

BRIEF REPORT

## Comparability of the age and sex distribution of the UK Clinical Practice Research Datalink and the total Dutch population

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### ABSTRACT

**Purpose** The UK Clinical Practice Research Datalink (CPRD) is increasingly being used by Dutch researchers in epidemiology and pharmacoepidemiology. It is however unclear if the UK CPRD is representative of the Dutch population and whether study results would apply to the Dutch population. Therefore, as first step, our objective was to compare the age and sex distribution of the CPRD with the total Dutch population.

**Methods** As a measure of representativeness, the age and sex distribution of the UK CPRD were visually and numerically compared with Dutch census data from the StatLine database of the Dutch National Bureau of Statistics in 2011.

**Results** The age distribution of men and women in the CPRD population was comparable to the Dutch male and female population. Differences of more than 10% only occurred in older age categories (75+ in men and 80+ in women).

**Conclusions** Results from observational studies that have used CPRD data are applicable to the Dutch population, and a useful resource for decision making in the Netherlands. Nevertheless, differences in drug exposure likelihood between countries should be kept in mind, as these could still cause variations in the actual population studied, thereby decreasing its generalizability. Copyright © 2016 John Wiley & Sons, Ltd.

KEY WORDS—representativeness; database; population-based; epidemiology; pharmacoepidemiology

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### INTRODUCTION

The United Kingdom (UK) Clinical Practice Research Datalink (CPRD) is one of the world's largest primary care databases and is frequently used for post-authorisation safety studies, pharmaco-epidemiology, and disease epidemiology.<sup>1–5</sup> Examples include the

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evaluation of side effects of dopamine agonists<sup>2</sup> or diabetes drugs<sup>3,4</sup>, and the epidemiology of fractures.<sup>5</sup>

From a global perspective, the healthcare system in the Netherlands, a small country not far from the UK, is largely comparable to that of the UK's National Health Service (NHS); i.e. everyone has equal access to medical care regardless of income or socioeconomic status. In both countries, the general practitioner (GP) is the gatekeeper of the public healthcare system, meaning patients cannot refer themselves to secondary or tertiary care without the GP's approval. These conditions are key for conducting population-based pharmacoepidemiological studies.

Although the Dutch public healthcare system has excellent conditions for establishing a large primary care database for pharmacoepidemiological research that is comparable to the CPRD in terms of sample size, this has not yet occurred. Smaller primary care databases do exist (e.g. Netherlands Information Network of General Practice (LINH), Integrated Primary Care Information (IPCI), PHARMO Database Network); however these are generally restricted by a limited set of medical codes (approximately 1000 different "International Classification of Primary Care" codes versus over 100 000 READ codes in the CPRD), few validation studies, considerable smaller sample size (e.g. 350 000 in LINH and 1.5 million in IPCI versus over 11 million in CPRD in 2011), and limited access to routinely collected lifestyle data, such as tobacco use, alcohol consumption, and socioeconomic status.<sup>6</sup> Furthermore, claims that these data are representative for the total Dutch population are seldom supported by published figures.<sup>7,8</sup> For these reasons, an increasing number of CPRD studies are being conducted by researchers from the Netherlands and are financially supported by Dutch universities and funding agencies such as ZonMw and NWO. A recent study showed that the CPRD is representative of the total UK population with respect to age and sex and covers 6.9% of the UK population.<sup>1,9</sup> A wide range of diagnoses in the CPRD have been validated in a number of studies, and data quality are further enhanced by NHS annual reward and incentive programme that details GP practice achievement results, the Quality and Outcomes Framework (QOF). The QOF awards GPs for regular recording of detailed data on a wide range of diseases. As a result, the CPRD contains millions of recordings for measurements such as blood pressure, cholesterol values, and lung function. In addition, the strength of CPRD's data partially explains why officials of the Food and Drug Administration in the United States perform studies using the CPRD

database for drug safety monitoring and regulatory decision making.<sup>10–12</sup>

Although there are many similarities between healthcare systems of the UK and the Netherlands, it is unclear whether results from CPRD studies would apply to the Dutch population. Therefore, our objective was to compare the age and sex distribution of the CPRD to the total Dutch population.

## METHODS

Using the same sample of data from the previously published CPRD data resource profile, the age and sex distribution of the CPRD primary care data on 27 March 2011 were visually and numerically compared with UK and Dutch census data in 2011.<sup>1</sup> The CPRD (formerly known as Value Added Medical Products, and later General Practice Research Database<sup>13,14</sup>) harnesses data from UK's general practices and produces a primary care dataset since 1987. Through the years, it has become one of the largest databases of longitudinal medical records from primary care in the world, with coverage of over 11.3 million patients from 674 practices. To date, 4.4 million active (alive, currently registered) patients meet quality criteria (approximately 6.9% of the UK population), who are broadly representative of the UK general population in terms of age, sex, and ethnicity. For this study, visual comparison was performed by inspecting the overlap between the respective lines in a graph (Figure 1). An additional comparison calculated the differences between proportional distributions of 5-year age groups of CPRD data versus Dutch census data in 2011. We are not aware of any objective methods to define representativeness of patients in a research database compared to a country's total population. We therefore described the absolute and proportional differences between the age and sex distributions of CPRD and Dutch Census data in order to leave this to the reader, and made a subjective decision to consider an age-sex specific difference of <10% representative (Table 1). Numbers for computing sex-stratified age categories of the total Dutch population in March 2011 were obtained from the StatLine database of the Dutch National Bureau of Statistics ([www.cbs.nl](http://www.cbs.nl)).

## RESULTS

In general, the age distribution of men and women in the CPRD population was comparable to the Dutch male and female population (Figure 1). Overall, the

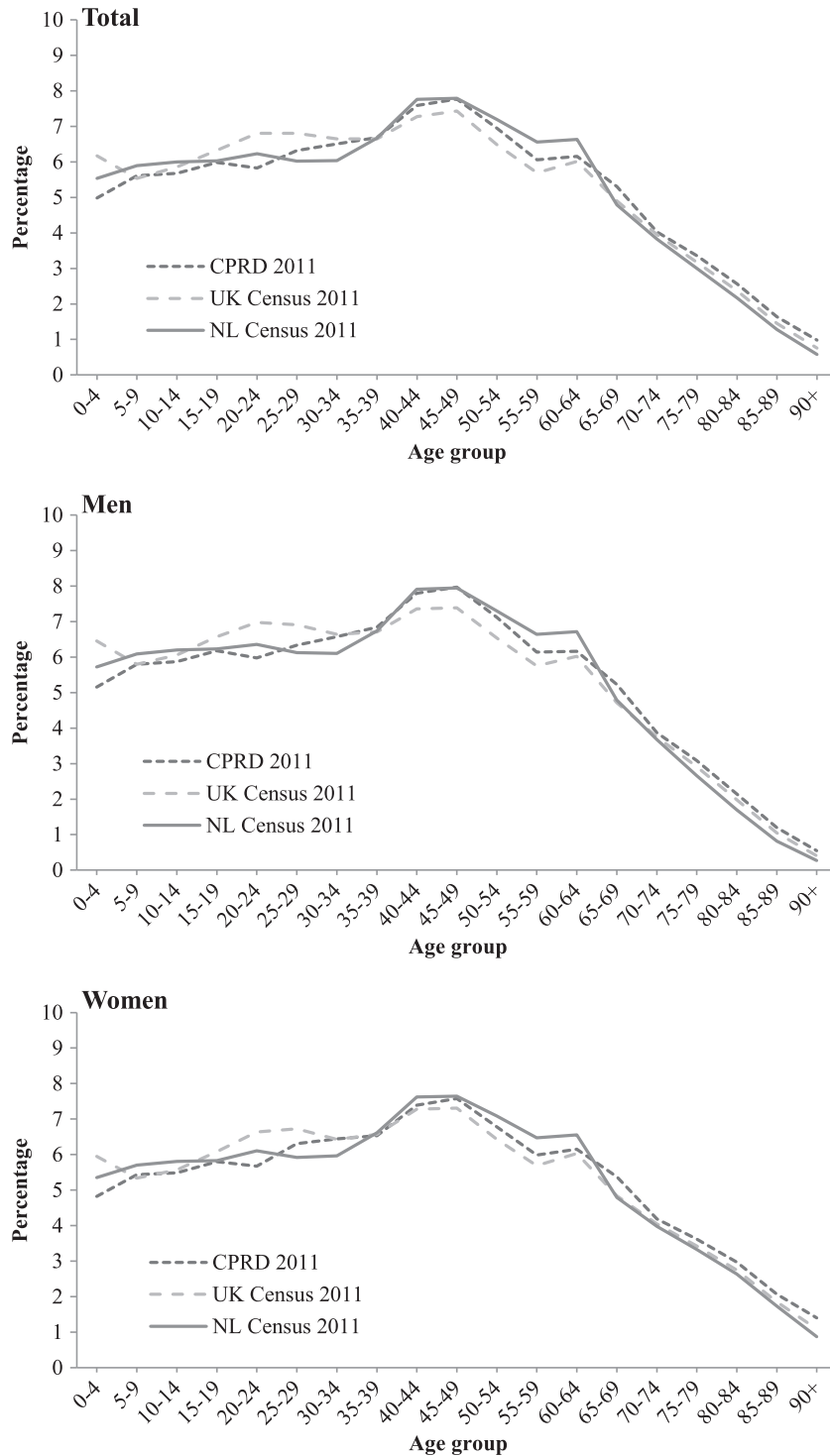


Figure 1. Age distribution of the CPRD primary care data on 27 March 2011 compared with UK and NL Census data from 2011, in both men and women (top panel), men only (middle panel), and women only (bottom panel). These data are based on a one-million patient sample of CPRD. Adapted from Herrett et al. *Int. J. Epidemiol* 2015

percentage men and women in the CPRD in 2011 was the same as in the Dutch population (49.5% men, 50.5% women). The additional comparison based on

calculating the differences between proportional distributions of 5-year age groups showed that differences of more than 10% occurred only in older age

Table 1. Differences between proportional age distributions of CPRD and the total Dutch population

Age group	Total				Men				Women			
	CPRD	NL Census	$\Delta^*$	$\Delta\%^\dagger$	CPRD	NL Census	$\Delta^*$	$\Delta\%^\dagger$	CPRD	NL Census	$\Delta^*$	$\Delta\%^\dagger$
0–4	4.99	5.54	–0.55	–9.94	5.15	5.72	–0.57	–9.98	4.82	5.35	–0.53	–9.90
5–9	5.61	5.89	–0.28	–4.75	5.80	6.09	–0.29	–4.74	5.43	5.70	–0.27	–4.77
10–14	5.68	6.00	–0.32	–5.38	5.87	6.20	–0.33	–5.32	5.49	5.80	–0.31	–5.43
15–19	5.99	6.03	–0.04	–0.65	6.18	6.23	–0.05	–0.80	5.80	5.83	–0.03	–0.50
20–24	5.83	6.23	–0.40	–6.44	5.98	6.35	–0.37	–5.89	5.68	6.10	–0.42	–7.00
25–29	6.32	6.02	0.30	4.96	6.34	6.13	0.21	3.41	6.31	5.92	0.39	6.54
30–34	6.51	6.03	0.47	7.83	6.57	6.11	0.46	7.65	6.44	5.96	0.48	8.01
35–39	6.69	6.67	0.01	0.20	6.84	6.74	0.10	1.62	6.53	6.61	–0.08	–1.22
40–44	7.59	7.77	–0.17	–2.22	7.80	7.91	–0.11	–1.42	7.39	7.62	–0.23	–3.03
45–49	7.77	7.79	–0.02	–0.31	7.97	7.95	0.02	0.22	7.58	7.64	–0.06	–0.86
50–54	6.95	7.19	–0.24	–3.41	7.12	7.30	–0.18	–2.44	6.78	7.09	–0.31	–4.38
55–59	6.06	6.56	–0.49	–7.54	6.14	6.64	–0.50	–7.62	5.99	6.47	–0.48	–7.46
60–64	6.15	6.64	–0.48	–7.24	6.16	6.72	–0.56	–8.30	6.15	6.55	–0.40	–6.18
65–69	5.30	4.79	0.51	<b>10.64</b>	5.23	4.79	0.44	9.18	5.37	4.79	0.58	<b>12.08</b>
70–74	4.03	3.83	0.20	5.27	3.87	3.67	0.20	5.31	4.19	3.98	0.21	5.23
75–79	3.36	3.00	0.36	<b>11.90</b>	3.09	2.66	0.43	<b>15.98</b>	3.62	3.33	0.29	8.71
80–84	2.56	2.17	0.39	<b>18.00</b>	2.15	1.70	0.45	<b>26.28</b>	2.97	2.64	0.33	<b>12.80</b>
85–89	1.64	1.28	0.36	<b>28.27</b>	1.20	0.82	0.38	<b>47.05</b>	2.07	1.73	0.34	<b>19.62</b>
90+	0.98	0.57	0.41	<b>70.52</b>	0.55	0.27	0.28	<b>102.20</b>	1.40	0.87	0.53	<b>60.92</b>

\* Absolute difference.

† Percentage difference between CPRD versus NL Census data (CPRD minus NL Census, divided by NL Census), with >10% regarded as different (BOLD). Abbreviations: CPRD: Clinical Practice Research Datalink; NL: Netherlands;  $\Delta$  difference.

categories, starting from 75+ in men, and 80+ in women (Table 1).

## DISCUSSION

In this study, we showed that the age and sex distribution of the CPRD was visually and numerically comparable to that of the total Dutch population in 2011.

To our knowledge, this is the first study to directly compare the age and sex distribution of the CPRD to the total Dutch population. Apart from LINH, a national data network compiling electronic medical records (EMR) of 92 primary care practices with 211 GPs and over 350 000 patients, we are not aware of any Dutch EMR database with data from GPs, which has published data on its representativeness according to the total Dutch population. The IPCI database is a longitudinal primary care database maintained by the department of Medical Informatics of the Erasmus Medical Centre in Rotterdam. In published papers of studies using the IPCI database it is frequently stated that the database is comparable to the total Dutch population in terms of age and sex.<sup>15,16</sup> However, we could not verify this claim in a (peer-reviewed) publication. In a report of the Netherlands Institute for Health Services Research (NIVEL), which maintains the LINH database, it is shown that LINH is generally comparable to the total Dutch population, with a slight underrepresentation of women of 75 years and older.<sup>8</sup> However, age- and sex-stratified proportions were

calculated as compared to the total LINH population and not as compared to the total LINH population stratified by sex, making direct comparison with our results difficult.

Our calculations of the differences between proportional distributions of 5-year age groups show that the CPRD is comparable to the Dutch population in terms of age and sex up to age 75 in men and age 80 in women. However, in Figure 1 it can be clearly seen that the age distribution of CPRD and Dutch census data almost overlap in these higher age groups. The large differences for higher age groups seen in Table 1 may be a spurious finding, because the calculations were based on very small proportions of the total population. Of note, some difference is also seen between CPRD and the UK population in Figure 1. Men and to a lesser extent women aged between 20 and 35 years of age are underrepresented in CPRD, which has been attributed to the fact that these individuals probably do not register with a GP.<sup>9</sup>

Several strengths have to be noted for this study. First, UK CPRD data were compared to data from the StatLine database of the Dutch National Bureau of Statistics, a reliable source of population-based information, regulated by national and European codes and laws.<sup>17</sup> Second, by calculating the differences between proportional distributions in all age groups, we demonstrated that the distributions were not only visually, but also numerically comparable. Last, by showing the overall representativeness of the CPRD

database of another population besides the UK population, CPRD may be used as rich data source for healthcare policymakers outside the UK.

There are also several limitations to this comparison. First, there are no objective methods to define representativeness of patients in a research database compared to a country's total population. To overcome this, we gave the reader insight into the various ways of comparing these data. Furthermore, the CPRD population was compared to the total Dutch population in terms of age and sex only. Therefore, we cannot rule out differences in for instance ethnicity, socioeconomic class, or lifestyle, which may in turn impact disease prevalence, exposure to important risk factors, or the degree of health care seeking behaviour. Based on the report of the OECD health indicators, the UK population has higher rates of tobacco and alcohol consumption, and especially obesity among adults, compared to the Dutch population.<sup>18</sup> Although the results of our study imply that the UK CPRD may also be representative of the total Dutch population, information on a specific population of drug users is ultimately necessary to know whether results from pharmacoepidemiological studies are transferrable to one's own region. As of yet, we have not looked into the comparability of various subpopulations in CPRD and The Netherlands. In addition, relative risks of disease outcomes found in CPRD could be extrapolated to the Dutch population, incidence rates or absolute risks cannot.

In conclusion, this study showed that the age and sex distribution of CPRD were generally comparable to that of the total Dutch population. Results from observational studies that have used CPRD data are applicable to the total Dutch population (similar to how relative risks from randomized clinical trials apply to their demarcated population), and a useful resource for decision making in the Netherlands. Nevertheless, differences in drug exposure likelihood between countries should be kept in mind, as these could still cause variations in the actual population studied, thereby decreasing its generalizability. In addition, the results of this study may encourage scientists from other countries with similar healthcare systems to perform comparable studies of CPRD representativeness.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## FUNDING

none.

## PRIOR POSTINGS AND PRESENTATIONS

None.

### KEY POINTS

- The age and sex distribution of the UK CPRD were comparable to the total Dutch population.
- Results from observational studies that have used CPRD data are applicable to the Dutch population.

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