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Article

Is self-rated health in adolescence a predictor of prescribed medication in adulthood? Findings from the Nord Trøndelag Health Study and the Norwegian Prescription Database

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ABSTRACT

Self-rated health (SRH) is a commonly used health indicator predicting morbidity and mortality in a range of populations. However, the relationship between SRH and medication is not well established. The aim of this study was to examine adolescent SRH as a predictor for prescribed medication later in young adulthood. Eighteen years' prospective data from the Nord-Trøndelag Health Study (HUNT) and the Norwegian Prescription Database (NorPD) were analyzed. Baseline data, gathered from 8982 adolescents (mean age 16.0 years) in the Young-HUNT I survey (1995–1997), were linked to individual data from NorPD, including information on all medications prescribed in 2013–2014. Gender-stratified negative binomial regression models were used to investigate the association between SRH and medication, also adjusted for age, baseline self-reported medicine use, physical and mental disability, smoking, and physical activity. Based on the Anatomical Therapeutic Chemical (ATC) Classification System, total consumption and consumption related to various ATC groups were examined.

The adjusted analyses showed a dose–response relationship for females, with poorer SRH predicting higher average medication for both total consumption and for the ATC groups "Musculoskeletal system" (M), "Nervous system" (N; Analgesics (N02), Opioids (N02A)) and "Respiratory system" (R). The predictive power of SRH, as well as the role of the adjustment factors, varies by gender and drug groups. This knowledge is important in order to identify risks for later disease and to capture pathological changes before and beyond the disease diagnosis, potentially preventing morbidity in the adult population.

Self-rated health (SRH or subjective, self-assessed, self-perceived health) is among the most commonly used indicators of present health status as seen from the individual's own perspective (Idler & Benyamini, 1997; Jylhä, 2009). It is commonly measured by a one-item question, where people are asked to rate their health status on a four- or five-point scale, from poor to excellent, or to compare their health with that of age peers (Jylhä, 2009). According to the literature, health is conceptualized during childhood and adolescence (Wade & Vingils, 1999; Breidablik, Meland & Lydersen, 2008). SRH thereafter seems to also be a stable construct (Boardman, 2006; Breidablik, Meland & Lydersen, 2009), in one study, over an 11-year period from adolescence to early adulthood (Vie, Hufthammer, Holmen, Meland & Breidablik, 2014). It encompasses biological, psychological and social dimensions (Fylkesnes & Forde, 1991; Manderbacka, 1998).

Several studies have showed that SRH measured by one single question is a powerful predictor of morbidity and mortality in a range of populations (Benyamini & Idler, 1999; Idler & Benyamini, 1997; Shadbolt, Barresi & Craft, 2002). Among adults, SRH has been related to functional ability (Idler & Kasl, 1995; Idler, Russell & Davis, 2000; Neufeld, Machacova, Mossey & Luborsky, 2013), health-risk behavior (Haddock et al., 2006), contact with primary care (Bath, 1999; Miilunpalo, Vuori, Oja, Pasanen & Urponen, 1997), hospitalization

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(Mutran & Ferraro, 1988; Doiron, Fiebiga, Joharb & Suziedelytec, 2015), and medical outcomes, i.e., diabetes mellitus (Wennberg et al., 2013) and cardiovascular disease (Møller, Kristensen & Hollnagel, 1996). Individuals reporting poor SRH are worse off than those who rate their health as good, and the predictive effect of SRH on health outcomes remains after controlling for both demographic factors and objective measures of health status (DeSalvo, Bloser, Reynolds, He & Muntner, 2006; Idler & Benyamini, 1997).

SRH has also been associated both with over-the-counter (OTC) medications and with prescription drugs. In Europe, in the cross-sectional study among 4824 adolescents, poor SRH predicted more frequent use of OTC medications (Holstein, Hansen, Andersen & Due, 2008), and in a sample of 6702 persons, aged 20–79 years, those who rated their health as poor were more likely to be daily (versus sporadic) users of analgesics and drugs against dyspepsia/peptic ulcer (Furu & Thelle, 2001). In another cross-sectional study amongst 3085 adults in Bangladesh (where essentially no prescription is needed to purchase medicine), bad SRH was associated with two times higher medicine consumption than self-reported "good health" (Haque,Tisha, Mustafa & Rahman, 2015). A Finnish study of 700 older community-dwelling people found poor SRH as one of the factors most significantly associated with analgesic use (Pokela, Bell, Lihavainen, Sulkava & Hartikainen, 2010). In a cross-sectional study poor subjective health also acted as an independent predictor of polypharmacy (five or more prescribed drugs) among 466 older general practice patients in Germany (Junius-Walker, Theile & Hummers-Pradier, 2007). In a one-year prospective framework an Australian study (with over 200,000 observations) self-assessed health indeed predicted future health, as measured by hospitalizations, out-of-hospital medical services and prescription drugs (Doiron et al., 2015). In contrast, in a cross sectional study among 131 Danish schoolchildren maternal health (including SRH) did not significantly influence child use of OTC analgesics in the past 3 months (Jensen et al. 2014).

However, there is a lack of prospective studies investigating the relationship between SRH and medication among younger subjects and future health (Gobina et al., 2011). As objective health status is also assumed to influence the person's subjective rating of their health (Murata, Kondo, Tamakoshi, Yatsuya & Toyoshima, 2006), longitudinal studies are needed to confirm the findings and the temporal relationship. Additionally, most current studies on young populations examine self-reported or OTC medications, whereas few studies examine the link between SRH and prescribed medication.

Prescribed medication is one of the health care systems' most important methods to treat, relieve, and sometimes cure diseases (Skoog, Midlöv, Borgquist, Sundquist & Halling, 2014), and the majority (over 50%) of medical consultations is found to result in a prescription (Loikas, Wettermark, von Euler, Bergman & Schenck-Gustafsson, 2013; Wilson, McDonald, Hayes & Cooney, 1992). In Norway, prescribed medication accounted for 86% of total number of defined daily doses (DDD) in 2014, and these fractions have remained relatively constant over time (Sakshaug, 2016). Further, prescribed medication is an important objective health indicator, as it is prescribed by a doctor intended to be used by a person in the diagnosis, cure, mitigation, treatment, or prevention of specific diseases. As the different drug groups as described by the Anatomical Therapeutic Chemical (ATC) Classification system (WHO Collaborating Centre for Drug Statistics Methodology, 2014) reflect different bodily systems (e.g. cardiovascular, musculoskeletal, nervous systems), information regarding the association between SRH and specific drug groups may give a more nuanced understanding of the relationship between SRH and specific health outcomes. Although the associations between SRH and later morbidity are well documented (Idler & Benyamini, 1997), its mechanisms are poorly understood, especially regarding which bodily systems are involved. A relevant question is whether subjective health perceptions predict disease from certain bodily systems more than others.

A theoretical framework that may be used to understand the underlying mechanisms through which SRH results in chronic or "objective" disease is the conceptual model of allostasis (McEwen & Seeman, 1999). Allostasis is the adaptive regulatory process that maintains homeostasis during exposure to physical, psychosocial and environmental challenges or stressors (McEwen & Seeman, 1999). Yet, excessive amounts of such activation may results in allostatic load (AL) leading to physiological dysregulation, which in turn may increase the risk of manifest disease in multiple bodily system. In view of this model, previous research has found poor SRH in adolescence to predict AL 11 years later via mechanisms of sustained activation of multiple bodily systems, including biomarkers representing the endocrine (HR), metabolic (HDL, triglycerides, diabetes risk profile) and anthropometric (WHR, BMI) system (Vie, Meland & Breidablik, 2014). In such a view an examination of the relation between SRH and different drug groups may increase our understanding of the relation between SRH and different bodily systems. Yet, except from the Australian one-year prospective study (Doiron et al., 2015), the current studies presented above, do not examine medication from several drug groups at one time.

The main aim of the present study was to examine to what degree SRH in adolescence predicts prescribed medication eighteen years later, in adult age. We examine both total consumption and the following ATC groups: the "Cardiovascular system", "Antiinfectives for systemic use", the "Musculoskeletal system", the "Nervous system" and the "Respiratory system", thereby also testing if SRH predicts certain medication group better than others.

Method

Study population

The study is based on the Norwegian Prescription Database (NorPD) and eighteen years' prospective data from the Nord-Trøndelag Health (HUNT) Study. The HUNT Study is a large population-based health study in the county of Nord-Trøndelag, Norway, based on self-reported questionnaires, interviews and clinical measurements. The baseline data for the present study were collected in the Young-HUNT1 survey (1995–1997), in which 10,202 adolescents (ages 12–20) were invited, and 8982 (4519 males and 4463 females) completed the questionnaire (response rate 88%) (Fig. 1). For a detailed description of the sample and design of the project, see Holmen et al. (2013) and Krokstad et al. (2013). Questionnaires are available at the HUNT website, https://www.ntnu.edu/hunt/data/que.

Using the unique 11-digit personal identity number assigned to every Norwegian citizen at birth, the data from Young-HUNT1, were accurately linked to individual data from the NorPD prescription database at the Norwegian Institute of Public Health (for details regarding the linkage procedure, see https://www.ntnu.edu/hunt/merging-registries; see also Holmen et al., 2013; Furu, 2008). The NorPD monitors drugs dispensed by prescription in Norway and the database contains a complete listing of all prescription drugs dispensed by pharmacies since 2004. It captures all prescriptions dispensed at pharmacies to individual patients in open care, and all pharmacies in Norway are obliged by law to forward prescription data to the NorPD (Furu, 2008). As the data are collected from pharmacies, it only captures prescriptions that are actually dispensed (and not over-the-counter medication or medication bought abroad). Hence, we only included dispensed prescription and the register has 100% coverage. In the present study, we include information on all prescribed medications for the years 2013 and 2014 (measured as the number of prescriptions, as information on defined daily dose (DDD) was frequently not available) (see also the NorPD website; http://www.norpd.no/).

The Norwegian Health Care system has a universal coverage, with a small co-payment in primary care (OECD Economic Surveys, 2005). General practice is the first line of medical healthcare, and is based on a

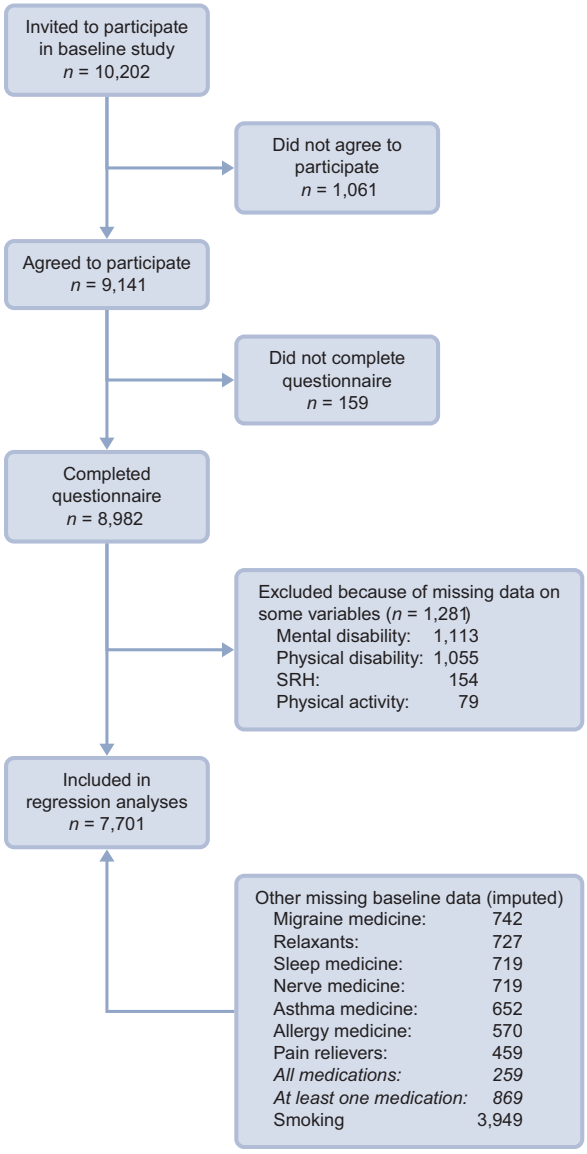

Fig. 1. Study population flow chart.

Regular General Practitioner Scheme, and a patient list system established for the entire population (St.meld. nr. 23, 1996–1997). Hence, most people who reside in Norway have access to a regular general practitioner (GP). The GPs are gatekeepers to specialist services and therefore exert large influence on specialist utilization (St.meld. nr. 23, 1996–1997).

Measures

Self-rated health (SRH) measured in the Young-HUNT1 survey is based on a four-point ordinal scale answer to the question "How is your health at the moment?", with the possible responses "Very good", "Good", "Not so good", and "Poor". Since few respondents (0.6%) reported their health as "Poor", we have grouped them together with the respondents reporting "Not so good" in the statistical analyses.

Medication

Prescribed medicines recorded in the NorPD are classified according to the ATC classification system as of 2015 (WHO, 2014). Based on the ATC system and previous findings linking SRH to different bodily system (Christian et al. 2011; Doiron et al., 2015; Janszky, Lekander, Blom, Georgiades & Ahnve, 2005; Pokela et al., 2010; Rogers, Everett, Saint Onge & Krueger, 2010; van der Linde et al., 2013; Vie et al., 2014), we define nine drug groups (Table 2), including a group for *all* prescriptions excluding contraceptives (G03A and G03B). Quantities of dispensed drugs are measured in terms of the number of prescriptions (as DDD information was not available for many of the prescriptions).

Unadjusted and adjusted analyses

We performed separate analyses for males and females, since gender has been associated with both SRH (Idler, 1993; Idler & Benyamini, 1997; Manderbacka, 1998) and medication (Fernández-Liz et al., 2008). Similarly, baseline *medicine use* (Bertoldi et al. 2012), *smoking* (Barendregt, Bonneux, & van der Maas, 1997; Lasser et al. 2000), *physical and mental disability* (Doiron et al., 2015), and *physical activity* (Dale et al. 2015) have all been associated with subjective health perceptions and may affect the relationship between SRH and medication by influencing both the independent and dependent variables. Research has also shown a joint effect of multiple lifestyle behaviors (e.g., smoking and physical activity) on health outcomes (Ford, Zhao, Tsai & Li, 2011). We therefore report the association between SRH and medication adjusted for all these predictors.

In the current study *baseline medicine use* was based on questions worded like "Do you take/use any of these medicines or dietary supplements?", including seven types of medications: pain relievers, migraine medicine, sleep medicine, nerve medicine, relaxants, asthma medicine, and allergy medicine. Daily use was recorded as "yes" if the person used at least one of these medicines daily. The question on *physical activity* had the response options "yes", "no" and "no, but used to participate in physical activity before" (the latter was treated as "no"). For *smoking*, there were similar options ("yes" and "no", but with some qualifiers, e.g. "no, but earlier I sometimes used to smoke" treated as no). *Physical and mental disability* was assessed by asking the participants if they had suffered from any long-term illness or injury of a physical or psychological nature that impaired their functioning in everyday life ("yes" and "no"). Table 1 shows demographic data for

Table 1
Demographic data for adolescents, stratified by self-reported health.

	Not so good/poor (*n* = 968)		Good (*n* = 5352)		Very good (*n* = 2508)		Overall (*n* = 8828)	
	Mean/*n*	SD/%	Mean/*n*	SD/%	Mean/*n*	SD/%	Mean/*n*	SD/%
Age	16.2	1.8	16.1	1.8	15.9	1.8	16.0	1.8
Sex, male	437	45%	2498	47%	1506	60%	4441	50%
Daily smoker	314	41%	1066	23%	227	10%	1607	21%
Daily medication	133	17%	409	9%	101	4%	643	8%
Physical disability	187	23%	322	7%	52	2%	561	7%
Mental disability	134	17%	204	4%	38	2%	376	5%
Physically active	314	33%	2588	49%	1708	68%	4610	52%

adolescents and the included variables, stratified by SRH.

Ethics

All study subjects and the parents or guardians of those under the age of 16 years gave written consent to participate in the HUNT study and to the use of data for research. It was informed that participation was voluntary. The study was approved by the Norwegian Data Inspectorate, the Regional and National Committees for Medical and Health Research Ethics and the Norwegian Directorate of Health.

Statistical methods

We report the crude number of prescriptions stratified by SRH as means with 95% percentile bootstrap confidence intervals (based on 10,000 replications), along with *p*-values from Welch ANOVA tests (Welch, 1951). This test was chosen because it is sensitive to differences in means while being insensitive to differences in variances.

To examine how much a single, coarsely categorized, question on self-reported health could predict the number of prescriptions, we fitted count regression models with SRH as a predictor. To assess whether SRH still had any predictive power on prescription use when including common (strong) predictors of prescription use, we included age (continuous), daily use of medication (yes/no), physical disability (yes/no), mental disability (yes/no), smoking (yes/no), and physical activity (yes/no) as additional predictors. Initial analyses revealed that Poisson count models did not fit the data well, because they predicted a smaller variation in the number of prescriptions than what was observed. To account for this overdispersion, we therefore fitted negative binomial regression models. We report the results from the models as exponentiated coefficients, which estimate the relative increase/decrease in the mean number of prescriptions for different levels of the predictors compared to their reference levels. For all models, we used "good SRH" as the reference level for SRH, since it is the most common SRH level, i.e. corresponding a "typical" person, and "no" for binary predictors.

All data analyses were done using R version 3.3.0 (R Core Team 2016). The negative binomial regression models were fitted using the "glm.nb" function in the "MASS" package (Venables & Ripley 2002). We examined the models for any problems with multicolinearity, using the VIF statistic. For all tests, we define *statistically significant* as having a *P*-value ≤ 0.05.

There were little missing data on SRH, and for the main analyses we therefore only report results on non-missing SRH status. For daily use of medication, we treat missing responses as "no" daily use. For the other variables, we use complete-case analysis, and report the number of observations the analyses are based on.

Results

Descriptive statistics

At baseline (T1), the vast majority (89%) of the respondents rated their health as "good" (61%) or "very good" (28%), while 11% rated their health as "not so good" (10%) or "poor" (0,6%). The overall prevalence of medication use was 9% (males 8%, females 10%). Table 2 shows the average number of prescribed medications, stratified by ATC group, sex, and SRH.

SRH as a predictor of prescribed medication

Table 3 and Fig. 2a show the results of sex-stratified negative binomial regression models for SRH in adolescence (T1) as a predictor of the number of prescribed medication in adult age (T2). For space reasons, we only report the (unadjusted and adjusted) estimated effect of SRH. There were no problems with multicolinearity, as all VIF values were < 2.

In the unadjusted analyses, for both sexes, SRH in adolescence predicted *total* drug consumption in adulthood. The result shows a dose–response relationship between SRH and medicine use, with poorer SRH in adolescence predicting higher average medication in adulthood. Adjusting for age, baseline medicine use, physical activity, smoking, and mental and physical disability attenuated the effect of SRH on later medication, and it was no longer statistically significant for men.

More specifically, the adjusted analyses showed a dose–response relationship, with poor SRH in adolescence predicting higher average medication for both total consumption and the ATC groups "Musculoskeletal system" (M), "Nervous system" (N; Analgesics (N02), "Opioids" (N02A)) and "Respiratory system" (R) for females. For males there was no statistically significant results for the adjusted analysis. Hence, prescribed medication for the "Cardiovascular system"; "Antiinfectives for systemic use"; "Anxiolytics/hypnotics/sedatives" and "Antipsychotics/antidepressants/psychostimulants" in adult age were not predicted by adolescence SRH in the adjusted analyses. All the adjustment variables *were* associated with later prescriptions, yet in different degrees, depending on medicine groups and gender. Especially baseline self-reported medication seems to play an important role as a predictor (for both genders): Those respondents reporting medicine use in adolescence were more likely to use prescription drugs in adult age.

For the cardiovascular system, the estimated effects showed dose–response relationships for both sexes, but none of the models achieved statistical significance.

For antiinfectives for systemic use, in the unadjusted analyses, we found a clear effect for females, but none for males. Adjusting for other predictors attenuated the estimated predictive effect of SRH.

For the muscolo-skeletal system, the unadjusted models showed statistically significant effects for both females and males. In the adjusted models these effects were attenuated, and for males no longer significant.

For the analgesics group, there were large effects of SRH for both females and males. Again, these were attenuated when adjusted for other predictors (and no longer significant for males).

For the anxiolytics/hypnotics/sedatives group the largest, and only statistical significant, effect was found for females.

For the opioid group, SRH had a predictive effect in the unadjusted analyses for both sexes, and for females it remained significant (but attenuated) after adjustment.

The antipsychotics/antidepressants/psychostimulants group only showed a predictive effect of SRH for females, and only before adjusting for other predictors.

The respiration group showed statistically significant effects for both unadjusted and adjusted analyses for females. For males, the estimated effect was much smaller, and significant only in the unadjusted model.

There was an association between SRH status and having an incomplete questionnaire ($P < 0.001$), where the people with some missing data reported worse SRH (17% reporting "poor"/"not so good" SRH, as compared to 10% for the people with complete data).

Discussion

The aim of the present study was to examine SRH in adolescence as a predictor of prescribed medication in adulthood, by using 18 years prospective data from a large population-based sample and register-based outcomes. More specifically, using the Anatomical Therapeutic Chemical (ATC) Classification System (WHO Collaborating Centre for Drug Statistics Methodology, 2014), we aimed to examine adolescence SRH as a predictor for both total medication consumption and for medication consumption related to specific ATC groups.

Adjusting for age, smoking, baseline medicine use, physical activity, and mental and physical disability, the analyses showed a dose–response relationship between SRH in adolescence and total

Table 2
Average number of prescribed medicines (with 95% confidence intervals) in young adulthood for different levels of SRH status in adolescence.

Group	ATC code(s)	Sex	Not so good / poor	Good	Very good	P-value[a]
Total, excl. contraceptives	All except G03A and G02B	Female	14.8 (12.5–17.8)	9.3 (8.7–9.8)	7.6 (6.8–8.7)	< .001
		Male	8.9 (6.8–11.7)	6.9 (6.2–7.7)	5.3 (4.6–6.1)	0.001
Cardiovascular system	C	Female	0.6 (0.3–0.9)	0.2 (0.2–0.3)	0.2 (0.1–0.2)	0.03
		Male	0.4 (0.2–0.7)	0.3 (0.2–0.4)	0.2 (0.2 to 0.3)	0.34
Antiinfectives for systemic use	J	Female	1.4 (1.2–1.6)	1.2 (1.1 to 1.3)	1.0 (0.9–1.1)	< .001
		Male	0.6 (0.5–0.7)	0.5 (0.5–0.6)	0.6 (0.5–0.6)	0.93
Musculoskeletal system	M	Female	1.2 (1.0–1.4)	0.8 (0.7–0.9)	0.6 (0.5–0.7)	< .001
		Male	0.8 (0.6–1.1)	0.6 (0.6–0.7)	0.5 (0.5–0.6)	0.02
Analgesics	N02	Female	2.1 (1.6–2.7)	1.2 (1.0–1.4)	0.7 (0.5–1.0)	< .001
		Male	1.6 (0.8–2.5)	0.8 (0.6–1.0)	0.5 (0.4–0.7)	0.02
Anxiolytics/hypnotics/sedatives	N05B, N05C(A-F)	Female	0.7 (0.4–1.1)	0.4 (0.3–0.5)	0.3 (0.1–0.4)	0.04
		Male	0.6 (0.2–1.2)	0.3 (0.2–0.4)	0.2 (0.–0.4)	0.30
Opioids	N02A	Female	1.0 (0.7–1.5)	0.6 (0.5–0.8)	0.3 (0.2–0.6)	0.006
		Male	1.2 (0.5–2.1)	0.6 (0.4–0.8)	0.4 (0.2–0.5)	0.04
Antipsychotics/antidepressants/psychostimulants	N05A, N06A,and N06B	Female	1.8 (1.1–2.9)	0.7 (0.6–0.8)	0.6 (0.4–0.8)	0.03
		Male	1.1 (0.7–1.5)	0.7 (0.5–0.9)	0.6 (0.3–1.0)	0.28
Respiration	R	Female	2.2 (1.8–2.6)	1.5 (1.4–1.6)	1.2 (1.0–1.4)	< .001
		Male	1.3 (1.1–1.6)	1.1 (1.0–1.2)	0.9 (0.8–1.1)	0.01

The medicines are classified according to the ATC classification system as of 2015 (WHO, 2014), in 9 groups, including a group for all prescriptions excluding contraceptives (n = 8828).
Abbreviations: WHO: World Health Organization; ATC: Anatomical Therapeutic Chemical; SRH: Self-rated health.
[a] Test of difference in mean number of prescribed medicines (Welch ANOVA test).

consumption in young adulthood, with poorer SRH predicting higher average medication for both total consumption and the ATC groups "Musculoskeletal system" (M); "Nervous system" (N; Analgesics (N02); Opioids (N02A)), and "Respiratory system" (R) for females, but not for males. The predictive power of SRH, as well as the role of the adjustment factors, varied by gender and drug groups.

The finding that adolescent SRH predicted prescribed medication (both total and with regard to the specific drug groups) in adult age corresponds with previous research, which has consistently shown SRH to predict morbidity and mortality (Idler & Benyamini, 1997; Benyamini & idler, 1999; Shadbolt et al., 2002) and also with a previous cross-sectional study showing associations between SRH and self-reported medicine use among adolescence (Holstein et al., 2008), and a one-year prospective study showing subjective health to predict prescribed medication among adults (Doiron et al., 2015). The current study expands on this, by demonstrating that SRH is also important with regard to prescribed medication, in a long-term perspective, from adolescence and eighteen years later to (young) adulthood. This indicates that subjective health perceptions early in life affect long-term health. Moreover, by demonstrating the association between SRH and the specific ATC groups across genders, the current findings indicate some possible psychological and physiological mechanisms (e.g. the musculoskeletal system and the nervous system), linking SRH in adolescence to future health outcomes.

As expected, the effect of SRH on later medication decreased in the adjusted analyses. All the adjustment variables were associated with later prescriptions, yet in different degrees, depending on medicine groups and gender.

We had some missing data on the other predictors included in the regression models, and missingness was related to SRH. The effect of this is that people with poor SRH are underrepresented in our study. As people with "poor"/"no so good" SRH might be less inclined to complete a large questionnaire, we suspect that of the people *actually analyzed*, the ones reported to have the lowest levels of SRH are somewhat more healthy than the corresponding people in the whole population.

Several explanations for the association between SHR and later objective health exist. In line with Idler and Benyamini (1997) one possible explanation for the current findings is that SRH elicit inclusive "summary ratings" of health, which likely capture diagnosed diseases, severity and comorbidity of conditions, but *also* self-perceived but not-yet-diagnosable bodily sensations related to disease processes. Second, SRH ratings are dynamic catching chronic, but also recent or recurrent health problems that otherwise may be missed during one-time "objective" evaluations (Idler & Benyamini, 1997). Third, SRH reflects, and also affects behavioral factors (e.g., smoking and physical activity) and emotional factors (e.g., depression) (Idler & Benyamini, 1997). Finally, SRH reflects a person's perceived resources (e.g., social support) that may influence later health (Benyamini, 2011). Clearly, the mechanisms are complex and although existing evidence provides support for each of these explanations, the actual mechanisms underlying the predictive validity of SRH in relation to subsequent health remain complex.

The current findings add to the literature by demonstrating that SRH relates to multiple bodily (both physiological and psychological) systems. The finding that SRH in adolescence predicted prescribed medications for the musculoskeletal system (ATC group M) for females corresponds with Doiron et al. (2015) showing that subjective health perception had significant effects on drugs and certain out-of-hospital medical services (by rheumatologists, physiotherapists and podiatrists). It should be noted that in Norway some painkillers that may be used for the musculoskeletal system including nonsteroidal anti-inflammatory drugs (NSAIDs) are available without a prescription. Consequently, our significant finding regarding SRH as a predictor for medication representing the musculoskeletal system can be treated as a more "pure" result, representing the association between SRH and more *serious* ailments that are associated with the musculoskeletal system.

The current study also shows that SRH in adolescence predicted the number of prescribed medications for the ATC-group N (nervous system). More specifically, the finding that SRH in adolescence predicted later use of analgesics for females supports the cross-sectional study who found a difference between sporadic and daily users of analgesics depending on the extent they rated their health as poor (Furu & Thelle, 2001). Another one-year prospective study found poor SRH to be one of the main factors associated with analgesic use (Pokela et al., 2010). Furthermore, the finding that SRH in adolescence (T1) predicted prescription for opioids is partly in line with a Danish study showing that users of opioids clearly had a poorer SRH compared with users of other drug groups (Rosholm & Christensen, 1997).

Table 3
Estimated predictive effect of SRH in adolescence (HUNT 1,1995–1997) on the number of prescriptions in young adulthood (NorPD, 2013–2014),*.

Sex	Group	Adjustment**	SRH: Not very good / poor			SRH: Very good			*P*-value[b]
			Estimate	95% CI	*P*-value[a]	Estimate	95% CI	*P*-value[a]	
Females	Total, excl. contraceptives	Unadjusted	1.51	1.32 to 1.73	< .001	0.80	0.72 to 0.88	< .001	< .001
		Adjusted	1.29	1.12 to 1.48	< .001	0.84	0.76 to 0.94	0.001	< .001
	Cardiovascular system	Unadjusted	1.49	0.89 to 2.66	0.15	0.75	0.49 to 1.14	0.17	0.08
		Adjusted	1.48	0.86 to 2.68	0.18	0.79	0.52 to 1.23	0.28	0.16
	Antiinfectives for systemic use	Unadjusted	1.21	1.03 to 1.42	0.02	0.86	0.76 to 0.98	0.02	0.001
		Adjusted	1.12	0.95 to 1.32	0.18	0.91	0.80 to 1.03	0.12	0.09
	Musculoskeletal system	Unadjusted	1.47	1.19 to 1.83	< .001	0.72	0.60 to 0.85	< .001	< .001
		Adjusted	1.21	0.97 to 1.53	0.10	0.77	0.65 to 0.92	0.004	0.002
	Analgesics	Unadjusted	1.69	1.25 to 2.32	< .001	0.65	0.51 to 0.82	< .001	< .001
		Adjusted	1.33	0.96 to 1.88	0.08	0.69	0.54 to 0.88	0.002	0.001
	Anxiolytics/hypnotics/sedatives	Unadjusted	1.56	0.90 to 2.88	0.13	0.56	0.37 to 0.88	0.01	0.005
		Adjusted	1.15	0.65 to 2.16	0.64	0.62	0.39 to 1.01	0.04	0.12
	Opioids	Unadjusted	1.46	1.02 to 2.12	0.04	0.55	0.42 to 0.74	< .001	< .001
		Adjusted	1.10	0.75 to 1.64	0.64	0.60	0.45 to 0.81	< .001	0.003
	Antipsychotics/antidepressants/	Unadjusted	1.99	1.19 to 3.56	0.01	0.78	0.52 to 1.19	0.24	0.006
	psychostimulants	Adjusted	1.31	0.76 to 2.39	0.35	0.81	0.54 to 1.25	0.32	0.32
	Respiration	Unadjusted	1.56	1.25 to 1.96	< .001	0.82	0.69 to 0.97	0.02	< .001
		Adjusted	1.31	1.05 to 1.66	0.02	0.81	0.68 to 0.96	0.01	< .001
Males	Total, excl. contraceptives	Unadjusted	1.25	1.05 to 1.51	0.02	0.79	0.71 to 0.88	< .001	< .001
		Adjusted	0.96	0.80 to 1.16	0.65	0.90	0.81 to 1.01	0.08	0.22
	Cardiovascular system	Unadjusted	1.49	0.74 to 3.39	0.29	0.73	0.46 to 1.17	0.18	0.14
		Adjusted	1.25	0.61 to 2.85	0.55	0.75	0.46 to 1.22	0.22	0.35
	Antiinfectives for systemic use	Unadjusted	1.00	0.79 to 1.25	0.98	0.99	0.86 to 1.14	0.90	0.99
		Adjusted	0.94	0.74 to 1.18	0.58	1.04	0.90 to 1.20	0.59	0.69
	Musculoskeletal system	Unadjusted	1.15	0.90 to 1.47	0.27	0.83	0.71 to 0.97	0.02	0.01
		Adjusted	1.03	0.80 to 1.32	0.83	0.92	0.78 to 1.08	0.28	0.53
	Analgesics	Unadjusted	2.07	1.43 to 3.07	< .001	0.62	0.49to0.80	< .001	< .001
		Adjusted	1.26	0.85 to 1.92	0.23	0.82	0.64 to 1.05	0.10	0.12
	Anxiolytics/hypnotics/sedatives	Unadjusted	1.98	0.88 to 5.31	0.13	0.80	0.47 to 1.41	0.43	0.12
		Adjusted	0.83	0.36 to 2.18	0.67	0.86	0.51 to 1.45	0.56	0.80
	Opioids	Unadjusted	2.05	1.34 to 3.28	0.002	0.57	0.43 to 0.77	< .001	< .001
		Adjusted	1.19	0.75 to 1.96	0.44	0.81	0.60 to 1.09	0.15	0.26
	Antipsychotics/antidepressants/	Unadjusted	1.25	0.59 to 3.07	0.59	1.00	0.62 to 1.66	0.99	0.85
	psychostimulants	Adjusted	0.94	0.45 to 2.28	0.89	1.37	0.84 to 2.28	0.21	0.42
	Respiration	Unadjusted	1.19	0.90 to 1.60	0.23	0.84	0.70 to 1.00	0.05	0.03
		Adjusted	0.96	0.72 to 1.29	0.78	0.91	0.76 to 1.08	0.29	0.56

Abbreviations: SRH: Self-rated health. CI: Confidence interval.

* Based on negative binomial regression models stratified by sex (n = 4,441 for males and n = 4,387 for females). The reference group is "good" SRH, and the estimates are count ratios, e.g. an estimate of 1.5 for "not very good / poor" SRH indicates an expected 50% increase in the number of prescriptions as compared to "good" SRH.

** The "adjusted" results are adjusted for age, daily use of medication, physical disability, mental disability, smoking, and physical activity.

[a] P-values for testing the if the number of prescriptions for the given SRH level differs from the number of prescriptions for the reference SRH level ("good" SRH, representing a "typical" person).

[b] P-values for testing the overall effect of SRH level on the number of prescriptions, i.e. if the number of prescriptions vary among the three SRH levels.

Finally, SRH in adolescence (T1) predicted the number of prescribed medication for respiration among females (and males in the unadjusted analysis). This finding corresponds with Latham and Peek (2013), which described significant associations between SRH and subsequent morbidity in arthritis and lung disease.

However, the predictive effect of SRH on ATC group C (the

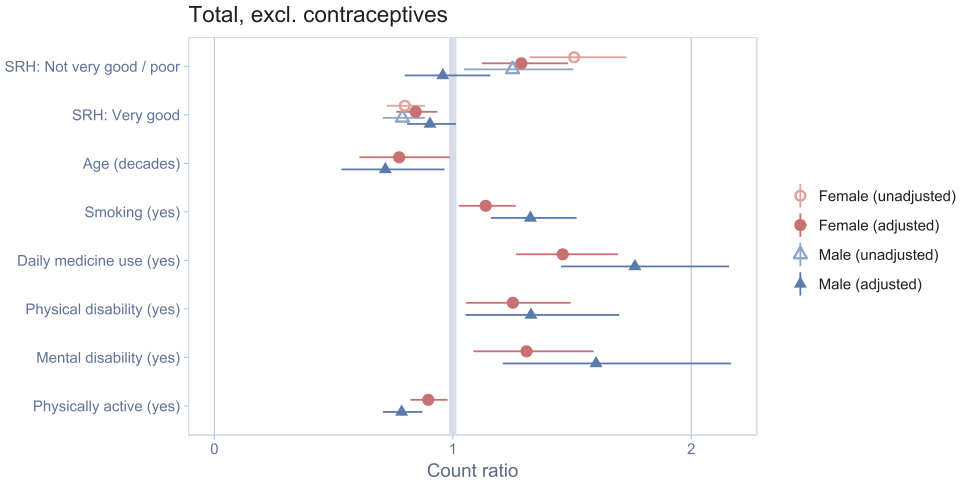

Fig. 2. (a). Estimated predictive effect of SRH and other potential risk factors in adolescence on the number of prescriptions in young adulthood. The reference group is "good" SRH, and the estimates are count ratios, e.g. an estimate of 1.5 for "not very good / poor" SRH indicates an expected 50% increase in the number of prescriptions as compared to "good" SRH. The horizontal lines show 95% confidence intervals.

cardiovascular system) did not achieve statistically significance, in contrast to previous research, revealing SRH as a strong predictor of cardiovascular disease (van der Linde et al., 2013). One reason for this may be our young (30–40 years old) and healthy population, where medication for cardiovascular disease are not prevalent.

Notably, the current study demonstrated sex differences regarding the association between SRH and future medication, both with regard to total consumption, consumption related to the specific ATC groups, and regarding the adjustment variables. Specifically, the adjusted analyses show that SRH predict total medicine consumption only among females. In reference to the specific ATC groups, SRH seem to influence future medication more broadly among females, as compared to males. Previous studies have found inconsistencies in sex differences regarding the predictive ability of SRH on both morbidity and mortality, with some studies demonstrating the relation between SRH and mortality for females (Halford, Ekselius, Anderzen, Arnetz & Svärdsudd, 2010), whereas in other studies it was demonstrated only for males (Benyamini & Idler, 1999; Deeg & Kriegsman, 2003). One possible explanation for these gender differences is that the study variables included may reflect gender differences it-self as there are significant differences in both health perceptions and drug prescription between females and males in Europe and the United States (Skoog et at., 2014). In general, females assess their health worse than males do (Currie et al., 2012), tend to have more health complaints, to use more prescription drugs as compared to males (Gobina et al., 2011). Females may also be more likely to pursue medical services (Jorm, Grayson, Creasey, Waite & Broe, 2000), increasing their probability of receiving prescriptions over time (Nordfjærn, Bjerkeset, Moylan, Berk & Gråwe, 2013). Second, the meaning of health and, accordingly, the interpretation of the SRH question may differ between males and females, as females may put weight on more widespread health problems, while males may put emphasis on diseases affecting longevity (Idler & Benyamini, 1997). Females may also base SRH on a wider range of health-related factors, as compared to males (Benyamini, Leventhal & Leventhal, 2000; Brunner, 2006). Third, the potential predictors of the association between SRH and future health may differ between males and females (Deeg & Kriegsman, 2003). Accordingly, the choice of predictors to adjust for may result in overestimation of the predictive ability of SRH in one or both genders.

In sum, the findings that SRHs act as a predictor for several ATC groups reflects its associations with multiple bodily systems and adds support to previous research linking SRH to stress theory-based psychobiological mechanisms, as well as multi-morbidity (Mavaddat, Valderas, van der Linde, Khaw & Kinmonth, 2014). Yet, the findings that the relative increase/decrease in prescription for different SRH response varies between medication groups, and further highlights the biological basis of SRH, suggesting that a limited focus on any one health domain may limit the ability to understand health outcomes for which self-rated health is predictive in a long-term perspective (Perruccio, Katz & Losina, 2012).

Strengths and limitations

To our knowledge, this is the first prospective study of SRH and prescribed medication that followed the investigated variables from adolescence to young adulthood. Most previous studies on SRH and health outcomes have focused on the elderly, and few studies investigate the relationship between SRH and health-outcomes from adolescence to adulthood. Further, most of the current research has a cross-sectional design, and longitudinal studies have been lacking to confirm the findings and clarify the temporal relationship between SRH and health-related outcomes. A major strength of this study is that we investigated SRH and medication by using an eighteen years' prospective design, allowing us to identify SRH as a protective or risk factor for ill health and subsequent medication.

The large population-based sample, as well as the high participation rate, reinforces the validity of the data. Additionally, the use of a comprehensive national prescription register, reduce selection or information biases, and minimize risk of errors in measurement of medicine use due to underreporting or inadequate recall by respondents. Yet, lack of information on adherence is a common concern when reporting prescription data for medication, as drug dispensed at pharmacy, but never or irregularly used, cannot be detected. Yet, as medication in the current study are seen as a measure for health and not necessarily medication intake, prescribed medication seem to be a valid measure of health as it is prescribed by a doctor and intended to treat, relieve, or cure specific diseases.

A further strength is the use of objective data when investigating the SRH–health relationship, as recommended in the SRH literature (Jylhä, Volpato & Guralnik, 2006). Furthermore, in contrast to current research on SRH and medication, we investigated both total and specific drug consumption, using the ATC classification system, recommended by the World Health Organization (WHO). However, one drawback is that the medication data are based on the number of prescriptions. DDD, which were not available on many of the prescriptions used in the current study, may be a better measure of medication use, as dose size may say something about the seriousness of diseases (Rønning, 2001). Yet, we believe that excluding prescriptions with missing DDD would introduce more bias than using the number of prescriptions as an aggregate measure of medicine use would. We also had some missing data on the other predictors included in the regression models, limiting the generalizability of the results.

In addition, factors that are unaccounted for in our analyses might be influencing the association between SRH and health. The lack of information on socioeconomic differences, for example, could be a limitation and may influence the results, as it has shown to be an important predictor of overall health and SRH (Goodman, Huang, Schafer-Kalkhoff & Adler, 2007). Parental education may also influence SRH among adolescents (Breidablik, Meland, Holmen & Lydersen, 2010). In addition, the health care attendance varies with many factors such as gender, age, SES, self-management etc. (Grasdal & Monstad, 2011; Vikum, Krokstad & Westin, 2012; Vikum, Johnsen & Krokstad, 2013). Further, the Young-HUNT Study has high attendance rate among adolescents attending school, while most non-participants were not in school when the study was conducted. Therefore, non-attending students may have more somatic or mental health problems than attending participants (Holmen et al., 2013). Finally, it should be acknowledged that both SRH and medicine use, are rather skewed variables, possibly influencing the findings.

Conclusion

The findings suggest that SRH predicts both mental and physical future health, as measured by prescribed medication. The predictive effect of SRH, as well as the influence of the various variables adjusted for, varies by type of medication and gender. This information may be used to identify those at risk for future medication and to further understand the predictive power of SRH. Given that SRH is mainly formed early in life and also seems to be a stable construct over time, the finding that SRH may be a marker for subclinical conditions and/or early morbidity, indicate that prevention and intervention efforts related to SRH early in life may be critical to promoting and maintaining health. SRH is also an important indicator of public health, as it reflects objective health status and can serve as a global measure of health status in the general population. Further, SRH could be used as a tool in the Norwegian healthcare system to identify those who are most in need of their services (Wu et al., 2013).

The unique value of this study is that it measures SRH earlier in life, which may improve the ability to predict, prevent and manage disease over a greater portion of the life span, resulting in improved health and greater efficiencies in delivering effective care. This should be of interest to the health-care community worldwide. In a global health

perspective, the current findings also contribute to better understanding of the specific predictive power of this important global measure of health. Clearly, there remain many unresolved questions about SRH and medication, not captured in the present study. Large longitudinal studies with several, and frequent follow-up points and relevant measurements should further explore the short-term dynamics as well as the long-term medical outcomes of SRH over time. Such knowledge may be used to identify the risk for later disease and capture pathological changes before and beyond the disease diagnosis, and as such prevent morbidity in the adult population.

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