ARTICLE

Co- and multi-morbidity patterns in an unselected Norwegian population: cross-sectional analysis based on the HUNT Study and theoretical reflections concerning basic medical models

Margret Olafia Tomasdottrir MDa, Linn Getz MD PhDb, Johann A. Sigurdsson MD Dr medc, Halfdan Petursson MD PhDd, Anna Luise Kirkengen MD Dr mede, Steinar Krokstad MD PhDf, Bruce McEwen PhDg and Irene Hetlevik MD Dr medb

a GP and Research Fellow, Department of Family Medicine, University of Iceland, Reykjavík, Iceland
b Professor, General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
c Professor, Department of Family Medicine, University of Iceland, Reykjavik, Iceland & General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
d Researcher, General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
e Professor, General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
f Director, HUNT Research Centre, The Nord-Trøndelag Health Study Centre (HUNT), Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
g Professor & Head of Laboratory, Laboratory of Neuroendocrinology, The Rockefeller University, New York, NY, USA
h Professor, General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

Abstract

Rationale and aims: Accumulating evidence shows that diseases tend to cluster in diseased individuals, so-called multimorbidity. The aim of this study was to analyze multimorbidity patterns, empirically and theoretically, to better understand the phenomenon.

Population and methods: The Norwegian population-based Nord-Trøndelag Health Study HUNT 3 (2006-8), with 47,959 individuals aged 20-79 years. A total of 21 relevant, longstanding diseases/malfunctions were eligible for counting in each participant. Multimorbidity was defined as two or more chronic conditions.

Results: Multimorbidity was found in 18% of individuals aged 20 years. The prevalence increased with age in both sexes. The overall age-standardized prevalence was 42% (39% for men, 46% for women). ‘Musculoskeletal disorders’ was the disease-group most frequently associated with multimorbidity. Three conditions, strategically selected to represent different diagnostic domains according to biomedical tradition; gastro-esophageal reflux, thyroid disease and dental problems, were all associated with both mental and somatic comorbid conditions.

Conclusions and implications: Multimorbidity appears to be prevalent in both genders and across age-groups, even in the affluent and relatively equitable Norwegian society. The disease clusters typically transcend biomedicine’s traditional demarcations between mental and somatic diseases and between diagnostic categories within each of these domains. A new theoretical approach to disease development and recovery is warranted, in order to adequately tackle ‘the challenge of multimorbidity’, both empirically and clinically. We think the concept allostatic load can be systematically developed to “capture” the interrelatedness of biography and biology and to address the fundamental significance of “that, which gains” versus “that, which drains” any given human being.

Keywords

Adverse life events, allostatic load, disease classification, disease clustering, multimorbidity, person-centered care, theory of science

Correspondence address

Professor Linn Getz, General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway. E-mail: linn.getz@ntnu.no

Accepted for publication: 30 May 2013
Introduction

By biomedical convention, most diseases are conceptualized, diagnosed and treated as single and independent entities [1-5]. Recently, however, we have witnessed rapidly increasing interest in co- and multimorbidity patterns [1-4,6-12]. Many, even most, consultations in primary care involve patients with multimorbidity [13]. Primary care providers typically carry the main clinical responsibility for multimorbid patients, except when uncommon conditions are involved [7]. Patients with a relatively low socio-economic status and a correspondingly high disease burden have been shown to use a comparable amount of primary care services, but less specialized out-patient care, compared to patients from higher socioeconomic strata [14,15].

Valid information about the frequency and nature of disease co-occurrence and clustering in individual persons is crucial for organizing effective healthcare, ranging from disease classification and reimbursement systems via training of personnel to development of clinical guidelines and preventive programs. Gathering reliable evidence is, however, demanding [16,17]. There is a well-documented association with age, but multimorbidity has been shown to be prevalent even in younger age groups [13,18]. A recent Scottish study, based on a comprehensive primary care database, found that, numerically, more than half of the individuals with multimorbidity were younger than 65 years [19]. Some co-morbid disease associations are particularly well-documented, such as the co-occurrence of depression and metabolic syndrome/cardiovascular disease [20-23]. Until now, prevalence estimates, organizational and therapeutic implications, as well as the general health impact of co-and multimorbidity, have received most scientific attention, but there is also rising interest in causal mechanisms and pathways, ranging from the genetic to the environmental level [24]. Research from various contexts documents that multimorbidity is increased by low socioeconomic status [19,25-29]. Job strain is also associated with worse health and increased disease burden [25,30-32]. Concerning biomolecular mechanisms, some researchers focus on specific pathways, such as systemic inflammation [22,33] or autonomic imbalance [34], while others apply a systems-oriented, life-course perspective [24,35,36]. The US Adverse Childhood Experiences study found a dose-response relationship between adverse childhood circumstances and the number of diseases in adult life, both in the somatic and mental domains [37,38]. Scientific explanations of how adversity gets “under the skin” have been developing and converging over the last decade [39-43].

To sum up, the scientific knowledge pertaining to multimorbidity is rapidly advancing, but still incomplete at every level [44], ranging from prevalence data and cluster descriptions across populations and subgroups (gender, ethnicity, social class), down to precise conceptualization of what - and how - lifetime experience become embodied [45] in a life-course perspective. The aim of the present study was to deepen existing knowledge about the distribution and nature of disease clustering and multimorbidity. We present and discuss data from a Norwegian population study which, by international comparison, represents an affluent, stable and ethnically homogenous society with only moderate degrees of social inequality.

Study population and methods

Our data come from the Nord-Trøndelag Health Study (HUNT), a renowned, longitudinal, total adult population-based study [46]. The third wave, HUNT 3, was carried out 2006-2008. All adults 20 years and above were invited to participate. In total 27,779 women and 23,060 men participated; the participation rate was 54% [46]. Our study group is shown in Table 1. An analysis of non-participants showed that the oldest and youngest groups were somewhat underrepresented, along with people of lower socioeconomic status [47]. The HUNT population has been considered fairly representative for Norway, but since Nord-Trøndelag lacks large cities, the social gradient in the HUNT population might be smaller than for Norway as a whole [15,46].

Table 1 Participants and participation rates according to age groups and gender

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>% of invited</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>4,276</td>
<td>30.0</td>
<td>2,517</td>
<td>1,759</td>
</tr>
<tr>
<td>30-39</td>
<td>6,906</td>
<td>43.9</td>
<td>4,024</td>
<td>2,882</td>
</tr>
<tr>
<td>40-49</td>
<td>9,982</td>
<td>56.3</td>
<td>5,440</td>
<td>4,542</td>
</tr>
<tr>
<td>50-59</td>
<td>11,391</td>
<td>65.8</td>
<td>5,981</td>
<td>5,410</td>
</tr>
<tr>
<td>60-69</td>
<td>9,741</td>
<td>70.6</td>
<td>5,112</td>
<td>4,629</td>
</tr>
<tr>
<td>70-79</td>
<td>5,663</td>
<td>65.9</td>
<td>3,036</td>
<td>2,627</td>
</tr>
<tr>
<td>Total</td>
<td>47,959</td>
<td>54.8</td>
<td>26,110</td>
<td>21,849</td>
</tr>
</tbody>
</table>

The HUNT 3 data were collected by means of questionnaires, interviews, clinical examinations and blood and urine samples. For the present analysis, we included participants aged 20-79 years. We selected 21 relevant disease conditions for an analysis of multimorbidity (Table 2). Twelve of these conditions were self-reported in response to the question “Have you had or do you have the following medical condition?” Regarding cardiovascular disease (CVD), we included the following conditions: a history of myocardial infarction, angina pectoris, heart failure, other heart disease and/or stroke. Hypertension was defined as a positive answer to the question “Do you take or have you taken antihypertensive medicine?” and/or severe hypertension (systole ≥180 mmHg and/or diastole ≥110) [48] at the clinical examination. To avoid double registration, the presence of self-reported CVD was used as an exclusion criterion, as the definition was based on use of medication. Hyperlipidemia was defined as fasting total cholesterol above 7.0 mmol/L and/or fasting triglycerides above 3.0 mmol/L. Chronic back pain was based on a report of having pain/stiffness in the back or neck that had
lasted more than 3 months during the last year. Thyroidal disease was defined as either hyper- or hypothyroidism; dental health problems when the participant defined dental health as bad or very bad; gastro-esophageal reflux as much heartburn/acid regurgitation during the last year and, finally, clinically relevant mental problems were defined as a positive answer to the global question: “Have you had or do you have mental health problems for which you have sought help?”

We estimated the prevalence of multimorbidity as a simple count of 2 or more co-occurring diseases and/or relevant conditions in the same person [9], age-specific as well as age-standardized (European standard) [49]. Prevalence numbers of mental health problems were estimated in relation to somatic health and odds ratios (ORs) were generated for the association of mental health problems with the number of somatic health problems. In our analyses of multimorbidity, missing values for independent diseases were defined as negative.

Regarding specific diseases and their associations, we focused on the group 40-59 years, where disease prevalences are typically higher than in younger age groups and multimorbidity prevalences lower than in older age groups. We excluded participants with missing data about the disease in question (Table 2). Associations of selected diseases were tested with Chi-square test and odds ratios, with 95% confidence intervals (CI) generated. We decided to look more closely at disease clustering around 3 strategically selected conditions which, according to biomedical tradition, would be regarded as relatively different and distinct: that is, gastro-esophageal reflux, thyroid disease and dental health problems (including periodontal disease). SPSS statistical program (version 20) was used for calculations.

**Ethical approval**

Each participant in the HUNT Study signed a written consent regarding the screening and the use of data for research purposes. The study was approved by the Norwegian Data Inspectorate and the Regional Committee for Ethics in Medical Research.

**Results**

We analyzed data from 47,959 eligible HUNT 3 participants, aged 20-79 years. Figure 1 shows the prevalence of multimorbidity and how it steadily increases from 14% among people aged 20, to 33% for people aged 40 to 62% for people aged 60 and to 77% for people aged 79 years. The overall age-standardized prevalence of multimorbidity in the age group 20-79 years was 42%. Bold numbers in the figure add information regarding the number of diseases/conditions. The data show a significant difference (p<0.001) in prevalence

### Table 2 Disease prevalences (%) in the age-group 40-59 years (absolute numbers within brackets)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Total</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>5.3</td>
<td>3.6</td>
<td>7.2</td>
</tr>
<tr>
<td>Renal disease</td>
<td>2.3</td>
<td>2.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13.0</td>
<td>13.2</td>
<td>12.7</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>20.2</td>
<td>17.2</td>
<td>23.7</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.8</td>
<td>2.3</td>
<td>3.4</td>
</tr>
<tr>
<td>Obesity</td>
<td>23.0</td>
<td>22.1</td>
<td>24.0</td>
</tr>
<tr>
<td>COPD</td>
<td>2.5</td>
<td>2.6</td>
<td>2.2</td>
</tr>
<tr>
<td>Asthma</td>
<td>9.2</td>
<td>9.5</td>
<td>8.9</td>
</tr>
<tr>
<td>Chronic back pain</td>
<td>37.1</td>
<td>42.2</td>
<td>31.2</td>
</tr>
<tr>
<td>Mental health problems</td>
<td>15.0</td>
<td>18.5</td>
<td>11.1</td>
</tr>
<tr>
<td>Cancer</td>
<td>3.2</td>
<td>4.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>6.4</td>
<td>6.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Gastro-esophageal reflux</td>
<td>7.2</td>
<td>6.7</td>
<td>7.9</td>
</tr>
<tr>
<td>Thyroidal diseases</td>
<td>6.7</td>
<td>10.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Dental health problems</td>
<td>7.5</td>
<td>7.1</td>
<td>8.1</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>10.6</td>
<td>13.7</td>
<td>7.1</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>4.1</td>
<td>6.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>3.2</td>
<td>3.7</td>
<td>2.7</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>2.0</td>
<td>1.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>1.1</td>
<td>1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>1.3</td>
<td>1.4</td>
<td>1.3</td>
</tr>
</tbody>
</table>
between genders; males had a total prevalence of 39%, compared to 46% among women.

The gender differences are further detailed in Table 2. They were most prominent for the most common diseases, with musculoskeletal conditions and mental health problems being far more common among women, whilst CVD and hyperlipidemia were more common in men (Table 2). In the age group 40-59 years, however, the most common diseases were equally prevalent for both genders;
chronic back pain, obesity, hyperlipidemia and mental health problems.

Figure 2 shows how the prevalence of mental health problems increased with the number of somatic health conditions. The association was greatest in the youngest group (20-39 years), with an OR increasing from 1.5 (95% CI 1.3-1.7) in the presence of one somatic disease to 6.9 (95% CI 4.5-10.6) in the presence of 5 or more somatic diseases. The results were similar for the 40-59 year group, where OR = 1.4 (95% CI 1.3-1.6) for one disease and OR = 5.1 (95% CI 4.3-6.0) for 5 or more diseases. The association was much weaker in the oldest age group (60-79 years), where the odds ratio did not differ significantly from 1.0 for one disease, but increased steadily from 1.3 (95% CI 1.1-1.6), with 2 diseases to 2.8 (95% CI 2.3-3.5) in the presence of 5 or more diseases.

We also analyzed the prevalence of multimorbidity with respect to single diseases among participants, aged 40-59 (Figure 3). Multimorbidity prevalence was highest in association with musculoskeletal diseases (fibromyalgia, ankylosing spondylitis, rheumatoid arthritis, osteoarthritis). A striking morbidity load was observed in association with gastro-esophageal reflux, thyroid disease and dental health problems. Consequently, we selected these “index” conditions and specifically addressed their degree of “overlap”, as illustrated by Venn diagrams in Figure 4. The degree of overlap between diseases ranged from 13% to 32%. The overlap between any 2 of the selected diseases (Table 3) had odds ratios ranging from 1.3 (95% CI 1.2-1.4) for the well-documented combination mental health problems metabolic diseases (obesity or diabetes) to 3.5 (95% CI 3.1-4.1) for mental health problems/fibromyalgia. All overlaps shown in Figure 4 were significantly greater than expected by chance (p<0.01).

Discussion

In this unsellected and general Norwegian population with only moderate degrees of social inequity, multimorbidity proved to be common in all adult age-groups. The prevalences of the most common diseases were comparable in both genders, while multimorbidity as such was more common among women. An overall age-standardized multimorbidity prevalence of 42% is in accordance with some earlier reports [6,17].

The dose-response association between the number of somatic and mental disorders was prominent in all but the oldest age group. This finding is in accordance with previous research [19]. Beyond this, our study provides additional documentation of disease clustering, indicating identifiable patterns linked to the selected index conditions gastro-esophageal reflux, thyroidal disease and dental/periodontal health, again in accordance with previous observations [50-60]. Our findings add to the accumulating documentation that patterns of morbidity are ubiquitous and transcend the biomedical dichotomies somatic/mental and organic/functional and also the diagnostic categories within the specialized medical domains. This can be seen as posing a fundamental challenge to biomedicine’s current way of conceptualizing risk, disease and recovery [24,61-63].

Looking for ways to deepen our scientific understanding of disease clustering and multimorbidity, we think it might be fruitful to study multimorbidity from the perspective of approach.

The concept was introduced by Silverman and Eyer in the 1980s [64] and has subsequently been nuanced, developed and debated, see for instance [26,35,36,40,41,65-74]. Allostasis essentially refers to the body’s (including the brain’s) dynamic adaptation to challenges across multiple physiological systems, through which the organism actively adjusts to predictable and unpredictable experiences and stressors, small and big, ‘physical’ and ‘mental’, over time. Allostatic load neutrally denotes the cumulative impact of strain over time, while allostatic overload denotes a “red flag” physiological risk scenario, where the organism’s adaptive and restorative capacity is overtaxed to such an extent that adaptability and flexibility is gradually lost [75]. The result is physiological dysregulation, at times expressed only in subtle but widespread perturbations. These might, in accordance with complexity theory, nevertheless have a significant cumulative impact on the entire organism. Allostatic overload provides ‘soil’ for disease development, influenced by individual, genetic susceptibilities, eventual maladaptive, non-favorable ways of living (unhealthy lifestyle) and even the microbiome [76,77]. With reference to a booming scientific interest in systems biology in general and systems medicine in particular [24], the allostasis concept might be compatible with a theoretical framework of the lived body, the lifelong embodiment of personal experience [78].

The main repository of the lived experience is the person’s brain, with its capacity for decoding and memory and its paramount regulatory monitoring of systemic mediators of the autonomic, neuroendocrine, metabolic and immune systems that can promote allostatic overload. Moreover, in a situation of allostatic overload, these systemic mediators affect not only peripheral targets, such as organs, tissues and cells, but also “fire back on” the brain itself, including regions involved in cognitive, emotional and self-regulatory functions and result in remodeling of neural architecture that alters these functions as well as epigenetic changes that alter DNA methylation and patterns of gene expression [79,80]. The principally inevitable wear and tear on the body and brain take a toll on every individual, but the more efficiently allostatic is “buffered” or “counterweighted”, the longer the ravages of cellular aging and disease development can in principle be delayed. Fortunately, the healthy brain has a considerable potential for reactivation of plasticity, providing new possibilities in the treatment of conditions previously believed to be very difficult, if not impossible, to change [36,81].

Grounded in the natural sciences, the concept allostasis can accommodate advancing scientific knowledge about biomolecular mechanisms and pathways. It is already an established framework for conceptualization of the detrimental impact of socioeconomic disadvantage and adverse lifetime experiences [26,36,41,57,58].

339
Figure 3 Number and distribution of disease clustering / multimorbidity by index diseases in the age-group 40-59 years. COPD = Chronic obstructive pulmonary disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>No other disease</th>
<th>One other disease</th>
<th>Two other diseases</th>
<th>3+ other diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibromyalgia</td>
<td>34</td>
<td>118</td>
<td>188</td>
<td>503</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>26</td>
<td>101</td>
<td>105</td>
<td>184</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>42</td>
<td>95</td>
<td>132</td>
<td>402</td>
</tr>
<tr>
<td>COPD</td>
<td>34</td>
<td>86</td>
<td>93</td>
<td>311</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>188</td>
<td>477</td>
<td>557</td>
<td>970</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>21</td>
<td>42</td>
<td>49</td>
<td>128</td>
</tr>
<tr>
<td>Diabetes</td>
<td>55</td>
<td>110</td>
<td>129</td>
<td>313</td>
</tr>
<tr>
<td>Gastro-esophageal reflux</td>
<td>107</td>
<td>268</td>
<td>271</td>
<td>530</td>
</tr>
<tr>
<td>Thyroidal diseases</td>
<td>148</td>
<td>262</td>
<td>237</td>
<td>478</td>
</tr>
<tr>
<td>Dental health problems</td>
<td>176</td>
<td>321</td>
<td>290</td>
<td>513</td>
</tr>
<tr>
<td>Renal disease</td>
<td>71</td>
<td>111</td>
<td>122</td>
<td>217</td>
</tr>
<tr>
<td>Hypertension</td>
<td>404</td>
<td>629</td>
<td>644</td>
<td>914</td>
</tr>
<tr>
<td>Mental health problems</td>
<td>493</td>
<td>797</td>
<td>739</td>
<td>1099</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>219</td>
<td>342</td>
<td>296</td>
<td>513</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>180</td>
<td>291</td>
<td>263</td>
<td>392</td>
</tr>
<tr>
<td>Asthma</td>
<td>323</td>
<td>488</td>
<td>397</td>
<td>763</td>
</tr>
<tr>
<td>Obesity</td>
<td>893</td>
<td>1350</td>
<td>1149</td>
<td>1509</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>55</td>
<td>75</td>
<td>55</td>
<td>90</td>
</tr>
<tr>
<td>Cancer</td>
<td>139</td>
<td>166</td>
<td>135</td>
<td>242</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>738</td>
<td>992</td>
<td>758</td>
<td>944</td>
</tr>
<tr>
<td>Chronic back pain</td>
<td>1825</td>
<td>2211</td>
<td>1746</td>
<td>2145</td>
</tr>
</tbody>
</table>

Figure 4 Five Venn-diagrams of associations between diseases in age-group 40-59 years. a) Association between cardiovascular group (cardiovascular diseases, hypertension or hyperlipidemia), mental health problems and metabolic diseases (diabetes or obesity). b) Association between mental health problems, fibromyalgia and thyroidal diseases. c) Association between mental health problems, rheumatoid arthritis (RA) and lung diseases (COPD or asthma). d) Association between musculoskeletal problems (chronic back pain, fibromyalgia, rheumatoid arthritis, osteoarthritis or ankylosing spondylitis), gastro-esophageal reflux and mental health problems and e) Association between musculoskeletal problems, dental problems and cardiovascular group.
From the perspectives of adaptation and resilience, evidence of restorative (salutogenic) factors and their relation to allostatic processes [82] can be encompassed in an ethnically and culturally sensitive manner, ranging from a clean environment, healthy nutrition and physical activity to societal justice, organizational fairness [30] and respectful, supportive relationships [74,83]. In our mind, even the most fundamental human issues can be evoked: as only one of several current research trajectories, linked to the concept of allostasis [73] and illuminated by philosophical and artistic representations of human nature. Associated with the concept of allostasis might be the traditional biomedical focus on single disease conditions according to the "disease silo" model [2], both the researchers who designed the survey and the participants, were “blinded” to the research questions, so expectation bias can be ruled out. Most diagnoses/diagnostic labels in our study are self-reported, in contrast to studies based on medical records. This can be considered both a weakness and a strength. Self-reported health information might better reflect the individual’s quality of life [89] and can be seen as providing a more person-centered overview of the medical history and experienced burden of disease than medical records do.

As the HUNT Study was conceived in accordance with the traditional biomedical focus on single disease conditions according to the “disease silo” model [2], both the researchers who designed the survey and the participants, were “blinded” to the research questions, so expectation bias can be ruled out. Most diagnoses/diagnostic labels in our study are self-reported, in contrast to studies based on medical records. This can be considered both a weakness and a strength. Self-reported health information might better reflect the individual’s quality of life [89] and can be seen as providing a more person-centered overview of the medical history and experienced burden of disease than medical records do.

Conclusions, implications and recommendations

Contributing evidence from an unselected, general population in an affluent Nordic society, our study confirms that disease clustering and patterns of multimorbidity seem to support that they are more the rule than the exception, at least in Western societies. So what practical implications do we see? On the level of primary practice, we advocate person-focused care as outlined by the late Barbara Starfield [4,90], including attention to the patient’s lived experience as appropriate [91] and wise participation rates were lowest in the youngest and oldest age groups, especially for young males. A comparison between participants and non-participants showed that the latter were of lower socioeconomic status and had higher prevalence of index diseases and higher mortality [46,47]. This might contribute to an underestimation of multimorbidity in our study.

From the perspectives of adaptation and resilience, evidence of restorative (salutogenic) factors and their relation to allostatic processes [82] can be encompassed in an ethnically and culturally sensitive manner, ranging from a clean environment, healthy nutrition and physical activity to societal justice, organizational fairness [30] and respectful, supportive relationships [74,83]. In our mind, even the most fundamental human issues can be evoked: as only one of several current research trajectories, linked to the concept of allostasis [73] and illuminated by philosophical and artistic representations of human nature. Associated with the concept of allostasis might be the traditional biomedical focus on single disease conditions according to the "disease silo" model [2], both the researchers who designed the survey and the participants, were “blinded” to the research questions, so expectation bias can be ruled out. Most diagnoses/diagnostic labels in our study are self-reported, in contrast to studies based on medical records. This can be considered both a weakness and a strength. Self-reported health information might better reflect the individual’s quality of life [89] and can be seen as providing a more person-centered overview of the medical history and experienced burden of disease than medical records do.
support of each individual’s adaptability and experience of health [92]. Consultation time should be allocated according to needs [29]. Disease-oriented guidelines should be adapted to clinical realities [93-95]. On a societal and political level, it is urgent to define and, as far as possible, eliminate the major contributions of social inequality and detrimental life circumstances to the burden of morbidity [29,91]. But our professional response to the challenge of multimorbidity must definitely extend even beyond practical, organizational and political action. A thorough analysis of the essence of the multimorbidity phenomenon is needed. The observation that so many diseases tend to cluster is likely to represent an artifact of pathophysiological substrates, on the one hand and an understanding of disease burdens springing from existential and experiential hardship, on the other [25,61,78]. A deeper understanding of the ultimate sources of pathogenesis and recovery is needed to aid researchers, clinicians and policymakers to move forward in a sensible and sustainable manner. As explained above, we think further, interdisciplinary work linked to the concept allostatic load might be fruitful.

Acknowledgements and Conflicts of Interest

The authors thank Henrik Vogt, MD and Research Fellow at the General Practice Research Unit in Trondheim, for contributing substantial knowledge to the discussion in general and in particular regarding current development in systems medicine. This has relevance for further work with the concept of allostatics and multimorbidity in the clinical setting.

The HUNT3 Survey was mainly funded by the Norwegian Ministry of Health, the Norwegian University of Science and Technology, the Norwegian Research Council (the FUGE program), Central Norway Regional Health Authority, the Nord-Trondelag County Council and the Norwegian Institute of Public Health. Funding was also contributed by some commercial enterprises and other contributors [46]. The present analysis received support from the Research Fund of the Icelandic College of Family Physicians. The authors declare no conflicts of interest.

References

[12] The International Research Community on Multimorbidity (IRCMo)’s blog on multimorbidity [website]. Available at: https://pages.usherbrooke.ca/crmcspl-blog/ (accessed 2 April 2013)
from an Australian biomedical study. *BMC Public Health* 10 (1) 718.


