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Full Length Research Paper

Chronic conditions and multimorbidity in the Swiss primary care population

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To provide valid and representative epidemiologic estimates of prevalent chronic condition and multimorbidity in the Swiss primary care population, prospective planned cross-sectional study was utilized. Swiss primary care, Swiss Sentinel Surveillance Network, calendar weeks 11 and 12, 2015. 175 general practitioners (GP) or pediatricians (PED) with 26'853 patient contact. Thurgau Morbidity Index (TMI) (scores from 0=healthy to 6=multiple severe chronic conditions). Patients were 55.8±21.6 or 6.1±5.7 years old (mean±SD, in GPs vs. PEDs) and 47% were males. In GP patients, median TMI was 2 (IQR: 1-3). The median numbers of chronic conditions and permanently-used prescribed drugs were 2 (0-5) and 2 (1-4), respectively, whereas in the PEDs medians were 0. 16.7% of the GP and 7.0% of the PED patients had been hospitalized at least once during the previous year; patients cared by family/proxies or community nurses had been hospitalized significantly more often than patients living in homes (50.1 vs. 35.4%, OR 1.41, p<0.001). 51.5% of the patients over 80 years of age were caredependent, and 45.5% of the patients over 90 were living in homes for the elderly. In a representative sample of Swiss primary care patients, a substantial part showed multimorbidity with a high burden for disease, treatment and care-dependency. Trial registration: www.clinicaltrials.gov NCT0229537, national study registrywww.kofam.ch SNCTP000001207.

Keywords: Multimorbidity, comorbidity, morbidity, drug treatment, drug utilization, polymedication, polypharmacy, caredependency, hospitalization, primary health care, patient care management, delivery of health care, adult, child, Switzerland.

INTRODUCTION

Due to the aging of most societies worldwide, there has been an increase in the prevalence of chronic conditions and multimorbidity (Uijen, 2008; Barnett 2012; PradosTorres 2014). We define multimorbidity as three or more conditions that cumulate in one subject, whether they are related or not. This needs to be distinguished from comorbidities, which describe conditions related to some disorder of primary interest. For example, renal failure, peripheral neuropathy and retinopathy are comorbidities of diabetes and thus form a cluster of interdependent

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conditions (Prados-Torres 2014). Most elderly people with multiple chronic conditions are cared for in primary care, and there are concerns that the system cannot keep pace with the chronic disease epidemic to provide appropriate care (Bodenheimer, 2009). Persons suffering from multimorbidity have a burden to bear, including function loss, becoming dependent on care, and suffering from pain. They need to commit substantial amounts of time for health care visits as well as for disease management. Patients with multiple chronic conditions are more likely to become socially isolated, and often times are confronted with increased costs, not to mention loss of years of life (Gijsen, 2001). The patients' families and proxies may be involved as informal care givers and deliver care which poses additional challenges in terms of time and resources required. Society is affected by higher costs, the need to provide healthcare facilities and a decrease of the workforce (Federal Office of Public Health, 2015).

However, valid and nationally representative epidemiologic data are often scarce in Switzerland and other countries. In addition, whereas Switzerland has solid data on inpatient services, there is an almost complete lack of data on outpatient services including primary care where patients with chronic conditions are primarily cared for. Data on the burden of chronic diseases are important to plan for appropriate health care services for patients with chronic conditions and multimorbidity.

Therefore, the aim of this study was to provide valid and representative epidemiologic estimates of the prevalence of chronic conditions and multimorbidity in the Swiss primary care population.

METHOD

Sample

This analysis was based on the data collected for another study in Swiss primary care patients (Gnädinger2015). The study took place in the Swiss Sentinel Surveillance Network (Sentinella), a network of approximately180 general practitioners (GPs) and pediatricians (PEDs). This system was founded in 1986 to survey transmissible diseases (http://www.sentinella.ch/de/info). Later, other issues relevant for family medicine were also investigated in this system. It performs a denominator analysis twice a year to define its patient collective. For this study, the analysis of physician-to-patient contacts (PPC) was expanded by the collection of data related to multimorbidity. Any patient consulting a GPor PED practice participating in Sentinella between March 7th and March 20th, 2015, was included. Patients refusing data transmission to the Sentinella system were excluded. Furthermore, to characterize their practices and to evaluate potential difficulties with the study methodology, the *Sentinella* physicians filled in two questionnaires, one at the beginning and one at the end of the study (Gnädinger M 17).

Written instructions were delivered to the physicians by the *Sentinella* administration(Appendix A). Detailed information on the definitions of the study parameters is shown in Appendix B. Appendix C lists frequently asked questions.

Ascertainment of chronic conditions and multimorbidity

The year of birth and gender were recorded for each patient. Physicians provided the Thurgau Morbidity Index (TMI) (Fischer2007) as the primary indicator for the prevalence of chronic conditions and multimorbidity, and their seriousness; it increases with the number of chronic conditions and their severity (Appendix B). As secondary indicators, we included the number of chronic conditions, the number of prescribed drugs taken regularly, the Evans Index (comorbidity-polypharmacy score)(Evans2012), any hospitalization during the previous twelvemonths, and care-dependency. Evans Index was calculated by the simple addition of the numbers of chronic conditions and drugs. Since the physicians filling in the questionnaires were not trained to use a detailed nursina scale to measure caredependency(Noelker2014), we created a simple four-step Likert-type scale item (i.e. no care, care by proxies, by community nurse, or by an institution); because the item was equivocal to PED patients, analysis was restricted to adult patients > 20 years. A repeat visit was defined as a second or further visit during the fourteen days of data collection; we could not differentiate between no repeat consultation or a missing answer since physicians only reported if a repeat visit occurred. For each physician, we ascertained the Sentinella coding number, the specialty, and the language region.

Assessment of how the study sample represented Swiss GPs and the target population

To determine the representativeness of our sample we performed some comparisons: firstly, we compared our records to the data obtained by the New Index AG, Olten (a merger of Swiss trust center organizations excluding the canton of Vaud) for 2014. Most physicians are contracted to a trust center; the data should, therefore, draw a representative picture of Swiss patients. Secondly, we compared the *Sentinella* physician characteristics (age, gender, specialization) with the dataset of 2014 obtained from the Swiss Medical Association (FMH)in Berne, including all Swiss physicians, with information on their specialization. Virtually all physicians working in Switzerland are members of the FMH. Thirdly, to verify complete inclusion, we compared our data with those from an earlier *Sentinella* fourteen-day analysis limited to the collection ofgender and age data performed in August 2014.And finally, to describe the practice size, we received the number of PPC for 2015 from the *Sentinella* administration.

Statistical methods

Values are given as frequencies, mean \pm SD or median [interquartile range (IQR)], depending on the distribution of the data. Because of non-normal distribution of the numbers of drugs and conditions as well as the ordinal data level of TMI or care-dependency variables, correlation analyses were assessed with Spearman's Rho. To assess the representativeness of the patients and participating physicians, we used unpaired T- or Chi-square tests to identify statistically significant inferences.

To assess the association of multimorbidity with hospitalization, we used the SPSS GENLINMIXED procedure, a procedure that fits generalized linear mixed models. Clustering of patients was addressed by using a mixed binary logistic regression with the fixed factors of gender, age, care-dependency, number of chronic drug treatments, number of chronic conditions, and TMI as well as the physician's practice number as a random factor. If one item was missing, the whole record was excluded from the analysis. We used SPSS 24.

RESULTS

Records

We received 26'853 PPC data records; 27.5% were transmitted electronically, the rest by mail as paper/pencil documents. 22'379 records concerned weeks 11 and 12, 2'504 week 13, while the remaining 1'970 records stem from weeks 8 - 10 and 14 - 26, respectively. The records of two physicians who provided more than two weeks of reporting were restricted to the calendar weeks 11 and 12 as scheduled.

Description of study physicians and comparison to all Swiss GPs and PEDs

During 2015, 151 practices were registered in the *Senti-nella* system (where a physician's code does not necessarily correspond to one physician only), corresponding to 193 physicians. Out of the 151 practices, 144 (94.7%), corresponds to 180 physicians, regularly reported to the

Sentinella system (which means that they announced PPCs for at least 39 weeks a year). 119 comprised one reporting physician, 19 two, 5 three, and 1 eight, summarizing a total of 180 physicians.122 (67.8%) were German-speaking, 44 French (24.4%) and 14 Italian (7.8%). Their characteristics are listed in Table 1 which also provides comparative information with FMH data on all Swiss physicians.

Response rate and difficulties in variable coding

Two practices reporting regularly to the *Sentinella* system and comprising of five GPs did not deliver morbidity data. This led to a sample of 142 practices and 175 physicians. During 2015, the mean number of PPC was 4'456±2'137 in GPs, and 5'297±2'715 in PEDs. Figure 1 summarizes the response rates of the different items. In 20'602 records concerning adult patients, all variables were coded in 18'297 cases (88.8%). As a measure of completeness of reporting two weeks of morbidity data, we assumed that a proportion of 3.3% or more of the yearly PPC would be sent to our study database; this was achieved by 161 (92.0%) of the physicians. Items concerning problems of the study physicians with coding of the morbidity variables are listed in table e1 (Appendix E) and the frequently asked questions in Appendix C.

Description of patients and comparison to all patients in Swiss primary care

Out of the 26'853 records,12'606 concerned male patients (47.0%), 14'209 females (52.9%), and in 38 (0.1%) of them information on gender was missing. Table 2 lists the age categories separately by gender and compares them with New Index data for GPs; Table 3 does so for PEDs. This comparison demonstrates that the patients consulting the Sentinella physicians are representative of the overall Swiss primary care collective. A comparison of a fourteen-day analysis of age and gender in August 2014 with the current data did not reveal any significant differences of age (47.2 \pm 27.5 vs. 47.5 \pm 27.1 years) and gender (47.0 vs. 47.5% males) proportions (2015 vs. 2014, respectively).

Prevalence of chronic disease and multimorbidity in Swiss primary care patients

TMI scale values in GP practices were: 0 in 4'752 patients (23.7%), 1 in 3'160 (15.7%), 2 in 3'972 (19.8%), 3 in 3'854 (19.2%), 4 in 2'099 (10.5%), 5 in 1'537 (7.5%) and 6 in 702 (3.7%) (Totaling 20'076 valid and 1'876 missing recordings). In PEDs, the results were: 0 in3'711 (85.4%), 1 in451 (10.4%), 2 in 130 (3.0%), 3 in 23 (0.5%), 4 in 20 (0.5%), 5 in 2 (0.0%), and 6 in 7 (0.2%), respectively (totaling 4'344 valid and 557 missing recordings).

Parame	eter		Sentinella collective 2015	FMH collective 2014
Number	r of physicians		180	6'929
Gender				
	male		71%	66%
	female		29%	34%
Age		categories		
U U	< 40	years	7%	9%
	40 – 49) years	24%	25%
	50 - 59	years	37%	34%
	60 years and ov	er	32%	32%
Special	ty			
•	GP		82%	86%
	PED		18%	14%

Table 1. Comparison of the Sentinella vs. FMH physician collectives: Comparisons of Sentinella and FMH groups by chi-square were not significant. The two practices that did not report morbidity data were also included in this table, because they were otherwise part of the Sentinella physician collective.

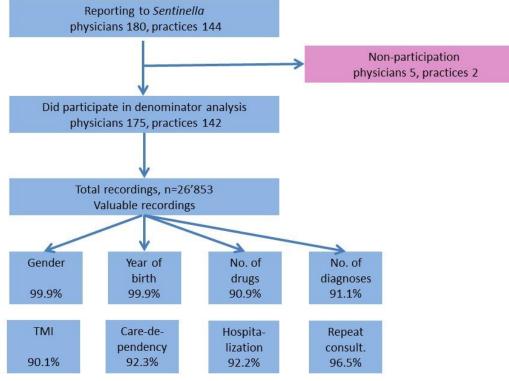


Figure 1. Flow chart of the study and reporting rates: Care-dependency was only evaluated for adults >19 years. The number of observations without missing values was 18.297 (only adult patients).

The distribution of TMI data by age group is shown in Figure 2.

The secondary indicators of multimorbidity showed a similar pattern. Table e2 (Appendix E) summarizes the morbidity variables (hospitalization, care-dependency, condition and drug counts, Evans index, TMI, and repeat

visit) by age categories and gender. The number of chronic **conditions** in GP patients was 2 (1-4) (median, interquartile range [IQR]) and in PEDs 0 (0-0). The spread of chronic conditions is depicted in Figure e1 (Appendix E). In GP patients, the median number of prescribed drugs taken regularly was 2 (0-5); in PEDs 0 (0-0); the

Table 2. Age and gender proportion of patients, percent values (%), GP data: *New Index data correspond to health (but *not* accident) insurance tariff, consultations and home visits, whole year 2014, n=12'180'910, 56.6% females. *Sentinella* data correspond to 21'918 consultation or home visit records (54.2% female patients). Median testing revealed that the male patient group of New Index was slightly older (p<0.001, median estimation by Hampel: *Sentinella* 55.2 y and New Index 56.3 y).

Age group, years	male patients		female patients	
	Sentinella	NewIndex*	Sentinella	NewIndex*
	n = 10'040	n = 5'282'285	n = 11'878	n = 6'898'625
91 and over	1.8	1.5	3.8	3.0
81 to 90	9.6	10.0	13.3	13.1
71 to 80	14.9	16.6	15.7	16.1
61 to 70	16.8	18.1	14.8	15.2
51 to 60	16.7	16.6	14.6	14.6
41 to 50	14.3	13.0	13.1	13.3
31 to 40	10.2	8.9	10.4	9.7
21 to 30	9.0	7.4	8.5	8.3
11 to 20	5.2	5.5	4.6	5.1
0 to 10	1.5	2.4	1.2	1.6

Table 3. Age and gender proportion of patients, percent values (%), pediatricians: *New Index data correspond to health (but *not* accident) insurance tariff, consultations and home visits, whole year 2014, n=1'624'908, 47.2% females. *Sentinella* data correspond to 4'897consultation or home visit records (47.6% female patients). Median testing revealed that the female patient group of New Index was slightly older (p<0.001, median estimation by Hampel: *Sentinella* 4.8 y and New Index 5.3 y).

Age group, years	male patients		female patients			
	Sentinella	NewIndex*	Sentinella	NewIndex*		
	n = 2'566	n = 857'850	n = 2'331	n = 767'058		
20 and over	0.9	1.5	0.8	3.0		
16 to 20	5.5	4.0	6.1	5.0		
11 to 15	16.4	17.9	16.1	18.4		
5 to 10	30.6	26.9	28.7	26.1		
4	6.4	7.4	6.7	7.2		
3	7.0	8.1	7.0	7.7		
2	11.1	10.4	12.0	9.9		
0 to 1	22.1	23.8	22.6	22.7		

maximum number of drugs was 25 in GPs and 7 in PEDs. Polymedication (>4 drugs) was present in 20.7% of the patients, increasing to 60.9% in very elderly (80+). The distribution of the number of chronic drugs by age is depicted in Figure 3. The median value of the **Evans' index** was 4 (1-9) in GPs and 0 (0-1) in PEDs; the age distribution is depicted in Figure e2 (Appendix E).

Hospitalization during the previous year was reported in 3'383 of 20'280 records (16.7%) in GPs (1'672 missing), and in 315 of 4'481 records (7.0%) in PEDs (420 missing). Logistic regression (GENLINMIXED procedure) showed positive and statistically significant associations of hospitalization with care-dependency, age, number of chronic drug treatments, number of chronic conditions, and TMI; female gender had a weak but not statistically significant negative association (Table 4). The model showed a negative predictive value of 96.6%, and positive predictive value of 24.9% for previous hospitalization. Outpatients (care-dependency grades 1 and 2) were

statistically significantly more frequently hospitalized than inpatients living in homes (grade 3) (50.1 vs. 35.4%, OR 1.41, p<0.001 by chi-square test); this association remained statistically significant also in the adjusted analysis (Table 4).

Multiple visits during the fortnight interval were recorded as follows: in GPs 1'703 out of 21'022 PPC (8.2%, 930 records excluded), and in PEDs 241 out of 4'901 (4.9%). Because of a misunderstanding, five physicians marked all patients known to the practices as repeat visits; their records were excluded. In the GP patient group, the mean age of records with a second or further visit was one year older compared to the initial visit records (56.9±21.7 vs. 55.8±21.7 years, p=0.042), while in PED practices the opposite was true (5.3±5.6 vs. 6.1±5.7 years, p=0.035). Gender distribution was not different in repeated as compared to first visits.

Age distribution of **care-dependency** is depicted in Figure 4. Because our questionnaire did not offer the answer

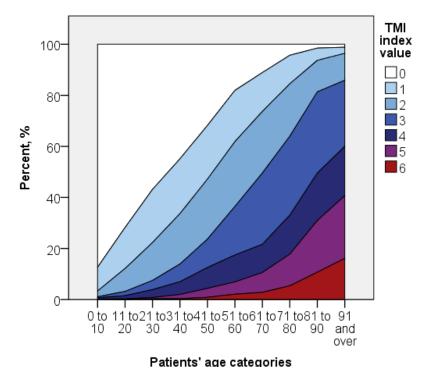


Figure 2. TMI values, percent %. The index values denote: "0" healthy, "1" premorbid, "2" one or two mild-to-moderate conditions, "3" three and more mild-to-moderate conditions, "4" one severe and less than three mild-to-moderate conditions, "5" one severe and three or more mild-to-moderate conditions, "6" two or more severe conditions. Graduations denote the entire class.

Table 4. Logistic regression using hospitalization in previous year as target variable. Crude and adjusted odds ratios (adult patients only).

	crude (mean, 95% CI)	adjusted (mean, 95% CI)
gender*	0.997 (0.904-1.055), p>0.05	0.908 (0.832-0.991), p= 0.030
age (per year)	1.029(1.027-1.032), p<0.001	0.994 (0.991-0.997), p<0.001
conditions (per naming)	1.294 (1.274-1.315), p<0.001	1.038 (1.015-1.062), p=0.001
drugs(per naming)	1.244 (1.229-1.259), p<0.001	1.031 (1.011-1.050), p=0.002
Thurgau Morbidity Index (per grade)	1.903 (1.849-1.958), p<0.001	1.650 (1.584-1.718), p<0.001
Care-dependency by:		
- family / proxies	6.844 (5.914-7.920), p<0.001	2.875 (2.445-3.380), p<0.001
-community nurse	8.474 (7.196-9.979), p<0.001	3.219 (2.743-3.949), p<0.001
- institution / home	4.297 (3.725-4.958), p<0.001	1.515 (1.284-1.788), p<0.001
		• •

*(1=male, 2=female), n=18'297.

"care of minors by parents", this item was equivocal and could not be evaluated in pediatric patients.

Correlations among measures of multimorbidity and regional variation

The correlation matrix (Spearman's Rho) revealed that all variables (previous hospitalization, care-dependency, num-

ber of prescribed drugs regularly taken, number of chronic diagnoses, TMI and Evans' index) were statistically significantly correlated with each other. They were also correlated with age and- except hospitalization-gender (Table 3, Appendix E). Compared to patients living in German or French speaking regions, we found a statistically significantly lower morbidity load of patients living in the Italian speaking region, i.e. TMI, number of drugs, number of conditions,

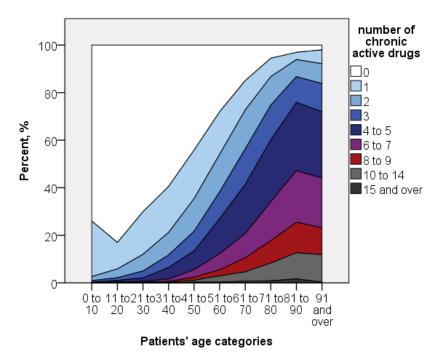


Figure 3. Number of prescribed drugs regularly taken, percent values (%). Graduations denote the entire class.

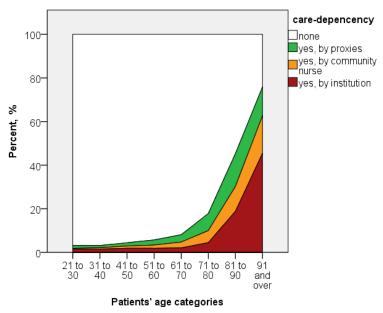
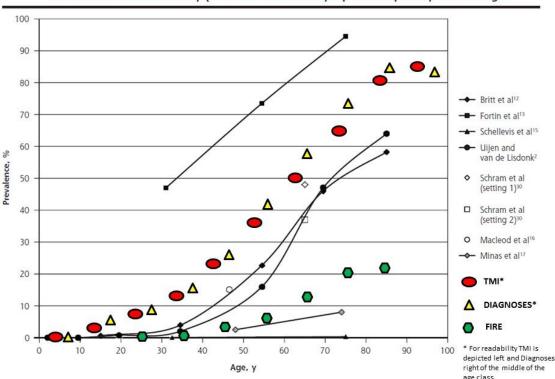


Figure 4. Care-dependency by age groups(percent values%, adult patients only). Graduations denote the entire class.

and Evans Index (Figures e3 to e6, Appendix E). However, the sample was small as expressed by the large error bars.

DISCUSSION

We collected morbidity data in primary care by the



Prevalence of multimorbidity (defined as ≥3 diseases) reported in primary care settings.

Figure 5. Comparison of Thurgau Morbidity Index (≥3) or chronic conditions (≥3) with literature (Fortin 2012, see figure 3 of that article, with permission). This review collected consultation-derived information in primary care settings from several studies and compared the prevalence of three or more chronic conditions by age groups. However, the Swiss FIRE data (Rizza 2012) were not consultation- but registry-based.

Sentinella network with representative physician and patient collectives in Switzerland with a high participation rate of 90%. In the adult patients, we found a median TMI value of 3, which means that half of the patients had at least three or more chronic conditions of mild to moderate severity. Similarly, half of the patients had three or more drug treatments. Half of the patients who are over 80 years of age were care-dependent. These data indicate a substantial burden from chronic disease and multimorbidity in the Swiss primary care population and an enormous financial and organizational load on the health system (Bähler, 2015) and on the patients, themselves and their families (Jaspers, 2015).

Thurgau Morbidity and Evans Index

In our study, the Thurgau Morbidity as well as the Evans indices rose with increasing age. The former index was developed to predict cost in insurance collectives (Fischer, 2007). The latter has shown to correlate with survival in trauma patients (Evans, 2012; Holmes, 2014), inhospital complications and the need for extended care facilities (Justiniano, 2015), and re-admissions (Housley, 2015). When coding TMI, the same condition can impact differently depending on whether it is either active or stable or whether it is socially sensitive or not. This fact solves the problem of diagnosis splitting of list-based indices (e.g. hypertension with or without end-organ damage), but introduces subjectivity to the coding of TMI. On the one hand, TMI does not differentiate between conditions of mild and moderate degree. On the other, we did not receive questions from the participating physicians that concerned the TMI (see Appendix C), which leads to the conclusion that after some training, TMI coding works easily and intuitively. However, as easy as it may be to code TMI for the GP, it may not be appropriate for automated index construction from existing databases. In contrast to an earlier study by Fischer et al. we found lower proportions of codes 2, 3 and 6 and more codes 0 and 1 (Figure e7, Appendix E); however, that study did not include consecutive patients as ours did and being designed to predict insurance costs it therefore tended to include a more ill patient collective (Fischer JE, personal communication).

Number of chronic conditions

We compared our data on morbidity with those from a review by Fortin et al. (2012) and determined it to be a good fit with earlier studies (Figure 5). As expected, within our data the TMI coding of 3 and over was slightly less frequent compared to the reporting of three and more chronic conditions, because the latter additionally included latent and past diagnoses. The computer-based Swiss data by Rizza et al. (2012) derived from the FIRE project showed a much lower rate of three and more conditions than ours. This difference may be explained by the fact that our data were consultation-based, whereas the ones by FIRE were registry-based (ill patients have more visits than healthy people). Furthermore, the FIRE physicians came up with significant under diagnosing of common disorders (Zellweger, 2014); perhaps this was less often the case in our cross-sectional study.

An overall population cohort study in the city of Lausanne on self-reported and measured multimorbidity found an overall prevalence of 23 – 56% depending on the definition used (Pache2015). Guidelines provide recommendations for patients with one single condition, but multimorbidity is the rule and not the exception in primary care (Treadwell, 2015). Following guidelines developed for each single condition in multimorbid patients may be complicated, resulting in conflicts, more costs, is time consuming for the patients, and sometimes even dangerous (Boyd, 2005; Markun, 2014).

Number of drugs taken regularly

A Swiss study on a health insurance collective revealed polypharmacy in 17% of the population, increasing to 50% in very elderly (80+) (Blozik 2013), This proportions are similar to the ones in the present study (20.7% and 60.9%, respectively). In contrast to an Italian study by Nobili et al. (2009), describing a mean number of 2.4±2.4 (±SD) prescribed drugs taken regularly by elderly patients aged 65 years and older in 2003, our patients in that age group used, on average 4.9±3.3 drugs. But there were some differences in the definition of regular treatments: in the work by Nobili, the cut-off was 12 months of treatment, while in ours it was one month. Nobili did not include herbal medicines, whereas we did in our study; furthermore, we also included topical treatment with possible systemic action. The Nobili data were registrybased, while ours stemmed from actual visits. Another publication by Skoog et al. (2014) confirmed our observation that drug prescription increases with age, female gender, and morbidity. In a cohort study on very elderly (80+), Wauters et al. (2016) described a median number of five regularly used drugs; female gender, low education, moderate alcohol consumption, multimorbidity, depression and lack of physical activity were linked to polypharmacy. A study on patients at the time of hospital discharge described an increased risk of polypharmacy (>16 drugs) in patients with two or more of the following high-risk diagnoses: COPD, cancer, diabetes mellitus, congestive heart failure, and coronary heart disease (Rohrer, 2013). The reduction in the proportion of young patients with a single regular treatment from the first to the second decade (24% vs. 18%, Figure 3) could possibly reflect the vitamin D rickets prophylaxis of 0 to threeyear-old infants. We did not evaluate the appropriateness of medication in our study patients; however, another study is now investigating reducing inappropriate medication in multimorbid patients (Hasler, 2015). A recent study by Rausch et al. described the total number of drugs and inappropriate drugs as associated with hospitalizations for unintentional poisoning (2017).

Hospitalization

We found that (previous) hospitalization was best predicted by the TMI value, and somewhat less by the caredependency scale. However, TMI values were not independent of the hospitalization status - hospital stay can redefine a given condition coding from mild/moderate to severe. Therefore, the correlation observed in our study may perhaps reflect an inverse causality, i.e. from the hospitalization to the TMI. Interestingly, institutionalized patients had a lower risk of being hospitalized as compared to people cared for by their family or proxies, as well as by the community nurse (OR 6.8 and 8.5 vs. 4.3); this association also remained statistically significant in the adjusted analysis. In the case of acute illness, this may be explained by resilient caring networks for institutionalized persons as compared to people living at home. Another explanation could be that caregivers were more reluctant to hospitalize patients with advanced disease living in homes because no curative treatment was possible and care could be delivered in the home as well.

Care-dependency

The current report of the European Observatory on Health Systems and Policies mentions that 4.2% of the Swiss population receive professional long-term care; 64% of them are at home and 36% in an institution. Additionally, 4.7% of the population (and 16.5% of those over 75) receives care by their family or proxies, not to mention persons cared for by migrant workers (De Pietro, 2015).

There are a lot of consequences of care-dependency such as loss of personal independency, a burden to the social network, and financial demand (Bähler, 2015, Jaspers, 2015). An ongoing study investigates the disease and treatment burden of Swiss primary care patients (Déruaz-Luyet, 2015). In our study, half of the patients in the age group over 80 were care-dependent and almost half of the seniors over 90 lived in homes for the elderly. A substantial proportion of the care was delivered by family and proxies as informal caregivers. And even if carried out by professionals, in contrast to other countries, in Switzerland more than half of the money spent on care is covered by private expenditures (OECD, 2011). This seems important as care for inpatients living in homes for the elderly costs six times more than care for outpatients (1.8% of general domestic product as compared to 0.3%, respectively) (OECD, 2011). This leads to people foregoing healthcare services due to financial reasons (Bodenmann, 2015).

Strengths and limitations

The strengths of the study include representative physician and patient collectives, prospective data collection by a research-experienced physician community, and a large sample size.

Possible weaknesses of our study are that we did not have the opportunity to implement systematic data quality control measures such as double entry or controls within one physician. Also, we did not ascertain specific chronic conditions but rather used aggregate measures of multimorbidity. TMI is not validated as a measure of morbidity and is prone to subjectivity in judgment of chronic condition severity. However, this is a challenge for any method to ascertain chronic conditions and their severity. Another limitation is that drugs unknown to the physicians could not be recorded.

CONCLUSION

In a representative sample of Swiss primary care patients, a substantial part shows multimorbidity with a high prevalence of chronic diseases, multiple drug treatment, and care-dependency. Such data are important for policy makers and health authorities who make decisions about the type and extent of primary care needed to address the chronic disease epidemic of the ageing population.

Contribution statement

MG led the study, did the pilot study (questionnaire development, data entering and processing) wrote all documents, conducted all contacts with the *Sentinella* administration, ethics committee, and others, programmed the electronic questionnaires, entered hand-written questionnaires into the database, did the data processing and wrote the publication after data collection.

AC is an expert on clinical pharmacology and drug safety.

DC is an expert on patient safety.

LH is French-speaking and helped to interpret the French questionnaires. She is an expert on multimorbidity. She is a member of the *Sentinella* program commission.

MP is head of Epidemiology, Biostatistics & Prevention Institute. He is responsible for the sound methodology.

AS had the idea for the study. He is vice president of the *Sentinella* program commission.

MZ is an expert on electronic data exchange in primary care.

All of them have seen all the study documents. All have contributed to revise the draft of this publication and approve the submitted version of this publication.

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Competing interests

The authors declare that they have no financial interest conflicts with this study.

Data sharing statement

No additional data are available.

Independent ethical committee (IEC)

The ethical committee of the Canton of Zurich waived our study since they decided that it did not need formal approval according to the regulations of the law on human research in Switzerland (KEK-ZH 2014-0400). The study was recorded in <u>www.ClinicalTrials.gov</u>: NCT02295371, as well as in our national study registry (<u>www.kofam.ch</u>; SNCTP000001207).

STROBE statement

Where applicable, our publication follows the general STROBE guidelines (<u>http://www.equator-network.org/</u>) (Appendix D).

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APPENDIX

Appendix A

Procedures for data collection in the practices (for paper and pencil patient records)

The practice nurse informed the patients that we had to note study statistics. She asked the patient whether the list of chronic drugs was still up-to-date. If not, she made a note for the doctor. She asked the patients whether they were cared for by their family or by the community nurse. She also asked the patients whether they had been hospitalized during the preceding year.

She filled in the following fields on the questionnaire: last name, first name, gender, year of birth, hospitalization, care-dependency, number of chronic conditions and previous visits during the fortnight interval. She made a postit note for every patient who had been seen during the study period.

She presented the patient files twice daily to the physician. He then controlled the fields that were coded by the nurse and encoded the fields "number of prescribed drugs taken regularly" and "Thurgau Morbidity Index" himself.

Doing it this way, the coding time per patient was 1.6 mins for the nurse and 0.7 mins for the physician (MG).

Appendix B

Determining the denominator

For this study, you should transmit only the data of the patient file and not enter new data. If you cannot answer an item, mark "unknown" or "9/99" (Morbidity index, drug or condition number). Each field requires an entry, except "repeat visit". Some information can be filled in by the practice nurse; but final checking and correcting before sending it to *Sentinella* administration is up to the physician.

Care-dependency

The possible answers are 1 = "yes, by proxies", 2 = "yes, by community nurse", 3 = "yes, by institution", 4 = "none", 5 = "unknown". If a person makes more than one yesanswer, then select the higher number. For the study, people requiring home help or meal service are coded with "2". Examples: Persons living in a home for the elderly are coded with "3". People living in a residence for the elderly and visited by a community nurse are coded with "2". People living at home and cared for by their family (i.e. children, demented) are coded with "1".

Number of drugs

Each pharmacological preparation which is *chronically* prescribed scores with one point per active substance included. We consider a treatment to be chronic if it is applied for at least one month. Medication for shorter treatment periods (e.g. antibiotics) should not be included. Eye drops, inhalations or nasal sprays count only if a *systemic* effect is intended (calcitonine nasal

0 1 0 0	
Does not count	Homeopathy, Schusslers salts, externals (without systemic effect), vitamins (if not medically indi- cated), on-demand medication, self-medication. Eve drops. Nasal spray without systemic effect.
	Short-time treatment (less than one month).
Counts as one drug	Herbal medicine, multivitamins (if medically indi- cated)
Counts per substance included	All other medication

Table 1. Recording of prescribed drugs taken regularly.

spray) or must be accepted as unavoidable (timolol eye drops). We also want to register transdermal, subcutaneous or vaginal hormone delivering systems, or medication prescribed by a specialist (gynecologist: contraceptive pills). Herbal medicine counts – independent of the number of plant extracts contained – as one drug. Homeopathy, Schüssler salts and so on are not counted. Multivitamins count only if taken for a medical condition (gastric bypass) and not if considered a tonic; they count as one drug. Oncologic treatment by a hospital also counts. Whether the patient applies the drug as scheduled or not, does not change his medication score. Medication on demand or self-medication is not counted. The qualifying date is the one of the recording. If you do not have assured data on medication, record "99".

Examples: Aclasta® (zoledronic acid) 5 mg once yearlyi.v.: 1 point. Calcimagon D3® (cholecalciferol, calcium carbonas) twice daily: 2 points. Exforge HCT® (valsartan, amlodipine, hydrochlorothiazide) once daily: 3 points. Testogel® gel (testosterone) one daily transdermal application: 1 point. ExcipialLipolotio® two daily applications: 0 point. ReBalance® 500 mg (hypericum perforatum) once daily: 1 point. Ceres petasites D6 alcoholic drops, 5 drops trice daily: 0 point. Implanon® (etonogestrel), subcutaneous, for three years: 1 point. Miacalcic® nasal spray 200 µg twice daily: 1 point.

Number of Conditions

Each chronic condition receives 1 point, regardless whether it is active (hypertension, actively treated), latent (elevated fasting blood glucose) or inactive (state after cholecystectomy); if the condition was important enough to be recorded in the patient file, it's important enough to count for this study! Exceptions: Drug allergies count as 1 point, even if they are multiple. An acute disease which is mainly chronic, but was not yet recorded as a chronic condition, should be counted for this study (activated knee osteoarthritis).

Thurgau Morbidity Index

You may note values from 0 to 6. Relevant for coding is the *worst* health state as caused by the chronic condition during the previous 12 months. When coding you follow the scheme from Figure 1. You start at the top. If the patient has at least **two severe conditions** (A), you code "6". If the patient has **one severe** condition and at least **three mild to moderate** conditions, the code is "5", if there are **less than three mild to moderate condition**, one codes "4" (B). If the patient has **no severe** condition but **at least three** mild to moderate ones, you encode "3", and if the patient has only **one or two** mild to moderate conditions, the code is "2" (C). If the patient has **no** chronic condition, but **risk factors** or **findings** to be regularly monitored, the code is "1". If none of the above mentioned is the case, the code is "0" (D, "healthy"). If your record is not sufficient to select a code, you register "9" for unknown.

We consider a condition to be **severe** if there is:

- an active malignant tumor (non-melanoma skin cancer excluded)
- a chronic condition with instability, decomposition, acute thrust
- conditions with severely impaired organ function
- severe systemic disease
- rapidly progressive disease
- conditions with severe social impairment

- all other conditions which are considered to be severe Cancer without relevant complaints is considered as mild to moderate (prostate). State after curative treatment of cancer is considered as "preclinical" or "healthy" (testicular). We consider the following conditions to be chronic: Primary chronic disease (osteoarthritis) or primary acute but not resolved after 12 months (hepatitis B).

Examples: A patient with currently compensated cardiac insufficiency was hospitalized three months earlier. His condition is considered to be severe. Rheumatoid arthritis treated with anti-TNF "biological treatment" without complaints counts to be mild to moderate. Osteoarthritis of the hip, operated six months before, scores for a severe condition, while the same patient, operated three years before and without complaints counts to be mild to moderate or preclinical. An obesity scores as mild to moderate, but if a gastric bypass operation had been performed during the previous 12 months, it counts to be severe. Addiction disease counts to be severe if stationary detoxification took place during the previous year or if its social consequences are severe.

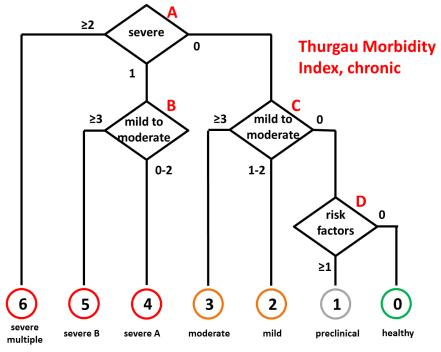


Figure 1. Thurgau Morbidity Index (chronic scale).

AIDS with a normalized immune system after medication is considered to be mild to moderate.

Hospitalization

If the patient had been hospitalized during the previous 12 months, you record "1", if not "2", if you do not know "3". The cause of hospitalization does not matter for coding.

Repeat visit

If the patient is seen for a second or further time during the fortnight period, you should mark the field, even if he or she consults for a different disease than the first time. In first visits, you leave the field empty.

Appendix C

Frequently asked questions (from: <u>www.medication-</u> incidents.ch)

Q: The nurse confounded the medication of two residents in a home for the elderly. Do I have to fill in *two* notification forms?

A: Yes, at least if you are in care of both residents.

Q: During treatment with prednisolone and methotrexate, a patient had oral candidiasis. Later we learned that she

had developed diabetes. Do I have to fill a form for that case?

A: No, this was a monitoring error (since you did not control on time for diabetes); the drugs were applied in the normal way, and the undesired drug reaction (diabetes during corticosteroid treatment) is not to be noted in our study.

Q: A patient was transferred from acute to geriatric care for continued i.v. antibiotic treatment. After three days, I was contacted by the family because the patient had not received his antibiotic treatment and was febrile. The i.v. antibiotics were not mentioned on the acute clinic transferring report. Do I have to report that case?

A: No! For two reasons: Firstly, you were not in care of the patient when the incident happened, and secondly, our study aims to investigate incidents in primary care, but your patient was transferred from one secondary care unit to another.

Q: Should I notify the daily problem of medication non-compliance of the patients?

A: No, only if an incident arises out of it (e.g. overmedication when taking medication as planned).

Q: Are children who are in a crèche to be considered as cared by an institution?

A: No, only children who are in an institution for a condition (like cerebral palsy or schizophrenia) count as cared by the institution; normal children count as cared by the parents (when sick) or not cared by others.

	Item No	Recommendation
Title andabstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract[yes]
		(b) Provide in the abstract an informative and balanced summary of what was done and what
		was found[yes]
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported [yes]
Objectives	3	State specific objectives, [yes]including any prespecified hypotheses[no]
Methods		
Study design	4	Present key elements of study design early in the paper[yes]
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection [yes]
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants[yes]
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. [yes] Givediagnosticcriteria, ifapplicable [no]
Data	8*	For each variable of interest, give sources of data and details of methods of assessment (mea-
sources/measurement		surement). Describe comparability of assessment methods if there is more than one group[yes]
Bias	9	Describe any efforts to address potential sources of bias[yes]
Study size	10	Explain how the study size was arrived at [yes]
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which
		groupings were chosen and why [yes]
Statisticalmethods	12	(a) Describe all statistical methods, including those used to control for confounding[yes]
		(b) Describe any methods used to examine subgroups and interactions[yes]
		(c) Explain how missing data were addressed[yes]
		(d) If applicable, describe analytical methods taking account of sampling strategy[no]
		(<u>e</u>) Describe any sensitivity analyses [no]
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible, ex-
		amined for eligibility, confirmed eligible, included in the study, completing follow-up, and ana-
		lysed[no]
		(b) Give reasons for non-participation at each stage[yes]
		(c) Consider use of a flow diagram[yes]
Descriptivedata	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information
		on exposures and potential confounders[yes]
		(b) Indicate number of participants with missing data for each variable of interest [yes]
Outcome data	15*	Report numbers of outcome events or summary measures[no]
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their preci-
		sion (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included[yes]
		(b) Report category boundaries when continuous variables were categorized[yes]
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period[no]
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses [yes]

Q: Do we have to fill in all items in patients consulting a second time during denominator analysis?

A: Yes, because we cannot assign the patients to their first visit by year of birth and gender alone.

Q: Does the anti-rickets prophylaxis with vitamin D in healthy toddlers count as medicine?

A: Yes.

Q: Are prisoners supposed to be regarded as institutionalized patients?

A: Yes, since usually they are not allowed to take their medication by themselves.

Appendix D

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at

Discussion		
Key results	18	Summarise key results with reference to study objectives[yes]
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias [yes]
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence[yes]
Generalisability	21	Discuss the generalisability (external validity) of the study results[yes]
Other informati	on	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based[yes]

*Give information separately for exposed and unexposed groups.

http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix E: e-Tables and e-Figures

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(Cl95%) by	age and linguistic region

e4 Mean number of prescribed drugs taken regularly(CI95%) by age and linguistic region

e5 Mean number of chronic conditions (CI95%) by age and linguistic region

e6 Mean Evan's Index (CI95%) by age and linguistic region

e7 Frequencies of Thurgau Morbidity Index values in comparison with historical data

We received questionnaires 145 from 180 Sentinella reporting physicians (response rate 80.6%, mostly there was only one questionnaire per practice). 16 respondents hat not participated the morbidity study or did not answer the questions concerning coding difficulties. The *effort* to fill in the morbidity questionnaires was considered: 61 (47.3%) "manageable", 56 (43.4%) "big effort", 12 (9.4%) "too much effort", but no one "impossible". *Time* to coding all morbidity items for one patient was estimated by 113 respondents (79.6%); the mean value was 3.5±2.0 min.

Difficulty with morbidity item coding										
Item	none	a little	important	massive						
Previous hospitalization	101 (78.3%)	25 (19.4%)	3 (2.3%)	0 (0.0%)						
Care-dependency	91 (70.5%)	31 (24.0%)	6 (4.7%)	1 (0.8%)						
Medication count	72 (55.8%)	44 (34.1%)	13 (10.1%)	0 (0.0%)						
Condition count	56 (43.4%)	51 (39.5%)	22 (17.1%)	0 (0.0%)						
TMI	52 (40.3%)	59 (45.7%)	17 (13.2%)	1 (0.8%)						
Repeat visit	96 (74.4%)	27 (20.9%)	6 (4.7%)	0 (0.0%)						

Table e1. Difficulties with morbidity item coding.

 Table e2.
 Morbidity indicators by age category and gender.

Age cate- gory	Hospitalisa- tion (percent)		Care- dependency* (percent)		Conditions (Median/IQR)		Drugs (Median/IQR)		Evans index (Median/IQR)		TMI (Median/IQR)		Repeat visit (per- cent)	
	Male	fe- male	male	fe- male	male	female	male	female	male	female	male	female	mal e	fe- male
0 - 10	7.2	8.3	n.a.	n.a.	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-0)	0 (0-0)	5.2	4.7
11 - 20	3.8	5.2	n.a.	n.a.	0 (0-1)	0 (0-1)	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	6.1	6.1
21 - 30	6.0	8.9	3.6	2.8	0 (0-1)	1 (0-1)	0 (0-0)	0 (0-1)	0 (0-2)	1 (0-2)	0 (0-1)	0 (0-1)	8.4	8.3

Table e2. Continued.

31 - 40	9.6	9.4	3.7	2.7	1 (0-2)	1 (0-2)	0 (0-1)	0 (0-1)	1 (0-3)	1 (0-4)	1 (0-2)	1(0-2)	7.6	8.4
41 - 50	11.5	9.4	5.2	3.7	1 (0-3)	1 (0-3)	1 (0-2)	1 (0-2)	2 (0-5)	3 (1-5)	1 (0-2)	1 (0-2)	8.6	7.4
51 - 60	13.8	14.3	5.5	6.0	2 (1-4)	2 (1-4)	2 (0-4)	2 (0-4)	4 (2-7)	4 (2-7)	2 (1-3)	2 (1-3)	8.3	7.5
61 - 70	19.6	16.0	6.4	9.7	3 (2-4)	3 (2-5)	3 (1-5)	3 (1-5)	6 (3-9)	6 (4-10)	3 (1-3)	2 (1-3)	7.8	8.0
71 - 80	27.3	22.9	17.7	18.0	4 (2-6)	4 (2-5)	4 (3-7)	4 (2-6)	8 (5-12)	8(5-12)	3 (2-4)	3 (2-4)	7.1	8.1
81 - 90	31.2	30.9	38.2	49.8	4 (3-7)	4 (3-6)	5 (3-7)	5 (4-8)	10 (7-14)	10(7-14)	4 (3-5)	3 (3-5)	10.8	9.1
91 and	31.7	32.0	79.0	74.7	5 (3-6)	4 (3-6)	5 (3-7)	5 (3-8)	10(7-13)	9(6-14)	4 (3-5)	4 (3-5)	8.0	8.7
over														

*Because of question ambiguity, the care-dependency category "care by parents / proxies" could not be evaluated in children and teenagers, so age categories 1 and 2 are without data.

Table e3. Correlation matrix (Spearman's Rho)

		Gender	Patient's age	Hospitalization in previous year	Care- dependency	Number of prescri- beddrugs regularly taken	Number of chronic conditions	Thurgau Morbidity Index (TMI)	Evans' index
Gender	correlation coefficient	1.000	.072	.008	.062**	.070	.058**	.051	.065
	Sig. (2-sided)		.000	.188	.000	.000	.000	.000	.000
	N	26815	26803	24749	20689	24413	24449	24407	24324
Patient's age	correlation coefficient	.072	1.000	.219	.356	.692	.719	.693	.725
	Sig. (2-sided)	.000		.000	0.000	0.000	0.000	0.000	0.000
	N	26803	26816	24752	20694	24419	24456	24412	24331
Hospitalization in previous year	correlation coefficient	.008	.219	1.000	.295	.291	.281	.337	.299
	Sig. (2-sided)	.188	.000		0.000	0.000	0.000	0.000	0.000
	N	24749	24752	24761	20544	23723	23874	23998	23718
Care- dependency	correlation coefficient	.062	.356	.295	1.000	.350	.308**	.397	.342
	Sig. (2-sided)	.000	0.000	0.000		0.000	0.000	0.000	0.000
	N	20689	20694	20544	20701	20175	20204	20156	20213
Number of prescribeddrugs	correlation coefficient	.070	.692	.291	.350	1.000	.817**	.781	.936
regularly taken	Sig. (2-sided)	.000	0.000	0.000	0.000		0.000	0.000	0.000
	Ν	24413	24419	23723	20175	24424	24255	23861	24272
Number of chronic condi-	correlation coefficient	.058**	.719	.281	.308**	.817**	1.000	.830**	.957**
tions	Sig. (2-sided)	.000	0.000	0.000	0.000	0.000		0.000	0.000
	Ν	24449	24456	23874	20204	24255	24461	23996	24282
Thurgau Mor- bidity Index	correlation coefficient	.051	.693	.337	.397**	.781	.830**	1.000	.840**
(TMI)	Sig. (2-sided)	.000	0.000	0.000	0.000	0.000	0.000		0.000
	Ν	24407	24412	23998	20156	23861	23996	24420	23864
Evans' index	correlation coefficient	.065	.725	.299	.342**	.936	.957	.840	1.000
	Sig. (2-sided)	.000	0.000	0.000	0.000	0.000	0.000	0.000	
	Ν	24324	24331	23718	20213	24272	24282	23864	24336

** The correlation is significant at the level of p=0.01 (2-sided).

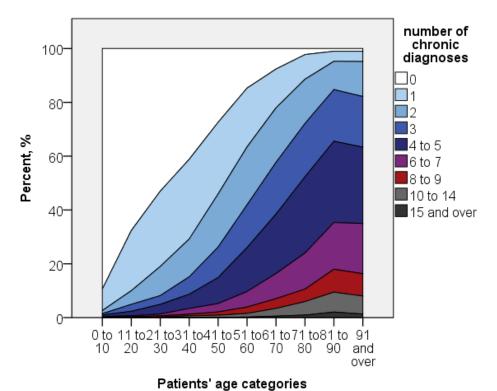


Figure e1. Number of chronic conditions, percent (%). Graduations denote the entire class.

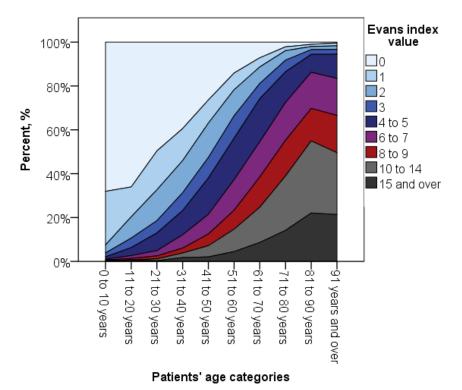
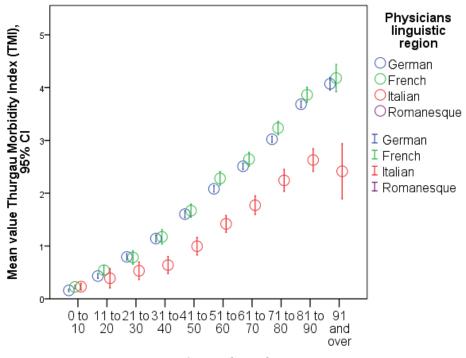
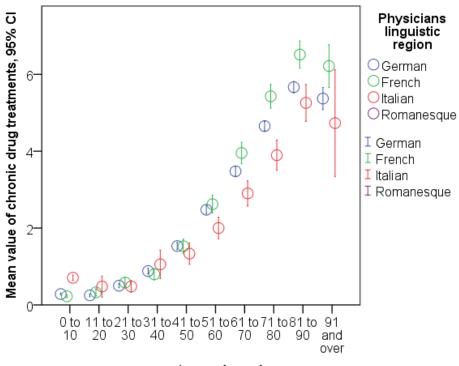


Figure e2. Evans index value, percent. Graduations denote the entire class.



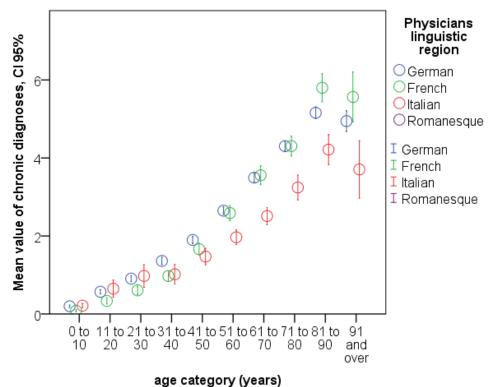
age category (years)

Figure e3.Mean Thurgau Morbidity index values (CI95%) by age and linguistic region.



age category (years)

Figure e4.Mean number of prescribed drugstaken regularly(CI95%) by age and linguistic region.



age category (years)

Figure e5.Mean number of chronic conditions(CI95%) by age and linguistic region.

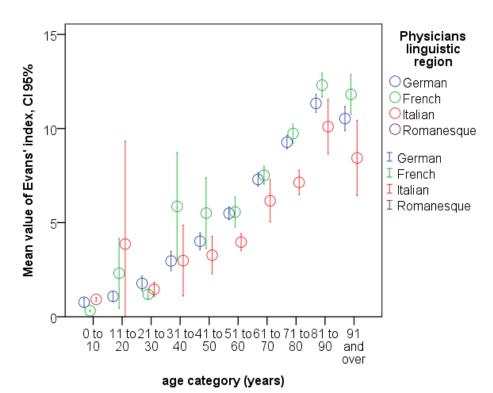


Figure e6.Mean Evan's Index (CI95%) by age and linguistic region.

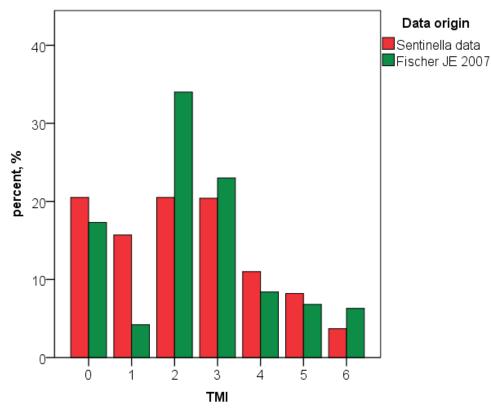


Figure e7. Frequencies of Thurgau Morbidity Index values in comparison with historical data (Fischer 2007) (all age groups and both sexes, GPs only). Fischer et al reported an intra-class correlation coefficient of 0.72 in trained physicians. In contrast to the data by Fischer et al. we found lower proportions of codes 2, 3 and 6 and more codes 0 and 1. However, the latter study did not include consecutive patients but rather a "convenience sample" preferring higher TMI codes for analyzing healthcare cost, also in the smaller groups of more severely diseased patients (personal communication of Joachim E. Fischer, Mannheim).