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The Increasing Age- and Gender- Specific Burden and Complexity of Multimorbidity in Taiwan, 2003-2013

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4 **The Increasing Age- and Gender- Specific Burden and Complexity of**
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7 **Multimorbidity in Taiwan, 2003-2013**
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31 Database

ABSTRACT

Objectives

Although there are accumulating evidence in multimorbidity in Western countries, that in Asian countries is very limited. This study aimed to estimate the population-based, age- and gender-specific prevalence and trends of multimorbidity in the Taiwanese population.

Design

Cross-sectional study based on claims data (National Health Insurance Research Database, Taiwan).

Participants

A subset of the NHIRD, which contains claim data for 2 million of randomly selected beneficiaries (~10% of total population) under Taiwan's mandatory National Health Insurance system.

Outcome measurements

The prevalence of multimorbidity in different age groups and both sexes in the years 2003 and 2013 was reported. We further revealed data on the prevalence of 20 common diseases or deficits in each age group and sex. As for clustering effect, we used graphic displays on the likelihood of co-occurrence with 1, 2, 3, and 4 or more other diseases or deficits for each selected disease or deficit in the years 2003 and

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4 2013.
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7 **Results**

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10 The prevalence of multimorbidity was 37.23 % in 2003 and 48.97 % in 2013. In 2013,
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12 the prevalence varied between 19.85 % in patients aged 20-29 years and 92.01% in
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14 those aged 80-89 years. In patients aged between 50 and 79 years, the prevalence of
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16 multimorbidity was higher in women than that in men. In men, the prevalence of
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18 chronic pulmonary disease and cardiovascular-related diseases was predominant
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20 while in women, the prevalence of osteoporosis, arthritis, cancer, and psychosomatic
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22 disorders were predominant. The co-occurring diseases/deficits within each
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24 disease/deficit varied across different age and gender groups.
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34 **Conclusions**

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37 The burden of multimorbidity was increasing and becoming more complex in Taiwan.
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40 It also varied across different age and gender groups. Fulfilling the needs of
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42 individuals with multimorbidity requires collaborative work across health care
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44 providers and needs to take into account age and gender disparities in multimorbidity.
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Strengths and limitations of this study

- This is the first nationwide study conducted in Taiwan to assess the age- and gender-specific burden and complexity of multimorbidity between 2003 and 2013.
- Multimorbidity was defined using existing methods to classify and consider geographic or ethnic discrepancies between Western and Asian countries.
- We identified multimorbidity based on the diagnoses recorded in the outpatient or inpatient visit. However, only up to three and up to five diagnoses were allowed to be recorded in each outpatient or inpatient visit in the NHIRD, the prevalence of multimorbidities may be underestimated

Introduction

Multimorbidity, defined as the coexistence of two or more chronic health conditions in the same person at the same time, has become a significant challenge to the healthcare systems worldwide. Previous studies have reported that multimorbidity was associated with worse clinical outcomes, poorer quality of life and increased medical expenditures at individual level^{1 2}At the nationwide level, multimorbidity also incurs significant social and economic burden due to complex health and welfare demands as well as associated costs to care for individuals with multimorbidity^{1 2}. These demands are expected to increase as the society aged as the prevalence of multimorbidity also increased with age³. However, effective strategies to manage multimorbidity remain unanswered. These may be due to the single-disease paradigm in the current clinical setting, which may result in fragmented care for patients manifesting multimorbidity.

To manage multimorbidity, it is necessary to measure the burden of multimorbidity.

However, the phenomenon of multimorbidity is not well understood. A simple count of diseases in each identified either through self-reporting⁴or by extracting information from electronic medical record using lists of diagnostic codes⁵⁻⁸ is the first and common approach. The extrapolation of the abovementioned studies,

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4 however, is difficult due to several limitations. First, most of the estimates came from
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7 selected medical institutions^{3 9-12} or limited to the specific population such as the
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10 elderly³. Some studies using a survey to collect the potential prevalence of
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13 multimorbidities in patients who visit their general practitioners^{13 14}. Population-
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16 based estimates are usually very limited. Second, the lists of diagnosis are likely to
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19 differ substantially between studies^{6 15 16}. To the best of our knowledge, there is
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22 currently no single set of codes that have been consistently used to identify patients
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25 with multimorbidity. Third, the prevalence of multimorbidity in Asian countries is
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28 very limited while the prevalence of multimorbidity may vary ethnically or
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31 geographically.
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37 To fill the current knowledge gap, this study aimed to estimate the population-based,
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40 age- and gender-specific prevalence and trends of multimorbidity using Taiwan's
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43 National Health Insurance Research Database (NHIRD).
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Methods

Data source

A population-based cross-sectional study was conducted using administrative claims data from Taiwan's National Health Insurance Research Database (NHIRD). The NHIRD is a nationwide claims-based database comprising anonymous eligibility and enrollment information, as well as claims for outpatient visits, admissions, procedures and prescription medications of more than 99 % of the entire population (23 million) in Taiwan ¹⁷.

We used a subset of the NHIRD, which contains claim data for 2 million of randomly selected beneficiaries to create an 11-year (2003-2013) panel of claims for analysis. In this study, we used two subsets of the NHIRD, the Longitudinal Health Insurance Database (LHID) 2005 and 2010 as our data source. These two datasets were made up of claims data on one million beneficiaries that were randomly captured from the Registry of Beneficiaries of the NHIRD in the years 2005 and 2010. Also, there were no significant differences in the gender distribution between patients in the LHID 2005 and the original NHIRD ($\chi^2=0.008$, $df=1$, p -value=0.931), and between those in the LHID 2010 and the original NHIRD ($\chi^2=0.067$, $df=1$, p -value=0.796)¹⁸. Therefore, the two subsets were thought to be representative enough of the original NHIRD, and

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4 the results obtained suggested generalizability to the whole Taiwanese population.
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10 A total of two million individuals, which composed approximately 10% of the total
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13 population in Taiwan, constituted the study population of this study. The identification
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16 numbers and all traceable personal identifiers of the insured in NHIRD were encrypted
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19 to ensure the confidentiality and privacy. In this way, this study was exempt from full
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22 review by the Institutional Review Board of the National Taiwan University Hospital,
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25 Taipei, Taiwan, and the requirement for providing informed consent was not imposed.
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31 **Ethical statement**

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34 The identification numbers for all of the entries in the NHIRD were encrypted to
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37 protect the privacy of the individual patients. The study protocol was approved by the
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40 Institution Review Board of the National Taiwan University Hospital (National
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43 Taiwan University Hospital Research Ethics Committee No. 201403069W).
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49 **Identification of common diseases or deficits**

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52 We defined cases as patients who had at least three diagnoses with 20 common diseases
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55 or deficits upon outpatient visits during the study period. Similar with most previous
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58 studies focusing on multimorbidity, we also specify multimorbidity in this study on
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4 condition that patients concurrently suffered from two or more of these 20 common
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7 diseases or deficits The 20 common diseases or deficits included hypertension, diabetes,
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10 congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular
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13 disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver
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16 disease, dementia, other neurological disorders, digestive disorder, osteoporosis,
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19 arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders,
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22 bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer. The
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25 detailed set of diagnostic codes regarding the definition of these common diseases or
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28 deficits was demonstrated in **Supplementary Table S1**. These diseases or deficits were
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31 selected based on the disease burden that they may fall on the whole society regarding
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34 considerable cost, the requirement for long-term care, reduced health-related quality of
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37 life, hospitalization, or death illustrated in previous studies^{6 19 20}. There was a lack of
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40 consensus over what diseases or deficits should be included in the definition of
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43 multimorbidity. Nevertheless, we sought the union of the diseases included in two of
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46 the previous studies investigating multimorbidity^{6 19} and those in a Taiwanese study
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49 evaluating the association between frailty and unplanned hospitalization, admission to
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52 intensive care units, and mortality²⁰. In this way, we believed that the list of diseases
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55 which we adopted to define multimorbidity was capable of reflecting the disease burden
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58 the population carried and was applicable in the Taiwanese population.
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Statistical Analysis

We reported descriptive data on the prevalence of multimorbidity in different age groups (categorized into eight groups including 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, and 90+) and both sexes (men and women) in the years 2003 and 2013.

The prevalence of multimorbidity was calculated by dividing the number of patients afflicted with multimorbidity by population size in each age group regarding the degree of multimorbidity (grouped into 2, 3, 4, and 5+). We further revealed data on the prevalence of each of the 20 common diseases or deficits in each age group and sex.

The individual prevalence was the estimated fraction with the number of patients with each disease or deficit in each age and sex group as the numerator and with population size in each group and sex as the denominator.

As for clustering effect, we used graphic displays on the likelihood of co-occurrence with 1, 2, 3, and 4 or more other diseases or deficits for each selected disease or deficit in the years 2003 and 2013. The likelihood was the estimated proportion with the number of patients suffering from the same disease or deficit with concurrent 1, 2, 3, and 4 or more other diseases or deficits divided by the number of patients with a specific disease or deficit. We also adopted graphics to demonstrate differences in the prevalence of multimorbidity and clustering effect between both sexes and among age

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4 groups in 2003 and 2013, respectively. All data in this study were analyzed using
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7 Python programming language with Mongo database software, version 3.6.4 and 4.0.2.
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13 **Results**

16 In general, the prevalence of at least one of 20 common diseases or deficits was
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18 37.23 % in 2003, and an approximately ten percent increase was observed in the year
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20 of 2013 (48.97 % in 2013, **Table 1**). The prevalence of at least one disease or deficit
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22 of 2013 (48.97 % in 2013, **Table 1**). The prevalence of at least one disease or deficit
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24 ranged from 16.74 % in patients aged 20-29 years to 78.05 % in those aged 80-89 years
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26 in 2003. In 2013, the prevalence varied between 19.85 % in patients aged 20-29 years
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28 and 92.01% in those aged 80-89 years. Increases in the prevalence of at least one disease
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30 or deficit were observed in all age groups, and the magnitude was from 3.11 % in
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32 patients aged 20-29 years to a dramatic 28.21 % in those aged 90 years or above in the
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34 years 2003 and 2013 (**Table 1**, Supplementary **Figure S1**). As for the multimorbidity,
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36 the increasing prevalence across all age groups and different intensity of multimorbidity
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38 was of great concern. For instance, the prevalence of three of 20 common diseases or
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40 deficits was 30.39 % in patients aged 60-69 years in 2003, and an approximately seven
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42 percent increase in prevalence was observed in 2013. In patients aged 90 years or above,
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44 the increase was even more significant. Compared to the prevalence of three diseases
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46 or deficits in 2003 (33.04 %, **Table 1**, Supplementary **Figure S1**), that in 2013 nearly
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4 doubled (66.52 %, **Table 1**, Supplementary **Figure S1**)
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7 A dramatically growing increase in the prevalence of multimorbidity was noticed
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10 in all age groups, especially in those aged 90 years or above, in men and women in the
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12 years 2003 and 2013 (**Figure 2**). Patterns of sex differences in the prevalence of
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14 multimorbidity were similar between the years 2003 and 2013. To be more specific, the
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16 prevalence of multimorbidity were comparable between men and women in patients
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18 aged 49 years or younger. In patients aged between 50 and 79 years, however, the
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20 prevalence of multimorbidity was higher in women than that in men. In patients aged
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22 80-89 years, the sex difference in the prevalence of multimorbidity was subtle. In
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24 patients aged 90 years, the sex difference in prevalence of multimorbidity was much
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26 higher in men than that in women (**Figure 2**).
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37 The prevalence of each of 20 common diseases or deficits was presented in **Table**
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40 **2**. The prevalence of all of the 20 common diseases or deficits remained comparable or
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42 increased in all age groups between the years 2003 and 2013. Significantly growing
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44 prevalence can be observed in cancer, dementia, cerebrovascular disease, and several
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46 cardiovascular-related diseases, including hypertension, diabetes, congestive heart
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48 failure, cardiac dysrhythmias, and peripheral vascular disease. The most frequently
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50 seen diseases in Taiwanese population consisted of hypertension, other neurological
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52 disorders, digestive disorder, and arthritis (including rheumatoid arthritis). Over half of
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4 patients aged elder than 70 years in 2013 were afflicted with hypertension, and nearly
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7 one-third of those suffering from other neurological disorder, digestive disorder, and
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10 arthritis (including rheumatoid arthritis). Although the prevalence of cancer and
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13 dementia was generally low in Taiwan, the disease burden caused by these two diseases
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16 cannot be overseen. There was nearly one-fifth of patients aged 90 years or above were
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19 affected by dementia and nearly one-sixth of patients aged 80 years or above lived with
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22 cancers in 2013. Also, there was a strikingly increasing trend in prevalence of older
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25 patients in these two diseases.
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28 As shown in **Table 3**, the prevalence of each common diseases or deficits
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30 increased in general between the years 2003 and 2013 in both men and women. In men,
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33 the prevalence of chronic pulmonary disease and cardiovascular-related diseases,
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36 including hypertension, congestive heart failure, peripheral vascular disease were
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39 predominant. In women, the prevalence of osteoporosis, arthritis (including rheumatoid
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42 arthritis), cancer, and psychosomatic disorders, including depression, anxiety, bipolar
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45 disorder, were predominant. As for dementia, interestingly, the prevalence in men was
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48 a bit higher in 2003, yet the condition was quite the other way in 2013.
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52 In **Figure 2**, we depicted sex differences in the prevalence of multimorbidity
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55 within individuals suffering from each common disease or deficit in 2003 and 2013.
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58 Generally, compared to the year of 2003, multimorbidity was more frequently seen in
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4 2013 in both sexes within all common diseases. Except for bipolar disorder and
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7 schizophrenia and psychotic disorders, which were least likely to occur with other
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10 diseases, other diseases might coexist with other diseases to some extents. In 2003,
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13 patients with anxiety, dissociative and somatoform disorders, digestive disorder, and
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16 hypertension were most likely to suffer from other diseases concurrently, but the sex
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19 difference was minor. In 2013, patients with the diseases mentioned above were most
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22 likely to have other diseases in the same time as well, the sex difference, on the contrary,
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25 was more noticeable. Specifically, a higher proportion of women suffering from anxiety,
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28 dissociative and somatoform disorders, and digestive disorder are of greater odds to
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31 have other concurrent diseases. Profound sex difference in multimorbidity can also be
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34 observed in patients with other diseases, including arthritis (including rheumatoid
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37 arthritis), osteoporosis, other neurological disorders, and liver disease, where women
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40 with the first three were of higher prevalence to concurrently have other diseases.
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46 **Discussions**

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49 To the best of our knowledge, this population-based study is the largest and the
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52 most comprehensive epidemiologic study to provide age- and gender-specific
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55 information on multimorbidity in the Taiwanese population. Previous studies are all
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58 limited to Western Countries, such as Canada⁶ or Australia¹³. Nevertheless, the
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4 etiology of multimorbidity may have geographical discrepancies. This information is
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7 therefore extremely fundamental for constructing national policies to combat the
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10 burden of multimorbidities, particularly in Asian countries. Our study also provides
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13 in-depth analyses of each selected disease/deficit and their concomitant comorbidities.
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16 This study could thus serve as valuable references for strategic thinking regarding
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19 sophisticated diseases management plans.
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25 We found that the prevalence of multimorbidities was increasing in the 10-years
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28 follow-up period. This increase is reasonable considering the threat of aging
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31 population ²¹ and is consistent with a previous study conducted in Ontario residents ⁶.
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34 The prevalence of multimorbidity among Ontarians rose from 17.4% in 2003 to
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37 24.3% in 2009, a 40% increase. In our study, the prevalence of multimorbidity rose
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40 from 20.07% in 2013 to 30.44 % in 2009, a 51.6% increase. Although the different
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43 magnitude of the increase could result from the various lists of diseases selected to
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46 count multimorbidity; the Ontario study includes 16 common chronic conditions⁶
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49 while our study includes 20 common chronic conditions. However, the speed of aging
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52 in the two different populations may explain the discrepancies better. The population
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55 is aging rapidly in Taiwan. Up until the end of 2010, 11% of Taiwan's population was
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58 aged more than 65 years. The ratio has been reached to 14% (the threshold for an
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4 “aged” society) by 2017, and the estimated ratio will expect to increase to 20% (the
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7 threshold for a “superaged” society) by 2025 in Taiwan ²².
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13 Multimorbidity, particularly in the elderly, is therefore very important for almost
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16 every country. In our study, we found that the prevalence of multimorbidity (2+
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18 diseases) in people aged 60-69, 70-79 and 80-89 were 56.84%, 74.64%, 82.64%,
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21 respectively, in 2013. The prevalence of multimorbidity (3+ diseases) in people aged
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24 60-69, 70-79 and 80-89 were 37.49%, 57.04%, 68.10%, respectively, in 2013. Facing
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27 such tremendous and complex medical demands, it is necessary to reform the current
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30 “single disease or specialty” paradigm into the “integrated and comprehensive
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33 medical care” model ²³. In our study, we also found that the combination and intensity
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36 of multimorbidity differed in older men and women. This finding may further indicate
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39 different medical needs for older men and women and gender-specific care plan for
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42 older people may be warranted. Our estimates are thus could serve as good references
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45 for countries facing such a rapid speed of aging to allocate medical and social welfare
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48 resources, including Taiwan or our neighbor country, Japan ²⁴ or other European
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51 countries²⁵.
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58 In addition to older people, the prevalence of multimorbidity among the younger
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4 population yield special attention. As most researches in multimorbidity have focused
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7 on older adults^{26 27}, evidence regarding this issue in young adults is very limited. In
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10 our study, the prevalence of multimorbidity (2+ diseases) in people aged 30-39, 40-49
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13 and 50-89 were 11.18%, 21.76%, and 37.75%, respectively, in 2013. This indicates
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16 the need for early intervention in those who already suffer from multimorbidity in
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19 their middle-ages as the intensity of multimorbidity gradually increase as shown in
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22 our study. Lifestyle factors such as smoking, drinking, exercise or diet in middle ages
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25 were reported to be associated with multimorbidity²⁸.
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31 Most importantly, our study contributes to the understanding of the in-depth details of
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34 multimorbidity. In addition to revealing very distinct predominant diseases/deficits in
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37 men and women, we also reported the burden of multimorbidity in each common
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40 chronic condition. From a clinical perspective, our findings can help further strata the
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43 patients within a specific disease/deficit group. For example, care for patients with
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46 diabetes mellitus and with one other comorbid conditions should be very different
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49 from patients with diabetes mellitus and with four other comorbid conditions. From a
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52 policy perspective, our findings can help allocate medical resources more efficiently.
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55 Our previous studies also support this strata strategy (or identifying high-risk group)
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58 we found that the increase of diabetic complications was positively associated with
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4 increased risk of hospitalization and healthcare costs^{29 30}.
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10 While we provide great epidemiologic information of age- and gender-specific, it
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12 has some limitations due to the nature of claims data. First, we identified the
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14 disease/deficit selection based on the diagnoses recorded in the outpatient or inpatient
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16 visit. However, only up to three and up to five diagnoses were allowed to be recorded
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18 in each outpatient or inpatient visit, the prevalence of multimorbidities may be
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20 underestimated. Second, as we used the NHIRD, the estimation about the
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22 multimorbidity in this study was from the perspective of the national insurance
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24 system. Patients who pay out-of-pocket for their diseases are not recorded in the
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26 NHIRD as well.
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40 Conclusively, our study is the first population-based study conducted in Taiwan
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42 providing age- and gender-specific information on multimorbidity. The burden of
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44 multimorbidity was increasing and becoming more complex in Taiwan. Providing for
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46 the needs of individuals with multimorbidity requires collaborative work across health
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48 care providers and may need to take into account age and gender disparities in
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50 multimorbidity.
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Figure legends

Figure 1. Prevalence of multi-morbidity in Taiwan by the number of common diseases or deficits*, sex, age group, and year. (a) Men and women in 2003. (b) Men and women in 2013.

Figure 2. Distribution of the proportion of individuals with multimorbidity in Taiwan within common diseases or deficits by sex and year.

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Table 1. Prevalence of multi-morbidity in Taiwan by number of common diseases or deficits*, age group, and year

2003							
Age groups	Taiwanese Population	Prevalence of at least one disease/deficit	Prevalence of multimorbidity, by degree of multimorbidity				
			2	3	4	5+	
20-29	285,406	16.74	4.01	1.15	0.36	0.12	
30-39	273,713	24.09	8.04	2.86	1.03	0.37	
40-49	269,568	35.91	16.01	7.08	2.92	1.12	
50-59	175,456	51.70	30.15	16.49	8.00	3.57	
60-69	114,876	66.52	47.08	30.39	17.13	8.70	
70-79	74,756	77.86	62.40	45.66	29.10	16.75	
80-89	20,002	78.05	64.32	48.74	32.39	19.58	
90+	1,946	62.23	45.68	33.04	21.12	12.69	
All	1,215,723	37.23	20.07	11.40	6.09	3.07	
2013							
Age groups	Taiwanese Population	Prevalence of at least one disease/deficit	Prevalence of multimorbidity, by degree of multimorbidity				
			2	3	4	5+	
20-29	245,613	19.85	5.21	1.49	0.47	0.15	
30-39	295,797	30.49	11.18	4.10	1.55	0.60	
40-49	277,889	43.45	21.76	10.08	4.35	1.83	
50-59	272,719	59.90	37.75	20.87	10.24	4.71	
60-69	173,213	75.39	56.84	37.49	21.74	11.70	
70-79	102,826	87.53	74.64	57.04	38.44	23.60	
80-89	52,978	92.01	82.64	68.10	49.71	33.06	
90+	8,492	90.44	80.96	66.52	48.39	32.54	
All	1,429,527	48.97	30.44	18.61	10.73	5.94	

*Hypertension, diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver disease, dementia, other neurological disorders, digestive disorder, osteoporosis, arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders, bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer

Table 2. Prevalence of 20 common diseases or deficits in Taiwan, by age group and year

Disease/ deficit	Year	Number with condition (prevalence)	Prevalence of each disease/ deficit, by age group							
			20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Hypertension	2003	126,651(10.42)	0.22	1.38	6.31	17.11	29.91	42.36	43.26	28.78
	2013	260,198(18.20)	0.43	2.38	9.54	22.91	39.64	55.39	61.71	56.64
Diabetes	2003	56,627(4.66)	0.20	0.77	3.00	8.51	14.04	16.31	12.51	5.86
	2013	126,991(8.88)	0.35	1.27	4.50	11.47	21.10	26.39	25.23	18.38
Congestive heart failure	2003	44,622(3.67)	0.06	0.38	1.80	5.35	10.43	17.25	19.95	15.88
	2013	71,026(4.97)	0.09	0.45	1.87	4.99	10.10	17.19	24.78	28.24
Coronary syndrome	2003	35,539(2.92)	0.04	0.25	1.19	3.98	8.75	14.82	16.05	11.20
	2013	60,367(4.22)	0.05	0.27	1.43	4.19	9.38	15.29	19.72	18.86
Cardiac dysrhythmias	2003	14,337(1.18)	0.14	0.31	0.69	1.47	2.89	5.24	6.67	5.29
	2013	29,098(2.04)	0.18	0.32	0.83	1.79	3.76	6.95	10.88	12.69
Peripheral vascular disease	2003	14,873(1.22)	0.07	0.13	0.44	1.23	3.34	7.10	8.70	4.78
	2013	28,562(2.00)	0.08	0.17	0.48	1.45	3.92	8.66	11.34	9.89
Cerebrovascular disease	2003	28,098(2.31)	0.14	0.25	0.86	2.74	6.59	12.09	15.26	11.51
	2013	56,770(3.97)	0.18	0.38	1.12	3.24	7.82	15.35	22.51	23.85
Chronic pulmonary disease	2003	37,897(3.12)	0.78	1.32	1.95	3.46	7.25	12.22	15.14	12.85
	2013	50,705(3.55)	0.74	1.26	1.80	3.02	5.77	10.73	17.17	21.15
Renal disease	2003	13,999(1.15)	0.18	0.34	0.77	1.57	2.80	4.54	5.07	3.44
	2013	38,748(2.71)	0.18	0.44	1.06	2.44	5.19	9.64	13.79	14.13
Liver disease	2003	43,555(3.58)	1.39	2.58	4.03	5.53	6.23	5.44	3.41	1.64
	2013	71,015(4.97)	0.79	2.88	5.13	7.28	8.56	8.05	5.69	4.03
Dementia	2003	5,194(0.43)	0.10	0.12	0.17	0.27	0.72	2.24	5.06	6.27
	2013	18,869(1.32)	0.13	0.19	0.30	0.51	1.27	4.89	12.77	20.54
Other neurological disorders	2003	124,029(10.20)	4.25	6.84	9.44	13.12	18.24	24.21	26.53	17.78
	2013	217,307(15.20)	6.54	10.37	13.29	16.90	21.42	29.04	33.85	31.03

Table 2. Prevalence of 20 common diseases or deficits in Taiwan, by age group and year (cont'd)

Disease/ deficit	Year	Number with condition (prevalence)	Prevalence of each disease/ deficit, by age group							
			20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Digestive disorder	2003	152,161(12.52)	6.81	8.54	11.19	14.94	21.03	29.22	32.39	25.95
	2013	227,327(15.90)	8.41	11.15	13.40	17.09	22.01	29.06	35.24	37.48
Osteoporosis	2003	14,732(1.21)	0.09	0.13	0.49	2.04	3.59	5.02	6.08	5.45
	2013	17,026(1.19)	0.07	0.11	0.23	0.74	2.10	5.23	7.67	9.15
Arthritis (including rheumatoid arthritis)	2003	149,434(12.29)	3.87	6.34	11.05	18.01	25.54	31.95	30.18	19.63
	2013	226,844(15.87)	4.18	7.28	12.01	19.46	27.70	37.45	37.03	29.30
Anxiety, dissociative and somatoform disorders	2003	52,029(4.28)	1.27	2.48	4.17	6.34	8.48	9.99	9.49	5.91
	2013	89,053(6.23)	1.69	3.45	5.82	8.00	10.29	11.91	11.18	8.44
Bipolar disorder	2003	8,251(0.68)	0.44	0.59	0.72	0.84	0.89	1.03	0.89	0.51
	2013	15,439(1.08)	0.51	0.80	1.25	1.30	1.44	1.50	1.32	0.92
Depression	2003	11,630(0.96)	0.64	0.82	0.97	1.14	1.27	1.51	1.61	1.13
	2013	24,712(1.73)	0.86	1.30	1.89	2.00	2.24	2.52	2.59	2.25
Schizophrenia and psychotic disorders	2003	7,472(0.61)	0.48	0.80	0.74	0.57	0.43	0.40	0.55	0.51
	2013	11,624(0.81)	0.42	0.82	1.10	1.00	0.77	0.65	0.55	0.67
Cancer	2003	37,438(3.08)	1.26	2.22	3.77	4.11	4.47	5.50	5.46	2.93
	2013	83,065(5.81)	1.36	2.97	5.68	7.22	9.19	11.54	12.57	12.16

Table 3. Prevalence of 20 common diseases or deficits in Taiwan, by sex, age group and year

Disease/ deficit	Year	Prevalence		Prevalence of each disease/ deficit, by age group															
				20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Hypertension	2003	10.52	10.33	0.33	0.11	1.90	0.92	7.29	5.42	17.13	17.09	27.66	31.83	39.89	44.96	41.16	45.18	29.55	28.31
	2013	19.40	17.13	0.68	0.21	3.58	1.35	12.67	6.71	25.93	20.10	40.55	38.81	51.88	58.30	58.03	65.22	54.02	58.70
Diabetes	2003	4.77	4.56	0.21	0.19	1.05	0.51	3.73	2.34	9.15	7.94	13.07	14.86	14.10	18.64	11.47	13.47	5.75	5.93
	2013	9.57	8.26	0.40	0.31	1.75	0.86	6.18	2.97	13.52	9.56	21.87	20.40	24.50	27.96	22.52	27.81	17.60	18.99
Congestive heart failure	2003	3.71	3.63	0.09	0.03	0.54	0.24	2.12	1.51	5.48	5.25	9.58	11.16	16.27	18.28	19.34	20.51	17.10	15.14
	2013	5.24	4.72	0.14	0.04	0.68	0.25	2.56	1.25	5.82	4.21	10.67	9.58	16.02	18.15	23.37	26.13	27.04	29.18
Coronary syndrome	2003	3.21	2.67	0.05	0.03	0.33	0.17	1.51	0.89	4.47	3.55	8.81	8.70	15.53	14.07	16.88	15.30	11.76	10.86
	2013	5.00	3.52	0.06	0.04	0.44	0.13	2.14	0.78	5.49	2.99	11.24	7.71	16.41	14.36	20.94	18.55	20.42	17.65
Cardiac dysrhythmias	2003	1.19	1.17	0.13	0.15	0.29	0.33	0.64	0.73	1.39	1.54	2.90	2.88	5.40	5.06	6.85	6.51	6.57	4.53
	2013	2.10	1.98	0.16	0.20	0.31	0.34	0.85	0.81	1.83	1.77	3.94	3.60	7.08	6.84	11.69	10.11	12.81	12.61
Peripheral vascular disease	2003	1.23	1.22	0.08	0.06	0.16	0.11	0.47	0.41	1.20	1.25	3.01	3.62	7.01	7.19	8.97	8.46	5.61	4.28
	2013	2.00	2.00	0.06	0.10	0.18	0.16	0.54	0.44	1.60	1.32	3.83	4.00	8.06	9.16	11.76	10.95	11.25	8.82
Cerebrovascular disease	2003	2.61	2.04	0.16	0.12	0.34	0.18	1.07	0.67	3.18	2.36	7.05	6.19	13.01	11.11	16.29	14.31	14.09	9.96
	2013	4.54	3.46	0.19	0.17	0.47	0.29	1.47	0.80	4.05	2.50	9.15	6.61	16.65	14.28	24.45	20.67	24.81	23.09

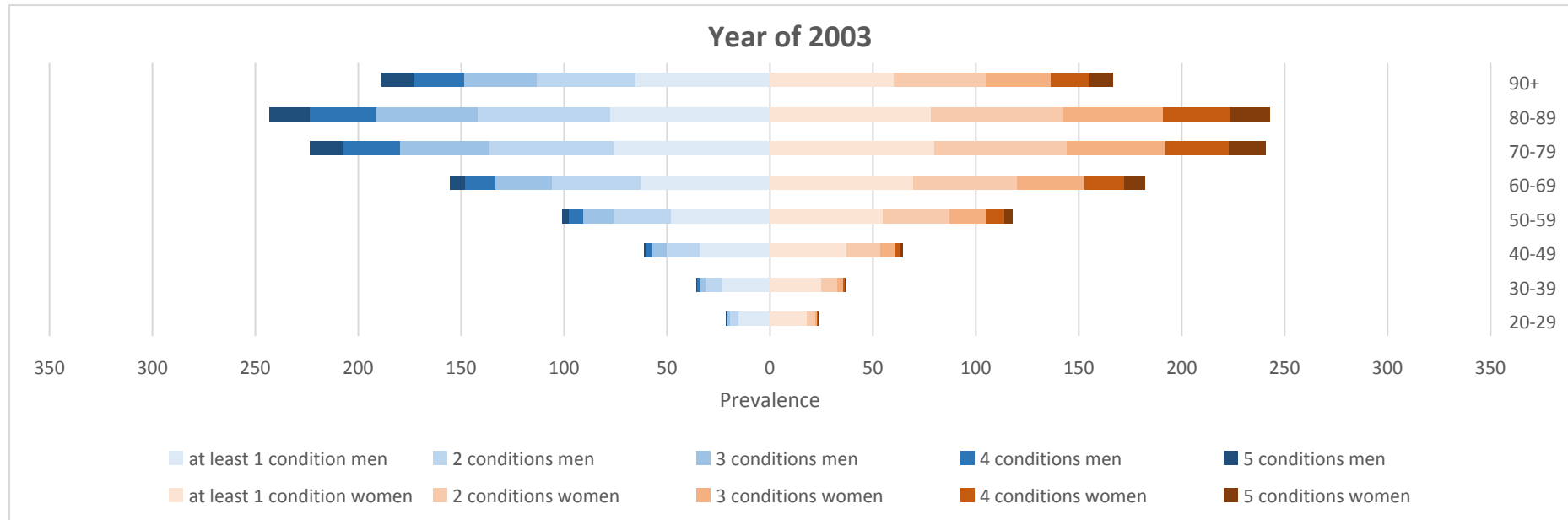
Table 3. Prevalence of 20 common diseases or deficits in Taiwan, by sex, age group and year (cont'd)

Disease/ deficit	Year	Prevalence		Prevalence of each disease/ deficit, by age group															
				20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Chronic pulmonary disease	2003	3.51	2.76	0.80	0.76	1.24	1.39	1.99	1.93	3.50	3.41	8.02	6.59	15.19	9.08	19.80	10.86	17.51	10.04
	2013	4.00	3.14	0.71	0.76	1.16	1.34	1.75	1.85	3.09	2.96	6.52	5.10	13.26	8.62	21.96	12.60	26.98	16.58
Renal disease	2003	1.29	1.03	0.22	0.15	0.42	0.27	0.86	0.68	1.68	1.48	3.02	2.62	4.90	4.16	6.09	4.14	4.51	2.80
	2013	3.26	2.22	0.21	0.15	0.58	0.32	1.42	0.72	3.04	1.89	6.25	4.23	11.26	8.29	15.84	11.85	16.96	11.91
Liver disease	2003	4.61	2.66	2.12	0.76	3.95	1.36	5.64	2.56	6.38	4.78	6.70	5.83	5.59	5.28	3.90	2.96	2.19	1.32
	2013	6.20	3.86	1.12	0.49	4.30	1.66	7.35	3.12	8.92	5.76	9.21	7.97	8.49	7.68	6.13	5.28	4.66	3.53
Dementia	2003	0.46	0.39	0.15	0.06	0.18	0.07	0.21	0.13	0.32	0.23	0.75	0.70	2.14	2.35	4.82	5.28	4.24	7.49
	2013	1.31	1.33	0.16	0.10	0.26	0.14	0.41	0.20	0.63	0.41	1.31	1.23	4.52	5.20	11.70	13.79	18.81	21.89
Other neurological disorders	2003	8.00	12.17	3.29	5.08	5.24	8.27	6.90	11.76	9.31	16.48	14.62	21.32	21.26	27.32	23.99	28.86	17.10	18.19
	2013	12.02	18.05	4.74	8.19	7.79	12.59	10.02	16.25	12.66	20.81	16.84	25.58	25.34	32.12	32.25	35.37	30.73	31.26

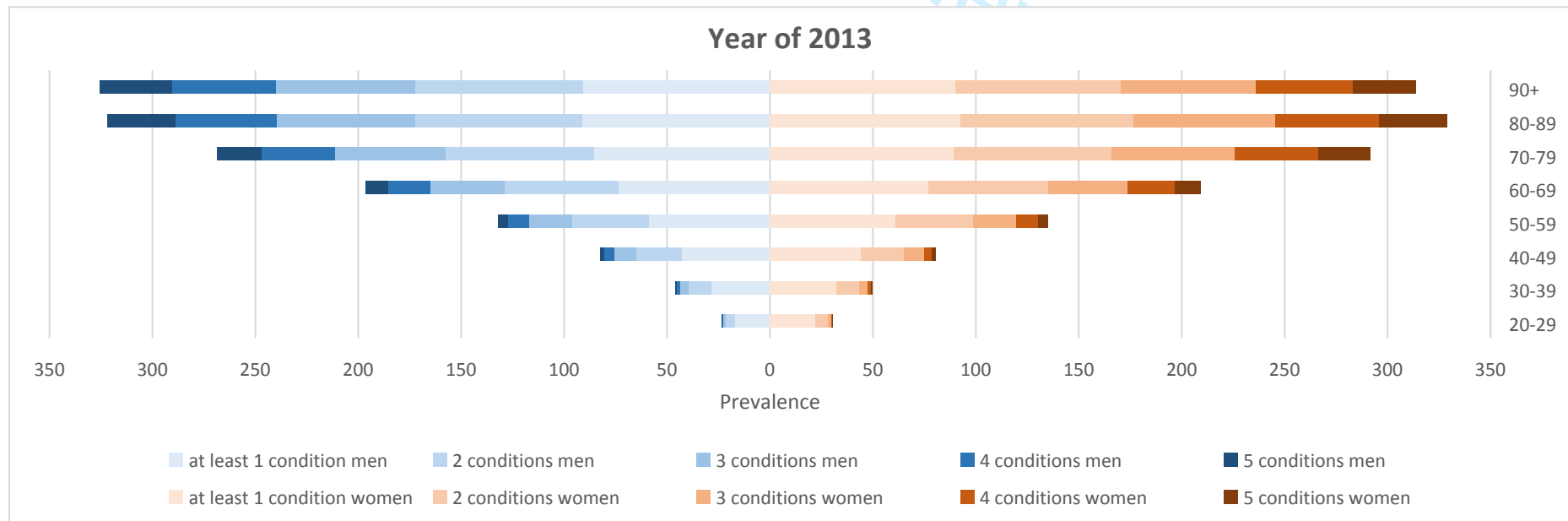
Table 3. Prevalence of 20 common diseases or deficits in Taiwan, by sex, age group and year (cont'd)

Disease/ deficit	Year	Prevalence		Prevalence of each disease/ deficit, by age group															
				20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Digestive disorder	2003	11.62	13.32	4.92	8.46	7.63	9.35	10.53	11.79	13.78	15.96	19.84	22.04	29.87	28.54	34.65	30.32	28.04	24.69
	2013	14.01	17.60	5.65	10.93	8.59	13.34	11.63	15.00	15.14	18.91	20.14	23.69	28.32	29.67	37.55	33.04	41.88	34.03
Osteoporosis	2003	0.45	1.89	0.13	0.05	0.14	0.13	0.26	0.70	0.41	3.48	0.91	5.87	2.07	8.14	2.75	9.14	4.10	6.26
	2013	0.58	1.74	0.09	0.05	0.15	0.08	0.26	0.21	0.45	1.02	0.76	3.31	1.98	7.93	3.72	11.43	5.25	12.21
Arthritis (including rheumatoid arthritis)	2003	12.26	12.32	4.81	3.05	7.46	5.35	11.49	10.65	16.09	19.70	22.43	28.20	30.16	33.85	29.71	30.61	22.85	17.70
	2013	15.32	16.36	4.89	3.53	8.75	6.03	12.75	11.34	18.01	20.80	24.02	31.04	32.67	41.43	35.62	38.37	30.49	28.36
Anxiety, dissociative and somatoform disorders	2003	3.36	5.10	1.11	1.42	2.05	2.86	3.26	5.01	4.47	7.99	6.27	10.36	8.18	11.91	8.46	10.44	6.43	5.60
	2013	4.90	7.42	1.50	1.86	2.95	3.87	4.76	6.78	5.99	9.87	7.55	12.78	9.09	14.26	9.34	12.94	7.93	8.84
Bipolar disorder	2003	0.55	0.79	0.43	0.45	0.44	0.72	0.55	0.87	0.63	1.02	0.72	1.03	0.87	1.20	0.76	1.02	0.55	0.49
	2013	0.84	1.29	0.51	0.51	0.65	0.93	0.95	1.52	0.97	1.62	1.04	1.79	1.10	1.84	1.09	1.54	0.99	0.86
Depression	2003	0.80	1.10	0.66	0.62	0.65	0.98	0.76	1.15	0.86	1.39	1.00	1.50	1.32	1.71	1.44	1.77	0.82	1.32
	2013	1.42	2.00	0.87	0.84	1.11	1.47	1.56	2.19	1.56	2.42	1.70	2.73	1.96	2.98	2.23	2.93	2.20	2.29
Schizophrenia and psychotic disorders	2003	0.68	0.56	0.62	0.37	0.96	0.65	0.81	0.68	0.51	0.62	0.34	0.51	0.37	0.43	0.49	0.61	0.41	0.58
	2013	0.89	0.75	0.50	0.35	0.98	0.68	1.32	0.91	1.04	0.97	0.70	0.85	0.51	0.77	0.49	0.60	0.59	0.74
Cancer	2003	2.21	3.85	0.90	1.58	1.22	3.11	1.80	5.56	2.80	5.26	4.26	4.66	6.22	4.73	6.82	4.21	4.38	2.06
	2013	5.06	6.49	1.02	1.67	1.82	3.95	3.41	7.73	5.76	8.57	9.09	9.29	13.37	10.02	15.81	9.49	16.21	8.99

Figure 1. Prevalence of multi-morbidity in Taiwan by number of common diseases or deficits*, sex, age group, and year
(a) Men and women in 2003



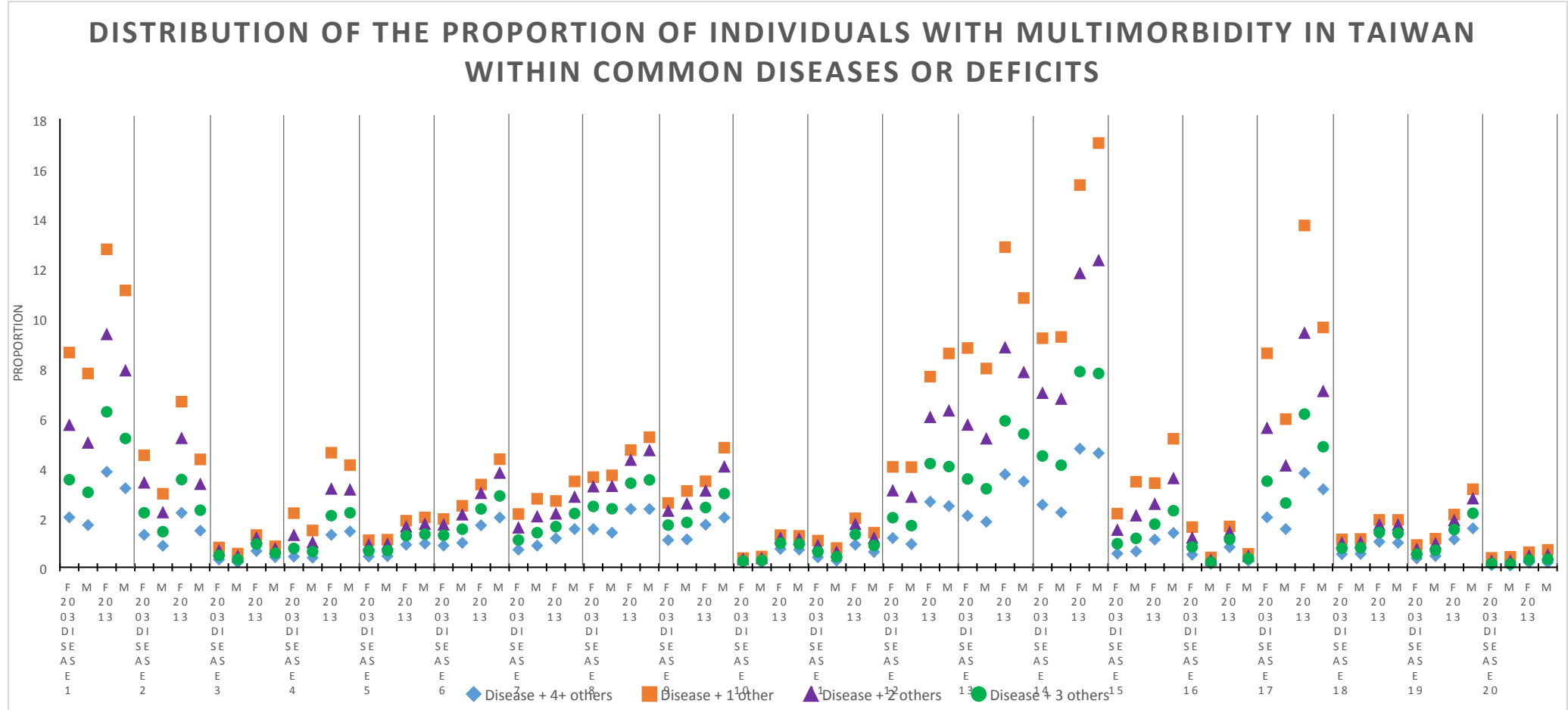
(b) Men and women in 2013



1 *Hypertension, diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular disease, cerebrovascular disease, chronic
2 pulmonary disease, renal disease, liver disease, dementia, other neurological disorders, digestive disorder, osteoporosis, arthritis (including rheumatoid
3 arthritis), anxiety dissociative and somatoform disorders, bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer
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Figure 2. Distribution of the proportion of individuals with multimorbidity in Taiwan within common diseases or deficits by sex and year



*Disease 1: Anxiety, dissociative and somatoform disorders; Disease 2: Arthritis (including rheumatoid arthritis); Disease 3: Bipolar disorder; Disease 4: Cancer; Disease 5: Cardiac dysrhythmias; Disease 6: Cerebrovascular disease; Disease 7: Chronic pulmonary disease; Disease 8: Congestive heart failure; Disease 9: Coronary syndrome; Disease 10: Dementia; Disease 11: Depression; Disease 12: Diabetes; Disease 13: Digestive disorders; Disease 14: Hypertension; Disease 15: Liver disease; Disease 16: Osteoporosis; Disease 17: Other neurological disorders; Disease 18: Peripheral vascular disease; Disease 19: Renal disease; Disease 20: Schizophrenia and psychotic disorders.

Table S1. ICD-9-CM codes regarding the definition of 20 common diseases or deficits

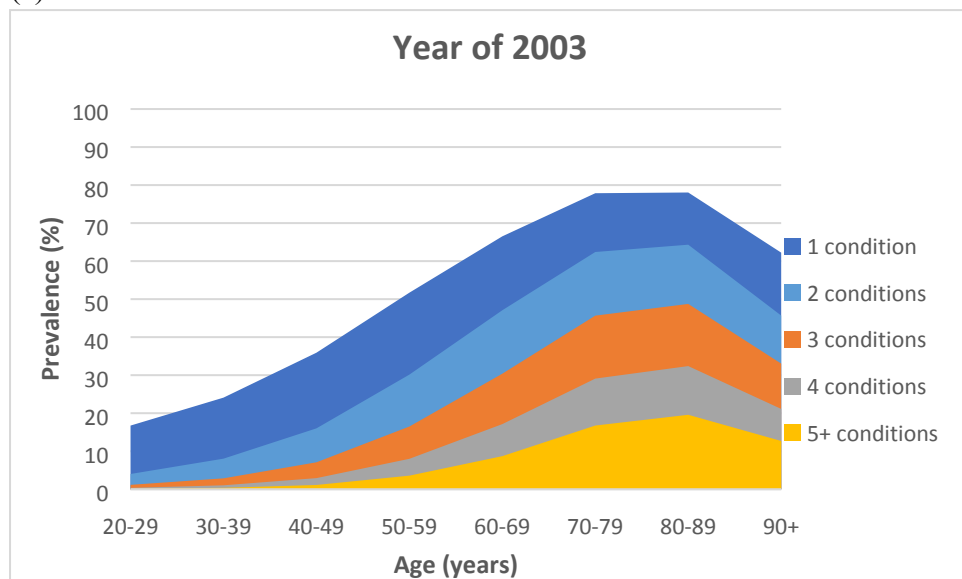
Disease/ Deficit	ICD-9-CM code
Hypertension	401, 402, 403, 404, 405
Diabetes	250
Congestive heart failure	39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 4254, 4255, 4257, 4258, 4259, 428
Coronary syndrome	410, 411, 412, 413, 414
Cardiac dysrhythmias	427
Peripheral vascular disease	0930, 4373, 4400, 4401, 44020, 44021, 44022, 44023, 44024, 44029, 44030, 44031, 44032, 4408, 4409, 44100, 44101, 44102, 44103, 4411, 4412, 4413, 4414, 4415, 4416, 4417, 4419, 4431, 44321, 44322, 44323, 44324, 44329, 44381, 44382, 44389, 4439, 4471, 5571, 5579, V434
Cerebrovascular disease	36234, 430, 431, 432, 43300, 43301, 43310, 43311, 43320, 43321, 43330, 43331, 43380, 43381, 43390, 43391, 434, 4350, 4351, 4352, 4353, 4358, 4359, 436, 437, 438
Chronic pulmonary disease	4168, 4169, 490, 491, 492, 493, 4940, 4941, 4950, 4951, 4952, 4953, 4954, 4955, 4956, 4957, 4958, 4959, 496, 500, 501, 502, 503, 504, 505, 5064, 5081, 5088
Renal disease	403, 404, 5820, 5821, 5822, 5824, 58281, 58289, 5829, 5830, 5831, 5832, 5834, 5836, 5837, 584, 585, 586, 5880, V420, V451, V560, V561, V562, V5631, V5632, V568
Liver disease	07022, 07023, 07032, 07033, 07044, 07054, 0706, 0709, 570, 5710, 5711, 5712, 5713, 57140, 57141, 57149, 5715, 5716, 5718, 5719, 5733, 5734, 5738, 5739, V427, 4560, 4561, 45620, 45621, 5722, 5723, 5724, 5728
Dementia	290, 2930, 2931, 29381, 29382, 29383, 29384, 29389, 2939, 2940, 2941, 2948, 2949, 3100, 3101, 3102, 3108, 3109, 3310, 3311, 3312
Other neurological disorders	3319, 332, 3334, 3335, 33392, 3340, 3341, 3342, 3343, 3344, 3348, 3349, 3350, 33510, 33511, 33519, 33520, 33521, 33522, 33523, 33524, 33529, 3358, 3359, 3362, 340, 3410, 3411, 34120, 34121, 34122, 3418, 3419, 34500, 34501, 34510, 34511, 3452, 3453, 34540, 34541, 34550, 34551, 34560, 34561, 34570, 34571, 34580, 34581, 34590, 34591, 3481, 3483, 34830, 34831, 34839, 780, 7843
Digestive disorder	530, 531, 532, 53300, 53301, 53310, 53311, 53320, 53321, 53330, 53331, 53340, 53341, 53350, 53351, 53360, 53361, 53370, 53371, 53390, 53391, 53400, 53401, 53410, 53411, 53420, 53421, 53430, 53431, 53440, 53441, 53450, 53451, 53460, 53461, 53470, 53471, 53490, 53491, 536, 558, 564
Osteoporosis	733
Arthritis (including rheumatoid arthritis)	274, 710, 711, 714, 715, 716, 718, 720, 727, 728, 729, 739

Table S1. ICD-9-CM codes regarding the definition of 20 common diseases or deficits (continued)

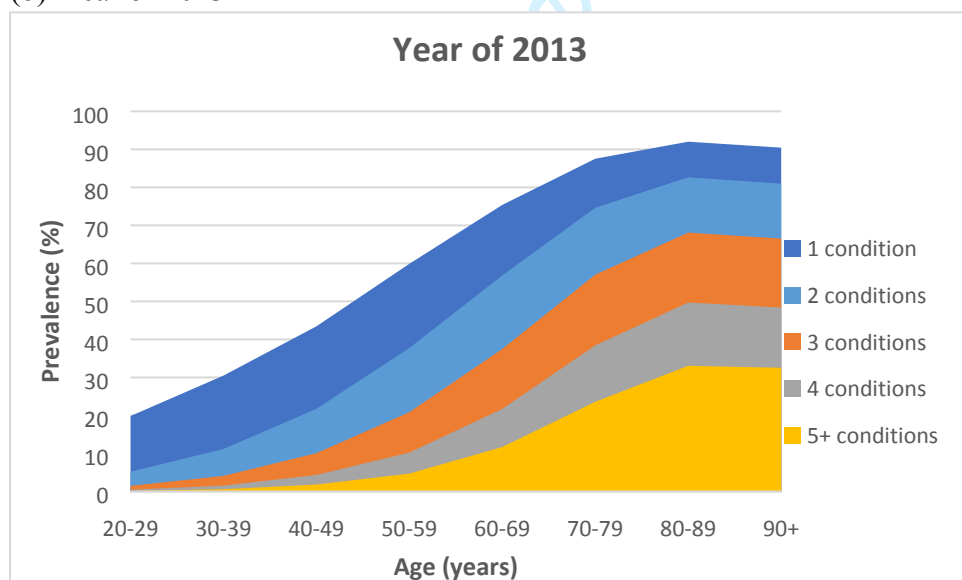
Disease/ Deficit	ICD-9-CM code
Anxiety, dissociative and somatoform disorders	30000-30002, 30009-30016, 30019-30023, 30029, 3003, 3005-3007, 30081, 30082, 30089, 3009, 3062, 3069, 30740-30749, 3080-3084, 3089, 316
Bipolar disorder	29600-29606, 29610-29616, 29640-29646, 29650-29656, 29660-29666, 2967, 29680-29682, 29689
Depression	29620-29626, 29630-29636, 29690, 29699, 2980, 3090, 3091, 311
Schizophrenia and psychotic disorders	29500-29505, 29510-29515, 29520-29525, 29530-29535, 29540-29545, 29550-29555, 29560-29565, 29570-29575, 29580-29585, 29590-29595, 2970-2973, 2978, 2979, 2981-2984, 2988, 2989, 29900, 29901, 29910, 29911, 29980, 29981, 29990, 29991
Cancer	140-239

Figure S1. Prevalence of multi-morbidity in Taiwan by number of common diseases or deficits*, age group, and year

(a) Year of 2003



(b) Year of 2013



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The Increasing Age- and Gender- Specific Burden and Complexity of Multimorbidity in Taiwan, 2003-2013

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Manuscripts

Revised Manuscript (clean)**The Increasing Age- and Gender- Specific Burden and Complexity of Multimorbidity in Taiwan, 2003-2013**

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42
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55 **Keywords:** disease burden, multimorbidity, National Health Insurance Research
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58 Database
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ABSTRACT

Objectives

Although there are accumulating evidence in multimorbidity in Western countries, that in Asian countries is very limited. This study aimed to estimate the population-based, age- and gender-specific prevalence and trends of multimorbidity in the Taiwanese population.

Design

Cross-sectional study based on claims data (National Health Insurance Research Database, Taiwan).

Participants

A subset of the NHIRD, which contains claim data for 2 million of randomly selected beneficiaries (~10% of total population) under Taiwan's mandatory National Health Insurance system.

Outcome measurements

The prevalence of multimorbidity in different age groups and both sexes in the years 2003 and 2013 was reported. We further revealed data on the prevalence of 20 common diseases in each age group and sex. As for clustering effect, we used graphic displays on the likelihood of co-occurrence with 1, 2, 3, and 4 or more other diseases for each selected disease in the years 2003 and 2013.

Results

The prevalence of multimorbidity (2+ diseases) was 20.07 % in 2003 and 30.44 % in 2013. In 2013, the prevalence varied between 5.21 % in patients aged 20-29 years and 80.96% in those aged 80-89 years. In patients aged between 50 and 79 years, the prevalence of multimorbidity was higher in women than that in men. In men, the prevalence of chronic pulmonary disease and cardiovascular-related diseases was predominant while in women, the prevalence of osteoporosis, arthritis, cancer, and psychosomatic disorders were predominant. The co-occurring diseases within each disease varied across different age and gender groups.

Conclusions

The burden of multimorbidity was increasing and becoming more complex in Taiwan. It also varied across different age and gender groups. Fulfilling the needs of individuals with multimorbidity requires collaborative work across health care providers and needs to take into account age and gender disparities in multimorbidity.

Strengths and limitations of this study

- This is the first nationwide study conducted in Taiwan to assess the age- and gender-specific burden and complexity of multimorbidity between 2003 and 2013.
- Multimorbidity was defined using existing methods to classify and consider geographic or ethnic discrepancies between Western and Asian countries.
- We identified multimorbidity based on the diagnoses recorded in the outpatient or inpatient visit. However, only up to three and up to five diagnoses were allowed to be recorded in each outpatient or inpatient visit in the NHIRD, the prevalence of multimorbidity may be underestimated

Introduction

Multimorbidity, defined as the coexistence of two or more chronic health conditions in the same person at the same time, has become a significant challenge to the healthcare systems worldwide. Previous studies have reported that multimorbidity was associated with worse clinical outcomes, poorer quality of life and increased medical expenditures at individual level.^{1 2} At the nationwide level, multimorbidity also incurs significant social and economic burden due to complex health and welfare demands as well as associated costs to care for individuals with multimorbidity^{1 2}. These demands are expected to increase as the society aged as the prevalence of multimorbidity also increased with age³. However, effective strategies to manage multimorbidity remain unanswered. These may be due to the single-disease paradigm in the current clinical setting, which may result in fragmented care for patients manifesting multimorbidity.

To manage multimorbidity, it is necessary to measure the burden of multimorbidity. However, the phenomenon of multimorbidity is not well understood. A simple count of diseases in each identified either through self-reporting⁴ or by extracting information from electronic medical record using lists of diagnostic codes⁵⁻⁸ is the first and common approach. The extrapolation of the abovementioned studies,

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4 however, is difficult due to several limitations. First, most of the estimates came from
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7 selected medical institutions ^{3 9-12} or limited to the specific population such as the
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10 elderly ³. Some studies using a survey to collect the potential prevalence of
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13 multimorbidity in patients who visit their general practitioners ^{13 14}. Population-based
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16 estimates are usually very limited. Second, the lists of diagnosis are likely to differ
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19 substantially between studies ^{6 15 16}. To the best of our knowledge, there is currently
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22 no single set of codes that have been consistently used to identify patients with
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25 multimorbidity. Third, the prevalence of multimorbidity in Asian countries is very
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28 limited while the prevalence of multimorbidity may vary ethnically or geographically.
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31 Based on two systematic reviews conducted by Pati S et al ¹⁷ and Hu X et al ¹⁸ and
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34 other studies ¹⁹⁻²¹, available evidence of multimorbidity in Asian countries were
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37 limited to specific area in one country ¹⁹⁻²¹ (i.e. no population-based data were
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40 available), limited by sample size (mostly including only hundreds of people) ¹⁹⁻²¹ and
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43 limited to the method that measure multimorbidity (mostly were self-reported).
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46 Similarly, they mainly focused on the prevalence of multimorbidity in the elderly ^{17 18}
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49 ²⁰. In addition, most of existing studies were cross-sectional one-time measurement of
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52 the prevalence of multimorbidity ^{17 18 20} and were not presented the time changes of
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55 burden of multimorbidity.
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4 To fill the current knowledge gap, this study aimed to estimate the population-based,
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7 age- and gender-specific prevalence and trends of multimorbidity using Taiwan's
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10 National Health Insurance Research Database (NHIRD).
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Methods

Data source

A population-based cross-sectional study was conducted using administrative claims data from Taiwan's National Health Insurance Research Database (NHIRD). The NHIRD is a nationwide claims-based database comprising anonymous eligibility and enrollment information, as well as claims for outpatient visits, admissions, procedures and prescription medications of more than 99 % of the entire population (23 million) in Taiwan ²².

We used a subset of the NHIRD, which contains claim data for 2 million of randomly selected beneficiaries to create an 11-year (2003-2013) panel of claims for analysis. In this study, we used two subsets of the NHIRD, the Longitudinal Health Insurance Database (LHID) 2005 and 2010 as our data source. These two datasets were made up of claims data on one million beneficiaries that were randomly sampled by the National Health Research Institute (NHRI), Taiwan. The one million beneficiaries in LHID 2005 were randomly selected from the year 2005 Registry for Beneficiaries of the NHIRD, which includes registration data of approximately 25.68 million beneficiaries of the National Health Insurance (NHI) program during the year 2005. The one million beneficiaries in LHID 2010 were randomly selected from the year 2010

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4 Registry for Beneficiaries of the NHIRD, which includes registration data of
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7 approximately 27.38 million beneficiaries of the NHI program during the year 2010.
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10 According to the statistics provided by the NHRI, there were no significant differences
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12 in the gender distribution between patients in the LHID 2005 and the original NHIRD
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14 ($\chi^2=0.008$, $df=1$, p -value=0.931), and between those in the LHID 2010 and the original
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16 NHIRD ($\chi^2=0.067$, $df=1$, p -value=0.796)²³. Therefore, the two subsets were thought to
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19 be representative enough of the original NHIRD, and the results obtained suggested
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22 generalizability to the whole Taiwanese population.
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31 A total of two million individuals, which composed approximately 10% of the total
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33 population in Taiwan, constituted the study population of this study. The identification
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35 numbers and all traceable personal identifiers of the insured in NHIRD were encrypted
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38 to ensure the confidentiality and privacy. In this way, this study was exempt from full
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41 review by the Institutional Review Board of the National Taiwan University Hospital,
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44 Taipei, Taiwan, and the requirement for providing informed consent was not imposed.
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52 **Ethical statement**

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55 The identification numbers for all of the entries in the NHIRD were encrypted to
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58 protect the privacy of the individual patients. The study protocol was approved by the
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4 Institution Review Board of the National Taiwan University Hospital (National
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7 Taiwan University Hospital Research Ethics Committee No. 201403069W).
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13 **Patient and public involvement**

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16 Patients were not involved in the design or conduct of this study.
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22 **Identification of common diseases**

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25 We defined cases as patients who had at least three diagnoses with 20 common diseases
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28 upon outpatient or inpatient visits during the study period. To ensure the specificity of
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31 every disease, only those who had at least 3 outpatient or 1 inpatient claims record of
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34 that specified diagnosis code in one year were considered as having that specified
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37 disease. This algorithm was adopted from many published studies using NHIRD to
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40 identify comorbidities²⁴⁻²⁶. For example, one individual must at least have three
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43 different visits for hypertension (e.g. March 1, May 2, and July 15, 2003) were
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46 considered as having hypertension in that year. Same algorithm was applied to other
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49 disease. Therefore, if this person also has at least three different visits for diabetes
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52 mellitus then he or she was defined as having two diseases (multimorbidity) in that
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55 year. Based on our algorithm, the diseases we selected in this study were chronic
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58 diseases.
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7 Similar with most previous studies focusing on multimorbidity, we also specify
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10 multimorbidity in this study on condition that patients concurrently suffered from two
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13 or more of these 20 common diseases. The 20 common diseases included hypertension,
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16 diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral
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19 vascular disease, cerebrovascular disease, chronic pulmonary disease, renal disease,
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22 liver disease, dementia, other neurological disorders, digestive disorder, osteoporosis,
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25 arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders,
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28 bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer. The
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31 detailed set of diagnostic codes regarding the definition of these common diseases was
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34 demonstrated in **Supplementary Table S1**. These diseases were selected based on the
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37 disease burden that they may fall on the whole society regarding considerable cost, the
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40 requirement for long-term care, reduced health-related quality of life, hospitalization,
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43 or death illustrated in previous studies^{6 25 27}. Three epidemiologists with clinical and
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46 research expertise in chronic diseases and multimorbidity took part in the discussions
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49 based on literature review of existing definitions of chronic disease across scientific
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52 papers. Since there was a lack of consensus over what diseases should be included in
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55 the definition of multimorbidity,, we sought the union of the diseases included in two
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58 of the previous studies investigating multimorbidity^{6 27} and those in a Taiwanese study
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4 (our previous study with a geriatric specialist involved) evaluating the association
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7 between multimorbidity and unplanned hospitalization, admission to intensive care
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10 units, and mortality²⁵. In this way, we believed that the list of diseases which we
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13 adopted to define multimorbidity was capable of reflecting the disease burden the
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16 population carried and was applicable in the Taiwanese population.
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22 **Statistical Analysis**

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25 We reported descriptive data on the prevalence of multimorbidity in different age
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28 groups (categorized into eight groups including 20-29, 30-39, 40-49, 50-59, 60-69, 70-
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31 79, 80-89, and 90+) and both sexes (men and women) in the years 2003 and 2013
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34 (annual point prevalence). Chi-square tests were used to compare prevalence in the
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37 years 2003 and 2013. The prevalence of multimorbidity was calculated by dividing the
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40 number of patients afflicted with multimorbidity by population size in each age group
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43 regarding the degree of multimorbidity (grouped into 2, 3, 4, and 5+). We further
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46 revealed data on the prevalence of each of the 20 common diseases in each age group
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49 and sex. The individual prevalence was the estimated fraction (percentage, %) with the
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52 number of patients with each disease in each age and sex group as the numerator and
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55 with population size in each group and sex as the denominator.
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58 As for clustering effect, we used graphic displays on the likelihood of co-
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4 occurrence with 1, 2, 3, and 4 or more other diseases for each selected disease in the
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7 years 2003 and 2013. The likelihood was the estimated proportion with the number of
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10 patients suffering from the same disease with concurrent 1, 2, 3, and 4 or more other
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13 diseases divided by the number of patients with a specific disease. We also adopted
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16 graphics to demonstrate differences in the prevalence of multimorbidity and clustering
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19 effect between both sexes and among age groups in 2003 and 2013, respectively. All
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22 data in this study were analyzed using Python programming language with Mongo
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25 database software, version 3.6.4 and 4.0.2.
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31 **Results**

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34 In general, the prevalence of at least one of 20 common diseases was 37.23 % in
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37 2003, and an approximately ten percent increase was observed in the year of 2013
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40 (48.97 % in 2013, **Table 1**). The prevalence of at least one disease ranged from 16.74
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43 % in patients aged 20-29 years to 78.05 % in those aged 80-89 years in 2003. In 2013,
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46 the prevalence varied between 19.85 % in patients aged 20-29 years and 92.01% in
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49 those aged 80-89 years. Increases in the prevalence of at least one disease were
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52 observed in all age groups, and the magnitude was from 3.11 % in patients aged 20-29
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55 years to a dramatic 28.21 % in those aged 90 years or above in the years 2003 and 2013
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58 (**Table 1**, Supplementary **Figure S1**). As for the multimorbidity, the increasing
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4 prevalence across all age groups and different intensity of multimorbidity was of great
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7 concern. For instance, the prevalence of three of 20 common diseases was 30.39 % in
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10 patients aged 60-69 years in 2003, and an approximately seven percent increase in
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13 prevalence was observed in 2013. In patients aged 90 years or above, the increase was
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16 even more significant. Compared to the prevalence of three diseases in 2003 (33.04 %, **Table 1**,
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18 **Table 1**, Supplementary **Figure S1**), that in 2013 nearly doubled (66.52 %, **Table 1**,
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21 Supplementary **Figure S1**)
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25 A dramatically growing increase in the prevalence of multimorbidity was noticed
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28 in all age groups, especially in those aged 90 years or above, in men and women in the
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31 years 2003 and 2013 (**Figure 1**). Patterns of sex differences in the prevalence of
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34 multimorbidity were similar between the years 2003 and 2013. To be more specific, the
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37 prevalence of multimorbidity were comparable between men and women in patients
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40 aged 49 years or younger. In patients aged between 50 and 79 years, however, the
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43 prevalence of multimorbidity was higher in women than that in men. In patients aged
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46 80-89 years, the sex difference in the prevalence of multimorbidity was subtle. In
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49 patients aged 90 years, the sex difference in prevalence of multimorbidity was much
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52 higher in men than that in women (**Figure 1**).
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55 The prevalence of each of 20 common diseases was presented in **Table 2**. The
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58 prevalence of all of the 20 common diseases remained comparable or increased in all
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4 age groups between the years 2003 and 2013. Significantly growing prevalence can be
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7 observed in cancer, dementia, cerebrovascular disease, and several cardiovascular-
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10 related diseases, including hypertension, diabetes, congestive heart failure, cardiac
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13 dysrhythmias, and peripheral vascular disease. The most frequently seen diseases in
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16 Taiwanese population consisted of hypertension, other neurological disorders, digestive
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19 disorder, and arthritis (including rheumatoid arthritis). Over half of patients aged elder
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22 than 70 years in 2013 were afflicted with hypertension, and nearly one-third of those
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24
25 suffering from other neurological disorder, digestive disorder, and arthritis (including
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28 rheumatoid arthritis). Although the prevalence of cancer and dementia was generally
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31 low in Taiwan, the disease burden caused by these two diseases cannot be overseen.
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34 There was nearly one-fifth of patients aged 90 years or above were affected by dementia
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37 and nearly one-sixth of patients aged 80 years or above lived with cancers in 2013.
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40 Also, there was a strikingly increasing trend in prevalence of older patients in these two
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43 diseases.
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46 As shown in **Table 3**, the prevalence of each common diseases increased in
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49 general between the years 2003 and 2013 in both men and women. In men, the
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52 prevalence of chronic pulmonary disease and cardiovascular-related diseases, including
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55 hypertension, congestive heart failure, peripheral vascular disease were predominant.
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58 In women, the prevalence of osteoporosis, arthritis (including rheumatoid arthritis),
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4 cancer, and psychosomatic disorders, including depression, anxiety, bipolar disorder,
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7 were predominant. As for dementia, interestingly, the prevalence in men was a bit
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10 higher in 2003, yet the condition was quite the other way in 2013.
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13 In **Figure 2**, we depicted sex differences in the prevalence of multimorbidity
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16 within individuals suffering from each common disease in 2003 and 2013. Generally,
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19 compared to the year of 2003, multimorbidity was more frequently seen in 2013 in both
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22 sexes within all common diseases. Except for bipolar disorder and schizophrenia and
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25 psychotic disorders, which were least likely to occur with other diseases, other diseases
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28 might coexist with other diseases to some extents. In 2003, patients with anxiety,
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31 dissociative and somatoform disorders, digestive disorder, and hypertension were most
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34 likely to suffer from other diseases concurrently, but the sex difference was minor. In
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37 2013, patients with the diseases mentioned above were most likely to have other
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40 diseases in the same time as well, the sex difference, on the contrary, was more
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43 noticeable. Specifically, a higher proportion of women suffering from anxiety,
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46 dissociative and somatoform disorders, and digestive disorder are of greater odds to
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49 have other concurrent diseases. Profound sex difference in multimorbidity can also be
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52 observed in patients with other diseases, including arthritis (including rheumatoid
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55 arthritis), osteoporosis, other neurological disorders, and liver disease, where women
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58 with the first three were of higher prevalence to concurrently have other diseases.
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Discussions

To the best of our knowledge, this population-based study is the largest and the most comprehensive epidemiologic study to provide age- and gender-specific information on multimorbidity in the Taiwanese population. Previous studies are all limited to Western Countries, such as Canada⁶ or Australia¹³. Nevertheless, the etiology of multimorbidity may have geographical discrepancies. Our study also fills the knowledge gap of existing studies conducted in Asian countries^{17 18} by providing the nationwide estimates of multimorbidity across different age groups and by providing the 10-years changes of burden of multimorbidity, which have not been done in existing studies. This information is therefore extremely fundamental for constructing national policies to combat the burden of multimorbidity, particularly in Asian countries. Our study also provides in-depth analyses of each selected disease and their concomitant comorbidities. This study could thus serve as valuable references for strategic thinking regarding sophisticated diseases management plans.

We found that the prevalence of multimorbidity was increasing in the 10-years follow-up period. This increase is reasonable considering the threat of aging population²⁸ and is consistent with a previous study conducted in Ontario residents⁶.

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4 The prevalence of multimorbidity among Ontarians rose from 17.4% in 2003 to
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7 24.3% in 2009, a 40% increase. In our study, the prevalence of multimorbidity rose
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10 from 20.07% in 2013 to 30.44 % in 2009, a 51.6% increase. Although the different
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13 magnitude of the increase could result from the various lists of diseases selected to
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16 count multimorbidity; the Ontario study includes 16 common chronic conditions⁶
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19 while our study includes 20 common chronic conditions. However, the speed of aging
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22 in the two different populations may explain the discrepancies better. The population
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25 is aging rapidly in Taiwan. Up until the end of 2010, 11% of Taiwan's population was
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28 aged more than 65 years. The ratio has been reached to 14% (the threshold for an
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31 “aged” society) by 2017, and the estimated ratio will expect to increase to 20% (the
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34 threshold for a “superaged” society) by 2025 in Taiwan ²⁹.

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40 Multimorbidity, particularly in the elderly, is therefore very important for almost
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43 every country. In our study, we found that the prevalence of multimorbidity (2+
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46 diseases) in people aged 60-69, 70-79 and 80-89 were 56.84%, 74.64%, 82.64%,
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49 respectively, in 2013. The prevalence of multimorbidity (3+ diseases) in people aged
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52 60-69, 70-79 and 80-89 were 37.49%, 57.04%, 68.10%, respectively, in 2013. Facing
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55 such tremendous and complex medical demands, it is necessary to reform the current
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58 “single disease or specialty” paradigm into the “integrated and comprehensive
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4 medical care” model³⁰. In our study, we also found that the combination and intensity
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7 of multimorbidity differed in older men and women. This finding may further indicate
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10 different medical needs for older men and women and gender-specific care plan for
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13 older people may be warranted. Our estimates are thus could serve as good references
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16 for countries facing such a rapid speed of aging to allocate medical and social welfare
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19 resources, including Taiwan or our neighbor country, Japan³¹ or other European
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22 countries³².

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28 In addition to older people, the prevalence of multimorbidity among the younger
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31 population yield special attention. As most researches in multimorbidity have focused
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34 on older adults^{33 34}, evidence regarding this issue in young adults is very limited. In
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37 our study, the prevalence of multimorbidity (2+ diseases) in people aged 30-39, 40-49
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40 and 50-89 were 11.18%, 21.76%, and 37.75%, respectively, in 2013. This indicates
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43 the need for early intervention in those who already suffer from multimorbidity in
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46 their middle-ages as the intensity of multimorbidity gradually increase as shown in
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49 our study. Lifestyle factors such as smoking, drinking, exercise or diet in middle ages
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52 were reported to be associated with multimorbidity³⁵.

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58 Most importantly, our study contributes to the understanding of the in-depth details of
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4 multimorbidity. In addition to revealing very distinct predominant diseases in men
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7 and women, we also reported the burden of multimorbidity in each common chronic
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10 condition. From a clinical perspective, our findings can help further strata the patients
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13 within a specific disease group. For example, care for patients with diabetes mellitus
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16 and with one other comorbid conditions should be very different from patients with
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19 diabetes mellitus and with four other comorbid conditions. From a policy perspective,
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22 our findings can help allocate medical resources more efficiently. Our previous
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25 studies also support this strata strategy (or identifying high-risk group) we found that
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28 the increase of diabetic complications was positively associated with increased risk of
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31 hospitalization and healthcare costs^{36 37}.

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37 While we provide great epidemiologic information of age- and gender-specific, it
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40 has some limitations due to the nature of claims data. First, we identified the disease
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43 based on the diagnoses recorded in the outpatient or inpatient visit. However, only up
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46 to three and up to five diagnoses were allowed to be recorded in each outpatient or
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49 inpatient visit, the prevalence of multimorbidity may be underestimated. Second, as
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52 we used the NHIRD, the estimation about the multimorbidity in this study was from
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55 the perspective of the national insurance system. Patients who pay out-of-pocket for
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58 their diseases are not recorded in the NHIRD as well. Thirdly, as there is no
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4 consensus of the number of diseases used to identify multimorbidity, comparisons of
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7 epidemiology of multimorbidity in different countries were very difficult. For
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10 example, a systematic review conducted by Pati S et al ¹⁷ revealed that among 13
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13 studies included in their systematic review, the number of health conditions analyzed
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16 per study varied from 7 to 22 with prevalence of multimorbidity varied from 4.5% to
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19 83%.

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25 Conclusively, our study is the first population-based study conducted in Taiwan
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28 providing age- and gender-specific information on multimorbidity. The burden of
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31 multimorbidity was increasing and becoming more complex in Taiwan. Providing for
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34 the needs of individuals with multimorbidity requires collaborative work across health
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37 care providers and may need to take into account age and gender disparities in
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40 multimorbidity.

41 42 43 44 **Acknowledgements**

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46
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52
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56 of the NHIA or NHRI. The authors have full access to all of the data in the study and
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59 take responsibility for the integrity of the data and the accuracy of the data analysis.
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Data sharing statement

Data for this study were provided by the National Health Insurance Administration, Taiwan following ethical approval, and may be available to other researchers who meet data access requirements.

Figure legends

Figure 1. Prevalence of multi-morbidity in Taiwan by the number of common diseases *, sex, age group, and year. (a) Men and women in 2003. (b) Men and women in 2013.

Figure 2. Prevalence of multi-morbidity in Taiwan within common diseases, by sex and year.

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Table 1. Prevalence of multi-morbidity in Taiwan by number of common diseases *, age group, and year

2003							
Age groups	Taiwanese Population	Prevalence of at least one disease (%)	Prevalence of multimorbidity, by degree of multimorbidity (%)				
			2	3	4	5+	
20-29	285,406	16.74	4.01	1.15	0.36	0.12	
30-39	273,713	24.09	8.04	2.86	1.03	0.37	
40-49	269,568	35.91	16.01	7.08	2.92	1.12	
50-59	175,456	51.70	30.15	16.49	8.00	3.57	
60-69	114,876	66.52	47.08	30.39	17.13	8.70	
70-79	74,756	77.86	62.40	45.66	29.10	16.75	
80-89	20,002	78.05	64.32	48.74	32.39	19.58	
90+	1,946	62.23	45.68	33.04	21.12	12.69	
All	1,215,723	37.23	20.07	11.40	6.09	3.07	
2013							
Age groups	Taiwanese Population	Prevalence of at least one disease (%)	Prevalence of multimorbidity, by degree of multimorbidity (%)				
			2	3	4	5+	
20-29	245,613	19.85 †	5.21	1.49	0.47	0.15	
30-39	295,797	30.49 †	11.18	4.10	1.55	0.60	
40-49	277,889	43.45 †	21.76	10.08	4.35	1.83	
50-59	272,719	59.90 †	37.75	20.87	10.24	4.71	
60-69	173,213	75.39 †	56.84	37.49	21.74	11.70	
70-79	102,826	87.53 †	74.64	57.04	38.44	23.60	
80-89	52,978	92.01 †	82.64	68.10	49.71	33.06	
90+	8,492	90.44 †	80.96	66.52	48.39	32.54	
All	1,429,527	48.97 †	30.44	18.61	10.73	5.94	

*Hypertension, diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver disease, dementia, other neurological disorders, digestive disorder, osteoporosis, arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders, bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer

†P<0.05 compared to prevalence in 2003 using chi-square tests.

Table 2. Prevalence of 20 common diseases in Taiwan, by age group and year

Disease	Year	Number with condition (prevalence, %)	Prevalence of each disease, by age group (%)							
			20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Hypertension	2003	126,651(10.42)	0.22	1.38	6.31	17.11	29.91	42.36	43.26	28.78
	2013	260,198(18.20) †	0.43	2.38	9.54	22.91	39.64	55.39	61.71	56.64
Diabetes	2003	56,627(4.66)	0.20	0.77	3.00	8.51	14.04	16.31	12.51	5.86
	2013	126,991(8.88) †	0.35	1.27	4.50	11.47	21.10	26.39	25.23	18.38
Congestive heart failure	2003	44,622(3.67)	0.06	0.38	1.80	5.35	10.43	17.25	19.95	15.88
	2013	71,026(4.97) †	0.09	0.45	1.87	4.99	10.10	17.19	24.78	28.24
Coronary syndrome	2003	35,539(2.92)	0.04	0.25	1.19	3.98	8.75	14.82	16.05	11.20
	2013	60,367(4.22) †	0.05	0.27	1.43	4.19	9.38	15.29	19.72	18.86
Cardiac dysrhythmias	2003	14,337(1.18)	0.14	0.31	0.69	1.47	2.89	5.24	6.67	5.29
	2013	29,098(2.04) †	0.18	0.32	0.83	1.79	3.76	6.95	10.88	12.69
Peripheral vascular disease	2003	14,873(1.22)	0.07	0.13	0.44	1.23	3.34	7.10	8.70	4.78
	2013	28,562(2.00) †	0.08	0.17	0.48	1.45	3.92	8.66	11.34	9.89
Cerebrovascular disease	2003	28,098(2.31)	0.14	0.25	0.86	2.74	6.59	12.09	15.26	11.51
	2013	56,770(3.97) †	0.18	0.38	1.12	3.24	7.82	15.35	22.51	23.85
Chronic pulmonary disease	2003	37,897(3.12)	0.78	1.32	1.95	3.46	7.25	12.22	15.14	12.85
	2013	50,705(3.55) †	0.74	1.26	1.80	3.02	5.77	10.73	17.17	21.15
Renal disease	2003	13,999(1.15)	0.18	0.34	0.77	1.57	2.80	4.54	5.07	3.44
	2013	38,748(2.71) †	0.18	0.44	1.06	2.44	5.19	9.64	13.79	14.13
Liver disease	2003	43,555(3.58)	1.39	2.58	4.03	5.53	6.23	5.44	3.41	1.64
	2013	71,015(4.97) †	0.79	2.88	5.13	7.28	8.56	8.05	5.69	4.03
Dementia	2003	5,194(0.43)	0.10	0.12	0.17	0.27	0.72	2.24	5.06	6.27
	2013	18,869(1.32) †	0.13	0.19	0.30	0.51	1.27	4.89	12.77	20.54
Other neurological disorders	2003	124,029(10.20)	4.25	6.84	9.44	13.12	18.24	24.21	26.53	17.78
	2013	217,307(15.20) †	6.54	10.37	13.29	16.90	21.42	29.04	33.85	31.03

Table 2. Prevalence of 20 common diseases or in Taiwan, by age group and year (cont'd)

Disease	Year	Number with condition (prevalence, %)	Prevalence of each disease, by age group (%)							
			20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Digestive disorder	2003	152,161(12.52)	6.81	8.54	11.19	14.94	21.03	29.22	32.39	25.95
	2013	227,327(15.90) †	8.41	11.15	13.40	17.09	22.01	29.06	35.24	37.48
Osteoporosis	2003	14,732(1.21)	0.09	0.13	0.49	2.04	3.59	5.02	6.08	5.45
	2013	17,026(1.19)	0.07	0.11	0.23	0.74	2.10	5.23	7.67	9.15
Arthritis (including rheumatoid arthritis)	2003	149,434(12.29)	3.87	6.34	11.05	18.01	25.54	31.95	30.18	19.63
	2013	226,844(15.87) †	4.18	7.28	12.01	19.46	27.70	37.45	37.03	29.30
Anxiety, dissociative and somatoform disorders	2003	52,029(4.28)	1.27	2.48	4.17	6.34	8.48	9.99	9.49	5.91
	2013	89,053(6.23) †	1.69	3.45	5.82	8.00	10.29	11.91	11.18	8.44
Bipolar disorder	2003	8,251(0.68)	0.44	0.59	0.72	0.84	0.89	1.03	0.89	0.51
	2013	15,439(1.08) †	0.51	0.80	1.25	1.30	1.44	1.50	1.32	0.92
Depression	2003	11,630(0.96)	0.64	0.82	0.97	1.14	1.27	1.51	1.61	1.13
	2013	24,712(1.73) †	0.86	1.30	1.89	2.00	2.24	2.52	2.59	2.25
Schizophrenia and psychotic disorders	2003	7,472(0.61)	0.48	0.80	0.74	0.57	0.43	0.40	0.55	0.51
	2013	11,624(0.81) †	0.42	0.82	1.10	1.00	0.77	0.65	0.55	0.67
Cancer	2003	37,438(3.08)	1.26	2.22	3.77	4.11	4.47	5.50	5.46	2.93
	2013	83,065(5.81) †	1.36	2.97	5.68	7.22	9.19	11.54	12.57	12.16

†P<0.05 compared to prevalence in 2003 using chi-square tests.

Table 3. Prevalence of 20 common diseases in Taiwan, by sex, age group and year

Disease	Year	Prevalence		Prevalence of each disease, by age group (%)															
		Prevalence (%)		20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Hypertension	2003	10.52	10.33	0.33	0.11	1.90	0.92	7.29	5.42	17.13	17.09	27.66	31.83	39.89	44.96	41.16	45.18	29.55	28.31
	2013	19.40	17.13	0.68	0.21	3.58	1.35	12.67	6.71	25.93	20.10	40.55	38.81	51.88	58.30	58.03	65.22	54.02	58.70
Diabetes	2003	4.77	4.56	0.21	0.19	1.05	0.51	3.73	2.34	9.15	7.94	13.07	14.86	14.10	18.64	11.47	13.47	5.75	5.93
	2013	9.57	8.26	0.40	0.31	1.75	0.86	6.18	2.97	13.52	9.56	21.87	20.40	24.50	27.96	22.52	27.81	17.60	18.99
Congestive heart failure	2003	3.71	3.63	0.09	0.03	0.54	0.24	2.12	1.51	5.48	5.25	9.58	11.16	16.27	18.28	19.34	20.51	17.10	15.14
	2013	5.24	4.72	0.14	0.04	0.68	0.25	2.56	1.25	5.82	4.21	10.67	9.58	16.02	18.15	23.37	26.13	27.04	29.18
Coronary syndrome	2003	3.21	2.67	0.05	0.03	0.33	0.17	1.51	0.89	4.47	3.55	8.81	8.70	15.53	14.07	16.88	15.30	11.76	10.86
	2013	5.00	3.52	0.06	0.04	0.44	0.13	2.14	0.78	5.49	2.99	11.24	7.71	16.41	14.36	20.94	18.55	20.42	17.65
Cardiac dysrhythmias	2003	1.19	1.17	0.13	0.15	0.29	0.33	0.64	0.73	1.39	1.54	2.90	2.88	5.40	5.06	6.85	6.51	6.57	4.53
	2013	2.10	1.98	0.16	0.20	0.31	0.34	0.85	0.81	1.83	1.77	3.94	3.60	7.08	6.84	11.69	10.11	12.81	12.61
Peripheral vascular disease	2003	1.23	1.22	0.08	0.06	0.16	0.11	0.47	0.41	1.20	1.25	3.01	3.62	7.01	7.19	8.97	8.46	5.61	4.28
	2013	2.00	2.00	0.06	0.10	0.18	0.16	0.54	0.44	1.60	1.32	3.83	4.00	8.06	9.16	11.76	10.95	11.25	8.82
Cerebrovascular disease	2003	2.61	2.04	0.16	0.12	0.34	0.18	1.07	0.67	3.18	2.36	7.05	6.19	13.01	11.11	16.29	14.31	14.09	9.96
	2013	4.54	3.46	0.19	0.17	0.47	0.29	1.47	0.80	4.05	2.50	9.15	6.61	16.65	14.28	24.45	20.67	24.81	23.09

Table 3. Prevalence of 20 common diseases in Taiwan, by sex, age group and year (cont'd)

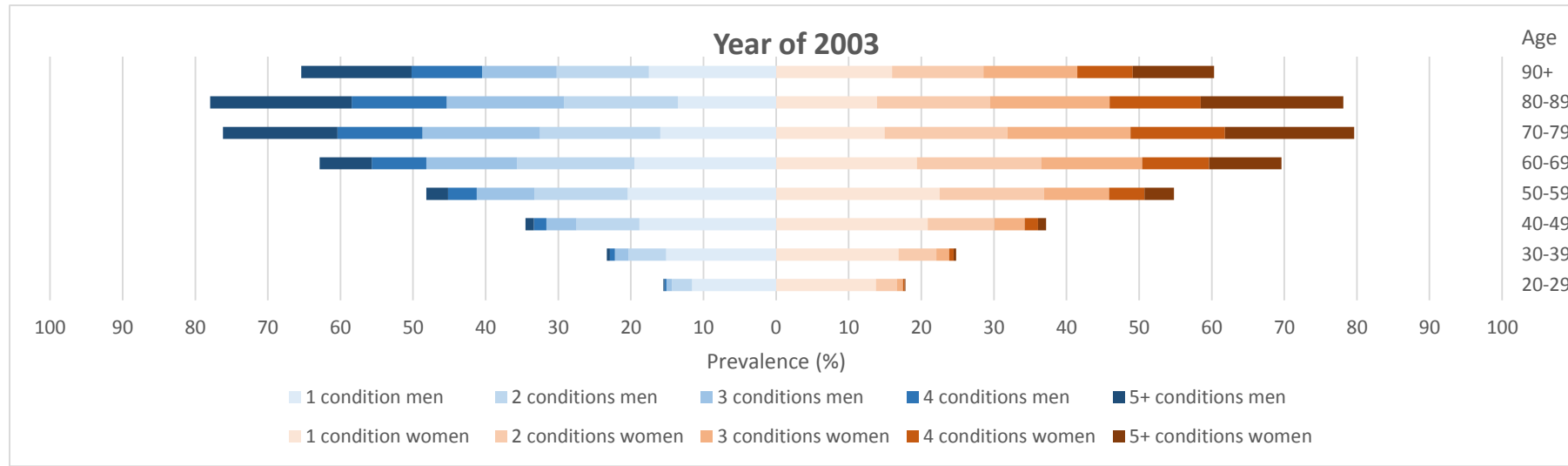
Disease	Year	Prevalence		Prevalence of each disease, by age group (%)															
		Prevalence (%)		20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Chronic pulmonary disease	2003	3.51	2.76	0.80	0.76	1.24	1.39	1.99	1.93	3.50	3.41	8.02	6.59	15.19	9.08	19.80	10.86	17.51	10.04
	2013	4.00	3.14	0.71	0.76	1.16	1.34	1.75	1.85	3.09	2.96	6.52	5.10	13.26	8.62	21.96	12.60	26.98	16.58
Renal disease	2003	1.29	1.03	0.22	0.15	0.42	0.27	0.86	0.68	1.68	1.48	3.02	2.62	4.90	4.16	6.09	4.14	4.51	2.80
	2013	3.26	2.22	0.21	0.15	0.58	0.32	1.42	0.72	3.04	1.89	6.25	4.23	11.26	8.29	15.84	11.85	16.96	11.91
Liver disease	2003	4.61	2.66	2.12	0.76	3.95	1.36	5.64	2.56	6.38	4.78	6.70	5.83	5.59	5.28	3.90	2.96	2.19	1.32
	2013	6.20	3.86	1.12	0.49	4.30	1.66	7.35	3.12	8.92	5.76	9.21	7.97	8.49	7.68	6.13	5.28	4.66	3.53
Dementia	2003	0.46	0.39	0.15	0.06	0.18	0.07	0.21	0.13	0.32	0.23	0.75	0.70	2.14	2.35	4.82	5.28	4.24	7.49
	2013	1.31	1.33	0.16	0.10	0.26	0.14	0.41	0.20	0.63	0.41	1.31	1.23	4.52	5.20	11.70	13.79	18.81	21.89
Other neurological disorders	2003	8.00	12.17	3.29	5.08	5.24	8.27	6.90	11.76	9.31	16.48	14.62	21.32	21.26	27.32	23.99	28.86	17.10	18.19
	2013	12.02	18.05	4.74	8.19	7.79	12.59	10.02	16.25	12.66	20.81	16.84	25.58	25.34	32.12	32.25	35.37	30.73	31.26

Table 3. Prevalence of 20 common diseases in Taiwan, by sex, age group and year (cont'd)

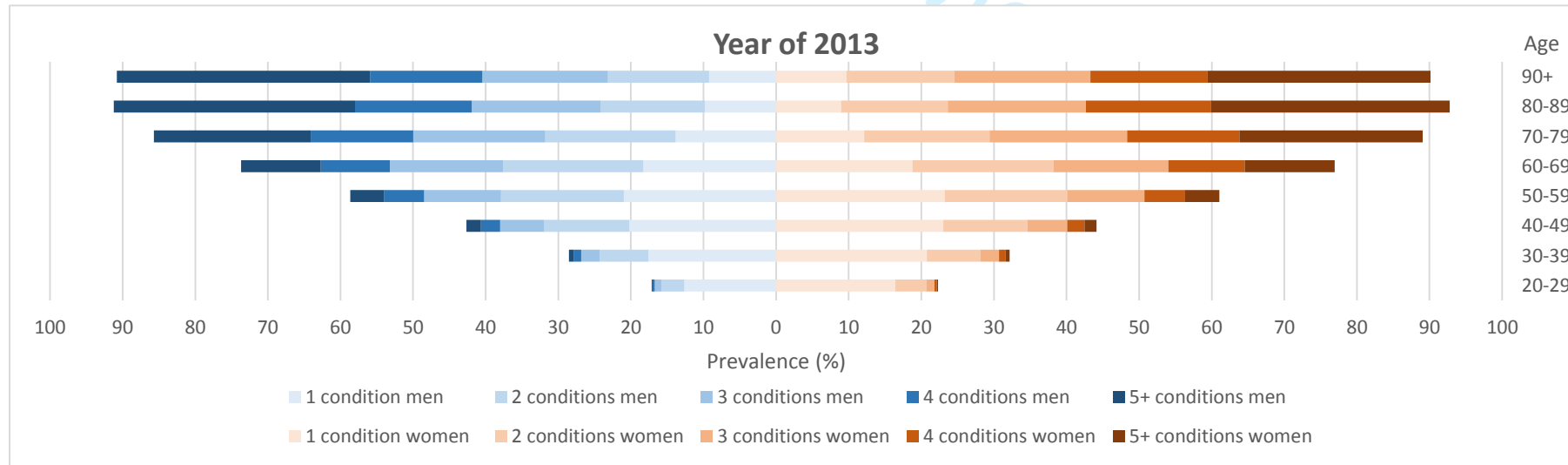
Disease	Year	Prevalence (%)		Prevalence of each disease, by age group (%)															
				20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Digestive disorder	2003	11.62	13.32	4.92	8.46	7.63	9.35	10.53	11.79	13.78	15.96	19.84	22.04	29.87	28.54	34.65	30.32	28.04	24.69
	2013	14.01	17.60	5.65	10.93	8.59	13.34	11.63	15.00	15.14	18.91	20.14	23.69	28.32	29.67	37.55	33.04	41.88	34.03
Osteoporosis	2003	0.45	1.89	0.13	0.05	0.14	0.13	0.26	0.70	0.41	3.48	0.91	5.87	2.07	8.14	2.75	9.14	4.10	6.26
	2013	0.58	1.74	0.09	0.05	0.15	0.08	0.26	0.21	0.45	1.02	0.76	3.31	1.98	7.93	3.72	11.43	5.25	12.21
Arthritis (including rheumatoid arthritis)	2003	12.26	12.32	4.81	3.05	7.46	5.35	11.49	10.65	16.09	19.70	22.43	28.20	30.16	33.85	29.71	30.61	22.85	17.70
	2013	15.32	16.36	4.89	3.53	8.75	6.03	12.75	11.34	18.01	20.80	24.02	31.04	32.67	41.43	35.62	38.37	30.49	28.36
Anxiety, dissociative and somatoform disorders	2003	3.36	5.10	1.11	1.42	2.05	2.86	3.26	5.01	4.47	7.99	6.27	10.36	8.18	11.91	8.46	10.44	6.43	5.60
	2013	4.90	7.42	1.50	1.86	2.95	3.87	4.76	6.78	5.99	9.87	7.55	12.78	9.09	14.26	9.34	12.94	7.93	8.84
Bipolar disorder	2003	0.55	0.79	0.43	0.45	0.44	0.72	0.55	0.87	0.63	1.02	0.72	1.03	0.87	1.20	0.76	1.02	0.55	0.49
	2013	0.84	1.29	0.51	0.51	0.65	0.93	0.95	1.52	0.97	1.62	1.04	1.79	1.10	1.84	1.09	1.54	0.99	0.86
Depression	2003	0.80	1.10	0.66	0.62	0.65	0.98	0.76	1.15	0.86	1.39	1.00	1.50	1.32	1.71	1.44	1.77	0.82	1.32
	2013	1.42	2.00	0.87	0.84	1.11	1.47	1.56	2.19	1.56	2.42	1.70	2.73	1.96	2.98	2.23	2.93	2.20	2.29
Schizophrenia and psychotic disorders	2003	0.68	0.56	0.62	0.37	0.96	0.65	0.81	0.68	0.51	0.62	0.34	0.51	0.37	0.43	0.49	0.61	0.41	0.58
	2013	0.89	0.75	0.50	0.35	0.98	0.68	1.32	0.91	1.04	0.97	0.70	0.85	0.51	0.77	0.49	0.60	0.59	0.74
Cancer	2003	2.21	3.85	0.90	1.58	1.22	3.11	1.80	5.56	2.80	5.26	4.26	4.66	6.22	4.73	6.82	4.21	4.38	2.06
	2013	5.06	6.49	1.02	1.67	1.82	3.95	3.41	7.73	5.76	8.57	9.09	9.29	13.37	10.02	15.81	9.49	16.21	8.99

Figure 1. Prevalence of multi-morbidity in Taiwan by number of common diseases *, sex, age group, and year

(a) Men and women in 2003

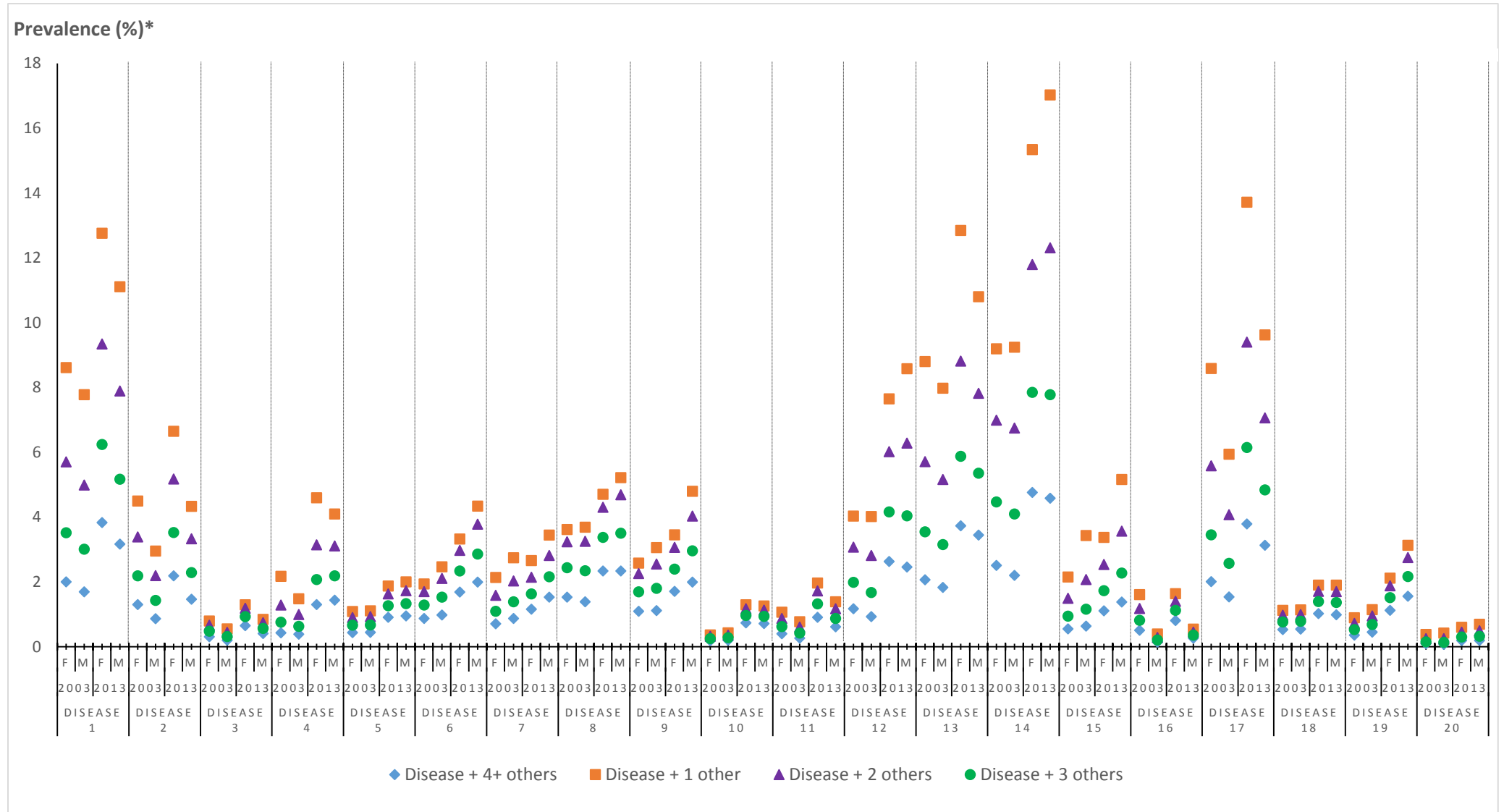


(b) Men and women in 2013



*Hypertension, diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver disease, dementia, other neurological disorders, digestive disorder, osteoporosis, arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders, bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer

Figure 2. Prevalence of multi-morbidity in Taiwan within common diseases, by sex and year.



*Prevalence (%): the number of patients suffering from a specific disease with concurrent 1, 2, 3, or 4+ other diseases divided by the number of patients with a specific disease. (Disease 1: Anxiety, dissociative and somatoform disorders; Disease 2: Arthritis (including rheumatoid arthritis); Disease 3: Bipolar disorder; Disease 4: Cancer; Disease 5: Cardiac dysrhythmias; Disease 6: Cerebrovascular disease; Disease 7: Chronic pulmonary disease; Disease 8: Congestive heart failure; Disease 9: Coronary syndrome; Disease 10: Dementia; Disease 11: Depression; Disease 12: Diabetes; Disease 13: Digestive disorders; Disease 14: Hypertension; Disease 15: Liver disease; Disease 16: Osteoporosis; Disease 17: Other neurological disorders; Disease 18: Peripheral vascular disease; Disease 19: Renal disease; Disease 20: Schizophrenia and psychotic disorders.)

Table S1. ICD-9-CM codes regarding the definition of 20 common diseases

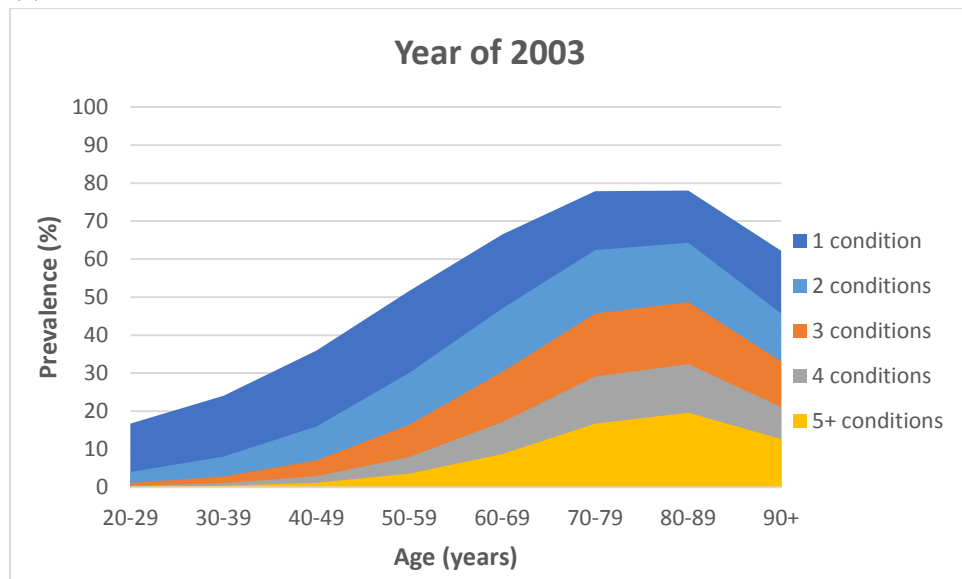
Disease	ICD-9-CM code
Hypertension	401, 402, 403, 404, 405
Diabetes	250
Congestive heart failure	39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 4254, 4255, 4257, 4258, 4259, 428
Coronary syndrome	410, 411, 412, 413, 414
Cardiac dysrhythmias	427
Peripheral vascular disease	0930, 4373, 4400, 4401, 44020, 44021, 44022, 44023, 44024, 44029, 44030, 44031, 44032, 4408, 4409, 44100, 44101, 44102, 44103, 4411, 4412, 4413, 4414, 4415, 4416, 4417, 4419, 4431, 44321, 44322, 44323, 44324, 44329, 44381, 44382, 44389, 4439, 4471, 5571, 5579, V434
Cerebrovascular disease	36234, 430, 431, 432, 43300, 43301, 43310, 43311, 43320, 43321, 43330, 43331, 43380, 43381, 43390, 43391, 434, 4350, 4351, 4352, 4353, 4358, 4359, 436, 437, 438
Chronic pulmonary disease	4168, 4169, 490, 491, 492, 493, 4940, 4941, 4950, 4951, 4952, 4953, 4954, 4955, 4956, 4957, 4958, 4959, 496, 500, 501, 502, 503, 504, 505, 5064, 5081, 5088
Renal disease	403, 404, 5820, 5821, 5822, 5824, 58281, 58289, 5829, 5830, 5831, 5832, 5834, 5836, 5837, 584, 585, 586, 5880, V420, V451, V560, V561, V562, V5631, V5632, V568
Liver disease	07022, 07023, 07032, 07033, 07044, 07054, 0706, 0709, 570, 5710, 5711, 5712, 5713, 57140, 57141, 57149, 5715, 5716, 5718, 5719, 5733, 5734, 5738, 5739, V427, 4560, 4561, 45620, 45621, 5722, 5723, 5724, 5728
Dementia	290, 2930, 2931, 29381, 29382, 29383, 29384, 29389, 2939, 2940, 2941, 2948, 2949, 3100, 3101, 3102, 3108, 3109, 3310, 3311, 3312
Other neurological disorders	3319, 332, 3334, 3335, 33392, 3340, 3341, 3342, 3343, 3344, 3348, 3349, 3350, 33510, 33511, 33519, 33520, 33521, 33522, 33523, 33524, 33529, 3358, 3359, 3362, 340, 3410, 3411, 34120, 34121, 34122, 3418, 3419, 34500, 34501, 34510, 34511, 3452, 3453, 34540, 34541, 34550, 34551, 34560, 34561, 34570, 34571, 34580, 34581, 34590, 34591, 3481, 3483, 34830, 34831, 34839, 780, 7843
Digestive disorder	530, 531, 532, 53300, 53301, 53310, 53311, 53320, 53321, 53330, 53331, 53340, 53341, 53350, 53351, 53360, 53361, 53370, 53371, 53390, 53391, 53400, 53401, 53410, 53411, 53420, 53421, 53430, 53431, 53440, 53441, 53450, 53451, 53460, 53461, 53470, 53471, 53490, 53491, 536, 558, 564
Osteoporosis	733
Arthritis (including rheumatoid arthritis)	274, 710, 711, 714, 715, 716, 718, 720, 727, 728, 729, 739

Table S1. ICD-9-CM codes regarding the definition of 20 common diseases (continued)

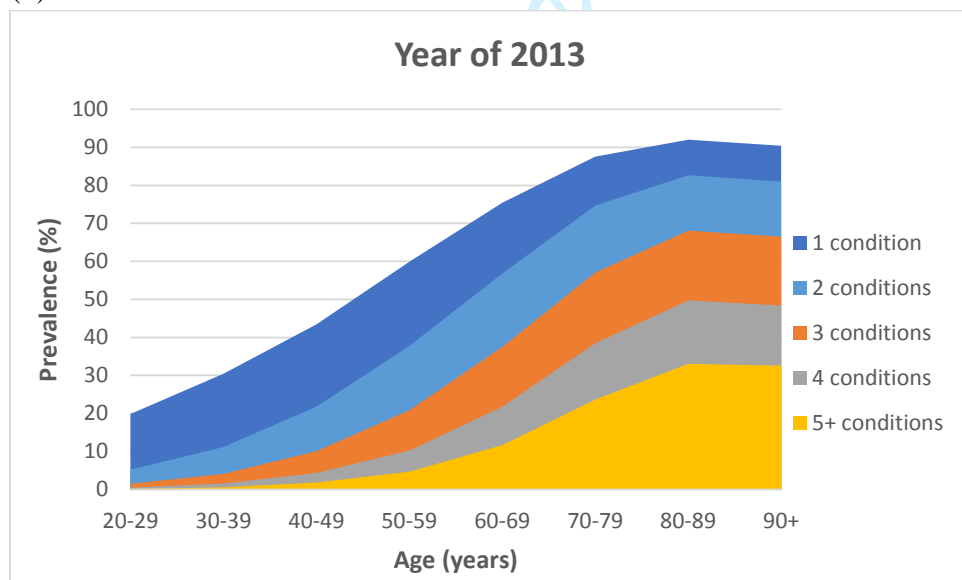
Disease	ICD-9-CM code
Anxiety, dissociative and somatoform disorders	30000-30002, 30009-30016, 30019-30023, 30029, 3003, 3005-3007, 30081, 30082, 30089, 3009, 3062, 3069, 30740-30749, 3080-3084, 3089, 316
Bipolar disorder	29600-29606, 29610-29616, 29640-29646, 29650-29656, 29660-29666, 2967, 29680-29682, 29689
Depression	29620-29626, 29630-29636, 29690, 29699, 2980, 3090, 3091, 311
Schizophrenia and psychotic disorders	29500-29505, 29510-29515, 29520-29525, 29530-29535, 29540-29545, 29550-29555, 29560-29565, 29570-29575, 29580-29585, 29590-29595, 2970-2973, 2978, 2979, 2981-2984, 2988, 2989, 29900, 29901, 29910, 29911, 29980, 29981, 29990, 29991
Cancer	140-239

Figure S1. Prevalence of multi-morbidity in Taiwan by number of common diseases, age group, and year

(a) Year of 2003



(b) Year of 2013



BMJ Open

The Increasing Age- and Gender-Specific Burden and Complexity of Multimorbidity in Taiwan, 2003-2013: A Cross-Sectional Study based on Nationwide Claims Data

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
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Manuscripts

Revised Manuscript (clean)**The Increasing Age- and Gender-Specific Burden and Complexity of
Multimorbidity in Taiwan, 2003-2013: A Cross-Sectional Study
based on Nationwide Claims Data**

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3
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29
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36

37 Hu RH, Hsiao FY, Chen LJ, and Hsu WY contributed to the study concept and
38
39
40 design. Hsiao FY, Hu RH, and Huang PT acquired and analyzed the data. Hsiao FY
41
42
43 and Chen LJ interpreted the data. Hu RH, Hsiao FY, Chen LJ, Huang PT, and Hsu
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58 Database
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ABSTRACT

Objectives

Although there is accumulating evidence regarding multimorbidity in Western countries, in Asian countries, this information is very limited. This study aimed to estimate the population-based, age- and gender-specific prevalence and trends of multimorbidity in the Taiwanese population.

Design

This was a cross-sectional study based on claims data (National Health Insurance Research Database, Taiwan).

Participants

The participants included a subset of the National Health Insurance Research Database, which contains claims data for 2 million randomly selected beneficiaries (~10% of the total population) under Taiwan's mandatory National Health Insurance system.

Outcome measurements

The prevalence of multimorbidity in different age groups and in both sexes in 2003 and 2013 was reported. We analyzed data on the prevalence of 20 common diseases in each age group and for both sexes. To investigate the clustering effect, we used graphical displays to analyze the likelihood of co-occurrence with 1, 2, 3, and 4 or

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4 more other diseases for each selected disease in 2003 and 2013.
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7 **Results**

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10 The prevalence of multimorbidity (two or more diseases) was 20.07% in 2003 and
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12 30.44% in 2013. In 2013, the prevalence varied between 5.21% in patients aged 20-29
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15 years and 80.96% in those aged 80-89 years. In patients aged 50-79 years, the
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17 prevalence of multimorbidity was higher in women than in men. In men, the
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19 prevalence of chronic pulmonary disease and cardiovascular-related diseases was
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22 prevalence of chronic pulmonary disease and cardiovascular-related diseases was
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24 predominant, while in women, the prevalence of osteoporosis, arthritis, cancer, and
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26 psychosomatic disorders was predominant. Co-occurring diseases varied across
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29 different age and gender groups.
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34 **Conclusions**

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37 The burden of multimorbidity is increasing and becoming more complex in Taiwan,
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39 and it was found to vary across different age and gender groups. Fulfilling the needs
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42 of individuals with multimorbidity requires collaborative work between healthcare
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45 providers and needs to take the age and gender disparities of multimorbidity into
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Strengths and limitations of this study

- This is the first nationwide study conducted in Taiwan to assess the age- and gender-specific burden and complexity of multimorbidity and was carried out between 2003 and 2013.
- Multimorbidity was defined using existing methods to classify and consider geographic or ethnic discrepancies between Western and Asian countries.
- We identified multimorbidity based on the diagnoses recorded at outpatient or inpatient visits. However, only up to three or five diagnoses were allowed to be recorded in each outpatient or inpatient visit in the NHIRD; therefore, the prevalence of multimorbidity may be underestimated

Introduction

Multimorbidity, defined as the coexistence of two or more chronic health conditions in the same person at the same time, has become a significant challenge to healthcare systems worldwide. Previous studies have reported multimorbidity to be associated with worse clinical outcomes, a poorer quality of life and increased medical expenditures at the individual level.^{1 2} At the national level, multimorbidity also incurs a significant social and economic burden due to complex health and welfare demands and the associated costs of caring for individuals with multimorbidity.^{1 2}. These demands are expected to increase as societies age, as the prevalence of multimorbidity increases with age.³ Nevertheless, effective strategies to manage multimorbidity remain elusive. This may be due to the single-disease paradigm in the current clinical setting, which may result in fragmented care for patients who manifest multimorbidity.

To manage multimorbidity, it is necessary to measure the burden of multimorbidity, but the phenomenon of multimorbidity is not well understood. A simple count of diseases in each patient, either through self-reporting⁴ or through extracting information from electronic medical records using lists of diagnostic codes⁵⁻⁸, has been the most common approach. The extrapolation of the abovementioned studies,

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4 however, is difficult due to several limitations. First, most of these estimates came
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7 from selected medical institutions ^{3 9-12} or are limited to the specific population such
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10 as the elderly ³. Some studies used a survey to ascertain the prevalence of
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13 multimorbidity in patients who visited their general practitioners ^{13 14}. However,
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16 population-based estimates are usually very limited. Second, the lists of diagnoses
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19 differ substantially between studies ^{6 15 16}. To the best of our knowledge, there is
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22 currently no single set of codes that have been consistently used to identify patients
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25 with multimorbidity. Third, the prevalence of multimorbidity in Asian countries is
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28 very limited, while the prevalence of multimorbidity may vary ethnically or
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31 geographically. Based on two systematic reviews conducted by Pati S et al ¹⁷ and Hu
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34 X et al ¹⁸, as well as on other studies ¹⁹⁻²¹, the available evidence of multimorbidity in
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37 Asian countries is limited to specific areas in one country ¹⁹⁻²¹ (i.e., no population-
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40 based data were available). Evidence is also limited by sample size (mostly including
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43 only hundreds of people) ¹⁹⁻²¹ and by the method used to measure multimorbidity
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46 (most studies used self-reported data). Similarly, previous studies have mainly
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49 focused on the prevalence of multimorbidity in the elderly ^{17 18 20}. In addition, most of
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52 existing studies were cross-sectional one-time measurements of the prevalence of
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55 multimorbidity ^{17 18 20} and did not investigate the burden of multimorbidity over time.
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4 To fill the current knowledge gap, this study aimed to estimate the population-based,
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7 age- and gender-specific prevalence and trends of multimorbidity using Taiwan's
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For peer review only

Methods

Data sources

This population-based cross-sectional study was conducted using administrative claims data from Taiwan's National Health Insurance Research Database (NHIRD).

The NHIRD is a nationwide claims-based database comprising anonymous eligibility and enrollment information, as well as claims for outpatient visits, admissions, procedures and prescription medications of more than 99% of the entire population (23 million) of Taiwan ²².

We used a subset of the NHIRD that contained claims data for 2 million randomly selected beneficiaries to create an 11-year (2003-2013) panel of claims for analysis. In this study, we used two subsets of the NHIRD—the 2005 and 2010 Longitudinal Health Insurance Databases (LHID)—as our data source. These two datasets were made up of claims data on one million beneficiaries that were randomly sampled by the National Health Research Institute (NHRI), Taiwan. The one million beneficiaries in LHID 2005 were randomly selected from the year 2005 Registry for Beneficiaries of the NHIRD, which includes registration data of approximately 25.68 million beneficiaries of the National Health Insurance (NHI) program during the year 2005. The one million beneficiaries in LHID 2010 were randomly selected from the year 2010 Registry for

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4 Beneficiaries of the NHIRD, which includes registration data of approximately 27.38
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7 million beneficiaries of the NHI program during the year 2010. According to the
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10 statistics provided by the NHRI, there were no significant differences in the gender
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13 distribution between patients in the LHID 2005 subset and the original NHIRD
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16 ($\chi^2=0.008$, $df=1$, $p\text{-value}=0.931$) or between those in the LHID 2010 subset and the
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19 original NHIRD ($\chi^2=0.067$, $df=1$, $p\text{-value}=0.796$)²³. Therefore, the two subsets were
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22 thought to be representative of the original NHIRD, and the results obtained suggested
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25 generalizability to the whole Taiwanese population. The sampling and data linkage
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28 process is provided in **Supplementary Figure S1**.

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34 A total of two million individuals, which comprised approximately 10% of the total
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37 population in Taiwan, constituted the study population.

42 43 **Ethical statement**

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46 The identification numbers for all of the entries in the NHIRD were encrypted to
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49 protect the privacy of the individual patients. The study protocol was approved by the
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52 Institutional Review Board of the National Taiwan University Hospital (National
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55 Taiwan University Hospital Research Ethics Committee No. 201403069W).

Patient and public involvement

Patients were not involved in the design or conduct of this study.

Identification of common diseases

We defined cases as patients who had at least three diagnoses from among 20 common diseases at outpatient or inpatient visits during the study period. To ensure the specificity of every disease, only those who had at least 3 outpatient or 1 inpatient claim records of that specified diagnosis code in one year were considered as having that specified disease. This algorithm was adopted from many published studies that have used NHIRD to identify comorbidities²⁴⁻²⁶. For example, one individual must have at least three different visits for hypertension (e.g., March 1, May 2, and July 15, 2003) to be considered as having hypertension in that year. The same algorithm was applied to other disease. Therefore, if this person also had at least three different visits for diabetes mellitus, then he or she was defined as having two diseases (multimorbidity) in that year. Based on our algorithm, the diseases we selected in this study were chronic diseases.

Similar with most previous studies focusing on multimorbidity, we also specified multimorbidity in this study as patients who concurrently suffered from two or more of

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4 the 20 common diseases. The 20 common diseases included hypertension, diabetes,
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7 congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular
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10 disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver
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13 disease, dementia, other neurological disorders, digestive disorders, osteoporosis,
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16 arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders,
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19 bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer. The
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22 detailed set of diagnostic codes regarding the definition of these common diseases is
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25 presented in **Supplementary Table S1**. These diseases were selected based on their
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28 disease burden, which impacts the whole of society regarding their considerable cost,
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31 the requirement for long-term care, reduced health-related quality of life,
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34 hospitalization, or death, as illustrated in previous studies ^{6 25 27}. Three epidemiologists
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37 with clinical and research expertise in chronic diseases and multimorbidity took part in
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40 the discussions of the literature regarding the existing definitions of chronic diseases
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43 across scientific papers. There was a lack of consensus over what diseases should be
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46 included in the definition of multimorbidity. Therefore, in the current study, we
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49 included all those diseases that were included in two previous multimorbidity studies ⁶
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52 ²⁷, as well as those from a Taiwanese study (our previous study that involved a geriatric
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55 specialist) evaluating the association between multimorbidity and unplanned
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58 hospitalizations, admission to intensive care units, and mortality ²⁵. In this way, we
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4 believed that the list of diseases which we adopted to define multimorbidity was capable
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7 of reflecting the disease burden of the Taiwanese population.
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10 11 12 13 **Statistical Analysis** 14

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16 We reported descriptive data on the prevalence of multimorbidity in different age
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18 groups (categorized into the following eight groups: 20-29, 30-39, 40-49, 50-59, 60-69,
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21 70-79, 80-89, and 90+ years) and both sexes (men and women) in the years 2003 and
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24 2013 (annual point prevalence). Chi-square tests were used to compare prevalences in
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27 the years 2003 and 2013. The prevalence of multimorbidity was calculated by dividing
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30 the number of patients afflicted with multimorbidity by the population size in each age
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33 group regarding the degree of multimorbidity (grouped into 2, 3, 4, and 5+). We further
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36 analyzed data on the prevalence of each of the 20 common diseases in each age group
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39 and sex. The individual prevalence was the estimated fraction (percentage, %), with the
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42 number of patients with each disease in each age group and sex as the numerator and
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45 the population size of each age group and sex as the denominator.
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52 To analyze the clustering effect, we used graphical displays of the likelihood of co-
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55 occurrence with 1, 2, 3, and 4 or more other diseases for each selected disease in the
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58 years 2003 and 2013. The likelihood was the estimated proportion of the number of
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4 patients suffering from the same disease with concurrent 1, 2, 3, and 4 or more other
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7 diseases divided by the number of patients with a specific disease. We also used
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10 graphics to illustrate differences in the prevalence of multimorbidity and the clustering
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13 effect between both sexes and among age groups in 2003 and 2013. All data in this
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16 study were analyzed using the Python programming language with Mongo database
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19 software, version 3.6.4 and 4.0.2.
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Results

In general, the prevalence of at least one of the 20 common diseases was 37.23% in 2003, and an approximately ten percent increase was observed in 2013 (48.97%, **Table 1**). The prevalence of at least one disease ranged from 16.74% in patients aged 20-29 years to 78.05% in those aged 80-89 years in 2003. In 2013, the prevalence varied between 19.85% in patients aged 20-29 years and 92.01% in those aged 80-89 years. Increases in the prevalence of at least one disease from 2003 to 2013 were observed in all age groups (**Table 1, Supplementary Figure S2**). Regarding multimorbidity, the increasing prevalence across all age groups and the different intensities of multimorbidity is of great concern. For instance, the prevalence of three of the 20 common diseases was 30.39% in patients aged 60-69 years in 2003, and an approximately seven percent increase in prevalence was observed in 2013. In patients aged 90 years or more, the increase was even more significant. Compared to the prevalence of three diseases in 2003 (33.04%, **Table 1, Supplementary Figure S2**), in 2013 it had nearly doubled (66.52%, **Table 1, Supplementary Figure S2**).

A dramatic increase in the prevalence of multimorbidity from 2003 to 2013 was found for all age groups, especially in those aged 90 years or more, for both men and women (**Figure 1**). Patterns of sex differences in the prevalence of multimorbidity were similar

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4 between 2003 and 2013. Specifically, the prevalences of multimorbidity were
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7 comparable between men and women in patients aged 49 years or younger. In patients
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10 aged between 50 and 79 years, however, the prevalence of multimorbidity was higher
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13 in women than in men. In patients aged 80-89 years, the sex difference in the prevalence
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16 of multimorbidity was subtle. In patients aged 90 years or more, the prevalence of
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19 multimorbidity was much higher in men than in women (**Figure 1**).

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25 The prevalence of each of the 20 common diseases is presented in **Table 2**. The
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28 prevalence of all 20 diseases remained comparable or increased in all age groups
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31 between the years 2003 and 2013. A significantly increased prevalence was observed
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34 for cancer, dementia, cerebrovascular disease, and several cardiovascular-related
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37 diseases, including hypertension, diabetes, congestive heart failure, cardiac
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40 dysrhythmias, and peripheral vascular disease. The most frequently observed diseases
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43 in the Taiwanese population consisted of hypertension, other neurological disorders,
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46 digestive disorders, and arthritis (including rheumatoid arthritis). Over half the patients
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49 greater than 70 years in 2013 were afflicted with hypertension, and nearly one-third of
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52 those suffered from other neurological disorders, digestive disorders, or arthritis
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55 (including rheumatoid arthritis). Although the prevalence of cancer and dementia was
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58 generally low in Taiwan, the disease burden caused by these two diseases cannot be
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4 overlooked. Nearly one-fifth of patients aged 90 years or older were affected by
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7 dementia, and nearly one-sixth of patients aged 80 years or older were afflicted with
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10 cancer in 2013. Additionally, there was a striking increasing trend in the prevalence of
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13 these two diseases in older patients.
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19 As shown in **Table 3**, in general, the prevalence of each common disease increased
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22 between the years 2003 and 2013 in both men and women. In men, the prevalence of
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25 chronic pulmonary disease and cardiovascular-related diseases, including hypertension,
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28 congestive heart failure, and peripheral vascular disease was predominant. In women,
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31 the prevalence of osteoporosis, arthritis (including rheumatoid arthritis), cancer, and
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34 psychosomatic disorders, including depression, anxiety, and bipolar disorder was
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37 predominant. Interestingly, the prevalence of dementia in men was slightly higher than
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40 in women in 2003; however, in 2013, the condition was much higher in women than in
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43 men.
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49 In **Figure 2**, we depicted sex differences in the prevalence of multimorbidity for
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52 individuals suffering from each common disease in 2003 and 2013. Generally,
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55 compared to 2003, multimorbidity was more frequently observed in 2013 in both sexes
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58 for all common diseases. Except for bipolar disorder, and schizophrenia and psychotic
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4 disorders, which were the least likely to occur with other diseases, the other studied
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7 diseases might be comorbid to some extent. In 2003, patients with anxiety, dissociative
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10 and somatoform disorders, digestive disorders, and hypertension were most likely to
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13 suffer from other diseases concurrently, but the differences by sex were minor. In 2013,
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16 patients with these diseases were most likely to have other diseases at the same time;
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19 however, the sex differences were more noticeable. Specifically, a higher proportion of
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22 women suffering from anxiety, dissociative and somatoform disorders, and digestive
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25 disorders have greater odds of having other concurrent diseases. A profound sex
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28 difference in multimorbidity could also be observed in patients with other diseases,
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31 including arthritis (including rheumatoid arthritis), osteoporosis, other neurological
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34 disorders, and liver disease, where women with the first three of these conditions had a
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37 higher prevalence of other concurrent diseases.
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Discussion

To the best of our knowledge, this population-based study is the largest and most comprehensive epidemiologic study to provide age- and gender-specific information on multimorbidity in the Taiwanese population. Previous studies of this topic have been limited to Western countries, such as Canada⁶ or Australia¹³. Nevertheless, the etiology of multimorbidity may have geographical discrepancies. Our study also fills the knowledge gap of existing studies conducted in Asian countries^{17 18} by providing nationwide estimates of multimorbidity across different age groups and illuminating the 10-year changes in the multimorbidity burden, which was not available from existing studies. This information is therefore fundamental for constructing national policies to combat the burden of multimorbidity, particularly in Asian countries. Our study also provides in-depth analyses of each selected disease and its concomitant comorbidities. This study could thus serve as a valuable reference for formulating strategic disease management plans.

We found that the prevalence of multimorbidity increased in the 10-year follow-up period. This increase is reasonable considering the aging population²⁸ and is consistent with a previous study conducted in Ontario⁶. The prevalence of multimorbidity among residents of Ontario rose from 17.4% in 2003 to 24.3% in

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4 2009, a 40% increase. In our study, the prevalence of multimorbidity rose from
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7 20.07% in 2013 to 30.44% in 2009, a 51.6% increase. The different magnitudes of the
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10 increase could have resulted from the various lists of diseases selected to assess
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13 multimorbidity; the Ontario study included 16 common chronic conditions⁶, while our
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16 study included 20 common chronic conditions. However, the rate of demographic
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19 aging in the two different populations may better explain the discrepancies. The
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22 population is aging rapidly in Taiwan. At the end of 2010, 11% of Taiwan's
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25 population was 65 years or older. The ratio of elderly people reached 14% (the
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28 threshold for an “aged” society) in 2017, and the estimated ratio is expected to
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31 increase to 20% (the threshold for a “superaged” society) in Taiwan by 2025 ²⁹.

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37 An understanding of multimorbidity, particularly in the elderly, is therefore very
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40 important for almost every country. In our study, we found that the prevalences of
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43 multimorbidity (2+ diseases) in people aged 60-69, 70-79 and 80-89 were 56.84%,
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46 74.64%, and 82.64%, respectively, in 2013. The prevalences of multimorbidity (3+
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49 diseases) in people aged 60-69, 70-79 and 80-89 were 37.49%, 57.04%, and 68.10%,
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52 respectively, in 2013. Facing such tremendous and complex medical demands, it is
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55 necessary to reform the current “single-disease or specialty” paradigm into a
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58 “integrated and comprehensive medical care” model ³⁰. We also found that the
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4 combination and intensity of multimorbidity differed in older men and women. This
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7 finding may further indicate different medical needs for older men and women, and
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10 gender-specific care plans for older people may be warranted. Our estimates can serve
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13 as a reference for countries facing a similar rapid speed of population aging to better
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16 allocate medical and social welfare resources, including for Taiwan, our neighbor
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19 country Japan ³¹ or other European countries ³².

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25 In addition to older people, the prevalence of multimorbidity among the younger
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28 population warrants special attention. As most studies of multimorbidity have focused
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31 on older adults ^{33 34}, evidence regarding this issue in young adults is very limited. In
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34 our study, the prevalences of multimorbidity (2+ diseases) in people aged 30-39, 40-
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37 49 and 50-89 were 11.18%, 21.76%, and 37.75%, respectively, in 2013. This indicates
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40 the need for early intervention in those who already suffer from multimorbidity in
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43 middle-age, as the intensity of multimorbidity gradually increases, as shown in our
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46 study. Lifestyle factors in middle-age, such as smoking, drinking, exercise and diet,
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49 have been reported to be associated with multimorbidity ³⁵.

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55 Most importantly, our study contributes to a better understanding of the in-depth
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58 details of multimorbidity. In addition to revealing very distinct predominant diseases
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4 in men and women, we also revealed the burden of multimorbidity in each common
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7 chronic condition. From a clinical perspective, our findings can help further stratify
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10 patients within specific disease groups. For example, patient care for those with
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13 diabetes mellitus and one other comorbid condition would be very different from
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16 patients with diabetes mellitus and four other comorbid conditions. From a policy
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19 perspective, our findings can help allocate medical resources more efficiently. Our
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22 previous studies have also supported this stratification strategy (identifying high-risk
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25 groups), and we found that an increase in diabetic complications was positively
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28 associated with an increased risk of hospitalization and increased healthcare costs ³⁶
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37 Here, we have provided epidemiologic information of age- and gender-specific
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40 multimorbidity; however, there are some limitations due to the nature of the claims
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43 data. First, we identified the disease based on the diagnoses recorded at the outpatient
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46 or inpatient visits. However, only up to three or up to five diagnoses were allowed to
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49 be recorded for each outpatient or inpatient visit, respectively; therefore, the
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52 prevalence of multimorbidity may be underestimated. Second, as we used the
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55 NHIRD, the estimations regarding multimorbidity were from the perspective of the
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58 national insurance system. Patients who pay out-of-pocket for their healthcare are not
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4 recorded in the NHIRD. Third, as there is no consensus on the number of diseases
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7 used to identify multimorbidity, epidemiological comparisons with different countries
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10 are difficult. For example, a systematic review conducted by Pati S et al ¹⁷ revealed
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13 that among 13 studies, the number of health conditions analyzed per study varied
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16 from 7 to 22, with the prevalence of multimorbidity varying from 4.5% to 83%.
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22 In summary, our study is the first population-based study conducted in Taiwan that
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25 provides age- and gender-specific information on multimorbidity. The burden of
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28 multimorbidity is increasing and becoming more complex in Taiwan. Providing for
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31 the needs of individuals with multimorbidity requires collaborative work across
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34 healthcare providers and may need to take into account age and gender disparities.
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However, the content of this article does not represent any official position of the NHIA or NHRI. The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement

Data for this study were provided by the National Health Insurance Administration, Taiwan, following ethical approval, and may be available to other researchers who meet data access requirements.

Figure legends

Figure 1. Prevalence of multimorbidity in Taiwan by number of common diseases *, sex, age group, and year. (a) Men and women in 2003. (b) Men and women in 2013.

Figure 2. Prevalence of multimorbidity in Taiwan within common diseases, by sex and year.

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Table 1. Prevalence of multimorbidity in Taiwan by number of common diseases *, age group, and year

2003							
Age group	Taiwanese population	Prevalence of at least one disease (%)	Prevalence of multimorbidity, by degree of multimorbidity (%)				
			2	3	4	5+	
20-29	285,406	16.74	4.01	1.15	0.36	0.12	
30-39	273,713	24.09	8.04	2.86	1.03	0.37	
40-49	269,568	35.91	16.01	7.08	2.92	1.12	
50-59	175,456	51.70	30.15	16.49	8.00	3.57	
60-69	114,876	66.52	47.08	30.39	17.13	8.70	
70-79	74,756	77.86	62.40	45.66	29.10	16.75	
80-89	20,002	78.05	64.32	48.74	32.39	19.58	
90+	1,946	62.23	45.68	33.04	21.12	12.69	
All	1,215,723	37.23	20.07	11.40	6.09	3.07	
2013							
Age group	Taiwanese population	Prevalence of at least one disease (%)	Prevalence of multimorbidity, by degree of multimorbidity (%)				
			2	3	4	5+	
20-29	245,613	19.85 †	5.21	1.49	0.47	0.15	
30-39	295,797	30.49 †	11.18	4.10	1.55	0.60	
40-49	277,889	43.45 †	21.76	10.08	4.35	1.83	
50-59	272,719	59.90 †	37.75	20.87	10.24	4.71	
60-69	173,213	75.39 †	56.84	37.49	21.74	11.70	
70-79	102,826	87.53 †	74.64	57.04	38.44	23.60	
80-89	52,978	92.01 †	82.64	68.10	49.71	33.06	
90+	8,492	90.44 †	80.96	66.52	48.39	32.54	
All	1,429,527	48.97 †	30.44	18.61	10.73	5.94	

*Hypertension, diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver disease, dementia, other neurological disorders, digestive disorders, osteoporosis, arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders, bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer

†P<0.05 compared to prevalence in 2003 using chi-squared tests.

Table 2. Prevalence of 20 common diseases in Taiwan, by age group and year

Disease	Year	Number with condition (prevalence, %)	Prevalence of each disease, by age group (%)							
			20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Hypertension	2003	126,651(10.42)	0.22	1.38	6.31	17.11	29.91	42.36	43.26	28.78
	2013	260,198(18.20) †	0.43	2.38	9.54	22.91	39.64	55.39	61.71	56.64
Diabetes	2003	56,627(4.66)	0.20	0.77	3.00	8.51	14.04	16.31	12.51	5.86
	2013	126,991(8.88) †	0.35	1.27	4.50	11.47	21.10	26.39	25.23	18.38
Congestive heart failure	2003	44,622(3.67)	0.06	0.38	1.80	5.35	10.43	17.25	19.95	15.88
	2013	71,026(4.97) †	0.09	0.45	1.87	4.99	10.10	17.19	24.78	28.24
Coronary syndrome	2003	35,539(2.92)	0.04	0.25	1.19	3.98	8.75	14.82	16.05	11.20
	2013	60,367(4.22) †	0.05	0.27	1.43	4.19	9.38	15.29	19.72	18.86
Cardiac dysrhythmias	2003	14,337(1.18)	0.14	0.31	0.69	1.47	2.89	5.24	6.67	5.29
	2013	29,098(2.04) †	0.18	0.32	0.83	1.79	3.76	6.95	10.88	12.69
Peripheral vascular disease	2003	14,873(1.22)	0.07	0.13	0.44	1.23	3.34	7.10	8.70	4.78
	2013	28,562(2.00) †	0.08	0.17	0.48	1.45	3.92	8.66	11.34	9.89
Cerebrovascular disease	2003	28,098(2.31)	0.14	0.25	0.86	2.74	6.59	12.09	15.26	11.51
	2013	56,770(3.97) †	0.18	0.38	1.12	3.24	7.82	15.35	22.51	23.85
Chronic pulmonary disease	2003	37,897(3.12)	0.78	1.32	1.95	3.46	7.25	12.22	15.14	12.85
	2013	50,705(3.55) †	0.74	1.26	1.80	3.02	5.77	10.73	17.17	21.15
Renal disease	2003	13,999(1.15)	0.18	0.34	0.77	1.57	2.80	4.54	5.07	3.44
	2013	38,748(2.71) †	0.18	0.44	1.06	2.44	5.19	9.64	13.79	14.13
Liver disease	2003	43,555(3.58)	1.39	2.58	4.03	5.53	6.23	5.44	3.41	1.64
	2013	71,015(4.97) †	0.79	2.88	5.13	7.28	8.56	8.05	5.69	4.03
Dementia	2003	5,194(0.43)	0.10	0.12	0.17	0.27	0.72	2.24	5.06	6.27
	2013	18,869(1.32) †	0.13	0.19	0.30	0.51	1.27	4.89	12.77	20.54
Other neurological disorders	2003	124,029(10.20)	4.25	6.84	9.44	13.12	18.24	24.21	26.53	17.78
	2013	217,307(15.20) †	6.54	10.37	13.29	16.90	21.42	29.04	33.85	31.03

Table 2. Prevalence of 20 common diseases in Taiwan, by age group and year (cont'd)

Disease	Year	Number with condition (prevalence, %)	Prevalence of each disease, by age group (%)							
			20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Digestive disorders	2003	152,161(12.52)	6.81	8.54	11.19	14.94	21.03	29.22	32.39	25.95
	2013	227,327(15.90) †	8.41	11.15	13.40	17.09	22.01	29.06	35.24	37.48
Osteoporosis	2003	14,732(1.21)	0.09	0.13	0.49	2.04	3.59	5.02	6.08	5.45
	2013	17,026(1.19)	0.07	0.11	0.23	0.74	2.10	5.23	7.67	9.15
Arthritis (including rheumatoid arthritis)	2003	149,434(12.29)	3.87	6.34	11.05	18.01	25.54	31.95	30.18	19.63
	2013	226,844(15.87) †	4.18	7.28	12.01	19.46	27.70	37.45	37.03	29.30
Anxiety, dissociative and somatoform disorders	2003	52,029(4.28)	1.27	2.48	4.17	6.34	8.48	9.99	9.49	5.91
	2013	89,053(6.23) †	1.69	3.45	5.82	8.00	10.29	11.91	11.18	8.44
Bipolar disorder	2003	8,251(0.68)	0.44	0.59	0.72	0.84	0.89	1.03	0.89	0.51
	2013	15,439(1.08) †	0.51	0.80	1.25	1.30	1.44	1.50	1.32	0.92
Depression	2003	11,630(0.96)	0.64	0.82	0.97	1.14	1.27	1.51	1.61	1.13
	2013	24,712(1.73) †	0.86	1.30	1.89	2.00	2.24	2.52	2.59	2.25
Schizophrenia and psychotic disorders	2003	7,472(0.61)	0.48	0.80	0.74	0.57	0.43	0.40	0.55	0.51
	2013	11,624(0.81) †	0.42	0.82	1.10	1.00	0.77	0.65	0.55	0.67
Cancer	2003	37,438(3.08)	1.26	2.22	3.77	4.11	4.47	5.50	5.46	2.93
	2013	83,065(5.81) †	1.36	2.97	5.68	7.22	9.19	11.54	12.57	12.16

†P<0.05 compared to prevalence in 2003 using chi-squared tests.

Table 3. Prevalence of 20 common diseases in Taiwan, by sex, age group and year

Disease	Year	Prevalence		Prevalence of each disease, by age group (%)															
		Prevalence (%)		20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Hypertension	2003	10.52	10.33	0.33	0.11	1.90	0.92	7.29	5.42	17.13	17.09	27.66	31.83	39.89	44.96	41.16	45.18	29.55	28.31
	2013	19.40	17.13	0.68	0.21	3.58	1.35	12.67	6.71	25.93	20.10	40.55	38.81	51.88	58.30	58.03	65.22	54.02	58.70
Diabetes	2003	4.77	4.56	0.21	0.19	1.05	0.51	3.73	2.34	9.15	7.94	13.07	14.86	14.10	18.64	11.47	13.47	5.75	5.93
	2013	9.57	8.26	0.40	0.31	1.75	0.86	6.18	2.97	13.52	9.56	21.87	20.40	24.50	27.96	22.52	27.81	17.60	18.99
Congestive heart failure	2003	3.71	3.63	0.09	0.03	0.54	0.24	2.12	1.51	5.48	5.25	9.58	11.16	16.27	18.28	19.34	20.51	17.10	15.14
	2013	5.24	4.72	0.14	0.04	0.68	0.25	2.56	1.25	5.82	4.21	10.67	9.58	16.02	18.15	23.37	26.13	27.04	29.18
Coronary syndrome	2003	3.21	2.67	0.05	0.03	0.33	0.17	1.51	0.89	4.47	3.55	8.81	8.70	15.53	14.07	16.88	15.30	11.76	10.86
	2013	5.00	3.52	0.06	0.04	0.44	0.13	2.14	0.78	5.49	2.99	11.24	7.71	16.41	14.36	20.94	18.55	20.42	17.65
Cardiac dysrhythmias	2003	1.19	1.17	0.13	0.15	0.29	0.33	0.64	0.73	1.39	1.54	2.90	2.88	5.40	5.06	6.85	6.51	6.57	4.53
	2013	2.10	1.98	0.16	0.20	0.31	0.34	0.85	0.81	1.83	1.77	3.94	3.60	7.08	6.84	11.69	10.11	12.81	12.61
Peripheral vascular disease	2003	1.23	1.22	0.08	0.06	0.16	0.11	0.47	0.41	1.20	1.25	3.01	3.62	7.01	7.19	8.97	8.46	5.61	4.28
	2013	2.00	2.00	0.06	0.10	0.18	0.16	0.54	0.44	1.60	1.32	3.83	4.00	8.06	9.16	11.76	10.95	11.25	8.82
Cerebrovascular disease	2003	2.61	2.04	0.16	0.12	0.34	0.18	1.07	0.67	3.18	2.36	7.05	6.19	13.01	11.11	16.29	14.31	14.09	9.96
	2013	4.54	3.46	0.19	0.17	0.47	0.29	1.47	0.80	4.05	2.50	9.15	6.61	16.65	14.28	24.45	20.67	24.81	23.09

Table 3. Prevalence of 20 common diseases in Taiwan, by sex, age group and year (cont'd)

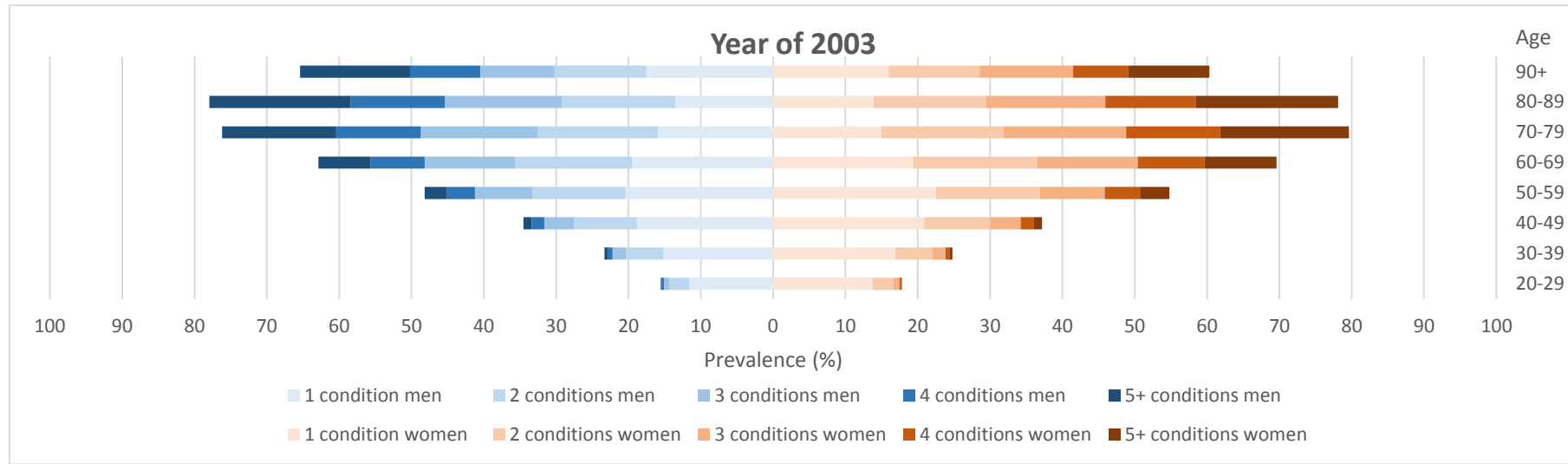
Disease	Year	Prevalence		Prevalence of each disease, by age group (%)															
		Prevalence (%)		20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Chronic pulmonary disease	2003	3.51	2.76	0.80	0.76	1.24	1.39	1.99	1.93	3.50	3.41	8.02	6.59	15.19	9.08	19.80	10.86	17.51	10.04
	2013	4.00	3.14	0.71	0.76	1.16	1.34	1.75	1.85	3.09	2.96	6.52	5.10	13.26	8.62	21.96	12.60	26.98	16.58
Renal disease	2003	1.29	1.03	0.22	0.15	0.42	0.27	0.86	0.68	1.68	1.48	3.02	2.62	4.90	4.16	6.09	4.14	4.51	2.80
	2013	3.26	2.22	0.21	0.15	0.58	0.32	1.42	0.72	3.04	1.89	6.25	4.23	11.26	8.29	15.84	11.85	16.96	11.91
Liver disease	2003	4.61	2.66	2.12	0.76	3.95	1.36	5.64	2.56	6.38	4.78	6.70	5.83	5.59	5.28	3.90	2.96	2.19	1.32
	2013	6.20	3.86	1.12	0.49	4.30	1.66	7.35	3.12	8.92	5.76	9.21	7.97	8.49	7.68	6.13	5.28	4.66	3.53
Dementia	2003	0.46	0.39	0.15	0.06	0.18	0.07	0.21	0.13	0.32	0.23	0.75	0.70	2.14	2.35	4.82	5.28	4.24	7.49
	2013	1.31	1.33	0.16	0.10	0.26	0.14	0.41	0.20	0.63	0.41	1.31	1.23	4.52	5.20	11.70	13.79	18.81	21.89
Other neurological disorders	2003	8.00	12.17	3.29	5.08	5.24	8.27	6.90	11.76	9.31	16.48	14.62	21.32	21.26	27.32	23.99	28.86	17.10	18.19
	2013	12.02	18.05	4.74	8.19	7.79	12.59	10.02	16.25	12.66	20.81	16.84	25.58	25.34	32.12	32.25	35.37	30.73	31.26

Table 3. Prevalence of 20 common diseases in Taiwan, by sex, age group and year (cont'd)

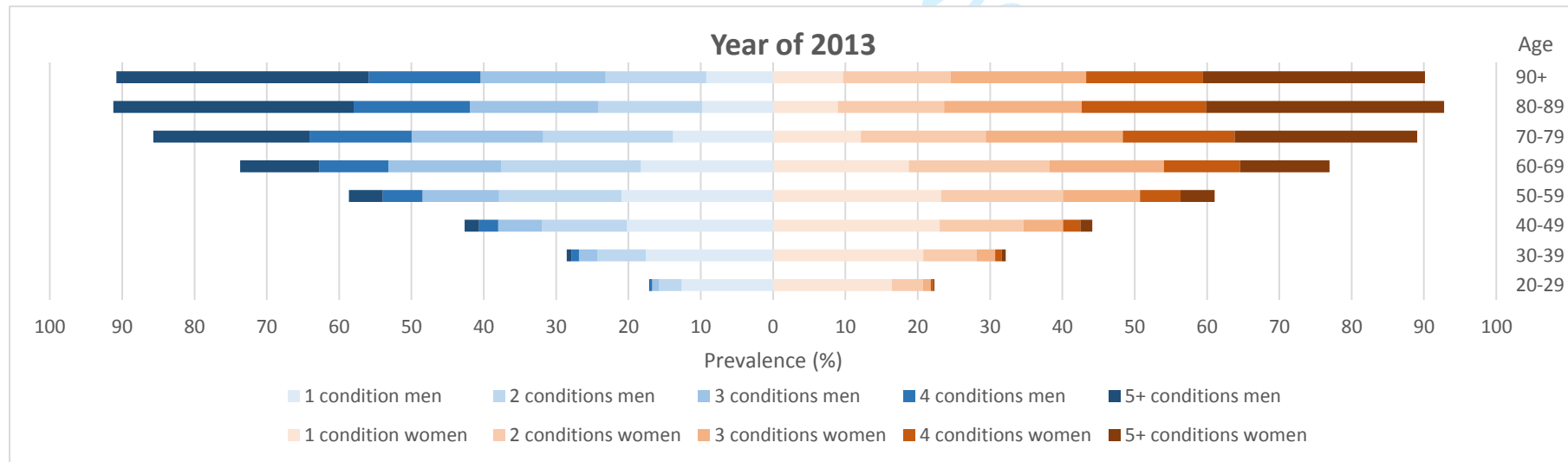
Disease	Year	Prevalence (%)		Prevalence of each disease, by age group (%)															
				20-29		30-39		40-49		50-59		60-69		70-79		80-89		90+	
		Male	Female	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Digestive disorders	2003	11.62	13.32	4.92	8.46	7.63	9.35	10.53	11.79	13.78	15.96	19.84	22.04	29.87	28.54	34.65	30.32	28.04	24.69
	2013	14.01	17.60	5.65	10.93	8.59	13.34	11.63	15.00	15.14	18.91	20.14	23.69	28.32	29.67	37.55	33.04	41.88	34.03
Osteoporosis	2003	0.45	1.89	0.13	0.05	0.14	0.13	0.26	0.70	0.41	3.48	0.91	5.87	2.07	8.14	2.75	9.14	4.10	6.26
	2013	0.58	1.74	0.09	0.05	0.15	0.08	0.26	0.21	0.45	1.02	0.76	3.31	1.98	7.93	3.72	11.43	5.25	12.21
Arthritis (including rheumatoid arthritis)	2003	12.26	12.32	4.81	3.05	7.46	5.35	11.49	10.65	16.09	19.70	22.43	28.20	30.16	33.85	29.71	30.61	22.85	17.70
	2013	15.32	16.36	4.89	3.53	8.75	6.03	12.75	11.34	18.01	20.80	24.02	31.04	32.67	41.43	35.62	38.37	30.49	28.36
Anxiety, dissociative and somatoform disorders	2003	3.36	5.10	1.11	1.42	2.05	2.86	3.26	5.01	4.47	7.99	6.27	10.36	8.18	11.91	8.46	10.44	6.43	5.60
	2013	4.90	7.42	1.50	1.86	2.95	3.87	4.76	6.78	5.99	9.87	7.55	12.78	9.09	14.26	9.34	12.94	7.93	8.84
Bipolar disorder	2003	0.55	0.79	0.43	0.45	0.44	0.72	0.55	0.87	0.63	1.02	0.72	1.03	0.87	1.20	0.76	1.02	0.55	0.49
	2013	0.84	1.29	0.51	0.51	0.65	0.93	0.95	1.52	0.97	1.62	1.04	1.79	1.10	1.84	1.09	1.54	0.99	0.86
Depression	2003	0.80	1.10	0.66	0.62	0.65	0.98	0.76	1.15	0.86	1.39	1.00	1.50	1.32	1.71	1.44	1.77	0.82	1.32
	2013	1.42	2.00	0.87	0.84	1.11	1.47	1.56	2.19	1.56	2.42	1.70	2.73	1.96	2.98	2.23	2.93	2.20	2.29
Schizophrenia and psychotic disorders	2003	0.68	0.56	0.62	0.37	0.96	0.65	0.81	0.68	0.51	0.62	0.34	0.51	0.37	0.43	0.49	0.61	0.41	0.58
	2013	0.89	0.75	0.50	0.35	0.98	0.68	1.32	0.91	1.04	0.97	0.70	0.85	0.51	0.77	0.49	0.60	0.59	0.74
Cancer	2003	2.21	3.85	0.90	1.58	1.22	3.11	1.80	5.56	2.80	5.26	4.26	4.66	6.22	4.73	6.82	4.21	4.38	2.06
	2013	5.06	6.49	1.02	1.67	1.82	3.95	3.41	7.73	5.76	8.57	9.09	9.29	13.37	10.02	15.81	9.49	16.21	8.99

Figure 1. Prevalence of multi-morbidity in Taiwan by number of common diseases *, sex, age group, and year

(a) Men and women in 2003

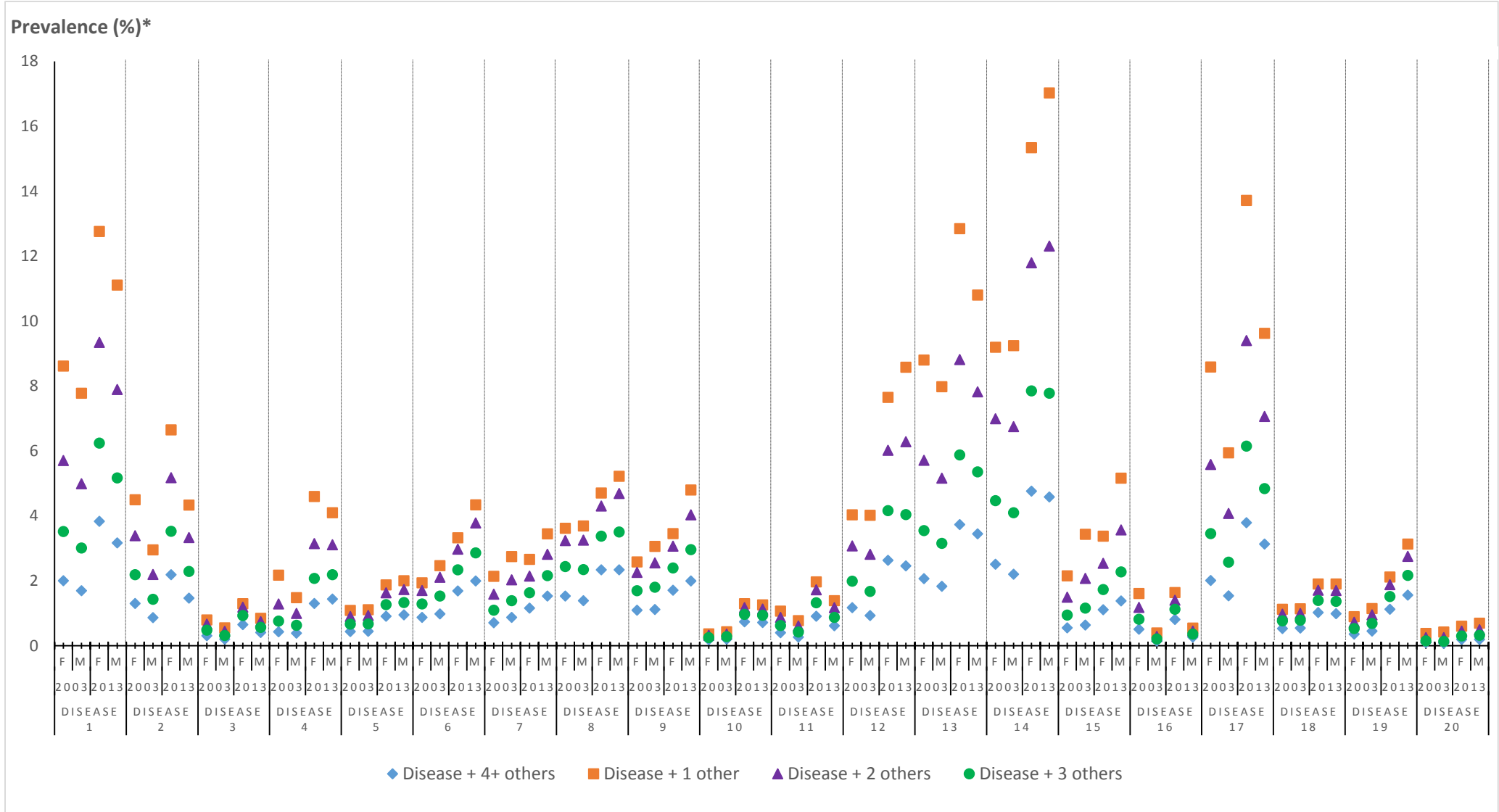


(b) Men and women in 2013



*Hypertension, diabetes, congestive heart failure, coronary syndrome, cardiac dysrhythmias, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, renal disease, liver disease, dementia, other neurological disorders, digestive disorder, osteoporosis, arthritis (including rheumatoid arthritis), anxiety dissociative and somatoform disorders, bipolar disorder, depression, schizophrenia and psychotic disorders, and cancer

Figure 2. Prevalence of multi-morbidity in Taiwan within common diseases, by sex and year.



*Prevalence (%): the number of patients suffering from a specific disease with concurrent 1, 2, 3, or 4+ other diseases divided by the number of patients with a specific disease. (Disease 1: Anxiety, dissociative and somatoform disorders; Disease 2: Arthritis (including rheumatoid arthritis); Disease 3: Bipolar disorder; Disease 4: Cancer; Disease 5: Cardiac dysrhythmias; Disease 6: Cerebrovascular disease; Disease 7: Chronic pulmonary disease; Disease 8: Congestive heart failure; Disease 9: Coronary syndrome; Disease 10: Dementia; Disease 11: Depression; Disease 12: Diabetes; Disease 13: Digestive disorders; Disease 14: Hypertension; Disease 15: Liver disease; Disease 16: Osteoporosis; Disease 17: Other neurological disorders; Disease 18: Peripheral vascular disease; Disease 19: Renal disease; Disease 20: Schizophrenia and psychotic disorders.)

Table S1. ICD-9-CM codes regarding the definition of 20 common diseases

Disease	ICD-9-CM code
Hypertension	401, 402, 403, 404, 405
Diabetes	250
Congestive heart failure	39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 4254, 4255, 4257, 4258, 4259, 428
Coronary syndrome	410, 411, 412, 413, 414
Cardiac dysrhythmias	427
Peripheral vascular disease	0930, 4373, 4400, 4401, 44020, 44021, 44022, 44023, 44024, 44029, 44030, 44031, 44032, 4408, 4409, 44100, 44101, 44102, 44103, 4411, 4412, 4413, 4414, 4415, 4416, 4417, 4419, 4431, 44321, 44322, 44323, 44324, 44329, 44381, 44382, 44389, 4439, 4471, 5571, 5579, V434
Cerebrovascular disease	36234, 430, 431, 432, 43300, 43301, 43310, 43311, 43320, 43321, 43330, 43331, 43380, 43381, 43390, 43391, 434, 4350, 4351, 4352, 4353, 4358, 4359, 436, 437, 438
Chronic pulmonary disease	4168, 4169, 490, 491, 492, 493, 4940, 4941, 4950, 4951, 4952, 4953, 4954, 4955, 4956, 4957, 4958, 4959, 496, 500, 501, 502, 503, 504, 505, 5064, 5081, 5088
Renal disease	403, 404, 5820, 5821, 5822, 5824, 58281, 58289, 5829, 5830, 5831, 5832, 5834, 5836, 5837, 584, 585, 586, 5880, V420, V451, V560, V561, V562, V5631, V5632, V568
Liver disease	07022, 07023, 07032, 07033, 07044, 07054, 0706, 0709, 570, 5710, 5711, 5712, 5713, 57140, 57141, 57149, 5715, 5716, 5718, 5719, 5733, 5734, 5738, 5739, V427, 4560, 4561, 45620, 45621, 5722, 5723, 5724, 5728
Dementia	290, 2930, 2931, 29381, 29382, 29383, 29384, 29389, 2939, 2940, 2941, 2948, 2949, 3100, 3101, 3102, 3108, 3109, 3310, 3311, 3312
Other neurological disorders	3319, 332, 3334, 3335, 33392, 3340, 3341, 3342, 3343, 3344, 3348, 3349, 3350, 33510, 33511, 33519, 33520, 33521, 33522, 33523, 33524, 33529, 3358, 3359, 3362, 340, 3410, 3411, 34120, 34121, 34122, 3418, 3419, 34500, 34501, 34510, 34511, 3452, 3453, 34540, 34541, 34550, 34551, 34560, 34561, 34570, 34571, 34580, 34581, 34590, 34591, 3481, 3483, 34830, 34831, 34839, 780, 7843
Digestive disorder	530, 531, 532, 53300, 53301, 53310, 53311, 53320, 53321, 53330, 53331, 53340, 53341, 53350, 53351, 53360, 53361, 53370, 53371, 53390, 53391, 53400, 53401, 53410, 53411, 53420, 53421, 53430, 53431, 53440, 53441, 53450, 53451, 53460, 53461, 53470, 53471, 53490, 53491, 536, 558, 564
Osteoporosis	733
Arthritis (including rheumatoid arthritis)	274, 710, 711, 714, 715, 716, 718, 720, 727, 728, 729, 739

Table S1. ICD-9-CM codes regarding the definition of 20 common diseases (continued)

Disease	ICD-9-CM code
Anxiety, dissociative and somatoform disorders	30000-30002, 30009-30016, 30019-30023, 30029, 3003, 3005-3007, 30081, 30082, 30089, 3009, 3062, 3069, 30740-30749, 3080-3084, 3089, 316
Bipolar disorder	29600-29606, 29610-29616, 29640-29646, 29650-29656, 29660-29666, 2967, 29680-29682, 29689
Depression	29620-29626, 29630-29636, 29690, 29699, 2980, 3090, 3091, 311
Schizophrenia and psychotic disorders	29500-29505, 29510-29515, 29520-29525, 29530-29535, 29540-29545, 29550-29555, 29560-29565, 29570-29575, 29580-29585, 29590-29595, 2970-2973, 2978, 2979, 2981-2984, 2988, 2989, 29900, 29901, 29910, 29911, 29980, 29981, 29990, 29991
Cancer	140-239

Figure S1. The sampling and data linkage process of the 2005 and 2010 Longitudinal Health Insurance Databases (LHID)

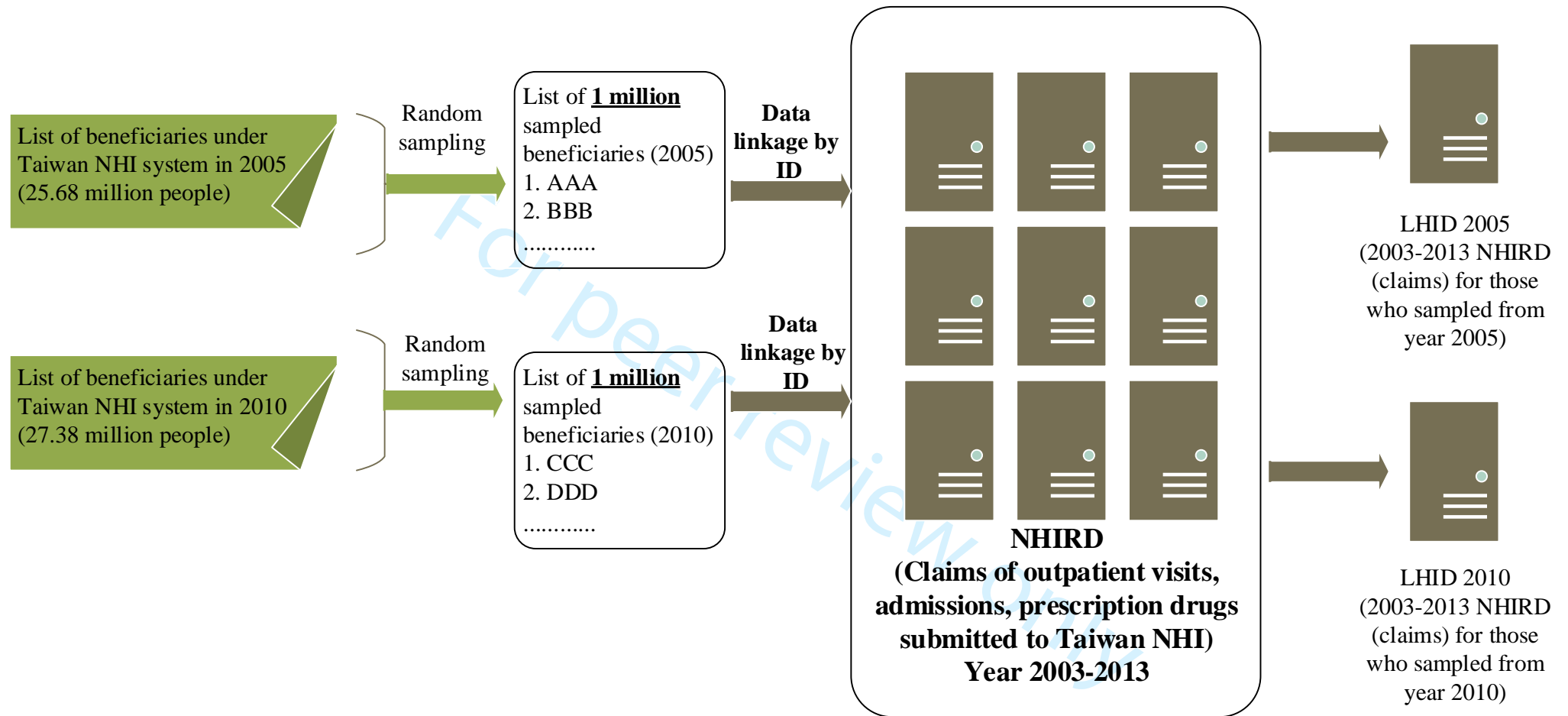
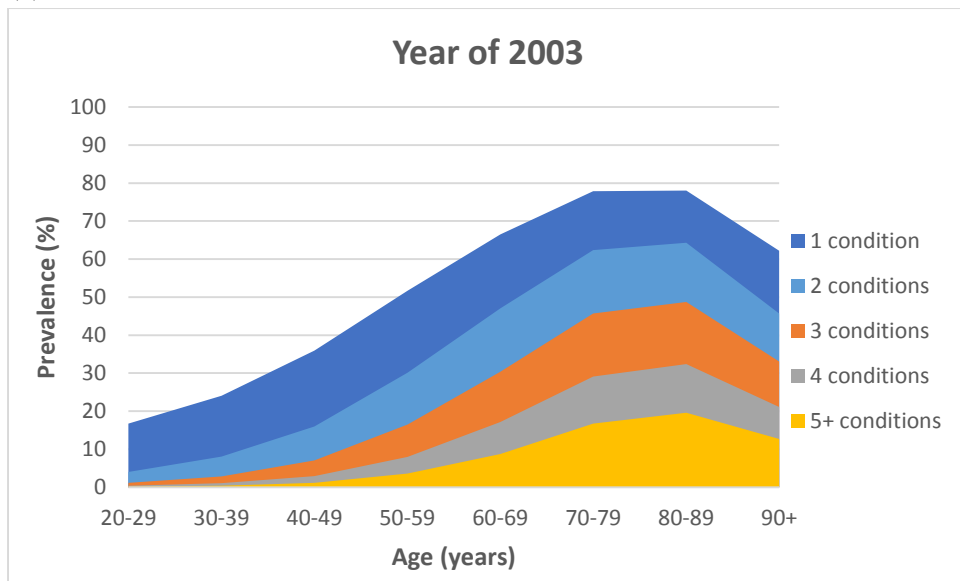
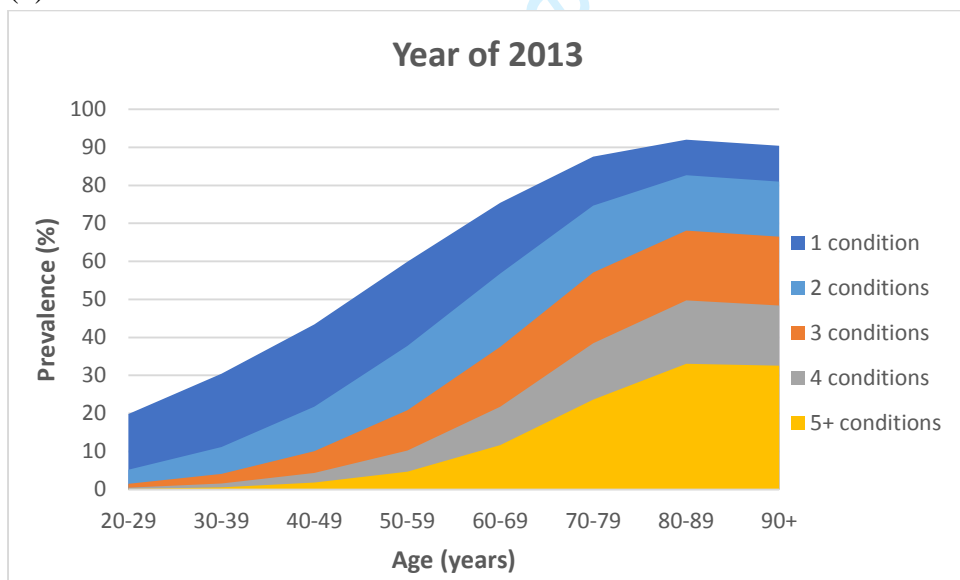


Figure S2. Prevalence of multi-morbidity in Taiwan by number of common diseases, age group, and year

(a) Year of 2003



(b) Year of 2013



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

	Item No	Recommendation	
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	p.1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	p.3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p.6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	p.8
Methods			
Study design	4	Present key elements of study design early in the paper	p.9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.9-10
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	p.9
		(b) <i>Cohort study</i> —For matched studies, give matching 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	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.11-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	p.9-10
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	p.9-10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.11-13
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	p.13-14
		(b) Describe any methods used to examine subgroups and interactions	p.13-14
		(c) Explain how missing data were addressed	Not applicable
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(e) Describe any sensitivity analyses	Not applicable

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Results			
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	p.9-10
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	p.15, 28
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	p.15-18, 28-33
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.15-18, 28-33
		(b) Report category boundaries when continuous variables were categorized	p.15-18, 28-33
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	p.15-18, 28-33
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.22-23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p.19-22
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.22-23
Other information			
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 present article is based	p.2

*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.

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.