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TITLE PAGE

Establishing a uniform operational definition of multimorbidity for primary care in Singapore based on retrospective, large administrative data

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ABSTRACT

Objectives: Multimorbidity is a norm in primary care. A consensus on its operational definition remains lacking especially in the list of chronic conditions considered. This study aimed to compare six different operational definitions of multimorbidity previously reported in the literature for the context of primary care in Singapore.

Methods: This is a retrospective study using anonymised primary care data. We defined multimorbidity as having three or more chronic conditions in an individual. Tabulation of the prevalence of single conditions and multimorbidity with each operational definition was done in our study population of 787,446 patients. Standardised prevalence rates (SPR) were obtained by adjusting for age, sex and ethnicity. We compared the operational definitions based on (1) number of chronic diseases, (2) presence of chronic diseases of high burden and (3) relevance in primary care in Singapore. IBM SPSS version 23 and Microsoft Office Excel 2019 were used for all statistical calculations and analyses.

Results: The SPRs of multimorbidity in primary care in Singapore varied from 5.7% to 17.2%. The lists by Fortin et al., Ge et al., Low et al. and Quah et al. included at least 12 chronic conditions, the recommended minimal number of conditions. Quah et al. considered the highest proportion of chronic diseases (92.3%) of high burden in primary care in Singapore, with SPRs of at least 1.0%. Picco et al. and Subramaniam et al. considered the fewest number of conditions of high relevance in primary care in Singapore.

Conclusions: Fortin et al.'s list of conditions is most suitable for describing multimorbidity in the primary care setting of Singapore. Pre-diabetes and 'physical disability' should be added to Fortin et al.'s list to augment its comprehensiveness. We propose a similar study methodology to be performed in other countries to identify the most suitable operational definition in their own context.

ARTICLE SUMMARY

Key messages

- The SPRs of multimorbidity in the primary care setting in Singapore varied widely depending on the operational definition utilised.
- Comparison of the operational definitions made based upon (1) number of chronic diseases, (2) presence of chronic diseases of high burden and (3) relevance in primary care in Singapore, revealed merits of Fortin et al.'s list when applied to the primary care population in Singapore.

Strengths and limitations of this study

- The strengths of this study include the utilisation of a large database, determination of the clinical relevance of a chronic condition through an iterative process and the employment of a systematic method in the comparison of all six operational definitions.
- The limitations of this study include the utilisation of a pre-determined number of International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) codes and not considering the impact of each chronic condition on affected individuals.

MAIN TEXT

1. BACKGROUND

Multimorbidity, the co-occurrence of multiple chronic health conditions in a single individual,[1] is a growing norm in primary care.[2-5] The term 'multimorbidity' has often been confused with the term 'comorbidity'.[6, 7] Comorbidity describes the simultaneous presence of multiple health conditions when there is an index condition. It is a concept that is commonly used by secondary and tertiary care clinicians. In contrast, multimorbidity describes the co-occurrence of two or more chronic medical conditions without specifying the index condition. Health outcomes are evaluated based on the interaction and burden of all co-existing chronic conditions.[8] Advocates of the concept of multimorbidity tend to focus on primary care, where the identification of an index disease is often neither obvious nor useful.[9]

The implications of multimorbidity are significant and widespread. From the patient's perspective, multimorbidity is associated with future functional decline,[10, 11] reduced health-related quality of life,[10, 12] inpatient admission and mortality.[13] From an economic standpoint, multimorbidity is associated with increased healthcare utilisation[14] and healthcare costs.[10] Single disease clinical practice guidelines that have traditionally been used for the management of chronic diseases are inappropriate in the management of patients with multimorbidity.[5, 15-17]

To this date, there is no consensus on an operational definition of multimorbidity.[18-20] This definition comprises two components: the list of chronic conditions considered and the cut-off for the number of chronic conditions used to determine the presence of multimorbidity.[21] The absence of a standardised operational definition has resulted in reported prevalence estimates of multimorbidity in Singapore to range widely from 16.3% to 89.4% [12, 14, 22-24] and has made comparability between published studies impossible.[21]

In 2017, an operational definition comprising 20 chronic conditions/categories of conditions was proposed by Fortin et al. as a common list of conditions for studying multimorbidity in primary care (Appendix 1-1).[21] These conditions were selected from a scoping review of relevant studies.

We identified six studies, two by Ge et al. [23, 25] (Appendix 1-2) and one each by Low et al. [24] (Appendix 1-3), Picco et al. [14] (Appendix 1-4), Quah et al. [12] (Appendix 1-5) and Subramaniam et al. [22] (Appendix 1-6), which were published between 2014 to 2019 in Singapore. These studies were identified on Medline Ovid between 2010 till 14 March 2020 and through direct correspondences with

the authors (Appendix 2). Heterogeneity was noted in both the methodologies and lists of chronic conditions utilised in each study.

The objective of this study was, therefore, to compare the different operational definitions of multimorbidity previously reported in the literature for the context of primary care in Singapore.

2. METHODS

2.1 Setting and Study Population

The study population was selected between 1 July 2015 and 30 June 2016. During this period, the public primary healthcare sector was organised into two main clusters in Singapore - National Healthcare Group Polyclinics (NHGP) and SingHealth Polyclinics (SHP). Together, the two clusters consisted of 18 polyclinics island-wide and employed 14% of primary care doctors. These polyclinics provide government-funded subsidised primary care, serving as a one-stop health centre providing a comprehensive range of healthcare services for the family, including, but not limited to the management of chronic diseases. According to the Primary Care Survey 2010 conducted by the Ministry of Health (MOH), Singapore, the polyclinics provided primary care services to 20% of the national population yet managed 45% of the chronic disease attendances nationally.[26] Private medical clinics run by general practitioners provided the remainder of primary care services in the country. The participants in this study were multi-ethnic patients aged 0 to 99 years old who consulted a doctor in NHGP at least once during the study period. A total of 787,446 patients from nine polyclinics were included in this study.

2.2 Data Source

Data from the study population were collected from the NHGP Business Informatics (BI) system. The BI system is an administrative database that captures each patient's consultation episodes and clinical parameters from structured data fields within the electronic medical records e.g. blood pressure readings, International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) diagnoses codes and laboratory data. For this study, we excluded all patient encounters that did not include an ICD-10 diagnosis code by a physician, such as vaccinations. Only de-identified data were collected in accordance with the personal data protection act.[27]

2.3 Definition of Chronic Condition and Multimorbidity

We adopted the definition of O'Halloran et al. for chronicity of a disease which is defined as one lasting at least six months, with a documented pattern of recurrence or deterioration, and having an impact on an individual's quality of life.[28]

While it was suggested to include two operational definitions of multimorbidity as there is no consensus on its definition (i.e. a cut-off of 'two or more' and 'three or more' chronic conditions), we adopted a cut-off of 'three or more' chronic conditions only to better identify patients with higher needs.[18]

2.4 Determination of Prevalence Rates of Single Conditions and Multimorbidity

The prevalence of a disease is defined as the proportion of the population at risk (PAR) that are cases at a point in time.[29] The PAR is defined as the group of people, healthy or sick, who would be counted as cases if they had the disease of interest, which forms the denominator for the calculation of prevalence.[29] For this study, the denominator or PAR was denoted by individuals aged 0 to 99 years who consulted a doctor in NHGP at least once between 1 July 2015 and 30 June 2016.

For the crude prevalence rate of single conditions, the numerator used was the number of unique patients with the single condition who had consulted a doctor in NHGP at least once between 1 July 2015 and 30 June 2016. For the crude prevalence rate of multimorbidity, the numerator used was the number of unique patients with multimorbidity who had consulted a doctor in NHGP at least once between 1 July 2015 and 30 June 2016.

Standardised prevalence rates (SPRs) were obtained by adjusting the study population to a standard population by using the direct standardisation method as detailed by Bains.[30] The 2016 Singapore population was used as the standard population.[31] Poisson approximation was utilised to calculate the confidence intervals of 95%.

2.5 Criteria for Comparison of Operational Definitions

Amongst the six studies conducted in Singapore, only five unique operational definitions were identified. The two studies by Ge et al. [23, 25] utilised the same operational definition. We compared six lists of chronic conditions from six different operational definitions of multimorbidity (Appendix 3) on the same study population. This included the list proposed by Fortin et al. that had been developed as a research tool to document the presence of multimorbidity in primary care [21] (Appendix 1-1) and the five lists used in the study of multimorbidity in Singapore (Appendix 1-2 to 1-6). A list of NHGP ICD-10 diagnosis codes was assembled by four senior family physicians based on the aforementioned definition of chronicity.[28]

Fortin et al. proposed that an ideal operational definition of multimorbidity should comprise at least 12 chronic diseases, each with a high impact or burden in the given population of interest.[18] Based on this, the comparison of the operational definitions of the six lists were focused on (1) the number of chronic diseases considered, (2) presence of chronic diseases of high burden and (3) relevance in the primary care setting in Singapore. We considered a chronic condition to be of significant burden in the primary care if it has a SPR of at least 1.0%. We tabulated the proportion of chronic diseases with a SPR of at least 1.0% in each list. The numerator used was the number of chronic conditions with a SPR of at least 1.0% and the denominator was the total number of chronic conditions in the list. The clinical relevance of a condition was based on consensus reached after iterative discussions between the clinicians, research team members and reference to statistics from the MOH, Singapore and local primary care initiatives such as the Chronic Disease Management Programme (CDMP).[32]

Statistics reported by the MOH have consistently ranked hyperlipidaemia, hypertensive disease and diabetes mellitus as the first, second and fourth top condition responsible for polyclinic attendances since 2012.[33] Hyperlipidaemia constituted 13.8% of polyclinic attendances in 2018, closely followed by hypertensive disease at 13.2%, acute upper respiratory tract infection at 9.4% and diabetes mellitus at 9.0%.

The Chronic Disease Management Programme (CDMP) [32] was introduced in 2006 to facilitate the provision of care to patients with chronic conditions through the development of evidence-based structured Disease Management Programmes and to reduce out-of-pocket payments for outpatient treatments by allowing patients to draw on their Medisave. The structured Disease Management Programmes facilitate the management of these conditions in the primary care setting. In 2018, the list of chronic conditions included in CDMP was increased to include 20 chronic conditions (Appendix 4).

2.6 Statistical Analysis

The sample size was determined by the number of patients aged 0 to 99 years who visited the NHGP for at least one doctor consultation between 1 July 2015 and 30 June 2016. We used listwise deletion method for complete case analysis. For descriptive statistics, we described the mean for continuous variables and their respective standard deviation. For categorical variables, we described proportions and their respective confidence intervals where appropriate.

SPRs were obtained by adjusting for age, sex and ethnicity. Age was stratified into four categories - ‘0 - 24’, ‘25 - 44’, ‘45 - 64’ and ‘65 - 99’. Sex was classified into male and female, and ethnicity was categorized into Chinese, Malay, Indian and Others. To compare the SPRs of multimorbidity among

age and sex, we tabulated age-stratified, sex-and-ethnicity SPR and sex-stratified, age-and-ethnicity SPR of multimorbidity between the different lists. No overlap of the 95% confidence intervals for the SPRs among the different lists was considered as statistically significant. IBM SPSS version 23 and Microsoft Office Excel 2019 were used for all statistical calculations and analyses.

3. RESULTS

The mean age of the 787,446 patients analysed in this study was 43.9 years. Females made up 50.9% of the patients and the Chinese formed the majority ethnic group at 68.2%. Of the four ethnicities, the Chinese had the highest mean age of 47.1 years and this was followed by the Indians at 39.7 years. 53.4% of the patients studied were from the '45 - 64' and '65 - 99' age groups (Table 1).

Table 1: Demographics of the study population

	Frequency	Percent	Mean Age (SD)
Total	787,446	100.0	43.9 (0.03)
Sex			
Female	400,965	50.9	45.3 (0.04)
Male	386,481	49.1	42.2 (0.04)
Ethnicity			
Chinese	537,234	68.2	47.1 (0.03)
Malay	127,501	16.2	35.1 (0.06)
Indian	78,452	10.0	39.7 (0.08)
Others	44,259	5.6	37.1 (0.09)
Age Groups			
0 - 24	201,839	25.6	
25 - 44	165,212	21.0	
45 - 64	252,206	32.0	
65 - 99	168,189	21.4	

The list recommended by Fortin et al. [21] gave the highest SPR of multimorbidity in the study population (17.2%). This was followed by the list recommended by Quah et al. [12] (16.8%), Low et al. [24] (14.6%), Ge et al. [23, 25] (13.0%), Subramaniam et al. [22] (5.9%) and Picco et al. [14] (5.7%) (Table 2).

Across the six lists, the SPRs of multimorbidity increased with increasing age, with the '65 to 99' years age group reporting the highest SPR of multimorbidity. The male sex is also noted to have higher SPRs of multimorbidity and the differences between the sexes are statistically significant (Table 2).

Table 2: Comparison of the standardised prevalence rates of multimorbidity among the six lists of chronic conditions

	Fortin et al. 2017	Ge et al. 2018 and 2019	Low et al. 2019	Picco et al. 2016	Quah et al. 2016	Subramaniam et al. 2014
Total	17.2 (17.2, 17.3)	13.0 (12.9, 13.0)	14.6 (14.5, 14.7)	5.7 (5.7, 5.8)	16.8 (16.7, 16.8)	5.9 (5.8, 5.9)
Sex						
Female	16.5 (16.4, 16.6)	11.7 (11.7, 11.8)	13.5 (13.4, 13.6)	5.4 (5.4, 5.5)	16.0 (15.9, 16.1)	5.6 (5.5, 5.6)
Male	18.0 (17.9, 18.1)	14.3 (14.1, 14.4)	15.8 (15.7, 15.9)	6.0 (5.9, 6.1)	17.6 (17.4, 17.7)	6.2 (6.1, 6.2)
Age Groups						
0 - 24	0.08 (0.07, 0.10)	0.02 (0.02, 0.03)	0.04 (0.03, 0.05)	0.01 (0.01, 0.01)	0.10 (0.08, 0.11)	0.02 (0.01, 0.02)
25 - 44	4.0 (3.9, 4.1)	2.2 (2.1, 2.3)	2.8 (2.7, 2.9)	0.5 (0.5, 0.5)	3.6 (3.5, 3.7)	0.6 (0.6, 0.7)
45 - 64	28.5 (28.3, 28.7)	20.2 (20.0, 20.4)	23.2 (23.0, 23.4)	7.8 (7.7, 7.9)	27.7 (27.5, 27.9)	8.1 (8.0, 8.2)
65 - 99	60.9 (60.5, 61.2)	50.9 (50.5, 51.2)	55.4 (55.0, 55.7)	26.1 (25.9, 26.4)	60.1 (59.7, 60.4)	26.3 (26.1, 26.6)

3.1 Criterion 1: Number of Chronic Conditions

A list of 57 NHGP ICD-10 diagnosis codes (Appendix 5) was matched to the chronic conditions in these six lists. Amongst the 20 conditions/categories of conditions proposed by Fortin et al.,[21] only 19 of them could be matched to the corresponding NHGP ICD-10 codes. We excluded the condition ‘chronic musculoskeletal condition causing pain or limitation’ from the list as the corresponding ICD-10 code was not reliably coded in the context at our primary care setting.

Low et al. [24] proposed a total of 48 chronic conditions, eight of which - ‘hip fracture’, ‘nephrosis’, ‘respiratory failure’, ‘secondary hypertension’, ‘spine fracture’, ‘coronary artery bypass graft’, ‘percutaneous coronary intervention’ and ‘kidney transplant’ had no corresponding NHGP ICD-10 codes and were likewise excluded from the list. Of the remaining 40 conditions, 16 conditions had overlapping ICD-10 codes. This included chronic conditions such as ‘anxiety’ and ‘general anxiety disorder’ which were matched to the same ICD-10 code: F41.1 ‘anxiety disorder, unspecified’. (Appendix 1-3). These conditions were reclassified to obtain a final list of 31 chronic conditions to avoid double-counting of chronic diseases and overestimation of multimorbidity.

Picco et al. [14] and Subramaniam et al. [22] only considered ten and eight conditions respectively, falling short of the recommended minimal number of 12 chronic conditions.[18]

3.2 Criterion 2: Prevalence amongst the Primary Care Population

We considered a chronic condition to be of high burden in the primary care setting if it has a SPR of at least 1.0%. The list proposed by Quah et al. [12] had the highest proportion (92.3%) of chronic conditions with a SPR of at least 1.0% (Appendix 1-5). This was followed by the list by Fortin et al. [21] (78.9%) (Appendix 1-1), Picco et al. [14] (70.0%) (Appendix 1-4), Subramaniam et al. [22] (62.5%) (Appendix 1-6), Ge et al. [23, 25] (52.9%) (Appendix 1-2) and lastly Low et al. [24] (41.9%) (Appendix 1-3).

3.3 Criterion 3: Relevance to Primary Care Services

Hypertensive disease and diabetes mellitus were represented in all six operational definitions, with SPRs of 20.93% and 11.86% respectively. Hyperlipidaemia, with the highest SPR of 24.97%, however, was absent in the lists of chronic conditions by Picco et al. [14] and Subramaniam et al..[22]

We compared the chronic conditions under CDMP with the lists of chronic conditions in the six operational definitions. The list of chronic conditions by Low et al. [24] included all 20 conditions under CDMP. This was followed by Ge et al. [23, 25] and Quah et al.,[12] with each considering 17 out of the 20 chronic conditions. Fortin et al. [21] considered 15 out of the 20 chronic conditions and Subramaniam et al. [22] and Picco et al. [14] only considered 10 and 8 of the 20 conditions respectively.

4. DISCUSSION

4.1 Summary of Results

The SPRs of multimorbidity in the primary care setting in Singapore varied widely depending on the operational definition utilised. The list of chronic conditions proposed by Fortin et al. [21] gave the highest SPR of multimorbidity (17.2%). The lists by Fortin et al.,[21] Ge et al.,[23, 25] Low et al. [24] and Quah et al. [12] included at least 12 chronic conditions with the list by Quah et al. [12] comprising the highest proportion of chronic diseases (92.3%) with a SPR of at least 1.0% that matched with a NHGP ICD-10 code. The lists by Picco et al. [14] and Subramaniam et al. [22] did not include hyperlipidaemia, a chronic condition of high relevance in the primary care setting in Singapore and both lists considered the fewest number of conditions under CDMP.

4.2 Comparison of Operational Definitions

Comparing the six operational definitions, it is clear that the lists proposed by Picco et al. [14] and Subramaniam et al. [22] had fallen short on several fronts. Both lists considered less than 12 chronic conditions and have comparatively lower proportions of chronic conditions with SPR of at least 1.0%. In addition, both considered the fewest number of chronic conditions under CDMP and failed to include hyperlipidaemia, which constitutes a large proportion of polyclinic attendances. These shortfalls likely contributed to the low SPRs of multimorbidity tabulated and underestimate multimorbidity in the primary care setting in Singapore.

While Low et al.'s list [24] comprised 31 chronic conditions, including all 20 conditions under CDMP, it reported the lowest proportion of chronic diseases (41.9%) with a SPR of at least 1.0%. This is likely due to two reasons. The first was that Low et al.'s list [24] is the longest amongst the six lists. While Low et al. [24] included 13 conditions with a SPR of at least 1.0%, (numerator), second only to Fortin et al. [21], its inclusion of a total of 31 chronic conditions (denominator), resulted in a less discriminating list. Second, the manner in which the list of chronic conditions was classified could be a contributory factor. Low et al. [24] had kept 'major depression', 'anxiety', 'schizophrenia' and 'bipolar disorder' as four separate chronic conditions (Appendix 1-3), whilst, other studies such as that by Quah et al. [12] had grouped them under a single chronic condition category - 'psychiatric conditions' (Appendix 1-5). When considered individually, only the chronic condition 'major depression' had a

SPR of at least 1.0%. While Low et al.'s list [24] is the most comprehensive, the presence of chronic conditions with overlapping ICD-10 codes prior to re-classification and the large number of chronic conditions with no corresponding NHGP ICD-10 codes make it less ideal as an operational definition for use in the primary care setting in Singapore.

The list by Ge et al.,[23, 25] which comprised 17 chronic conditions and considered a large number of chronic conditions under CDMP also had a low proportion of chronic diseases (52.9%) with a SPR of at least 1.0%. Ge et al. [23, 25] had likewise considered the psychiatric diseases individually (Appendix 1-2) as opposed to grouping them as a single chronic condition. In addition, Ge et al.'s list [23, 25] did not include conditions commonly seen in primary care such as thyroid conditions and diseases of the gastrointestinal tract, which were present in Fortin et al. [21] (Appendix 1-1) and Quah et al.'s lists [12] (Appendix 1-5). 'Thyroid disorder (Fortin et al. [21]) / Thyroid diseases (Quah et al. [12])' have a SPR of 2.36%. 'Chronic hepatitis (Fortin et al. [21])' and 'Stomach problem (reflux, heart burn, or gastric ulcer) (Fortin et al. [21])' have SPRs of 3.02% and 2.52% respectively, while 'Gastrointestinal diseases (Quah et al. [12])' has a SPR of 5.76%. The list proposed by Ge et al. [23, 25] is thus not ideal as the exclusion of these chronic conditions would underestimate the prevalence of multimorbidity in the primary care setting in Singapore.

Quah et al.'s list [12] of 13 conditions, encompassing 17 CDMP conditions, comprised the largest proportion of chronic conditions (92.3%) with SPRs of at least 1.0%. This is contributed by two reasons. First, Quah et al. [12] had included the chronic condition 'physical disability', which had a SPR of 1.05%. This chronic condition was absent in all the other five lists. Second, Quah et al. [12] had classified chronic diseases affecting similar organ systems into a single chronic condition category (Appendix 1-5). For example, a large number of ICD-10 conditions such as Parkinson's disease, dementia, epilepsy and stroke were all classified under a single chronic condition 'neurological conditions'. The use of Quah et al.'s list [12] would fail to capture individuals with more than one disease of the neurological system and fail to give a discerning estimate of the prevalence of multimorbidity.

While the list of 19 chronic conditions proposed by Fortin et al. [21] captured fewer chronic conditions under CDMP and had a lower proportion of chronic conditions (78.9%) with a SPR of at least 1.0% compared to that by Quah et al.,[12] its inclusion of key chronic conditions of relevance to primary care makes it most suitable as an operational definition for use in the primary care setting in Singapore. Fortin et al. [21] included the chronic condition 'chronic urinary problem', which was matched to the ICD-10 code 'hyperplasia of prostate'. The SPR tabulated was 1.07% and benign prostatic hyperplasia is also a chronic condition recognised under CDMP, underscoring its importance in the population. In addition, Fortin et al. [21] considered the chronic condition 'osteoporosis', a chronic disease recognised under CDMP. While the SPR tabulated for 'osteoporosis' stands at 0.57%, this is likely to increase in the future in view of Singapore's rapidly ageing population.[34]

4.2 Proposing a New Operational Definition of Multimorbidity

When applied to the primary care population in Singapore, the list proposed by Fortin et al. [21] had comparatively outshone the others based on the aforementioned criteria. Although we noted that Fortin et al.'s [21] list of chronic conditions [21] was not as comprehensive as Quah et al.'s,[12] Quah et al.'s list [12] included many categories which were organ systems and encompassed all the available ICD-10 codes within that system which is less discerning as that of Fortin et al.'s.[21]

We propose the use of a modified list of chronic conditions adapted from Fortin et al.'s list [21] for use in the primary care setting in Singapore (Appendix 6). We suggest the inclusion of pre-diabetes (ICD-10 codes: E09 and E099) under the chronic condition 'diabetes' and the addition of the chronic condition 'physical disability' to Fortin et al.'s existing list of chronic conditions [21] to increase its comprehensiveness.

The relevance of pre-diabetes in Singapore is indisputable with the Singapore government placing greater emphasis on diabetes management and aggressive intervention for individuals with pre-diabetes.[35] Pre-diabetes is also recognised under CDMP and has a SPR of 3.65% (3.61, 3.69). The inclusion of pre-diabetes under the chronic condition 'diabetes' increased the SPR from 11.86% to 14.28% (14.20, 14.35).

The inclusion of 'physical disability', with a SPR of 1.05%, which is matched to the ICD-10 code 'hearing loss' is important in the context of Singapore's ageing population as the prevalence of hearing impairment has been reported to increase with age and has serious ramifications physically, mentally, socially and financially for affected individuals.[36]

We acknowledge that Fortin et al. [21] did not recognise several conditions under CDMP (Appendix 4), namely, 'schizophrenia', 'bipolar disorder', 'Parkinson's disease', 'epilepsy' and 'psoriasis', however, the SPRs of each of these chronic conditions is low and is unlikely to result in much variation in the prevalence estimates of multimorbidity. In addition, in Singapore, these chronic conditions are still largely managed by their relevant specialties and do not form a large proportion of primary care attendances.

With the proposed new operational definition, we calculated the SPR of multimorbidity to be 18.1%. The pattern of multimorbidity across the different sex, ethnicity and age groups remain consistent with that of Fortin et al.'s.[21]

4.3 Strengths of our study

Our study leveraged on the utilisation of a large database upon which the six different operational definitions were consistently applied. The determination of the clinical relevance of a chronic condition was also achieved through an iterative process, with discussions held among clinicians and research team members. In addition, a systematic method was employed in the comparison of all six operational definitions.

4.4 Limitations of our study

Our study has several limitations. Firstly, the utilisation of electronic medical records would rely heavily on accurate and consistent data reporting. This limitation was mitigated by the use of standardised ICD-10 codes. Secondly, the number of ICD-10 codes depicting chronic conditions is fixed and pre-determined in our electronic health records system. Nine chronic conditions/categories of conditions, thus, could not be reliably coded with the NHGP ICD-10 codes. This included the chronic condition proposed by Fortin et al. [21] 'chronic musculoskeletal condition causing pain or limitation', a common complaint in the primary care setting.[12] The available list of ICD-10 codes may change as we move on to the new generation electronic medical records system in the future. Thirdly, our study reports low SPRs of psychiatric conditions. This is incongruent with reports from the Singapore Mental Health Study, which reported higher lifetime prevalence rates.[37] One possible reason is that patients with psychiatric illnesses tend to consult spiritual healers or religious leaders for help instead of their primary care physicians.[37, 38] Lastly, we did not estimate the impact of each chronic condition on affected individuals. This was a criterion that was utilised by Fortin et al. in his selection of chronic conditions for inclusion in their operational definition.[21]

5. CONCLUSION

We compared six operational definitions and found that Fortin et al.'s list of chronic conditions [21] (Appendix 1-1) was most applicable to the primary care setting in Singapore, fulfilling the aforementioned criteria. We propose the addition of pre-diabetes and the chronic condition 'physical disability' into Fortin et al.'s list of conditions [21] to augment its comprehensiveness in our setting (Appendix 6).

Multimorbidity is a growing healthcare conundrum afflicting multiple countries globally. We utilised criteria previously proposed by Fortin et al. [21] in the formulation of a standardised operational definition contextualized to primary care in Singapore. The creation of such standardised operational definitions for use in individual countries would allow for meaningful comparisons to be made across research studies done within the country. We propose that similar studies should be conducted in different geographical countries/regions in the world to describe the most suitable list of chronic conditions for multimorbidity in their own context.

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Contributors

ESL and PSSL initiated and conceptualised the study. ESL and YX developed the analysis approach. YAJL conducted the data analysis for this study. YAJL wrote the first draft of the manuscript. YX, PSSL and ESL provided inputs and assisted in the interpretation of the findings. ESL critically reviewed the final version of the article. All authors have read and approved the final manuscript.

Competing Interests

None declared.

Data Sharing

Data are not available for online access. Readers who wish to gain access to the data can write to the senior author ESL at eng_sing_lee@nhgp.com.sg with their requests. Access can be granted subject to approval of the National Healthcare Group Domain Specific Review Board (DSRB) and in line with the National Healthcare Group Research Data Policy. This is a requirement mandated for this research study by our DSRB and funders.

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APPENDICES

Appendix 1-1: List of Chronic Conditions (Fortin et al. 2017)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.79 (24.86, 25.07)
2	Hypertension (high blood pressure)	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis &/or rheumatoid arthritis	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		11	M15.9 (Osteoarthritis (OA) - Generalised)			
		12	M19.99 (Arthritis, unspecified, site unspecified)			
5	Obesity	13	E66.9 (Obesity, unspecified)	48,893	6.21	5.29 (5.24, 5.34)
6	Cardiovascular disease (angina, MI, AF, poor circulation of lower limbs)	14	I25.9 (Chronic ischaemic heart disease, unspecified)	43,559	5.53	3.74 (3.71, 3.78)
		15	I48 (Atrial fibrillation and flutter)			
		16	I70.20 (Atherosclerosis of arteries of extremities, unspecified)			
		17	I73.9 (Peripheral vascular disease, unspecified)			
7	Asthma, COPD, or chronic bronchitis	18	J44.9 (Chronic Obstructive Pulmonary Disease, Unspecified)	32,611	4.14	3.68 (3.63, 3.72)
		19	J45.9 (Asthma, unspecified)			
8	Chronic hepatitis	20	K76.9 (Liver disease, unspecified)	25,918	3.29	3.02 (2.98, 3.06)
		21	Z22.51 (Carrier of viral hepatitis B)			
9	Stomach problem (reflux, heartburn, or gastric ulcer)	22	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	22,233	2.82	2.52 (2.48, 2.56)
		23	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
10	Thyroid disorder	24	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		25	E05.9 (Thyrotoxicosis, unspecified)			
11	Stroke and TIA	26	G45.9 (Transient cerebral ischaemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		27	I64 (Stroke, not specified as haemorrhage or infarction)			
12	Heart failure (including valve problems or replacement)	28	I50.0 (Congestive heart failure)	20,538	2.61	1.97 (1.94, 2.00)
		29	I51.9 (Heart disease, unspecified)			
13	Kidney disease or failure	30	N03.9 (Unspecified nephritic syndrome, unspecified)	22,221	2.82	1.82 (1.79, 1.84)
		31	N18.9 (Chronic kidney disease, unspecified)			
14	Depression or anxiety	32	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	14,910	1.89	1.81 (1.78, 1.84)
		33	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		34	F41.1 (Anxiety disorder, unspecified)			
15	Chronic urinary problem	35	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)

16	Any cancer in the last 5 years	36	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
17	Osteoporosis	37	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
18	Dementia or Alzheimer's disease	38	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
19	Colon problem (irritable bowel)	39	K58.9 (Irritable bowel syndrome without diarrhoea)	1,517	0.19	0.20 (0.19, 0.21)
20	Chronic musculoskeletal condition causing pain or limitation	No matching ICD-10 code		-	-	-

Appendix 1-2: List of Chronic Conditions (Ge et al. 2018 and 2019)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Dyslipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Osteoarthritis/Gout/RA	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	38,755	4.92	3.89 (3.85, 3.93)
		11	M10.99 (Gout, unspecified, site unspecified)			
		12	M15.9 (Osteoarthritis (OA) - generalized)			
5	Asthma	13	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Heart attack/IHD	14	I25.9 (Chronic ischemic heart disease, unspecified)	36,401	4.62	3.15 (3.12, 3.19)
7	Stroke/TIA	15	G45.9 (Transient cerebral ischemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		16	I64 (Stroke, not specified as haemorrhage or infarction)			
8	CKD	17	N18.9 (Chronic kidney disease, unspecified)	21,638	2.75	1.76 (1.73, 1.78)
9	Depression	18	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		19	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
10	Anxiety disorder	20	F41.1 (Anxiety disorder, unspecified)	6,085	0.77	0.75 (0.73, 0.77)
11	Cancer	21	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
12	Osteoporosis	22	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
13	Chronic bronchitis/emphysema/COPD	23	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)
14	Schizophrenia	24	F20.9 (Schizophrenia, unspecified)	2,889	0.37	0.33 (0.31, 0.34)
15	Heart failure	25	I50.0 (Congestive heart failure)	3,469	0.44	0.29 (0.28, 0.30)
16	Dementia/Alzheimer's	26	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
17	Parkinson's disease	27	G20 (Parkinson's disease)	1,900	0.24	0.15 (0.14, 0.15)

Appendix 1-3: List of Chronic Conditions (Low et al. 2019)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Lipid disorders	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Angina Coronary heart disease Myocardial infarction	10	I25.9 (Chronic ischaemic heart disease, unspecified)	51,264	6.51	4.65 (4.61, 4.70)
		11	I51.9 (Heart disease, unspecified)			
5	Asthma	12	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Moderate liver disease Severe liver disease	13	K76.9 (Liver disease, unspecified)	18,658	2.37	2.13 (2.09, 2.16)
7	Renal disease	14	N28.9 (Disorder of kidney and ureter, unspecified)	21,112	2.68	1.94 (1.91, 1.97)
8	CKD on dialysis or pre-dialysis Chronic kidney disease	15	N18.9 (Chronic kidney disease, unspecified)	21,638	2.75	1.76 (1.73, 1.78)
9	Osteoarthritis	16	M15.9 (Osteoarthritis (OA) - generalized)	18,378	2.33	1.72 (1.70, 1.75)
10	Haemorrhagic stroke Ischemic stroke Stroke	17	I64 (Stroke, not specified as haemorrhage or infarction)	19,808	2.52	1.72 (1.69, 1.74)
11	Hypothyroidism	18	E03.9 (Hypothyroidism)	14,133	1.79	1.51 (1.48, 1.53)
12	Major depression	19	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		20	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
13	Benign prostatic hyperplasia (BPH)	21	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
14	Hyperthyroidism	22	E05.9 (Thyrotoxicosis)	7,873	1.00	1.00 (0.97, 1.02)
15	Anxiety General anxiety disease	23	F41.1 (Anxiety disorder, unspecified)	6,085	0.77	0.75 (0.73, 0.77)
16	Cancer (w/o metastasis) Metastatic carcinoma	24	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
17	Arrhythmia Atrial fibrillation	25	I48 (Atrial fibrillation and flutter)	7,241	0.92	0.58 (0.57, 0.60)
18	Osteoporosis	26	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
19	Chronic obstructive pulmonary disease	27	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)
20	Epilepsy	28	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)	2,734	0.35	0.33 (0.32, 0.35)
21	Schizophrenia	29	F20.9 (Schizophrenia, unspecified)	2,889	0.37	0.33 (0.31, 0.34)
22	Heart failure	30	I50.0 (Congestive heart failure)	3,469	0.44	0.29 (0.28, 0.30)

23	Dementia	31	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
24	Peripheral vascular disease	32	I73.9 (Peripheral vascular disease, unspecified)	2,598	0.33	0.21 (0.21, 0.22)
25	Rheumatoid arthritis	33	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	2,010	0.26	0.19 (0.18, 0.20)
26	Parkinson's disease	34	G20 (Parkinson's disease)	1,900	0.24	0.15 (0.14, 0.15)
27	Nephritis	35	N03.9 (Unspecified nephritic syndrome, unspecified)	770	0.10	0.08 (0.07, 0.08)
28	Major lower extremity amputation	36	Z89.5 (Acquired absence of leg at or below knee)	236	0.03	0.02 (0.02, 0.02)
		37	Z89.6 (Acquired absence of leg above knee)			
29	Minor lower extremity amputation	38	Z89.4 (Acquired absence of foot and ankle)	122	0.02	0.01 (0.01, 0.01)
30	Bipolar disorder	39	F31.9 (Bipolar affective disorder, unspecified)	51	0.01	0.01 (0.01, 0.01)
31	Psoriasis	40	L40.8 (Other psoriasis)	0	0.00	0.00
32	Hip fracture	No matching ICD-10 code				-
33	Nephrosis	No matching ICD-10 code				-
34	Respiratory failure	No matching ICD-10 code				-
35	Secondary hypertension	No matching ICD-10 code				-
36	Spine fracture	No matching ICD-10 code				-
37	Coronary artery bypass graft	No matching ICD-10 code				-
38	Percutaneous coronary intervention	No matching ICD-10 code				-
39	Kidney transplant	No matching ICD-10 code				-

Appendix 1-4: List of Chronic Conditions (Picco et al. 2016)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	High blood pressure	1	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
2	Diabetes	2	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		3	E11.9 (Type 2 diabetes mellitus without complication)			
		4	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		5	E14.3 (Diabetes mellitus with retinopathy)			
		6	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		7	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		8	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
3	Arthritis or Rheumatism	9	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		10	M15.9 (Osteoarthritis (OA) - generalized)			
		11	M19.99 (Arthritis, unspecified, site unspecified)			
4	Heart trouble (including heart attack, angina, heart failure and valve disease)	12	I51.9 (Heart disease, unspecified)	56,797	7.21	5.11 (5.06, 5.15)
		13	I50.0 (Congestive heart failure)			
		14	I25.9 (Chronic ischaemic heart disease, unspecified)			
		15	I48 (Atrial fibrillation and flutter)			
5	Breathlessness or Asthma	16	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Stroke	17	I64 (Stroke, not specified as haemorrhage or infarction)	19,808	2.52	1.72 (1.69, 1.74)
7	Depression	18	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		19	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
8	Cancer	20	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
9	TIA	21	G45.9 (Transient cerebral ischaemic attack, unspecified)	5,158	0.66	0.46 (0.45, 0.48)
10	COPD	22	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)

Appendix 1-5: List of Chronic Conditions (Quah et al. 2016)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		11	M19.99 (Arthritis, unspecified, site unspecified)			
		12	M15.9 (Osteoarthritis (OA) - generalized)			
5	Respiratory diseases	13	J30.4 (Allergic rhinitis, unspecified)	68,048	8.64	8.73 (8.65, 8.80)
		14	J44.9 (Chronic obstructive pulmonary disease, unspecified)			
		15	J45.9 (Asthma, unspecified)			
6	Gastrointestinal diseases	16	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	49,847	6.33	5.76 (5.70, 5.81)
		17	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
		18	K58.9 (Irritable bowel syndrome without diarrhoea)			
		19	K76.9 (Liver disease, unspecified)			
		20	K82.9 (Disease of gallbladder, unspecified)			
		21	Z22.51 (Carrier of viral hepatitis B)			
7	Heart diseases	22	I25.9 (Chronic ischaemic heart disease, unspecified)	56,797	7.21	5.11 (5.06, 5.15)
		23	I48 (Atrial fibrillation and flutter)			
		24	I50.0 (Congestive heart failure)			
		25	I51.9 (Heart disease, unspecified)			
8	Chronic kidney disease	26	N03.9 (Unspecified nephritic syndrome, unspecified)	38,350	4.87	3.36 (3.32, 3.39)
		27	N18.9 (Chronic kidney disease, unspecified)			
		28	N28.9 (Disorder of kidney and ureter, unspecified)			
9	Neurological conditions	29	F03 (Unspecified dementia)	31,093	3.95	2.79 (2.75, 2.82)
		30	G20 (Parkinson's disease)			
		31	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)			
		32	G45.9 (Transient cerebral ischemic attack, unspecified)			
		33	G60.9 (Hereditary and idiopathic neuropathy, unspecified)			
		34	I64 (Stroke, not specified as haemorrhage or infarction)			
10	Thyroid diseases	35	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		36	E05.9 (Thyrotoxicosis, unspecified)			
11	Psychiatric conditions	37	F20.9 (Schizophrenia, unspecified)	18,182	2.31	2.18 (2.15, 2.22)
		38	F29 (Unspecified nonorganic psychosis)			
		39	F31.9 (Bipolar affective disorder, unspecified)			

		40	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)			
		41	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		42	F41.1 (Anxiety disorder, unspecified)			
12	Physical disability	43	H91.9 (Hearing loss, unspecified)	10,514	1.34	1.05 (1.03, 1.08)
		44	Q79.9 (Congenital malformation of musculoskeletal system, unspecified)			
13	Cancer	45	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)

Appendix 1-6: List of Chronic Conditions (Subramaniam et al. 2014)

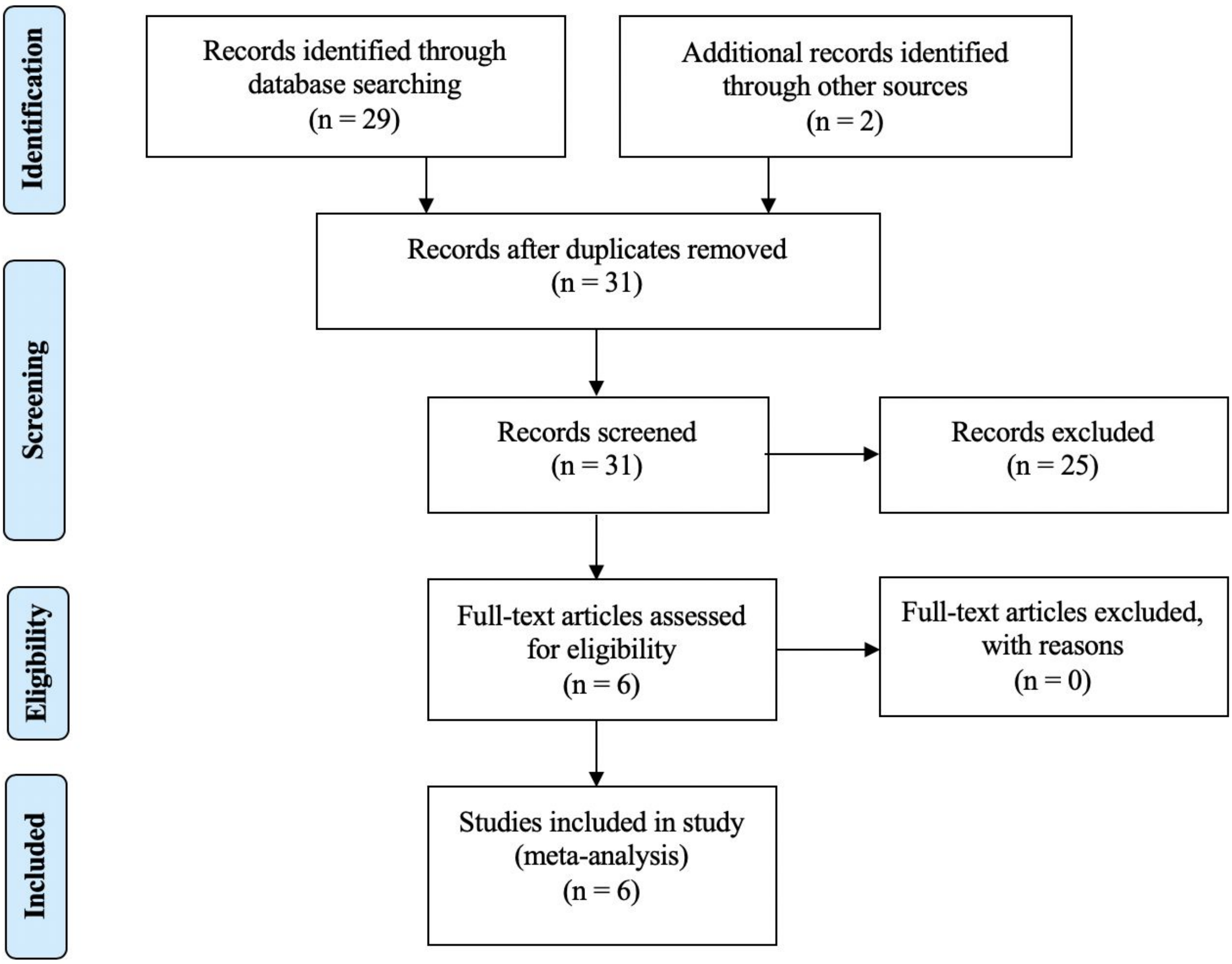
S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hypertension and high blood pressure	1	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
2	Diabetes	2	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		3	E11.9 (Type 2 diabetes mellitus without complication)			
		4	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		5	E14.3 (Diabetes mellitus with retinopathy)			
		6	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		7	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		8	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
3	Chronic pain (arthritis or rheumatism, back problems including disk or spine, migraine headaches)	9	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	107,090	13.60	11.24 (11.17, 11.31)
		10	M15.9 (Osteoarthritis (OA) - generalized)			
		11	M19.99 (Arthritis, unspecified, site unspecified)			
		12	G43.9 (Migraine, unspecified)			
		13	G50.0 (Trigeminal neuralgia)			
4	Respiratory disorders (asthma, chronic lung disease such as chronic bronchitis or emphysema)	14	J30.4 (Allergic rhinitis, unspecified)	68,048	8.64	8.73 (8.65, 8.80)
		15	J44.9 (Chronic obstructive pulmonary disease, unspecified)			
		16	J45.9 (Asthma, unspecified)			
5	Cardiovascular disorders (stroke or major paralysis, heart attack, coronary heart disease, angina, congestive heart failure or other heart disease)	17	I25.9 (Chronic ischaemic heart disease, unspecified)	73,922	9.39	6.65 (6.60, 6.70)
		18	I48 (Atrial fibrillation and flutter)			
		19	I50.0 (Congestive heart failure)			
		20	I51.9 (Heart disease, unspecified)			
		21	G45.9 (Transient cerebral ischaemic attack, unspecified)			
		22	I64 (Stroke, not specified as haemorrhage or infarction)			
6	Cancer	23	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
7	Neurological disorders (epilepsy, convulsion, Parkinson's disease)	24	G20 (Parkinson's disease)	4,609	0.59	0.48 (0.46, 0.49)
		25	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)			
8	Ulcer and chronic inflamed bowel (stomach ulcer, chronic inflamed bowel, enteritis or colitis)	26	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)	3,131	0.40	0.34 (0.33, 0.35)
		27	K58.9 (Irritable bowel syndrome without diarrhoea)			

Appendix 2a: Literature Search Strategy

Database: Ovid MEDLINE(R): 1946 to March Week 1 2020

S/N	Search Terms	Results
1	exp comorbidity/ or multiple chronic conditions/ or multimorbidity	106,975
2	(multimorbid* or multi-morbid* or comorbid* or co-morbid*).ab,ti,kw.	144,228
3	((multiple or coexist* or co-exist* or concurrent* or simultaneous*) adj3 (disease* or illness* or diagnos* or condition* or morbid* or disorder*)).ab,ti,kw.	61,543
4	1 or 2 or 3	263,334
5	(prevalence or association).ab,ti,kw.	1,385,219
6	(Singapore).ab,ti,kw.	12,889
7	4 and 5 and 6	166
8	Set following limits: English language, Human studies, Full Text, 2010 to Current	29

Appendix 2b: PRISMA Flow Diagram



Appendix 3: A Summary of the Differences between Reported Studies on Multimorbidity

	Fortin et al. (Published in 2017)	Ge et al. (Published in 2018)	Ge et al. (Published in 2019)	Low et al. (Published in 2019)	Picco et al. (Published in 2016)	Quah et al. (Published in 2016)	Subramaniam et al. (Published in 2014)
Number of conditions	20	17	17	48	10	14	8
Definition of chronic disease	Conditions that usually last 12 months or more	Diseases that are irreversible and persistent throughout adulthood	Diseases characterised by a long duration and are of a generally slow progression that are irreversible and persistent throughout adulthood	No	No	No	No
Source of list of chronic conditions	Developed from a scoping review of 44 publications on multimorbidity	Not mentioned	Not mentioned	Selected from 3 indexes - the Singapore Chronic Disease Management Programme[1], the Charlson Comorbidity Index[2] and the Elixhauser Comorbidity Index[3]	Not mentioned	Conditions from Singapore Mental Health Study[4] 2010	Modified Composite International Diagnostic Interview (CIDI)[5]
Sources of data	Self-reported* (conditions that have been confirmed by a doctor or for which they are on medications)	At least one of the sources was self-reported or from the NHG Chronic Disease Management System (CDMS) database[6]	Self-reported	Singapore Eastern Regional Health System[7]	Self-reported	Self-reported	Self-reported
Cut-point	Not mentioned	2 conditions	2 conditions	2 conditions	2 conditions	2 conditions	2 conditions
Reference population	Practice-based population	General population	General population	Practice-based population (tertiary hospitals, community hospitals, primary care polyclinics)	General population	Practice-based population (one primary care polyclinic)	General population

[1] The Chronic Disease Management Programme (CDMP) is an initiative introduced by the Ministry of Health (MOH), Singapore, in 2016 and involves the development of evidence-based structured Disease Management Programmes required in the management of their chronic diseases.
[2] The Charlson Comorbidity Index is a weighted index of 19 chronic conditions that was originally developed to predict the risk of short-term mortality from comorbid disease among patients being treated for primary breast cancer at a single hospital in 1987.
[3] The Elixhauser Comorbidity Index is an index of 30 chronic conditions that was developed to predict hospital charges, length of stay and in-patient mortality among patients 18 years and older from 438 hospitals in California in the year 1992.
[4] The Singapore Mental Health Study (SMHS) is a nationwide epidemiological study undertaken in 2009-2010 that provides insight into some of the common mental health illnesses in the adult Singapore resident population.
[5] The Composite International Diagnostic Interview (CIDI) was designed to allow investigators to reliably assess mental disorders according to the most widely accepted nomenclatures in different populations and cultures by combining questions from the Diagnostic Interview Schedule with questions designed to elicit Present State Examination items in 1988.
[6] The NHG Chronic Disease Management System (CDMS) database is a chronic disease registry within NHG that was commissioned for use in 2014 linking administrative and key clinical data of patients with chronic diseases across the National Healthcare Group cluster in Singapore.
[7] The Singapore Eastern Regional Health System was developed from the integration of the Singapore Health Services (SingHealth) and Eastern Health Alliance (EHA) in 2017.

Age-group	Not mentioned	≥ 21 years old	≥ 21 years old	0 to 85+ years old	≥ 60 years old	≥ 65 years old	≥ 18 years old
Measured levels of multimorbidity[8]	No	No	Yes Disease count	Yes Disease count	No	Yes 1. Disease count 2. Drug count	No
Patient-reported outcomes	No	Yes Physical function	Yes 1. Health-related quality of life 2. Self-rated health	No	No	Yes 1. Health-related quality of life 2. Functional disability 3. Chronic musculoskeletal pain	Yes Health-related quality of life

[8] Levels of multimorbidity refers to the combined effects of the multiple conditions that an individual has. This may be based on disease count, that is, the number of chronic conditions the patient has; or other variables such as drug count, which is the number of chronic medications an individual is prescribed.

Appendix 4: List of chronic conditions under Chronic Disease Management Programme (CDMP)

S/N	Conditions
1	Diabetes mellitus and pre-diabetes
2	Hypertension
3	Lipid disorders
4	Asthma
5	Chronic obstructive pulmonary disease (COPD)
6	Chronic kidney disease (nephritis/nephrosis)
7	Schizophrenia
8	Major depression
9	Bipolar disorder
10	Anxiety
11	Stroke
12	Dementia
13	Osteoarthritis
14	Parkinson's disease
15	Benign prostatic hyperplasia (BPH)
16	Epilepsy
17	Osteoporosis
18	Psoriasis
19	Rheumatoid arthritis (RA)
20	Ischemic heart disease (IHD)

Appendix 5a: List of ICD-10 diagnosis codes matched to the chronic conditions studied by each author

S/N	ICD-10 Codes	Fortin et al. 2017	Ge et al. 2018 and 2019	Low et al. 2019	Picco et al. 2016	Quah et al. 2016	Subramaniam et al. 2014
1	E78.5	✓	✓	✓		✓	
2	I10	✓	✓	✓	✓	✓	✓
3	E11.9	✓	✓	✓	✓	✓	✓
4	M19.99	✓			✓	✓	✓
5	J30.4					✓	✓
6	E66.9	✓					
7	J45.9	✓	✓	✓	✓	✓	✓
8	I25.9	✓	✓	✓	✓	✓	✓
9	K21.9	✓				✓	
10	K76.9	✓		✓		✓	
11	M10.99		✓				
12	N28.9			✓		✓	
13	N18.9	✓	✓	✓		✓	
14	I51.9	✓		✓	✓	✓	✓
15	M15.9	✓	✓	✓	✓	✓	✓
16	I64	✓	✓	✓	✓	✓	✓
17	E03.9	✓		✓		✓	
18	N40	✓		✓			
19	F32.90	✓	✓	✓	✓	✓	
20	Z22.51	✓				✓	
21	E05.9	✓		✓		✓	
22	H91.9					✓	
23	G43.9						✓
24	F41.1	✓	✓	✓		✓	
25	C80	✓	✓	✓	✓	✓	✓
26	I48	✓		✓	✓	✓	✓
27	M81.99	✓	✓	✓			
28	E14.31	✓	✓	✓	✓	✓	✓
29	G45.9	✓	✓	✓	✓	✓	✓
30	J44.9	✓	✓	✓	✓	✓	✓
31	K82.9					✓	
32	G40.90			✓		✓	✓
33	F20.9		✓	✓		✓	
34	E10.9	✓	✓	✓	✓	✓	✓
35	I50.0	✓	✓	✓	✓	✓	✓
36	F03	✓	✓	✓		✓	
37	F32.20	✓	✓	✓	✓	✓	
38	I73.9	✓		✓			
39	K58.9	✓				✓	✓
40	M06.99	✓	✓	✓	✓	✓	✓
41	F29					✓	
42	E14.73	✓	✓	✓	✓	✓	✓
43	G20		✓	✓		✓	✓
44	K27.9	✓				✓	✓
45	G60.9					✓	
46	Q79.9					✓	
47	I70.20	✓					
48	E14.2	✓	✓	✓	✓	✓	✓
49	N03.9	✓		✓		✓	
50	G50.0						✓
51	Z89.5			✓			
52	E14.3	✓	✓	✓	✓	✓	✓
53	F31.9			✓		✓	
54	Z89.6			✓			
55	Z89.4			✓			
56	E14.64	✓	✓	✓	✓	✓	✓
57	L40.8			✓			

Appendix 5b: Descriptors of ICD-10 diagnosis codes

S/N	ICD-10 Codes	Descriptors
1	E78.5	Hyperlipidaemia, unspecified
2	I10	Essential (primary) hypertension
3	E11.9	Type 2 diabetes mellitus without complication
4	M19.99	Arthritis, unspecified, site unspecified
5	J30.4	Allergic rhinitis, unspecified
6	E66.9	Obesity, unspecified
7	J45.9	Asthma, unspecified
8	I25.9	Chronic ischaemic heart disease, unspecified
9	K21.9	Gastro-oesophageal reflux disease without oesophagitis
10	K76.9	Liver disease, unspecified
11	M10.99	Gout, unspecified, site unspecified
12	N28.9	Disorder of kidney and ureter, unspecified
13	N18.9	Chronic kidney disease, unspecified
14	I51.9	Heart disease, unspecified
15	M15.9	Osteoarthritis (OA) - Generalised
16	I64	Stroke, not specified as haemorrhage or infarction
17	E03.9	Hypothyroidism, unspecified
18	N40	Hyperplasia of prostate
19	F32.90	Depressive episode, unspecified, not specified as arising in the postnatal period
20	Z22.51	Carrier of viral hepatitis B
21	E05.9	Thyrotoxicosis, unspecified
22	H91.9	Hearing loss, unspecified
23	G43.9	Migraine, unspecified
24	F41.1	Anxiety disorder, unspecified
25	C80	Malignant neoplasm without specification of site
26	I48	Atrial fibrillation and flutter
27	M81.99	Other osteoporosis, site unspecified
28	E14.31	Unspecified diabetes mellitus with background retinopathy
29	G45.9	Transient cerebral ischaemic attack, unspecified
30	J44.9	Chronic Obstructive Pulmonary Disease, Unspecified
31	K82.9	Disease of gallbladder, unspecified
32	G40.90	Epilepsy, unspecified, without mention of intractable epilepsy
33	F20.9	Schizophrenia, unspecified
34	E10.9	Type 1 diabetes mellitus without complication
35	I50.0	Congestive heart failure
36	F03	Unspecified dementia
37	F32.20	Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period
38	I73.9	Peripheral vascular disease, unspecified
39	K58.9	Irritable bowel syndrome without diarrhoea
40	M06.99	Rheumatoid arthritis, unspecified, site unspecified
41	F29	Unspecified nonorganic psychosis
42	E14.73	Unspecified diabetes mellitus with foot ulcer due to multiple causes
43	G20	Parkinson's disease
44	K27.9	Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation
45	G60.9	Hereditary and idiopathic neuropathy, unspecified
46	Q79.9	Congenital malformation of musculoskeletal system, unspecified
47	I70.20	Atherosclerosis of arteries of extremities, unspecified
48	E14.2	Diabetes mellitus with incipient diabetic nephropathy
49	N03.9	Unspecified nephritic syndrome, unspecified
50	G50.0	Trigeminal neuralgia
51	Z89.5	Acquired absence of leg at or below knee
52	E14.3	Diabetes mellitus with retinopathy
53	F31.9	Bipolar affective disorder, unspecified
54	Z89.6	Acquired absence of leg above knee
55	Z89.4	Acquired absence of foot and ankle
56	E14.64	Unspecified diabetes mellitus with hypoglycaemia
57	L40.8	Other psoriasis

Appendix 6: List of Chronic Conditions in Proposed Operational Definition of Multimorbidity

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.79 (24.86, 25.07)
2	Hypertension (high blood pressure)	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes (including pre-diabetes)	3	E09 (Impaired glucose regulation)	150,294	19.09	14.28 (14.20, 14.35)
		4	E099 (Impaired glucose regulation without complication)			
		5	E10.9 (Type 1 diabetes mellitus without complication)			
		6	E11.9 (Type 2 diabetes mellitus without complication)			
		7	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		8	E14.3 (Diabetes mellitus with retinopathy)			
		9	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		10	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		11	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis &/or rheumatoid arthritis	12	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		13	M15.9 (Osteoarthritis (OA) - Generalised)			
		14	M19.99 (Arthritis, unspecified, site unspecified)			
5	Obesity	15	E66.9 (Obesity, unspecified)	48,893	6.21	5.29 (5.24, 5.34)
6	Cardiovascular disease (angina, MI, AF, poor circulation of lower limbs)	16	I25.9 (Chronic ischaemic heart disease, unspecified)	43,559	5.53	3.74 (3.71, 3.78)
		17	I48 (Atrial fibrillation and flutter)			
		18	I70.20 (Atherosclerosis of arteries of extremities, unspecified)			
		19	I73.9 (Peripheral vascular disease, unspecified)			
7	Asthma, COPD, or chronic bronchitis	20	J44.9 (Chronic Obstructive Pulmonary Disease, Unspecified)	32,611	4.14	3.68 (3.63, 3.72)
		21	J45.9 (Asthma, unspecified)			
8	Chronic hepatitis	22	K76.9 (Liver disease, unspecified)	25,918	3.29	3.02 (2.98, 3.06)
		23	Z22.51 (Carrier of viral hepatitis B)			
9	Stomach problem (reflux, heartburn, or gastric ulcer)	24	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	22,233	2.82	2.52 (2.48, 2.56)
		25	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
10	Thyroid disorder	26	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		27	E05.9 (Thyrotoxicosis, unspecified)			
11	Stroke and TIA	28	G45.9 (Transient cerebral ischaemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		29	I64 (Stroke, not specified as haemorrhage or infarction)			
12	Heart failure (including valve problems or replacement)	30	I50.0 (Congestive heart failure)	20,538	2.61	1.97 (1.94, 2.00)
		31	I51.9 (Heart disease, unspecified)			
13	Kidney disease or failure	32	N03.9 (Unspecified nephritic syndrome, unspecified)	22,221	2.82	1.82 (1.79, 1.84)
		33	N18.9 (Chronic kidney disease, unspecified)			
14	Depression or anxiety	34	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	14,910	1.89	1.81 (1.78, 1.84)
		35	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		36	F41.1 (Anxiety disorder, unspecified)			
15	Chronic urinary problem	37	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
16	Physical disability	38	H91.9 (Hearing loss, unspecified)	10,514	1.34	1.05

		39	Q79.9 (Congenital malformation of musculoskeletal system, unspecified)			(1.03, 1.08)
17	Any cancer in the last 5 years	40	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
18	Osteoporosis	41	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
19	Dementia or Alzheimer's disease	42	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
20	Colon problem (irritable bowel)	43	K58.9 (Irritable bowel syndrome without diarrhoea)	1,517	0.19	0.20 (0.19, 0.21)

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TITLE PAGE

Comparing the prevalence of multimorbidity using different operational definitions in primary care in Singapore based on a cross-sectional study using retrospective, large administrative data

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ABSTRACT

Objectives: Multimorbidity is a norm in primary care. A consensus on its operational definition remains lacking especially in the list of chronic conditions considered. This study aimed to compare six different operational definitions of multimorbidity previously reported in the literature for the context of primary care in Singapore.

Methods: This is a retrospective study using anonymised primary care data. We defined multimorbidity as having three or more chronic conditions in an individual. Tabulation of the prevalence of single conditions and multimorbidity with each operational definition was done in our study population of 787,446 patients. Standardised prevalence rates (SPR) were obtained by adjusting for age, sex and ethnicity. We compared the operational definitions based on (1) number of chronic diseases, (2) presence of chronic diseases of high burden and (3) relevance in primary care in Singapore. IBM SPSS version 23 and Microsoft Office Excel 2019 were used for all statistical calculations and analyses.

Results: The SPRs of multimorbidity in primary care in Singapore varied from 5.7% to 17.2%. The lists by Fortin et al., Ge et al., Low et al. and Quah et al. included at least 12 chronic conditions, the recommended minimal number of conditions. Quah et al. considered the highest proportion of chronic diseases (92.3%) of high burden in primary care in Singapore, with SPRs of at least 1.0%. Picco et al. and Subramaniam et al. considered the fewest number of conditions of high relevance in primary care in Singapore.

Conclusions: Fortin et al.'s list of conditions is most suitable for describing multimorbidity in the primary care setting of Singapore. Pre-diabetes and 'physical disability' should be added to Fortin et al.'s list to augment its comprehensiveness. We propose a similar study methodology to be performed in other countries to identify the most suitable operational definition in their own context.

ARTICLE SUMMARY

Strengths and limitations of this study

- Strengths of this study include the utilisation of a large database and the determination of the clinical relevance of a chronic condition through an iterative process.
- Another strength of this study is the employment of a systematic method in the comparison of all six operational definitions.
- The limitations of this study include the utilisation of a single administrative database and the use of a pre-determined number of International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) codes.
- This study also did not consider the impact of each chronic condition on affected individuals.

MAIN TEXT

1. BACKGROUND

Multimorbidity, the co-occurrence of multiple chronic health conditions in a single individual,[1] is a growing norm in primary care.[2-5] 'Multimorbidity' has often been confused with 'comorbidity'.[6, 7] Comorbidity describes the simultaneous presence of multiple health conditions when there is an index condition. In contrast, multimorbidity describes the co-occurrence of two or more chronic medical conditions without specifying the index condition. Health outcomes are evaluated based on the interaction and burden of all co-existing chronic conditions.[8] Advocates of the concept of multimorbidity tend to focus on primary care, where the identification of an index disease is often neither obvious nor useful.[9]

The implications of multimorbidity are significant and widespread. From the patient's perspective, multimorbidity is associated with future functional decline,[10, 11] reduced health-related quality of life,[10, 12] inpatient admission and mortality.[13] From an economic standpoint, multimorbidity is associated with increased healthcare utilisation[14] and healthcare costs.[10] Single disease clinical practice guidelines (CPGs) that have traditionally been used for the management of chronic diseases are inappropriate in the management of patients with multimorbidity.[5, 15-17]

To this date, there is no consensus on an operational definition of multimorbidity.[18-20] This definition comprises two components: the list of chronic conditions considered and the cut-off for the number of chronic conditions used to determine the presence of multimorbidity.[21] The absence of a standardised operational definition has resulted in reported prevalence estimates of multimorbidity in Singapore to range widely from 16.3% to 89.4% [12, 14, 22-24] and has made comparability between published studies impossible.[21] Wide variations in prevalence estimates also prevent accurate estimations of disease burden and hinder resource distribution for effective disease management.[25]

In 2017, an operational definition comprising 20 chronic conditions/categories of conditions was proposed by Fortin et al. as a common list of conditions for studying multimorbidity in primary care (Appendix 1-1).[21] These conditions were selected from a scoping review of relevant studies.

We identified six studies, two by Ge et al. [23, 26] (Appendix 1-2) and one each by Low et al. [24] (Appendix 1-3), Picco et al. [14] (Appendix 1-4), Quah et al. [12] (Appendix 1-5) and Subramaniam et al. [22] (Appendix 1-6), which were published between 2014 to 2019 in Singapore. These studies were identified on Medline Ovid between 2010 till 14 March 2020 and through direct correspondences with

the authors (Appendix 2). Heterogeneity was noted in both the methodologies and lists of chronic conditions utilised in each study.

The objective of this study was to compare the different operational definitions of multimorbidity previously reported in the literature for the context of primary care in Singapore.

2. METHODS

2.1 Setting and Study Population

The study population was selected between 1 July 2015 and 30 June 2016. During this period, the public primary healthcare sector was organised into two main clusters in Singapore - National Healthcare Group Polyclinics (NHGP) and SingHealth Polyclinics (SHP). The two clusters shared 18 polyclinics island-wide and provided government-funded subsidised primary care including chronic disease management. According to annual statistics published by the Ministry of Health (MOH), Singapore, 3,916,771 individuals (approximately 70% of the 2016 Singapore population [27]) consulted a doctor in the polyclinics in 2016. Out of which, 58.9% attended the NHGP.[28] The participants in this study were multi-ethnic patients aged 0 to 99 years old who consulted a doctor in NHGP at least once during the study period. A total of 787,446 patients from nine polyclinics were included in this study.

2.2 Data Source

Data from the study population were collected from the NHGP Business Informatics (BI) system. The BI system is an administrative database that captures each patient's consultation episodes and clinical parameters from structured data fields within the electronic medical records (EMRs) e.g. blood pressure readings, International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) diagnoses codes and laboratory data. We excluded all patient encounters that did not include an ICD-10 diagnosis code by a physician. Only de-identified data were collected in accordance with the personal data protection act.[29]

2.3 Patient and Public Involvement

No patients were involved in this study.

2.4 Definition of Chronic Condition and Multimorbidity

We adopted the definition of O'Halloran et al. for chronicity of a disease which is defined as one lasting at least six months, with a documented pattern of recurrence or deterioration, and having an impact on an individual's quality of life.[30]

While we acknowledge that most studies have defined multimorbidity using a cut-off of 'two or more' chronic conditions,[31] in keeping with the World Health Organization's definition of multimorbidity,[32] we adopted a cut-off of 'three or more' chronic conditions to better identify patients with higher needs.[18]

2.5 Determination of Prevalence Rates of Single Conditions and Multimorbidity

The prevalence of a disease is defined as the proportion of the population at risk (PAR) that are cases at a point in time.[33] The PAR is defined as the group of people, healthy or sick, who would be counted as cases if they had the disease of interest. This forms the denominator for the calculation of prevalence.[33] For this study, the PAR was denoted by individuals aged 0 to 99 years who consulted a doctor in NHGP at least once during the study period.

For the crude prevalence rate of single conditions, the numerator used was the number of unique patients with the single condition who had consulted a doctor in NHGP at least once during the study period. For the crude prevalence rate of multimorbidity, the numerator used was the number of unique patients with multimorbidity who had consulted a doctor in NHGP at least once during the study period.

Standardised prevalence rates (SPRs) were obtained by adjusting the study population to a standard population by using the direct standardisation method as detailed by Bains.[34] The 2016 Singapore population was used as the standard population.[27] Poisson approximation was utilised to calculate the confidence intervals of 95%.

2.6 Criteria for Comparison of Operational Definitions

Amongst the six studies conducted in Singapore, only five unique operational definitions were identified. The two studies by Ge et al. [23, 26] utilised the same operational definition. We compared six lists of chronic conditions from six different operational definitions of multimorbidity (Appendix 3) on the same study population. This included the list proposed by Fortin et al. that had been developed as a research tool to document the presence of multimorbidity in primary care [21] (Appendix 1-1) and the five lists used in the study of multimorbidity in Singapore (Appendix 1-2 to 1-6). A list of NHGP ICD-10 diagnosis codes was assembled by four senior family physicians based on the aforementioned definition of chronicity.[30]

Fortin et al. proposed that an ideal operational definition of multimorbidity should comprise at least 12 chronic diseases, each with a high impact or burden in the population of interest.[18] Based on this, the comparison of the six operational definitions were focused on (1) the number of chronic diseases considered, (2) presence of chronic diseases of high burden and (3) relevance in the primary care setting in Singapore. We considered a chronic condition to be of significant burden in the primary care if it has a SPR of at least 1.0%. We tabulated the proportion of chronic diseases with a SPR of at least 1.0% in each list. The numerator used was the number of chronic conditions with a SPR of at least 1.0% and the denominator was the total number of chronic conditions in the list. The clinical relevance of a condition was based on consensus reached after iterative discussions between the clinicians, research team members and reference to statistics from the MOH and local primary care initiatives such as the Chronic Disease Management Programme (CDMP).[35]

Statistics reported by the MOH have consistently ranked hyperlipidaemia, hypertensive disease and diabetes mellitus as the first, second and fourth top condition responsible for polyclinic attendances since 2012.[36] Hyperlipidaemia constituted 13.8% of polyclinic attendances in 2018, closely followed by hypertensive disease at 13.2%, acute upper respiratory tract infection at 9.4% and diabetes mellitus at 9.0%.

The Chronic Disease Management Programme (CDMP) [35] was introduced in 2006 to facilitate the provision of care to patients with chronic conditions through the development of evidence-based structured Disease Management Programmes and to reduce out-of-pocket payments for outpatient treatments by allowing patients to draw on their Medisave. The structured Disease Management Programmes facilitate the management of these conditions in the primary care setting. In 2018, the list of chronic conditions included in CDMP was increased to include 20 chronic conditions (Appendix 4).

2.7 Statistical Analysis

The sample size was determined by the number of patients aged 0 to 99 years who visited the NHGP for at least one doctor consultation during the study period. We used listwise deletion method for complete case analysis. For descriptive statistics, we described the mean for continuous variables and their respective standard deviation. For categorical variables, we described proportions and their respective confidence intervals where appropriate.

SPRs were obtained by adjusting for age, sex and ethnicity. Age was stratified into four categories - '0 - 24', '25 - 44', '45 - 64' and '65 - 99'. Sex was classified into male and female, and ethnicity was categorized into Chinese, Malay, Indian and Others. To compare the SPRs of multimorbidity among

age and sex, we tabulated age-stratified, sex-and-ethnicity SPR and sex-stratified, age-and-ethnicity SPR of multimorbidity between the different lists. No overlap of the 95% confidence intervals for the SPRs among the different lists was considered as statistically significant. IBM SPSS version 23 and Microsoft Office Excel 2019 were used for all statistical calculations and analyses.

3. RESULTS

The mean age of the 787,446 patients analysed in this study was 43.9 years. Females made up 50.9% of the patients and the Chinese formed the majority ethnic group at 68.2%. Of the four ethnicities, the Chinese had the highest mean age of 47.1 years. 53.4% of the patients studied were from the '45 - 64' and '65 - 99' age groups (Table 1).

Table 1: Demographics of the study population

	Frequency	Percent	Mean Age (SD)
Total	787,446	100.0	43.9 (0.03)
Sex			
Female	400,965	50.9	45.3 (0.04)
Male	386,481	49.1	42.2 (0.04)
Ethnicity			
Chinese	537,234	68.2	47.1 (0.03)
Malay	127,501	16.2	35.1 (0.06)
Indian	78,452	10.0	39.7 (0.08)
Others	44,259	5.6	37.1 (0.09)
Age Groups			
0 - 24	201,839	25.6	
25 - 44	165,212	21.0	
45 - 64	252,206	32.0	
65 - 99	168,189	21.4	

The list recommended by Fortin et al. [21] gave the highest SPR of multimorbidity in the study population (17.2%). Across the six lists, the SPRs of multimorbidity increased with increasing age. The male sex reported higher SPRs of multimorbidity and the differences between the sexes are statistically significant (Table 2).

Table 2: Comparison of the standardised prevalence rates of multimorbidity among the six lists of chronic conditions

	Fortin et al. 2017	Ge et al. 2018 and 2019	Low et al. 2019	Picco et al. 2016	Quah et al. 2016	Subramaniam et al. 2014
Total	17.2 (17.2, 17.3)	13.0 (12.9, 13.0)	14.6 (14.5, 14.7)	5.7 (5.7, 5.8)	16.8 (16.7, 16.8)	5.9 (5.8, 5.9)
Sex						
Female	16.5 (16.4, 16.6)	11.7 (11.7, 11.8)	13.5 (13.4, 13.6)	5.4 (5.4, 5.5)	16.0 (15.9, 16.1)	5.6 (5.5, 5.6)
Male	18.0 (17.9, 18.1)	14.3 (14.1, 14.4)	15.8 (15.7, 15.9)	6.0 (5.9, 6.1)	17.6 (17.4, 17.7)	6.2 (6.1, 6.2)
Age Groups						
0 - 24	0.08 (0.07, 0.10)	0.02 (0.02, 0.03)	0.04 (0.03, 0.05)	0.01 (0.01, 0.01)	0.10 (0.08, 0.11)	0.02 (0.01, 0.02)
25 - 44	4.0 (3.9, 4.1)	2.2 (2.1, 2.3)	2.8 (2.7, 2.9)	0.5 (0.5, 0.5)	3.6 (3.5, 3.7)	0.6 (0.6, 0.7)
45 - 64	28.5 (28.3, 28.7)	20.2 (20.0, 20.4)	23.2 (23.0, 23.4)	7.8 (7.7, 7.9)	27.7 (27.5, 27.9)	8.1 (8.0, 8.2)
65 - 99	60.9 (60.5, 61.2)	50.9 (50.5, 51.2)	55.4 (55.0, 55.7)	26.1 (25.9, 26.4)	60.1 (59.7, 60.4)	26.3 (26.1, 26.6)

3.1 Criterion 1: Number of Chronic Conditions

A list of 57 NHGP ICD-10 diagnosis codes (Appendix 5) was matched to the chronic conditions in these six lists. Amongst the 20 conditions/categories of conditions proposed by Fortin et al.,[21] only 19 of them could be matched to the corresponding NHGP ICD-10 codes. We excluded the condition 'chronic musculoskeletal condition causing pain or limitation' from the list as the corresponding ICD-10 code was not reliably coded at our primary care setting. Similarly, as only 13 out of 14 conditions/categories of conditions proposed by Quah et al. [12] could be matched to corresponding NHGP ICD-10 codes, the condition 'back problems' was excluded from the list.

Low et al. [24] proposed a total of 48 chronic conditions, eight of which - 'hip fracture', 'nephrosis', 'respiratory failure', 'secondary hypertension', 'spine fracture', 'coronary artery bypass graft', 'percutaneous coronary intervention' and 'kidney transplant' had no corresponding NHGP ICD-10 codes and were excluded from the list. Of the remaining 40 conditions, 16 conditions had overlapping ICD-10 codes. This included chronic conditions such as 'anxiety' and 'general anxiety disorder' which were matched to the same ICD-10 code: F41.1 'anxiety disorder, unspecified' (Appendix 1-3). These conditions were reclassified to obtain a final list of 31 chronic conditions to avoid double-counting of chronic diseases and overestimation of multimorbidity.

Picco et al. [14] and Subramaniam et al. [22] only considered ten and eight conditions respectively, falling short of the recommended minimal number of 12 chronic conditions.[18]

3.2 Criterion 2: Prevalence amongst the Primary Care Population

We considered a chronic condition to be of high burden in the primary care setting if it has a SPR of at least 1.0%. The list proposed by Quah et al. [12] had the highest proportion (92.3%) of chronic conditions with a SPR of at least 1.0% (Appendix 1-5). This was followed by the list by Fortin et al. [21] (78.9%) (Appendix 1-1), Picco et al. [14] (70.0%) (Appendix 1-4), Subramaniam et al. [22] (62.5%) (Appendix 1-6), Ge et al. [23, 26] (52.9%) (Appendix 1-2) and lastly Low et al. [24] (41.9%) (Appendix 1-3).

3.3 Criterion 3: Relevance to Primary Care Services

Hypertensive disease and diabetes mellitus were represented in all six operational definitions, with SPRs of 20.93% and 11.86% respectively. Hyperlipidaemia, with the highest SPR of 24.97%, however, was absent in the lists of chronic conditions by Picco et al. [14] and Subramaniam et al..[22]

We compared the chronic conditions under CDMP with the lists of chronic conditions in the six operational definitions. The list of chronic conditions by Low et al. [24] included all 20 conditions under CDMP. This was followed by Ge et al. [23, 26] and Quah et al.,[12] with each considering 17 out of the 20 chronic conditions. Fortin et al. [21] considered 15 out of the 20 chronic conditions and Subramaniam et al. [22] and Picco et al. [14] only considered 10 and 8 of the 20 conditions respectively.

4. DISCUSSION

4.1 Summary of Results

The SPRs of multimorbidity in the primary care setting in Singapore varied widely depending on the operational definition utilised. The list of chronic conditions proposed by Fortin et al. [21] gave the highest SPR of multimorbidity (17.2%). The lists by Fortin et al.,[21] Ge et al.,[23, 26] Low et al. [24] and Quah et al. [12] included at least 12 chronic conditions with the list by Quah et al. [12] comprising the highest proportion of chronic diseases (92.3%) with a SPR of at least 1.0% that matched with a NHGP ICD-10 code. The lists by Picco et al. [14] and Subramaniam et al. [22] did not include hyperlipidaemia, a chronic condition of high relevance in the primary care setting in Singapore and both lists considered the fewest number of conditions under CDMP.

4.2 Comparison of Operational Definitions

Comparing the six operational definitions, it is clear that the lists proposed by Picco et al. [14] and Subramaniam et al. [22] had fallen short on several fronts. Both lists considered less than 12 chronic conditions and have comparatively lower proportions of chronic conditions with SPR of at least 1.0%. In addition, both considered the fewest number of chronic conditions under CDMP and failed to include hyperlipidaemia, which constitutes a large proportion of polyclinic attendances. These shortfalls likely contributed to the low SPRs of multimorbidity tabulated and underestimate multimorbidity in the primary care setting in Singapore.

While Low et al.'s list [24] comprised 31 chronic conditions, including all 20 conditions under CDMP, it reported the lowest proportion of chronic diseases (41.9%) with a SPR of at least 1.0%. This is likely due to two reasons. The first was that Low et al.'s list [24] is the longest amongst the six lists. While Low et al. [24] included 13 conditions with a SPR of at least 1.0%, (numerator), second only to Fortin et al. [21], its inclusion of a total of 31 chronic conditions (denominator), resulted in a less discriminating list. Second, the manner in which the list of chronic conditions was classified could be a contributory factor. Low et al. [24] had kept 'major depression', 'anxiety', 'schizophrenia' and 'bipolar disorder' as four separate chronic conditions (Appendix 1-3), whilst, other studies such as that by Quah et al. [12] had grouped them under a single chronic condition category - 'psychiatric conditions' (Appendix 1-5). When considered individually, only the chronic condition 'major depression' had a SPR of at least 1.0%. While Low et al.'s list [24] is the most comprehensive, the presence of chronic conditions with overlapping ICD-10 codes prior to re-classification and the large number of chronic conditions with no corresponding NHGP ICD-10 codes make it less ideal as an operational definition for use in the primary care setting in Singapore.

The list by Ge et al.,[23, 26] which comprised 17 chronic conditions and considered a large number of chronic conditions under CDMP also had a low proportion of chronic diseases (52.9%) with a SPR of at least 1.0%. Ge et al. [23, 26] had likewise considered the psychiatric diseases individually (Appendix 1-2) as opposed to grouping them as a single chronic condition. In addition, Ge et al.'s list [23, 26] did not include conditions commonly seen in primary care such as thyroid conditions and diseases of the gastrointestinal tract, which were present in Fortin et al. [21] (Appendix 1-1) and Quah et al.'s lists [12] (Appendix 1-5). 'Thyroid disorder (Fortin et al. [21]) / Thyroid diseases (Quah et al. [12])' have a SPR of 2.36%. 'Chronic hepatitis (Fortin et al. [21])' and 'Stomach problem (reflux, heart burn, or gastric ulcer) (Fortin et al. [21])' have SPRs of 3.02% and 2.52% respectively, while 'Gastrointestinal diseases (Quah et al. [12])' has a SPR of 5.76%. The list proposed by Ge et al. [23, 26] is thus not ideal as the exclusion of these chronic conditions would underestimate multimorbidity in the Singapore primary care setting.

Quah et al.'s list [12] of 13 conditions, encompassing 17 CDMP conditions, comprised the largest proportion of chronic conditions (92.3%) with SPRs of at least 1.0%. This is contributed by two reasons. First, Quah et al. [12] had included the chronic condition 'physical disability', which had a SPR of 1.05% and was absent in all the other five lists. Second, Quah et al. [12] had classified chronic diseases affecting similar organ systems into a single chronic condition category (Appendix 1-5). For example, several ICD-10 conditions such as Parkinson's disease, dementia, epilepsy and stroke were all classified under a single category 'neurological conditions'. While we acknowledge that individuals who suffer diseases of the same organ system often follow up with the same specialist and treatment options are often complementary and hence the rationality behind this manner of classification, [37] it is of our view that this is not always applicable to all chronic conditions of the same organ system. For example, in Parkinson's disease, the focus of care is on maintaining functional capabilities, whilst in epilepsy, care is focused on the avoidance of seizure triggers and seizure first aid. This manner of classification, as adopted by Quah at el., [12] risks overlooking individuals who require greater care and would fail to give a discerning estimate of multimorbidity. It is of our view that clinical judgement should be exercised in defining 'disease entities' taking into account the care needs of each chronic condition.

While the list of 19 chronic conditions proposed by Fortin et al. [21] captured fewer chronic conditions under CDMP and had a lower proportion of chronic conditions (78.9%) with a SPR of at least 1.0% compared to that by Quah et al.,[12] its inclusion of key chronic conditions of relevance to primary care makes it most suitable as an operational definition for use in the primary care setting in Singapore. Fortin et al. [21] included the chronic condition 'chronic urinary problem', which was matched to the ICD-10 code 'hyperplasia of prostate'. The SPR tabulated was 1.07% and benign prostatic hyperplasia is also recognised under CDMP, underscoring its importance in the population. In addition, Fortin et al. [21] considered the chronic condition 'osteoporosis', a chronic disease recognised under CDMP. While the SPR tabulated for 'osteoporosis' stands at 0.57%, this is likely to increase in the future in view of Singapore's rapidly ageing population.[38]

4.2 Proposing a New Operational Definition of Multimorbidity

When applied to the primary care population in Singapore, the list proposed by Fortin et al. [21] had comparatively outshone the others based on the aforementioned criteria.

We propose the use of a modified list of chronic conditions adapted from Fortin et al.'s list [21] for use in the primary care setting in Singapore (Appendix 6). We suggest the inclusion of pre-diabetes (ICD-10 codes: E09 and E099) under the chronic condition 'diabetes' and the addition of the chronic condition 'physical disability' to Fortin et al.'s existing list of chronic conditions [21] to increase its comprehensiveness.

The relevance of pre-diabetes in Singapore is indisputable with the Singapore government placing greater emphasis on diabetes management and aggressive intervention for individuals with pre-diabetes.[39] Pre-diabetes is also recognised under CDMP and has a SPR of 3.65% (3.61, 3.69). The inclusion of pre-diabetes under the chronic condition 'diabetes' increased the SPR from 11.86% to 14.28% (14.20, 14.35).

The inclusion of 'physical disability', with a SPR of 1.05%, which includes the ICD-10 code 'hearing loss' is important in the context of Singapore's ageing population as the prevalence of hearing impairment has been reported to increase with age and has serious ramifications physically, mentally, socially and financially for affected individuals.[40]

We acknowledge that Fortin et al. [21] did not recognise several conditions under CDMP (Appendix 4), namely, 'schizophrenia', 'bipolar disorder', 'Parkinson's disease', 'epilepsy' and 'psoriasis', however, the SPRs of each of these chronic conditions is low and is unlikely to result in much variation in the prevalence estimates of multimorbidity. In addition, in Singapore, these chronic conditions are still largely managed by their relevant specialties and do not form a large proportion of primary care attendances.

With the proposed new operational definition, we calculated the SPR of multimorbidity to be 18.1%. The pattern of multimorbidity across the different sex, ethnicity and age groups remain consistent with that of Fortin et al.'s.[21]

4.3 Strengths of our study

Our study leveraged on the utilisation of a large database upon which the six different operational definitions were consistently applied. The determination of the clinical relevance of a chronic condition was also achieved through an iterative process, with discussions held among clinicians and research team members. In addition, a systematic method was employed in the comparison of all six operational definitions.

4.4 Limitations of our study

Our study has several limitations. Firstly, we only utilised data from a single administrative source - the EMRs. The use of a single data source risks underestimating the prevalence estimates of chronic conditions.[41] Furthermore, the utilization of EMRs relies heavily on accurate and consistent data reporting. This limitation was, however, mitigated by the use of standardised ICD-10 codes. Secondly, the number of ICD-10 codes depicting chronic conditions is fixed and pre-determined in our EMRs. Ten chronic conditions/categories of conditions could not be reliably coded with the NHGP ICD-10 codes. This included the chronic condition proposed by Fortin et al. [21] 'chronic musculoskeletal condition causing pain or limitation', a common complaint in the primary care setting.[12] The fixed number of NHGP ICD-10 codes available also limited the inclusivity of chronic conditions such as 'physical disability' which only included the ICD-10 codes 'hearing loss' and 'congenital malformation of the musculoskeletal system'. The available list of ICD-10 codes may change as we move on to the new generation EMRs system in the future. Thirdly, our study reports low SPRs of psychiatric conditions. This is incongruent with reports from the Singapore Mental Health Study, which reported higher lifetime prevalence rates.[42] One possible reason is that patients with psychiatric illnesses tend to consult spiritual healers for help instead of their primary care physicians.[42, 43] Lastly, we did not estimate the impact of each chronic condition on affected individuals. This was a criterion that was utilised by Fortin et al. in his selection of chronic conditions for inclusion in their operational definition.[21]

5. CONCLUSION

We compared six operational definitions and found that Fortin et al.'s list of chronic conditions [21] (Appendix 1-1) was most applicable to the primary care setting in Singapore, fulfilling the aforementioned criteria. We propose the addition of pre-diabetes and the chronic condition 'physical disability' into Fortin et al.'s list of conditions [21] to augment its comprehensiveness in our setting (Appendix 6).

Multimorbidity is a growing global healthcare conundrum. We utilised criteria previously proposed by Fortin et al. [21] in the formulation of a standardised operational definition contextualized to primary care in Singapore. The creation of such standardised operational definitions for use in individual countries would allow for meaningful comparisons to be made across research studies done within the country. Common patterns of multimorbidity within the country can then be reliably identified, facilitating the creation of specific multimorbidity CPGs that are relevant to the primary care setting of the country. The CPGs can focus on coordinating care across various specialties for the different conditions, medications management to avoid polypharmacy and management of shared disease risk factors which are not covered with the current single disease CPGs.[44] We propose that similar studies be conducted in different geographical countries/regions in the world to describe the most suitable list of chronic conditions for multimorbidity in their own context.

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Contributors

ESL and PSSL initiated and conceptualised the study. ESL and YX developed the analysis approach. YAJL conducted the data analysis for this study. YAJL wrote the first draft of the manuscript. YX, PSSL and ESL provided inputs and assisted in the interpretation of the findings. ESL critically reviewed the final version of the article. All authors have read and approved the final manuscript.

Competing Interests

None declared.

Data Sharing

Data are not available for online access. Readers who wish to gain access to the data can write to the senior author ESL at eng_sing_lee@nhgp.com.sg with their requests. Access can be granted subject to approval of the National Healthcare Group Domain Specific Review Board (DSRB) and in line with the National Healthcare Group Research Data Policy. This is a requirement mandated for this research study by our DSRB and funders.

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APPENDICES

Appendix 1-1: List of Chronic Conditions (Fortin et al. 2017)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.79 (24.86, 25.07)
2	Hypertension (high blood pressure)	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis &/or rheumatoid arthritis	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		11	M15.9 (Osteoarthritis (OA) - Generalised)			
		12	M19.99 (Arthritis, unspecified, site unspecified)			
5	Obesity	13	E66.9 (Obesity, unspecified)	48,893	6.21	5.29 (5.24, 5.34)
6	Cardiovascular disease (angina, MI, AF, poor circulation of lower limbs)	14	I25.9 (Chronic ischaemic heart disease, unspecified)	43,559	5.53	3.74 (3.71, 3.78)
		15	I48 (Atrial fibrillation and flutter)			
		16	I70.20 (Atherosclerosis of arteries of extremities, unspecified)			
		17	I73.9 (Peripheral vascular disease, unspecified)			
7	Asthma, COPD, or chronic bronchitis	18	J44.9 (Chronic Obstructive Pulmonary Disease, Unspecified)	32,611	4.14	3.68 (3.63, 3.72)
		19	J45.9 (Asthma, unspecified)			
8	Chronic hepatitis	20	K76.9 (Liver disease, unspecified)	25,918	3.29	3.02 (2.98, 3.06)
		21	Z22.51 (Carrier of viral hepatitis B)			
9	Stomach problem (reflux, heartburn, or gastric ulcer)	22	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	22,233	2.82	2.52 (2.48, 2.56)
		23	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
10	Thyroid disorder	24	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		25	E05.9 (Thyrotoxicosis, unspecified)			
11	Stroke and TIA	26	G45.9 (Transient cerebral ischaemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		27	I64 (Stroke, not specified as haemorrhage or infarction)			
12	Heart failure (including valve problems or replacement)	28	I50.0 (Congestive heart failure)	20,538	2.61	1.97 (1.94, 2.00)
		29	I51.9 (Heart disease, unspecified)			
13	Kidney disease or failure	30	N03.9 (Unspecified nephritic syndrome, unspecified)	22,221	2.82	1.82 (1.79, 1.84)
		31	N18.9 (Chronic kidney disease, unspecified)			
14	Depression or anxiety	32	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	14,910	1.89	1.81 (1.78, 1.84)
		33	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		34	F41.1 (Anxiety disorder, unspecified)			
15	Chronic urinary problem	35	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
16	Any cancer in the last 5 years	36	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)

17	Osteoporosis	37	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
18	Dementia or Alzheimer's disease	38	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
19	Colon problem (irritable bowel)	39	K58.9 (Irritable bowel syndrome without diarrhoea)	1,517	0.19	0.20 (0.19, 0.21)
20	Chronic musculoskeletal condition causing pain or limitation	No matching ICD-10 code		-	-	-

Appendix 1-2: List of Chronic Conditions (Ge et al. 2018 and 2019)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Dyslipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Osteoarthritis/Gout/RA	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	38,755	4.92	3.89 (3.85, 3.93)
		11	M10.99 (Gout, unspecified, site unspecified)			
		12	M15.9 (Osteoarthritis (OA) - generalized)			
5	Asthma	13	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Heart attack/IHD	14	I25.9 (Chronic ischemic heart disease, unspecified)	36,401	4.62	3.15 (3.12, 3.19)
7	Stroke/TIA	15	G45.9 (Transient cerebral ischemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		16	I64 (Stroke, not specified as haemorrhage or infarction)			
8	CKD	17	N18.9 (Chronic kidney disease, unspecified)	21,638	2.75	1.76 (1.73, 1.78)
9	Depression	18	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		19	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
10	Anxiety disorder	20	F41.1 (Anxiety disorder, unspecified)	6,085	0.77	0.75 (0.73, 0.77)
11	Cancer	21	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
12	Osteoporosis	22	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
13	Chronic bronchitis/emphysema/COPD	23	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)
14	Schizophrenia	24	F20.9 (Schizophrenia, unspecified)	2,889	0.37	0.33 (0.31, 0.34)
15	Heart failure	25	I50.0 (Congestive heart failure)	3,469	0.44	0.29 (0.28, 0.30)
16	Dementia/Alzheimer's	26	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
17	Parkinson's disease	27	G20 (Parkinson's disease)	1,900	0.24	0.15 (0.14, 0.15)

Appendix 1-3: List of Chronic Conditions (Low et al. 2019)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Lipid disorders	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Angina Coronary heart disease Myocardial infarction	10	I25.9 (Chronic ischaemic heart disease, unspecified)	51,264	6.51	4.65 (4.61, 4.70)
		11	I51.9 (Heart disease, unspecified)			
5	Asthma	12	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Moderate liver disease Severe liver disease	13	K76.9 (Liver disease, unspecified)	18,658	2.37	2.13 (2.09, 2.16)
7	Renal disease	14	N28.9 (Disorder of kidney and ureter, unspecified)	21,112	2.68	1.94 (1.91, 1.97)
8	CKD on dialysis or pre-dialysis Chronic kidney disease	15	N18.9 (Chronic kidney disease, unspecified)	21,638	2.75	1.76 (1.73, 1.78)
9	Osteoarthritis	16	M15.9 (Osteoarthritis (OA) - generalized)	18,378	2.33	1.72 (1.70, 1.75)
10	Haemorrhagic stroke Ischemic stroke Stroke	17	I64 (Stroke, not specified as haemorrhage or infarction)	19,808	2.52	1.72 (1.69, 1.74)
11	Hypothyroidism	18	E03.9 (Hypothyroidism)	14,133	1.79	1.51 (1.48, 1.53)
12	Major depression	19	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		20	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
13	Benign prostatic hyperplasia (BPH)	21	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
14	Hyperthyroidism	22	E05.9 (Thyrotoxicosis)	7,873	1.00	1.00* (0.97, 1.02)
15	Anxiety General anxiety disease	23	F41.1 (Anxiety disorder, unspecified)	6,085	0.77	0.75 (0.73, 0.77)
16	Cancer (w/o metastasis) Metastatic carcinoma	24	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
17	Arrhythmia Atrial fibrillation	25	I48 (Atrial fibrillation and flutter)	7,241	0.92	0.58 (0.57, 0.60)
18	Osteoporosis	26	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
19	Chronic obstructive pulmonary disease	27	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)
20	Epilepsy	28	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)	2,734	0.35	0.33 (0.32, 0.35)
21	Schizophrenia	29	F20.9 (Schizophrenia, unspecified)	2,889	0.37	0.33 (0.31, 0.34)
22	Heart failure	30	I50.0 (Congestive heart failure)	3,469	0.44	0.29 (0.28, 0.30)
23	Dementia	31	F03 (Unspecified dementia)	3,571	0.45	0.27

						(0.26, 0.28)
24	Peripheral vascular disease	32	I73.9 (Peripheral vascular disease, unspecified)	2,598	0.33	0.21 (0.21, 0.22)
25	Rheumatoid arthritis	33	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	2,010	0.26	0.19 (0.18, 0.20)
26	Parkinson's disease	34	G20 (Parkinson's disease)	1,900	0.24	0.15 (0.14, 0.15)
27	Nephritis	35	N03.9 (Unspecified nephritic syndrome, unspecified)	770	0.10	0.08 (0.07, 0.08)
28	Major lower extremity amputation	36	Z89.5 (Acquired absence of leg at or below knee)	236	0.03	0.02 (0.02, 0.02)
		37	Z89.6 (Acquired absence of leg above knee)			
29	Minor lower extremity amputation	38	Z89.4 (Acquired absence of foot and ankle)	122	0.02	0.01 (0.01, 0.01)
30	Bipolar disorder	39	F31.9 (Bipolar affective disorder, unspecified)	51	0.01	0.01 (0.01, 0.01)
31	Psoriasis	40	L40.8 (Other psoriasis)	0	0.00	0.00
32	Hip fracture	No matching ICD-10 code				-
33	Nephrosis	No matching ICD-10 code				-
34	Respiratory failure	No matching ICD-10 code				-
35	Secondary hypertension	No matching ICD-10 code				-
36	Spine fracture	No matching ICD-10 code				-
37	Coronary artery bypass graft	No matching ICD-10 code				-
38	Percutaneous coronary intervention	No matching ICD-10 code				-
39	Kidney transplant	No matching ICD-10 code				-

*The standardized prevalence rate of 'hyperthyroidism' is 0.9980% (0.9737, 1.0222).

Appendix 1-4: List of Chronic Conditions (Picco et al. 2016)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	High blood pressure	1	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
2	Diabetes	2	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		3	E11.9 (Type 2 diabetes mellitus without complication)			
		4	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		5	E14.3 (Diabetes mellitus with retinopathy)			
		6	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		7	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		8	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
3	Arthritis or Rheumatism	9	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		10	M15.9 (Osteoarthritis (OA) - generalized)			
		11	M19.99 (Arthritis, unspecified, site unspecified)			
4	Heart trouble (including heart attack, angina, heart failure and valve disease)	12	I51.9 (Heart disease, unspecified)	56,797	7.21	5.11 (5.06, 5.15)
		13	I50.0 (Congestive heart failure)			
		14	I25.9 (Chronic ischaemic heart disease, unspecified)			
		15	I48 (Atrial fibrillation and flutter)			
5	Breathlessness or Asthma	16	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Stroke	17	I64 (Stroke, not specified as haemorrhage or infarction)	19,808	2.52	1.72 (1.69, 1.74)
7	Depression	18	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		19	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
8	Cancer	20	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
9	TIA	21	G45.9 (Transient cerebral ischaemic attack, unspecified)	5,158	0.66	0.46 (0.45, 0.48)
10	COPD	22	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)

Appendix 1-5: List of Chronic Conditions (Quah et al. 2016)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		11	M19.99 (Arthritis, unspecified, site unspecified)			
		12	M15.9 (Osteoarthritis (OA) - generalized)			
5	Respiratory diseases	13	J30.4 (Allergic rhinitis, unspecified)	68,048	8.64	8.73 (8.65, 8.80)
		14	J44.9 (Chronic obstructive pulmonary disease, unspecified)			
		15	J45.9 (Asthma, unspecified)			
6	Gastrointestinal diseases	16	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	49,847	6.33	5.76 (5.70, 5.81)
		17	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
		18	K58.9 (Irritable bowel syndrome without diarrhoea)			
		19	K76.9 (Liver disease, unspecified)			
		20	K82.9 (Disease of gallbladder, unspecified)			
		21	Z22.51 (Carrier of viral hepatitis B)			
7	Heart diseases	22	I25.9 (Chronic ischaemic heart disease, unspecified)	56,797	7.21	5.11 (5.06, 5.15)
		23	I48 (Atrial fibrillation and flutter)			
		24	I50.0 (Congestive heart failure)			
		25	I51.9 (Heart disease, unspecified)			
8	Chronic kidney disease	26	N03.9 (Unspecified nephritic syndrome, unspecified)	38,350	4.87	3.36 (3.32, 3.39)
		27	N18.9 (Chronic kidney disease, unspecified)			
		28	N28.9 (Disorder of kidney and ureter, unspecified)			
9	Neurological conditions	29	F03 (Unspecified dementia)	31,093	3.95	2.79 (2.75, 2.82)
		30	G20 (Parkinson's disease)			
		31	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)			
		32	G45.9 (Transient cerebral ischemic attack, unspecified)			
		33	G60.9 (Hereditary and idiopathic neuropathy, unspecified)			
		34	I64 (Stroke, not specified as haemorrhage or infarction)			
10	Thyroid diseases	35	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		36	E05.9 (Thyrotoxicosis, unspecified)			
11	Psychiatric conditions	37	F20.9 (Schizophrenia, unspecified)	18,182	2.31	2.18 (2.15, 2.22)
		38	F29 (Unspecified nonorganic psychosis)			
		39	F31.9 (Bipolar affective disorder, unspecified)			
		40	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)			

		41	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		42	F41.1 (Anxiety disorder, unspecified)			
12	Physical disability	43	H91.9 (Hearing loss, unspecified)	10,514	1.34	1.05 (1.03, 1.08)
		44	Q79.9 (Congenital malformation of musculoskeletal system, unspecified)			
13	Cancer	45	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
14	Back problems	No matching ICD-10 code		-	-	

Appendix 1-6: List of Chronic Conditions (Subramaniam et al. 2014)

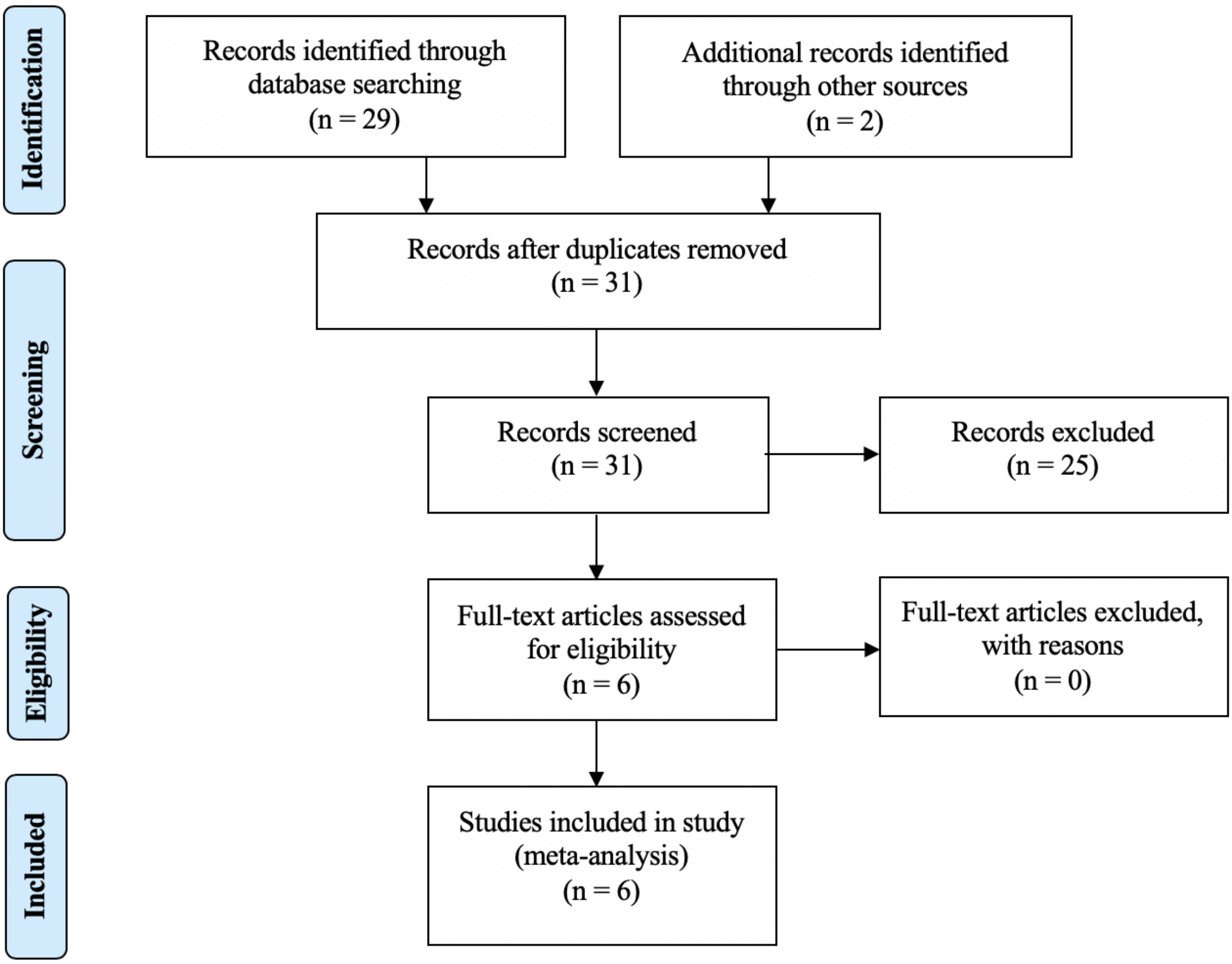
S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hypertension and high blood pressure	1	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
2	Diabetes	2	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		3	E11.9 (Type 2 diabetes mellitus without complication)			
		4	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		5	E14.3 (Diabetes mellitus with retinopathy)			
		6	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		7	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		8	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
3	Chronic pain (arthritis or rheumatism, back problems including disk or spine, migraine headaches)	9	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	107,090	13.60	11.24 (11.17, 11.31)
		10	M15.9 (Osteoarthritis (OA) - generalized)			
		11	M19.99 (Arthritis, unspecified, site unspecified)			
		12	G43.9 (Migraine, unspecified)			
		13	G50.0 (Trigeminal neuralgia)			
4	Respiratory disorders (asthma, chronic lung disease such as chronic bronchitis or emphysema)	14	J30.4 (Allergic rhinitis, unspecified)	68,048	8.64	8.73 (8.65, 8.80)
		15	J44.9 (Chronic obstructive pulmonary disease, unspecified)			
		16	J45.9 (Asthma, unspecified)			
5	Cardiovascular disorders (stroke or major paralysis, heart attack, coronary heart disease, angina, congestive heart failure or other heart disease)	17	I25.9 (Chronic ischaemic heart disease, unspecified)	73,922	9.39	6.65 (6.60, 6.70)
		18	I48 (Atrial fibrillation and flutter)			
		19	I50.0 (Congestive heart failure)			
		20	I51.9 (Heart disease, unspecified)			
		21	G45.9 (Transient cerebral ischaemic attack, unspecified)			
		22	I64 (Stroke, not specified as haemorrhage or infarction)			
6	Cancer	23	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
7	Neurological disorders (epilepsy, convulsion, Parkinson's disease)	24	G20 (Parkinson's disease)	4,609	0.59	0.48 (0.46, 0.49)
		25	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)			
8	Ulcer and chronic inflamed bowel (stomach ulcer, chronic inflamed bowel, enteritis or colitis)	26	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)	3,131	0.40	0.34 (0.33, 0.35)
		27	K58.9 (Irritable bowel syndrome without diarrhoea)			

Appendix 2a: Literature Search Strategy

Database: Ovid MEDLINE(R): 1946 to March Week 1 2020

S/N	Search Terms	Results
1	exp comorbidity/ or multiple chronic conditions/ or multimorbidity	106,975
2	(multimorbid* or multi-morbid* or comorbid* or co-morbid*).ab,ti,kw.	144,228
3	((multiple or coexist* or co-exist* or concurrent* or simultaneous*) adj3 (disease* or illness* or diagnos* or condition* or morbid* or disorder*)).ab,ti,kw.	61,543
4	1 or 2 or 3	263,334
5	(prevalence or association).ab,ti,kw.	1,385,219
6	(Singapore).ab,ti,kw.	12,889
7	4 and 5 and 6	166
8	Set following limits: English language, Human studies, Full Text, 2010 to Current	29

Appendix 2b: PRISMA Flow Diagram



Appendix 3: A Summary of the Differences between Reported Studies on Multimorbidity

	Fortin et al. (Published in 2017)	**Ge et al. (Published in 2018)**	**Ge et al. (Published in 2019)**	**Low et al. (Published in 2019)**	**Picco et al. (Published in 2016)**	**Quah et al. (Published in 2016)**	**Subramaniam et al. (Published in 2014)**
Number of conditions	20	17	17	48	10	14	8
Definition of chronic disease	Conditions that usually last 12 months or more	Diseases that are irreversible and persistent throughout adulthood	Diseases characterised by a long duration and are of a generally slow progression that are irreversible and persistent throughout adulthood	No	No	No	No
Source of list of chronic conditions	Developed from a scoping review of 44 publications on multimorbidity	Not mentioned	Not mentioned	Selected from 3 indexes - the Singapore Chronic Disease Management Programme[1], the Charlson Comorbidity Index[2] and the Elixhauser Comorbidity Index[3]	Not mentioned	Conditions from Singapore Mental Health Study[4] 2010	Modified Composite International Diagnostic Interview (CIDI)[5]
Sources of data	Self-reported* (conditions that have been confirmed by a doctor or for which they are on medications)	At least one of the sources was self-reported or from the NHG Chronic Disease Management System (CDMS) database[6]	Self-reported	Singapore Eastern Regional Health System[7]	Self-reported	Self-reported	Self-reported
Cut-point	Not mentioned	2 conditions	2 conditions	2 conditions	2 conditions	2 conditions	2 conditions
Reference population	Practice-based population	General population	General population	Practice-based population (tertiary hospitals, community hospitals, primary care polyclinics)	General population	Practice-based population (one primary care polyclinic)	General population
Age-group	Not mentioned	≥ 21 years old	≥ 21 years old	0 to 85+ years old	≥ 60 years old	≥ 65 years old	≥ 18 years old

[1] The Chronic Disease Management Programme (CDMP) is an initiative introduced by the Ministry of Health (MOH), Singapore, in 2016 and involves the development of evidence-based structured Disease Management Programmes required in the management of their chronic diseases.

[2] The Charlson Comorbidity Index is a weighted index of 19 chronic conditions that was originally developed to predict the risk of short-term mortality from comorbid disease among patients being treated for primary breast cancer at a single hospital in 1987.

[3] The Elixhauser Comorbidity Index is an index of 30 chronic conditions that was developed to predict hospital charges, length of stay and in-patient mortality among patients 18 years and older from 438 hospitals in California in the year 1992.

[4] The Singapore Mental Health Study (SMHS) is a nationwide epidemiological study undertaken in 2009-2010 that provides insight into some of the common mental health illnesses in the adult Singapore resident population.

[5] The Composite International Diagnostic Interview (CIDI) was designed to allow investigators to reliably assess mental disorders according to the most widely accepted nomenclatures in different populations and cultures by combining questions from the Diagnostic Interview Schedule with questions designed to elicit Present State Examination items in 1988.

[6] The NHG Chronic Disease Management System (CDMS) database is a chronic disease registry within NHG that was commissioned for use in 2014 linking administrative and key clinical data of patients with chronic diseases across the National Healthcare Group cluster in Singapore.

[7] The Singapore Eastern Regional Health System was developed from the integration of the Singapore Health Services (SingHealth) and Eastern Health Alliance (EHA) in 2017.

Measured levels of multimorbidity[8]	No	No	Yes Disease count	Yes Disease count	No	Yes 1. Disease count 2. Drug count	No
Patient-reported outcomes	No	Yes Physical function	Yes 1. Health-related quality of life 2. Self-rated health	No	No	Yes 1. Health-related quality of life 2. Functional disability 3. Chronic musculoskeletal pain	Yes Health-related quality of life

[8] Levels of multimorbidity refers to the combined effects of the multiple conditions that an individual has. This may be based on disease count, that is, the number of chronic conditions the patient has; or other variables such as drug count, which is the number of chronic medications an individual is prescribed.

Appendix 4: List of chronic conditions under Chronic Disease Management Programme (CDMP)

S/N	Conditions
1	Diabetes mellitus and pre-diabetes
2	Hypertension
3	Lipid disorders
4	Asthma
5	Chronic obstructive pulmonary disease (COPD)
6	Chronic kidney disease (nephritis/nephrosis)
7	Schizophrenia
8	Major depression
9	Bipolar disorder
10	Anxiety
11	Stroke
12	Dementia
13	Osteoarthritis
14	Parkinson's disease
15	Benign prostatic hyperplasia (BPH)
16	Epilepsy
17	Osteoporosis
18	Psoriasis
19	Rheumatoid arthritis (RA)
20	Ischemic heart disease (IHD)

Appendix 5a: List of ICD-10 diagnosis codes matched to the chronic conditions studied by each author

S/N	ICD-10 Codes	Fortin et al. 2017	Ge et al. 2018 and 2019	Low et al. 2019	Picco et al. 2016	Quah et al. 2016	Subramaniam et al. 2014
1	E78.5	✓	✓	✓		✓	
2	I10	✓	✓	✓	✓	✓	✓
3	E11.9	✓	✓	✓	✓	✓	✓
4	M19.99	✓			✓	✓	✓
5	J30.4					✓	✓
6	E66.9	✓					
7	J45.9	✓	✓	✓	✓	✓	✓
8	I25.9	✓	✓	✓	✓	✓	✓
9	K21.9	✓				✓	
10	K76.9	✓		✓		✓	
11	M10.99		✓				
12	N28.9			✓		✓	
13	N18.9	✓	✓	✓		✓	
14	I51.9	✓		✓	✓	✓	✓
15	M15.9	✓	✓	✓	✓	✓	✓
16	I64	✓	✓	✓	✓	✓	✓
17	E03.9	✓		✓		✓	
18	N40	✓		✓			
19	F32.90	✓	✓	✓	✓	✓	
20	Z22.51	✓				✓	
21	E05.9	✓		✓		✓	
22	H91.9					✓	
23	G43.9						✓
24	F41.1	✓	✓	✓		✓	
25	C80	✓	✓	✓	✓	✓	✓
26	I48	✓		✓	✓	✓	✓
27	M81.99	✓	✓	✓			
28	E14.31	✓	✓	✓	✓	✓	✓
29	G45.9	✓	✓	✓	✓	✓	✓
30	J44.9	✓	✓	✓	✓	✓	✓
31	K82.9					✓	
32	G40.90			✓		✓	✓
33	F20.9		✓	✓		✓	
34	E10.9	✓	✓	✓	✓	✓	✓
35	I50.0	✓	✓	✓	✓	✓	✓
36	F03	✓	✓	✓		✓	
37	F32.20	✓	✓	✓	✓	✓	
38	I73.9	✓		✓			
39	K58.9	✓				✓	✓
40	M06.99	✓	✓	✓	✓	✓	✓
41	F29					✓	
42	E14.73	✓	✓	✓	✓	✓	✓
43	G20		✓	✓		✓	✓
44	K27.9	✓				✓	✓
45	G60.9					✓	
46	Q79.9					✓	
47	I70.20	✓					
48	E14.2	✓	✓	✓	✓	✓	✓
49	N03.9	✓		✓		✓	
50	G50.0						✓
51	Z89.5			✓			
52	E14.3	✓	✓	✓	✓	✓	✓
53	F31.9			✓		✓	
54	Z89.6			✓			
55	Z89.4			✓			
56	E14.64	✓	✓	✓	✓	✓	✓
57	L40.8			✓			

Appendix 5b: Descriptors of ICD-10 diagnosis codes

S/N	ICD-10 Codes	Descriptors
1	E78.5	Hyperlipidaemia, unspecified
2	I10	Essential (primary) hypertension
3	E11.9	Type 2 diabetes mellitus without complication
4	M19.99	Arthritis, unspecified, site unspecified
5	J30.4	Allergic rhinitis, unspecified
6	E66.9	Obesity, unspecified
7	J45.9	Asthma, unspecified
8	I25.9	Chronic ischaemic heart disease, unspecified
9	K21.9	Gastro-oesophageal reflux disease without oesophagitis
10	K76.9	Liver disease, unspecified
11	M10.99	Gout, unspecified, site unspecified
12	N28.9	Disorder of kidney and ureter, unspecified
13	N18.9	Chronic kidney disease, unspecified
14	I51.9	Heart disease, unspecified
15	M15.9	Osteoarthritis (OA) - Generalised
16	I64	Stroke, not specified as haemorrhage or infarction
17	E03.9	Hypothyroidism, unspecified
18	N40	Hyperplasia of prostate
19	F32.90	Depressive episode, unspecified, not specified as arising in the postnatal period
20	Z22.51	Carrier of viral hepatitis B
21	E05.9	Thyrotoxicosis, unspecified
22	H91.9	Hearing loss, unspecified
23	G43.9	Migraine, unspecified
24	F41.1	Anxiety disorder, unspecified
25	C80	Malignant neoplasm without specification of site
26	I48	Atrial fibrillation and flutter
27	M81.99	Other osteoporosis, site unspecified
28	E14.31	Unspecified diabetes mellitus with background retinopathy
29	G45.9	Transient cerebral ischaemic attack, unspecified
30	J44.9	Chronic Obstructive Pulmonary Disease, Unspecified
31	K82.9	Disease of gallbladder, unspecified
32	G40.90	Epilepsy, unspecified, without mention of intractable epilepsy
33	F20.9	Schizophrenia, unspecified
34	E10.9	Type 1 diabetes mellitus without complication
35	I50.0	Congestive heart failure
36	F03	Unspecified dementia
37	F32.20	Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period
38	I73.9	Peripheral vascular disease, unspecified
39	K58.9	Irritable bowel syndrome without diarrhoea
40	M06.99	Rheumatoid arthritis, unspecified, site unspecified
41	F29	Unspecified nonorganic psychosis
42	E14.73	Unspecified diabetes mellitus with foot ulcer due to multiple causes
43	G20	Parkinson's disease
44	K27.9	Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation
45	G60.9	Hereditary and idiopathic neuropathy, unspecified
46	Q79.9	Congenital malformation of musculoskeletal system, unspecified
47	I70.20	Atherosclerosis of arteries of extremities, unspecified
48	E14.2	Diabetes mellitus with incipient diabetic nephropathy
49	N03.9	Unspecified nephritic syndrome, unspecified
50	G50.0	Trigeminal neuralgia
51	Z89.5	Acquired absence of leg at or below knee
52	E14.3	Diabetes mellitus with retinopathy
53	F31.9	Bipolar affective disorder, unspecified
54	Z89.6	Acquired absence of leg above knee
55	Z89.4	Acquired absence of foot and ankle
56	E14.64	Unspecified diabetes mellitus with hypoglycaemia
57	L40.8	Other psoriasis

Appendix 6: List of Chronic Conditions in Proposed Operational Definition of Multimorbidity

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.79 (24.86, 25.07)
2	Hypertension (high blood pressure)	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes (including pre-diabetes)	3	E09 (Impaired glucose regulation)	150,294	19.09	14.28 (14.20, 14.35)
		4	E099 (Impaired glucose regulation without complication)			
		5	E10.9 (Type 1 diabetes mellitus without complication)			
		6	E11.9 (Type 2 diabetes mellitus without complication)			
		7	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		8	E14.3 (Diabetes mellitus with retinopathy)			
		9	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		10	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		11	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis &/or rheumatoid arthritis	12	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		13	M15.9 (Osteoarthritis (OA) - Generalised)			
		14	M19.99 (Arthritis, unspecified, site unspecified)			
5	Obesity	15	E66.9 (Obesity, unspecified)	48,893	6.21	5.29 (5.24, 5.34)
6	Cardiovascular disease (angina, MI, AF, poor circulation of lower limbs)	16	I25.9 (Chronic ischaemic heart disease, unspecified)	43,559	5.53	3.74 (3.71, 3.78)
		17	I48 (Atrial fibrillation and flutter)			
		18	I70.20 (Atherosclerosis of arteries of extremities, unspecified)			
		19	I73.9 (Peripheral vascular disease, unspecified)			
7	Asthma, COPD, or chronic bronchitis	20	J44.9 (Chronic Obstructive Pulmonary Disease, Unspecified)	32,611	4.14	3.68 (3.63, 3.72)
		21	J45.9 (Asthma, unspecified)			
8	Chronic hepatitis	22	K76.9 (Liver disease, unspecified)	25,918	3.29	3.02 (2.98, 3.06)
		23	Z22.51 (Carrier of viral hepatitis B)			
9	Stomach problem (reflux, heartburn, or gastric ulcer)	24	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	22,233	2.82	2.52 (2.48, 2.56)
		25	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
10	Thyroid disorder	26	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		27	E05.9 (Thyrotoxicosis, unspecified)			
11	Stroke and TIA	28	G45.9 (Transient cerebral ischaemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		29	I64 (Stroke, not specified as haemorrhage or infarction)			
12	Heart failure (including valve problems or replacement)	30	I50.0 (Congestive heart failure)	20,538	2.61	1.97 (1.94, 2.00)
		31	I51.9 (Heart disease, unspecified)			
13	Kidney disease or failure	32	N03.9 (Unspecified nephritic syndrome, unspecified)	22,221	2.82	1.82 (1.79, 1.84)
		33	N18.9 (Chronic kidney disease, unspecified)			
14	Depression or anxiety	34	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	14,910	1.89	1.81 (1.78, 1.84)
		35	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		36	F41.1 (Anxiety disorder, unspecified)			
15	Chronic urinary problem	37	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
16	Physical disability	38	H91.9 (Hearing loss, unspecified)	10,514	1.34	1.05

		39	Q79.9 (Congenital malformation of musculoskeletal system, unspecified)			(1.03, 1.08)
17	Any cancer in the last 5 years	40	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
18	Osteoporosis	41	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
19	Dementia or Alzheimer's disease	42	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
20	Colon problem (irritable bowel)	43	K58.9 (Irritable bowel syndrome without diarrhoea)	1,517	0.19	0.20 (0.19, 0.21)

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Comparing the prevalence of multimorbidity using different operational definitions in primary care in Singapore based on a cross-sectional study using retrospective, large administrative data

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TITLE PAGE

Comparing the prevalence of multimorbidity using different operational definitions in primary care in Singapore based on a cross-sectional study using retrospective, large administrative data

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ABSTRACT

Objectives: Multimorbidity is a norm in primary care. A consensus on its operational definition remains lacking especially in the list of chronic conditions considered. This study aimed to compare six different operational definitions of multimorbidity previously reported in the literature for the context of primary care in Singapore.

Design, Setting and Participants: This is a retrospective study using anonymised primary care data from a study population of 787,446 patients. We defined multimorbidity as having three or more chronic conditions in an individual. The prevalence of single conditions and multimorbidity with each operational definition was tabulated and standardised prevalence rates (SPR) were obtained by adjusting for age, sex and ethnicity. We compared the operational definitions based on (1) number of chronic diseases, (2) presence of chronic diseases of high burden and (3) relevance in primary care in Singapore. IBM SPSS version 23 and Microsoft Office Excel 2019 were used for all statistical calculations and analyses.

Results: The SPRs of multimorbidity in primary care in Singapore varied from 5.7% to 17.2%. The lists by Fortin et al., Ge et al., Low et al. and Quah et al. included at least 12 chronic conditions, the recommended minimal number of conditions. Quah et al. considered the highest proportion of chronic diseases (92.3%) of high burden in primary care in Singapore, with SPRs of at least 1.0%. Picco et al. and Subramaniam et al. considered the fewest number of conditions of high relevance in primary care in Singapore.

Conclusions: Fortin et al.'s list of conditions is most suitable for describing multimorbidity in the Singapore primary care setting. Pre-diabetes and 'physical disability' should be added to Fortin et al.'s list to augment its comprehensiveness. We propose a similar study methodology be performed in other countries to identify the most suitable operational definition in their own context.

ARTICLE SUMMARY

Strengths and limitations of this study

- Strengths of this study include the utilisation of a large database and the determination of the clinical relevance of a chronic condition through an iterative process.
- Another strength of this study is the employment of a systematic method in the comparison of all six operational definitions.
- The limitations of this study include the utilisation of a single administrative database and the use of a pre-determined number of International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) codes.
- This study also did not consider the impact of each chronic condition on affected individuals.

MAIN TEXT

1. BACKGROUND

Multimorbidity, the co-occurrence of multiple chronic health conditions in a single individual,[1] is a growing norm in primary care.[2-5] 'Multimorbidity' has often been confused with 'comorbidity'.[6, 7] Comorbidity describes the simultaneous presence of multiple health conditions when there is an index condition. In contrast, multimorbidity describes the co-occurrence of two or more chronic medical conditions without specifying the index condition. Health outcomes are evaluated based on the interaction and burden of all co-existing chronic conditions.[8] Advocates of the concept of multimorbidity tend to focus on primary care, where the identification of an index disease is often neither obvious nor useful.[9]

The implications of multimorbidity are significant and widespread. From the patient's perspective, multimorbidity is associated with future functional decline,[10, 11] reduced health-related quality of life,[10, 12] inpatient admission and mortality.[13] From an economic standpoint, multimorbidity is associated with increased healthcare utilisation[14] and healthcare costs.[10] Single disease clinical practice guidelines (CPGs) that have traditionally been used for the management of chronic diseases are inappropriate in the management of patients with multimorbidity.[5, 15-17]

To this date, there is no consensus on an operational definition of multimorbidity.[18-20] This definition comprises two components: the list of chronic conditions considered and the cut-off for the number of chronic conditions used to determine the presence of multimorbidity.[21] The absence of a standardised operational definition has resulted in reported prevalence estimates of multimorbidity in Singapore to range widely from 16.3% to 89.4% [12, 14, 22-24] and has made comparability between published studies impossible.[21] Wide variations in prevalence estimates also prevent accurate estimations of disease burden and hinder resource distribution for effective disease management.[25]

In 2017, an operational definition comprising 20 chronic conditions/categories of conditions was proposed by Fortin et al. as a common list of conditions for studying multimorbidity in primary care (Appendix 1-1).[21] These conditions were selected from a scoping review of relevant studies.

We identified six studies, two by Ge et al. [23, 26] (Appendix 1-2) and one each by Low et al. [24] (Appendix 1-3), Picco et al. [14] (Appendix 1-4), Quah et al. [12] (Appendix 1-5) and Subramaniam et al. [22] (Appendix 1-6), which were published between 2014 to 2019 in Singapore. These studies were identified on Medline Ovid between 2010 till 14 March 2020 and through direct correspondences with

the authors (Appendix 2). Heterogeneity was noted in both the methodologies and lists of chronic conditions utilised in each study.

The objective of this study was to compare the different operational definitions of multimorbidity previously reported in the literature for the context of primary care in Singapore.

2. METHODS

2.1 Setting and Study Population

The study population was selected between 1 July 2015 and 30 June 2016. During this period, the public primary healthcare sector was organised into two main clusters in Singapore - National Healthcare Group Polyclinics (NHGP) and SingHealth Polyclinics (SHP). The two clusters shared 18 polyclinics island-wide, providing government-funded subsidised primary care. According to statistics published by the Ministry of Health (MOH), Singapore, 3,916,771 individuals (approximately 70% of the 2016 Singapore population [27]) consulted a doctor in the polyclinics in 2016. Out of which, 58.9% attended the NHGP.[28] The choice to draw data only from the NHGP was based on pragmatic reasons. The participants in this study were multi-ethnic patients aged 0 to 99 years old who consulted a doctor in NHGP at least once during the study period. A total of 787,446 patients from nine polyclinics were included in this study.

2.2 Data Source

Data from the study population were collected from the NHGP Business Informatics (BI) system. The BI system is an administrative database that captures each patient's consultation episodes and clinical parameters from structured data fields within the electronic medical records (EMRs) e.g. blood pressure readings, International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) diagnoses codes and laboratory data. We excluded all patient encounters that did not include an ICD-10 diagnosis code by a physician. Only de-identified data were collected in accordance with the personal data protection act.[29]

2.3 Patient and Public Involvement

No patients were involved in this study.

2.4 Definition of Chronic Condition and Multimorbidity

We adopted the definition of O'Halloran et al. for chronicity of a disease which is defined as one lasting at least six months, with a documented pattern of recurrence or deterioration, and having an impact on an individual's quality of life.[30]

While we acknowledge that most studies have defined multimorbidity using a cut-off of 'two or more' chronic conditions,[31] in keeping with the World Health Organization's definition of multimorbidity,[32] we adopted a cut-off of 'three or more' chronic conditions to better identify patients with higher needs.[18]

2.5 Determination of Prevalence Rates of Single Conditions and Multimorbidity

The prevalence of a disease is defined as the proportion of the population at risk (PAR) that are cases at a point in time.[33] The PAR is defined as the group of people, healthy or sick, who would be counted as cases if they had the disease of interest. This forms the denominator for the calculation of prevalence.[33] For this study, the PAR was denoted by individuals aged 0 to 99 years who consulted a doctor in NHGP at least once during the study period.

For the crude prevalence rate of single conditions, the numerator used was the number of unique patients with the single condition who had consulted a doctor in NHGP at least once during the study period. For the crude prevalence rate of multimorbidity, the numerator used was the number of unique patients with multimorbidity who had consulted a doctor in NHGP at least once during the study period.

Standardised prevalence rates (SPRs) were obtained by adjusting the study population to a standard population by using the direct standardisation method as detailed by Bains.[34] The 2016 Singapore population was used as the standard population.[27] Poisson approximation was utilised to calculate the confidence intervals of 95%.

2.6 Criteria for Comparison of Operational Definitions

Amongst the six studies conducted in Singapore, only five unique operational definitions were identified. The two studies by Ge et al. [23, 26] utilised the same operational definition. We compared six lists of chronic conditions from six different operational definitions of multimorbidity (Appendix 3) on the same study population. This included the list proposed by Fortin et al. that had been developed as a research tool to document the presence of multimorbidity in primary care [21] (Appendix 1-1) and the five lists used in the study of multimorbidity in Singapore (Appendix 1-2 to 1-6). A list of NHGP ICD-10 diagnosis codes was assembled by four senior family physicians based on the aforementioned definition of chronicity.[30]

Fortin et al. proposed that an ideal operational definition of multimorbidity should comprise at least 12 chronic diseases, each with a high impact or burden in the population of interest.[18] Based on this, the comparison of the six operational definitions were focused on (1) the number of chronic diseases considered, (2) presence of chronic diseases of high burden and (3) relevance in the primary care setting in Singapore. We considered a chronic condition to be of significant burden in the primary care if it has a SPR of at least 1.0%. We tabulated the proportion of chronic diseases with a SPR of at least 1.0% in each list. The numerator used was the number of chronic conditions with a SPR of at least 1.0% and the denominator was the total number of chronic conditions in the list. The clinical relevance of a condition was based on consensus reached after iterative discussions between the clinicians, research team members and reference to statistics from the MOH and local primary care initiatives such as the Chronic Disease Management Programme (CDMP).[35]

Statistics reported by the MOH have consistently ranked hyperlipidaemia, hypertensive disease and diabetes mellitus as the first, second and fourth top condition responsible for polyclinic attendances since 2012.[36] Hyperlipidaemia constituted 13.8% of polyclinic attendances in 2018, closely followed by hypertensive disease at 13.2%, acute upper respiratory tract infection at 9.4% and diabetes mellitus at 9.0%.

The CDMP [35] was introduced in 2006 to facilitate the provision of care to patients with chronic conditions through the development of evidence-based structured Disease Management Programmes and to reduce out-of-pocket payments for outpatient treatments by allowing patients to draw on their Medisave. The structured Disease Management Programmes facilitate the management of these conditions in the primary care setting. In 2018, the list of chronic conditions included in CDMP was increased to include 20 chronic conditions (Appendix 4).

2.7 Statistical Analysis

The sample size was determined by the number of patients aged 0 to 99 years who visited the NHGP for at least one doctor consultation during the study period. We used listwise deletion method for complete case analysis. For descriptive statistics, we described the mean for continuous variables and their respective standard deviation. For categorical variables, we described proportions and their respective confidence intervals where appropriate.

SPRs were obtained by adjusting for age, sex and ethnicity. Age was stratified into four categories - '0 - 24', '25 - 44', '45 - 64' and '65 - 99'. Sex was classified into male and female, and ethnicity was categorized into Chinese, Malay, Indian and Others. To compare the SPRs of multimorbidity among

age and sex, we tabulated age-stratified, sex-and-ethnicity SPR and sex-stratified, age-and-ethnicity SPR of multimorbidity between the different lists. No overlap of the 95% confidence intervals for the SPRs among the different lists was considered as statistically significant. IBM SPSS version 23 and Microsoft Office Excel 2019 were used for all statistical calculations and analyses.

3. RESULTS

The mean age of the 787,446 patients analysed in this study was 43.9 years. Females made up 50.9% of the patients and the Chinese formed the majority ethnic group at 68.2%. Of the four ethnicities, the Chinese had the highest mean age of 47.1 years. 53.4% of the patients studied were from the '45 - 64' and '65 - 99' age groups (Table 1).

Table 1: Demographics of the study population

	Frequency	Percent	Mean Age (SD)
Total	787,446	100.0	43.9 (0.03)
Sex			
Female	400,965	50.9	45.3 (0.04)
Male	386,481	49.1	42.2 (0.04)
Ethnicity			
Chinese	537,234	68.2	47.1 (0.03)
Malay	127,501	16.2	35.1 (0.06)
Indian	78,452	10.0	39.7 (0.08)
Others	44,259	5.6	37.1 (0.09)
Age Groups			
0 - 24	201,839	25.6	
25 - 44	165,212	21.0	
45 - 64	252,206	32.0	
65 - 99	168,189	21.4	

The list recommended by Fortin et al. [21] gave the highest SPR of multimorbidity in the study population (17.2%). Across the six lists, the SPRs of multimorbidity increased with increasing age. The male sex reported higher SPRs of multimorbidity and the differences between the sexes are statistically significant (Table 2).

Table 2: Comparison of the standardised prevalence rates of multimorbidity among the six lists of chronic conditions

	Fortin et al. 2017	Ge et al. 2018 and 2019	Low et al. 2019	Picco et al. 2016	Quah et al. 2016	Subramaniam et al. 2014
Total	17.2 (17.2, 17.3)	13.0 (12.9, 13.0)	14.6 (14.5, 14.7)	5.7 (5.7, 5.8)	16.8 (16.7, 16.8)	5.9 (5.8, 5.9)
Sex						
Female	16.5 (16.4, 16.6)	11.7 (11.7, 11.8)	13.5 (13.4, 13.6)	5.4 (5.4, 5.5)	16.0 (15.9, 16.1)	5.6 (5.5, 5.6)
Male	18.0 (17.9, 18.1)	14.3 (14.1, 14.4)	15.8 (15.7, 15.9)	6.0 (5.9, 6.1)	17.6 (17.4, 17.7)	6.2 (6.1, 6.2)
Age Groups						
0 - 24	0.08 (0.07, 0.10)	0.02 (0.02, 0.03)	0.04 (0.03, 0.05)	0.01 (0.01, 0.01)	0.10 (0.08, 0.11)	0.02 (0.01, 0.02)
25 - 44	4.0 (3.9, 4.1)	2.2 (2.1, 2.3)	2.8 (2.7, 2.9)	0.5 (0.5, 0.5)	3.6 (3.5, 3.7)	0.6 (0.6, 0.7)
45 - 64	28.5 (28.3, 28.7)	20.2 (20.0, 20.4)	23.2 (23.0, 23.4)	7.8 (7.7, 7.9)	27.7 (27.5, 27.9)	8.1 (8.0, 8.2)
65 - 99	60.9 (60.5, 61.2)	50.9 (50.5, 51.2)	55.4 (55.0, 55.7)	26.1 (25.9, 26.4)	60.1 (59.7, 60.4)	26.3 (26.1, 26.6)

3.1 Criterion 1: Number of Chronic Conditions

A list of 57 NHGP ICD-10 diagnosis codes (Appendix 5) was matched to the chronic conditions in these six lists. Amongst the 20 conditions/categories of conditions proposed by Fortin et al.,[21] only 19 of them could be matched to the corresponding NHGP ICD-10 codes. We excluded the condition ‘chronic musculoskeletal condition causing pain or limitation’ from the list as the corresponding ICD-10 code was not reliably coded at our primary care setting. Similarly, as only 13 out of 14 conditions/categories of conditions proposed by Quah et al. [12] could be matched to corresponding NHGP ICD-10 codes, the condition ‘back problems’ was excluded from the list.

Low et al. [24] proposed a total of 48 chronic conditions, eight of which - ‘hip fracture’, ‘nephrosis’, ‘respiratory failure’, ‘secondary hypertension’, ‘spine fracture’, ‘coronary artery bypass graft’, ‘percutaneous coronary intervention’ and ‘kidney transplant’ had no corresponding NHGP ICD-10 codes and were excluded from the list. Of the remaining 40 conditions, 16 conditions had overlapping ICD-10 codes. This included chronic conditions such as ‘anxiety’ and ‘general anxiety disorder’ which were matched to the same ICD-10 code: F41.1 ‘anxiety disorder, unspecified’ (Appendix 1-3). These conditions were reclassified to obtain a final list of 31 chronic conditions to avoid double-counting of chronic diseases and overestimation of multimorbidity.

Picco et al. [14] and Subramaniam et al. [22] only considered ten and eight conditions respectively, falling short of the recommended minimal number of 12 chronic conditions.[18]

3.2 Criterion 2: Prevalence amongst the Primary Care Population

We considered a chronic condition to be of high burden in the primary care setting if it has a SPR of at least 1.0%. The list proposed by Quah et al. [12] had the highest proportion (92.3%) of chronic conditions with a SPR of at least 1.0% (Appendix 1-5). This was followed by the list by Fortin et al. [21] (78.9%) (Appendix 1-1), Picco et al. [14] (70.0%) (Appendix 1-4), Subramaniam et al. [22] (62.5%) (Appendix 1-6), Ge et al. [23, 26] (52.9%) (Appendix 1-2) and lastly Low et al. [24] (41.9%) (Appendix 1-3).

3.3 Criterion 3: Relevance to Primary Care Services

Hypertensive disease and diabetes mellitus were represented in all six operational definitions, with SPRs of 20.93% and 11.86% respectively. Hyperlipidaemia, with the highest SPR of 24.97%, however, was absent in the lists of chronic conditions by Picco et al. [14] and Subramaniam et al..[22]

We compared the chronic conditions under CDMP with the lists of chronic conditions in the six operational definitions. The list of chronic conditions by Low et al. [24] included all 20 conditions under CDMP. This was followed by Ge et al. [23, 26] and Quah et al.,[12] with each considering 17 out of the 20 chronic conditions. Fortin et al. [21] considered 15 out of the 20 chronic conditions and Subramaniam et al. [22] and Picco et al. [14] only considered 10 and 8 of the 20 conditions respectively.

4. DISCUSSION

4.1 Summary of Results

The SPRs of multimorbidity in the primary care setting in Singapore varied widely depending on the operational definition utilised. The list of chronic conditions proposed by Fortin et al. [21] gave the highest SPR of multimorbidity (17.2%). The lists by Fortin et al.,[21] Ge et al.,[23, 26] Low et al. [24] and Quah et al. [12] included at least 12 chronic conditions with the list by Quah et al. [12] comprising the highest proportion of chronic diseases (92.3%) with a SPR of at least 1.0% that matched with a NHGP ICD-10 code. The lists by Picco et al. [14] and Subramaniam et al. [22] did not include hyperlipidaemia, a chronic condition of high relevance in the primary care setting in Singapore and both lists considered the fewest number of conditions under CDMP.

4.2 Comparison of Operational Definitions

Comparing the six operational definitions, it is clear that the lists proposed by Picco et al. [14] and Subramaniam et al. [22] had fallen short on several fronts. Both lists considered less than 12 chronic conditions and have comparatively lower proportions of chronic conditions with SPR of at least 1.0%. In addition, both considered the fewest number of chronic conditions under CDMP and failed to include hyperlipidaemia, which constitutes a large proportion of polyclinic attendances. These shortfalls likely contributed to the low SPRs of multimorbidity tabulated and underestimate multimorbidity in the primary care setting in Singapore.

While Low et al.'s list [24] comprised 31 chronic conditions, including all 20 conditions under CDMP, it reported the lowest proportion of chronic diseases (41.9%) with a SPR of at least 1.0%. This is likely due to two reasons. The first was that Low et al.'s list [24] is the longest amongst the six lists. While Low et al. [24] included 13 conditions with a SPR of at least 1.0%, (numerator), second only to Fortin et al. [21], its inclusion of a total of 31 chronic conditions (denominator), resulted in a less discriminating list. Second, the manner in which the list of chronic conditions was classified could be a contributory factor. Low et al. [24] had kept 'major depression', 'anxiety', 'schizophrenia' and 'bipolar disorder' as four separate chronic conditions (Appendix 1-3), whilst, other studies such as that by Quah et al. [12] had grouped them under a single chronic condition category - 'psychiatric conditions' (Appendix 1-5). When considered individually, only the chronic condition 'major depression' had a SPR of at least 1.0%. While Low et al.'s list [24] is the most comprehensive, the presence of chronic conditions with overlapping ICD-10 codes prior to re-classification and the large number of chronic conditions with no corresponding NHGP ICD-10 codes make it less ideal as an operational definition for use in the primary care setting in Singapore.

The list by Ge et al.,[23, 26] which comprised 17 chronic conditions and considered a large number of chronic conditions under CDMP also had a low proportion of chronic diseases (52.9%) with a SPR of at least 1.0%. Ge et al. [23, 26] had likewise considered the psychiatric diseases individually (Appendix 1-2) as opposed to grouping them as a single chronic condition. In addition, Ge et al.'s list [23, 26] did not include conditions commonly seen in primary care such as thyroid conditions and diseases of the gastrointestinal tract, which were present in Fortin et al. [21] (Appendix 1-1) and Quah et al.'s lists [12] (Appendix 1-5). 'Thyroid disorder (Fortin et al. [21]) / Thyroid diseases (Quah et al. [12])' have a SPR of 2.36%. 'Chronic hepatitis (Fortin et al. [21])' and 'Stomach problem (reflux, heart burn, or gastric ulcer) (Fortin et al. [21])' have SPRs of 3.02% and 2.52% respectively, while 'Gastrointestinal diseases (Quah et al. [12])' has a SPR of 5.76%. The list proposed by Ge et al. [23, 26] is thus not ideal as the exclusion of these chronic conditions would underestimate multimorbidity in the Singapore primary care setting.

Quah et al.'s list [12] of 13 conditions, encompassing 17 CDMP conditions, comprised the largest proportion of chronic conditions (92.3%) with SPRs of at least 1.0%. This is contributed by two reasons. First, Quah et al. [12] had included the chronic condition 'physical disability', which had a SPR of 1.05% and was absent in all the other five lists. Second, Quah et al. [12] had classified chronic diseases affecting similar organ systems into a single chronic condition category (Appendix 1-5). For example, several ICD-10 conditions such as Parkinson's disease, dementia, epilepsy and stroke were all classified under a single category 'neurological conditions'. While we acknowledge that individuals who suffer diseases of the same organ system often follow up with the same specialist and treatment options are often complementary and hence the rationality behind this manner of classification, [37] it is of our view that this is not always applicable to all chronic conditions of the same organ system. For example, in Parkinson's disease, the focus of care is on maintaining functional capabilities, whilst in epilepsy, care is focused on the avoidance of seizure triggers and seizure first aid. This manner of classification, as adopted by Quah at el., [12] risks overlooking individuals who require greater care and would fail to give a discerning estimate of multimorbidity. It is of our view that clinical judgement should be exercised in defining 'disease entities' taking into account the care needs of each chronic condition.

While the list of 19 chronic conditions proposed by Fortin et al. [21] captured fewer chronic conditions under CDMP and had a lower proportion of chronic conditions (78.9%) with a SPR of at least 1.0% compared to that by Quah et al.,[12] its inclusion of key chronic conditions of relevance to primary care makes it most suitable as an operational definition for use in the primary care setting in Singapore. Fortin et al. [21] included the chronic condition 'chronic urinary problem', which was matched to the ICD-10 code 'hyperplasia of prostate'. The SPR tabulated was 1.07% and benign prostatic hyperplasia is also recognised under CDMP, underscoring its importance in the population. In addition, Fortin et al. [21] considered the chronic condition 'osteoporosis', a chronic disease recognised under CDMP. While the SPR tabulated for 'osteoporosis' stands at 0.57%, this is likely to increase in the future in view of Singapore's rapidly ageing population.[38]

4.2 Proposing a New Operational Definition of Multimorbidity

When applied to the primary care population in Singapore, the list proposed by Fortin et al. [21] had comparatively outshone the others based on the aforementioned criteria.

We propose the use of a modified list of chronic conditions adapted from Fortin et al.'s list [21] for use in the primary care setting in Singapore (Appendix 6). We suggest the inclusion of pre-diabetes (ICD-10 codes: E09 and E099) under the chronic condition 'diabetes' and the addition of the chronic condition 'physical disability' to Fortin et al.'s existing list of chronic conditions [21] to increase its comprehensiveness.

The relevance of pre-diabetes in Singapore is indisputable with the Singapore government placing greater emphasis on diabetes management and aggressive intervention for individuals with pre-diabetes.[39] Pre-diabetes is also recognised under CDMP and has a SPR of 3.65% (3.61, 3.69). The inclusion of pre-diabetes under the chronic condition 'diabetes' increased the SPR from 11.86% to 14.28% (14.20, 14.35).

The inclusion of 'physical disability', with a SPR of 1.05%, which includes the ICD-10 code 'hearing loss' is important in the context of Singapore's ageing population as the prevalence of hearing impairment has been reported to increase with age and has serious ramifications physically, mentally, socially and financially for affected individuals.[40]

We acknowledge that Fortin et al. [21] did not recognise several conditions under CDMP (Appendix 4), namely, 'schizophrenia', 'bipolar disorder', 'Parkinson's disease', 'epilepsy' and 'psoriasis', however, the SPRs of each of these chronic conditions is low and is unlikely to result in much variation in the prevalence estimates of multimorbidity. In addition, in Singapore, these chronic conditions are still largely managed by their relevant specialties and do not form a large proportion of primary care attendances.

With the proposed new operational definition, we calculated the SPR of multimorbidity to be 18.1%. The pattern of multimorbidity across the different sex, ethnicity and age groups remain consistent with that of Fortin et al.'s.[21]

4.3 Strengths of our study

Our study leveraged on the utilisation of a large database upon which the six different operational definitions were consistently applied. The determination of the clinical relevance of a chronic condition was also achieved through an iterative process, with discussions held among clinicians and research team members. In addition, a systematic method was employed in the comparison of all six operational definitions.

4.4 Limitations of our study

Our study has several limitations. Firstly, we only utilised data from a single administrative source - the EMRs. The use of a single data source risks underestimating the prevalence estimates of chronic conditions.[41] Furthermore, the utilization of EMRs relies heavily on accurate and consistent data reporting. This limitation was, however, mitigated by the use of standardised ICD-10 codes. Secondly, the number of ICD-10 codes depicting chronic conditions is fixed and pre-determined in our EMRs. Ten chronic conditions/categories of conditions could not be reliably coded with the NHGP ICD-10 codes. This included the chronic condition proposed by Fortin et al. [21] 'chronic musculoskeletal condition causing pain or limitation', a common complaint in the primary care setting.[12] The fixed number of NHGP ICD-10 codes available also limited the inclusivity of chronic conditions such as 'physical disability' which only included the ICD-10 codes 'hearing loss' and 'congenital malformation of the musculoskeletal system'. The available list of ICD-10 codes may change as we move on to the new generation EMRs system in the future. Thirdly, our study reports low SPRs of psychiatric conditions. This is incongruent with reports from the Singapore Mental Health Study, which reported higher lifetime prevalence rates.[42] One possible reason is that patients with psychiatric illnesses tend to consult spiritual healers for help instead of their primary care physicians.[42, 43] Lastly, we did not estimate the impact of each chronic condition on affected individuals. This was a criterion that was utilised by Fortin et al. in his selection of chronic conditions for inclusion in their operational definition.[21]

5. CONCLUSION

We compared six operational definitions and found that Fortin et al.'s list of chronic conditions [21] (Appendix 1-1) was most applicable to the primary care setting in Singapore, fulfilling the aforementioned criteria. We propose the addition of pre-diabetes and the chronic condition 'physical disability' into Fortin et al.'s list of conditions [21] to augment its comprehensiveness in our setting (Appendix 6).

Multimorbidity is a growing global healthcare conundrum. We utilised criteria previously proposed by Fortin et al. [21] in the formulation of a standardised operational definition contextualized to primary care in Singapore. The creation of such standardised operational definitions for use in individual countries would allow for meaningful comparisons to be made across research studies done within the country. Common patterns of multimorbidity within the country can then be reliably identified, facilitating the creation of specific multimorbidity CPGs that are relevant to the primary care setting of the country. The CPGs can focus on coordinating care across various specialties, medications management to avoid polypharmacy and management of shared disease risk factors which are not covered with the current single disease CPGs.[44] We propose that similar studies be conducted in different geographical countries/regions in the world to describe the most suitable list of chronic conditions for multimorbidity in their own context.

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Contributors

ESL and PSSL initiated and conceptualised the study. ESL and YX developed the analysis approach. YAJL conducted the data analysis for this study. YAJL wrote the first draft of the manuscript. YX, PSSL and ESL provided inputs and assisted in the interpretation of the findings. ESL critically reviewed the final version of the article. All authors have read and approved the final manuscript.

Competing Interests

None declared.

Data Sharing

Data are not available for online access. Readers who wish to gain access to the data can write to the senior author ESL at eng_sing_lee@nhgp.com.sg with their requests. Access can be granted subject to approval of the National Healthcare Group Domain Specific Review Board (DSRB) and in line with the National Healthcare Group Research Data Policy. This is a requirement mandated for this research study by our DSRB and funders.

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APPENDICES

Appendix 1-1: List of Chronic Conditions (Fortin et al. 2017)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.79 (24.86, 25.07)
2	Hypertension (high blood pressure)	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis &/or rheumatoid arthritis	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		11	M15.9 (Osteoarthritis (OA) - Generalised)			
		12	M19.99 (Arthritis, unspecified, site unspecified)			
5	Obesity	13	E66.9 (Obesity, unspecified)	48,893	6.21	5.29 (5.24, 5.34)
6	Cardiovascular disease (angina, MI, AF, poor circulation of lower limbs)	14	I25.9 (Chronic ischaemic heart disease, unspecified)	43,559	5.53	3.74 (3.71, 3.78)
		15	I48 (Atrial fibrillation and flutter)			
		16	I70.20 (Atherosclerosis of arteries of extremities, unspecified)			
		17	I73.9 (Peripheral vascular disease, unspecified)			
7	Asthma, COPD, or chronic bronchitis	18	J44.9 (Chronic Obstructive Pulmonary Disease, Unspecified)	32,611	4.14	3.68 (3.63, 3.72)
		19	J45.9 (Asthma, unspecified)			
8	Chronic hepatitis	20	K76.9 (Liver disease, unspecified)	25,918	3.29	3.02 (2.98, 3.06)
		21	Z22.51 (Carrier of viral hepatitis B)			
9	Stomach problem (reflux, heartburn, or gastric ulcer)	22	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	22,233	2.82	2.52 (2.48, 2.56)
		23	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
10	Thyroid disorder	24	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		25	E05.9 (Thyrotoxicosis, unspecified)			
11	Stroke and TIA	26	G45.9 (Transient cerebral ischaemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		27	I64 (Stroke, not specified as haemorrhage or infarction)			
12	Heart failure (including valve problems or replacement)	28	I50.0 (Congestive heart failure)	20,538	2.61	1.97 (1.94, 2.00)
		29	I51.9 (Heart disease, unspecified)			
13	Kidney disease or failure	30	N03.9 (Unspecified nephritic syndrome, unspecified)	22,221	2.82	1.82 (1.79, 1.84)
		31	N18.9 (Chronic kidney disease, unspecified)			
14	Depression or anxiety	32	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	14,910	1.89	1.81 (1.78, 1.84)
		33	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		34	F41.1 (Anxiety disorder, unspecified)			
15	Chronic urinary problem	35	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
16	Any cancer in the last 5 years	36	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)

17	Osteoporosis	37	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
18	Dementia or Alzheimer's disease	38	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
19	Colon problem (irritable bowel)	39	K58.9 (Irritable bowel syndrome without diarrhoea)	1,517	0.19	0.20 (0.19, 0.21)
20	Chronic musculoskeletal condition causing pain or limitation	No matching ICD-10 code		-	-	-

Appendix 1-2: List of Chronic Conditions (Ge et al. 2018 and 2019)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Dyslipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Osteoarthritis/Gout/RA	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	38,755	4.92	3.89 (3.85, 3.93)
		11	M10.99 (Gout, unspecified, site unspecified)			
		12	M15.9 (Osteoarthritis (OA) - generalized)			
5	Asthma	13	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Heart attack/IHD	14	I25.9 (Chronic ischemic heart disease, unspecified)	36,401	4.62	3.15 (3.12, 3.19)
7	Stroke/TIA	15	G45.9 (Transient cerebral ischemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		16	I64 (Stroke, not specified as haemorrhage or infarction)			
8	CKD	17	N18.9 (Chronic kidney disease, unspecified)	21,638	2.75	1.76 (1.73, 1.78)
9	Depression	18	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		19	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
10	Anxiety disorder	20	F41.1 (Anxiety disorder, unspecified)	6,085	0.77	0.75 (0.73, 0.77)
11	Cancer	21	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
12	Osteoporosis	22	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
13	Chronic bronchitis/emphysema/COPD	23	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)
14	Schizophrenia	24	F20.9 (Schizophrenia, unspecified)	2,889	0.37	0.33 (0.31, 0.34)
15	Heart failure	25	I50.0 (Congestive heart failure)	3,469	0.44	0.29 (0.28, 0.30)
16	Dementia/Alzheimer's	26	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
17	Parkinson's disease	27	G20 (Parkinson's disease)	1,900	0.24	0.15 (0.14, 0.15)

Appendix 1-3: List of Chronic Conditions (Low et al. 2019)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Lipid disorders	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Angina Coronary heart disease Myocardial infarction	10	I25.9 (Chronic ischaemic heart disease, unspecified)	51,264	6.51	4.65 (4.61, 4.70)
		11	I51.9 (Heart disease, unspecified)			
5	Asthma	12	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Moderate liver disease Severe liver disease	13	K76.9 (Liver disease, unspecified)	18,658	2.37	2.13 (2.09, 2.16)
7	Renal disease	14	N28.9 (Disorder of kidney and ureter, unspecified)	21,112	2.68	1.94 (1.91, 1.97)
8	CKD on dialysis or pre-dialysis Chronic kidney disease	15	N18.9 (Chronic kidney disease, unspecified)	21,638	2.75	1.76 (1.73, 1.78)
9	Osteoarthritis	16	M15.9 (Osteoarthritis (OA) - generalized)	18,378	2.33	1.72 (1.70, 1.75)
10	Haemorrhagic stroke Ischemic stroke Stroke	17	I64 (Stroke, not specified as haemorrhage or infarction)	19,808	2.52	1.72 (1.69, 1.74)
11	Hypothyroidism	18	E03.9 (Hypothyroidism)	14,133	1.79	1.51 (1.48, 1.53)
12	Major depression	19	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		20	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
13	Benign prostatic hyperplasia (BPH)	21	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
14	Hyperthyroidism	22	E05.9 (Thyrotoxicosis)	7,873	1.00	1.00* (0.97, 1.02)
15	Anxiety General anxiety disease	23	F41.1 (Anxiety disorder, unspecified)	6,085	0.77	0.75 (0.73, 0.77)
16	Cancer (w/o metastasis) Metastatic carcinoma	24	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
17	Arrhythmia Atrial fibrillation	25	I48 (Atrial fibrillation and flutter)	7,241	0.92	0.58 (0.57, 0.60)
18	Osteoporosis	26	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
19	Chronic obstructive pulmonary disease	27	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)
20	Epilepsy	28	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)	2,734	0.35	0.33 (0.32, 0.35)
21	Schizophrenia	29	F20.9 (Schizophrenia, unspecified)	2,889	0.37	0.33 (0.31, 0.34)
22	Heart failure	30	I50.0 (Congestive heart failure)	3,469	0.44	0.29 (0.28, 0.30)
23	Dementia	31	F03 (Unspecified dementia)	3,571	0.45	0.27

						(0.26, 0.28)
24	Peripheral vascular disease	32	I73.9 (Peripheral vascular disease, unspecified)	2,598	0.33	0.21 (0.21, 0.22)
25	Rheumatoid arthritis	33	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	2,010	0.26	0.19 (0.18, 0.20)
26	Parkinson’s disease	34	G20 (Parkinson’s disease)	1,900	0.24	0.15 (0.14, 0.15)
27	Nephritis	35	N03.9 (Unspecified nephritic syndrome, unspecified)	770	0.10	0.08 (0.07, 0.08)
28	Psoriasis	36	L40.8 (Other psoriasis)	651	0.08	0.08 (0.07, 0.08)
29	Major lower extremity amputation	37	Z89.5 (Acquired absence of leg at or below knee)	236	0.03	0.02 (0.02, 0.02)
		38	Z89.6 (Acquired absence of leg above knee)			
30	Minor lower extremity amputation	39	Z89.4 (Acquired absence of foot and ankle)	122	0.02	0.01 (0.01, 0.01)
31	Bipolar disorder	40	F31.9 (Bipolar affective disorder, unspecified)	51	0.01	0.01 (0.01, 0.01)
32	Hip fracture	No matching ICD-10 code				-
33	Nephrosis	No matching ICD-10 code				-
34	Respiratory failure	No matching ICD-10 code				-
35	Secondary hypertension	No matching ICD-10 code				-
36	Spine fracture	No matching ICD-10 code				-
37	Coronary artery bypass graft	No matching ICD-10 code				-
38	Percutaneous coronary intervention	No matching ICD-10 code				-
39	Kidney transplant	No matching ICD-10 code				-

*The standardized prevalence rate of ‘hyperthyroidism’ is 0.9980% (0.9737, 1.0222).

Appendix 1-4: List of Chronic Conditions (Picco et al. 2016)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	High blood pressure	1	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
2	Diabetes	2	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		3	E11.9 (Type 2 diabetes mellitus without complication)			
		4	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		5	E14.3 (Diabetes mellitus with retinopathy)			
		6	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		7	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		8	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
3	Arthritis or Rheumatism	9	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		10	M15.9 (Osteoarthritis (OA) - generalized)			
		11	M19.99 (Arthritis, unspecified, site unspecified)			
4	Heart trouble (including heart attack, angina, heart failure and valve disease)	12	I51.9 (Heart disease, unspecified)	56,797	7.21	5.11 (5.06, 5.15)
		13	I50.0 (Congestive heart failure)			
		14	I25.9 (Chronic ischaemic heart disease, unspecified)			
		15	I48 (Atrial fibrillation and flutter)			
5	Breathlessness or Asthma	16	J45.9 (Asthma, unspecified)	28,778	3.65	3.37 (3.33, 3.42)
6	Stroke	17	I64 (Stroke, not specified as haemorrhage or infarction)	19,808	2.52	1.72 (1.69, 1.74)
7	Depression	18	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	9,941	1.26	1.20 (1.17, 1.23)
		19	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
8	Cancer	20	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
9	TIA	21	G45.9 (Transient cerebral ischaemic attack, unspecified)	5,158	0.66	0.46 (0.45, 0.48)
10	COPD	22	J44.9 (Chronic obstructive pulmonary disease, unspecified)	5,080	0.65	0.41 (0.40, 0.42)

Appendix 1-5: List of Chronic Conditions (Quah et al. 2016)

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.97 (24.86, 25.07)
2	Hypertension	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes	3	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		4	E11.9 (Type 2 diabetes mellitus without complication)			
		5	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		6	E14.3 (Diabetes mellitus with retinopathy)			
		7	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		8	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		9	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis	10	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		11	M19.99 (Arthritis, unspecified, site unspecified)			
		12	M15.9 (Osteoarthritis (OA) - generalized)			
5	Respiratory diseases	13	J30.4 (Allergic rhinitis, unspecified)	68,048	8.64	8.73 (8.65, 8.80)
		14	J44.9 (Chronic obstructive pulmonary disease, unspecified)			
		15	J45.9 (Asthma, unspecified)			
6	Gastrointestinal diseases	16	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	49,847	6.33	5.76 (5.70, 5.81)
		17	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
		18	K58.9 (Irritable bowel syndrome without diarrhoea)			
		19	K76.9 (Liver disease, unspecified)			
		20	K82.9 (Disease of gallbladder, unspecified)			
		21	Z22.51 (Carrier of viral hepatitis B)			
7	Heart diseases	22	I25.9 (Chronic ischaemic heart disease, unspecified)	56,797	7.21	5.11 (5.06, 5.15)
		23	I48 (Atrial fibrillation and flutter)			
		24	I50.0 (Congestive heart failure)			
		25	I51.9 (Heart disease, unspecified)			
8	Chronic kidney disease	26	N03.9 (Unspecified nephritic syndrome, unspecified)	38,350	4.87	3.36 (3.32, 3.39)
		27	N18.9 (Chronic kidney disease, unspecified)			
		28	N28.9 (Disorder of kidney and ureter, unspecified)			
9	Neurological conditions	29	F03 (Unspecified dementia)	31,093	3.95	2.79 (2.75, 2.82)
		30	G20 (Parkinson's disease)			
		31	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)			
		32	G45.9 (Transient cerebral ischemic attack, unspecified)			
		33	G60.9 (Hereditary and idiopathic neuropathy, unspecified)			
		34	I64 (Stroke, not specified as haemorrhage or infarction)			
10	Thyroid diseases	35	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		36	E05.9 (Thyrotoxicosis, unspecified)			
11	Psychiatric conditions	37	F20.9 (Schizophrenia, unspecified)	18,182	2.31	2.18 (2.15, 2.22)
		38	F29 (Unspecified nonorganic psychosis)			
		39	F31.9 (Bipolar affective disorder, unspecified)			
		40	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)			

		41	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		42	F41.1 (Anxiety disorder, unspecified)			
12	Physical disability	43	H91.9 (Hearing loss, unspecified)	10,514	1.34	1.05 (1.03, 1.08)
		44	Q79.9 (Congenital malformation of musculoskeletal system, unspecified)			
13	Cancer	45	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
14	Back problems	No matching ICD-10 code		-	-	

Appendix 1-6: List of Chronic Conditions (Subramaniam et al. 2014)

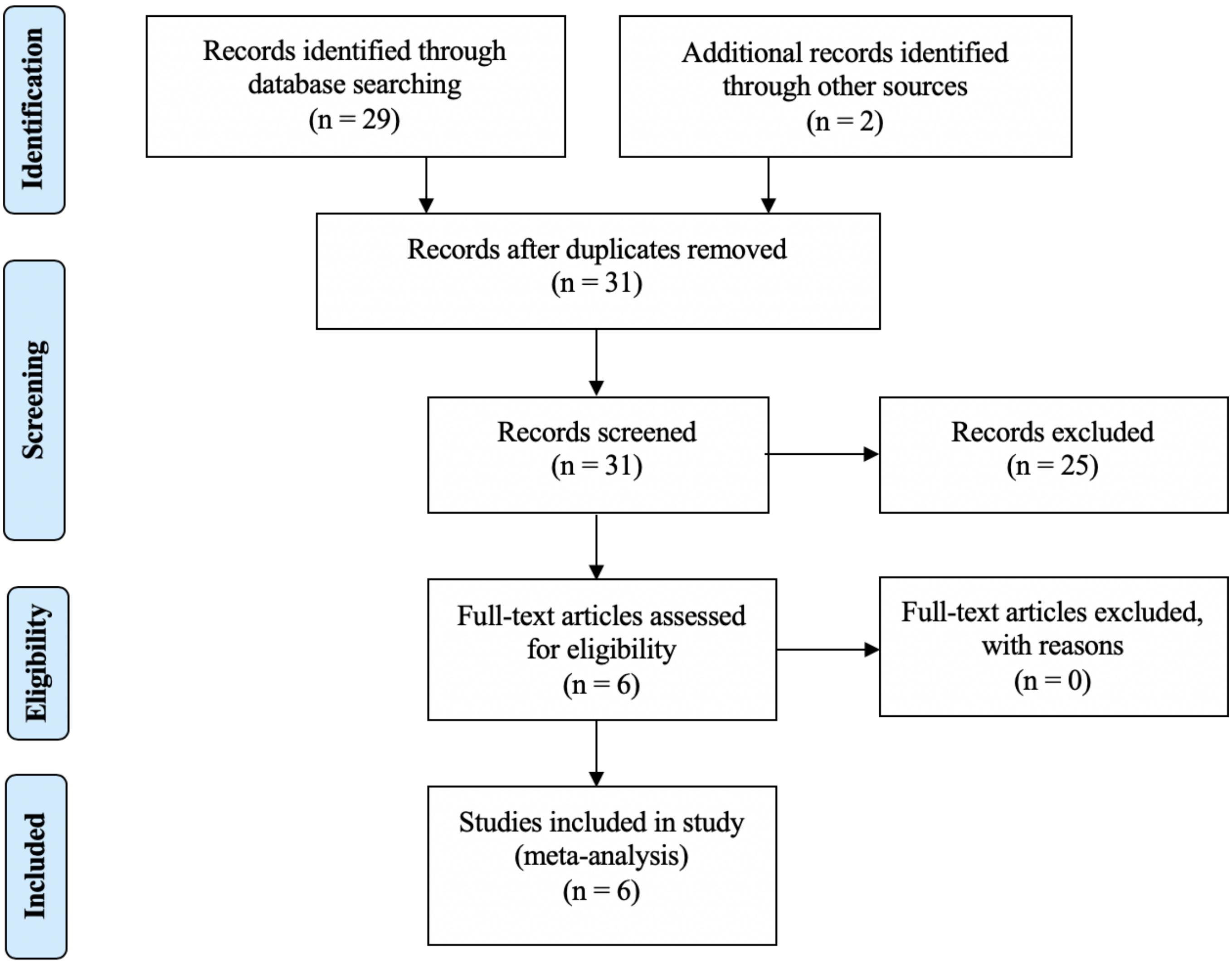
S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hypertension and high blood pressure	1	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
2	Diabetes	2	E10.9 (Type 1 diabetes mellitus without complication)	125,058	15.88	11.86 (11.79, 11.93)
		3	E11.9 (Type 2 diabetes mellitus without complication)			
		4	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		5	E14.3 (Diabetes mellitus with retinopathy)			
		6	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		7	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		8	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
3	Chronic pain (arthritis or rheumatism, back problems including disk or spine, migraine headaches)	9	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	107,090	13.60	11.24 (11.17, 11.31)
		10	M15.9 (Osteoarthritis (OA) - generalized)			
		11	M19.99 (Arthritis, unspecified, site unspecified)			
		12	G43.9 (Migraine, unspecified)			
		13	G50.0 (Trigeminal neuralgia)			
4	Respiratory disorders (asthma, chronic lung disease such as chronic bronchitis or emphysema)	14	J30.4 (Allergic rhinitis, unspecified)	68,048	8.64	8.73 (8.65, 8.80)
		15	J44.9 (Chronic obstructive pulmonary disease, unspecified)			
		16	J45.9 (Asthma, unspecified)			
5	Cardiovascular disorders (stroke or major paralysis, heart attack, coronary heart disease, angina, congestive heart failure or other heart disease)	17	I25.9 (Chronic ischaemic heart disease, unspecified)	73,922	9.39	6.65 (6.60, 6.70)
		18	I48 (Atrial fibrillation and flutter)			
		19	I50.0 (Congestive heart failure)			
		20	I51.9 (Heart disease, unspecified)			
		21	G45.9 (Transient cerebral ischaemic attack, unspecified)			
		22	I64 (Stroke, not specified as haemorrhage or infarction)			
6	Cancer	23	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
7	Neurological disorders (epilepsy, convulsion, Parkinson's disease)	24	G20 (Parkinson's disease)	4,609	0.59	0.48 (0.46, 0.49)
		25	G40.90 (Epilepsy, unspecified, without mention of intractable epilepsy)			
8	Ulcer and chronic inflamed bowel (stomach ulcer, chronic inflamed bowel, enteritis or colitis)	26	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)	3,131	0.40	0.34 (0.33, 0.35)
		27	K58.9 (Irritable bowel syndrome without diarrhoea)			

Appendix 2a: Literature Search Strategy

Database: Ovid MEDLINE(R): 1946 to March Week 1 2020

S/N	Search Terms	Results
1	exp comorbidity/ or multiple chronic conditions/ or multimorbidity	106,975
2	(multimorbid* or multi-morbid* or comorbid* or co-morbid*).ab,ti,kw.	144,228
3	((multiple or coexist* or co-exist* or concurrent* or simultaneous*) adj3 (disease* or illness* or diagnos* or condition* or morbid* or disorder*)).ab,ti,kw.	61,543
4	1 or 2 or 3	263,334
5	(prevalence or association).ab,ti,kw.	1,385,219
6	(Singapore).ab,ti,kw.	12,889
7	4 and 5 and 6	166
8	Set following limits: English language, Human studies, Full Text, 2010 to Current	29

Appendix 2b: PRISMA Flow Diagram



Appendix 3: A Summary of the Differences between Reported Studies on Multimorbidity

	Fortin et al. (Published in 2017)	Ge et al. (Published in 2018)	Ge et al. (Published in 2019)	Low et al. (Published in 2019)	Picco et al. (Published in 2016)	Quah et al. (Published in 2016)	Subramaniam et al. (Published in 2014)
Number of conditions	20	17	17	48	10	14	8
Definition of chronic disease	Conditions that usually last 12 months or more	Diseases that are irreversible and persistent throughout adulthood	Diseases characterised by a long duration and are of a generally slow progression that are irreversible and persistent throughout adulthood	No	No	No	No
Source of list of chronic conditions	Developed from a scoping review of 44 publications on multimorbidity	Not mentioned	Not mentioned	Selected from 3 indexes - the Singapore Chronic Disease Management Programme[1], the Charlson Comorbidity Index[2] and the Elixhauser Comorbidity Index[3]	Not mentioned	Conditions from Singapore Mental Health Study[4] 2010	Modified Composite International Diagnostic Interview (CIDI)[5]
Sources of data	Self-reported* (conditions that have been confirmed by a doctor or for which they are on medications)	At least one of the sources was self-reported or from the NHG Chronic Disease Management System (CDMS) database[6]	Self-reported	Singapore Eastern Regional Health System[7]	Self-reported	Self-reported	Self-reported
Cut-point	Not mentioned	2 conditions	2 conditions	2 conditions	2 conditions	2 conditions	2 conditions
Reference population	Practice-based population	General population	General population	Practice-based population (tertiary hospitals, community hospitals, primary care polyclinics)	General population	Practice-based population (one primary care polyclinic)	General population
Age-group	Not mentioned	≥ 21 years old	≥ 21 years old	0 to 85+ years old	≥ 60 years old	≥ 65 years old	≥ 18 years old

[1] The Chronic Disease Management Programme (CDMP) is an initiative introduced by the Ministry of Health (MOH), Singapore, in 2016 and involves the development of evidence-based structured Disease Management Programmes required in the management of their chronic diseases.
[2] The Charlson Comorbidity Index is a weighted index of 19 chronic conditions that was originally developed to predict the risk of short-term mortality from comorbid disease among patients being treated for primary breast cancer at a single hospital in 1987.
[3] The Elixhauser Comorbidity Index is an index of 30 chronic conditions that was developed to predict hospital charges, length of stay and in-patient mortality among patients 18 years and older from 438 hospitals in California in the year 1992.
[4] The Singapore Mental Health Study (SMHS) is a nationwide epidemiological study undertaken in 2009-2010 that provides insight into some of the common mental health illnesses in the adult Singapore resident population.
[5] The Composite International Diagnostic Interview (CIDI) was designed to allow investigators to reliably assess mental disorders according to the most widely accepted nomenclatures in different populations and cultures by combining questions from the Diagnostic Interview Schedule with questions designed to elicit Present State Examination items in 1988.
[6] The NHG Chronic Disease Management System (CDMS) database is a chronic disease registry within NHG that was commissioned for use in 2014 linking administrative and key clinical data of patients with chronic diseases across the National Healthcare Group cluster in Singapore.
[7] The Singapore Eastern Regional Health System was developed from the integration of the Singapore Health Services (SingHealth) and Eastern Health Alliance (EHA) in 2017.

Measured levels of multimorbidity[8]	No	No	Yes Disease count	Yes Disease count	No	Yes 1. Disease count 2. Drug count	No
Patient-reported outcomes	No	Yes Physical function	Yes 1. Health-related quality of life 2. Self-rated health	No	No	Yes 1. Health-related quality of life 2. Functional disability 3. Chronic musculoskeletal pain	Yes Health-related quality of life

[8] Levels of multimorbidity refers to the combined effects of the multiple conditions that an individual has. This may be based on disease count, that is, the number of chronic conditions the patient has; or other variables such as drug count, which is the number of chronic medications an individual is prescribed.

Appendix 4: List of chronic conditions under Chronic Disease Management Programme (CDMP)

S/N	Conditions
1	Diabetes mellitus and pre-diabetes
2	Hypertension
3	Lipid disorders
4	Asthma
5	Chronic obstructive pulmonary disease (COPD)
6	Chronic kidney disease (nephritis/nephrosis)
7	Schizophrenia
8	Major depression
9	Bipolar disorder
10	Anxiety
11	Stroke
12	Dementia
13	Osteoarthritis
14	Parkinson's disease
15	Benign prostatic hyperplasia (BPH)
16	Epilepsy
17	Osteoporosis
18	Psoriasis
19	Rheumatoid arthritis (RA)
20	Ischemic heart disease (IHD)

Appendix 5a: List of ICD-10 diagnosis codes matched to the chronic conditions studied by each author

S/N	ICD-10 Codes	Fortin et al. 2017	Ge et al. 2018 and 2019	Low et al. 2019	Picco et al. 2016	Quah et al. 2016	Subramaniam et al. 2014
1	E78.5	✓	✓	✓		✓	
2	I10	✓	✓	✓	✓	✓	✓
3	E11.9	✓	✓	✓	✓	✓	✓
4	M19.99	✓			✓	✓	✓
5	J30.4					✓	✓
6	E66.9	✓					
7	J45.9	✓	✓	✓	✓	✓	✓
8	I25.9	✓	✓	✓	✓	✓	✓
9	K21.9	✓				✓	
10	K76.9	✓		✓		✓	
11	M10.99		✓				
12	N28.9			✓		✓	
13	N18.9	✓	✓	✓		✓	
14	I51.9	✓		✓	✓	✓	✓
15	M15.9	✓	✓	✓	✓	✓	✓
16	I64	✓	✓	✓	✓	✓	✓
17	E03.9	✓		✓		✓	
18	N40	✓		✓			
19	F32.90	✓	✓	✓	✓	✓	
20	Z22.51	✓				✓	
21	E05.9	✓		✓		✓	
22	H91.9					✓	
23	G43.9						✓
24	F41.1	✓	✓	✓		✓	
25	C80	✓	✓	✓	✓	✓	✓
26	I48	✓		✓	✓	✓	✓
27	M81.99	✓	✓	✓			
28	E14.31	✓	✓	✓	✓	✓	✓
29	G45.9	✓	✓	✓	✓	✓	✓
30	J44.9	✓	✓	✓	✓	✓	✓
31	K82.9					✓	
32	G40.90			✓		✓	✓
33	F20.9		✓	✓		✓	
34	E10.9	✓	✓	✓	✓	✓	✓
35	I50.0	✓	✓	✓	✓	✓	✓
36	F03	✓	✓	✓		✓	
37	F32.20	✓	✓	✓	✓	✓	
38	I73.9	✓		✓			
39	K58.9	✓				✓	✓
40	M06.99	✓	✓	✓	✓	✓	✓
41	F29					✓	
42	E14.73	✓	✓	✓	✓	✓	✓
43	G20		✓	✓		✓	✓
44	K27.9	✓				✓	✓
45	G60.9					✓	
46	Q79.9					✓	
47	I70.20	✓					
48	E14.2	✓	✓	✓	✓	✓	✓
49	N03.9	✓		✓		✓	
50	G50.0						✓
51	Z89.5			✓			
52	E14.3	✓	✓	✓	✓	✓	✓
53	F31.9			✓		✓	
54	Z89.6			✓			
55	Z89.4			✓			
56	E14.64	✓	✓	✓	✓	✓	✓
57	L40.8			✓			

Appendix 5b: Descriptors of ICD-10 diagnosis codes

S/N	ICD-10 Codes	Descriptors
1	E78.5	Hyperlipidaemia, unspecified
2	I10	Essential (primary) hypertension
3	E11.9	Type 2 diabetes mellitus without complication
4	M19.99	Arthritis, unspecified, site unspecified
5	J30.4	Allergic rhinitis, unspecified
6	E66.9	Obesity, unspecified
7	J45.9	Asthma, unspecified
8	I25.9	Chronic ischaemic heart disease, unspecified
9	K21.9	Gastro-oesophageal reflux disease without oesophagitis
10	K76.9	Liver disease, unspecified
11	M10.99	Gout, unspecified, site unspecified
12	N28.9	Disorder of kidney and ureter, unspecified
13	N18.9	Chronic kidney disease, unspecified
14	I51.9	Heart disease, unspecified
15	M15.9	Osteoarthritis (OA) - Generalised
16	I64	Stroke, not specified as haemorrhage or infarction
17	E03.9	Hypothyroidism, unspecified
18	N40	Hyperplasia of prostate
19	F32.90	Depressive episode, unspecified, not specified as arising in the postnatal period
20	Z22.51	Carrier of viral hepatitis B
21	E05.9	Thyrotoxicosis, unspecified
22	H91.9	Hearing loss, unspecified
23	G43.9	Migraine, unspecified
24	F41.1	Anxiety disorder, unspecified
25	C80	Malignant neoplasm without specification of site
26	I48	Atrial fibrillation and flutter
27	M81.99	Other osteoporosis, site unspecified
28	E14.31	Unspecified diabetes mellitus with background retinopathy
29	G45.9	Transient cerebral ischaemic attack, unspecified
30	J44.9	Chronic Obstructive Pulmonary Disease, Unspecified
31	K82.9	Disease of gallbladder, unspecified
32	G40.90	Epilepsy, unspecified, without mention of intractable epilepsy
33	F20.9	Schizophrenia, unspecified
34	E10.9	Type 1 diabetes mellitus without complication
35	I50.0	Congestive heart failure
36	F03	Unspecified dementia
37	F32.20	Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period
38	I73.9	Peripheral vascular disease, unspecified
39	K58.9	Irritable bowel syndrome without diarrhoea
40	M06.99	Rheumatoid arthritis, unspecified, site unspecified
41	F29	Unspecified nonorganic psychosis
42	E14.73	Unspecified diabetes mellitus with foot ulcer due to multiple causes
43	G20	Parkinson's disease
44	K27.9	Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation
45	G60.9	Hereditary and idiopathic neuropathy, unspecified
46	Q79.9	Congenital malformation of musculoskeletal system, unspecified
47	I70.20	Atherosclerosis of arteries of extremities, unspecified
48	E14.2	Diabetes mellitus with incipient diabetic nephropathy
49	N03.9	Unspecified nephritic syndrome, unspecified
50	G50.0	Trigeminal neuralgia
51	Z89.5	Acquired absence of leg at or below knee
52	E14.3	Diabetes mellitus with retinopathy
53	F31.9	Bipolar affective disorder, unspecified
54	Z89.6	Acquired absence of leg above knee
55	Z89.4	Acquired absence of foot and ankle
56	E14.64	Unspecified diabetes mellitus with hypoglycaemia
57	L40.8	Other psoriasis

Appendix 6: List of Chronic Conditions in Proposed Operational Definition of Multimorbidity

S/N	Conditions	S/N	ICD-10 Codes	Patient Count	Crude Prevalence Rate	Standardised Prevalence Rate (95% CI)
1	Hyperlipidaemia	1	E78.5 (Hyperlipidaemia, unspecified)	257,114	32.65	24.79 (24.86, 25.07)
2	Hypertension (high blood pressure)	2	I10 (Essential (primary) hypertension)	221,760	28.16	20.93 (20.84, 21.02)
3	Diabetes (including pre-diabetes)	3	E09 (Impaired glucose regulation)	150,294	19.09	14.28 (14.20, 14.35)
		4	E099 (Impaired glucose regulation without complication)			
		5	E10.9 (Type 1 diabetes mellitus without complication)			
		6	E11.9 (Type 2 diabetes mellitus without complication)			
		7	E14.2 (Diabetes mellitus with incipient diabetic nephropathy)			
		8	E14.3 (Diabetes mellitus with retinopathy)			
		9	E14.31 (Unspecified diabetes mellitus with background retinopathy)			
		10	E14.64 (Unspecified diabetes mellitus with hypoglycaemia)			
		11	E14.73 (Unspecified diabetes mellitus with foot ulcer due to multiple causes)			
4	Arthritis &/or rheumatoid arthritis	12	M06.99 (Rheumatoid arthritis, unspecified, site unspecified)	100,838	12.81	10.43 (10.36, 10.50)
		13	M15.9 (Osteoarthritis (OA) - Generalised)			
		14	M19.99 (Arthritis, unspecified, site unspecified)			
5	Obesity	15	E66.9 (Obesity, unspecified)	48,893	6.21	5.29 (5.24, 5.34)
6	Cardiovascular disease (angina, MI, AF, poor circulation of lower limbs)	16	I25.9 (Chronic ischaemic heart disease, unspecified)	43,559	5.53	3.74 (3.71, 3.78)
		17	I48 (Atrial fibrillation and flutter)			
		18	I70.20 (Atherosclerosis of arteries of extremities, unspecified)			
		19	I73.9 (Peripheral vascular disease, unspecified)			
7	Asthma, COPD, or chronic bronchitis	20	J44.9 (Chronic Obstructive Pulmonary Disease, Unspecified)	32,611	4.14	3.68 (3.63, 3.72)
		21	J45.9 (Asthma, unspecified)			
8	Chronic hepatitis	22	K76.9 (Liver disease, unspecified)	25,918	3.29	3.02 (2.98, 3.06)
		23	Z22.51 (Carrier of viral hepatitis B)			
9	Stomach problem (reflux, heartburn, or gastric ulcer)	24	K21.9 (Gastro-oesophageal reflux disease without oesophagitis)	22,233	2.82	2.52 (2.48, 2.56)
		25	K27.9 (Peptic ulcer, unspecified as acute or chronic, without haemorrhage or perforation)			
10	Thyroid disorder	26	E03.9 (Hypothyroidism, unspecified)	20,781	2.64	2.36 (2.32, 2.39)
		27	E05.9 (Thyrotoxicosis, unspecified)			
11	Stroke and TIA	28	G45.9 (Transient cerebral ischaemic attack, unspecified)	23,628	3.00	2.07 (2.04, 2.10)
		29	I64 (Stroke, not specified as haemorrhage or infarction)			
12	Heart failure (including valve problems or replacement)	30	I50.0 (Congestive heart failure)	20,538	2.61	1.97 (1.94, 2.00)
		31	I51.9 (Heart disease, unspecified)			
13	Kidney disease or failure	32	N03.9 (Unspecified nephritic syndrome, unspecified)	22,221	2.82	1.82 (1.79, 1.84)
		33	N18.9 (Chronic kidney disease, unspecified)			
14	Depression or anxiety	34	F32.20 (Severe depressive episode without psychotic symptoms, not specified as arising in the postnatal period)	14,910	1.89	1.81 (1.78, 1.84)
		35	F32.90 (Depressive episode, unspecified, not specified as arising in the postnatal period)			
		36	F41.1 (Anxiety disorder, unspecified)			
15	Chronic urinary problem	37	N40 (Hyperplasia of prostate)	13,031	1.65	1.07 (1.05, 1.09)
16	Physical disability	38	H91.9 (Hearing loss, unspecified)	10,514	1.34	1.05

		39	Q79.9 (Congenital malformation of musculoskeletal system, unspecified)			(1.03, 1.08)
17	Any cancer in the last 5 years	40	C80 (Malignant neoplasm without specification of site)	7,940	1.01	0.68 (0.66, 0.69)
18	Osteoporosis	41	M81.99 (Other osteoporosis, site unspecified)	7,283	0.92	0.57 (0.56, 0.59)
19	Dementia or Alzheimer's disease	42	F03 (Unspecified dementia)	3,571	0.45	0.27 (0.26, 0.28)
20	Colon problem (irritable bowel)	43	K58.9 (Irritable bowel syndrome without diarrhoea)	1,517	0.19	0.20 (0.19, 0.21)

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