC CYSTITIS 5902 RENAL/PERIRENAL ABSCESS 5959 CYSTITIS NOS 5903 PYELOURETERITIS CYSTICA 5990 URIN TRACT INFECTION NOS	07/2

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	<b>Denominator:</b> Population in MSA or county.	
Adult Asthma exacerbation	Adult Asthma Admission Rate           Numerator:           Discharges with ICD-9-CM principal diagnosis           code of asthma (see below).	J45, J46
	All discharges of age 18 years and older.	
	<b>Exclude:</b> Transfers <sup>1</sup> .	
	MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	
	ICD-9-CM diagnosis codes: 49300 EXT ASTHMA W/O STAT ASTH 49320 CH OB ASTH W/O STAT ASTH 49301 EXT ASTHMA W STATUS ASTH 49321 CH OB ASTHMA W STAT ASTH 49302 EXT ASTHMA W STATUS ACEX OCT00- 49322 CH OB ASTHMA W STAT ACEX	
	49310 INT ASTHMA W/O STAT ASTH OCT00- 49311 INT ASTHMA W STATUS ASTH 49390 ASTHMA W/O STATUS ASTHM 49312 INT ASTHMA W STATUS ACEX OCT00-	
	49391 ASTHMA W STATUS ASTHMAT 49392 ASTHMA W STATUS AC EXAC OCT00-	N .
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	51.
Amputations (diabetes-related)	Rate of Lower-extremity Amputation among Patients with Diabetes	Z89.4-Z89.7
	<b>Numerator:</b> Discharges with ICD-9-CM procedure code for lower-extremity amputation (see below) in any field and diagnosis code of diabetes in any field (see below).	*qualify only if registered with diabetes in the Danish National Diabetes Register or if registered with a diagnosis of diabetes (ICD-10:E10- 14, H36.0, O24, excluding O24.4) at
	All discharges of age 18 years and older.	the same admission as the ACSC

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<b>Exclude:</b> Trauma (see below). Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	
MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM procedure codes:</b> 8410 LOWER LIMB AMPUTAT NOS 8415 BELOW KNEE AMPUTAT NEC 8411 TOE AMPUTATION 8416 DISARTICULATION OF KNEE 8412 AMPUTATION THROUGH FOOT 8417 ABOVE KNEE AMPUTATION 8413 DISARTICULATION OF ANKLE 8418 DISARTICULATION OF HIP 8414 AMPUTAT THROUGH MALLEOLI 8419 HINDQUARTER AMPUTATION ICD-9-CM diagnosis codes for diabetes: 25000 DMII WO CMP NT ST UNCNTR 25050 DMII OPHTH NT ST UNCNTRL 25001 DMI WO CMP NT ST UNCNTRL 25051 DMI OPHTH NT ST UNCNTRLD 25002 DMII WO CMP UNCNTRLD 25052 DMII OPHTH UNCNTRLD 25003 DMI WO CMP UNCNTRLD 25053 DMI OPHTH UNCNTRLD 25010 DMII KETO NT ST UNCNTRLD 25060 DMII NEURO NT ST UNCNTRLD 25061 DMI NEURO NT ST UNCNTRLD 25012 DMII KETO NT ST UNCNTRLD 25062 DMII NEURO NT ST UNCNTRLD 25063 DMI NEURO UNCNTRLD 25013 DMI KETOACD UNCONTROLD 25063 DMI NEURO UNCNTRLD 25020 DMII HPRSM NT ST UNCNTRLD 25071 DMI CIRC NT ST UNCNTRLD 25072	EXCLUSION: Traumatic amputations of lower limb \$78.0-\$78.9, \$88.0-\$88.9, \$98.0- \$98.4, T05.3-T05.5

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	25032 DMII OTH COMA UNCONTROLD 25082
	DMII OTH UNCNTRLD
	25033 DMI OTH COMA UNCONTROLD 25083
	DMI OTH UNCNTRLD
	25040 DMII RENL NT ST UNCNTRLD 25090
	DMII UNSPF NT ST UNCNTRL
	25041 DMI RENL NT ST UNCNTRLD 25091
	DMI UNSPF NT ST UNCNTRLD
	25042 DMII RENAL UNCNTRLD 25092 DMII
	UNSPF UNCNTRLD
	25043 DMI RENAL UNCNTRLD 25093 DMI
	UNSPF UNCNTRLD
	Exclude: Trauma
	ICD-9-CM diagnosis codes:
	8950 AMPUTATION TOE 8971 AMPUTAT BK,
	UNILAT-COMPL
	8951 AMPUTATION TOE-COMPLICAT 8972
	WILLAT-COMPL 8950 AMPUTATION TOE-COMPLICAT BK, UNILAT-COMPL 8951 AMPUTATION TOE-COMPLICAT 8972 AMPUT ABOVE KNEE, UNILAT 8960 AMPUTATION FOOT, UNILAT 8973 AMPUT ABV KN, UNIL-COMPL 8961 AMPUT FOOT, UNILAT-COMPL 8974 AMPUTAT LEG, UNILAT NOS 8962 AMPUTATION FOOT, BILAT 8975 AMPUT LEG, UNIL NOS-COMP 8963 AMPUTAT FOOT, BILAT-COMP 8976 AMPUT ATION LEG, BILAT
	8960 AMPUTATION FOOT, UNILAT 8973
	AMPUT ABV KN, UNIL-COMPL
	8961 AMPUT FOOT, UNILAT-COMPL 8974
	AMPUTAT LEG, UNILAT NOS
	8962 AMPUTATION FOOT, BILAT 8975
	AMPUT LEG, UNIL NOS-COMP
	8963 AMPUTAT FOOT, BILAT-COMP 8976
	AMPUTATION LEG, BILAT
	8970 AMPUT BELOW KNEE, UNILAT 8977
	AMPUTAT LEG, BILAT-COMPL
	<b>Denominator:</b> Population in MSA or county, age
	18 years and older.
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a mission date with an overlap of +/- 1 day this. . or obstetric diagnoses were present as a secondary diag. <sup>1</sup>Transfers imply that if a discharge date is followed by another admission date with an overlap of +/- 1 day this is counted as one admission. <sup>2</sup>The exclusion of obstetric admissions was performed if any diagnostic codes for obstetric diagnoses were present as a secondary diagnosis at the same admission as the ACSC. The obstetric diagnostic codes included: O0.0-O99.9.

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Covariates
Appendix 5: Information on socioeconomic position (SEP) obtained from Statistics Denmark.
Education level
< 10 years
10-15 years
> 15 years
Civil status
Living alone/single
Cohabitation
Partners
Married

from the Danish National Patient	ICD-8	ICD-10
Myocardial infarction	410	121;122;123
Congestive heart failure	427.09, 427.10, 427.11, 427.19, 428.99, 782.49	150; 111.0; 113.0; 113.2
Peripheral vascular disease	427.19, 428.99, 782.49 440, 441, 442, 443, 444, 445,	170; 171; 172; 173; 174; 177
Cerebrovascular disease	430-438	160-169; G45; G46
Dementia	290.09-290.19, 293.09	F00-F03; F05.1; G30
Chronic pulmonary disease	490-493, 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3 J84.1; J92.0; J96.1; J98.2; J98.3
Connective tissue disease	712, 716, 734, 446, 135.99	M05; M06; M08; M09;M30;M31; M32; M33; M34; M35; M36; D86
Ulcer disease	530.91, 530.98, 531-534,	K22.1; K25-K28
Mild liver disease	571, 573.01, 573.04	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0
Diabetes mellitus	249.00, 249.06, 249.07, 249.09, 250.00, 250.06, 250.07, 250.09	E10.0, E10.1; E10.9; E11.0; E11.1; E11.9
Hemiplegia	344	G81; G82
Moderate/severe renal	403,404,580-583, 584,	I12; I13; N00-N05; N07; N11; N14;
Disease	590.09, 593.19, 753.10- 753.19, 792	N17-N19; Q61
Diabetes mellitus with	249.01-249.05, 249.08,	E10.2-E10.8; E11.2-E11.8
chronic complications	250.01-250.05, 250.08	C00 C75
Any tumour Leukaemia	140-194	C00-C75
	204-207	C91-C95
Lymphoma Moderate/severe liver	200-203, 275.59	C81-C85; C88; C90; C96
	070.00, 070.02, 070.04,	B15.0; B16.0; B16.2; B19.0; K70.4;
Disease	070.06, 070.08, 573.00, 456.00-456.09	K72; K76.6; I85
Metastatic solid tumour	436.00-456.09 195-198, 199	C76-C80

AIDS	079.83	B21-B24

ACSC Outcome	ACSC-predisposing medical comorbidity
Chronic conditions	
Angina	Myocardial infarction <sup>1</sup>
CHF exacerbation	CHF <sup>1</sup>
HTN	Myocardial infarction <sup>1</sup>
	CHF <sup>1</sup>
	Cerebrovascular disease <sup>1</sup>
	Peripheral vascular disease <sup>1</sup>
Diabetes-related ACSCs	Diabetes <sup>2</sup>
COPD exacerbation	Chronic pulmonary disease <sup>1</sup>
	or
	Redemption of at least 2 prescriptions of drugs for obstructive airway diseases within 6 months <sup>3</sup>
Adult asthma exacerbation	Chronic pulmonary disease <sup>1</sup>
	or
	Redemption of at least 2 prescriptions of drugs for obstructive airway diseases within 6 months <sup>3</sup>
Acute conditions	
Perforated appendicitis	-
Pneumonia	-
UTI	-
<sup>2</sup> Obtained from the Danish National D	atient Register using the algorithm defined in the Charlson Comorbidity Index (see appendix biabetes Register (see appendix 8) rescriptions Registry (see appendix 9).

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Appendix 8: Information on diabetes obtained from the Danish National Diabetes Register.			
Algoritm: Individuals were classified as having diabetes on the day where at least one of the following six			
criteria was met:			
1. A diagnosis of diabetes made at any Danish hospital as registered in the Danish National Patient Register			
(ICD-8:249, 250; ICD-10:E10-14, H36.0, O24, excluding O24.4).			
2 A referral to chiropody of diabetic patients as registered in the Danish National Health Service			

- 2. A referral to chiropody of diabetic patients as registered in the Danish National Health Service Register.(Andersen *et al.* 2011)
- 3. Five blood glucose measurements within one year as registered in the Danish National Health Service Register.
- 4. Two blood glucose measurements per year for five consecutive years as registered in the Danish National Health Service Register.
- 5. Two redemptions of oral anti-diabetic drugs within six months as registered in the Danish National Prescription Registry.
- 6. Two redemptions of prescribed insulin as registered in the Danish National Prescription Registry.

Appendix 9: ATC codes for drugs for obstructive airway disease obtained from the Danish National			
Prescription Registry.	Prescription Registry.		
ATC codes	Type of drug		
R03	Drugs for obstructive airway diseases		
R03A	Adrenergics, inhalants		
R03B	Other drugs for obstructive airway diseases, inhalants		
R03C	Adrenergics for systemic use		
R03D	Other systemic drugs for obstructive airway diseases		

Appendix 10: Information on substance abuse disorders obtained from the Danish National Patient			
Register and the Danish Psychiatric C	Central Register.		
	ICD-8	ICD-10	
Drug related			
Opioids	304.09, 304.19	F11.0–F11.9	
Cannabinoids	304.59	F12.0–F12.9	
Sedatives/hypnotics	304.29, 304.39	F13.0–F13.9	
Cocaine	304.49	F14.0–F14.9	
Other stimulants	304.69	F15.0–15.9	
Hallucinogens	304.79	F16.0–F16.9	
Other and multiple drugs	304.89, 304.99	F18.0–F19.9	
Alcohol related			
Alcohol psychosis and abuse	291.09-291.99	F10.0–F10.9	
syndrome	303.09-303.99		
Cirrhosis and steatosis of the liver	571.09, 571.10, 571.19	K70.0–K70.9	
Esophageal varices	456.00, 456.01, 456.09	I85.0–I85.9	

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STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Corresponding Manuscript Page Number
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term	1
The and about act	1	in the title or the abstract $\mathbf{X}$	1
		( <i>b</i> ) Provide in the abstract an informative and balanced	2-3
		summary of what was done and what was found $\mathbf{X}$	
Introduction		······································	
Background/rationale	2	Explain the scientific background and rationale for the	4
Dackground/Tationale		investigation being reported <b>X</b>	-
Objectives	3	State specific objectives, including any prespecified	5
Objectives		hypotheses X	5
		hypotheses A	
Methods			_
Study design	4	Present key elements of study design early in the paper <b>X</b>	5
Setting	5	Describe the setting, locations, and relevant dates, including	5
		periods of recruitment, exposure, follow-up, and data	
	-	collection X	
Participants	6	(a) Cohort study—Give the eligibility criteria, and the	5-6
		sources and methods of selection of participants. Describe	
		methods of follow-up X	
		Case-control study—Give the eligibility criteria, and the	
		sources and methods of case ascertainment and control	
		selection. Give the rationale for the choice of cases and	
		controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the	
		sources and methods of selection of participants	27/4
		(b) Cohort study—For matched studies, give matching	N/A
		criteria and number of exposed and unexposed	
		<i>Case-control study</i> —For matched studies, give matching	
		criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	6-9
		confounders, and effect modifiers. Give diagnostic criteria,	
		if applicable X	
Data sources/	8*	For each variable of interest, give sources of data and	6-9
measurement		details of methods of assessment (measurement). Describe	
		comparability of assessment methods if there is more than	
		one group X	0
Bias	9	Describe any efforts to address potential sources of bias X	9
Study size	10	Explain how the study size was arrived at N/A	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the	8-10
		analyses. If applicable, describe which groupings were	
<u> </u>		chosen and why X	0.10
Statistical methods	12	(a) Describe all statistical methods, including those used to	9-10
		control for confounding X	
		(b) Describe any methods used to examine subgroups and	10

(c) Explain how missing data were addressed X     9       (d) Cohort study—If applicable, explain how loss to     NA       Glow-up was addressed NA     Case-control study—If applicable, explain how matching     0       of cases and controls was addressed     Case-control study—If applicable, explain how matching     0       of cases and controls was addressed     Case-controls was addressed     To		interactions X	
follow-up was addressed NA Case-control study—If applicable, explain how matching of cases and controls was addressed methods taking account of sampling strategy (o) Describe any sensitivity analyses X Continued on next page			
Concentral study—If applicable, explain how matching of cases and countrols was addressed       Concentral study—If applicable, explain how matching         Concentral study—If applicable, explain how matching       Concentral study—If applicable, explain how matching         Concentral study—If applicable, explain how matching       Concentral study—If applicable, explain how matching         Concentral study—If applicable, explain how matching       Concentral study—If applicable, explain how matching         Concentral study—If applicable, explain how matching       Concentral study—If applicable, explain how matching         Continued on new page       Continued on new page       Continued on new page			N/A
of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy (c) Describe any sensitivity analyses X 10 Continued on next page		÷	
Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses <b>X</b> 10			
(e) Describe any sensitivity analyses X 10			
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		$(\underline{e})$ Describe any sensitivity analyses <b>X</b>	10
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Results			Corresponding Manuscript Page Number
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-11
		X (b) Give reasons for non-participation at each stage N/A	NI/ A
			N/A
Description	1.4*	(c) Consider use of a flow diagram	N/A 11. 27. 28 (Table 1)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	11, 27-28 (Table 1)
		confounders X	
		(b) Indicate number of participants with missing data for each variable of interest <b>X</b>	27-28 (Table 1)
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount) <b>X</b>	11
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <b>X</b>	11
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	N/A
Main results	16	<ul> <li>(a) Give unadjusted estimates and, if applicable, confounder- adjusted estimates and their precision (eg, 95% confidence interval).</li> <li>Make clear which confounders were adjusted for and why they were included X</li> </ul>	11, 13, 30-31 (Table 2), 33 (Table 4)
		(b) Report category boundaries when continuous variables were categorized <b>X</b>	8-10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses <b>X</b>	12-13, 32 (Table 3), 34-35
			(Figures 1 and 2)
Discussion			
Key results	18	Summarise key results with reference to study objectives X	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude	15-16
		of any potential bias X	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar	15-16
		studies, and other relevant evidence X	
Generalisability	21	Discuss the generalisability (external validity) of the study results X	15-16
Other information	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the	1, 10

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\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

<text> Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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# Depression and Risk for Hospitalizations and Rehospitalizations for Ambulatory Care-Sensitive Conditions in Denmark: a Population-Based Cohort Study

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# Depression and Risk for Hospitalizations and Rehospitalizations for Ambulatory Care-Sensitive Conditions in Denmark: a Population-Based Cohort Study

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# ABSTRACT

**Objective:** Hospitalizations for ambulatory care-sensitive conditions (ACSCs), a group of chronic and acute illnesses considered not to require inpatient treatment if timely and appropriate ambulatory care is received, and early rehospitalizations are common and costly. We sought to determine whether individuals with depression are at increased risk for hospitalizations for ACSCs, and rehospitalization for the same or another ACSC, within 30 days.

Design: National, population-based cohort study.

Setting: Denmark.

Participants: 5,049,353 individuals ≥ 18 years old between January 1, 2005 and December 31, 2013.

**Measurements:** Depression was ascertained via psychiatrist diagnoses in the Danish Psychiatric Central Register or antidepressant prescription redemption from the Danish National Prescription Registry. Hospitalizations for ACSCs and rehospitalizations within 30 days were identified using the Danish National Patient Register.

**Results:** Overall, individuals with depression were 2.35-times more likely to be hospitalized for an ACSC (95% Confidence Interval [95%CI]: 2.32, 2.37) versus those without depression after adjusting for age, sex, and calendar period, and 1.45-times more likely after adjusting for socioeconomic factors, comorbidities, and primary care utilization (95%CI: 1.43, 1.46). After adjusting for ACSC-predisposing comorbidity, depression was associated with significantly greater risk for hospitalizations for all chronic (e.g., angina, diabetes complications, congestive heart failure exacerbation) and acute ACSCs (e.g., pneumonia) compared to those without depression. Compared to those without depression, persons with depression were 1.21-times more likely to be rehospitalized within 30 days for the same ACSC (95%CI: 1.18, 1.24) and

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1.19-times more likely to be rehospitalized within 30 days for a different ACSC (95%CI: 1.15,

1.23).

**Conclusions:** Individuals with depression are at increased risk for hospitalizations for ACSCs, and once discharged are at elevated risk for rehospitalizations within 30 days for ACSCs.

# ARTICLE SUMMARY

- A strength of our study is that we followed a nationwide, population-based cohort with nearly no loss to follow-up.
- Our use of data from a country with a national healthcare system with universal access to health care and a relatively homogeneous population may impact generalizability to other countries with more ethnically diverse populations and different healthcare settings.
- Although we lack data on potential mediators of an association between depression and ambulatory care-sensitive condition (ACSC)-related hospitalizations such as health-risk behaviors (e.g., smoking, sedentary lifestyle), previous studies that controlled for health-risk behaviors found that the association between depression and greater risk for ACSC-related hospitalizations was independent of these factors.
- Our data lacks the degree of detail required to determine if adequate treatment for depression could moderate the adverse outcomes seen here.

## **INTRODUCTION**

Hospitalizations for chronic illnesses and their sequelae are a major contributor to rising healthcare costs in Western societies.<sup>1</sup> In the U.S., an estimated 10% of all hospitalizations may be preventable,<sup>2</sup> such as those for ambulatory care-sensitive conditions (ACSCs), a set of chronic (e.g., diabetes with complications, congestive heart failure [CHF], chronic obstructive pulmonary disease [COPD] exacerbation) and acute illnesses (e.g., bacterial pneumonia, urinary tract infection [UTI]) considered not to require inpatient treatment if patients receive timely and appropriate ambulatory care.<sup>3</sup> Hospitalizations for ACSCs have been estimated to cost the U.S. \$31.9 billion and £1.4 billion in the U.K. annually.<sup>4,5</sup> Moreover, early rehospitalizations, some of which may be due to ACSCs, are common and costly to health systems.<sup>6</sup> With the advent of accountable care organizations in the U.S. and other efforts to improve healthcare delivery worldwide, health systems are increasingly trying to prevent hospitalizations for ACSCs and early rehospitalizations in an effort to reduce healthcare spending.<sup>7-9</sup>

Depression is highly prevalent worldwide,<sup>10</sup> and is independently associated with more chronic disease sequelae,<sup>11</sup> greater healthcare costs,<sup>12</sup> and increased mortality.<sup>13</sup> Importantly, depression is amenable to treatment and could be a potentially modifiable risk factor for ACSCrelated hospitalizations. Depression may increase hospitalizations for ACSCs through factors such as reduced adherence to chronic disease treatments and reduced self-care.<sup>14</sup> While prior studies have found higher risk of hospitalizations for ACSCs and/or early rehospitalizations among persons with depression, they have been limited to single centers,<sup>15,16</sup> specific chronic disease populations,<sup>17</sup> geographically-defined health systems,<sup>16,17</sup> and older adults.<sup>18</sup> Furthermore, previous research on depression and risk of rehospitalizations within 30 days has not focused on potentially preventable rehospitalizations,<sup>15,16,18,19</sup> such as rehospitalizations

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within 30 days for an ACSC, an outcome that is arguably of particular importance to health systems and health policy makers. Also, it remains unknown whether depressed individuals are at greater risk of ACSC-related hospitalizations and rehospitalizations simply because they are more likely to have underlying chronic diseases.<sup>20,21</sup>

Utilizing data from a population-based cohort of five million Danish adults, we sought to determine if individuals with depression, defined by a clinical diagnosis and/or receiving antidepressant treatment, are at increased risk for hospitalizations for ACSCs after adjusting for demographics, socioeconomic factors, comorbidity (ACSC-predisposing and non-ACSC-predisposing comorbidity), and primary care utilization. Further, we examined whether persons with depression who have been hospitalized for an ACSC are at greater risk for rehospitalization for the same, or another ACSC, within 30 days. We hypothesized that depression would be independently associated with increased risk for hospitalizations for ACSCs as well as rehospitalizations within 30 days for either the same or a different ACSC.

## **METHODS**

#### Population

We conducted a population-based cohort study of all adults  $\geq$  18 years old, alive and residing in Denmark at least one day between January 1, 2005 and December 31, 2013. The cohort was constructed using data from the Danish Civil Registration System,<sup>22</sup> which includes data on sex, date of birth, vital status, and emigration since January 1, 1968. In the register, Danish residents are each assigned a unique personal identification number which links to person-level data.<sup>22</sup>

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# Primary Independent Variable

Our primary independent variable of interest was depression as identified by either psychiatric diagnosis or filling at least one antidepressant prescription. Depression was treated as a time-dependent variable (i.e., an individual without a recorded depression diagnosis or antidepressant prescription redemption at baseline could be diagnosed with depression or redeem an antidepressant prescription during the follow-up period, moving from the "unexposed" to the "exposed" group). Information on psychiatric diagnoses was obtained from the Danish Psychiatric Central Register<sup>23</sup> (see Appendix 1), which includes diagnostic information on all psychiatric hospitalizations from 1969 onwards and outpatient specialty mental health visits from 1995 onwards.<sup>23</sup> Prescription fills for antidepressant prescriptions (i.e. selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and other non-tricyclic (TCA) antidepressants, see Appendix 1) were identified using the Danish National Prescription Registry.<sup>24</sup> This register includes data on all prescriptions dispensed at Danish pharmacies since 1995, including purchase date and classification of drugs according to the Anatomical Therapeutic Chemical Classification.<sup>25</sup> We excluded TCA prescriptions from our depression definition because of their frequent use for insomnia and/or pain. We also excluded bupropion or trazodone prescriptions since neither was approved for treating depression in Denmark during the study period. Individuals with schizophrenia, schizoaffective disorders or bipolar disorder were censored at date of diagnosis (see Appendix 2) and excluded from analyses.

Outcomes of Interest

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Our primary outcome of interest was hospitalization for one of 12 ACSCs as defined by the Agency for Healthcare Research and Quality (AHRQ) (see Appendix 3).<sup>2</sup> Prior to December 31, 1993, register-based diagnoses were based on the Danish version of the International Classification of Diseases, 8th Revision (ICD-8).<sup>26</sup> From January 1, 1994 forward, the Danish version of the ICD-10<sup>27</sup> was used. Since the AHRQ-defined ACSCs were originally derived using ICD-9 diagnoses, we included eight AHRQ-defined ACSCs (i.e., angina without concomitant cardiovascular procedures, COPD exacerbation, CHF exacerbation, diabetes with short-term complications, diabetes with long-term complications, uncontrolled diabetes, hypertension (HTN), and appendicitis with perforation) that were translated into ICD-10 diagnosis codes and validated in a previous study.<sup>28</sup> We also included four AHRO-defined ACSCs (i.e., bacterial pneumonia, diabetes-related lower extremity amputations, UTIs, and adult asthma exacerbations) based on ICD-10 codes used in prior Danish register-based studies.<sup>29-32</sup> We further divided ACSCs into five "chronic" ACSCs (i.e., angina, CHF exacerbation, HTN, diabetes-related, COPD/adult asthma exacerbation) and three "acute" ACSCs (i.e., appendicitis with perforation, pneumonia, and UTI). We used the Danish National Patient Register,<sup>33</sup> which contains information on all medical hospitalizations since January 1, 1977 and outpatient visits since January 1, 1995,<sup>33</sup> to obtain information on hospitalizations with principal discharge diagnoses for ACSCs occurring between January 1, 2005 and December 31, 2013. If a discharge was followed by an admission within one day, it was considered a transfer and counted as one admission only. We excluded hospitalizations with secondary obstetric diagnoses (ICD-10 codes: 000.0-099.9).

Our secondary outcome of interest was rehospitalization for an ACSC within 30 days of discharge from the initial ACSC-related hospitalization. We counted rehospitalizations that were

for the same ACSC, or for a different ACSC, using data from the Danish National Patient Register.

Socioeconomic Factors, Comorbid Medical Conditions, and Substance Abuse Disorders

Information on marital/partnered status and education was obtained from Statistics Denmark and the Danish Educational Registers, respectively (see Appendix 4).<sup>34,35</sup> We categorized marital/partnered status as living with a partner (i.e., married, registered partnership, or cohabitation) or living alone (i.e., living without a partner, including widows/widowers). We classified maximum educational level attained into the following three categories based on the United Nations Educational, Scientific and Cultural Organization's International Standard Classification of Education: low (<10 years), middle (10–15 years), and high (>15 years).<sup>36</sup>

For the five chronic ACSCs, we defined ACSC-predisposing medical comorbidity specific for each ACSC in question (see Appendix 5). Information on ACSC-predisposing medical comorbidity and non-ACSC predisposing medical comorbidity was obtained from the Danish National Patient Register and based on Charlson Comorbidity Index (CCI) categories<sup>37</sup> (see Appendix 6) (e.g., myocardial infarction as ACSC-predisposing medical comorbidity for angina hospitalization, etc.), with two exceptions. Diabetes diagnoses were obtained from the Danish National Diabetes Register between January 1, 1990 and December 31, 2013 (see Appendix 7).<sup>38</sup> Chronic pulmonary disease was identified as either a diagnosis based on the CCI category obtained from the Danish National Patient Register or  $\geq$  two prescription redemptions within a six month period for medications treating obstructive airway diseases (see Appendix 8) as obtained from the Danish National Prescription Registry. Non-ACSC predisposing medical comorbidity included all remaining CCI diagnostic categories. We did not define ACSCpredisposing medical comorbidity for the three acute ACSCs.

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Data on substance abuse (excluding tobacco abuse) was obtained from the Danish Psychiatric Central Register or the Danish National Patient Register (see Appendix 9). *Primary Care Utilization* 

We obtained information on day-time face-to-face visits with primary care physicians (PCPs) or other primary care staff from the Danish National Health Service Register,<sup>39</sup> which has been collecting primary care administrative data since January 1, 1990. To reduce the chances of including a primary care visit that directly resulted in an ACSC-related hospitalization, we constructed a time-dependent variable counting the number of primary care visits from 10-375 days before any given day. We categorized primary care visits into three equally-sized categories of low, medium, or high utilization based on observed frequencies (i.e., 0-2, 3-9 or  $\geq$ 10 visits). *Statistical Analysis* 

We compared individuals with depression to those without depression using Poisson regression models in order to estimate incidence rate ratios (IRRs) for hospitalizations for ACSCs and subsequent rehospitalization within 30 days for an ACSC. We estimated corresponding 95% Confidence Intervals (95%CIs) using cluster robust variance estimation to account for interperson correlation and dichotomy of rehospitalization. In these analyses, our outcomes of interest were a count of the number of hospitalizations for ACSCs. Age and calendar period were adjusted for using two-year and one-year age and time bands, respectively. All variables (including depression status), except sex, were treated as time-dependent. Individuals contributed at-risk time from January 1, 2005 or from their 18<sup>th</sup> birthday, whichever came last, in different time bands based upon the different covariate combinations they enter with during follow-up. Within each of these combinations, we counted the number of ACSC-related

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hospitalizations that occurred after registration of a depression diagnosis and/or redemption of an antidepressant prescription. Censoring occurred at date of death, emigration, date of bipolar disorder or schizophrenia diagnosis, or on December 31, 2013, whichever came first.

For each ACSC-related hospitalization outcome, we fitted five risk models, adjusting sequentially for demographics (i.e., age, sex and calendar period), socioeconomic factors (i.e., marital/partnered status and education), ACSC-predisposing medical comorbidity (with each comorbid condition entered individually), other comorbidity (i.e., non-ACSC-predisposing medical comorbidity entered individually and substance abuse), and primary care utilization. All model covariates were chosen *a priori* based on prior studies identifying their potential associations with both depression and healthcare utilization outcomes.<sup>12,16,17,40</sup> To address missing data on education, we conducted multiple imputation using five imputed data sets according to methods developed by Rubin.<sup>41</sup>

We performed two pre-specified sub-analyses. First, we examined whether the association between depression and risk for ACSC-related hospitalizations was modified by age. To do so, we repeated our Poisson regressions stratified by three age categories:  $\leq$  40 years old, 41-64 years old, and  $\geq$  65 years old. Second, we examined the associated risk for hospitalizations for chronic and acute ACSCs based on time since depression diagnosis in models adjusted for demographics.

In order to determine if an association between depression and risk for hospitalizations for ACSCs was impacted by our depression definition, we performed a pre-specified sensitivity analysis in which we repeated our regressions using three different depression definitions: antidepressant prescription alone, outpatient psychiatric visit-based diagnosis alone or psychiatric hospitalization for depression.

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We fitted three models examining risk for rehospitalization within 30 days for an ACSC. The first model adjusted for demographics, the second included adjustment for socioeconomic factors and the third for medical and substance abuse comorbidities. Our outcome of interest in these models was time to rehospitalization for an ACSC within 30 days of discharge from the initial ACSC-related hospitalization. Individuals were at risk for the outcome on the day of discharge from their ACSC-related hospitalization. All variables in these analyses excluding sex were treated as time-dependent.

We used two-sided significance tests for all analyses with statistical significance set at P < 0.05. Analyses were performed using STATA 13 (Stata Corporation, College Station, TX).

#### **RESULTS**

We followed a cohort of 5,049,353 individuals for a total of 38,674,363 person-years at risk, including 1,319,896 (26.1%) persons diagnosed with depression or who had redeemed an antidepressant prescription during the study period. Of those with depression, 1,182,495 (89.6%) cases were from antidepressant prescription fills while 137,401 (10.4%) cases were diagnosed by mental health specialists in outpatient or inpatient contacts. The mean age at initially registered depression diagnosis was 49.1 (standard deviation: 19.2) years old.

Table 1 displays the characteristics of our cohort by depression status. During the nine year follow-up period, we identified 1,255,640 hospitalizations for ACSCs, including 542,184 (43.2%) among persons with depression. There were 71.4 ACSC-related hospitalizations per 1,000 person-years among those with depression versus 23.0 per 1,000 person-years among those with depression versus 23.0 per 1,000 person-years among those with depression versus 23.0 per 1,000 person-years among

[Please insert Table 1 here]

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Compared to those without depression, the IRR for having any ACSC-related hospitalization was 2.35 (95% CI: 2.32, 2.37) for individuals with depression after adjusting for demographics. This association remained robust after adjusting for socioeconomic factors, and decreased though remained significant after adjusting for possible mediators including comorbidities and PCP visits during the previous year (Table 2).

In comparison to persons without depression, depression was associated with increased risk for hospitalizations for all of the chronic ACSCs even after adjusting for specific chronic ACSC-predisposing medical comorbidity (Table 2), particularly for hospitalizations for angina (IRR: 1.77; 95%CI: 1.73, 1.81), COPD/asthma exacerbations (IRR: 1.88; 95%CI: 1.84, 1.93), and diabetes-related hospitalizations (IRR: 1.83; 95%CI: 1.77, 1.89). Although these results were attenuated by adjusting for additional comorbidity and PCP visits during the previous year, depression remained independently associated with increased risk for hospitalizations for all chronic ACSCs, especially for hospitalizations for COPD/asthma exacerbations (IRR: 1.61; 95%CI: 1.57, 1.65), and diabetes-related hospitalizations (IRR: 1.69; 95%CI: 1.63, 1.75) (Table 2).

Similarly, depression was associated with increased risk for hospitalizations for all three acute ACSCs even after adjusting for medical and substance abuse comorbidity (appendicitis with perforation: IRR: 1.26; 95%CI: 1.21, 1.33; pneumonia: IRR: 1.55; 95%CI: 1.53, 1.56; UTI: 1.74; 95%CI: 1.71, 1.77). These associations remained significant after adjusting for PCP visits during the preceding year.

[Please insert Table 2 here]

When we stratified by age categories, we found that the association between depression and risk for hospitalizations for ACSCs was especially potent for individuals 40 years old or

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younger (IRR: 2.06; 1.98, 2.13). Depression was also independently associated with increased risk for hospitalizations for ACSCs among middle-aged and older adults (Table 3). [Please insert Table 3 here]

In the first year after depression diagnosis, the associated risk for hospitalization for a chronic ACSC was nearly 3-times greater than those without depression (IRR: 2.89; 95%CI: 2.83, 2.96) (Figure 1). The associated risk remained nearly 2.4-times greater than for those without depression (IRR: 2.39, 95%CI: 2.34, 2.43) 10 or more years after depression diagnosis. During the first year after depression diagnosis, the associated risk for hospitalization for an acute ACSC was 3 1/3-times greater than for those without depression (IRR: 3.33, 95%CI: 3.27, 3.40), and the associated risk remained 2 <sup>1</sup>/<sub>4</sub>-times higher at  $\geq$  10 years after depression diagnosis (IRR: 2.25; 95%CI: 2.22, 2.29) (Figure 2).

[Please insert Figure 1 here]

[Please insert Figure 2 here]

In our sensitivity analysis in which we examined whether our results regarding risk for hospitalization for any ACSC were impacted by depression definition, we found that depression defined by antidepressant prescription alone (IRR: 2.31; 95%CI: 2.28, 2.33), outpatient psychiatric visit-based diagnosis alone (IRR: 2.66; 95%CI: 2.56, 2.77) or psychiatric hospitalization for depression (IRR: 2.69; 95%CI: 2.62, 2.77) were all associated increased risk for hospitalization for an ACSC after adjusting for demographics. These associations remained significant after adjusting for socioeconomic factors, comorbidities, and PCP visits in the previous year (antidepressant prescription alone: IRR: 1.44; 95%CI: 1.43, 1.45; outpatient psychiatric visit-based diagnosis: IRR: 1.54; 95%CI: 1.48, 1.60; psychiatric hospitalization for depression: IRR: 1.50; 95%CI: 1.46, 1.54).

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Approximately 6.8% of all ACSC-related hospitalizations during the follow-up period were followed by an ACSC-related rehospitalization within 30 days, of which 73.0% were for the same ACSC and 27.0% were for a different ACSC. Of the 85,046 ACSC-related rehospitalizations within 30 days, 42,791 (50.3%) were among those with depression. Compared to those without depression, depression was associated with 1.36-times greater risk for rehospitalization within 30 days for the same ACSC (95%CI: 1.32, 1.39) and 1.44-times greater risk for rehospitalization within 30 days for a different ACSC (95%CI: 1.39, 1.49) after adjusting for age, sex, and calendar period (Table 4). After adjusting for socioeconomic factors and comorbidities, while attenuated, depression remained independently associated with greater risk for rehospitalization within 30 days for the same ACSC (IRR: 1.21; 95%CI: 1.18, 1.24) or another ACSC (IRR: 1.19; 95%CI: 1.15, 1.23).

[Please insert Table 4 here]

## **DISCUSSION**

In this nationwide, population-based longitudinal study of over 5 million individuals, we found that depression was independently associated with higher risk for hospitalizations for both chronic and acute ACSCs and that the associated risk remained high for at least 10 years. To our knowledge, the present study is the first to show that depression was associated with higher risk of rehospitalization for the same or another ACSC within 30 days of an ACSC-related hospitalization. Importantly, we identified that the associated risk of hospitalizations for ACSCs was greater among persons with depression even when we adjusted for the higher prevalence of predisposing chronic diseases in this population.

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An increased risk of hospitalization and subsequent rehospitalization for an ACSC among depressed individuals is troubling in light of evidence that some ACSC-related hospitalizations may have negative effects on long-term functioning, cognition and mental health.<sup>42</sup> Depression in-and-of-itself is known to increase the risk of cognitive decline and functional impairment,<sup>43,44</sup> both of which increase risk of ACSC-related hospitalizations.<sup>18,45</sup> Therefore, depressed individuals could be especially at risk for a vicious cycle of hospitalizations, rehospitalizations, and rapid decline.

This study has important implications for development of interventions to prevent costly ACSC-related hospitalizations and rehospitalizations. A potential explanation for our findings is that depressed individuals may not receive timely and/or appropriate ambulatory care for chronic diseases such as diabetes or cardiovascular disease as well as acute diseases such as pneumonia or UTIs. Yet, we found that depression was independently associated with increased risk for hospitalizations for these conditions even in a country, Denmark, with universal access to primary care. Therefore, it could be reasonable to conclude that simply increasing access to primary care may not ameliorate these problems. This interpretation is supported by recent studies evaluating the impact of health care reform in Massachusetts that found improving access to care was not associated with reductions in ACSC-related hospitalizations or rehospitalizations within 30 days among high-risk populations.<sup>46,47</sup>

If expanding access to primary care by itself is insufficient to prevent hospitalizations for ACSCs among at-risk populations such as those with depression, then additional research is needed to identify cost-effective interventions that could reduce these potentially preventable events. One possibility is through ongoing efforts to integrate psychiatric care into primary care and other ambulatory care medical settings. Collaborative care for depression and comorbid

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conditions in primary care settings has been proven effective and cost-effective,<sup>48-53</sup> and its costeffectiveness is in part due to reductions in hospitalizations for comorbid medical conditions.<sup>54</sup> Further studies of sufficient duration and size are needed to determine if collaborative care could prevent ACSC-related hospitalizations among individuals with depression. More research is also needed to ascertain if integrating aspects of collaborative care into existing interventions focusing on improving transitional care from the hospital back to primary care<sup>55,56</sup> could prevent early rehospitalizations for ACSCs. Such research would be of particular interest to accountable care organizations and health policy makers aiming to reduce healthcare costs while simultaneously improving patient outcomes and overall quality of care.

Our study has several strengths and limitations. We followed a nationwide, populationbased cohort with nearly no loss to follow-up. However, our use of data from a country with a national healthcare system with universal access to health care and a relatively homogeneous population may impact generalizability. Yet, these factors may enhance internal validity by decreasing the degree socioeconomic factors play in healthcare-seeking behavior, and potentially suggest that our estimates may be overly conservative. Further, our depression definition was based on a combination of psychiatric diagnoses and antidepressant prescription records, potentially introducing selection bias since patients with more severe depression are more likely to be prescribed antidepressants and/or referred to psychiatrists,<sup>57,58</sup> and is further exacerbated by inability to capture depressed individuals who have not sought treatment.<sup>59</sup> However, our sensitivity analysis examining different depression definitions did not yield differing results, and our primary depression definition has been used in prior related research.<sup>43</sup>

While we lack data on potential mediators of an association between depression and ACSC-related hospitalizations such as health-risk behaviors (e.g., smoking, sedentary lifestyle),

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previous studies in this area that controlled for health-risk behaviors found that the association between depression and greater risk for ACSC-related hospitalizations was independent of these factors.<sup>17,18</sup> Our data lacks the degree of detail required to determine if adequate treatment for depression could moderate the adverse outcomes seen here. Also, the registers lack detail to sufficiently ascertain illness severity, so we cannot fully exclude the possibility that our findings reflect that when compared to the general population, depressed individuals may present with higher acuity of medical illnesses and a greater burden of comorbidity, necessitating hospitalization for optimal treatment.

In conclusion, in a nationwide study in Denmark, we found that compared to individuals without depression, depression was associated with increased risk for hospitalizations for ACSCs. Furthermore, once hospitalized for an ACSC, depression was associated with greater risk for rehospitalization within 30 days for the same, or another, ACSC. Further research that clarifies the mechanisms linking depression and ACSC-related hospitalizations, and that develops interventions that prevent ACSC-related hospitalizations in persons with depression, is needed given the burden that recurrent hospitalizations places on individuals and society.

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**Authorship:** Drs. Davydow, Ribe, Pedersen, Prior, Vedsted, Unützer and Vestergaard, and Messrs. Fenger-Grøn and Pedersen fulfill all three of the ICJME criteria for authorship, including: 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content, and 3) final approval of the version to be published.

**Transparency Declaration:** Dr. Davydow affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

**Guarantor:** Dr. Vestergaard has had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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#### Table 1. Study cohort characteristics

	<b>Depression (n = 1,319,896)</b>			Without Dep	Without Depression (n = 3,782,713)		
Measure	Number of Hospitalizations for ACSCs	Person-Years at Risk	Percentage risk time spent in category (%)	Number of Hospitalizations for ACSCs	Person-Years at Risk	Percentage risk time spent in category (%)	
Total	542,184	7,596,536	100.0	713,456	31,077,828	100.0	
Age (years)	20.121		<b>2</b> 2.2		11.040.404	20.4	
$\leq 40$	28,434	1,771,769	23.3	69,350	11,940,484	38.4	
41-64	158,633	3,697,843	48.7	197,925	13,201,867	42.5	
$\geq$ 65	355,117	2,126,924	28.0	446,181	5,935,477	19.1	
Sex							
Male	231,216	2,884,303	38.0	393,065	16,114,603	51.8	
Female	310,968	4,712,233	62.0	320,391	14,963,225	48.2	
Calendar period							
2005	47,853	661,461	8.7	79,756	3,564,097	11.5	
2006	57,932	711,984	9.4	90,186	3,523,904	11.3	
2007	46,477	761,231	10.0	67,588	3,494,327	11.2	
2008	51,896	805,396	10.6	71,465	3,475,920	11.2	
2009	63,150	848,956	11.2	83,274	3,452,336	11.1	
2010	51,567	895,574	11.8	64,832	3,425,594	11.0	
2011	74,991	938,720	12.4	89,372	3,405,029	11.0	
2012	74,535	972,971	12.8	85,424	3,378,860	10.9	
2013	73,783	1,000,243	13.2	81,559	3,358,761	10.8	
Marital status							
Living with partner	226,573	3,585,166	47.2	348,530	15,922,753	51.2	
Living alone	315,611	4,011,370	52.8	364,926	15,155,075	48.8	
Education (years)							
< 10	265,781	2,751,794	36.2	312,769	8,845,177	28.5	

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10-15	178,680	3,182,588	41.9	249,363	14,267,047	45.9
$\geq 16$	47,039	1,284,597	16.9	75,866	6,318,611	20.3
Missing	50,684	377,558	5.0	75,458	1,646,993	5.3
Comorbidity						
MI	89,475	261,404	3.4	109,123	556,446	1.8
CHF	118,101	212,889	2.8	137,507	367,223	1.2
Diabetes	155,739	761,878	10.0	165,161	1,567,720	5.0
Cerebrovascular	126,796	615,389	8.1	98,828	834,803	2.7
disease	120,150	010,000	011	,020		,
Peripheral vascular	79,566	283,055	3.7	70,493	443,853	1.4
disease	,			, , , , , , ,	,	
Chronic pulmonary	229,594	674,995	8.9	208,423	1,339,308	4.3
disease	- )				<u> </u>	
Dementia	44,638	217,259	2.9	19,519	110,040	0.3
Connective tissue	42,814	269,168	3.5	39,087	514,840	1.7
disease	<b>y</b> -				- ,	
Peptic ulcer disease	69,733	327,298	4.3	53,974	464,831	1.5
Renal disease	45,769	123,767	1.6	50,315	245,853	0.8
Mild liver disease	19,437	129,645	1.7	11,845	159,553	0.5
Moderate/severe	5,287	27,978	0.4	3,516	34,556	0.1
liver disease	- ,	- <u>)</u>			- ,	
Paraplegia	7,123	31,836	0.4	4,893	46,060	0.1
Cancer	102,324	608,120	8.0	118,072	1,430,995	4.6
Metastatic carcinoma	12,338	58,013	0.8	13,715	116,930	0.4
HIV/AIDS	1,011	10,673	0.1	998	22,685	0.1
Substance abuse disorders	87,977	792,810	10.4	42,932	881,074	2.8
Primary care visits in prior						
year						
0-2	119,055	2,487,888	32.7	196,845	17,355,110	55.8
3-9	223,859	3,739,020	49.2	317,381	11,687,211	37.6
$\geq 10$	199,270	1,369,628	18.0	199,230	2,035,670	6.5

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.SC = ambulatory care-sensitive . .IV = Human Immunodeficiency Virus; MI = . Abbreviations (in alphabetical order): ACSC = ambulatory care-sensitive condition; AIDS = Acquired Immunodeficiency Syndrome; CHF = congestive heart failure; HIV = Human Immunodeficiency Virus; MI = myocardial infarction.

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#### Table 2. The risk of hospitalizations for ambulatory care-sensitive conditions associated with depression compared to

#### individuals without depression

Outcome	<u>Model 1</u> Adjusted for demographics <sup>a</sup>	<u>Model 2</u> Adjusted for variables in Model 1 and socioeconomic factors <sup>b</sup>	<u>Model 3</u> Adjusted for variables in Model 2 and ACSC- predisposing comorbidity	Model 4 Adjusted for variables in Model 3 and non-ACSC- predisposing comorbidity <sup>h</sup> and substance abuse disorders	<u>Model 5</u> Adjusted for variables in Model 4 and PCP visits in the previous year
		<b>Incidence</b> Rate	e Ratio (95% Confid	ence Interval)	
Any ACSC	$2.35(2.32, 2.37)^{\dagger}$	$2.27 (2.25, 2.29)^{\dagger}$		$1.53 (1.51, 1.54)^{\dagger}$	$1.45(1.43, 1.46)^{\dagger}$
<b>Type of ACSC</b> <i>Chronic ACSCs</i> Angina COPD/Asthma exacerbation CHF exacerbation Diabetes-related HTN	$\begin{array}{c} 2.03 \ (1.99, \ 2.08)^{\dagger} \\ 3.17 \ (3.09, \ 3.24)^{\dagger} \\ 1.72 \ (1.67, \ 1.76)^{\dagger} \\ 2.88 \ (2.79, \ 2.98)^{\dagger} \\ 1.52 \ (1.48, \ 1.57)^{\dagger} \end{array}$	$\begin{array}{c} 2.00 \; (1.96, 2.05)^{\dagger} \\ 2.97 \; (2.90, 3.04)^{\dagger} \\ 1.67 \; (1.62, 1.71)^{\dagger} \\ 2.66 \; (2.57, 2.75)^{\dagger} \\ 1.48 \; (1.44, 1.53)^{\dagger} \end{array}$	$1.77 (1.73, 1.81)^{c^{\ddagger}}$ $1.88 (1.84, 1.93)^{d^{\ddagger}}$ $1.22 (1.19, 1.25)^{e^{\ddagger}}$ $1.83 (1.77, 1.89)^{f^{\ddagger}}$ $1.37 (1.33, 1.41)^{g^{\ddagger}}$	$\begin{array}{c} 1.52 \ (1.49,  1.56)^{\dagger} \\ 1.66 \ (1.62,  1.70)^{\dagger} \\ 1.09 \ (1.06,  1.12)^{\dagger} \\ 1.86 \ (1.80,  1.93)^{\dagger} \\ 1.30 \ (1.26,  1.34)^{\dagger} \end{array}$	$\begin{array}{l} 1.35 \left(1.32, 1.38\right)^{\dagger} \\ 1.61 \left(1.57, 1.65\right)^{\dagger} \\ 1.06 \left(1.03, 1.09\right)^{\dagger} \\ 1.69 \left(1.63, 1.75\right)^{\dagger} \\ 1.18 \left(1.14, 1.21\right)^{\dagger} \end{array}$
Acute ACSCs Appendicitis with perforation Pneumonia UTI	$1.31 (1.25, 1.37)^{\ddagger}$ $2.35 (2.33, 2.38)^{\ddagger}$ $2.38 (2.34, 2.42)^{\ddagger}$	$\begin{array}{c} 1.31 \ (1.25, \ 1.37)^{\ddagger} \\ 2.29 \ (2.27, \ 2.32)^{\ddagger} \\ 2.34 \ (2.31, \ 2.38)^{\ddagger} \end{array}$	. ( , ,	$1.26 (1.21, 1.33)^{\dagger}$ $1.55 (1.53, 1.56)^{\dagger}$ $1.74 (1.71, 1.77)^{\dagger}$	$1.21 (1.16, 1.27)^{\ddagger}$ $1.50 (1.48, 1.52)^{\ddagger}$ $1.63 (1.60, 1.66)^{\ddagger}$

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<u>Abbreviations (in alphabetical order)</u>: ACSC = ambulatory care-sensitive condition; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HTN = hypertension; PCP = primary care physician; UTI = urinary tract infection.

<sup>a</sup> Age, sex and calendar period.

<sup>b</sup> Educational level and marital status.

<sup>c</sup> Adjusted for myocardial infarction.

<sup>d</sup>Adjusted for chronic pulmonary disease.

<sup>e</sup> Adjusted for CHF.

<sup>f</sup>Adjusted for diabetes mellitus.

<sup>g</sup> Adjusted for myocardial infarction, CHF, cerebrovascular disease and peripheral vascular disease.

<sup>h</sup> Charlson Comorbidity Index diagnoses not previously adjusted for.

 $^{+}P < 0.001$ 

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## Table 3. The effect of age on the association of depression with risk of hospitalization for an

#### ambulatory care-sensitive condition

Age categories	Adjusted for demographics	Adjusted for socioeconomic factors	Adjusted for comorbidities	Adjusted for PCP visits
	uemographies	<b>Incidence Rate Ratio</b>	comorbiunces	
		(95% Confidence Interval)		
$\leq$ 40 years old	2.88 (2.78, 3.00) <sup>‡</sup>	$2.83 (2.72, 2.93)^{\dagger}$	$2.34(2.25, 2.43)^{\dagger}$	$2.06(1.98, 2.13)^{\dagger}$
41 – 64 years old	2.93 (2.88, 2.98) <sup>‡</sup>	2.74 (2.69, 2.78) <sup>‡</sup>	1.94 (1.91, 1.97) <sup>‡</sup>	1.73 (1.70, 1.76) <sup>†</sup>
Age≥65 years old	$2.30(2.28, 2.32)^{\dagger}$	2.18 (2.15, 2.20) <sup>‡</sup>	1.34 (1.33, 1.36) <sup>‡</sup>	1.31 (1.30, 1.32) <sup>‡</sup>
	PCP = primary care	ohysician.		
<sup>+</sup> P < 0.001				

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in Model 2,

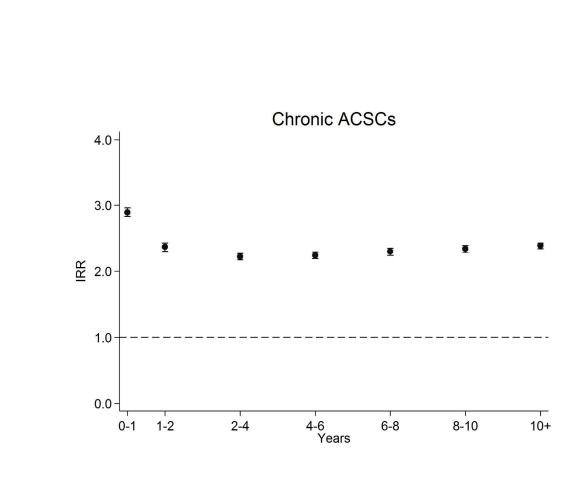
Table 4. The risk of rehospitalization within 30 days for the same or another ambulatory

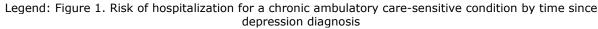
care-sensitive condition among those with depression compared to individuals without				
depression				
		Model 1	Model 2	<u>Model 3</u> Adjusted for variables

Model 1

Outcome	Adjusted for demographics	in Model 1 and socioeconomic factors	comorbidity and substance abuse disorders
		e Rate Ratio	
		dence Interval)	
Same ACSC	1.36 (1.32, 1.39) <sup>‡</sup>	$1.34(1.31, 1.38)^{\dagger}$	$1.21 (1.18, 1.24)^{\dagger}$
Another ACSC	$1.44 (1.39, 1.49)^{\dagger}$	$1.42(1.37, 1.47)^{\dagger}$	1.19 (1.15, 1.23)‡
<u>Abbreviation</u> : ACSC =	ambulatory care-sensitive	condition.	
<sup>+</sup> <i>P</i> < 0.001			

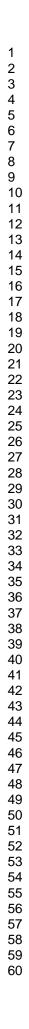
Adjusted for variables

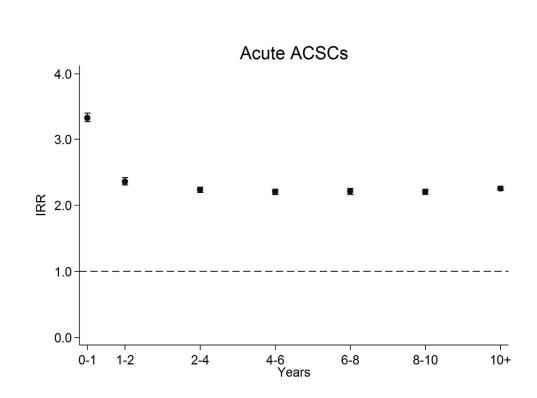


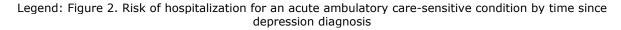


Caption: Abbreviations (in alphabetical order): ACSCs = ambulatory care-sensitive conditions; IRR = incidence rate ratio. 529x384mm (300 x 300 DPI)

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Caption: Abbreviations (in alphabetical order): ACSCs = ambulatory care-sensitive conditions; IRR = incidence rate ratio. 529x384mm (300 x 300 DPI)

## **Supplementary Online Material**

# <u>APPENDIX 1</u>: Information on depression obtained from the Danish Psychiatric Central Register and the Danish National Prescription Registry

#### A diagnosis of depression was identified if at least one of the following criteria applied:

- 1. Registration of a diagnosis of depression in the Danish Psychiatric Central Register. And/or
- 2. Registration of at least one prescription of antidepressants redeemed in the Danish National Prescription Registry

#### Diagnosis according to a record of depression in the Danish Psychiatric Central Register:

296.09, 296.29, 296.99, 298.09, F32,	F33
300.49, and 300.19	

# Diagnosis according to a record of prescriptions for antidepressants in the Danish National Prescription Registry:

Name	Drug	ATC-codes
SSRI (Selective serotonin re-uptake inhibitors)	Fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, and escitalopram	N06AB
MAOIs (Monoamine oxidase inhibitors)	Isocarboxazid and moclobemide	N06AF, N06AG
Other antidepressants	Mianserin, nefazodone, mirtazapine, venlafaxine, reboxetine, duloxetine, and agomelatine	N06AX

# <u>APPENDIX 2</u>: Information on severe mental illness obtained from the Danish Psychiatric Central Register.

	ICD-8	ICD-10
Schizophrenia	295 (excluding 295.79)	F20
Schizoaffective disorders	295.79, 296.8	F25

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Bipolar affective disorders	296.19, 296.39	F30, F31

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Discharges with a surgical procedure in any field (010-8699). Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS         Denominator: Population in MSA or county, age 18 years and older.         COPD (Chronic obstructive pulmonary disorder) exacerbation         COPD (Chronic obstructive pulmonary disorder)         Coppl (Chronic obstructive pulmonary disorder)         COPD (Chronic obstructive pulmonary disorder)         Coppl (Chronic obstructive pulmonary disorder)         Coppl (Chronic obstructive pulmonary disorder)	Register.	entified by the Agency for Healthcare Research a	nd Quality as ACSCs in their rend
Angina       Angina Without Procedure Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for angina (see below).       120.0, 120.1, 120.8, 120.9, 124. I24.1, 124.8, 124.9         All discharges with ICD-9-CM principal diagnosis code for angina (see below).       120.0, 120.1, 120.8, 120.9, 124. I24.1, 124.8, 124.9         All discharges of age 18 years and older.       Exclude: Discharges with a surgical procedure in any field (010-8699). Transfers <sup>1</sup> .       120.0, 120.1, 120.8, 120.9, 124. I24.1, 124.8, 124.9         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> EXCLUSIONS: All surgical procedures (stat with a K in the Danish versi the NCSP, which means surgical Prinzmetrafter: MIS CORONARY OCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS       120.0-J20.9*, J40.0-J40.9*, J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.	•	entitied by the Agency for Heathcare Research a	nu Quanty as Aeses in their repe
Numerator: Discharges with ICD-9-CM principal diagnosis code for angina (see below).I24.1, I24.8, I24.9All discharges of age 18 years and older.EXCLUSIONS: All surgical procedures (star with a K in the Danish versi the NCSP, which means surgional procedures)Exclude: Discharges with a surgical procedure in any field (010-8699).Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 41111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOSJ20.0-J20.9*, J40.0-J40.9*, (J20.0-J20.9*, J40.0-J40.9*, (I-OPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).J20.0-J20.9*, J40.0-J40.9*, (J41.0, J41.1, J42.0-J42.9, J43.)	Disease	Description in the AHRQ list	ICD-10
Numerator: Discharges with ICD-9-CM principal diagnosis code for angina (see below).I24.1, I24.8, I24.9All discharges of age 18 years and older.EXCLUSIONS: All surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan surgical procedures (stan with a K in the Danish versi the NCSP, which means surgical procedures (stan surgical procedures (stan surgical	Angina	Angina Without Procedure Admission Rate	I20 0 I20 1 I20 8 I20 9 I24 0
Discharges with ICD-9-CM principal diagnosis code for angina (see below).       Exclude:         All discharges of age 18 years and older.       Exclude:         Discharges with a surgical procedure in any field (010-8699).       Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         4111 INTERMED CORONARY SYND 4130       ANGINA DECUBITUS         41181 CORONARY OCLSN W/O MI 4131       PRINZMETAL ANGINA         41182 CORONARY OCCLSN W/O MI 4131       PRINZMETAL ANGINA         41189 AC ISCHEMIC HRT DIS NEC 4139       ANGINA PECTORIS NEC/NOS         Denominator: Population in MSA or county, age 18 years and older.       J20.0-J20.9*, J40.0-J40.9*, (COPD) Admission Rate         COPD (Chronic obstructive pulmonary liscases (core for COPD (see below).       J41.0, J41.1, J42.0-J42.9, J43.9, J44.0-J44.9, J47.0-J47.	ing ina		120.0, 120.1, 120.0, 120.9, 121.0
code for angina (see below).       All discharges of age 18 years and older.         All discharges of age 18 years and older.       Exclude:         Discharges with a surgical procedure in any field (010-8699).       Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         4111 INTERMED CORONARY SYND 4130       ANGINA DECUBITUS         41181 CORONARY OCCLSN W/O MI 4131       PRINZMETAL ANGINA         41189 AC ISCHEMIC HRT DIS NEC 4139       ANGINA PECTORIS NEC/NOS         Denominator: Population in MSA or county, age 18 years and older.       J20.0-J20.9*, J40.0-J40.9*, 143.0, J41.1, J42.0-J42.9, J43.9, J44.0-J44.9, J47.0-J47.2         COPD (Chronic obstructive pulmonary lisease (COPD) Admission Rate Numerator:       Discharges with ICD-9-CM principal diagnosis code for COPD (see below).			124.1, 124.0, 124.9
All discharges of age 18 years and older.       All surgical procedures (star with a K in the Danish versities NCSP, which means surgical procedure in any field (010-8699). Transfers <sup>1</sup> .       All surgical procedures (star with a K in the Danish versities NCSP, which means surgical procedures).         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS       J20.0-J20.9*, J40.0-J40.9*, J20.0-J20.9*, J40.0-J40.9*, Isorder) exacerbation         COPD (Chronic obstructive pulmonary lisorder) exacerbation       Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).       J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.			
All discharges of age 18 years and older.       with a K in the Danish versit the NCSP, which means surgities by the NCSP, which means surgities with a surgical procedure in any field (010-8699).       with a K in the Danish versit the NCSP, which means surgities the NCSP, which means surgities with a grant of the NCSP, which means surgities the NCSP, which means the NCSP, which means the NCSP, which means the NCSP, which means surgities the NCSP, which means the			
Exclude:       Discharges with a surgical procedure in any field (010-8699).       With a K in the Damish versus the NCSP, which means surgical procedure in any field (010-8699).         Transfers <sup>1</sup> .       MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS       Denominator: Population in MSA or county, age 18 years and older.         COPD (Chronic obstructive pulmonary lisorder) exacerbation       Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).       J20.0-J20.9*, J40.0-J40.9*, J43.9, J44.0-J44.9, J47.0-J47.		All discharges of age 18 years and older	
Discharges with a surgical procedure in any field (010-8699). Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS         Denominator: Population in MSA or county, age 18 years and older.         COPD (Chronic obstructive pulmonary disorder) exacerbation         Chronic Obstructive pulmonary disorder) exacerbation         Chronic Obstructive pulmonary disorder) exacerbation         Chronic Obstructive pulmonary disorder)         Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).		The discharges of uge to years and older.	with a K in the Danish versio
Discharges with a surgical procedure in any field (010-8699). Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS         Denominator: Population in MSA or county, age 18 years and older.         COPD (Chronic obstructive pulmonary lisorder) exacerbation         Chronic Obstructive pulmonary Discharges with ICD-9-CM principal diagnosis code for COPD (see below).		Exclude:	the NCSP, which means surg
(010-8699). Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM diagnosis codes:</b> 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS <b>Denominator:</b> Population in MSA or county, age 18 years and older. <b>COPD (Chronic obstructive pulmonary</b> <b>lisorder) exacerbation COPD (Chronic obstructive pulmonary</b> <b>lisorder) exacerbation Chronic Obstructive Pulmonary Disease</b> (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).			
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MDC 14 (pregnancy, childbirth, and puerperium)2ICD-9-CM diagnosis codes:4111 INTERMED CORONARY SYND 4130ANGINA DECUBITUS41181 CORONARY OCCLSN W/O MI 4131PRINZMETAL ANGINA41189 AC ISCHEMIC HRT DIS NEC 4139ANGINA PECTORIS NEC/NOSDenominator: Population in MSA or county, age 18 years and older.COPD (Chronic obstructive pulmonary lisorder) exacerbationChronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43.			
ICD-9-CM diagnosis codes:         4111 INTERMED CORONARY SYND 4130         ANGINA DECUBITUS         41181 CORONARY OCCLSN W/O MI 4131         PRINZMETAL ANGINA         41189 AC ISCHEMIC HRT DIS NEC 4139         ANGINA PECTORIS NEC/NOS         Denominator: Population in MSA or county, age         18 years and older.         COPD (Chronic obstructive pulmonary lisorder) exacerbation         Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).			
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41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOSDenominator: Population in MSA or county, age 18 years and older.COPD (Chronic obstructive pulmonary lisorder) exacerbationChronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.4			
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Denominator: Population in MSA or county, age 18 years and older.J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.4COPD (Chronic obstructive pulmonary lisorder) exacerbationChronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.4			
18 years and older.         COPD (Chronic obstructive pulmonary lisorder) exacerbation       Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).       J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.9		ANGINA PECTORIS NEC/NOS	
18 years and older.         COPD (Chronic obstructive pulmonary lisorder) exacerbation       Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).       J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.9			
COPD (Chronic obstructive pulmonary lisorder) exacerbationChronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43.9, J43.9, J44.0-J44.9, J47.0-J47.4			
<b>disorder) exacerbation</b> (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below). J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.9		18 years and older.	
<b>lisorder) exacerbation</b> (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below). J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.			
Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below).J41.0, J41.1, J42.0-J42.9, J43. J43.9, J44.0-J44.9, J47.0-J47.9			J20.0-J20.9*, J40.0-J40.9*,
Discharges with ICD-9-CM principal diagnosis code for COPD (see below).	lisorder) exacerbation		
Discharges with ICD-9-CM principal diagnosis code for COPD (see below). J43.9, J44.0-J44.9, J47.0-J47.9			J41.0, J41.1, J42.0-J42.9, J43.8
code for COPD (see below).			J43.9. J44.0-J44.9. J47.0-J47.9
All discharges of age 18 years and older.		code for COPD (see below).	
All discharges of age 18 years and older.			
		All discharges of age 18 years and older.	

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	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	*qualify only if accompanied by secondary diagnosis of any of the other codes listed under COPD
	ICD-9-CM diagnosis codes: 4660 AC BRONCHITIS* 4920 EMPHYSEMATOUS BLEB 490 BRONCHITIS NOS* 4928 EMPHYSEMA NEC 4910 SIMPLE CHR BRONCHITIS 494	N
	BRONCHIECTASIS -OCT00 4911 MUCOPURUL CHR BRONCHITIS 4940 BRONCHIECTAS W/O AC EXAC 49120 OBS CHR BRNC W/O ACT EXA OCT00- 49121 OBS CHR BRNC W ACT EXA 4941 BRONCHIECTASIS W AC EXAC 4918 CHRONIC BRONCHITIS NEC OCT00- 4919 CHRONIC BRONCHITIS NOS 496 CHR AIRWAY OBSTRUCT NEC	December 2015. Downloaded from http://bmjopen.bmj.com/ on Apri
	* Qualifies only if accompanied by secondary diagnosis of 491.xx, 492.x, or 496 (i.e., any other code on this list).	/bmjopen.bmj.co
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	m/ on Ap
CHF (Congestive heart failure) exacerbation	Congestive Heart Failure (CHF) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for CHF (see below).	I09.0-I09.9 I11.0, I13.0, I13.2, I13.9, I50.0, 201 I50.1, I50.9, I46.9
	All discharges of age 18 years and older. <b>Exclude:</b> Discharges with cardiac procedure codes (see below) in any field. Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	EXCLUSION: Cardiac procedures: Protected KFNG02, KFNG05, KFNA, KFNC, KFT, KFW, KFQ, BFCA01-BFCA07
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1 2 3			36/bmjopen-2015-
4		ICD 0 CM diagnosis and as	-009878 on
5		ICD-9-CM diagnosis codes: 39891 RHEUMATIC HEART FAILURE 40413	878
6		BEN HYP HRT/REN W CHF&RF	or
7		40201 MAL HYPERT HRT DIS W CHF 40491	N
8		HYPER HRT/REN NOS W CHF	December 2015
9		40211 BENIGN HYP HRT DIS W CHF 40493	Cen l
10		HYP HT/REN NOS W CHF&RF	nbe
11		40291 HYPERTEN HEART DIS W CHF 4280	N N
12		CONGESTIVE HEART FAILURE	018
13		40401 MAL HYPER HRT/REN W CHF 4281	•
14 15		LEFT HEART FAILURE	OO W
16		40403 MAL HYP HRT/REN W CHF&RF 4289	Downloaded
17		HEART FAILURE NOS 40411 BEN HYPER HRT/REN W CHF	ad
18		Exclude ICD-9-CM procedure codes:	d f
19		3601 PTCA-1 VESSEL W/O AGENT 3619 HRT	ron
20		REVAS BYPS ANAS NEC	
21		3602 PTCA-1 VESSEL WITH AGNT 375 HEART	
22		TRANSPLANTATION	
23		3605 PTCA-MULTIPLE VESSEL 3770 INT	<u>n</u> o
24		INSERT PACEMAK LEAD	per
25		3606 INSERT CORONARY ART STENT OCT95-	
26		3771 INT INSERT LEAD IN VENT	<u>,                                    </u>
27		3610 AORTOCORONARY BYPASS NOS 3772	Š.
28		INT INSER LEAD ATRI-VENT	o o
29		3611 AORTOCOR BYPAS-1 COR ART 3773 INT	
30		INSER LEAD IN ATRIUM	pr <u>i</u>
31 32		3612 AORTOCOR BYPAS-2 COR ART 3774 INT OR REPL LEAD EPICAR	17
32 33		3613 AORTOCOR BYPAS-3 COR ART 3775	from http://bmjopen.bmj.com/ on April 17, 2024
34		REVISION OF LEAD	024
35		3614 AORTCOR BYPAS-4+ COR ART 3776	by
36		REPL TV ATRI-VENT LEAD	ng
37		3615 1 INT MAM-COR ART BYPASS 3777	est
38		REMOVAL OF LEAD W/O REPL	י. ד
39		3616 2 INT MAM-COR ART BYPASS 3778	ote
40		INSER TEMP PACEMAKER SYS	cte
41		3617 ABD-CORON ART BYPASS OCT96- 3779	d b
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	<b>Denominator:</b> Population in MSA or county, age 18 years and older.		
Diabetes (with short-term complications)	<ul> <li>Diabetes Short-term Complications Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for short-term complications (ketoacidosis, hyperosmolarity, coma) (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Transfers<sup>1</sup>. MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 25010 DM KETO T2, DM CONT 25022 DM W/ HYPROSM T2, DM UNCNT 25011 DM KETO T1, DM CONT 25023 DM W/ HYPROSM T1, DM UNCNT 25012 DM KETO T2, DM UNCONT 25030 DM COMA NEC T2, DM CONT 25013 DM KETO T1, DM UNCONT 25031 DM COMA NEC T1, DM CONT 25020 DM W/ HYPROSM T2, DM CONT 25032 DM COMA NEC T2, DM UNCONT 25021 DM W/ HYPROSM T1, DM CONT 25033 DM COMA NEC T1, DM UNCONT</li> <li>Penominator: Population in MSA or county, age 18 years and older.</li> </ul>	E10.0, E10.1, E11.0, E11.1,	
Diabetes (uncontrolled (without short- term or long-term complications))	Uncontrolled Diabetes Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for uncontrolled diabetes, without mention of	E10.9, E11.9	

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 $\begin{array}{c} 20\\ 21\\ 22\\ 23\\ 24\\ 25\\ 26\\ 27\\ 28\\ 29\\ 30\\ 31\\ 32\\ 33\\ 35\\ 36\\ 37\\ 38\\ 40\\ 41\\ 43\\ 44\\ 5\\ 46\\ 47\\ 48\\ \end{array}$ 

 $\begin{array}{c} 21 \\ 22 \\ 23 \\ 25 \\ 26 \\ 27 \\ 28 \\ 29 \\ 30 \\ 31 \\ 32 \\ 33 \\ 35 \\ 36 \\ 37 \\ 38 \\ 39 \\ 40 \\ 41 \end{array}$ 

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Exclude: Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 25002 DM, T2, UNCONT 25003 DM, T1, UNCONT         Denominator: Population in MSA or county, age 18 years and older. May be combined with diabetes short-term complications as a single indicator.         Diabetes (with long-term omplications)         Diabetes Long-term Complications Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).         All discharges of age 18 years and older.         Exclude: Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
Transfers <sup>1</sup> .       MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:       25002 DM, T2, UNCONT         25003 DM, T1, UNCONT       Denominator: Population in MSA or county, age         18 years and older.       May be combined with diabetes short-term complications as a single indicator.         Diabetes (with long-term complications admission Rate       E         Numerator:       Disbetes Long-term Complications Admission (complications)         Diabetes long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).         All discharges of age 18 years and older.         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         25002 DM, T2, UNCONT         25003 DM, T1, UNCONT         Denominator: Population in MSA or county, age         18 years and older.         May be combined with diabetes short-term         complications as a single indicator.         Diabetes (with long-term omplications admission momplications)         Diabetes Long-term Complications Admission momplications         Bischarges with ICD-9-CM principal diagnosis code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).         All discharges of age 18 years and older.         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
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25003 DM, T1, UNCONTDenominator: Population in MSA or county, age 18 years and older. May be combined with diabetes short-term complications as a single indicator.Diabetes (with long-term complications)Diabetes Long-term Complications Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).All discharges of age 18 years and older.Exclude: Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
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Diabetes (with long-term complications)       Diabetes Long-term Complications Admission Rate       E         Numerator:       Discharges with ICD-9-CM principal diagnosis code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).       All discharges of age 18 years and older.         Exclude:       Transfers <sup>1</sup> .       MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:       25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
Rate         Numerator:         Discharges with ICD-9-CM principal diagnosis         code for long-term complications (renal, eye,         neurological, circulatory, or complications not         otherwise specified) (see below).         All discharges of age 18 years and older.         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         25040 DM RENAL COMP T2 CONT 25070 DM         CIRCU DIS T2 CONT	
Rate       Numerator:         Discharges with ICD-9-CM principal diagnosis       code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).         All discharges of age 18 years and older.         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         25040 DM RENAL COMP T2 CONT 25070 DM         CIRCU DIS T2 CONT	10.2-E10.8, E11.2-E11.8
Numerator:         Discharges with ICD-9-CM principal diagnosis         code for long-term complications (renal, eye,         neurological, circulatory, or complications not         otherwise specified) (see below).         All discharges of age 18 years and older.         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes:         25040 DM RENAL COMP T2 CONT 25070 DM         CIRCU DIS T2 CONT	,
<ul> <li>code for long-term complications (renal, eye, neurological, circulatory, or complications not otherwise specified) (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Transfers<sup>1</sup>. MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT</li> </ul>	
neurological, circulatory, or complications not otherwise specified) (see below). All discharges of age 18 years and older. <b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM diagnosis codes:</b> 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
otherwise specified) (see below). All discharges of age 18 years and older. <b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM diagnosis codes:</b> 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
All discharges of age 18 years and older. <b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM diagnosis codes:</b> 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
<ul> <li>Exclude: Transfers<sup>1</sup>. MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT</li> </ul>	
Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM diagnosis codes:</b> 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
<b>ICD-9-CM diagnosis codes:</b> 25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
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CIRCU DIS T1 CONT 25042 DM RENAL COMP T2 UNCNT 25072 DM	
25042 DM RENAL COMP T2 UNCNT 25072 DM CIRCU DIS T2 UNCNT	
25043 DM RENAL COMP T1 UNCNT 25073 DM	

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	CIRCU DIS T1 UNCNT 25050 DM EYE COMP T2 CONT 25080 DM W COMP NEC T2 CONT 25051 DM EYE COMP T1 CONT 25081 DM W COMP NEC T1 CONT 25052 DM EYE COMP T2 UNCNT 25082 DM W COMP NEC T2 UNCNT 25053 DM EYE COMP T1 UNCNT 25083 DM W COMP NEC T1 UNCNT 25060 DM NEURO COMP T2 CONT 25090 DM W COMPL NOS T2 CONT 25061 DM NEURO COMP T1 CONT 25091 DM W COMPL NOS T1 CONT 25062 DM NEURO COMP T2 UNCNT 25092 DM W COMPL NOS T2 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT	
(TN (Hypertension)	<ul> <li>Hypertension Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for hypertension (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Discharges with cardiac procedure codes (see below) in any field. Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 4010 MALIGNANT HYPERTENSION 40310 BENIGN HYP HRT DIS W/OUT RF 4019 HYPERTENSION NOS 40390 HYPERTEN HEART DIS W/OUT RF</li> </ul>	I10.0-I10.9, I11.9, I12.9, I13.9 EXCLUSION: Cardiac procedures: KFNG02, KFNG05, KFNA, KFNC, KFT, KFW, KFQ, BFCA01-BFCA07

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	40200 MAL HYPERTEN HRT DIS W/OUT CHF 40400 MAL HYPER HRT/REN W/OUT CHF/RF			
	40210 BEN HYPERTEN HRT DIS W/OUT CHF 40410 BEN HYPER HRT/REN W/OUT CHF/RF 40290 HYPERTENSIVE HRT DIS W/OUT CHF 40490 HYPER HRT/REN NOS W/OUT CHF/RF			
	40300 MAL HYPERT HRT DIS W/OUT RF Exclude ICD-9-CM procedure codes: 3601 PTCA-1 VESSEL W/O AGENT 3619 HRT REVAS BYPS ANAS NEC			
	3602 PTCA-1 VESSEL WITH AGNT 375 HEART TRANSPLANTATION 3605 PTCA-MULTIPLE VESSEL 3770 INT			
	INSERT PACEMAK LEAD 3606 INSERT CORONARY ART STENT OCT95- 3771 INT INSERT LEAD IN VENT 3610 AORTOCORONARY BYPASS NOS 3772			
	INT INSER LEAD ATRI-VENT 3611 AORTOCOR BYPAS-1 COR ART 3773 INT INSER LEAD IN ATRIUM 3612 AORTOCOR BYPAS-2 COR ART 3774 INT			
	OR REPL LEAD EPICAR 3613 AORTOCOR BYPAS-3 COR ART 3775 REVISION OF LEAD 3614 AORTCOR BYPAS-4+ COR ART 3776			
	REPL TV ATRI-VENT LEAD 3615 1 INT MAM-COR ART BYPASS 3777 REMOVAL OF LEAD W/O REPL	Or		
	3616 2 INT MAM-COR ART BYPASS 3778 INSER TEMP PACEMAKER SYS 3617 ABD-CORON ART BYPASS OCT96- 3779 REVIS OR RELOCATE POCKET			
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.			
Perforated appendicitis	Perforated Appendix Admission Rate Numerator: Discharges with ICD-9-CM diagnosis code for	K35.0, K35.1, K35.2, K35.3		

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	in any field.	600
	All discharges of age 18 years and older.	878 or
	<b>Exclude:</b> Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	1 2 Decembe
	<b>ICD-9-CM diagnosis codes (outcome of interest):</b> 5400 AC APPEND W PERITONITIS 5401 ABSCESS OF APPENDIX	ar 2015. Dow
	<b>ICD-9-CM diagnosis codes (population at risk):</b> 5400 AC APPEND W PERITONITIS 5409 ACUTE APPENDICITIS NOS 5401 ABSCESS OF APPENDIX 541 APPENDICITIS NOS	December 2015. Downloaded from http://bmjopen.bmj
	<b>Denominator:</b> Number of discharges with diagnosis code for appendicitis in any field in MSA or county.	//bmjopen.bmj.c
Pneumonia	Bacterial Pneumonia Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for bacterial pneumonia (see below).	J13-J14.9, J15.3-J15.4, J15.7-J13.9         J16.0-J16.9, J18.0-J18.9 <u>EXCLUSION:</u> Sickle cell disorders         D57.0-D57.9
	All discharges of age 18 years and older.	Sickle cell disorders 77 D57.0-D57.9
	<b>Exclude:</b> Discharges with diagnosis code for sickle cell anemia or HB-S disease (see below) in any field. Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	124 by guest. Protected by copyright
	ICD-9-CM diagnosis codes: 481 PNEUMOCOCCAL PNEUMONIA 48230	ectec

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	4822 H.INFLUENZAE PNEUMONIA 48231 GRP A STREP PNEUMONIA 4829 BACTERIAL PNEUMONIA NOS 48232 GRP B STREP PNEUMONIA 4830 MYCOPLASMA PNEUMONIA 48239 OTH STREP PNEUMONIA 4831 CHLAMYDIA PNEUMONIA 0CT96- 485 BRONCOPNEUMONIA ORG NOS 4838 OTH SPEC ORG PNEUMONIA 486 PNEUMONIA, ORGANISM NOS <b>Exclude ICD-9-CM diagnosis codes:</b> 28260 SICKLE-CELL ANEMIA NOS 28263 SICKLE-CELL/HB-C DISEASE 28261 HB-S DISEASE W/O CRISIS 28269 SICKLE-CELL ANEMIA NEC 28262 HB-S DISEASE WITH CRISIS	
Is (urinary tract infections)	Urinary Tract Infection Admission Rate         Numerator:         Discharges with ICD-9-CM principal diagnosis         code of urinary tract infection (see below).         Exclude:         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD 0 CM diagnosis codes:	N10.0-N12.9, N15.1-15.9, N N30.9, N34.0-N34.9, N39.0
	ICD-9-CM diagnosis codes:59000 CHR PYELONEPHRITIS NOS 59080PYELONEPHRITIS NOS59001 CHR PYELONEPH W MED NECR 59081PYELONEPHRIT IN OTH DIS59010 AC PYELONEPHRITIS NOS 5909INFECTION OF KIDNEY NOS59011 AC PYELONEPHR W MED NECR 5950AC CYSTITIS5902 RENAL/PERIRENAL ABSCESS 5959CYSTITIS NOS5903 PYELOURETERITIS CYSTICA 5990 URINTRACT INFECTION NOS	

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	<b>Denominator:</b> Population in MSA or county.	36/bmjopen-2015-009878
Adult Asthma exacerbation	Adult Asthma Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code of asthma (see below).All discharges of age 18 years and older.Exclude: Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 49300 EXT ASTHMA W/O STAT ASTH 49320 CH OB ASTH W/O STAT ASTH 49301 EXT ASTHMA W STATUS ASTH 49321 CH OB ASTHMA W STATUS ACEX OCT00- 49322 CH OB ASTHMA W STAT ACEX 49310 INT ASTHMA W/O STAT ASTH OCT00-	J45, J46 0n 2 December 2015. Downloaded from http://bmjopen.bmj.com/ on April 17, 202
	49311 INT ASTHMA W STATUS ASTH 49390 ASTHMA W/O STATUS ASTHM 49312 INT ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ASTHMAT 49392 ASTHMA W STATUS AC EXAC OCT00- <b>Denominator:</b> Population in MSA or county, age 18 years and older.	bmj.com/ on April 17, 202
Amputations (diabetes-related)	Rate of Lower-extremity Amputation among Patients with Diabetes Numerator: Discharges with ICD-9-CM procedure code for lower-extremity amputation (see below) in any field and diagnosis code of diabetes in any field (see below).All discharges of age 18 years and older.	289.4-289.7 *qualify only if registered with diabetes in the Danish National Diabetes Register or if registered with a diagnosis of diabetes (ICD-10:ETO- 14, H36.0, O24, excluding O24.4) at the same admission as the ACSC of
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1 2		36/bmjopen-2015
3 4		-009878 on
5	Exclude:	878
6	Trauma (see below).	on on
7	Transfers <sup>1</sup> .	
8 9	MDC 14 (pregnancy, childbirth, and puerperium) $^2$	EXCLUSION: Traumatic amputations of lowsr limb
10		<b>Traumatic amputations of low</b> $\mathbf{\widehat{s}}$ <b>r</b>
11		limb ह
12	ICD-9-CM procedure codes: 8410 LOWER LIMB AMPUTAT NOS 8415	
13	BELOW KNEE AMPUTAT NEC	S78.0-S78.9, S88.0-S88.9, S98.0
14	8411 TOE AMPUTATION 8416	
15	DISARTICULATION OF KNEE	S98.4, T05.3-T05.5 Downloaded from http://bmjopen.bmj.com/ on April 17, 2024
16	8412 AMPUTATION THROUGH FOOT 8417	
17	ABOVE KNEE AMPUTATION	dec
18	8413 DISARTICULATION OF ANKLE 8418	1 frc
19	DISARTICULATION OF HIP	E E E E E E E E E E E E E E E E E E E
20	8414 AMPUTAT THROUGH MALLEOLI 8419	The second
21 22	HINDQUARTER AMPUTATION	
23	ICD-9-CM diagnosis codes for diabetes: 25000 DMII WO CMP NT ST UNCNTR 25050	<u>n</u>
24	DMII OPHTH NT ST UNCNTRL	ope
25	25001 DMI WO CMP NT ST UNCNTRL 25051	n.b
26	DMI OPHTH NT ST UNCNTRLD	<u>.</u>
27	25002 DMII WO CMP UNCNTRLD 25052 DMII	
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29	25003 DMI WO CMP UNCNTRLD 25053 DMI	V on April 17, 202
30	OPHTH UNCNTRLD	, prii
31	25010 DMII KETO NT ST UNCNTRLD 25060	17
32 33	DMII NEURO NT ST UNCNTRL 25011 DMI KETO NT ST UNCNTRLD 25061	, 20
34	DMI NEURO NT ST UNCNTRLD 25001	024
35	25012 DMII KETOACD UNCONTROLD 25062	- by
36	DMII NEURO UNCNTRLD	guest.
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38	DMI NEURO UNCNTRLD	P
39	25020 DMII HPRSM NT ST UNCNTRL 25070	ote
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8960 AMPUTATION FOOT, UNILAT 8973 AMPUT ABV KN, UNIL-COMPL 8961 AMPUT FOOT, UNILAT-COMPL 8974 AMPUTAT LEG, UNILAT NOS 8962 AMPUTATION FOOT, BILAT 8975 AMPUT LEG, UNIL NOS-COMP 8963 AMPUTAT FOOT, BILAT-COMP 8976 AMPUTATION LEG, BILAT 8970 AMPUT BELOW KNEE, UNILAT 8977 AMPUTAT LEG, BILAT-COMPL	April 17, 2024 by guest. Protected by copyright.
<b>Denominator:</b> Population in MSA or county, age 18 years and older.	cied by co
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Γ	is followed by another admission date with an overlap of +/- 1 day this is counted as one admission. <sup>2</sup> The exclu
<sup>1</sup> Transfers imply that if a discharge date a obstetric admissions was performed if an The obstetric diagnostic codes included:	in the presence of the present of the present of the present of the present of the presence o
<b>Appendix 4: Information</b> <b>Statistics Denmark</b>	mation on socioeconomic position (SEP) obtained from
Education level	Δ.
< 10 years	
10-15 years	
> 15 years	
<i>Civil status</i>	
Living alone/single	
Cohabitation	
Partners	
Married	
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	BMJ Open ne ACSC-predisposing medical comorbidity obtained from the Danish Danish National Diabetes Register and the Danish National Prescripti	njopen-2(
Appendix 5: Information on th	e ACSC-predisposing medical comorbidity obtained from the Danish	015-00
National Patient Register, the B Registry.	Danish National Diabetes Register and the Danish National Prescripti	ion <sup>878</sup>
ACSC Outcome	ACSC-predisposing medical comorbidity	on 2
Chronic conditions		De
Angina	Myocardial infarction <sup>1</sup>	cembe
CHF exacerbation	CHF <sup>1</sup>	r 20
HTN	Myocardial infarction <sup>1</sup>	 
	CHF <sup>1</sup>	Do
	Cerebrovascular disease <sup>1</sup>	wnl
	Peripheral vascular disease <sup>1</sup>	oad
Diabetes-related ACSCs	Diabetes <sup>2</sup>	d f
COPD exacerbation	Chronic pulmonary disease <sup>1</sup>	- ion
	ACSC-predisposing medical comorbidity         Myocardial infarction <sup>1</sup> CHF <sup>1</sup> Myocardial infarction <sup>1</sup> CHF <sup>1</sup> Myocardial infarction <sup>1</sup> CHF <sup>1</sup> Cerebrovascular disease <sup>1</sup> Peripheral vascular disease <sup>1</sup> Diabetes <sup>2</sup> Chronic pulmonary disease <sup>1</sup> or         Redemption of at least 2 prescriptions of drugs for obstructive air diseases within 6 months <sup>3</sup> Chronic pulmonary disease <sup>1</sup> or         Redemption of at least 2 prescriptions of drugs for obstructive air diseases within 6 months <sup>3</sup>	http://bmjo
	Redemption of at least 2 prescriptions of drugs for obstructive air diseases within 6 months <sup>3</sup>	tway
		j.com/
Adult asthma exacerbation	Chronic pulmonary disease <sup>1</sup>	on Apr
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	Redemption of at least 2 prescriptions of drugs for obstructive air diseases within 6 months <sup>3</sup>	way by
		gues
Acute conditions		F
Perforated appendicitis	-	rotect
Pneumonia	-	ed by
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5 BMJ Open UTI - <sup>1</sup> Obtained from the Danish National Patient Register using the algorithm defined in the Charlson Con Index (see appendix 6).		
UTI	-	
Obtained from the Danish Nati	onal Patient Register using the alg	orithm defined in the Charlson Comort
	onal Diabetes Register (see append	
	ional Prescriptions Registry (see appendiculation of the second	
	chronic diseases included in the (	Charlson Comorbidity Index
obtained from the Danish Nat	ICD-8	ICD-10
Myocardial infarction	410	I21;I22;I23
Congestive heart failure	427.09, 427.10, 427.11,	150; 111.0; 113.0; 113.2
congestive neart fanale	427.19, 428.99, 782.49	130, 111.0, 113.0, 113.2
Peripheral vascular disease	440, 441, 442, 443, 444,	170; 171; 172; 173; 174; 177
	445,	
Cerebrovascular disease	430-438	I60-I69; G45; G46
Dementia	290.09-290.19, 293.09	F00-F03; F05.1; G30
Chronic pulmonary disease	490-493, 515-518	J40-J47; J60-J67; J68.4; J70.1;
		J70.3; J84.1; J92.0; J96.1; J98.2; J98.3
Connective tissue disease	712, 716, 734, 446, 135.99	M05; M06; M08; M09;M30;M31;
		M32; M33; M34; M35; M36; D86
Ulcer disease	530.91, 530.98, 531-534,	K22.1; K25-K28
Mild liver disease	571, 573.01, 573.04	B18; K70.0-K70.3; K70.9; K71;
Dishotos mallitus	240.00 240.06 240.07	K73; K74; K76.0
Diabetes mellitus	249.00, 249.06, 249.07, 249.09, 250.00, 250.06,	E10.0, E10.1; E10.9; E11.0; E11.1; E11.9
	2+7.07, 250.00, 250.00,	L11.1, L11.7

obtained from the Danish Nati	ronic diseases included in the C onal Patient Register	charison Comorbiuity midex
	ICD-8	ICD-10
Myocardial infarction	410	I21;I22;I23
Congestive heart failure	427.09, 427.10, 427.11,	150; 111.0; 113.0; 113.2
	427.19, 428.99, 782.49	
Peripheral vascular disease	440, 441, 442, 443, 444,	170; 171; 172; 173; 174; 177
	445,	
Cerebrovascular disease	430-438	I60-I69; G45; G46
Dementia	290.09-290.19, 293.09	F00-F03; F05.1; G30
Chronic pulmonary disease	490-493, 515-518	J40-J47; J60-J67; J68.4; J70.1;
		J70.3; J84.1; J92.0; J96.1; J98.2; J98.3
Connective tissue disease	712, 716, 734, 446, 135.99	M05; M06; M08; M09;M30;M31;
		M32; M33; M34; M35; M36; D86
Ulcer disease	530.91, 530.98, 531-534,	K22.1; K25-K28
Mild liver disease	571, 573.01, 573.04	B18; K70.0-K70.3; K70.9; K71;
		K73; K74; K76.0
Diabetes mellitus	249.00, 249.06, 249.07,	E10.0, E10.1; E10.9; E11.0;
	249.09, 250.00, 250.06,	E11.1; E11.9

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	250.07, 250.09	
Hemiplegia	344	G81; G82
Moderate/severe renal	403,404,580-583, 584,	I12; I13; N00-N05; N07; N11;
Disease	590.09, 593.19, 753.10-	N14; N17-N19; Q61
	753.19, 792	
Diabetes mellitus with	249.01-249.05, 249.08,	E10.2-E10.8; E11.2-E11.8
chronic complications	250.01-250.05, 250.08	
Any tumour	140-194	C00-C75
Leukaemia	204-207	C91-C95
Lymphoma	200-203, 275.59	C81-C85; C88; C90; C96
Moderate/severe liver	070.00, 070.02, 070.04,	B15.0; B16.0; B16.2; B19.0;
Disease	070.06, 070.08, 573.00,	K70.4; K72; K76.6; I85
	456.00-456.09	
Metastatic solid tumour	195-198, 199	C76-C80
AIDS	079.83	B21-B24

•	
Ap	opendix 7: Information on diabetes obtained from the Danish National Diabetes Register.
Al	gorithm: Individuals were classified as having diabetes on the day where at least one of the
fol	lowing six criteria was met:
1.	A diagnosis of diabetes made at any Danish hospital as registered in the Danish National Patient
	Register (ICD-8:249, 250; ICD-10:E10-14, H36.0, O24, excluding O24.4).
2.	A referral to chiropody of diabetic patients as registered in the Danish National Health Service
	Register.(Andersen <i>et al.</i> 2011)
3.	Five blood glucose measurements within one year as registered in the Danish National Health
	Service Register.
4.	Two blood glucose measurements per year for five consecutive years as registered in the Danish
	National Health Service Register.
5.	Two redemptions of oral anti-diabetic drugs within six months as registered in the Danish National
	Prescription Registry.
6.	Two redemptions of prescribed insulin as registered in the Danish National Prescription Registry.

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Appendix 8: ATC National Prescripti	codes for drugs for obstructive airway disease obtained from the Danish on Registry.
ATC codes	Type of drug
R03	Drugs for obstructive airway diseases
R03A	Adrenergics, inhalants
R03B	Other drugs for obstructive airway diseases, inhalants
R03C	Adrenergics for systemic use
R03D	Other systemic drugs for obstructive airway diseases

Appendix 9: Information on substance abuse disorders obtained from the Danish National Patient Register and the Danish Psychiatric Central Register.

ychiatric Central Regist	er.
ICD-8	ICD-10
304.09, 304.19	F11.0–F11.9
304.59	F12.0–F12.9
304.29, 304.39	F13.0–F13.9
304.49	F14.0–F14.9
304.69	F15.0–15.9
304.79	F16.0–F16.9
304.89, 304.99	F18.0–F19.9
291.09-291.99	F10.0–F10.9
303.09-303.99	
571.09, 571.10, 571.19	K70.0-K70.9
456.00, 456.01, 456.09	I85.0–I85.9
	ICD-8 304.09, 304.19 304.59 304.29, 304.39 304.49 304.69 304.69 304.79 304.89, 304.99 291.09–291.99 303.09–303.99 571.09, 571.10, 571.19

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# The risk of ACSCs and rehospitalizations for AGSCs among persons with depression

		Considerations	
Study			
population:	<ul> <li>Depression study</li> <li>All persons born in Denmark, alive and minimum 18 years of age and still living in Denmark at some time between January 1, 1999 and December 31, 2013.</li> <li>Sub-analysis: Stratified by age categories: ≤ 40, 41-65, ≥ 65 (i.e., adult, middle-aged, older adults)</li> </ul>		
Follow-up:	January 1, 2005-December 31,2013	This enables us to make sure who has a mental disorder between 1995 and 2005	~
Censor-in	18 years of birthday or study start, whichever comes last.	We do not want to include children. And also, this definition is a part of the AHRQ list. No age maximum.	7/
Censor-out	Emigration, death, SMI diagnosis or study end whichever comes first.	We will censor out persons with SMI!	
Dropping individuals	<ul> <li>Out-censored before in- censored (children and young persons dying before their 18th years birthday, or emigration, SMI diagnosis or death before study start).</li> </ul>		

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xposure		
	Depression	<ul> <li>Time-dependent variable (see Appendix 1):</li> <li><u>All cases</u> of depression between 1969 and 2013 (diagnoses-in and outpatient contacts) and between 1995 and 2013 (prescriptions). Remember that depression identified by redemptions need at least 2 prescriptions within 6 months.</li> </ul>
		Sub-analysisRisk of ACSC-related hospitalizations by depression diagnosis-type (i.e., our rough proxy for depression severity):1)Psychiatric hospitalization for depression2)Outpatient depression diagnosis only3)Antidepressant prescriptions only
	Dual diagnosis	If a person has a primary care determined depression it is overruled by a diagnosis from the registers (the secondary health care).
Outcome		
	<ol> <li>The number of hospitalizations for ACSCs (Ambulatory care sensitive conditions) during follow- up</li> <li>hospitalization rates for the following categories:</li> </ol>	<ol> <li><u>The algorithm</u>: We have modified this outcome measure because it is classified according to ICD-9 (and diagnoses in Denmark are according to ICD-8 before 1994 and ICD-10 since 1995).</li> </ol>
	Using codes from the Danish ACSC validation paper(Schiotz <i>et al.</i> 2011): -Angina -COPD exacerbation -Congestive heart failure exacerbation -Diabetes-short term compl. -Diabetes long-term compl. -Diabetes- uncontrolled	We have used a <u>validated algorithm</u> from a Danish 'translated versions' in a Danish article (Schiotz <i>et al.</i> 2011). However, as this version does not include all of the categories of ACSCs from the AHRQ list, we have additionally included for all practical purposes, the rest of the categories (pneumonia, amputations, urinary tract infections, and asthma) (and a translation of the codes from ICD-9 to 10 have been conducted with inspiration

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-Hypertension -Appendicitis	from algorithms from previous Danish papers).	
Using codes with inspiration from Danish register-based studies (or own algorithms): -Bacterial Pneumonia(Nielsen et al. 2012) -Lower extremities amputations (Jorgensen et al. 2014) -Urinary tract infections -Adult asthma exacerbation (Andersen et al. 2013) combine COPD exacerbation and adult asthma exacerbation into a single category for analyses 2. The number of rehospitalizations within 30 days after the index ACSC hospitalization for the same ACSC or for a different ACSC	<ul> <li>This means that the only diseases not included in this model (compared to the original AHRQ list) are dehydration, immunizations, and IUGR.</li> <li>2) Inpatient contacts only: Per definition ACSCs includes ONLY inpatient.</li> <li>3) Principal discharge diagnosis (see Danish article or Davydow 2013)</li> <li>4) Appendicitis with perforation</li> <li>5) Epidemiological considerations One of the major epidemiological considerations</li> <li>One of the major epidemiological considerations for this study is the fact that persons with mental illness have higher rates for chronic diseases and are also more likely to receive poor quality of care treatment. If we show these persons have higher risk of ACSC we will have difficulty disentangling the increased risk of chronic diseases from the increased risk of suboptimal treatment. But the causal mechanism is likely to include both, and it will have to be discussed!!</li> <li>6) Exclusions: <ul> <li>All transfers: Unfortunately we do</li> </ul> </li> </ul>	
	not have access to data on transfers between hospitals. If a discharge date is followed by another admission date with an overlap of 1 day then we only count this as 1 admission. See the table for how to count the ACSCs.	
	- Procedures for angina: Exclusions	

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		of angina cases who has had ANY surgical procedures (NCSP surgical codes) at the SAME admission. - Specific exclusions concerning	
		diabetic amputations and concerning pneumonia	
Covariates			
Demographic	Age, gender, calendar period.	We are adjusting for age as a time- dependent variable divided into 2 years age- bands.	
		We are adjusting for calendar period as a time-dependent variable divided into 1 year-time-bands.	
Socio- economic position (SEP)	Depression paper Marital status (married, registered partners, cohabitant or single). Income (OECD-adjusted household income)		
Comorbidity	Educational level		40.
Medical comorbidity (See Appendices 6- 8)	Diagnoses included in the Charlson Comorbidity index except for diabetes, which will come from the Diabetes Register, COPD/asthma exacerbations which will come from the combination of the CCI chronic pulmonary disease category and prescriptions.	Time-dependent We will identify hospital contacts for the chronic somatic diseases included in the CCI. Each diagnosis will be entered into the models as a time-dependent covariate. From 1995 onwards, outpatient contacts are also included.	0 1 1
		Adjusting for each category of disease from the CCI (instead of using an index).	

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	Substance abuse	See appendix 10	
Health care utilization	Primary care visits (Face-to-Face-contacts=0101 contacts)	# of GP visits during the follow-up period for each individual	
		Time-dependent	
	In the analyses, we will categorize according to the interquartile range of PCP visits in the cohort We will count PCP visits from 10-	This could be confounded by indication, but reduced contacts to GP and hospitals could also be an intermediate variable between mental illness and ACSC.	
<u></u>	375 days before any given day.	6	
Statistical Analyses			
	Poisson regression with variance adjusted for clustering. <u>Outcome measures</u> : -number of hospitalizations per	I. The outcome will be the number of these events since we will be using Poisson regression models. The outcome measure is rate ratio	
	person years (rate measure). -rate ratios, RR	which approximates the relative risks.	
		-We make the analysis for any ACSC and subsequently the analyses for each category , dividing into "chronic" ACSCs and "acute" ACSCs.	h
		a) <u>Sub-analyses for the time since</u> <u>analyses</u> b) <u>Analyses with adjustments</u>	07/1
		For depression study Adjustment: Models 1-5: 1) age, gender and calendar period, 2)SEP, 3) ACSC-predisposing comorbidity for chronic ACSCs, 4) non-ACSC- predisposing comorbidity and substance abuse, 5) GP contacts	
		<ul> <li>a) Sub-analysis: Stratified by age</li> <li>categories: ≤ 40, 41-65, ≥ 65 (i.e.,</li> <li>adult, middle-aged, older adults),</li> </ul>	



		<ul> <li>adjusted in sequence of Models 1- 5</li> <li>b) Sensitivity analysis: depression diagnosis type analysis (hospitalization for depression vs. outpatient depression vs. prescription alone), adjusted in sequence of Models 1-5</li> <li>c) Time since depression diagnosis (adjusted for age, sex and calendar period)</li> <li>II. 30-day rehospitalizations for the same or another ACSC adjusted for demographics, then SES and comorbidity</li> </ul>
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Regarding transfers		
	Second a	dmission
First admission	ACSC	Non-ACSC
ACSC	Count the second ASCS*	Count the ACSC-admission
Non-ACSC	Count the ACSC-admission	Count as 0

\*This means that if the ACSC diagnoses are two different that it will be the second admission that counts.

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Appendices			015-009
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EXPOSURES (Appendices 1-3)			December
APPENDIX 1: Information on depr National Prescription	ession obtained from the Danish n Registry	Psychiatric Ce	entral Register and the Dani
A diagnosis of depression was identified	l if at least one of the following criteria	applied:	nloade
<ul> <li>And/or</li> <li>2. Registration of at least one prescription National Prescription Registry</li> <li>Diagnosis according to a record of depresent of the prescription of the pres</li></ul>	evia.		Downloaded from http://bmjopen.bmj.com/ on April 17, 2024
ICD-8	ICD-10		0
296.09, 296.29, 296.99, 298.09, 300.49, and 300.19	F32, F33		on April 1
	intions for antidoprossants in the Danie	ch National Droc	
Diagnosis according to a record of prescr Name	Drug	ATC-codes	
			Gription Registry:

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		N06AG
Other antidepressants	Mianserin, nefazodone, mirtazapine, venlafaxine, reboxetine, duloxetine, and agomelatine	N06AX

	ICD-8	ICD-10
Schizophrenia	295 (excluding 295.79)	F20
Schizoaffective disorders	295.79, 296.8	F25
Bipolar affective disorders	296.19, 296.39	F30, F31

Schizoaffective disorders 295.79, 296.8 F25   Bipolar affective disorders 296.19, 296.39 F30, F31   Dutcome   Definition of outcome measures for the ACSC (see Appendix 4)   Categories   Any of the categories		ICD-8	ICD-10	
Bipolar affective disorders 296.19, 296.39 F30, F31  Dutcome  Definition of outcome measures for the ACSC (see Appendix 4)  Categories  Ny ACSC Any of the categories  Ype of ACSC Any of the categories  Ype of ACSC Any of the categories  COPD/adult asthma exacerbation CHF exacerbation Diabetes-related ACSC The 3 diabetes categories + amputations HTN Perforated appendicitis Pneumonia	Schizophrenia	295 (excluding 295.79)	F20	
Dutcome         Definition of outcome measures for the ACSC (see Appendix 4)         Categories         uny ACSC         Any of the categories         ype of ACSC         Angina         COPD/adult asthma         exacerbation         CHF exacerbation         Diabetes-related ACSC         The 3 diabetes categories + amputations         HTN         Perforated appendicitis         Pneumonia	Schizoaffective disorders	295.79, 296.8	F25	
Definition of outcome measures for the ACSC (see Appendix 4)Categoriesany ACSCAny of the categoriesany and CSCAny of the categoriesAnginaCoPD/adult asthmaexacerbationCOPD/adult asthmaexacerbationCHF exacerbationDiabetes-related ACSCThe 3 diabetes categories + amputationsHTNPerforated appendicitisPneumoniaImage: Complex and the categories + amputation is a categ	Bipolar affective disorders	296.19, 296.39	F30, F31	
Any ACSC Any of the categories ype of ACSC Angina COPD/adult asthma exacerbation CHF exacerbation Diabetes-related ACSC The 3 diabetes categories + amputations HTN Perforated appendicitis Pneumonia	Definition of outcome measure			]
ype of ACSC         Angina         COPD/adult asthma         exacerbation         CHF exacerbation         Diabetes-related ACSC         The 3 diabetes categories + amputations         HTN         Perforated appendicitis         Pneumonia	Any ACSC	-		
Angina       Angina         COPD/adult asthma       exacerbation         exacerbation       Exacerbation         Diabetes-related ACSC       The 3 diabetes categories + amputations         HTN       Perforated appendicitis         Pneumonia       Image: Comparison of the second secon	Type of ACSC			
exacerbationCHF exacerbationDiabetes-related ACSCThe 3 diabetes categories + amputationsHTNPerforated appendicitisPneumonia				
CHF exacerbationDiabetes-related ACSCThe 3 diabetes categories + amputationsHTNPerforated appendicitisPneumoniaImage: Comparison of the state	COPD/adult asthma			
Diabetes-related ACSCThe 3 diabetes categories + amputationsHTNPerforated appendicitisPneumoniaImage: Comparison of the second	exacerbation			
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Hospitalizations for 12 of the conditions ide prevention quality indicator	entified by the Agency for Healthcare Research an	d Quality as ACSCs in their reportion	
Disease	Description in the AHRQ list	ICD-10	
Angina	<ul> <li>Angina Without Procedure Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for angina (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Discharges with a surgical procedure in any field (010-8699). Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 4111 INTERMED CORONARY SYND 4130 ANGINA DECUBITUS 41181 CORONARY OCCLSN W/O MI 4131 PRINZMETAL ANGINA 41189 AC ISCHEMIC HRT DIS NEC 4139 ANGINA PECTORIS NEC/NOS</li> <li>Denominator: Population in MSA or county, age 18 years and older.</li> </ul>	I20.0, I20.1, I20.8, I20.9, I24.0, or I24.1, I24.8, I24.9 EXCLUSIONS: All surgical procedures (starting with a K in the Danish version of the NCSP, which means surgical)	
COPD (Chronic obstructive pulmonary disorder) exacerbation	Chronic Obstructive Pulmonary Disease (COPD) Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for COPD (see below). All discharges of age 18 years and older.	J20.0-J20.9*, J40.0-J40.9*, J41.0, J41.1, J42.0-J42.9, J43.8, st. J43.9, J44.0-J44.9, J47.0-J47.9 *qualify only if accompanied by	
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ge 65 of 85	BMJ Open         Transfers <sup>1</sup> .         MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> <b>ICD-9-CM diagnosis codes:</b> 4660 AC BRONCHITIS * 4920         EMPHYSEMATOUS BLEB         490 BRONCHITIS NOS* 4928 EMPHYSEMA         NEC         4910 SIMPLE CHR BRONCHITIS 494         BRONCHIECTASIS - OCT00         4911 MUCOPURUL CHR BRONCHITIS 4940         BRONCHIECTAS W/O AC EXAC         4912 OBS CHR BRNC W/O ACT EXA OCT00-         49121 OBS CHR BRNC W/O ACT EXA OCT00-         49121 OBS CHR BRNC W ACT EXA 4941         BRONCHIECTASIS W AC EXAC         4918 CHRONIC BRONCHITIS NEC OCT00-         4919 CHRONIC BRONCHITIS NOS 496 CHR         AIRWAY OBSTRUCT NEC         * Qualifies only if accompanied by secondary         diagnosis of 491.xx, 492.x, or 496 (i.e., any other code         on this list).         Denominator: Population in MSA or county, age         B years and older.         Discharges with ICD-9-CM principal diagnosis code for CHF (see below).         All discharges of age 18 years and older.         Exclude:       Discharges with cardiac procedure codes (see	Secondary diagnosis of any of the other codes listed under COPIE 2015. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Downloaded from http://bmjopen.bmj.com/ on April 109.0-109.9 link.com/ on April 10
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ICD-9-CM diagnosis codes: 39891 RHEUMATIC HEART FAILURE 40413 BEN HYP HRT/REN W CHF&RF 40201 MAL HYPERT HRT DIS W CHF 40491 HYPER HRT/REN NOS W CHF 40211 BENIGN HYP HRT DIS W CHF 40493 HYP HT/REN NOS W CHF&RF 40291 HYPER TRT NALURE 40401 MAL HYPER HRT/REN W CHF 4280 CONGESTIVE HEART FAILURE 40403 MAL HYPER HRT/REN W CHF 4281 LEFT HEART FAILURE 40403 MAL HYP HRT/REN W CHF 4289 HEART FAILURE NOS 40411 BEN HYPER HRT/REN W CHF Exclude ICD-9-CM procedure codes: 3601 PTCA-1 VESSEL W/O AGENT 3619 HRT REVAS BYPS ANAS NEC 3602 PTCA-1 VESSEL W/O AGENT 3619 HRT REVAS BYPS ANAS NEC 3605 PTCA-1 VESSEL WITH AGNT 375 HEART TRANSPLANTATION 3605 PTCA-1 UESSEL WITH AGNT 375 HEART TRANSPLANTATION 3606 INSERT CORONARY ART STENT OCT95- 3771 INT INSERT LEAD IN VENT 3610 AORTOCORONARY BYPASS NOS 3772 INT INSER LEAD ATRI-VENT 3611 AORTOCOR BYPAS-1 COR ART 3773 INT INSER LEAD IN ATRIUM 3612 AORTOCOR BYPAS-2 COR ART 3774 INT INSER LEAD IN ATRIUM 3613 AORTOCOR BYPAS-3 COR ART 3775 REVISION OF LEAD 3614 AORTOCOR BYPAS-3 COR ART 3776 REPL LY ATRI-VENT LEAD 3615 1 INT MAM-COR ART BYPASS 3777 REMOVAL OF LEAD W/O REPL 3616 2 INT MAM-COR ART BYPASS 3778 INSER TEMP PACEMAKE SYS 3617 ABD-CORON ART BYPASS OCT96- 3779	15-009878 on 2 December 2015. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by

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	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	
Diabetes (with short-term complications)	<ul> <li>Diabetes Short-term Complications Admission Rate</li> <li>Numerator:</li> <li>Discharges with ICD-9-CM principal diagnosis code for short-term complications (ketoacidosis, hyperosmolarity, coma) (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes:</li> <li>25010 DM KETO T2, DM CONT 25022 DM W/ HYPROSM T2, DM UNCNT</li> <li>25011 DM KETO T1, DM CONT 25023 DM W/ HYPROSM T1, DM UNCNT</li> <li>25012 DM KETO T2, DM UNCONT 25030 DM COMA NEC T2, DM CONT</li> <li>25013 DM KETO T1, DM UNCONT 25031 DM COMA NEC T1, DM CONT</li> <li>25020 DM W/ HYPROSM T2, DM CONT 25032</li> <li>DM COMA NEC T2, DM UNCONT</li> <li>25021 DM W/ HYPROSM T2, DM CONT 25033</li> <li>DM COMA NEC T1, DM UNCONT</li> <li>25021 DM W/ HYPROSM T1, DM CONT 25033</li> <li>DM COMA NEC T1, DM UNCONT</li> <li>25021 DM W/ HYPROSM T1, DM CONT 25033</li> <li>DM COMA NEC T1, DM UNCONT</li> </ul>	E10.0, E10.1, E11.0, E11.1,
Diabetes (uncontrolled (without short- term or long-term complications))	Uncontrolled Diabetes Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code for uncontrolled diabetes, without mention of	E10.9, E11.9

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	All discharges of age 18 years and older.	
	<b>Exclude:</b> Transfers <sup>1</sup> .	
	MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	
	ICD-9-CM diagnosis codes:	
	25002 DM, T2, UNCONT 25003 DM, T1, UNCONT	
	<b>Denominator:</b> Population in MSA or county, age	
	18 years and older. May be combined with diabetes short-term	
	complications as a single indicator.	
Diabetes (with long-term	Diabetes Long-term Complications Admission	E10.2-E10.8, E11.2-E11.8
omplications)	Rate	
	Numerator: Discharges with ICD-9-CM principal diagnosis	
	code for long-term complications (renal, eye,	
	neurological, circulatory, or complications not	
	All discharges of age 18 years and older.	1
	Exclude:	
	Transfers <sup>1</sup> . MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	h 07/
	ICD-9-CM diagnosis codes:	
	25040 DM RENAL COMP T2 CONT 25070 DM CIRCU DIS T2 CONT	
	25041 DM RENAL COMP T1 CONT 25071 DM	
	CIRCU DIS T1 CONT	
	25042 DM RENAL COMP T2 UNCNT 25072 DM	
	CIRCU DIS T2 UNCNT	
	25043 DM RENAL COMP T1 UNCNT 25073 DM CIRCU DIS T1 UNCNT	
		1

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9 of 85	25050 DM EYE COMP T2 CONT 25080 DM W COMP NEC T2 CONT 25051 DM EYE COMP T1 CONT 25081 DM W COMP NEC T1 CONT 25052 DM EYE COMP T2 UNCNT 25082 DM W COMP NEC T2 UNCNT 25053 DM EYE COMP T1 UNCNT 25083 DM W COMP NEC T1 UNCNT 25060 DM NEURO COMP T2 CONT 25090 DM W COMPL NOS T2 CONT 25061 DM NEURO COMP T1 CONT 25091 DM W COMPL NOS T1 CONT 25062 DM NEURO COMP T2 UNCNT 25092 DM W COMPL NOS T2 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT 25063 DM NEURO COMP T1 UNCNT 25093 DM W COMPL NOS T1 UNCNT Denominator: Population in MSA or county, age 18 years and older.	110.0-110.9, 111.9, 112.9, 113.9 EXCLUSION:
	<ul> <li>Discharges with ICD-9-CM principal diagnosis code for hypertension (see below).</li> <li>All discharges of age 18 years and older.</li> <li>Exclude: <ul> <li>Discharges with cardiac procedure codes (see below) in any field.</li> <li>Transfers<sup>1</sup>.</li> <li>MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> </ul> </li> </ul>	EXCLUSION: Cardiac procedures: KFNG02, KFNG05, KFNA, KFNC, KFT, KFW, KFQ, BFCA01-BFCA07
	ICD-9-CM diagnosis codes: 4010 MALIGNANT HYPERTENSION 40310 BENIGN HYP HRT DIS W/OUT RF 4019 HYPERTENSION NOS 40390 HYPERTEN HEART DIS W/OUT RF 40200 MAL HYPERTEN HRT DIS W/OUT CHF	

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	40400 MAL HYPER HRT/REN W/OUT CHF/RF	
	40210 BEN HYPERTEN HRT DIS W/OUT CHF	
	40410 BEN HYPER HRT/REN W/OUT CHF/RF 40290 HYPERTENSIVE HRT DIS W/OUT CHF	
	40290 HYPERTENSIVE HRT DIS W/OUT CHF 40490 HYPER HRT/REN NOS W/OUT CHF/RF	
	40490 MAL HYPERT HRT DIS W/OUT RF	
	Exclude ICD-9-CM procedure codes:	
	3601 PTCA-1 VESSEL W/O AGENT 3619 HRT	
	REVAS BYPS ANAS NEC	
	3602 PTCA-1 VESSEL WITH AGNT 375 HEART	
	TRANSPLANTATION	
	3605 PTCA-MULTIPLE VESSEL 3770 INT	
	INSERT PACEMAK LEAD	
	3606 INSERT CORONARY ART STENT OCT95-	
	3771 INT INSERT LEAD IN VENT	
	3610 AORTOCORONARY BYPASS NOS 3772	
	INT INSER LEAD ATRI-VENT	
	3611 AORTOCOR BYPAS-1 COR ART 3773 INT	
	INSER LEAD IN ATRIUM	
	3612 AORTOCOR BYPAS-2 COR ART 3774 INT	
	OR REPL LEAD EPICAR	
	3613 AORTOCOR BYPAS-3 COR ART 3775	
	REVISION OF LEAD	
	3614 AORTCOR BYPAS-4+ COR ART 3776	
	REPL TV ATRI-VENT LEAD	
	3615 1 INT MAM-COR ART BYPASS 3777	
	REMOVAL OF LEAD W/O REPL 3616 2 INT MAM-COR ART BYPASS 3778	
	INSER TEMP PACEMAKER SYS	
	3617 ABD-CORON ART BYPASS OCT96- 3779	
	REVIS OR RELOCATE POCKET	
	<b>Denominator:</b> Population in MSA or county, age	
	18 years and older.	
erforated appendicitis	Perforated Appendix Admission Rate	K35.0, K35.1, K35.2, K35.3
	Numerator:	
	Discharges with ICD-9-CM diagnosis code for perforations or abscesses of appendix (see below)	
	in any field.	
	m any neta.	1

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	Final discular ges of age 18 years and order.       B000000000000000000000000000000000000
Pneumonia	Bacterial Pneumonia Admission Rate Numerator:       J13-J14.9, J15.3-J15.4, J15.7-J16.9, J16.0-J16.9, J18.0-J18.9         Discharges with ICD-9-CM principal diagnosis code for bacterial pneumonia (see below).       J16.0-J16.9, J18.0-J18.9         All discharges of age 18 years and older.       EXCLUSION: Sickle cell disorders Discharges with diagnosis code for sickle cell anemia or HB-S disease (see below) in any field. Transfers <sup>1</sup> .       Discharges with diagnosis code for sickle cell anemia or HB-S disease (see below) in any field. Transfers <sup>1</sup> .       MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup> ICD-9-CM diagnosis codes: 481 PNEUMOCOCCAL PNEUMONIA 48230 STREP PNEUMONIA UNSPEC 4822 H.INFLUENZAE PNEUMONIA 48231 GRP       POPOCOCCAL PNEUMONIA 48231 GRP
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LITIS (urinary tract infactions)	A STREP PNEUMONIA 4829 BACTERIAL PNEUMONIA NOS 48232 GRP B STREP PNEUMONIA 4830 MYCOPLASMA PNEUMONIA 48239 OTH STREP PNEUMONIA 4831 CHLAMYDIA PNEUMONIA OCT96- 485 BRONCOPNEUMONIA ORG NOS 4838 OTH SPEC ORG PNEUMONIA 486 PNEUMONIA, ORGANISM NOS <b>Exclude ICD-9-CM diagnosis codes:</b> 28260 SICKLE-CELL ANEMIA NOS 28263 SICKLE-CELL/HB-C DISEASE 28261 HB-S DISEASE W/O CRISIS 28269 SICKLE-CELL ANEMIA NEC 28262 HB-S DISEASE WITH CRISIS <b>Urinary Tract Infection Admission Bate</b>	36/bmjopen-2015. Downloaded from N10.0.N12.9. N15.1.15.9. N30
UTIs (urinary tract infections)	<ul> <li>Urinary Tract Infection Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis code of urinary tract infection (see below).</li> <li>Exclude: Transfers<sup>1</sup>. MDC 14 (pregnancy, childbirth, and puerperium)<sup>2</sup></li> <li>ICD-9-CM diagnosis codes: 59000 CHR PYELONEPHRITIS NOS 59080 PYELONEPHRITIS NOS 59001 CHR PYELONEPH W MED NECR 59081 PYELONEPHRITI IN OTH DIS 59010 AC PYELONEPHRITIS NOS 5909 INFECTION OF KIDNEY NOS 59011 AC PYELONEPHR W MED NECR 5950 AC CYSTITIS 5902 RENAL/PERIRENAL ABSCESS 5959 CYSTITIS NOS 5903 PYELOURETERITIS CYSTICA 5990 URIN TRACT INFECTION NOS</li> </ul>	N10.0-N12.9, N15.1-15.9, N30.0 N30.9, N34.0-N34.9, N39.0
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	<b>Denominator:</b> Population in MSA or county.	1000-1 1
Adult Asthma exacerbation	Adult Asthma Admission Rate Numerator: Discharges with ICD-9-CM principal diagnosis	on 2
	code of asthma (see below).	Decem
	All discharges of age 18 years and older.	iber 2
	<b>Exclude:</b> Transfers <sup>1</sup> .	015. [
	MDC 14 (pregnancy, childbirth, and puerperium) $^2$	Down
	ICD-9-CM diagnosis codes: 49300 EXT ASTHMA W/O STAT ASTH 49320 CH OB ASTH W/O STAT ASTH	December 2015. Downloaded from http://bmjopen.bmj.com/ on April 17,
	49301 EXT ASTHMA W STATUS ASTH 49321 CH OB ASTHMA W STAT ASTH 49302 EXT ASTHMA W STATUS ACEX	om http://
	OCT00- 49322 CH OB ASTHMA W STAT ACEX 49310 INT ASTHMA W/O STAT ASTH OCT00- 49311 INT ASTHMA W STATUS ASTH 49390	bmjopen
	ASTHMA W/O STATUS ASTHM 49312 INT ASTHMA W STATUS ACEX OCT00- 49391 ASTHMA W STATUS ASTHMAT	.bmj.co
	49392 ASTHMA W STATUS AC EXAC OCT00-	n/ on
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	April 17,
Amputations (diabetes-related)	Rate of Lower-extremity Amputation among Patients with Diabetes	Z89.4-Z89.7
	Numerator: Discharges with ICD-9-CM procedure code for lower-extremity amputation (see below) in any field and diagnosis code of diabetes in any field (see below).	*qualify only if registered with diabetes in the Danish National Diabetes Register or if registered y a diagnosis of diabetes (ICD-10:E30 14, H36.0, O24, excluding O24.4) at
	All discharges of age 18 years and older.	the same admission as the ACSC
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Trauma (see below). Transfers <sup>1</sup> .	80
MDC 14 (pregnancy, childbirth, and puerperium) <sup>2</sup>	n 2
MDC 14 (pregnancy, childbirth, and puerperfulit)	
	EXCLUSION:
ICD-9-CM procedure codes:	limb
8410 LOWER LIMB AMPUTAT NOS 8415	1
BELOW KNEE AMPUTAT NEC	S78.0-S78.9, S88.0-S88.9, S98.6
8411 TOE AMPUTATION 8416	
DISARTICULATION OF KNEE	590.4, 105.5-105.5 S
8412 AMPUTATION THROUGH FOOT 8417 ABOVE KNEE AMPUTATION	S98.4, T05.3-T05.5 Downloaded from http://bmjopen.bmj.com/ on April 17, 2024
8413 DISARTICULATION OF ANKLE 8418	ade
DISARTICULATION OF HIP	d fr
8414 AMPUTAT THROUGH MALLEOLI 8419	O m
HINDQUARTER AMPUTATION	n ti
ICD-9-CM diagnosis codes for diabetes:	p://
25000 DMII WO CMP NT ST UNCNTR 25050	<u> </u>
DMII OPHTH NT ST UNCNTRL	
25001 DMI WO CMP NT ST UNCNTRL 25051 DMI OPHTH NT ST UNCNTRLD	en.t
25002 DMII WO CMP UNCNTRLD 25052 DMII	<u>, i</u>
OPHTH UNCNTRLD	S S
25003 DMI WO CMP UNCNTRLD 25053 DMI	N O
OPHTH UNCNTRLD	
25010 DMII KETO NT ST UNCNTRLD 25060	April April
DMII NEURO NT ST UNCNTRL	117
25011 DMI KETO NT ST UNCNTRLD 25061 DMI NEURO NT ST UNCNTRLD	, 2
25012 DMII KETOACD UNCONTROLD 25062	024
DMII NEURO UNCNTRLD	by
25013 DMI KETOACD UNCONTROLD 25063	u ĝ
DMI NEURO UNCNTRLD	est.
25020 DMII HPRSM NT ST UNCNTRL 25070	Pr
DMII CIRC NT ST UNCNTRLD	guest. Protected by
25021 DMI HPRSM NT ST UNCNTRLD 25071	
DMI CIRC NT ST UNCNTRLD	<u>u</u>

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	DMII CIRC UNCNTRLD 25023 DMI HPROSMLR UNCONTROLD 25073 DMI CIRC UNCNTRLD 25030 DMII O CM NT ST UNCNTRLD 25080 DMII OTH NT ST UNCNTRLD 25031 DMI O CM NT ST UNCNTRL 25081 DMI OTH NT ST UNCNTRLD 25032 DMII OTH COMA UNCONTROLD 25082 DMII OTH UNCNTRLD 25033 DMI OTH COMA UNCONTROLD 25083 DMI OTH UNCNTRLD 25040 DMII RENL NT ST UNCNTRLD 25090 DMII UNSPF NT ST UNCNTRL 25041 DMI RENL NT ST UNCNTRLD 25091 DMI UNSPF NT ST UNCNTRLD 25042 DMII RENAL UNCNTRLD 25092 DMII UNSPF UNCNTRLD 25043 DMI RENAL UNCNTRLD 25093 DMI UNSPF UNCNTRLD	
	Exclude: Trauma ICD-9-CM diagnosis codes: 8950 AMPUTATION TOE 8971 AMPUTAT BK, UNILAT-COMPL 8951 AMPUTATION TOE-COMPLICAT 8972 AMPUT ABOVE KNEE, UNILAT 8960 AMPUTATION FOOT, UNILAT 8973 AMPUT ABV KN, UNIL-COMPL 8961 AMPUT FOOT, UNILAT-COMPL 8974 AMPUTAT LEG, UNILAT NOS 8962 AMPUTATION FOOT, BILAT 8975 AMPUT LEG, UNIL NOS-COMP 8963 AMPUTAT FOOT, BILAT-COMP 8976 AMPUTATION LEG, BILAT 8970 AMPUT BELOW KNEE, UNILAT 8977 AMPUTAT LEG, BILAT-COMPL	
	<b>Denominator:</b> Population in MSA or county, age 18 years and older.	

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 Amission date with an overlap of +/-.

 .or obstetric diagnoses were present as a seco.

 <sup>1</sup>Transfers imply that if a discharge date is followed by another admission date with an overlap of +/- 1 day this is counted as one admission. <sup>2</sup>The exclusion by obstetric admissions was performed if any diagnostic codes for obstetric diagnoses were present as a secondary diagnosis at the same admission as the ACS. The obstetric diagnostic codes included: 00.0-099.9. 2 December 2015. Downloaded from http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by copyright. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Covariates
Appendix 5: Information on socioeconomic position (SEP) obtained from Statistics Denmark.
Education level
< 10 years
10-15 years
> 15 years
Civil status
Living alone/single
Cohabitation
Partners
Married

Annendiy & Information on abranic discosses included in the Charleon Comerchidity Index abtained					
Appendix 6: Information on chronic diseases included in the Charlson Comorbidity Index obtained from the Danish National Patient Register					
it officiel Duffish Patients and a dufficiel i	ICD-8	ICD-10			
Myocardial infarction	410	I21;I22;I23			
Congestive heart failure	427.09, 427.10, 427.11,	150; 111.0; 113.0; 113.2			
	427.19, 428.99, 782.49	10 0, 11100, 11010, 11012			
Peripheral vascular disease	440, 441, 442, 443, 444, 445,	170; 171; 172; 173; 174; 177			
Cerebrovascular disease	430-438	I60-I69; G45; G46			
Dementia		F00-F03; F05.1; G30			
	290.09-290.19, 293.09				
Chronic pulmonary disease	490-493, 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3;			
		J84.1; J92.0; J96.1; J98.2; J98.3			
Connective tissue disease	712, 716, 734, 446, 135.99	M05; M06; M08; M09;M30;M31;			
		M32; M33; M34; M35; M36; D86			
Ulcer disease	530.91, 530.98, 531-534,	K22.1; K25-K28			
Mild liver disease	571, 573.01, 573.04	B18; K70.0-K70.3; K70.9; K71;			
		K73; K74; K76.0			
Diabetes mellitus	249.00, 249.06, 249.07,	E10.0, E10.1; E10.9; E11.0; E11.1;			
	249.09, 250.00, 250.06,	E11.9			
	250.07, 250.09				
Hemiplegia	344	G81; G82			
Moderate/severe renal	403,404,580-583, 584,	I12; I13; N00-N05; N07; N11; N14;			
Disease	590.09, 593.19, 753.10-	N17-N19; Q61			
	753.19, 792				
Diabetes mellitus with	249.01-249.05, 249.08,	E10.2-E10.8; E11.2-E11.8			
chronic complications	250.01-250.05, 250.08				
Any tumour	140-194	C00-C75			
Leukaemia	204-207	C91-C95			
Lymphoma	200-203, 275.59	C81-C85; C88; C90; C96			
Moderate/severe liver	070.00, 070.02, 070.04,	B15.0; B16.0; B16.2; B19.0; K70.4;			
Disease	070.06, 070.08, 573.00,	K72; K76.6; I85			
	456.00-456.09	· · ·			
Metastatic solid tumour	195-198, 199	C76-C80			

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ACSC Outcome	onal Diabetes Register and the Danish National Prescription Registry. ACSC-predisposing medical comorbidity
Chronic conditions	
Angina	Myocardial infarction <sup>1</sup>
CHF exacerbation	CHF <sup>1</sup>
HTN	Myocardial infarction <sup>1</sup> CHF <sup>1</sup> Cerebrovascular disease <sup>1</sup>
Diabetes-related ACSCs	Peripheral vascular disease <sup>1</sup> Diabetes <sup>2</sup>
COPD exacerbation	Chronic pulmonary disease <sup>1</sup>
	or
	Redemption of at least 2 prescriptions of drugs for obstructive airway diseases within 6 months <sup>3</sup>
Adult asthma exacerbation	Chronic pulmonary disease <sup>1</sup>
	or
	Redemption of at least 2 prescriptions of drugs for obstructive airway diseases within 6 months <sup>3</sup>
Acute conditions	
Perforated appendicitis	-
Pneumonia	-
UTI	-
<sup>1</sup> Obtained from the Danish National Pa <sup>2</sup> Obtained from the Danish National Di <sup>3</sup> Obtained from the Danish National Pro-	

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Appendix 8: Information on diabetes obtained from the Danish National Diabetes Register.
Algoritm: Individuals were classified as having diabetes on the day where at least one of the following six
criteria was met:
1. A diagnosis of diabetes made at any Danish hospital as registered in the Danish National Patient Register
(ICD-8:249, 250; ICD-10:E10-14, H36.0, O24, excluding O24.4).

- 2. A referral to chiropody of diabetic patients as registered in the Danish National Health Service Register.(Andersen *et al.* 2011)
- 3. Five blood glucose measurements within one year as registered in the Danish National Health Service Register.
- 4. Two blood glucose measurements per year for five consecutive years as registered in the Danish National Health Service Register.
- 5. Two redemptions of oral anti-diabetic drugs within six months as registered in the Danish National Prescription Registry.
- 6. Two redemptions of prescribed insulin as registered in the Danish National Prescription Registry.

## Appendix 9: ATC codes for drugs for obstructive airway disease obtained from the Danish National<br/>Prescription Registry.ATC codesType of drug<br/>Drugs for obstructive airway diseasesR03Drugs for obstructive airway diseasesR03AAdrenergics, inhalantsR03BOther drugs for obstructive airway diseases, inhalantsR03CAdrenergics for systemic useR03DOther systemic drugs for obstructive airway diseases

Appendix 10: Information on substance abuse disorders obtained from the Danish National Patient					
<b>Register and the Danish Psychiatric C</b>	Central Register.				
	ICD-8	ICD-10			
Drug related					
Opioids	304.09, 304.19	F11.0–F11.9			
Cannabinoids	304.59	F12.0–F12.9			
Sedatives/hypnotics	304.29, 304.39	F13.0–F13.9			
Cocaine	304.49	F14.0–F14.9			
Other stimulants	304.69	F15.0–15.9			
Hallucinogens	304.79	F16.0–F16.9			
Other and multiple drugs	304.89, 304.99	F18.0–F19.9			
Alcohol related					
Alcohol psychosis and abuse	291.09-291.99	F10.0–F10.9			
syndrome	303.09-303.99				
Cirrhosis and steatosis of the liver	571.09, 571.10, 571.19	K70.0-K70.9			
Esophageal varices	456.00, 456.01, 456.09	I85.0–I85.9			

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STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Corresponding Manuscript Page Number
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term	1
		in the title or the abstract <b>X</b>	
		(b) Provide in the abstract an informative and balanced	2-3
		summary of what was done and what was found X	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the	4
U		investigation being reported X	
Objectives	3	State specific objectives, including any prespecified	5
5		hypotheses X	
Methods			
Study design	4	Present key elements of study design early in the paper X	5
Setting	5	Describe the setting, locations, and relevant dates, including	5
Setting	2	periods of recruitment, exposure, follow-up, and data	U
		collection X	
Participants	6	(a) Cohort study—Give the eligibility criteria, and the	5-6
	-	sources and methods of selection of participants. Describe	
		methods of follow-up <b>X</b>	
		<i>Case-control study</i> —Give the eligibility criteria, and the	
		sources and methods of case ascertainment and control	
		selection. Give the rationale for the choice of cases and	
		controls	
		Cross-sectional study—Give the eligibility criteria, and the	
		sources and methods of selection of participants	
		(b) Cohort study—For matched studies, give matching	N/A
		criteria and number of exposed and unexposed	
		Case-control study—For matched studies, give matching	
		criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	6-9
		confounders, and effect modifiers. Give diagnostic criteria,	
		if applicable X	
Data sources/	8*	For each variable of interest, give sources of data and	6-9
measurement		details of methods of assessment (measurement). Describe	
		comparability of assessment methods if there is more than	
		one group <b>X</b>	
Bias	9	Describe any efforts to address potential sources of bias X	9
Study size	10	Explain how the study size was arrived at N/A	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the	8-10
		analyses. If applicable, describe which groupings were	
		chosen and why X	
Statistical methods	12	(a) Describe all statistical methods, including those used to	9-10
		control for confounding X	
		(b) Describe any methods used to examine subgroups and	10

(c) Tsplini how missing data were addressed X     9       (d) Cohorr study—II applicable, explain how loss to     NA       follow-up was addressed NA     Case-control study—III applicable, explain how matching     0       of cases and controls was addressed VA     Case-control study—III applicable, explain how matching     0       of cases and controls was addressed VA     Case-control study—III applicable, explain how matching     0       of cases and controls was addressed VA     Case-control study—III applicable, explain how matching     0       of control study—III applicable, advective analytical methods taking account of sampling strategy     III     IIII			interactions X	
follow-up was addressed N/A Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses X 10 Continued on next page				
Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy (c) Describe any sensitivity analyses X 10				N/A
of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses X 10 Continued on next page			<u>^</u>	
Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses X 10				
(e) Describe any sensitivity analyses X 10				
(a) Describe any sensitivity analyses X       10			Cross-sectional study-If applicable, describe analytical	
(a) Describe any sensitivity analyses X       10			methods taking account of sampling strategy	
			( $\underline{e}$ ) Describe any sensitivity analyses <b>X</b>	10
	(	Continued on next page		

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Results			Corresponding Manuscript Page Number
Participants	13*	<ul> <li>(a) Report numbers of individuals at each stage of study—eg</li> <li>numbers potentially eligible, examined for eligibility, confirmed</li> <li>eligible, included in the study, completing follow-up, and analysed</li> <li>X</li> </ul>	10-11
		(b) Give reasons for non-participation at each stage N/A	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive	14*	(a) Give characteristics of study participants (eg demographic,	11, 27-28 (Table 1)
data		clinical, social) and information on exposures and potential	
		confounders X	
		(b) Indicate number of participants with missing data for each	27-28 (Table 1)
		variable of interest X	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total	11
		amount) <b>X</b>	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary	11
		measures over time X	
		Case-control study-Report numbers in each exposure category, or	N/A
		summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or	N/A
		summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-	11, 13, 30-31 (Table
		adjusted estimates and their precision (eg, 95% confidence interval).	2), 33 (Table 4)
		Make clear which confounders were adjusted for and why they were	
		included X	
		(b) Report category boundaries when continuous variables were	8-10
		categorized X	
		(c) If relevant, consider translating estimates of relative risk into	N/A
		absolute risk for a meaningful time period N/A	
Other analyses	17	Report other analyses done—eg analyses of subgroups and	12-13, 32 (Table 3)
		interactions, and sensitivity analyses X	34-35
			(Figures 1 and 2)
Discussion			
Key results	18	Summarise key results with reference to study objectives X	14
Limitations	19	Discuss limitations of the study, taking into account sources of	15-16
		potential bias or imprecision. Discuss both direction and magnitude	
		of any potential bias X	
Interpretation	20	Give a cautious overall interpretation of results considering	15-16
		objectives, limitations, multiplicity of analyses, results from similar	
		studies, and other relevant evidence X	
Generalisability	21	Discuss the generalisability (external validity) of the study results ${\bf X}$	15-16
Other information	on		
Funding	22	Give the source of funding and the role of the funders for the	1, 10
		present study and, if applicable, for the original study on which the	
		present article is based <b>X</b>	

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\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

<text> Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.