ICU Survivors Have a Substantial Higher Risk of Developing New Chronic Conditions Compared to a Population-Based Control Group

Ilse van Beusekom, MSc[1,2]; Ferishta Bakhshi-Raiez, PhD[1,2]; Marike van der Schaaf, PhD[3,4]; Wim B. Busschers, MSc[1,2]; Nicolette F. de Keizer, PhD[1,2]; Dave A. Dongelmans, MD, PhD[2,5]

Objectives: To describe the types and prevalence of chronic conditions in an ICU population and a population-based control group during the year before ICU admission and to quantify the risk of developing new chronic conditions in ICU patients compared with the control group.

Design: We conducted a retrospective cohort study, combining a national health insurance claims database and a national quality registry for ICUs. Claims data in the timeframe 2012–2014 were combined with clinical data of patients who had been admitted to an ICU during 2013. To assess the differences in risk of developing new chronic conditions, ICU patients were compared with a population-based control group using logistic regression modeling.

Setting: Eighty-one Dutch ICUs.

Patients: All patients admitted to an ICU during 2013. A population-based control group was created, and weighted on the age, gender, and socio-economic status of the ICU population.

Interventions: None.

Measurements and Main Results: ICU patients (n = 56,760) have more chronic conditions compared with the control group (n = 75,232) during the year before ICU admission ($p < 0.0001$). After case-mix adjustment ICU patients had a higher risk of developing chronic conditions, with odds ratios ranging from 1.67 (CI, 1.29–2.17) for asthma to 24.35 (CI, 14.00–42.34) for epilepsy, compared with the control group.

Conclusions: Due to the high prevalence of chronic conditions and the increased risk of developing new chronic conditions, ICU follow-up care is advised and may focus on the identification and treatment of the new developed chronic conditions. (*Crit Care Med* 2019; 47:324–330)

Key Words: chronic conditions; chronic obstructive pulmonary disease; diabetes mellitus; heart diseases; intensive care unit; population-based study

ICU patients are life threatening ill. Five decades ago, at the onset of ICU care, up to 33% of the patients did not survive their ICU admission (1, 2). As a result of improved medical technology, knowledge and treatment, the mortality rates dropped to 10–15% during the last decade (3–6). Due to this decrease in mortality, the focus on ICU outcome measures shifted from solely ICU mortality to long-term survival, morbidity, and quality of life after discharge.

After hospital discharge, many ICU survivors suffer long-term complaints as part of the Post Intensive Care Syndrome (PICS) leading to financial difficulties, restrictions in societal participation and decreased quality of life (7, 8). The term "PICS" was introduced to describe the presence of one or more impairments in mental, cognitive, and physical functioning after critical illness (9).

Recent studies have shown that ICU patients have increased healthcare costs and increased hospital admissions before their ICU admission (10–12). Comorbidities present before ICU admission have been recognized as predictors for hospital resource use before and after ICU discharge (11–13). This might indicate that patients have an impaired health status even before ICU admission, since comorbidities, in general, are associated with mortality, morbidity, and quality of life (13, 14). Yet, little is known about the prevalence of chronic

[1]Department of Medical Informatics, Amsterdam UMC, Amsterdam Public Health Research Institute, University of Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands.

[2]National Intensive Care Evaluation (NICE) foundation, Amsterdam, The Netherlands.

[3]Department of Rehabilitation, Amsterdam UMC, Amsterdam Movement Sciences, University of Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands.

[4]Centre of Applied Research, Faculty of Health, Amsterdam University of Applied Sciences, Amsterdam, The Netherlands.

[5]Department of Intensive Care Medicine, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands.

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For information regarding this article, E-mail: i.vanbeusekom@amc.uva.nl

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conditions within the total ICU population before ICU admission, the types of chronic conditions ICU patients suffer, and the risk of developing new chronic conditions after ICU discharge. Furthermore, it is unknown whether there is a difference between ICU patients and the general population with respect to the types, prevalence and the development of chronic conditions.

The aim of this study was: 1) to describe the types and prevalence of chronic conditions in an ICU population and a population-based control group during the year before ICU admission and 2) to quantify the risk of developing new chronic conditions in ICU patients and the population-based control group during the year after ICU admission.

MATERIALS AND METHODS

We conducted a retrospective cohort study, combining data of the Dutch National Intensive Care Evaluation (NICE) registry (15) with data of the health insurance claims database of Vektis (16).

Dutch NICE Database

The NICE registry is a national quality registry in which, during the study period, 90% of all Dutch ICUs are participating (15). The ICUs are collecting data for all patients admitted to their ICU, which includes: age, gender, ICU admission and discharge data, primary diagnosis at ICU admission, severity of illness, ICU mortality, and in-hospital mortality. Extensive information about the collected items, data quality, and data reliability has been published before (17).

All patients from the NICE registry, 18 years old of age or older during the year of ICU admission, admitted to an ICU during the year 2013 and discharged from the ICU before January 1, 2014, were included in the NICE registry subset.

Vektis Insurance Claims Database

Health insurance is compulsory for Dutch citizens, and 99% of the Dutch inhabitants have private healthcare insurance (18). The Vektis databases (16) contain reimbursement data on all medical treatments paid for by Dutch insurance companies, as well as demographic information, such as gender, date of birth, socio-economic status (SES), and a proxy for date of death, for all registered residents of the Netherlands.

Vektis also contains claims for pharmaceutical care, including information on provided drugs, the Anatomical Therapeutic Chemical (ATC) code, the date the drug was supplied, and the quantity supplied. To determine the chronic conditions, Pharmaceutical Cost Groups (PCGs) were used as a proxy. PCGs are based on the idea that a patient with a certain chronic condition can be identified by claims for specific prescribed drugs (19, 20).

We used the PCGs to identify chronic conditions during the whole study period since clinical diagnosis are not available from NICE or Vektis. The validity of pharmacy-based claims data for the assessment of chronic conditions and prevalence estimates have been demonstrated before in different country's (20–24). A complete description of the definitions of chronic conditions and ATC codes, as used in the year 2014, is given in **Appendix 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/E214).

All patients in the Vektis database who had a claim for an ICU day in the year 2013 and were 18 years of age or older during the year of ICU admission were included in the ICU-subset of the Vektis database. Based on this ICU-subset, a population-based control group was created from all registered inhabitants of the Netherlands in the Vektis database. The population-based control group was frequency matched based on the combination of the age, gender, and SES of patients from the ICU-subset, and had no claims for ICU care during 2013. Only ICU patients with no missing data for gender, age, and SES were used in the frequency matching process which was undertaken before the linking process.

Linking Process

The subset extracted from the NICE database and the ICU-subset of the Vektis database were linked using a deterministic linkage algorithm (25). The linking process is extensively described in a previous published study (12).

Statistical Analysis

The year before ICU admission is defined as January 1, 2012, until December 31, 2012, and the year after ICU admission as January 1, 2014, until December 31, 2014.

Median and interquartile ranges are given for nonnormally distributed data and numbers, and proportions are used to present categorical data. The chi-square test was used to test for differences in proportions between the ICU population and control group. A p value of less than 0.05 was considered to indicate a statistically significant difference.

To assess the difference in risk of developing one or more new chronic conditions after ICU discharge, logistic regression modeling was used, with age, gender, and SES as possible explanatory variables. When a person did not have any chronic conditions during 2012 and 2013 and did have a chronic condition during 2014, we considered the chronic condition new and thus developed after ICU discharge. We plotted the estimated risk of developing one or more new chronic conditions, for both study populations, as a function of age and corrected for median SES and gender. Only people with no chronic conditions during 2012 and 2013 were taken into account.

For the most prevalent new chronic conditions within the ICU population, the differences in risk of developing the specified chronic condition, between ICU patients and the control group were evaluated. The specified chronic condition was the independent variable and age, gender, SES, and having preexisting chronic conditions before admission were taken into account as possible explanatory variables. Only people which did not have the specified chronic condition during 2012 and 2013 were taken into account.

For analyses regarding the differences between 2012 and 2014, only people who survived at least until the December 31, 2014 were taken into account. For all analyses, only the

first ICU admission of ICU patients was included. Statistical analyses were performed in SAS (Version 7.1; SAS Institute, Cary, NC).

The control group was divided into two subgroups, and post hoc analyses were performed. Control persons who had been admitted to a hospital or had an outpatient appointment with a specialist were identified as "hospital population" and control persons who had not been admitted to a hospital nor had an outpatient appointment with a specialist were identified as "nonhospital population." A detailed description of the two subpopulations is given in Appendix 1 (Supplemental Digital Content 1, http://links.lww.com/CCM/E214).

Ethics

The need for ethical approval for this study was waived by the Medical Ethics Committee of the Academic Medical Center and stored under number W17_296.

RESULTS

The study population consisted of 56,760 ICU patients and 75,232 control persons. **Figure 1** gives an overview of the data linking process. ICU patients who could not be linked between the two registries (12.8%) or who did not survive hospital admission (13.6%) were excluded from all analyses. Of the 56,760 unique ICU patients, 3,732 patients (6.6%) were admitted to the ICU more than once, with the number of readmissions ranging from 1 to 11 times. **Table 1** gives insight in the characteristics of the ICU population and the control group. Of the ICU population, 55.4% had one or more chronic conditions during the year before admission, within the control group this was 38.4%. **Table 2** describes the prevalence of specific chronic conditions within both study populations during 2012.

Appendix 2 (Supplemental Digital Content 2, http://links.lww.com/CCM/E215) provides an overview of the logistic regression analyses. Since the variables age, gender, SES, and preexisting chronic conditions were frequently found effect modifiers, crude odds are reported, the odds for males and females with a median age, a median SES and no preexisting chronic conditions, and the effects of the interaction terms within the study populations.

The odds of developing one or more new chronic conditions are estimated to be 5.29 (CI, 4.90–5.72) times higher for male ICU patients compared with similar persons from the control group and 4.39 (CI, 3.99–4.83) times higher for female ICU patients compared with similar persons from the control group. Within the ICU population, women are less likely to develop one or more new chronic conditions, compared with men (odds ratio [OR], 0.76; CI, 0.70–0.83). The difference between men and women in the control group was not significant ($p = 0.06$). **Figure 2** gives an overview of the risk of developing one or more new chronic conditions for both populations in relation to age and gender.

High cholesterol, heart diseases, chronic obstructive pulmonary disease (COPD), depression, diabetes mellitus (DM) 2, asthma, epilepsy, and DM 1 are the most prevalent newly developed chronic conditions in the ICU population during the year after ICU admission (**Appendix 3**, Supplemental Digital Content 3, http://links.lww.com/CCM/E216). ICU patients had a higher risk of developing those chronic conditions (Appendix 2, Supplemental Digital Content 2, http://links.lww.com/CCM/E215).

Within both study populations, older people had a higher risk of developing most specified chronic conditions. However, within both study populations older patients are less likely to develop depression, and within the ICU population, older people are less likely to develop epilepsy (OR, 0.99; CI, 0.98–0.99).

Women in the ICU population are less likely to develop high cholesterol and DM 2 compared with men in the ICU population and women in the control group are less likely to develop high cholesterol,

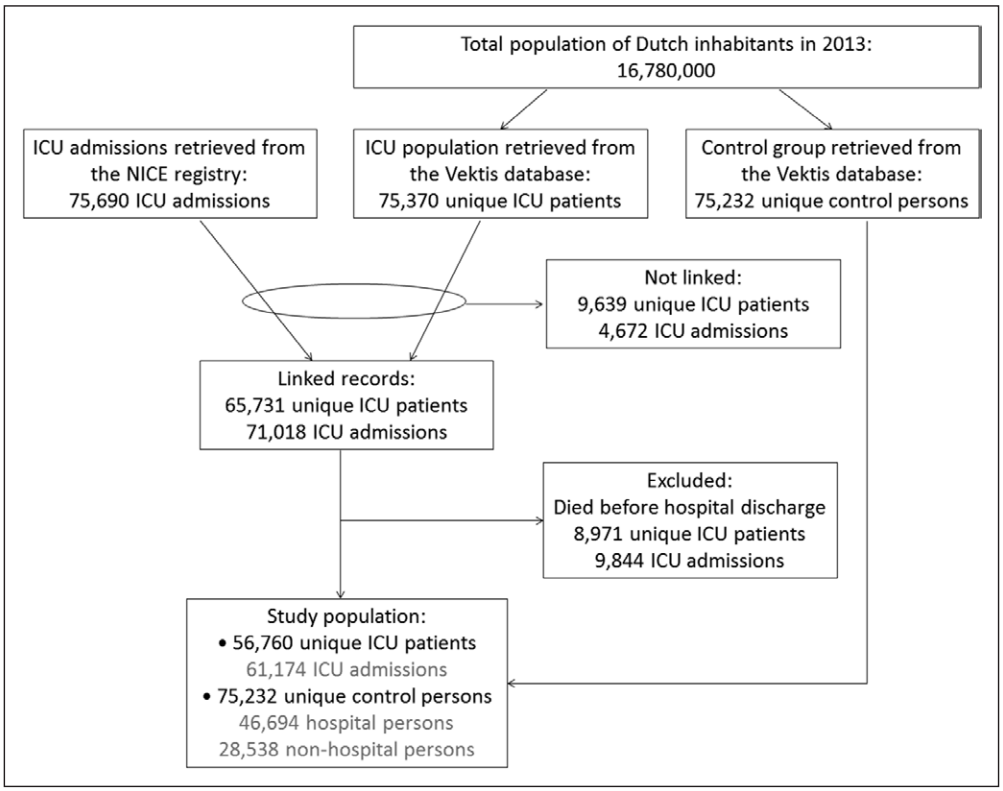

Figure 1. Flowchart of the linking process. NICE = National Intensive Care Evaluation.

TABLE 1. Characteristics of the ICU Population and the Control Group During 2012

Characteristics	ICU Population, *n* = 56,760	Control Group, *n* = 75,232
Male, *n* (%)	34,111 (60.1)	44,742 (59.5)
Age, median (IQR)	65 (53–73)	65 (55–74)
Socio-economic status, median (IQR)	0.2 (–0.6 to 0.8)	0.2 (–0.6 to 0.8)
Died during 2013, *n* (%)	3,465 (6.1)	1,659 (2.2)
Died during 2014, *n* (%)	4,291 (8.1)	1,685 (2.3)

IQR = interquartile range.

TABLE 2. Prevalence of Chronic Conditions Within the ICU Population and the Control Group During 2012

Chronic Condition	ICU Population, *n* = 56,760, *n* (%)	Control Group, *n* = 75,232, *n* (%)	*p*
Population with one or more chronic conditions	31,472 (55.4)	28,902 (38.4)	< 0.0001
Population with two or more chronic conditions	10,856 (19.1)	7,029 (9.3)	< 0.0001
Chronic condition			
High cholesterol	9,348 (16.5)	10,576 (14.1)	< 0.0001
Heart diseases	7,954 (14.0)	4,997 (6.6)	< 0.0001
Chronic obstructive pulmonary disease	4,454 (7.8)	2,445 (3.2)	< 0.0001
DM 2	4,274 (7.5)	4,087 (5.4)	< 0.0001
DM 1	3,705 (6.5)	2,254 (3.0)	< 0.0001
Depression	3,427 (6.0)	2,656 (3.5)	< 0.0001
Asthma	2,808 (4.9)	2,418 (3.2)	< 0.0001
Thyroid diseases	1,954 (3.4)	2,058 (2.7)	< 0.0001
Glaucoma	1,432 (2.5)	1,924 (2.6)	0.69
Neuropathic pains	1,106 (1.9)	543 (0.7)	< 0.0001
Psychoses, Alzheimer's disease, and addictions	1,018 (1.8)	601 (0.8)	< 0.0001
Epilepsy	983 (1.7)	551 (0.7)	< 0.0001
Rheumatism	609 (1.1)	551 (0.7)	< 0.0001
Hormone sensitive tumors	553 (1.0)	692 (0.9)	0.31
Kidney diseases	489 (0.9)	151 (0.2)	< 0.0001
Transplantations	419 (0.7)	163 (0.2)	< 0.0001
Crohn's disease	263 (0.5)	246 (0.3)	< 0.0001
Parkinson's disease	243 (0.4)	346 (0.5)	0.39
Diseases of the central neurologic system	201 (0.4)	56 (0.1)	< 0.0001
Cystic fibrosis/pancreas enzymes	153 (0.3)	49 (0.1)	< 0.0001
HIV	87 (0.2)	59 (0.1)	< 0.0001

DM = diabetes mellitus.

heart diseases, COPD, DM 2, and DM 1 compared with men in the control group.

ICU patients with preexisting chronic conditions are more likely to develop heart diseases, COPD, DM 2, and DM 1 compared with ICU patients with no preexisting chronic conditions. Within the control group, persons with preexisting chronic conditions have a higher risk of developing all studied chronic conditions compared with control persons with no preexisting chronic conditions.

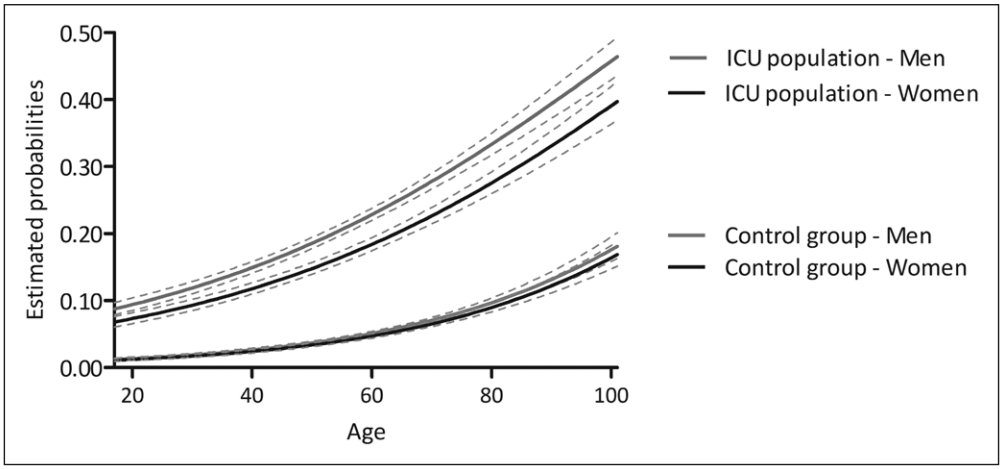

Figure 2. Risk of developing one or more new chronic conditions.

The results of the post hoc analyses are described in Appendix 3 (Supplemental Digital Content 3, http://links.lww.com/CCM/E216), **Appendix 4** (Supplemental Digital Content 4, http://links.lww.com/CCM/E217), **Appendix 5** (Supplemental Digital Content 5, http://links.lww.com/CCM/E218), **Appendix 6** (Supplemental Digital Content 6, http://links.lww.com/CCM/E219), **Appendix 7** (Supplemental Digital Content 7, http://links.lww.com/CCM/E220), and **Appendix 8** (Supplemental Digital Content 8, http://links.lww.com/CCM/E221), respectively. Male ICU patients have an odds of 8.46 (CI, 7.54–9.49) for developing one or more new chronic conditions compared with similar persons from the nonhospital population and an odds of 3.86 (CI, 3.53–4.21) compared with similar persons from the hospital population.

DISCUSSION

Our analysis demonstrated that ICU patients have more chronic conditions during the year before ICU admission compared with a population-based control group. Furthermore, ICU survivors without preexisting chronic conditions were five-fold more likely to develop a chronic condition compared with surviving control patients without preexisting chronic conditions. Additional chronic conditions increase complexity of care for patients surviving critical illness or injury. These data support the need for routine ICU follow-up to assist with assessment of chronic condition persistence, severity, impact on cognitive and motor function, and coordination of healthcare.

To our knowledge, this is the first study that describes in depth the differences in the prevalence of chronic conditions between an ICU population and a population-based control group during the year before ICU admission and the development of new chronic conditions over time. Studies have used the count of preexisting Charlson Comorbidities Index to compare the number of chronic conditions during admission. They reported that ICU patients had significantly more chronic conditions compared with a hospitalized control group (11, 26). The results of these studies are in line with the results of our study.

The fact that ICU patients have more chronic conditions and have a higher chance of developing new chronic conditions after discharge is important insight. Previous studies have shown that people with more chronic conditions generally have a higher risk of dying, a decreased quality of life, a decreased functional status, and an increased healthcare resource use (12–14). ICU follow-up care has been recommended to address the long-term, and severe complains ICU patients suffer after discharge. In sight of the results of our study, we suggest that ICU follow-up care should be offered to ICU survivors and special attention should be given to identifying new chronic conditions in an early stage so they can be treated accurately.

Female gender is a common risk factor for (multi)morbidity (27, 28) and studies have shown that women experience a lower self-reported health status, more (multi)morbidity and higher healthcare resource use compared with men (12, 29–31). Our study is partly in line with those studies and shows that within the ICU population women have a higher prevalence of chronic conditions at baseline compared with men (data not shown). However, our study also shows that within both study populations, men had higher estimated risk of developing new chronic conditions compared with women. A possible explanation for these outcomes is that on average men have less consultations with general practitioners (GPs) (32). Since chronic conditions are primarily diagnosed and managed by GPs, men could be less likely to be diagnosed before ICU admission. Furthermore, since PCGs measure treatment rather than the condition per se, we cannot exclude that the lower baseline prevalence in men represents (in part) undertreatment. If so, the higher estimated risk of developing a new chronic condition would, at least in part, represent a higher degree of treated patients rather than more patients with a chronic condition.

Although ICU patients have more chronic conditions during the year before ICU admission, the most prevalent types of chronic conditions are comparable among the ICU population and the general population. We adjusted for some demographic differences between the two populations. However, it might be that other demographic factors not included in our dataset, might further explain the differences in risk of developing new chronic conditions. Nevertheless, we believe that factors related to the ICU admission, such as the acute illness, side-effects of treatment or complications, may play an important role in the development of new chronic conditions in ICU patients. Further research on this topic is essential.

A limitation of this study is the use of administrative claims data to identify chronic conditions and not the clinical

diagnoses described in the healthcare records of the patient. However, all drugs that were used for the classification of the chronic conditions can only be prescribed by a medical doctor. Furthermore, a latent chronic condition can be diagnosed during ICU admission and treated from that moment onwards, whereas a latent chronic condition in the control group may not be diagnosed during our study. This can lead to a overestimation of the differences in the development of new chronic conditions between the ICU population and the control group. Therefore, with post hoc analyses, we identified subpopulations of the control group: hospital population and nonhospital population. The supplementary analyses showed that ICU patients had still a higher risk of developing new chronic conditions compared with the hospital population. Furthermore, we excluded people who did not survive the entire study period for the analyses regarding the development of new chronic conditions. Within the ICU population, the mortality rate and the prevalence of chronic conditions are higher compared with the control group. People with more chronic conditions are more likely to have worse health outcomes and are more likely to pass away. By excluding deceased ICU patients, we expect that the differences in development of new chronic conditions between the ICU population and the control group are slightly larger than we estimated. There is limited evidence on the relation between mechanisms common to critical illness and the development of chronic conditions. A recently performed systematic review and meta-analysis concluded that stress hyperglycemia during ICU admission is associated with increased risk of incident diabetes. However, the strength of that association remains uncertain because of statistical and clinical heterogeneity among the included studies (33). We were not able to find an association between ICU related mechanisms and all other new chronic conditions described in our study. Further research is necessary to gain more insight in the association between mechanisms common to critical illness and/or the treatments provided in the ICU and the development of chronic conditions in order to coordinate ICU (follow-up) care. Despite these limitations, we still believe the differences we found are clinically significant. Through the unique collaboration of a national health insurance claims database and a national clinical ICU registry, we were able to include almost all patients admitted to a Dutch ICU. Since we included almost all ICU patients of an entire country, we also believe that the results we found are representative for other western countries with similar healthcare systems.

CONCLUSIONS

We showed that ICU patients have more chronic conditions during the year before ICU admission compared with a population-based control group and a five times higher odds on developing one or more new chronic conditions compared with the control group. Due to the high prevalence of chronic conditions and the increased risk of developing new chronic conditions ICU follow-up care is advised and may focus on the identification and treatment of the new developed chronic conditions. To this end, further research on the relation of ICU related factors and development of chronic conditions after ICU discharge is essential.

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