


## ORIGINAL ARTICLE

# Neurovascular disease in Switzerland: 10-year trends show non-traditional risk factors on the rise and higher exposure in women

Martin Hänsel<sup>1</sup>  | Klaus Steigmiller<sup>2</sup> | Andreas R. Luft<sup>1</sup> | Catherine Gebhard<sup>3</sup> | Ulrike Held<sup>2</sup> | Susanne Wegener<sup>1</sup> 

<sup>1</sup>Department of Neurology and Clinical Neuroscience Center, University Hospital Zurich and University of Zurich, Zurich, Switzerland

<sup>2</sup>Department of Biostatistics at Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland

<sup>3</sup>Department of Nuclear Medicine, University Hospital Zurich and University of Zurich, Zurich, Switzerland

## Correspondence

Susanne Wegener, Department of Neurology, University Hospital Zurich, Frauenklinikstrasse 26, 8091 Zurich, Switzerland.  
Email: [susanne.wegener@usz.ch](mailto:susanne.wegener@usz.ch)

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## Abstract

**Background and purpose:** Effective risk factor modification is the prerequisite to prevent neurovascular disease such as stroke or vascular dementia. Non-traditional vascular risk factors (nt-vrfs) including stress significantly add to the risk of neurovascular disease arising from traditional vascular risk factors (t-vrfs). In order to discover sex-specific changes that may underlie previously reported inclines in the prevalence of neurovascular and cardiovascular disease in women, 10-year trends in the prevalence of vrfs in Switzerland were assessed.

**Methods:** Anonymized data from 22,134 participants (51% women) of the governmental Swiss Health Survey, performed every 5 years (2007, 2012 and 2017), were obtained. Epidemiological parameters, t-vrfs and nt-vrfs were analyzed in a cross-sectional study design.

**Results:** Over the observation period, the number of women having full-time jobs increased considerably (2007 38%, 2012 39%, 2017 44%). This was accompanied by a substantial rise in the prevalence of nt-vrfs in women and men including stress at work (2007, not available; 2012 women/men 58%/60%; 2017 women/men 66%/65%), low locus of control (women/men: 2007 21%/19%, 2012 22%/19%, 2017 25%/22%) and sleep disorders (women/men: 2007 30%/22%, 2012 28%/20%, 2017 32%/26%). Amongst t-vrfs, only the prevalence of obesity and hypercholesterolemia increased over time in both sexes, whilst other t-vrfs remained stable (hypertension [27%], diabetes [5%]) or decreased (smoking [9.4 cigarettes/day]).

**Conclusions:** A rise in women's economic participation alongside a higher affection with nt-vrfs in the female Swiss population emphasizes the need to improve vascular risk stratification and implement effective preventive measures for neurovascular and cardiovascular disease.

## KEYWORDS

cardiovascular disease, cardiovascular risk factors, prevalence, sex, stroke, Switzerland

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## INTRODUCTION

Stroke and ischaemic heart disease are the most common causes of death and disability worldwide [1]. Diabetes, arterial hypertension, high low-density lipoprotein cholesterol level, obesity and kidney dysfunction along with behavioral risk factors (diet, tobacco, alcohol consumption, physical inactivity) are well-known modifiable traditional vascular risk factors (t-vrfs) [2–4]. They account for approximately 70% of all vascular disease (VD) [5].

A rise in VD was shown to be the primary cause of mortality in women in the United States between 1997 and 2012 [6]. In particular, the incidence of VD in younger women aged 35–54 years was reported to increase, the reason remaining unclear [7, 8]. The consequences of VD for neurological health are manifold: whilst stroke and vascular dementia are direct manifestations of VD in the brain, vascular dysfunction increases the burden of other neurological diseases as well. This includes Alzheimer's disease, neuro-inflammatory disorders and symptomatic epilepsy [9–11]. Whilst sex differences in neurovascular aging are increasingly acknowledged, studies about social trends, sex- or gender-specific lifestyle and psychosocial risk factors for neurovascular disease are still rare [12, 13]. Recently, nt-vrfs including stress, loss of control, depression and sleep disorders have been identified as independent predictors of future vascular events [14, 15]. Accumulating evidence suggests that treating these risk factors is an efficient means to reduce cardiovascular morbidity and mortality [5, 12, 14, 15]. However, knowledge about sex-specific temporal trends in nt-vrfs is lacking, which is a serious problem considering that changes in vrfs might have tremendous impact on the development of future neurovascular and cardiovascular disease in women.

In Switzerland, vrfs were studied nationwide during the “stroke prevention campaign” in 2001 [16, 17]. However, the data are >15 years old and no sex-specific trends were reported. Data from the Swiss Health Survey, a well-balanced and representative sample, were used to assess 10-year trends in cardiovascular risk factors in Switzerland. Specifically, our goal was to assess sex differences and trends in t-vrfs and nt-vrfs between women and men.

## METHODS

### Swiss Health Survey

Data were generated by the Swiss Health Survey (source Bundesamt für Statistik, BFS), a governmental Swiss-wide survey which has been performed every 5 years since 1992. The data from 2007, 2012 and 2017 were used in a cross-sectional study design.

The sampling plan consisted of a simple one-stage random sample of persons and households without replacement and with stratification on the cantonal level. Data preparation consisted of various plausibility checks by the BFS and a weighting to generate a representative sample for all persons over 15 years of age living in a private household in Switzerland. The weighting took account of the

sampling plan and the occurrence of non-responses. It also included calibration of the size of the households, region, sex, nationality, civil status and age group such that the sample was representative for the Swiss population above 15 years of age. For more information about the survey, see the Supplementary methods. Reporting in this paper follows the STROBE guidelines (Supplementary Data S1).

From over 450 items of the Swiss Health Survey, t-vrfs and nt-vrfs were identified. Items were classified into t-vrfs (hypertension, diabetes mellitus, hypercholesterolemia, body mass index, alcohol consumption, nicotine consumption, physical activity, passive smoking, drug consumption, contraception) versus nt-vrfs (stress at work, feeling exhausted at work, job satisfaction, job resignation, working despite illness, problems arranging work with family duties, working in leisure time, locus of control, energy and vitality, quality of life, sleep disorders, major depression), according to other studies [5, 18, 19]. Further, epidemiological parameters were specified: education level, urbanism, employment level, job situation, net earnings. Inconclusive answers from the primary data such as “I do not know”, “no answer”, “not questioned”, “data error”, “proxy answer” and “no consensus” were excluded. Therefore, the number of data points at each item may differ.

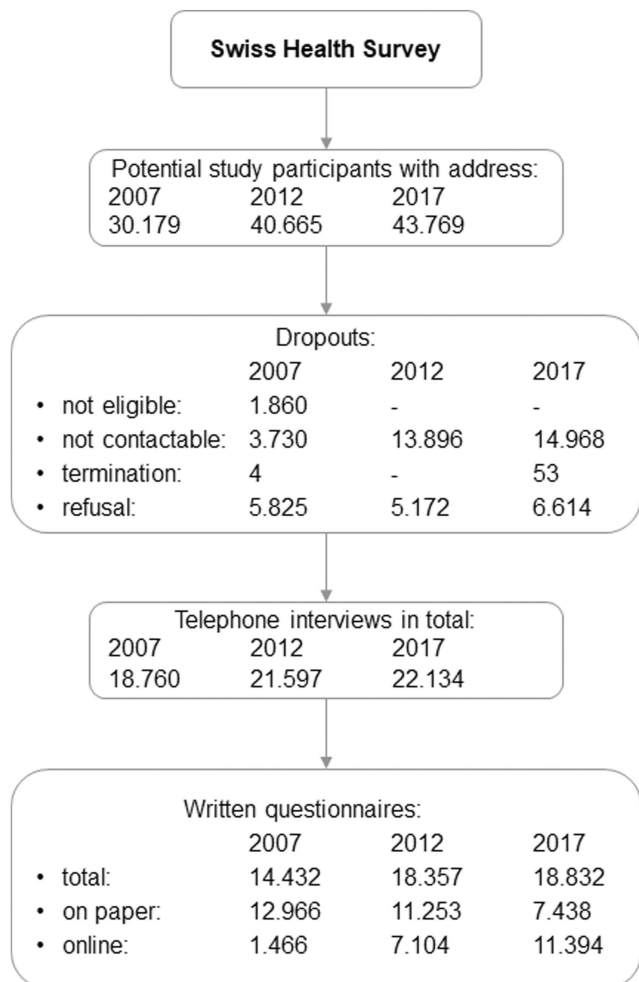
### Statistical methods

The statistical analysis followed a design-based approach without final population correction in which the design feature of the Swiss Health Survey was accounted for. Calculations on subpopulations respected the survey design. The recommended weights of the telephone or written interviews as suggested by the BFS were used for all evaluations. All estimates were calculated together with 95% Wald and logit-Wald confidence intervals (CIs) for continuous and categorical variables, respectively. Since data in this study were not collected in a clinical study but in a survey using a complex sampling design, all analyses based on the data need to account for the sampling design through weights. Therefore, simple statistical tests cannot be used. For these reasons, it was preferred to abstain from using statistical tests but instead use CIs. In the case of non-overlapping CIs, differences of means are significant to the 5% significance level. Analyses were performed using R 4.0.3 [20] and the package ‘survey 4.0’ [21]. Because all values are population-weighted, the results are shown as percentages except for the metric data.

## RESULTS

### Swiss Health Survey recruitment 2007–2017

The recruitment of the Swiss Health Survey for the years 2007/2012/2017 is shown in the flowchart (Figure 1). In 2007/2012/2017, 18,760/21,597/22,134 participants were included through telephone interviews. According to the survey design, all subsequent results refer to estimates of the Swiss population older



**FIGURE 1** Flowchart of the Swiss Health Survey recruitment 2007–2017. Flowchart of the Swiss Health Survey with potential participants in 2007/2012/2017, including dropouts and resulting telephone interviews, as well as written questionnaires in total. The primary goal of collecting these data was to study the health condition of the Swiss population, detecting changes in health conditions and monitoring the impact of health policy activities. In 2017, the BFS contacted 43,769 people in Switzerland by regular mail followed by a telephone interview. For the first round (telephone interview), out of 13,117 people they could not, 1152 were absent, 53 people stopped during the telephone interview and 6614 did not want to start the interview. In total, 22,134 telephone interviews were conducted. Out of these participants, 18,832 filled out a secondary written questionnaire with further in-depth questions. In 2007/2012 there were 30,179/40,665 potential study participants, there were 11,419/19,068 dropouts and in total 18,760/21,597 telephone interviews were made. From these participants 14,432/18,357 people answered the written questionnaire. Because it was voluntary to participate in the study, there is a voluntary bias as a potential selection bias. However, due to the large number of cases ( $n = 22,134$ ) and the structured process to overcome inclusion bias applied by the BFS, it is thought that the influence of this bias on the results can be considered minor

than 15 years living in a private household, that is, not the actual study participants. Only the weighted results are shown with percentage values. To improve readability, the CIs are not shown in

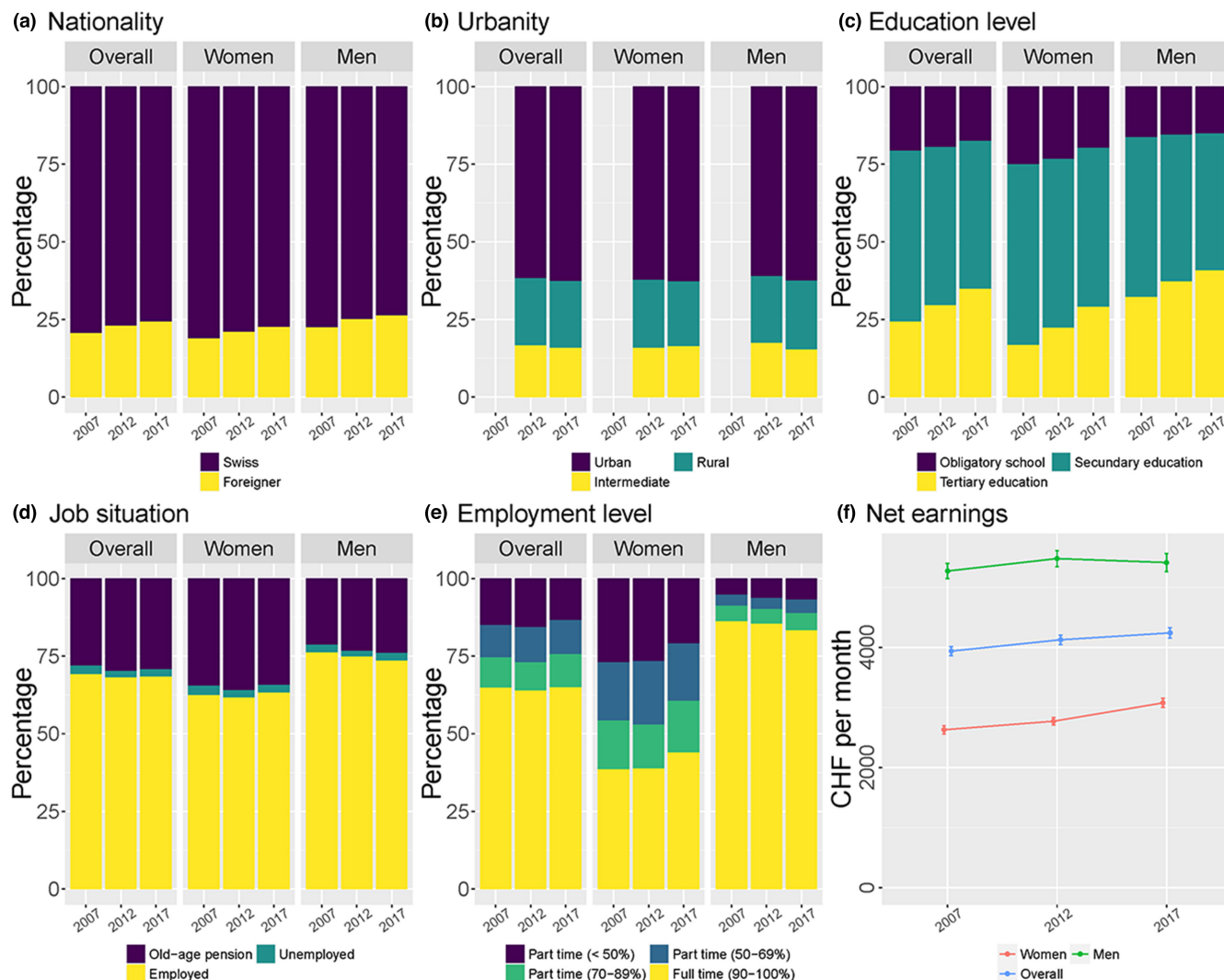
the text (the CIs and detailed results of the survey are shown in Tables S1–S3).

## Epidemiological characteristics

The ratio of men and women remained largely stable over the observation period (49% vs. 51%). The mean age of the study participants increased slightly (45.8/47.4/47.5 years) from 2007 to 2017 with female participants being older than males (48.2 vs. 46.8 years for 2017; see Figure S1 showing histograms of age for female/male sex). The fraction of foreigners living in Switzerland in 2017 was around 24% and increased by 3% between 2007 and 2017 (Figure 2a). The ratio of men and women living in a city or a rural area did not change between 2012 and 2017 (Figure 2b). The level of secondary education (vocational training) and tertiary education (college, polytechnic degree, university) increased every 5 years and more so in women. In 2017, there were more women with secondary education level than men (51% vs. 44%), but more men with tertiary education level than women (41% vs. 29%) (Figure 2c). Women were less frequently employed than men (63% vs. 74%; Figure 2d). The overall employment level in the last 10 years remained nearly the same (Figure 2e). Men more frequently had a full-time job (83% vs. 44%). From 2012 to 2017, the percentage of women with full-time jobs increased from 39% to 44%. Of note, net earnings increased more in women (from 2600 CHF to 3100 CHF) than in men (5300 CHF to 5400 CHF) but were still about 43% less than those of men in 2017 (not adjusted for employment level) (Figure 2f).

## Traditional vascular risk factors (t-vrfs) and lifestyle factors

The reported prevalence of hypertension increased from 22% to 27% between 2007 and 2012 (Figure 3a), but remained stable between 2012 and 2017, as did the fraction of people with diabetes (5%) in both sexes (Figure 3b). Reported dyslipidemia increased slightly in both men and women between 2007 and 2017 (Figure 3c). The overall body mass index rose from 24.2 (2007) to 24.8 (2017). Accordingly, obesity was more common in 2017 compared to 2007. Women more often had normal body weight compared to men (62% vs. 48% in 2017) (Figure 3d). The level of physical activity increased between 2007 and 2017 (Figure 3f), especially the percentage of people feeling “sufficiently active” (three times per week highly intensive training), which went up from 35% to 45%. Women were more often non-smokers (77%) than men (70%) (Figure 3g). The consumption of cigarettes decreased from 10.6 to 9.4 per day between 2007 and 2017 (Figure 3h). There was a significant decrease in passive smoking between 2007 (37 min/day) and 2017 (17 min/day) with a sharp decline in 2012 in both sexes (Figure 3i). This positive trend correlates with the smoking ban in closed rooms in Switzerland, implemented in 2010. The overall consumption of drugs (cannabis, cocaine and other drugs) during the 12 months before the interview



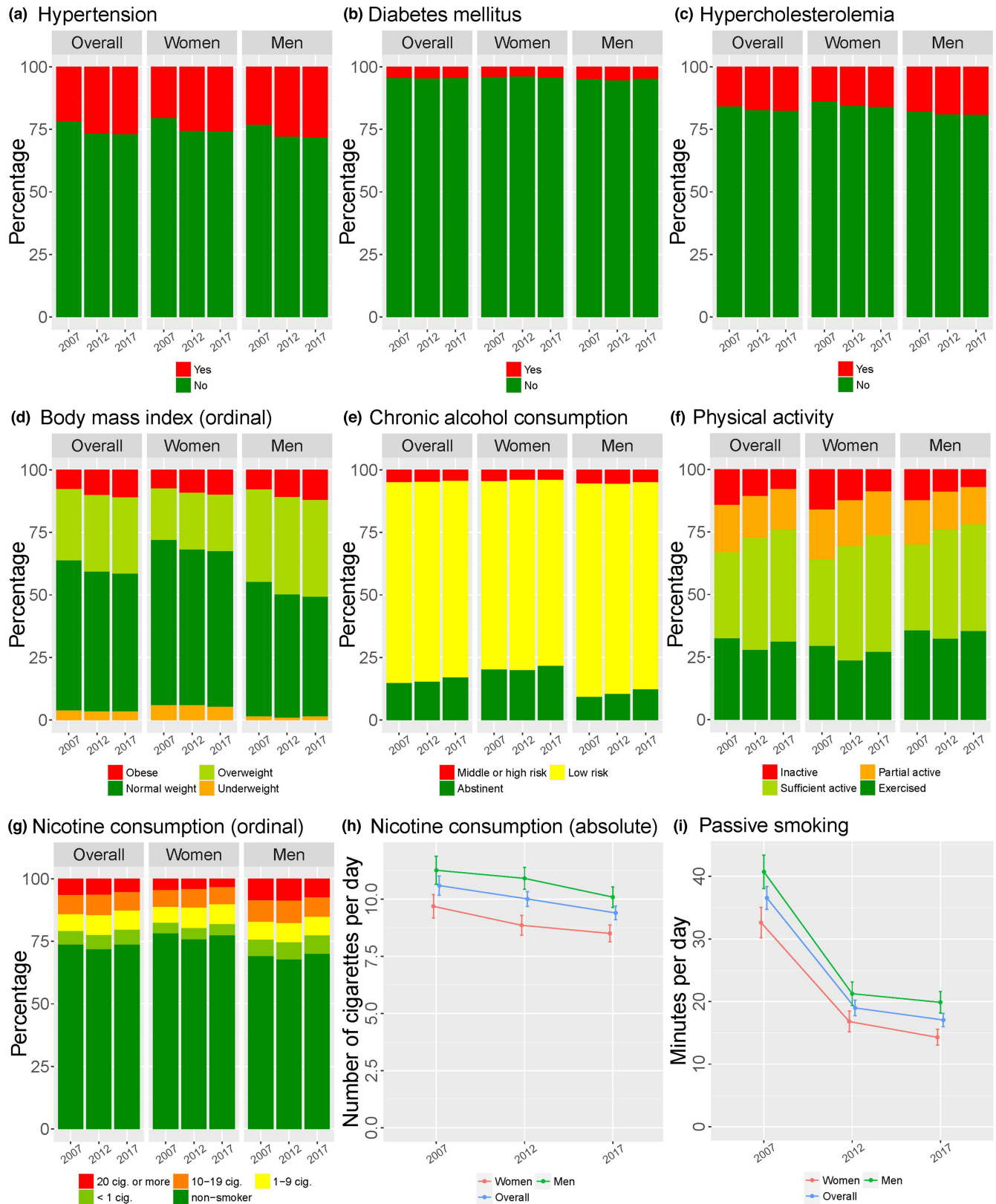
**FIGURE 2** Epidemiological factors of the Swiss Health Survey 2007–2017. Charts of all Swiss people, separated by sex, showing epidemiological factors including (a) nationality, (b) urbanism, (c) education level, (d) job situation, (e) employment level and (f) net earnings for the years 2007/2012/2017 [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

increased slightly from 2007 to 2017 (Figure 4a; details are shown in Figure 4b–4e).

### Non-traditional vascular risk factors (nt-vrfs)

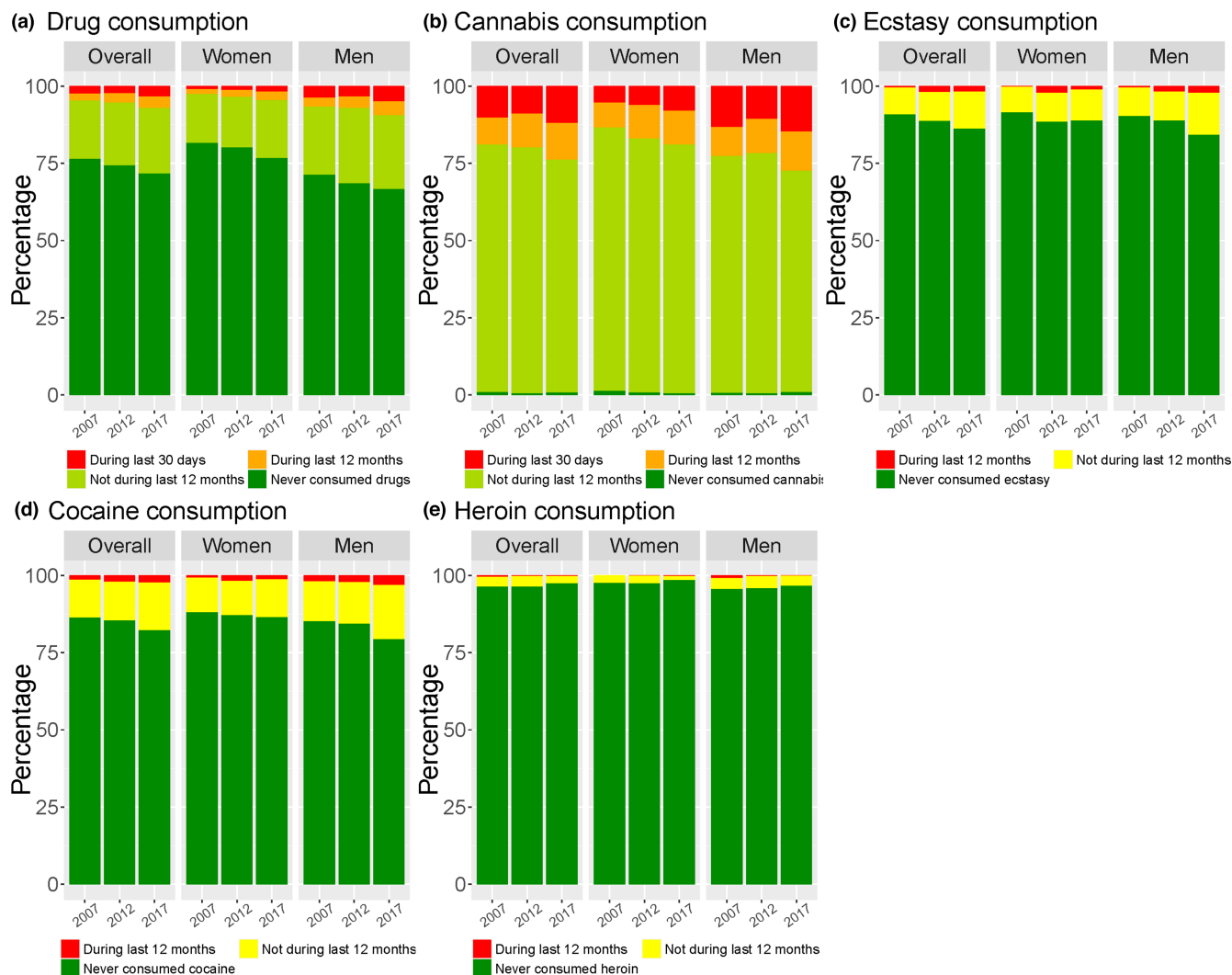
There was a clear increase in nt-vrfs over the 10-year observation period. Stress at work increased in both women and men. The relative increases in the categories “mostly” and “sometimes” for stress at work were both +4% in women and +2% in men over the last 5 years (Figure 5a). The overall feeling of job resignation increased slightly between 2007 and 2017 in both sexes, especially the overall cumulative fraction of “high” and “very high” job resignation (Figure 5b). The feeling to be exhausted at work was increasingly reported in 2017, especially in women (Figure 5c). The fraction of participants saying that exhaustion at work was “not the case at all” remained stable at 38% in men but decreased from 40% to 36% in women.

Arranging work with family duties was perceived as problematic in 7% of all participants in 2012 and 9% in 2017 (Figure 5d). More men never had problems arranging work with family duties compared to women. About 31% of women and men worked despite illness during the last 12 months in 2017 (not questioned in 2007/2012). The fraction of women working despite illness was higher (32%) than that of men (30%), but women were less often ill (38%) compared to men (40%). The “locus of control”, a personal resource as an empowerment to dealing with problems, decreased between 2007 and 2017 (Figure 5f). The fraction of people considering themselves with “low locus of control” increased, especially in women (25%) compared to men (22%). The prevalence of major depression went up from 2012 to 2017 (Figure 5g). More people reported severe, rather severe and intermediate major depression: 6% (2012) and 9% (2017), particularly more women. The overall percentage of participants reporting low energy and vitality went up from 23% to 29% with a higher fraction of women (33%) compared to men (26%; Figure 5h). Men more often felt



**FIGURE 3** Traditional vascular risk factors and lifestyle factors of the Swiss Health Survey 2007–2017. Charts of all Swiss people, separated by sex, which show the traditional vascular risk factors including (a) hypertension, (b) diabetes mellitus, (c) hypercholesterolemia, (d) body mass index (ordinal), (e) chronic alcohol consumption, (f) physical activity, (g) nicotine consumption (ordinal), (h) nicotine consumption (absolute) and (i) passive smoking for the years 2007/2012/2017 [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]





**FIGURE 4** Drug consumption and drug subanalyses of the Swiss Health Survey 2007–2017. Drug consumption (except alcohol) including all Swiss people (a) for the years 2007/2012/2017 separated by sex, and subanalyses of all ever-drug-users for (b) cannabis consumption, (c) ecstasy consumption, (d) cocaine consumption and (e) heroin consumption for the years 2007/2012/2017, separated by sex [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

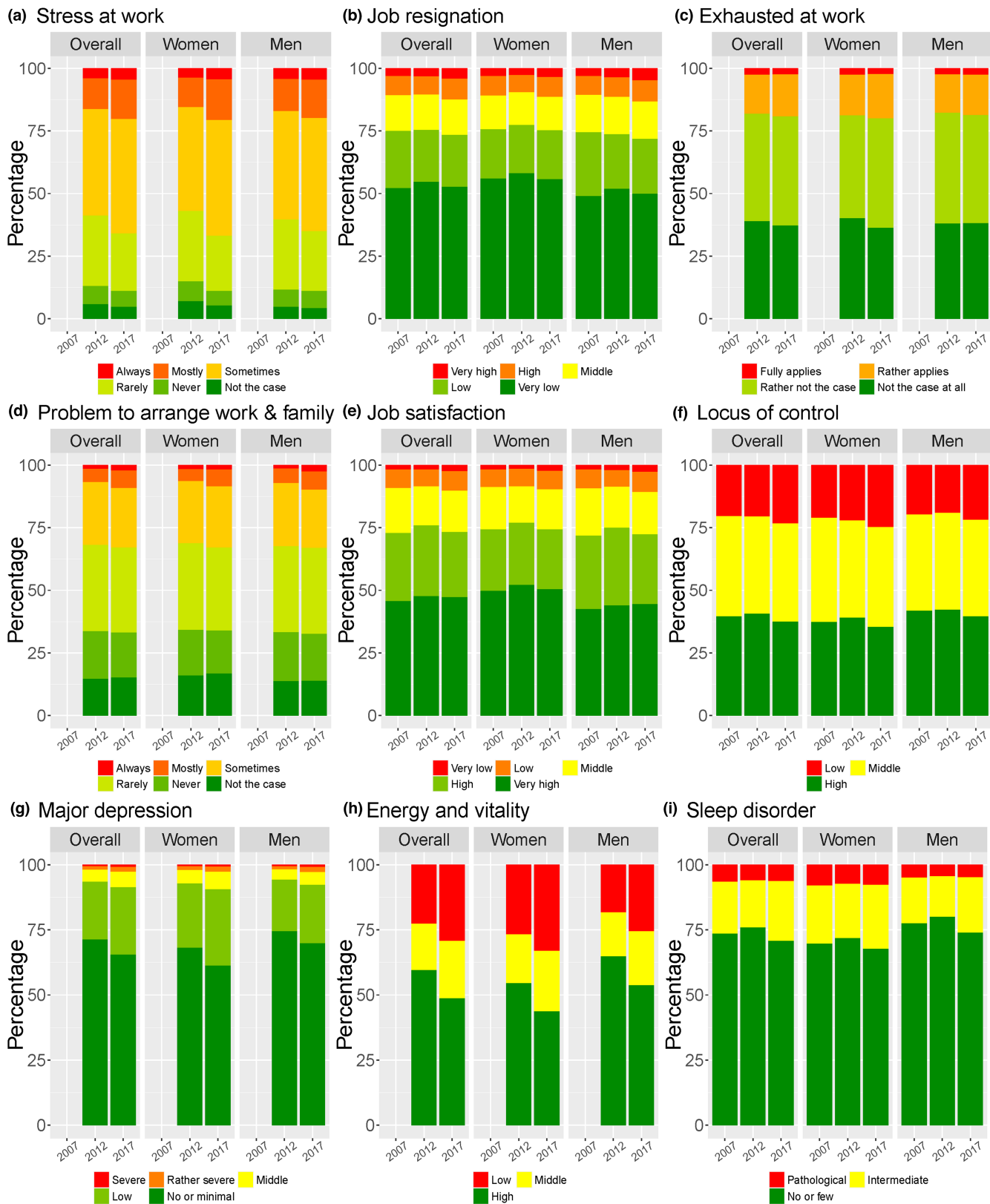
to have high levels of energy and vitality than women (54% vs. 44%) in 2017. Sleep disorders were a bit more common in 2017 compared to 2007 (Figure 5). The fraction of individuals with no or few sleeping problems decreased from 74% to 71%, whilst those with intermediate sleep disorders went up. Women had more often intermediate (25% vs. 21%) and severe sleeping problems than men (8% vs. 5%).

## DISCUSSION

The importance of t-vrfs and nt-vrfs for prevention of VD is undisputed. For decades, VD has been perceived as more prevalent in men. However, overall cardiovascular mortality is higher and the incidence of VD is increasing in women [22]. Whilst in the elderly (>65 years of age) stroke incidence rates declined in some high-income countries (HICs) over the last 10 years, it increased in the younger population, particularly in women [23, 24]. In younger women aged 35–54 years,

VD incidence and case fatality is on the rise [8]. Societal changes and global health developments with significant impact on health behavior and preventive measures might account, at least in part, for this trend [8, 12–15]. In Switzerland and other HICs alike, the social participation of women has been increasing over the past decades, along with higher employment rates [25]. The role of stress at work affecting the work–life balance and part of increasing psychosocial risk factors has been shown in several studies [15, 26]. At the same time, new knowledge about sex differences in cardiovascular aging highlights the impact of t-vrfs and nt-vrfs for physical and mental health [26]. Therefore, societal trends in women's life may increase the risk of developing both vrfs and nt-vrfs.

A systematic analysis from the Swiss Health Survey (2007–2017) was performed to investigate trends and sex differences in a wide spectrum of t-vrfs, lifestyle factors and nt-vrfs over 10 years. In our study, an increase of nt-vrfs was found in both sexes, which was more pronounced in women than in men, whilst most t-vrfs



**FIGURE 5** Non-traditional vascular risk factors of the Swiss Health Survey 2007–2017. Charts of all Swiss people, separated by sex, which show the non-traditional cardiovascular risk factors including (a) stress at work, (b) job resignation, (c) exhausted at work, (d) problems arranging work and family, (e) job satisfaction, (f) locus of control, (g) major depression, (h) energy and vitality and (i) sleep disorder for the years 2007/2012/2017 [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

remained stable in both sexes. In particular the number of women reporting low energy and vitality, low locus of control and exhaustion at work rose considerably in recent years. To our knowledge, these results are the first to document a 10-year trend of increasing nt-vrfs within a large cohort of participants living in an HIC, with sex differences concerning women. Potentially, this rise of nt-vrfs could be a reason for the steady increase of female VD [3].

### Traditional vascular risk factors and lifestyle factors

In addition to the "stroke prevention campaign" in 2001, there were only few other investigations of cardiovascular risk factors in Switzerland, all studying selected cohorts and not analyzing sex differences [27–30].

Generally, arterial hypertension was identified as the most important risk factor for global disease burden in 2010 [31]. In our cohort, the percentage of hypertension (27%) was stable over the last 5 years with a higher fraction of hypertension in men compared to women, but with a prevalence of less than 1/3, far below that of other HICs [32]. In line with previous studies, there was no increase in the prevalence of diabetes between 2007 and 2017 [33]. A high cholesterol level belongs to the top three potentially modifiable risk factors for ischaemic heart diseases [34]. Whereas, especially in the United States and other HICs a decline in people with high cholesterol level was observed (from 18% in 2000 to 11% in 2014) [35], our data suggest a stable/slightly increased prevalence in Switzerland over the last 10 years (2007/2017: men 18%/19%, women 14%/16%). Compared to other studies, a rise in obesity was observed over the last 10 years from 8% to 11% in 2017, but on a lower level than in the United States (2014 39.6%) [3] or Germany (2016 23.6%). The decrease in tobacco consumption in the Swiss population is a very positive development, especially in the light of a 25% greater risk for coronary heart disease in female compared to male smokers. The smoking ban cut daily passive smoking time in half from 37 to 19 min per day between 2007 and 2012. Physical inactivity is responsible for 1 to 2 million deaths per year worldwide, and the worldwide prevalence of physical inactivity is higher (35%) than that of smoking (26%) [36]. As a positive trend, and in line with US data, the proportion of people with an inactive (<30 min/week) or only partially active (30–149 min/week) lifestyle in Switzerland decreased from 33% (2007) to 24% (2017) [37]. Although drugs are not considered classical t-vrfs, like other health behaviors (tobacco consumption, nutrition, physical inactivity) they increase the risk of VD [3]. A relative increase was found in drug abuse over the last 10 years in Switzerland. The higher illicit consumption of cocaine, cannabis and ecstasy, particularly in men (2017 3% vs. 1%, 27% vs. 19%, 2% vs. 1%), was noticeable and similar to previous reports in Germany and Austria [38].

### Non-traditional vascular risk factors

The list of verified nt-vrfs is constantly growing. Our data confirm that the number of individuals experiencing substantial stress at

work has significantly increased over time in Switzerland. The potential relationship between (work-related) stress and VD is well known [39]. In the light of these findings, the trend of rising stress at work, job resignation and feeling exhausted at work in the Swiss population, particularly in women, is alarming. A relatively new marker of stress and nt-vrfs is working despite illness, also called sickness presenteeism. 31% of Swiss people did work despite illness in 2017, with a higher fraction of women. Compared to other studies such as the European Working Conditions Survey from 2012 (44,000 people in 34 countries), the Swiss prevalence (30% in men and 32% in women) was lower than in the EU (41% men, 45% women) [40]. However, VD risk is double in people with sickness presenteeism [41]. Another important finding is the increasing percentage of females reporting a rise in both low energy/vitality and low locus of control between 2007 and 2017. A low locus of control is associated with lower levels of leisure time and physical activity, and thus impacts other vrfs [42]. Furthermore, depression went up in the Swiss population between 2012 and 2017 in the categories severe/rather severe/middle. In fact, the higher prevalence of depression in women is alarming, considering that this nt-vrf was previously shown to double the risk of VD [43]. The comorbidity of sleep disorders and psychiatric disorders is well known. Hence, it is not surprising that the fraction of intermediate sleep disorders is rising, and in particular intermediate and severe sleeping problems are increasing, affecting more women compared to men. The prevalence of self-reported sleep disturbances in 2010 in the United States was about 14%–18% in men and 18%–25% in women, and on a lower level than in our reported data 7 years later in Switzerland (32% in women, 26% in men) [44].

### Strengths and limitations

The large number of participants, the well-grounded sampling plan, the weighting to correct for missing responses and the calibration for the correct representation of subgroups (e.g., sex, nationality, civilian status, age groups) are methodological strengths of this study. However, our study has several limitations related to its cross-sectional and observational study design. First, due to the observational nature of this study, temporal trends in environmental risk factors, including air pollution, were not available for this analysis [23].

Second, a potential selection bias may have occurred (a) due to the considerable number of dropouts, although this was accounted for by introducing weights in the sample plan of the BFS (see Supplementary methods), and (b) because people not living in their own household (e.g., living in retirement homes, prison, military, cloister) were not included. Third, the questionnaire was voluntary and questions could have been answered according to social desirability. Fourth, not everyone is aware of her/his medical condition; therefore, the answers rely on the knowledge of the survey participants. On the other hand, higher awareness of certain risk conditions such as hypertension or dyslipidemia by participants could be perceived as an increase in prevalence. However, the BFS performed various



plausibility checks to evaluate the validity of the responses; therefore they checked the plausibility of prior answers during the written questionnaires and telephone interviews with similar questions, for example regarding the actual medication. All prior surveys from 2007 to 2017 were conducted by applying similar methods; hence, the temporal trends can be considered reliable and are an important monitoring tool by the BFS to detect epidemiological trends early.

## CONCLUSION

Our data provide new insights into trends of cardiovascular risk behavior and health conditions in Switzerland between 2007 and 2017. It is shown that t-vrfs remained mostly stable, but that nt-vrfs are on the rise in Switzerland. This trend is more pronounced in women compared to men. Our results underscore the fact that sex differences exist for nt-vrfs, with a worrisome trend towards a particular increase in women. Further investigations and activities in prevention and public awareness are needed to target nt-vrfs for decreasing VD in women and men alike.

## AUTHOR CONTRIBUTIONS

**Martin Hänsel:** Data curation (lead); formal analysis (supporting); investigation (lead); writing – original draft (lead). **Klaus Steigmiller:** Formal analysis (equal); methodology (equal); software (equal); visualization (lead); writing – review and editing (supporting). **Andreas R. Luft:** Funding acquisition (equal); resources (equal); writing – review and editing (equal). **Catherine Gebhard:** Conceptualization (equal); funding acquisition (equal); writing – review and editing (equal). **Ulrike Held:** Formal analysis (equal); methodology (equal); software (equal); supervision (equal); validation (equal); writing – review and editing (supporting). **Susanne Wegener:** Conceptualization (lead); funding acquisition (lead); investigation (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (supporting).

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## CONFLICT OF INTEREST

The authors declare they have no conflict of interest pertaining to the current work.

## DATA AVAILABILITY STATEMENT

The data used in this article were provided by the Bundesamt für Statistik [BFS] by permission. Open access is not permitted; however, upon reasonable request the steering committee of the Bundesamt für Statistik may allow further follow-up analyses.

## ORCID

Martin Hänsel  <https://orcid.org/0000-0001-9300-1130>

Susanne Wegener  <https://orcid.org/0000-0003-4369-7023>

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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