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Doctoral Thesis

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SAMANDRAG

Maksimalt oksygenopptak (VO_{2peak}) er rekna som ein av dei viktigaste prognostiske markørane for framtidig hjarte-/karsjukdom og tidleg død. Ettersom direkte måling av VO_{2peak} er tidkrevjande og kostbart har implementeringa i førebyggjande helsearbeid og klinisk praksis vore begrensa. Både VO_{2peak} og ei rekkje andre sentrale helseparameter, kan betrast ved ei viss mengd fysisk aktivitet i kvardagen, og dagens globale anbefalingar er at alle vaksne bør utføre minst 150 minutt med moderat intensitet eller minst 75 minutt med høg intensitet per veke. Utforminga av anbefalingane inneber at det totale energiforbruket, og dermed helsegevinstane, kan oppnås ved ulike tilnærmingar der kortare varigheit kan kompenserast med høgare intensitet og vice versa. I dette prosjektet nytta me data på direkte målt VO_{2peak} frå 4631 deltakarar i den siste Helseundersøkelsen i Nord-Trøndelag (HUNT 3, 2006-08) til først å utvikle ein prediksjonsmodell for å kunne estimere VO_{2peak} og vidare undersøke om denne modellen kunne predikere framtidig hjerte-/kardødeligheit og død uansett årsak i ein stor befolkning. Me såg vidare på korleis ulike tilnærmingar til dagens anbefalingar for fysisk aktivitet var assosiert med direkte målt VO_{2peak} i utvalet frå HUNT. Hovedfunna i avhandlinga er at VO_{2peak} kan estimerast relativt nøyaktig ved ein regresjonsmodell med lett tilgjengelige variablar som alder, kroppssamansetning, fysisk aktivitetsnivå og kvilepuls og at modellen kan nyttast til å kategorisere personar med låg eller høg direkte målt VO_{2peak}. Denne modellen vart nytta til å estimere VO_{2peak} i eit stort utval friske deltakarar frå HUNT 1 (1984-86) som vart fulgt fram til registrert dødsdato eller slutten av 2010. For kvar 3,5 $mL \cdot kg^{-1} \cdot min^{-1}$ høgare estimert VO_{2peak} var risikoen for død av hjarte-/karsjukdom 21 % lågare for personar av begge kjønn som var under 60 år ved undersøkelsen, medan risikoen uansett dødsårsak var henholdsvis 15 % og 8 % lågare for menn og kvinner. Vidare viser me at grupper som rapporterer fysisk aktivitetsvanar i tråd med dagens anbefalingar, anten ved moderat relativ intensitet over lengre tid eller høg intensitet over kortare tid, i gjennomsnitt hadde tilfredsstillande høg og tilnærma lik VO_{2peak}. Samtidig viser me at eit relativt begrensa antal personar som rapporterte ein tidsbruk under minimum anbefaling, men med svært høg relativ intensitet, også hadde tilsvarande høg VO_{2peak}. Også når tidsbruken eller det samla energiforbruket var konstant fann me at dei som rapporterte høg intensitet hadde høgare VO_{2peak} enn dei som rapporterte låg eller moderate intensitet.

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SUMMARY

Directly measured peak oxygen uptake (VO_{2peak}) is established as an important prognostic marker of cardiovascular disease and premature mortality, but is rarely evaluated for prevention purposes or in primary care settings due to costly and time-consuming procedures. Both VO_{2peak} and several other health parameters can, however, be improved and maintained by regular exercise, and today`s recommendations suggest that all adults should do at least 150 minutes of moderate intensity or 75 minutes or vigorous intensity exercise per week. Hence, the total recommended volume or energy expenditure may be reached by strictly different approaches. In the current thesis, data on directly measured VO_{2peak} in 4631 individuals from the third wave of the Nord-Trøndelag Health Study (HUNT 3, 2006-08), were used to first derive a simple prediction model for VO_{2peak} that potentially could supplement direct measurements in healthcare settings and for research purposes. Next, the clinical utility of this model was examined by its ability to predict all-cause and cardiovascular mortality in a large sample of healthy men and women from the HUNT 1 (1984-86) cohort. Furthermore, we examined how different combinations of intensity and total time spent at habitual exercise were associated with VO_{2peak} in apparently healthy, community dwelling individuals from HUNT 3. The findings in this thesis indicate that VO_{2peak} can be predicted with reasonable accuracy by using easily available clinical and self-reported variables such as age, body composition, self-reported physical activity and resting heart rate, and that the model can be used to correctly classify subjects in the correct tail of the VO_{2peak} distribution. For each metabolic equivalent (i.e. MET, ~3.5 $mL \cdot kg^{-1} \cdot min^{-1}$) higher CRF, the risk of CVD mortality was 21% lower in both men and women who were below 60 years at baseline, while the corresponding risk of all-cause mortality was 15% and 8% lower in men and women, respectively, for each MET higher CRF. Furthermore, we demonstrate that habitual exercise patterns of moderate intensity for a long total duration or vigorous intensity for a relatively short duration, adding up to the total volume as recommended by the health authorities, both were associated with a beneficial VO_{2peak} –level. However, a higher VO_{2peak} was observed among those reporting vigorous intensity compared to low and moderate intensity for a similar time spent, and energy expenditure used during exercise.

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Funding source: Norwegian Council on Cardiovascular Disease

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First and foremost I will express my gratitude to my main supervisor Professor Ulrik Wisløff. You opened the door into the scientific world for me as a fresh master student, and have literally kept it open since then. Your never-ending optimism and enthusiasm, along with creative ideas and wide scientific knowledge, have provided me the self-confidence to do independent research. A huge thank you also to co-supervisor Professor Imre Janszky, your expertise in epidemiology and statistics are beyond remarkable and your thoughtful comments on study design and interpretation have been invaluable. The collaboration with you and Professor Lars Vatten has been of utmost importance for our research group in general and me in particular. I also want to thank Javaid Nauman and Stian Aspenes for fruitful discussions and your important contributions to the studies.

All other colleagues and friends in the Cardiac Exercise Research Group; the working environment you are making, both scientifically and socially, is simply outstanding!

Finally, I want to thank my parents for your encouragement and support throughout these years and life itself.

Bjarne M. Nes, Trondheim, 2013

LIST OF PAPERS

The thesis is based on the following original papers and is referred to by their roman numbers throughout the text.

Paper I

Nes, BM, Janszky, I, Vatten, LJ, Nilsen, TIL, Aspenes, ST & Wisløff, U. (2011) Estimating VO_{2peak} from a nonexercise prediction model: The HUNT Study, Norway. *Medicine & Science in Sports & Exercise*. **43**(11):2024-2030

Paper II

Nes, BM, Janszky, I, Bertheussen, GF, Aspenes, ST, Vatten, LJ, & Wisløff, U. (2012) Exercise patterns and peak oxygen uptake in a healthy population: The HUNT Study. *Medicine & Science in Sports & Exercise*. **44**(10):1881-1889

Paper III

Nes, BM, Vatten, LJ, Nauman, J, Janszky, I & Wisløff, U. (2013) Estimated cardiorespiratory fitness as a predictor of long-term all-cause and cardiovascular disease mortality: The HUNT Study in Norway. *Medicine & Science in Sports & Exercise*. *Accepted for publication.*

ABBREVIATIONS

ACLS	Aerobics Center Longitudinal Study
ACSM	American College of Sports Medicine
BMI	Body mass index
CI	Confidence interval
CRF	Cardiorespiratory fitness
GLM	General linear model
HUNT	Nord-Trøndelag Health Study
MET	Metabolic equivalent
PA	Physical activity
R^2	Coefficient of determination (variance explained)
RHR	Resting heart rate
SD	Standard deviation
SEE	Standard error of the estimate
VO_{2max}	Maximal oxygen uptake
VO_{2peak}	Peak oxygen uptake
WC	Waist circumference
WHO	World Health Organization

DEFINITIONS

Cardiorespiratory fitness:

The ability to perform large-muscle dynamic moderate-to-high intensity exercise for prolonged periods[1].

Exercise:

Physical activity that is planned, structured and repetitive and has as a final or intermediate objective the improvement or maintenance of physical fitness[2,3].

Maximal/peak oxygen uptake ($VO_{2max/peak}$):

The highest rate at which oxygen can be taken up and utilized by the body during strenuous, dynamic exercise with a large muscle mass[4].

Metabolic equivalent (MET):

METs is the ratio of the rate of energy expended during an activity to the rate of energy expended at rest[2]. 1 MET is the rate of energy expenditure while sitting at rest and is, by convention, defined as 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ [5].

Non-exercise model:

A multiple regression model derived to estimate the level of cardiorespiratory fitness without exercise testing

Physical activity:

Any voluntary movement produced by skeletal muscles that result in energy expenditure above resting levels[2,3].

Physical fitness:

A set of attributes that people have or achieve that relates to the ability to perform physical activity[3].

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BACKGROUND

The past century represented a dramatic epidemiological transition in the burden of disease worldwide. While communicable diseases have been the leading cause of deaths for many decades, recent reports states that preventable, non-communicable diseases (i.e. cardiovascular disease, cancer, chronic pulmonary diseases and type 2 diabetes) now account for at least 60% of all deaths globally[6]. The majority of these diseases share a number of common modifiable risk factors, where the most prominent are unhealthy diet, high blood pressure, high cholesterol, tobacco smoking, obesity and physical inactivity[7]. The Global Burden of Disease Study conservatively estimated that lack of physical activity (PA) alone accounted for ~3.2 million deaths worldwide in 2010[7]. In comparison ~5.7 million deaths were attributed to smoking and ~1.4 million to child and maternal under-nutrition. Similarly important is that inactivity may be causally related to several other high ranked risk factors, and combined with an increasing prevalence worldwide, inactivity might now be regarded as one of the leading global health problems[8,9]. Additionally, a certain amount of regular PA is a prerequisite for maintaining or improving several aspects of physical fitness, and in particular cardiorespiratory fitness (CRF), which is suggested to be an even stronger predictor of morbidity and premature mortality than inactivity[10,11].

Against this backdrop, the public health attention to PA levels has evolved rapidly over the last 20 years. Several national governments, as well as global organizations such as World Health Organization (WHO) and the United Nations, have placed increased PA higher on the agenda and launched strategies and action plans aiming to combat the growing burden of inactivity related disease[12-16]. Individual patient counseling in primary care, however, are commonly restricted to assessment of more traditional health indicators (commonly referred to as `vital signs`) such as pulse rate, blood pressure, respiratory rate and body temperature[17]. Established cardiovascular risk factors such as overweight, dyslipidemia, smoking and family history of disease have also gained recognition and are commonly evaluated collectively through so-called risk-score models such as the Framingham Risk Score, Q-Risk or the European Score prediction chart[18-20]. Physical inactivity, and in particular low CRF, has received less attention despite a growing body of evidence supporting its important prognostic utility[21-25]. However, through the *Exercise is Medicine*® initiative, the American College of Sports Medicine (ACSM) in partnership with the American Medical Association, now encourages that measurement of PA status should be included as a vital sign at every clinical visit. A large healthcare system, Kaiser Permanente in California (USA), comprising more than 3.4 million residents and 4000 physicians, has served as a role model and pioneered the inclusion of the PA vital sign[26]. At every visit, for every patient, two questions on frequency and duration of moderate-to-vigorous PA are used to calculate minutes per week of exercise which is automatically recorded in the electronic medical journals.

An individuals` CRF, however, is not routinely examined in healthcare settings despite that CRF appears to be strongly associated with overall health status and future risk of chronic disease in both high-risk and apparently healthy persons[24,27-29]. Indeed, some studies suggest that the CRF level is a better predictor than traditional health parameters such as hypertension, smoking, overweight, dyslipidemia and type 2 diabetes[24,30]. Nevertheless, regular measurement of CRF is presently limited to prognostic evaluation in heart disease patients or as the cardinal performance measure in endurance athletes[31,32].

Physical activity and cardiorespiratory fitness as separate risk factors

Although closely related and often used interchangeably, PA and CRF have strictly different meanings. PA is a behavior which is commonly quantified by the total volume performed i.e. by multiplying the number of bouts or sessions (*frequency*), the time of participation of each single session (*duration*) and the physiological effort associated with the PA (*intensity*), respectively[2]. On the other hand, CRF is a physiological attribute related to the ability to do strenuous exercise and is highly dependent on the upper limit of the cardiovascular system to supply and extract oxygen[3]. Both PA and CRF are inversely related to cardiovascular disease, its risk factors, and premature cardiovascular and all-cause mortality[33-37]. Some studies report that PA and CRF are related to these health outcomes independent of each other and it has also been suggested that the health-promoting effect goes through different mechanisms[38,39]. A meta-analysis from 2001 proposed that PA and CRF certainly have different relationships to cardiovascular risk[39]. While a relatively linear risk reduction was observed across strata of self-reported PA, a considerably greater benefit was found in the lower end of the CRF spectrum (until approximately the 20th percentile). The finding that the greatest risk improvement is observed between the least fit and the next least fit groups are consistent among several large population based studies, although specific cut-off values associated with increased risk are yet to be established[28,40,41]. Nevertheless, few studies have examined the combined effect of PA and CRF in order to elucidate what is more important for future health outcomes. Recently, Lee et al. examined the combined associations and relative contributions of PA and CRF with all-cause mortality in ~42,000 healthy men and women from the

Aerobics Center Longitudinal Study (ACLS) cohort[10]. They reported that men and women who did not meet the recommended level of PA, but were among the 40% most fit for their age group, had lowered risk of premature mortality. On the contrary, those who met the recommended level of PA, but were among the 20% with lowest CRF, did not have significantly lower relative risks compared to those who were both inactive and unfit. Similarly, Sassen et al. reported that the relation between PA and cardiovascular risk factors disappeared when the level of CRF was adjusted for, while adjustment for PA volume did not attenuate the relationship between CRF and cardiovascular risk[42]. Moreover, high intensity PA was the main characteristic of PA in determining the risk factor prevalence. Consequently, one may propose that a low level of CRF warrants consideration as a risk factor independent of overall PA level. Also, it may be speculated that the association between PA and health and longevity are largely mediated by CRF.

Maximal/peak oxygen uptake ($VO_{2max/peak}$)

Maximal oxygen uptake (VO_{2max}) is recognized as the gold standard measurement of CRF[32]. VO_{2max} is defined as the highest rate of oxygen uptake obtained during strenuous, dynamical work involving large muscle groups[3]. The oxygen uptake (VO_2) is set by the Fick equation (VO_2 = heart rate × cardiac stroke volume × arteriovenous O_2-difference) and VO_{2max} is therefore equal to the maximal ability of the cardiopulmonary system to supply, and skeletal muscles and the heart muscle cells to extract, oxygen during dynamical muscle work. The measurement of VO_{2max} is generally performed by ventilatory gas analysis during an incremental treadmill or bicycle protocol to exhaustion[43]. In principle, the term VO_{2max} implies that a maximal physiologic limit is achieved and objective criteria are suggested to consolidate that the rate of oxygen transport are maximized[44]. The plateau criterion implies that no further increase in oxygen uptake is seen despite increase in workload. As a secondary criterion of VO_{2max}, the respiratory exchange ratio (RER) should generally exceed a pre-specified level, typically ≥1.05-1.10, in order to certify that a near maximum effort is obtained. However, both the ability to reach a plateau, and the corresponding RER, vary considerably among individuals, despite maximal exercise, and in most clinical settings the term VO_{2peak} seems more appropriate[44].

Lack of established reference values of VO_{2peak} and consensus on clinically relevant cut-off values that defines increased risk for different populations may have limited the implementation of CRF measurement in healthcare settings[32]. Other reasons may be that the procedure for direct measurement is time-consuming, expensive, requires extra facilities, trained personnel and a high degree of motivation and effort from the individual with possible accompanying risks. Some of these constraints have been overcome by the development of exercise protocols that estimates VO_{2peak} from surrogate measures such as total treadmill time, heart rate at sub-maximal levels, perceived exertion or maximal watt production[45-47]. Although these protocols may be more cost-effective and applicable for mass testing, the feasibility in most time-limited healthcare settings seems questionable. Recently, a group of leading experts in the field, on behalf of the American Heart Association, have claimed for a national registry for CRF in the United States with the possibility of international expansion[32]. The expert group specifically emphasized the need for establishment of normative data for the population using directly measured VO_2 by maximal exercise testing and the potential to derive prediction formulas for CRF from other variables in the registry.

Non-exercise models of peak oxygen uptake

The strong statistical association between VO_{2peak} and certain health indicators such as age, PA, body composition, smoking status, resting heart rate, nutritional status and occupation have facilitated the development of multivariable regression models that combined explains a substantial proportion of the variance in VO_{2peak}. Such prediction models, commonly referred to in the literature as *non-exercise models*, predict VO_{2peak} reasonably well and are therefore suggested as surrogate measures when exercise testing is inapplicable. Already in 1973, a classical study by Bruce and colleagues indicated the feasibility of predicting VO_{2peak} from easily obtainable variables such as sex, age, weight and physical exercise habits in 295 healthy adults[45]. In the coming decades several studies attempted to examine the associations between CRF and anthropometrical or behavioral data, or a combination of both[48-50].

The first study that was deliberately designed to develop and cross-validate a non-exercise model for assessment of VO_{2peak} was probably that from Jackson et al in 1990[51]. Their cohort consisted of 2009, predominantly male (~90%), NASA employees who performed a graded maximal exercise test as part of their annual health examination. A multiple regression analysis revealed that age, sex, self-reported PA and body composition (BMI or percent body fat) were predictors of VO_{2peak}. Together these variables explained 61% of the variance in VO_{2peak} when BMI was included in the model and slightly more with percent body fat. The precision of the model was comparable or better (standard error of the estimate, SEE, was ~5.5 $mL \cdot kg^{-1} \cdot min^{-1}$ for the two models, respectively) than the Åstrand-

Rhyming test, which is a well-established sub-maximal exercise tests widely used to estimate VO_{2peak}. Cross-validation in a sub-sample from the same cohort and in hypertensive individuals and persons with a positive electrocardiogram confirmed the accuracy of the model. The study contained a relatively low number of females (n=150 for the validation sample and n=43 for the cross-validation sample), but its applicability was later confirmed by a validation study in 165 females 18-45 years[52]. A limitation of the study was that the non-exercise model systematically underestimated CRF in well-trained participants with a VO_{2peak} >55 $mL·kg^{-1}·min^{-1}$. This limitation was later confirmed by a validation study in well-trained college students with a mean age of 21 years[53].

In 2005, an international group of experts expanded on the work by Jackson et al. by deriving and cross-validating non-exercise models in three large epidemiological databases (total n=38,137)[54]. Similar variables as in the original study were used to develop new cohort-specific models in a larger group of NASA employees, participants in the ACLS Study at the Cooper Clinic, and the Allied Dunbar National Fitness Survey (ADNFS) in the UK. The NASA model was the most accurate and showed the highest cross-validity when applied to the other cohorts. The superior model fit is likely explained by the measurement method used for determining CRF, since in the NASA cohort CRF was measured directly as VO_{2peak}, whereas it was estimated from maximal and sub-maximal exercise testing, respectively, in ACLS and ADNFS. Subsequent validation studies have confirmed its validity in healthy elderly[55].

Associations between physical activity and peak oxygen uptake

It is well established from randomized controlled trials that exercise training and VO_{2peak} is causally related, and structured PA is recognized as the main method to improve VO_{2peak}[2,56]. Nevertheless, most population based studies including healthy participants indicate a weak to moderate relationship between self-reported habitual PA and VO_{2peak}[57]. For example, a cross-sectional study from the Baltimore Longitudinal Study of Aging reported quite moderate correlations between overall self-reported PA and VO_{2peak} in 1116 healthy individuals over a wide age-range (r=0.28 and r=0.27 in men and women, respectively)[57]. After adjustment for age Lakka et al. reported a weak correlation (r=0.11) between VO_{2peak} and a wide range of conditioning PA in middle-aged men[38]. Similar associations have been reported in other populations with different age-ranges[58-60].

The relatively weak association between PA levels and VO_{2peak} at the population level, and stronger association with health outcomes for the latter, has generally been attributed to how PA has been measured[61]. Self-reported PA by questionnaires, the most widely used approach in population studies, are inherently prone to bias which threatens internal validity[62]. On the contrary, CRF levels can be measured directly with low measurement error and high reproducibility[63]. In recent years, however, objective measurement of PA by activity monitors has been introduced also in large-scale studies[64,65]. The correlation between objectively measured PA and VO_{2peak}, however, is not very different from those obtained for self-reported PA with correlations generally ranging from 0.15-0.40[66-68]. Hence, the inherent bias of self-report data does not seem to fully account for the weak association. Other influencing factors in the PA-VO_{2peak} dose-response relationship are genetics, sex, age and individual fitness level[69,70]. The heritability of VO_{2peak} have been estimated to be at least 50% and may hence be a primary contributor to the observed heterogeneity in VO_{2peak} between subjects with similar exercise patterns[71,72]. Genetics have also been shown to play a major role in the observed responsiveness to a standardized exercise program[73,74]. Moreover, the separate domains of PA, including frequency, duration and intensity of activity, have seldom been taken into account in population studies. Talbot et al. reported markedly different associations with VO_{2peak} for high-, moderate- and low-intensity activity, respectively in a heterogeneous population of community dwellers[57]. Activities requiring vigorous absolute intensity (≥6 metabolic equivalents, METs) were moderately associated with VO_{2peak} (r=0.33 and 0.27 in men and women, respectively), while a weak association was found for moderate intensity (r=0.12 and 0.17 for men and women, respectively) and no association was observed for light intensity (r=0.08 and 0.06 for men and women, respectively). Several other observational studies have reported stronger associations between VO_{2peak} and self-reported vigorous intensity PA, compared to moderate intensity or total volume of PA[60,75,76]. Only a handful population based studies, however, have examined how different intensities during unsupervised, freely selected exercise are associated with VO_{2peak} at the same or a higher total duration or volume performed.

Current physical activity recommendations for apparently healthy adults

The WHO`s global PA recommendations for healthy adults is to achieve a minimum of 150 minutes of *moderate* intensity PA throughout the week or at least 75 minutes of *vigorous* intensity PA per week[13]. The recommended total duration could be obtained by accumulating bouts of at least 10 minutes and should preferably be spread throughout the week.

Conceptually similar recommendations were first launched in 1995, almost simultaneously as the first public health guidelines for PA in the U.S. were published by the ACSM and Centers for Disease Control and Prevention, which set the stage for a governmental report from the U.S. Surgeon General[16]. The primary recommendations were highly consistent across the different expert panels and represented a paradigm shift from an *exercise for fitness* approach to *PA for health promotion*. These guidelines were cornerstone publications that were soon adopted, with no or minor modifications, by a number of countries worldwide, including Norway[77].

The ACSM and the American Heart Association have extended on the primary recommendations and developed group-specific recommendations for physical activity for elderly[78,79], heart disease patients[80], diabetes patients and more[81]. Additionally, the ACSM have developed specific recommendations for the purpose of exercise prescription in primary care, with special emphasis on the quantity and quality of exercise needed for developing and maintaining CRF[2]. Basically, these recommendations coincide with the general guidelines for health promotion and disease prevention, but are extended to include musculoskeletal and neuromotor fitness.

The primary recommendation before 1995 was to undertake vigorous intensity activity in bouts of at least 20 minutes with the aim of increasing physical fitness[82]. The highlighting of moderate intensity activity, such as brisk walking, was a somewhat controversial topic when the recommendations were first published[83]. Apparently, the new recommendations were based on a tentative conclusion that recommending moderate intensity activity, and allowing for accumulating bouts throughout the day, was the best-buy approach for promoting PA in an increasingly sedentary population. However, a large number of studies, although mostly published after the shift in recommendations, have confirmed the benefit of moderate intensity activity to reduce morbidity and premature mortality[37,84]. Notably, the recommendations can now be reached by either moderate or vigorous intensity activity, or a combination of both, provided a certain total volume of energy expenditure is satisfied. An inherent implication is that there is a 2:1 ratio between time spent at vigorous and moderate intensity activity with concern to health outcomes. This seems to be based on an assumption that it is the total amount of work that matters and that energy expenditure will be equal by doubling the total duration of moderate as compared to vigorous intensity activity. In this case, the benefits of recommending and undertaking vigorous intensity PA are solely restricted to being a time efficient alternative. What has been less clear, however, is whether higher intensities confers benefits compared to moderate intensities for the same amount of energy expenditure. Although this has been proposed by small scale randomized trials[85], most epidemiological studies that have proposed larger benefits of higher intensity have not taken into account that PA undertaken at higher intensity also confers a higher total volume of exercise. Moreover, some recent large-scale studies have reported risk reductions for both cardiovascular disease and all-cause mortality at PA volumes as low as half of that expressed in current recommendations[86]. The recommended amount and intensity of exercise have also never been validated against directly measured VO_{2peak} at the population level.

AIMS AND HYPOTHESES

The main aim of the current thesis was to further examine the correlates of VO_{2peak} in a large, healthy population and explore the possibility of accurately estimating VO_{2peak} without exercise testing. Furthermore we wanted to examine how freely selected, self-reported exercise patterns were associated with VO_{2peak} in a large sample of healthy, community dwelling men and women.

SPECIFIC AIMS

Prediction of VO_{2peak} from non-exercise variables

To derive and cross-validate a simple, non-exercise based prediction model of VO_{2peak} that could potentially be incorporated in healthcare settings.

We hypothesized that age and a set of modifiable clinical and self-reported variables could explain a large proportion of the variance in VO_{2peak} and thus be used to predict VO_{2peak} without exercise testing.

The association between self-reported exercise patterns and VO_{2peak}

To cross-sectionally examine how different combinations of intensity and total time spent at habitual exercise were associated with VO_{2peak} in an apparently healthy, free-living population.

We hypothesized that vigorous intensity of exercise was associated with higher VO_{2peak} than low and moderate intensity for the same time spent and total volume performed on habitual exercise.

Estimated VO_{2peak} and long-term mortality

To evaluate the predictive value of estimated VO_{2peak} from a non-exercise model for long-term (~24 years) mortality in men and women who were healthy at baseline.

We hypothesized that estimated VO_{2peak} at baseline were inversely associated with the risk of premature CVD and all-cause mortality.

MATERIAL AND METHODS

The Nord-Trøndelag Health Study (HUNT)

The Nord-Trøndelag Health Study (Norwegian spelling: *"Helseundersøkelsen i Nord-Trøndelag»*, abbreviated HUNT) is a longitudinal, population-based health survey in Norway. Nord-Trøndelag County is located in the middle of the country, covers both inland and coastal areas and consists of 24 smaller municipalities (Figure 2). Briefly, the county is regarded demographically similar to Norway as a whole, except from an education level and income slightly below the national average[87]. The population is stable and homogenous regarding ethnicity (mostly Caucasians) and socio-economic status and has a low net migration. The HUNT Study is regarded as one of the most comprehensive population-based health surveys in the world and invites all residents above 20 years of age to participate. The survey has been carried out at three occasions, the first in 1984-86 (HUNT 1), the second in 1995-97 (HUNT 2) and the third in 2006-08 (HUNT 3). From the first survey in the mid-eighties, the study has been consecutively expanded to include a large number of sub-studies which examines different aspects relevant to the major public health issues of the time. The main strength of the HUNT Study is the wide range of information, excellent data quality, involvement of a whole unselected population, easy linkage to other health registries and a generally high participation rate. In HUNT 1 ~89% of those invited chose to participate, while the corresponding rates for HUNT 2 and 3 were ~69% and ~54%, respectively (Figure 1). The HUNT Study is collaboration between the HUNT Research Centre (at Department of Public Health, The Faculty of Medicine, NTNU), Nord-Trøndelag County Council and the Norwegian Institute of Public Health. The current thesis contains data from HUNT 1 and HUNT 3.

Figure 1: Flow-chart of invited and participated adults (≥20 years) in the three HUNT surveys including the HUNT Fitness Study.

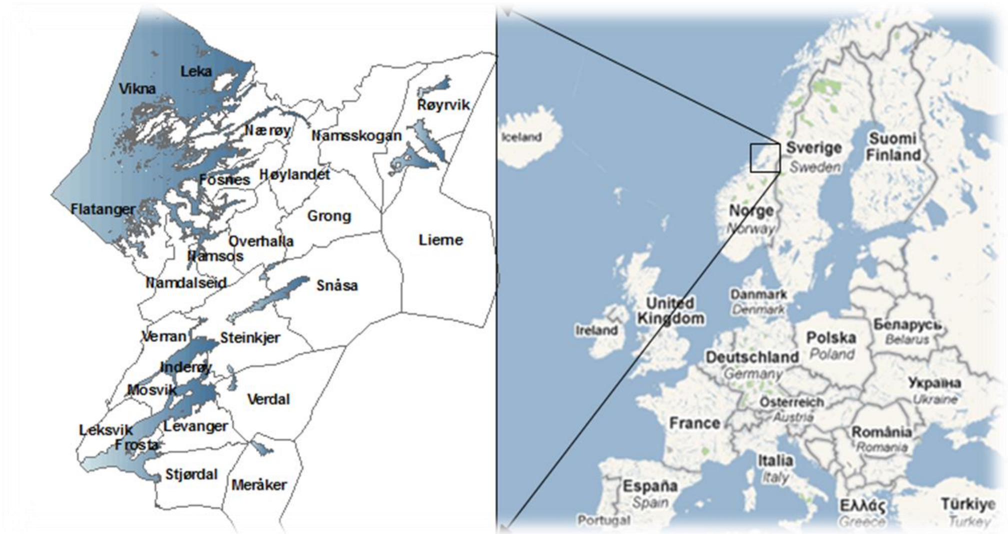

Figure 2: Nord-Trøndelag County with its 24 municipalities. Courtesy: Krokstad et al. 2012.

The HUNT Fitness Study

The HUNT Fitness Study was a sub-study in HUNT 3 designed to obtain normal values of VO_{2peak} in a healthy population. The study was carried out between June 2007 and June 2008. Four municipalities within the county (Stjørdal, Verdal, Levanger and Namsos) were chosen in advance and the VO_{2peak} testing was performed in connection with the basic HUNT examination. Exclusion criteria for participation in the HUNT Fitness Study were known cardiovascular disease, cancer, obstructive lung disease and use of blood pressure medication. Further exclusions were done for blindness, pregnancy and any physical impairment preventing intense treadmill walking. Before exercise testing all participants also had to pass a brief medical interview involving the abovementioned exclusion criteria. A total of 12,609 persons were offered participation in the HUNT Fitness Study and at study closure 4631 individuals (2,368 women and 2,263 men, age: 19-90 years) had their VO_{2peak} tested. At present, these data provides one of the largest reference materials of objectively measured VO_{2peak} over a wide age range. A detailed description of the enrollment procedure and a participation flow-chart is presented elsewhere[88]. In addition to measurement of VO_{2peak} the HUNT Fitness Study also involved measurement of endothelial function from flow-mediated dilatation (FMD) of the brachial artery using ultrasound technology (Vivid-I, GE Healthcare, USA), and apprehension of questionnaire-based information about pain and health-related quality of life. These data, however, were not used in the thesis.

Clinical measurements

All clinical measurements were performed by trained nurses at the local HUNT examination facility. Height and body weight was read to the nearest centimeter (cm) and 0.5 kilogram (kg), respectively, using internally standardized measures (Model DS-102, Arctic Heating AS, Nøtterøy, Norway). Body mass index (BMI) was calculated by dividing body weight by the squared value of height in meters. Waist circumference (WC) was only measured in HUNT 3 and read to the nearest centimeter using a steel band horizontally at the height of the umbilicus. Blood pressure was measured three times by an automatic oscillometry (Dinamap 845XT, Critikon) and the mean of the second and third reading was used for analysis. Resting heart rate in HUNT 1 was measured by palpating the radial pulse over 15 seconds after at least four minutes of seated rest. In the case of irregular pulse or difficulties counting heart beats, the test was extended to 30 seconds, if necessary with a stethoscope placed over the heart. In The HUNT Fitness Study, the lowest heart rate was registered by 3-point electrocardiogram during FMD measurement with the participants lying in supine position on a bench for 10 minutes in a dim lit and quiet room. Blood samples were drawn from the participants in HUNT 3 and non-fasting glucose, triglycerides, total cholesterol and HDL cholesterol was analyzed in addition to some biomarkers not relevant for the present thesis.

Peak oxygen uptake measurements

Prior to the maximal exercise test, all participants carried out a 10 minute warm-up period. After a brief introduction to treadmill walking or running, preferably without hand-rail grasp, the speed was individually adjusted to a work-load causing slightly increased breathing and hart rate. Before entering the test treadmill (DK7830; DK City, Taichung, Taiwan) all participants were equipped with a face-mask (Hans Rudolph, Shawnee, KS) and heart rate monitor (Polar S610 or RS400; Polar Electro Oy, Kempele, Finland) and instructed in detail about test procedures. Oxygen uptake (VO_2) and heart rate were then measured continuously during an incremental, individualized treadmill protocol until exhaustion. VO_2 kinetics was measured directly by a portable mixing chamber gas analyzer (MetaMax II; Cortex, Leipzig, Germany). The initial workload was chosen from the warm-up pace, and speed and/or inclination was then increased whenever the participant reached an oxygen uptake that was stable over 30 seconds. As a prolongation of the warm-up period, and before exhaustion was reached, most participants had their steady-state VO_2 measured during one (*n*=2773) or two (*n*=2543) submaximal levels. For each level, speed (km/h), inclination (%), heart rate and subjective level of exertion on the Borg 6-20 scale was registered in addition to VO_2. A test was considered maximal (VO_{2max}) if the VO_2 did not increase more than 2 $mL \cdot kg^{-1} \cdot min^{-1}$ despite increased workload, combined with a respiratory exchange ratio at or above 1.05. Since 12.6% of the participants did not reach both the VO_{2max} criteria, the term VO_{2peak} are used throughout this thesis and in the corresponding papers. An individual`s VO_{2peak} was registered as the mean of the three successively highest 10 seconds VO_2 registrations. A detailed description of the test protocol is previously published by our group[89]. The test equipment was calibrated with volume calibration repeated every third test and two point gas calibration every fifth. Before and after each test the ambient room air was routinely checked. Before the start of the study the validity of the MetaMax II apparatus were tested by comparison against Douglas bag and iron lung (Cortex Biophysik). Direct measurements of VO_{2peak} are preferable to indirect estimation due to higher precision and reliability[62]. However, the methods are more complicated and warrants trained personnel.

Self-reported information

Some essential information was questionnaire-based in both HUNT 1 and HUNT 3. In all three papers all data on leisure time PA (exercise) were collected through a self-administered questionnaire included with the invitation letter. The questions covered the three essential domains of PA; frequency, intensity and duration. The frequency question was stated as "How often do you exercise?" with the response options "Never", "Less than once a week", "Once a week", "2-3 times a week" and "Almost every day". The intensity question was stated as "If you exercise as frequently as once or more a week: How hard do you push yourself?", with the response options "I take it easy without breaking a sweat or losing my breath", "I push myself so hard that I lose my breath and break into sweat" and "I push myself near exhaustion". The duration question was stated as "How long does each session last?", with the response options "Less than 15 minutes", "15-29 minutes", "30 minutes to one hour" and "More than one hour". In Paper I and III the individual responses to each question was weighted to form a physical activity index score (PA-Index). The individual weighting was chosen on the basis of each variables association with VO_{2peak} in a multiple linear regression model. The new index was compared to two previously published PA indexes used in the HUNT cohort, but preferred on the basis of a stronger total association with VO_{2peak}. In Paper II, the response options were collapsed into categories which roughly corresponded to current recommendations for PA for the general population. Inactive people were defined as those reporting none or less than once a week of regular PA. The questionnaire applied was the same in all three papers, with the exception for the intensity questions used in Paper II. This question was taken from a questionnaire handed out in connection with the VO_{2peak} testing and was chosen because it gave more detailed information on relative exercise intensity. Participants were asked to assess their usual intensity of exercise on the well-known Borg 6- to 20-point scale which is frequently validated against objective measures such as heart rate and VO_2[90,91]. Other self-reported variables include smoking status (“Never smoked”, “Former smoker” and “Current smoker”), alcohol consumption last 14 days (“None”, “1-4 times”, “5-10 times” and “More than 10 times”), marital status (“Married”, “Unmarried”, “Widow/widower” and ”Divorced/separated”), family history of disease and attained education (“9 years or less”, “10-12 years” and “More than 12 years”).

Other register data

The unique 11-digit identification number allocated to all Norwegian citizens make it possible to link data from the HUNT database and other health registries. In Norway, it is mandatory for physicians or public health officers to report deaths to the National Cause of Death Registry. The underlying cause of death is registered using the International Classification of Disease (ICD) coding system. In Paper III, the primary end-point was deaths caused by cardiovascular disease (ICD: *9th Revision:* 390-459, *10th Revision:* I00-I99) and all causes. The information on causes of death was complete through December 31st, 2010.

Ethics

The data collections in all HUNT surveys, including The HUNT Fitness Study and the specific studies included in the thesis are approved by the Regional committee for medical research ethics, The Norwegian Data Inspectorate and Health Directorate and are performed in conformity with Norwegian law and the Declaration of Helsinki. In HUNT 2 and 3 all participants signed a document of informed consent, while in HUNT 1 attendance and participation in the medical examination was considered as approval of informed consent. The mortality follow-up in Paper III was approved by HUNT Research Centre and Statistics Norway which is the responsible unity for collection and organization of the data.

METHODOLOGICAL CONSIDERATIONS

The validity of a study is concerning the degree to which a study reaches a correct conclusion and can be broadly separated into internal and external validity. Internal validity is the validity of the inferences made as they pertain to the members of the study population while external validity is the extent to which the inferences can be generalized to people outside the study population (*generalizability*). In the following the internal and external validity of the studies included in the thesis will be discussed. The precision of the specific results (control of random errors) are discussed in the Results and discussion section.

Internal validity (control of systematic error)

Systematic errors in estimates are often referred to as biases, as opposite to validity. Potential bias are commonly sub-classified into three different types; *selection bias, information bias* and *confounding*.

Selection bias

Selection bias refers to systematic error introduced by procedures used for selection of participants into the study or factors that influence study participation. Such bias appears if the relation of the exposure to the outcome is different for those who participate in a study and those who theoretically would be eligible for the study[92]. The HUNT studies in general invite the total adult population of a county and have a high participation rate and these factors may reduce bias due to selection. The participation rate, however, declined somewhat from being exceptionally high (89%) in HUNT 1 to a considerably lower, but acceptable in most age groups, in HUNT 3 (54%). However, a recent study of attendants and non-attendants in HUNT 3 proposed that there is generally no reason to be concerned about biased associations, although it depends on the given research question[93]. Moreover, the most pronounced difference between attendants and non-attendants were a higher prevalence of cardiovascular disease and diabetes among the latter, and these groups were not included in our studies.

The relatively low participation rate in The HUNT Fitness Study (44.7% of those invited) may also make Paper I and II subject to self-selection bias. Accordingly, it may be possible that those volunteering for exercise testing were also more fit than the corresponding healthy sample of non-attendants. However, almost all of those who were invited to testing from the basic HUNT study agreed to participate in the VO_{2peak} test. Yet, many potential participants chose to withdraw their participation in the study, partly because of long waiting lines due to limited capacity at the test facilities. Nevertheless, a comparison of participants in the HUNT Fitness Study and the overall healthy population in HUNT 3 revealed only minor mean differences for several important health indicators[88]. For example, in female Fitness Study participants systolic blood pressure was 123.5 mmHg compared to 124.3 mmHg in the total healthy population, diastolic blood pressure was 69.7 mmHg compared to 69.8 mmHg and waist circumference were 0.86 m compared to 0.88 m, respectively. In men, systolic blood pressure was 132 mmHg in the Fitness Study sample compared to 131 mmHg in the healthy HUNT population and diastolic blood pressure 76 mmHg compared to 75 mmHg. BMI were slightly lower in The Fitness Study participants (25.4 compared to 26.1 in women and 26.6 compared to 27.0 in men) and a lower proportion reported to be inactive defined as exercising less than once per week (14.1% compared to 20.6%). The HUNT Fitness Study participants are therefore considered to be fairly representative of the general population of apparently healthy, free-living men and women in Nord-Trøndelag County.

Information bias

Information bias is commonly arising because of errors or inconsistency in the measurement of the exposure or outcome variables. Misclassification is a common source of information bias for categorical variables collected from self-report. Misclassification can be differential or non-differential depending on the variables relationship to the other variables. Differential misclassification occurs when the value of a variable depends on the actual value of another variable, while non-differential misclassification implies that the value of a variable is not dependent on the actual value of another variable[92].

All clinical variables measured in HUNT are collected by trained nurses using standardized equipment and procedures which consolidates high construct validity. The main outcome variable, $VO_{2peak,}$ was measured by ventilatory gas analysis which is considered as the gold standard measurement of cardiorespiratory fitness[62]. The non-exercise predicted VO_{2peak}, however, are prone to misclassification bias when categorized as in Paper III. The misclassification, however, is probably non-differential (i.e. random) which typically leads to more conservative or underestimated associations. Another obvious source of information bias in the current thesis is the use of self-reported measures of PA.

Assessment of physical activity (PA)

Several different methods for assessment of PA are available and the preferred method depends largely on the degree of accuracy needed as opposed to the feasibility and cost of the method of choice. For example, the doubly labeled water method are recognized as the gold standard method of assessing energy expenditure in free-living individuals, but its expense and complicated procedure limits the usefulness in epidemiological settings[62]. This method is therefore mostly used to validate less accurate measurement methods such as self-report questionnaires. In recent years, however, the introduction of accelerometers and pedometers that individuals wear on their hip or arms during daily living has made it possible to measure PA quite accurately also in population studies[94]. Self-report measures of PA, as opposed to objective measurement, may induce misclassification bias due to a tendency to over- or underreporting of a certain behavior due to social desirability or simply because recalling specific behaviors is a complex cognitive task. The misclassification caused by incorrect recall of PA may be differential (i.e. non-random) if more active people, especially those taking part in vigorous PA and sports, are more likely to accurately recall their activity[95]. Indeed, the questionnaire applied in Papers I-III was more accurate in measuring vigorous than low- and moderate intensity activity in a previous validation study[96]. Furthermore, self-reported PA has consistently been shown to overestimate the objective level of PA[94]. This may indicate bias due to social desirability, suggesting that people tend to over-rate their actual PA level. This assumption is reflected in recent studies showing that compliance to PA recommendations, as measured by objective methods (accelerometers or pedometers), are considerably lower than previous prevalence estimates based on self-report[94]. The estimated compliance to the PA recommendations in the general population therefore varies greatly depending on how PA is measured. Nonetheless, simple self-report questionnaires have been the method of choice in the field of PA epidemiology over several decades. Indeed, most of the evidence that form the basis of today`s PA recommendations are based on self-report and we can thus conclude that PA questionnaires certainly have contributed to the field of PA and health[97].

However, one must keep in minds that self-report questionnaires and accelerometers in essence measures different things. While most questionnaires in general asks the participant about a certain behavior, accelerometers merely measures movements. Hence, the disagreement between the measurement methods may not just be a question about accuracy. The difference may also be attributed to the fact that self-report measurement takes into account the interpretation of people about what they really do. For instance, an hour at the gym or playing football may not equal an hour of dynamic movement, still the total time period engaged in the activity may be the maximum accuracy people are able to recall and interpret. Furthermore, there is at present no consensus about how to translate certain accelerometer counts into certain intensities, particularly relative intensity, for different groups such as elderly populations. Accordingly, we may speculate that self-report data are more easily translated into comprehensible public health guidelines. Moreover, the association between objectively measured PA by accelerometers and health outcomes and premature mortality is yet to be established. Hence, we might expect that the introduction of objective PA measurement in population studies ultimately leads to a shift in the recommended amount and intensity of PA for health promotion.

Confounding

Confounding is an important issue in observational studies because confounding factors can potentially obscure the true association between exposure and outcome. Confounding may bias any association observed if one or more variables are associated with the exposure and also causally related to the outcome variable[92]. Thus, the effect of the exposure is mixed together with the effect of another variable. Confounding therefore introduces bias in studies examining cause-effect issues (Paper II and III), but is not of particular concern in pure prediction models (Paper I). The error introduced by confounding factors in non-randomized studies can be dealt with by statistically controlling for these variables in multivariable models (*adjustment*), by excluding participants at specific levels of the confounding variable (*restriction*) or by doing separate analysis for different levels of the confounder (*stratification*).

The HUNT studies include a wide range of variables that allows for statistical adjustment for several potential confounders. Selection of potential confounders and how to deal with them is, however, a careful process that should be based on prior knowledge and not merely statistical grounds. Age and sex were the most obvious confounders in our studies since both are strong determinants of VO_{2peak} and may causally affect both PA levels and risk of mortality. Women have systematically lower VO_{2peak} than men across all adult age-groups and for the ease of interpretation we chose to stratify our analysis by sex in all studies, instead of including sex as a covariate in the linear models. All analyses were adjusted for age. Another important confounding factor in most observational studies with recourse to hard-endpoints (i.e. mortality or cardiovascular disease) is the existence of undetected subclinical disease which may lead to biased interpretation of the cause-effect relationship (*reverse causation*). For instance, low VO_{2peak} may be caused by an underlying disease that concurrently increases risk of premature mortality. We cannot fully exclude the possibility of this in Paper III. However, the large sample size and broad range of information on baseline health status allowed us exclude a large number of participants anticipated to have a subclinical disease at baseline (i.e. self-reported long-term functional impairment, motion impairment and angina pectoris). Moreover, excluding the first 5 years of follow-up in a sub-analysis did not change the results appreciably which might have been the case if low-fit subjects had the specific diseases already at baseline.

Importantly, a variable that is associated with both the exposure and the outcome might be on the causal pathway between exposure and outcome (a *mediator*) and should then not be regarded as a confounder. PA and VO_{2peak} (exposure variables in Paper II and III, respectively) positively affects a broad range of factors that may be on the causal pathway to the outcome (i.e. VO_{2peak} or cardiovascular mortality) and adjusting for these intermediate variables may lead to overly conservative estimates. For instance, we chose not to adjust for blood pressure in Paper III since it is well known that PA can reduce blood pressure in a causal manner and that blood pressure is causally related to mortality risk[98]. However, we excluded participants on blood pressure medication (*restriction*) although the need for pharmacological reduction in blood pressure may be caused by low PA or VO_{2peak} and also is known to causally reduce mortality, because medication use might be associated with underlying subclinical disease or a genetic vulnerability that increases risk[99].

External validity (generalizability)

Generalizability refers to whether the results apply to people outside the population under study. The homogenous nature of the HUNT population, including the HUNT Fitness Study sample, may limit generalizability of the results to other populations. Nord-Trøndelag county, however, is geographical and demographically representative of Norway as a whole, also regarding health[100]. A limitation, however, may be lack of larger cities and a low proportion of immigrants of non-European background. However, this non-representativeness is assumed to be unrelated to the associations we studied. The association between CRF and cardiovascular or all-cause mortality is well-established, and similarly strong, for a wide range of population samples and is therefore probably not confounded by race, ethnicity, socio-economic status or geographic residence[33,34,101]. Participants invited to the HUNT Fitness Study were apparently healthy, and hence not representative of unselected populations normally containing a large proportion of people with cardiovascular or pulmonary diseases.

Nevertheless, as compared to previously published data on VO_{2peak} from comparable populations, the participants in HUNT had a somewhat higher VO_{2peak}[102-104]. Therefore, the lack of an external validation sample is a limitation of Paper I. However, previous studies have shown that similar models derived in healthy samples can be applied to groups receiving anti-hypertensive medication and people with a positive exercise electrocardiogram[51]. Moreover, cross-validation analysis in individuals from the HUNT Fitness Study with clustered cardiovascular risk factors (n=224) or hypertension (n=938) indicated that the model was valid also when applied to these subgroups. In the hypertensive group of men and women the mean difference between measured and predicted VO_{2peak} was negligible and the correlation was similar to that observed in the total sample (men, r=0.77, SD 5.58 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, women, r=0.68, SD 4.84). In the group with a clustering of cardiovascular risk factors, as previously defined by Aspenes et al.[27], the mean difference were 0.5 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ (r=0.77, SD 4.87 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$) Hence, the non-exercise model may be applicable also to high-risk subjects although derivation of population specific models may be preferable.

Statistical analyses

Paper I and II were designed as cross-sectional studies and included participants from the HUNT Fitness Study. Paper III was a prospective follow-up study of apparently healthy participants in HUNT 1. Analyses were done separately for men and women in all three papers. Precision of estimated means and hazard ratios were indicated by 95% confidence intervals. All statistical p-values were two-sided and the statistical procedures were conducted using PASW Statistics version 18.0 (Copyright 1993-2007 Polar Engineering and Consulting) or STATA for Windows version 12.1 (StataCorp LP, 1985-2007).

In *Paper I,* multiple linear regression analyses with VO_{2peak} as the dependent variable were used to develop the non-exercise models. Inclusion of potential predictor variables were done hierarchically, meaning they were entered one by one or in blocks of two or more variables based on a priori assumptions of the variables` association with VO_{2peak}. This method is preferable because the investigator easily can control the entry of predictor variables based on theoretical considerations[105]. An alternative regression method could be stepwise or backward regression which allows the computer program to select a set of the “best” predictors based on correlation coefficients. This approach, however, has several pitfalls because it is entirely data driven and the obtained model may not be the optimal regarding both internal and external validity[106]. Two important statistical measures were used to evaluate the accuracy of the models, namely the standard error of estimate (SEE) and the squared multiple regression coefficient (R^2)[107]. SEE refers to the random error of prediction for a regression line and are equal to a standard error score of 1 in terms of the units of the dependent variable. SEE is calculated as the sum of squared differences between actual and predicted values, divided by the total number of subjects. On the other hand, R^2, also called the coefficient of determination, is a measure of the strength of association and tells us what proportion of the variation of a variable (i.e. VO_{2peak}) that can be explained by a set of predictor variables. The models were further examined for accuracy by examining subgroups of age, PA-level and VO_{2peak} for constant errors (CE) and total errors (TE). CE are a measure of systematic over- or under-prediction and were calculated as the mean difference between measured and predicted VO_{2peak} (*mean residuals*) within the subgroups. A negative CE value indicates that the model, at average, tended to overestimate VO_{2peak} in that particular subgroup, while a positive value indicates a potential under-prediction. In contrast, TE combines the systematic error and the random error (SEE) and represents the total error of the model when applied to the particular subgroup. Any systematic over- or under-prediction among subgroups could be corrected by adding or subtracting the appropriate CE value from a cross-validation statistics for a particular sub-group, to the *y*-intercept of the original equation. Theoretically, this method would result in a constant error of zero for the modified equation when used in the intended population[108]. To test this hypothesis a cross-validation study in an independent sample would be necessary. The final model was, however, internally cross-validated by splitting the data-set into a derivation and a cross-validation sample. The regression analysis was performed on the derivation sample and the obtained model used to predict VO_{2peak} for each individual in the cross-validation sample. The correlation between observed scores and the predicted scores constitute the cross-validity coefficient which were squared and compared to the original R^2 of the validation sample. CE and TE values were estimated for the cross-validation sample when the model obtained from the derivation sample was used. Here, CE and TE represent the systematic and total error values of a model derived in one sample and validated in another sample. PRESS-statistics (Predicted Residual Sum of Squares) represents an alternative to simple-data splitting as an internal cross-validation procedure. This method may be preferable to data-splitting in smaller samples because it allows all observations to be included in both derivation and cross-validation. When the PRESS procedure was applied to the data material in Paper I we observed a R^2 of 0.61 and 0.55 and a SEE of 5.71 and 5.15, in men and women, respectively. Hence, this method did not add anything to simple data-splitting in the present cohort.

In *Paper II*, a general linear model (GLM) was used, with VO_{2peak} as the dependent variable, to determine the association between different groups of self-reported exercise patterns and VO_{2peak}. Adjustment was made for age only or age, BMI, smoking status and occupational PA. From the sub-maximal steady-state VO_2-measures and the VO_{2peak}-test, the test-subject's individual perceived exertion on the Borg scale association with VO_2 was calculated ($Y = a \cdot X + b$, where Y is VO_2 and X is Borg). For a given Borg scale rating a corresponding VO_2 value as a percentage of VO_{2peak} was established based on the individual treadmill test. The individual energy expenditure during self-reported exercise was calculated by multiplying the VO_2 ($L \cdot min^{-1}$) corresponding to the self-reported Borg scale rating by 5 $kcal \cdot min^{-1}$ (equivalent to ~1 L VO_2 for 1 minute). Furthermore, average energy expenditure was multiplied by the self-reported weekly duration of exercise to estimate total energy expenditure. Estimated resting energy expenditure was subtracted to obtain an estimate of net energy expenditure caused by exercise. In order to assess the independent effect of relative intensity within groups with different net energy expenditure, VO_{2peak} was entered as a dependent variable and intensity groups as independent variable with estimated weekly energy expenditure (kcal/week) and age as continuous variables as covariates. The analyses were then done separately for quartiles of weekly energy expenditure. Hence, we could separate the effect of intensity independent of its contribution to total energy expenditure. An implicit limitation of this cross-sectional study is that it cannot suggest causal pathways, but merely indicate associations and this limitation has to be acknowledged when interpreting the results[109].

In *Paper III*, Cox-proportional hazard models were used to assess the association of mortality with estimated VO_{2peak}. The Cox-model offers the opportunity to include numerous covariates and hence efficiently control for confounding. The outcome variables were death from cardiovascular disease and death from all-causes. We adjusted for age by entering age as the time-scale. Using age as the time-scale instead of time-on-study limits the introduction of bias than can occur when age is highly correlated with the predictor variable of interest, which is the case with estimated VO_{2peak}. We also did stratified analysis for younger and older subjects due to a moderate effect modification by age 60. Effect modification may appear when the influence of two variables on the outcome variable are not additive in their respective effects (i.e. the association between estimated VO_{2peak} and mortality were different for younger and older subjects). The validity of the prediction models were assessed by examining measures of discrimination and calibration[110]. Discrimination was assessed by calculating the area under the receiver operating curves (AUC, also known as Harrell`s *c*-statistic) and its 95% confidence intervals for estimated CRF and each modifiable constituent component, respectively. The AUC describes the probability that a classifier will assign a higher risk to a randomly chosen participant who died than a randomly chosen participant who survived until end of follow-up. Hence, a risk prediction by pure chance yields a *c*-statistic of 0.50, and higher values reflect better discrimination. The calibration refers to the degree of similarity between the observed and predicted risk (i.e. low-fit participants with a given predicted risk will actually experience events at the same rate). The Cox-regression model was calibrated by comparing the mean incidence proportion of events (CVD and all-cause, respectively) for each quintile of predicted risk and each estimated VO_{2peak}-group, with the multi-adjusted predicted risk obtained by the Cox-models.

RESULTS AND DISCUSSION

The current thesis shows that peak oxygen uptake (VO_{2peak}) can be predicted with reasonable accuracy from easily available clinical and self-reported variables. The final multiple regression model (non-exercise model) could predict long-term cardiovascular and all-cause mortality in people who were apparently healthy and below 60 years at baseline. Furthermore, we demonstrate that habitual exercise patterns of moderate relative intensity for a long total duration or vigorous intensity for a relatively short duration, adding up to the total volume as recommended by the health authorities, both were associated with a beneficial VO_{2peak} –level.

Non-exercise models of peak oxygen uptake

To our knowledge, the non-exercise models in Paper I are the first developed in a Scandinavian population and among the few derived from a large sample that included similar amounts of men and women with directly measured VO_{2peak} as the outcome variable. The accuracy of these models, as judged by R^2 (0.61 and 0.56 for men and women, respectively) and SEE (5.7 and 5.1 for men and women, respectively), are comparable to previously published models containing similar, large samples and a wide age range (Table 1)[51,54,104,111]. Non-exercise models that report considerably lower SEE and higher R^2 were generally based on smaller and more selected samples and may therefore have limited generalizability[112,113]. A large sample size is crucial for obtaining a useful prediction equation[114]. More predictor variables applied to smaller samples may spuriously increase the explanatory power[107]. The vast majority of previous non-exercise models include the variables sex, age, PA level and body composition, while some also include smoking, resting heart rate or height[51,54,115]. The non-exercise model in Paper I differ from most previous studies in that we made sex-specific models instead of including a dummy-coded sex variable. Sex differences in body composition are well-documented and may support sex-specific models as long as the sample size is large. Moreover, inclusion of product terms revealed interactions with sex for age, BMI and WC, respectively, which further support the preference of sex-specific models. Although WC/BMI was the strongest modifiable predictor in our sample, habitual PA levels are a key determinant of CRF and should therefore be measured with precision. In an attempt to improve the accuracy of prediction, Japanese researchers have included objective assessment of PA in their prediction models[116,117]. Hence, they would possibly overcome the accompanying bias associated with self-report measures of PA. When including time spent in moderate-to-vigorous PA or limited to vigorous PA as measured by accelerometers together with age and BMI or waist circumference, respectively, they observed a considerably higher R^2 and lower SEE compared to previous models (R^2, 0.71-0.86, SEE, 3.0-4.2). However, to obtain an objective measure of PA, it is required that the individual wears an activity monitor for up to 7 consecutive days, which may not be feasible in most healthcare settings[118].

In Paper I, we instead attempted to make a PA index from self-reported data that correlated well with VO_{2peak}. Hence, we examined the independent contributions of frequency, duration and intensity of PA and weighted each PA dimension differently according to the obtained ß-coefficients in a multiple regression analysis. It is proposed from several large-scale studies that intensity of PA are more strongly associated with VO_{2peak} than frequency or duration[60,75]. The index takes this into account by weighting higher relative intensity more than higher frequency and duration of PA, respectively (see Table 4 in Paper I). The correlation between the PA-Index and VO_{2peak} were 0.39 and 0.44 in women and men, respectively. We might, however, speculate that questionnaires making use of absolute intensity (activities assumed to require a certain energy expenditure), are more suitable in predicting VO_{2peak} since the absolute intensity during exercise are inherently limited by the maximal exercise capacity. For example, the Duke Activity Status Index (DASI) asks participants about their ability to perform 12 common daily activities that requires different levels of functional capacity. This index has been shown to correlate moderately well (r=0.58) with directly measured VO_{2peak} in an independent sample of healthy subjects[119]. Similarly, the Veterans Specific Activity Questionnaire (VSAQ) lists 13 activities with a corresponding MET-value and was shown to correlate moderately well with VO_{2peak} (r=0.42) in people referred for exercise testing for clinical reasons[120].

Table 1: Non-exercise models of VO_{2peak} derived from original data

Authors	Participants	Age	N	% female	Predictor variables	R^2	SEE	SEE (%)
Jackson et al.(1990)[51]	Healthy NASA employees	18-70	2009	9.7%	Age, sex, PA, BMI or %BF, RHR	0.61 0.66	5.70 (BMI) 5.35 (%BF)	14.4% 13.5%
Jurca et al.(2005)[54]	NASA ACLS ADNFS	20-70	1863 46,190 1706	21.6% 22.4% 50.0%	Age, sex, BMI, RHR, PA	0.65 0.60 0.58	5.08 (NASA) 5.25 (ACSL) 6.90 (ADNFS)	13.2% 13.0% 15.6%
Matthews et al.(1999)[104]	Healthy volunteers	19-79	799	51.2%	Age, age^2, sex, PA, height, weight or BMI	0.74 0.73	5.64 (H,W) 5.76 (BMI)	15.2% 15.5%
Whaley et al. (1995)[111]	Former exercise study particpants	-	2350	39.8%	Age, sex, PA, %BF Above+RHR, smoking status	0.70 0.85	5.61 5.38	14.5% 14.0%
Wier et al. (2006)[115]	Healthy NASA employees	19-82	2801	13.7%	Age, sex, PA and BMI, WC or % BF, respectively	0.66 0.67 0.64	4.80 (WC) 4.72 (%BF) 4.90 (BMI)	13.4% 13.2% 13.7%
Bruce et al. (1973)[45]	Healthy volunteers	48	295	53.2%	Age, sex, PA, weight	0.65	4.84	13.0%
Heil et al. (1995)[112]	Healthy volunteers	20-79	439	52.2%	Age, age^2, %BF, PA, sex	0.77 0.72 0.72	4.90 4.64 (♀) 5.02 (♂)	12.7% 13.8% 11.4%
Bradshaw et al. (2005)[113]	Healthy wellness program participants	18-65	100	50.0%	Age, sex, BMI, PFA, PA	0.86	3.45	8.6%
Nes et al. (2011)	Healthy HUNT participants	19-90	4260	51.6%	Age, PA-I, WC, RHR	0.67 0.61 0.56	5.47 5.70 (♂) 5.14 (♀)	13.7% 12.8% 14.3%

BMI, body mass index, %BF, body fat percentage, PA, self-reported physical activity, PA-I, physical activity index, RHR, resting heart rate, WC, waist circumference, PFA, perceived functional ability, NASA, National Aeronautics and Space Administration, ACSL, Aerobics Center Longitudinal Study, ADNFS, Allied Dunbar National Fitness Survey

In the model used for prospective mortality follow-up (Paper III), BMI was used instead of WC as a measure of body composition since WC was not measured in HUNT 1. However, both variables were examined extensively during the derivation of the model and yielded only small differences in R^2 and SEE as shown in Table 2. Previous studies have shown that inclusion of waist or BMI in multivariable models did not change model characteristics substantially[115,121]. Noteworthy, BMI was a strong predictor of VO_{2peak}, despite that VO_{2peak} were defined as the amount of oxygen consumption per kilo body mass ($mL \cdot kg^{-1} \cdot min^{-1}$). The finding that BMI were highly associated with VO_{2peak} may indicate that simply dividing VO_2 by body mass do not fully account for the influence of body mass on VO_{2peak} as intended. Some studies have also examined the predictive ability of percent body fat in non-exercise models and found similar or slightly better model fit[112,115,122]. However, percent body fat is estimated by measuring thickness of a minimum of three skinfolds and a possibly higher precision may not justify the time requirement needed to measure it properly.

Table 2: Multiple regression coefficients for predicting VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) in the total sample with waist or BMI included in the model

Variable	Men		Women	
	WC-model	BMI-model	WC-model	BMI-model
Intercept	100.27	92.05	74.74	70.77
Age	-0.296	-0.327	-0.247	-0.244
PA-Index	0.226	0.257	0.198	0.213
WC/BMI	-0.369	-0.933	-0.259	-0.749
RHR	-0.155	-0.167	-0.114	-0.107
R	0.782	0.770	0.745	0.753
R^2	0.612	0.593	0.555	0.568
SEE	5.70	5.84	5.14	5.06

PA-Index, physical activity index, WC, waist circumference, BMI, body mass index RHR, resting heart rate, R, multiple regression coefficient, R^2, squared multiple regression coefficient, SEE, standard error of estimate

The accuracy of the present models, in terms of SEE and R^2, are comparable to submaximal exercise testing of VO_{2peak}. For example the Multistage shuttle run test[123,124], the Rockport 1-mile walk test[125], the modified Bruce protocol[45,126], the single-stage submaximal treadmill test[127,128], the Åstrand-Rhyming test[46,129] and the ACSM prediction equation[130] all report SEE within the range of 3.5 to 6.5 $mL \cdot kg^{-1} \cdot min^{-1}$. However, most submaximal tests are population-specific and direct comparison may be limited without thorough cross-validation of both methods in an independent sample. We are aware of two other studies that validated non-exercise testing models and submaximal testing methods in the same sample. Jackson et al. (1990) reported similar correlations with directly measured VO_{2peak} for their non-exercise model (r=0.79), compared to the Åstrand-Rhyming submaximal test (r=0.78), in a healthy cross-validation sample[51]. However, the submaximal exercise test considerably overestimated VO_{2peak} for the whole range of fitness levels, while the non-exercise model underestimated VO_{2peak} among high-fit subjects. Mailey et al. (2010) validated the non-exercise model from Jurca et al. (2005) in elderly subjects, and found fairly similar cross-validity correlations between VO_{2peak} and maximal METs estimated from the non-exercise model (r=0.66) and the Rockport 1-mile walk test (r=0.68), respectively[55]. Moreover, the non-exercise model was more closely related to cardiovascular risk factor clustering compared to the Rockport test[55].

One reason why non-exercise models, as well as submaximal testing methods, fail to fully account for the variance in directly measured VO_{2peak} may be that the individual variability attributed to genetics are high. Several lines of evidence suggest that heritability may be responsible for more than 50% of the variability of VO_{2peak} in heterogeneous populations[72]. This is congruent with the results in Paper I, and others[45,51,54], showing that ~40% of the variance are left unexplained after including a wide range of modifiable and non-modifiable predictor variables. CRF are, however, frequently measured by maximal treadmill tests that, in comparison to sub-maximal and non-exercise tests, may better capture the heterogeneity in VO_{2peak}[45,131]. These protocols have been used in epidemiological studies and yield fairly accurate estimates of VO_{2peak} (r~0.90, SEE~3-4.0 $mL \cdot kg^{-1} \cdot min^{-1}$)[132]. However, these protocols suffer from many of the same limitations as direct measurement in terms of time-use, personnel requirement, equipment and participant efforts.

A possible limitation of most established non-exercise models is that they were derived from cross-sectional data. Therefore the accuracy of these models to estimate temporal changes in VO_{2peak} is not known. Accordingly, one does not know whether changes in the modifiable predictor variables over time, by training or detraining, may be detected by non-exercise prediction of VO_{2peak}. Furthermore, most cross-sectional models, including ours, found that VO_{2peak} was linearly related to age and hence included age as a linear term. However, longitudinal VO_{2peak} data suggest a non-linear decline with increasing age[133,134]. A recent study from the ACLS cohort attempted to overcome these problems by developing models from longitudinal exercise test data using linear mixed models[122]. These models are promising for capturing temporal changes in VO_{2peak} and warrants further attention.

Table 3: Descriptive data and cardiovascular risk factors by quintiles of estimated VO_{2peak}

Women	**Quintile 1** <31.0 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 2** 31.1-34.4 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 3** 34.5-37.3 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 4** 37.4-40.7 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 5** >40.7 $mL \cdot kg^{-1} \cdot min^{-1}$
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	28.2±4.6	32.4±4.6	35.4±5.2	38.8±5.2	44.4±6.8
Age (years)	62.1±9.8	55.0±8.9	47.8±9.3	42.1±9.0	33.9±8.4
BMI (m/kg^2)	28.8±4.1	26.2±3.3	25.3±3.4	24.0±2.9	22.5±2.1
Waist (cm)	96.8±10.1	88.7±8.3	85.5±8.0	82.3±7.4	76.1±6.4
Resting HR ($beats \cdot min^{-1}$)	65±10	62±9	60±8	58±8	56±8
Smoking status (% no/yes)	76/24	78/22	71/29	79/21	77/23
Systolic BP (mmHg)	137±17	127±15	121±13	118±11	115±10
Diastolic BP (mmHg)	75±10	71±10	69±9	68±9	66±8
Non-fasting glucose (ml/dl)	5.5±1.0	5.3±1.0	5.1±0.9	5.0±0.9	4.8±0.8
Total cholesterol	6.21±1.0	5.90±1.11	5.41±1.01	4.98±0.89	4.60±0.70
HDL cholesterol	1.50±0.37	1.51±0.34	1.51±0.35	1.51±0.33	1.54±0.30
Triglycerides	1.58±0.69	1.38±0.81	1.17±0.54	0.98±0.41	0.91±0.43
Men	**Quintile 1** <38.2 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 2** 38.3-42.2 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 3** 42.3-45.8 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 4** 45.8-50.3 $mL \cdot kg^{-1} \cdot min^{-1}$	**Quintile 5** >50.3 $mL \cdot kg^{-1} \cdot min^{-1}$
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	34.6±5.2	40.0±5.9	44.2±5.4	48.6±6.2	54.7±6.9
Age (years)	61.7±10.3	55.2±9.9	48.7±9.7	44.0±8.3	34.2±10.0
BMI (m/kg^2)	29.1±3.4	27.3±3.0	26.7±2.4	25.6±2.4	24.1±2.4
Waist (cm)	104.0±8.1	98.4±6.9	94.9±6.0	91.1±5.9	85.3±6.2
Resting HR ($beats \cdot min^{-1}$)	62±9	59±9	57±8	55±7	53±8
Smoking status (% no/yes)	80/20	78/22	75/25	79/21	82/18
Systolic BP (mmHg)	139±15	134±14	131±13	129±12	125±11
Diastolic BP (mmHg)	80±10	79±9	77±9	75±9	69±9
Non-fasting glucose (ml/dl)	6.0±2.2	5.7±2.0	5.4±1.3	5.2±0.9	5.0±1.2
Total cholesterol	5.69±1.00	5.74±0.90	5.59±0.98	5.44±0.97	4.74±0.93
HDL cholesterol	1.18±0.27	1.22±0.28	1.25±0.29	1.25±0.28	1.28±0.27
Triglycerides	2.07±1.12	2.03±1.38	1.82±1.16	1.75±1.00	1.26±0.60

Mean ± standard deviation,VO_{2peak}, peak oxygen uptake, BMI, body mass index, HR, heart rate, BP, blood pressure,
Quintiles of estimated VO_{2peak} from the non-exercise model in Paper I using waist circumference as measure of body composition

Cross-validity of the model

Given the SEE of the current models (5.7 and 5.1 $mL \cdot kg^{-1} \cdot min^{-1}$ for men and women, respectively) there is a relatively wide scatter around the line of identity for measured and predicted values. Implicitly, a predicted VO_{2peak} for an individual will be lower or higher than the true value in most participants. Moreover, the degree of inaccuracy may further increase when a model derived from a given population are applied to a different population. Therefore, different cross-validation techniques are commonly used to estimate how accurately a predictive model will perform in an independent data set. Such methods are important in guarding against a spuriously high model-fit that may appear when multiple predictors are included in a regression model. The problem of over-fitting a model can be detected by simple data-splitting procedures as presented in Paper I. Here, the regression model was developed on a randomly drawn part of the sample and tested on the other half of the sample.

Overall, the cross-validation statistics revealed high model stability as evidenced by small differences between measured and predicted values and relatively stable total error, across subgroups of age and PA levels in both sexes (see Table 5 in Paper I). The model seems to be most accurate among those with a medium fitness level reporting none or mostly low-intensity PA and those who were above 35 years for men and 50 years for women. However, in accordance with previous studies[51,104], the model tended to overestimate VO_{2peak} in low-fit subjects and subsequently, underestimate VO_{2peak} in high-fit subjects. When the model was applied to the cross-validation sample it tended to underestimate and overestimate VO_{2peak}, respectively, by at average ~4-5 $mL \cdot kg^{-1} \cdot min^{-1}$ in low- and high-fit men and women.

Table 4: Age and sex-specific quintile cut-off values for measured VO_{2peak} (mL·kg^{-1}·min^{-1})

	Total sample	<60 years	≥60 years
Men			
Q_1	<36.1	<38.9	<31.6
Q_2	36.1-41.5	38.9-44.2	31.6-34.8
Q_3	41.5-46.5	44.3-48.5	34.9-39.1
Q_4	46.6-52.0	48.6-53.5	39.2-43.4
Q_5	>52.0	>53.5	>43.4
Women			
Q_1	<29.1	<31.2	<25.0
Q_2	29.1-33.3	31.2-34.9	25.0-27.9
Q_3	33.4-37.2	35.0-39.1	28.0-30.7
Q_4	37.3-42.0	39.2-43.2	30.8-33.8
Q_5	>42.0	>43.2	>33.8

Q_{1-5}, quintiles of measured VO_{2peak}

Cross-classification

In a health perspective the systematic under-prediction among high-fit subjects may not sustain a pressing problem, because moderate and high fitness is not associated with high disease risk. At the extremes of CRF, such as among heart disease patients or top level endurance athletes, VO_{2peak} should be directly measured with regularity because relatively small increments/decrements may have great impact on prognosis or performance[135]. The ability to easily and correctly classify low-fit apparently healthy subjects, however, is of crucial importance since several dose-response studies suggest that the largest increase in risk are between low-fit and medium-fit persons[28,39]. We evaluated the ability of the non-exercise models to classify an individual`s VO_{2peak} by cross-classification procedures. In Paper I we show that the model was quite accurate in classifying high- and low-fit subjects since ~90% of the participants were correctly classified into the same or adjacent quartile of measured VO_{2peak} (see Table 6, Paper I). In practice this implies, given that the quartile cut-points are used, that a woman with a predicted VO_{2peak} below 32 mL·kg^{-1}·min^{-1} probably has a measured VO_{2peak} at least below 35 mL·kg^{-1}·min^{-1} and a man with a predicted value below 40 mL·kg^{-1}·min^{-1} is very likely to have a measured VO_{2peak} below 44 mL·kg^{-1}·min^{-1}. In a previous study from the HUNT Fitness Study, Aspenes et al. showed that men and women with a measured VO_{2peak} below 44 mL·kg^{-1}·min^{-1} and 35 mL·kg^{-1}·min^{-1}, respectively, had an increased prevalence of cardiovascular risk factor clustering[27]. Hence, we might be able to capture high-risk subjects by using the right cut-offs. The distribution of some cardiovascular risk factors stratified by quintiles of estimated VO_{2peak} in the HUNT Fitness Study participants is shown in Table 3. Several clinical cardiovascular risk factors differ in a dose-response manner across estimated VO_{2peak} categories. In the following we show that the model was reasonably accurate in cross-classifying low-fit subjects into the correct tail of the measured VO_{2peak} distribution (i.e. 1^{st} and 2^{nd} quintile). The age- and sex-specific cut-off values for measured VO_{2peak} in the total sample and men and women above and below 60 years are presented in Table 4.

Table 5 shows cross-classification of low-fit participants (1^{st} quintile of measured VO_{2peak}) across quintiles of predicted VO_{2peak} based on the BMI-model. Hence, the percentages represent the sensitivity of the model to capture those with a low measured VO_{2peak}. In the total sample slightly above 40% were correctly classified into the lowest quintile. However, more than 80% were correctly classified within one quintile. Hence, a predicted VO_{2peak} below 41.5 and 33.3 $mL·kg^{-1}·min^{-1}$ in men and women, respectively, would capture most participants with a measured VO_{2peak} below 36.1 and 29.1 $mL·kg^{-1}·min^{-1}$. Extreme misclassification occurred very rarely as only 2.2 and 3.6% of the low-fit men and women, respectively, were predicted to be in the two highest categories of VO_{2peak}. In subgroups the non-exercise model were, as expected, less accurate in classifying low-fit subjects of normal weight and those reporting a high PA level. However, a relatively few subjects fell into these categories (n=63 and n=111 for normal weight men and women, respectively and n=25 and n=23 for highly active men and women in 1^{st} quintile of VO_{2peak}). On the other hand, the majority of subjects who were predicted to be in the lowest quintile actually had a measured VO_{2peak} in the 1^{st} (~70% in both men and women) or 2^{nd} quintile (>90% in men and women). Only 1-2% of those predicted to have low fitness did actually have a VO_{2peak} in the two highest quintiles. Therefore, we can be relatively confident that those with a low predicted VO_{2peak} actually has a low VO_{2peak} (high positive predictive value). These numbers are in accordance with two previous studies that evaluated the classification accuracy of non-exercise testing[104,136]. Hence, we considered the model as accurate enough to correctly identify low-fit and high-fit subjects in an epidemiological study (Paper III).

Table 5: Cross-classification of participants with low measured VO_{2peak} into categories of predicted VO_{2peak}

	Classification into predicted quintiles (%)							
	Men				**Women**			
Low measured VO_{2peak} (Q_1)	***N*[a]**	Q_1	Q_{1-2}	Q_{4-5}	***N*[a]**	Q_1	Q_{1-2}	Q_{4-5}
Total sample	414/2067	41.5	84.0	2.2	439/2193	42.8	80.4	3.6
<60 years[b]	321/1601	45.5	86.0	2.8	349/1745	36.1	73.6	5.5
≥60 years[b]	94/466	50.0	72.3	5.7	90/448	43.3	66.6	15.5
Low activity[c]	247/759	51.8	89.0	1.6	254/795	56.3	87.4	2.0
Moderate activity[c]	142/954	28.2	81.9	2.1	162/1038	26.5	72.2	6.2
High activity[c]	25/354	16.0	48.0	8.0	23/360	8.7	60.9	4.3
Normal weight[d]	63/644	12.7	63.5	4.8	111/1182	13.5	62.1	12.6
Overweight[d]	222/1143	36.5	85.1	2.7	182/733	37.4	78.6	1.1
Obese[d]	129/280	64.3	92.2	0.0	146/278	71.9	96.6	0.0

Q_{1-5}, quintiles of predicted VO_{2peak}
[a]number in lowest quintile of VO_{2peak} and total number in subgroup
[b]age-specific quintile from Table 4
[c]Tertiles of PA-Index
[d]BMI <25 (normal), 25-30 (overweight), >30 (obese)

Estimated VO_{2peak} and mortality

In Paper III we used the non-exercise model of Paper I to estimate VO_{2peak} in a large sample of healthy men and women who took part in the first HUNT Study in 1984-85. Furthermore, we assessed the association with all-cause and cardiovascular mortality after ~24 years of follow-up. Previous population-based studies have confirmed that exercise tested CRF is a powerful and independent predictor of premature mortality in asymptomatic populations[24,28,137] and in people with cardiovascular disease[24,34,36,138]. Assuming that the non-exercise model were able to correctly classify VO_{2peak} in an independent sample from the HUNT population, we hypothesized an increased risk of mortality among those estimated to have low VO_{2peak} at baseline and an overall inverse association between mortality and estimated VO_{2peak}.

Indeed, the observed risk reductions associated with higher estimated VO_{2peak} in participants below 60 years at baseline, were comparable to those obtained in population based studies that estimated CRF from maximal treadmill tests[24,31]. A meta-analysis by Kodama and co-workers reported a summarized risk reduction for all-cause mortality of 13% per MET (~3.5 $mL \cdot kg^{-1} \cdot min^{-1}$) higher CRF[31]. Among the 19 studies that were included, the reported risk reductions ranged from 4 to 26% per MET higher CRF. Hence, our findings of 8-14% reduction in all-cause mortality and 21% reduction in cardiovascular mortality per estimated MET seem to be well within the expected range. In participants below 60 years, we observed a 12 and 17% lower risk of all-cause mortality and ~25% lower risk of cardiovascular mortality in men and women, respectively, with medium CRF compared to those in the lowest quintile. It could be argued, however, that prediction of mortality from a non-exercise model does not provide more information than what is already available from the respective variables included in the model (i.e. age, BMI, PA and RHR). In Paper III, however, we show that estimated VO_{2peak} had a better discriminative ability than each of its constituent components separately, also when age was statistically controlled for. This may not be surprising since BMI, PA, RHR are all independent predictors of premature mortality[139-141]. However, estimated VO_{2peak} was also a better predictor than a composite score derived from the sum of z-scores for each variable. Consequently, we might propose that the non-exercise model were able to discriminate participants by VO_{2peak} and therefore might add to the prognostic utility of each separate risk factor.

Only one other study has examined the association between estimated CRF from a non-exercise model and premature mortality. Stamatakis and co-workers used one of the models from Jurca et al. to estimate CRF in 32,319 healthy men and women[142]. In general, their findings of a 12-15% decrease in all-cause and 25-27% decrease in cardiovascular mortality per SD increase in estimated METs (SD was ~1.6-1.7 METs) are close to those obtained in Paper III. That study pooled data from eight different cohorts and had a shorter follow-up time (~9 years). The prognostic utility of non-exercise testing of CRF should be evaluated further in other populations. A few other studies have, however, attempted to predict premature mortality from more simple CRF estimates without performing exercise testing. Among 906 women referred for coronary angiography, maximal METs estimated from the DASI questionnaire predicted adverse cardiovascular events and all-cause mortality[143]. Each estimated MET was associated with an 8% decrease in risk of adverse cardiovascular events and 7% decrease in risk of all-cause mortality. Similarly, a study that estimated METs from the VSAQ questionnaire during a mean follow-up of 4.5 years, reported a 10% survival benefit during per each MET in 1185 men referred for exercise testing for clinical reasons[144]. Moreover, a prospective cohort study including 858 middle-aged participants from Scotland found that self-rated fitness were an independent and similarly strong predictor of all-cause mortality as self-rated overall health status[145]. Although the risk reductions reported in these studies were generally lower compared to Paper III and that from Stamatakis et al., and may vary according to baseline hazards, the findings at least suggest that including self-rated fitness levels may increase the accuracy of future non-exercise models and their association with hard endpoints.

Intensity and volume of physical activity in relation to health outcomes

Today`s recommendations for PA allows for shorter total duration of PA spend at vigorous intensities or longer total duration of moderate intensity as long as the total volume exceeds ~500 MET/min per week (minutes per week · intensity in METs, corresponds to ~1000 kcal). An implication of this statement is that the benefits of higher intensity, as opposed to low or moderate, are attributed essentially to the higher energy expenditure per time unit. However, accumulating evidence from randomized trials indicate that high intensity training may yield health benefits independent of its contribution to the total energy expenditure[85,146]. Some epidemiological evidence are also emerging, including a large prospective cohort study involving 416,175 individuals that were followed for ~8 years[86]. In that study, self-reported PA was separated into moderate and vigorous intensity for five different categories of total weekly energy expenditure. For a similar or lower estimated energy expenditure, reporting vigorous intensity activities was associated with lower risk of death from cardiovascular disease, diabetes and all-causes. Moreover, a study of men in the Health Professionals` Follow-up Study found a significantly lower risk of coronary heart disease for vigorous compared to low and moderate intensity after statistically controlling for total energy expenditure[147]. Also, a previous HUNT study showed that a single weekly exercise session of high intensity considerably reduced the risk of cardiovascular mortality compared to no activity, while no additional benefit was observed by increasing the duration or frequency of exercise sessions[148].

However, it is suggested that self-reported PA by questionnaires are more imprecise in measuring low and moderate intensity exercise (misclassification bias) and we might suspect that most people who are doing vigorous intensity activity also do considerable amounts of moderate intensity activity[95]. Hence, the inability to separate the effects of high and moderate intensity activity in relation to health outcomes has been a problem of observational studies. The incorporation of objective measurement of PA by accelerometers in population based studies, however, may be superior to self-report measures concerning the independent effects of moderate and vigorous intensity PA. Recently, Jansen and Ross showed that vigorous intensity PA measured by accelerometers had a considerably larger influence on metabolic syndrome prevalence compared to moderate intensity PA after controlling for total energy expenditure dose[149]. Intriguingly, ~75 min of vigorous PA had double the benefit of ~150 min of moderate PA when energy expenditure was kept constant.

Intensity and volume of exercise in relation to peak oxygen uptake (VO_{2peak})

Several short-term randomized controlled trials have indicated that vigorous intensity exercise, relative to the individual`s VO_{2peak} or maximal heart rate, yield larger improvements in VO_{2peak} than moderate intensity exercise for a similar amount of total work performed[150-153]. For practical reasons randomized trials generally mimic only two or three out of an infinitely number of possible exercise patterns (i.e. combinations of frequency, duration and intensity) in free-living individuals. Furthermore, such trials are hampered by relatively short follow-up time (solely <1 year, usually 8-12 weeks) and small and/or selected samples. Whether these benefits are maintained over a longer time frame, i.e. over the course of a lifetime, and hence relevant for public health guidelines, is therefore a matter of controversy. On the contrary, observational studies may better capture more permanent PA behavior and provide complementary information on dose-response issues. In Paper II, we cross-sectionally examined how self-reported, freely selected exercise patterns of longer total duration at moderate intensity and shorter durations at vigorous intensity were associated with VO_{2peak} in healthy adults. Briefly, similar VO_{2peak} was observed in groups approximating those patterns, but considerably higher net estimated energy expenditure were found among the longer duration-moderate intensity groups. Interestingly, however, groups reporting shorter exercise time than recommended (i.e. less than 75 minutes per week, mean ~45-50 minutes) at vigorous intensity, had comparable VO_{2peak} values to those in the moderate intensity-long duration groups. Despite this, the energy expenditure was considerably lower than the total recommended volume. Possible dose-response relationships between PA at low, moderate and vigorous intensity and VO_{2peak} from these data are shown in Figure 3 and 4. Our observation of substantially higher VO_{2peak} levels among those reporting vigorous-intensity, as compared to moderate and low intensity at similar total duration, is in accordance with data from randomized controlled trials[57,76] (Figure 3, see also Figure 1 in Paper II). Although not essentially novel, this information is important since lack of time is one of the most stated barriers to habitual exercise[154,155]. The intensity-dependent associations were, however, attenuated after adjusting for weekly net energy expenditure (Figure 4, see also Figure 2 in Paper II). In men, VO_{2peak} was still slightly higher for vigorous intensity PA, as compared to moderate intensity at all total volumes performed. Among women, however, at least the recommended total volume of 1000 $kcal \cdot week^{-1}$ seemed to be necessary to achieve benefits from vigorous intensity PA when net energy expenditure was constant between the two intensity groups.

In Paper II we assessed the intensity of exercise using the Borg 6-20 scale. The Borg scale is considered as a valid measure of relative intensity and correlated well with relative VO_2 and heart rate at different stages of incremental treadmill walking or running in the present population. Contrary to the majority of observational studies, intensity of exercise was therefore assessed relative to the individuals` exercise capacity not in absolute MET values[124,125]. This may be more appropriate when the age-span is large and CRF levels differ widely among participants. For example, an absolute intensity of 7 METs (VO_2 ~25 mL·kg^{-1}·min^{-1}) corresponded to 82% of VO_{2peak}, and 14-15 on the Borg scale (*vigorous* intensity) for an average 60-year-old woman, while it corresponded to only 45% of VO_{2peak} and Borg scale 8-9 (*low* intensity) for a 20-year-old man among the participants in Paper II. Hence, undertaking PA requiring 7 MET may yield a substantially different exercise stimulus at different tails of the CRF distribution. Hence, the perceived exertion of activities requiring a certain absolute intensity may be negatively associated with the individuals` level of CRF[156]. Moreover, it is practically important because current guidelines support perceived exertion as the primary method in exercise prescription[2,140,157]. Paper II was also novel in that we estimated self-reported PA energy expenditure on the basis of the concurrent VO_2 associated with each individual`s Borg scale ratings at the incremental treadmill test. Previous studies have provided crude estimates of energy expenditure from self-report data by assigning certain MET values to specific activities based on the compendium by Ainsworth et al[158,159]. Hence, we used a more direct approach in determining individual energy expenditure. However, we acknowledge that people may rate the exertion different in a test setting as compared to recalling usual exercise intensity in daily life. Hence, the estimated energy expenditure may be subject to bias when translating perceived exertion on the treadmill to habitual exercise. However, reporting a shorter total duration and/or lower intensity than recommended was consistently associated with estimated net energy expenditure below 1000 kcal·week$^{-1.}$ Moreover, a doubling of total time spent within the different intensity groups was associated with an approximately doubling of net energy expenditure (see Table 4 in Paper II).

The findings in Paper II in no way negate current PA recommendations, but suggest that vigorous relative intensity certainly compensates for lower total exercise time and may also be beneficial to moderate intensity PA at similar net energy expenditure, at least in men and active women. Indeed, the observed differences in VO_{2peak} may seem small, but as previously mentioned, a difference of 1 MET (~3.5 mL·kg^{-1}·min^{-1}) may provide a reduced relative risk of premature mortality in the order of 10-25% which must be considered as a clinically relevant difference[31]. Broadly recommending sporadic vigorous intensity exercise may, however, be controversial due to possible increased risk of musculoskeletal injury and triggering of heart attacks in subgroups with underlying disease[160,161]. Furthermore, the modest estimated energy expenditure in the low volume-vigorous intensity groups may not be sufficient for preventing weight gain[162]. Hence, reducing sedentary time and, accordingly, accumulating low intensity activity through daily life activities should be highly encouraged in addition to exercise training and may yield health benefits independent of increased VO_{2peak}[163,164]. Furthermore, the results herein may be explained by relatively fit people being more likely to engage in more frequent and/or more vigorous PA. Hence, causality can only be determined by large-scale randomized trials with careful control of exercise behavior and drop-outs.

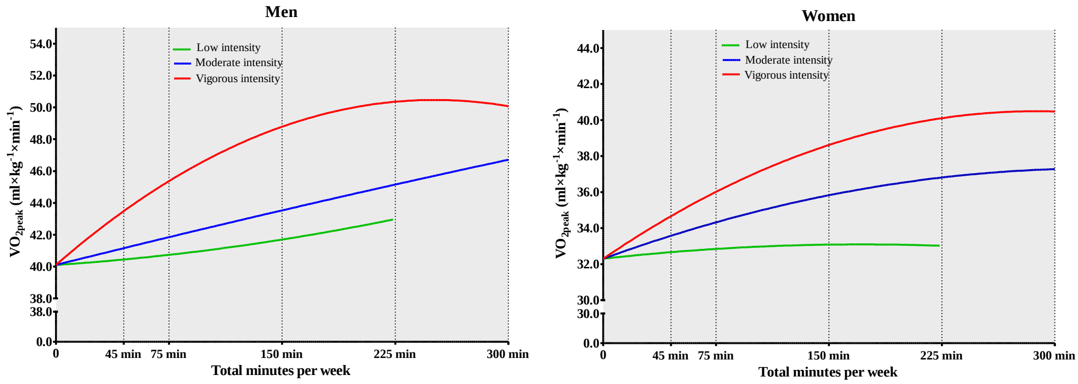

Figure 3: Weekly exercise time and VO_{2peak} in men and women at different intensities. Low intensity (Borg scale 6-11, ~40-65% of VO_{2peak}), moderate intensity (Borg scale 12-13, ~70-72% of VO_{2peak}) and vigorous intensity (Borg scale 14-20, >80% of VO_{2peak}). The curves were smoothed through the mean VO_{2peak} for groups reporting different total exercise time at low-, moderate and vigorous intensity, respectively.

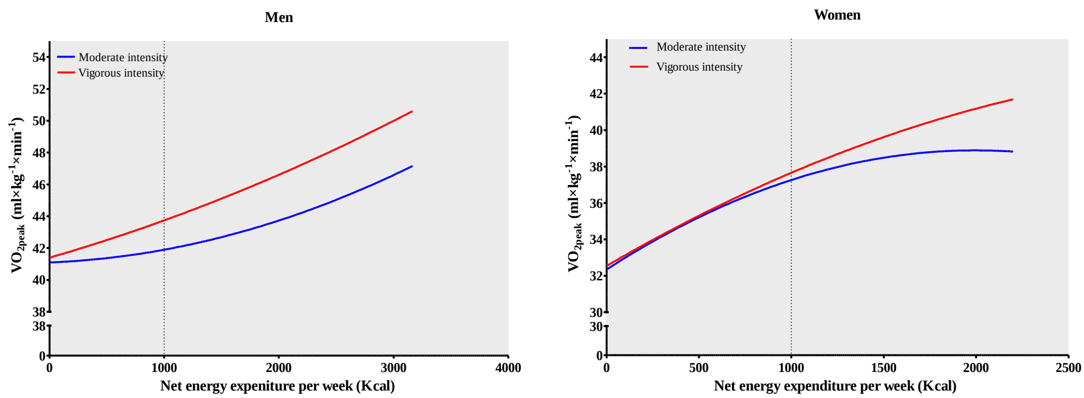

Figure 4: Total kcal per week spent at exercise and VO_{2peak} in men and women at different intensities. Moderate intensity (Borg scale 12-13, ~70-72% of VO_{2peak}) and vigorous intensity (Borg scale 14-20, >80% of VO_{2peak}). The curves were smoothed through the mean VO_{2peak} for groups with different energy expenditure at moderate and vigorous intensity, respectively.

Practical application of the results

The current thesis may provide an opportunity for physicians and other health personnel to put focus also on the individual level of CRF in clinical consultations. The non-exercise model from Paper I can easily be incorporated in computer programs that estimates the CRF level (see www.ntnu.no/cerg/vo2max) or in prediction charts (see Appendix). When a low level of CRF is identified a maximal exercise test using ventilatory gas analysis could be considered to objectively determine VO_{2peak} and provide an accurate baseline level before eventually entering a structured exercise program. However, one should be aware that the estimation are limited in capturing individuals who are low-fit despite of being highly active and of normal weight etc. (potentially so-called non-responders). A conversation about the agreement between self-rated fitness and self-reported exercise patterns may help in detecting these relatively rare cases. Furthermore, focus should be set on the major modifiable determinant of CRF, namely the habitual PA pattern. The current PA recommendations provide a good starting point for such a discussion. The accumulation of 150 minutes of moderate-intensity exercise per week, preferably spread throughout the week, might be sufficient to improve fitness, but at least 75 minutes of vigorous intensity exercise is also satisfactory if time is limited. Precise definitions of frequency, duration and intensity should be provided. Moreover, exercise prescription should be tailored to the individuals` characteristics by taking into account age and baseline CRF, preferably by prescribing exercise intensity on a relative scale and also by considering the accompanying risks of certain activities in high risk groups.

Future research

We recognize that the non-exercise models may need further refinement to be applicable for broad implementation in clinical practice. Firstly, it should be externally validated in a different cohort, preferably containing a larger number of high-risk subjects. Secondly, future studies should elucidate whether precision could be increased, without compromising simplicity, by further refinement of the PA variable and potentially including measures of self-rated CRF. Thirdly, longitudinal studies should also examine whether changes in estimated VO_{2peak} are associated with different health outcomes. The HUNT database may be applicable for such a study if VO_{2peak} could be estimated with the same model at minimum two time points (i.e. HUNT 1 and 2).

The issue of dose-response between PA and VO_{2peak} and their relation to different health outcomes also warrants further consideration. Paper II introduces a novel approach to estimate energy expenditure of exercise from the Borg scale in community-dwelling populations that could be used in prospective analysis of PA and future health. Planned follow-up studies of the HUNT Fitness Study population may also unveil how different exercise patterns and VO_{2peak} interact as prognostic factors for cardiovascular and all-cause mortality as well as more rare outcomes such as specific types of cancers.

Conclusions

The current thesis provides an internally well-validated prediction model that could estimate VO_{2peak} reasonably well without exercise testing on the basis of age, an index of habitual PA, body composition and resting heart rate. Furthermore, we demonstrated that the non-exercise test could predict long-term cardiovascular and all-cause mortality, at least in men and women below 60 years at baseline. Notably, the relative risk reductions were similar to those reported by studies utilizing direct measurement of VO_{2peak}. Lastly, we provide evidence that exercise patterns in accordance with current recommendations were associated with a beneficial VO_{2peak} both among participants preferring a high amount at a moderate relative intensity and a lower amount at a vigorous intensity.

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PAPER I

Nes, BM, Janszky, I, Vatten, LJ, Nilsen, TIL, Aspenes, ST & Wisløff, U. (2011) Estimating VO_{2peak} from a non-exercise prediction model: The HUNT Study, Norway. *Medicine & Science in Sports & Exercise*. **43**(11):2024-2030

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PAPER II

Nes, BM, Janszky, I, Bertheussen, GF, Aspenes, ST, Vatten, LJ, & Wisløff, U. (2012)
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PAPER III

Nes, BM, Vatten, LJ, Nauman, J, Janszky, I & Wisløff, U. (2013) Estimated cardiorespiratory fitness as a predictor of long-term all-cause and cardiovascular disease mortality: the HUNT study in Norway. *Medicine & Science in Sports & Exercise. Accepted for publication.*

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APPENDIX

1. **Prediction chart for estimation of VO_{2peak}**
2. **Questionnaire used in Paper I, *HUNT 3 (2006-08)***
3. **Questionnaire used in Paper II, *The HUNT Fitness Study***
4. **Information used in Paper II, *The HUNT Fitness Study***
5. **Questionnaire used in Paper III, *HUNT 1 (1984-86)***

STEP 1

PHYSICAL ACTIVITY INDEX

Choose the option that best matches your usual exercise habits. Examples of exercise can be walking, skiing, cycling, swimming and indoor or outdoor sports.

How often do you exercise?	
Never or less than once per week	0
Once a week	1
Two to three times a week	**2**
Almost every day	3
How hard do you usually push yourself?	*
I take it easy without losing my breath or breaking into sweat	0
I lose my breath and break into sweat	**5**
Almost to exhaustion	10
For how long do usually exercise?	*
Less than 30 minutes per session	1
More than 30 minutes per session	**1.5**
	=
Your physical activity index score:	**15** → Add to STEP 2

STEP 2

Estimate cardiorespiratory fitness	**MEN**		**WOMEN**	
Constant	**100.27**		**74.74**	
	–		–	
Age in years	**40**	x 0.296	**35**	x 0.247
	–		–	
Waist circumference (cm)	**85**	x 0.369	**85**	x 0.259
	–		–	
Resting heart rate (beats per min)	**70**	x 0.155	**65**	x 0.114
	+		+	
Physical activity score	**15**	x 0.226	**15**	x 0.198
	=		=	
Estimated peak oxygen uptake:	**50**	**ml·kg^{-1}·min^{-1}**	**40**	**ml·kg^{-1}·min^{-1}**

Invitasjon til HUNT 3

Viktig
Enkelt
Gratis

Du inviteres herved til å delta i den tredje store Helseundersøkelsen i Nord-Trøndelag (HUNT 3). Ved å delta får du en enkel undersøkelse av din egen helse, og du gir samtidig et viktig bidrag til medisinsk forskning.

Hver deltaker er like viktig, enten du er ung eller gammel, frisk eller syk, er HUNT-veteran eller møter for første gang. Tilsvarende undersøkelse er tidligere gjennomført i 1984-86 (HUNT 1) og 1995-97 (HUNT 2 og Ung-HUNT). For å kunne studere årsaker til sykdom, er det viktig at også de som tidligere har deltatt møter fram.

Vennligst fyll ut spørreskjemaet, og ta det med når du møter til undersøkelse.

Undersøkelsen tar vanligvis ca 1/2 time. Du vil få brev med resultater fra dine prøver etter noen uker. Dersom noen av resultatene er utenom det normale, vil du bli anbefalt undersøkelse hos fastlegen din.

Du kan lese mer om HUNT 3 i den vedlagte brosjyren eller på www.hunt.ntnu.no. Har du spørsmål, kan du også ringe til HUNT forskningssenter, tlf 74075180.

Vel møtt til undersøkelsen!

Vennlig hilsen

Steinar Krokstad
Førsteamanuensis
Prosjektleder HUNT 3

Jostein Holmen
Professor, daglig leder
HUNT forskningssenter

Stig A. Slørdahl
Professor, dekanus
Det medisinske fakultet, NTNU

Tid og sted for oppmøte

Dersom det foreslåtte tidspunktet ikke passer for deg, behøver du ikke bestille ny time. Du kan møte når det passer deg innenfor åpningstiden, men det kan da bli noe ventetid. Du kan også møte i en annen kommune, hvis det skulle passe bedre. Takk for at du deltar!

Åpningstida:

hunt 3
Helseundersøkelsen i Nord-Trøndelag

NTNU
HUNT forskningssenter






En time for bedre folkehelse

VESTVIK REKLAME AS. FOTO: HARALD SÆTERØY OG JOHAN ARNT NESGÅRD.

Slik fyller du ut skjemaet

- Skjemaet vil bli lest maskinelt.
- Det er derfor viktig at du krysser av riktig: **Rett** ☒ **Galt**
- Krysser du feil sted, retter du ved å fylle boksen slik: ■
- Skriv tydelige tall: 0 1 2 3 4 5 6 7 8 9
- Bruk bare svart eller blå penn. Ikke bruk blyant eller tusj.

HELSE OG DAGLIGLIV

1 Hvordan er helsa di nå?

☐ Dårlig ☐ Ikke helt god ☐ God ☐ Svært god

2 Har du noen langvarig (minst 1 år) sykdom, skade eller lidelse av fysisk eller psykisk art som nedsetter dine funksjoner i ditt daglige liv? ☐ Ja ☐ Nei

Hvis ja:
Hvor mye vil du si at dine funksjoner er nedsatt?

	Litt nedsatt	Middels nedsatt	Mye nedsatt
Er bevegelseshemmet	☐	☐	☐
Har nedsatt syn	☐	☐	☐
Har nedsatt hørsel	☐	☐	☐
Hemmet pga. kroppslig sykdom	☐	☐	☐
Hemmet pga. psykisk sykdom	☐	☐	☐

3 Har du kroppslige smerter nå som har vart mer enn 6 måneder? ☐ Ja ☐ Nei

4 Hvor sterke kroppslige smerter har du hatt i løpet av de siste 4 uker?

☐ Ingen ☐ Meget svake ☐ Svake ☐ Moderate ☐ Sterke ☐ Meget sterke

5 I hvilken grad har din fysiske helse eller følelsesmessige problemer begrenset deg i din vanlige sosiale omgang med familie eller venner i løpet av de siste 4 uker?

☐ Ikke i det hele tatt ☐ En del ☐ Litt ☐ Mye ☐ Kunne ikke ha sosial omgang

HELSETJENESTER

6 Har du i løpet av de siste 12 måneder vært hos:

	Ja	Nei
Fastlege/allmennlege	☐	☐
Annen legespesialist utenfor sykehus	☐	☐
Konsultasjon uten innleggelse		
- ved psykiatrisk poliklinikk	☐	☐
- ved annen poliklinikk i sykehus	☐	☐
Kiropraktor	☐	☐
Homøopat, akupunktør, soneterapeut, håndspålegger eller annen alternativ behandler	☐	☐

7 Har du vært innlagt i sykehus i løpet av de siste 12 måneder? ☐ Ja ☐ Nei

SYKDOMMER OG PLAGER

8 Har du hatt noe anfall med pipende eller tung pust de siste 12 måneder? ☐ Ja ☐ Nei

9 Har du noen gang de siste 5 år brukt medisiner for astma, kronisk bronkitt, emfysem eller KOLS? ☐ Ja ☐ Nei

10 Bruker du, eller har du brukt, medisin mot høyt blodtrykk? ☐ Ja ☐ Nei

11 Har du, eller har du noen gang hatt, noen av disse sykdommene/plagene:
(Sett ett kryss pr. linje)

Hvis ja, hvor gammel var du **første** gang?
Eksempel: 3 4 *år gammel*

	Ja	Nei	Hvis ja, hvor gammel var du første gang?
Hjerteinfarkt	☐	☐	___ *år gammel*
Angina pectoris (hjertekrampe)	☐	☐	___ *år gammel*
Hjertesvikt	☐	☐	___ *år gammel*
Annen hjertesykdom	☐	☐	___ *år gammel*
Hjerneslag/hjerneblødning	☐	☐	___ *år gammel*
Nyresykdom	☐	☐	___ *år gammel*
Astma	☐	☐	___ *år gammel*
Kronisk bronkitt, emfysem, KOLS	☐	☐	___ *år gammel*
Diabetes (sukkersyke)	☐	☐	___ *år gammel*
Psoriasis	☐	☐	___ *år gammel*
Eksem på hendene	☐	☐	___ *år gammel*
Kreftsykdom	☐	☐	___ *år gammel*
Epilepsi	☐	☐	___ *år gammel*
Leddgikt (reumatoid artritt)	☐	☐	___ *år gammel*
Bechterews sykdom	☐	☐	___ *år gammel*
Sarkoidose	☐	☐	___ *år gammel*
Beinskjørhet (osteoporose)	☐	☐	___ *år gammel*
Fibromyalgi	☐	☐	___ *år gammel*
Slitasjegikt (artrose)	☐	☐	___ *år gammel*
Psykiske plager som du har søkt hjelp for	☐	☐	___ *år gammel*

12 Har du noen gang fått påvist for høyt blodsukker? ☐ Ja ☐ Nei

Hvis ja: I hvilken situasjon første gang?

☐ Ved helseundersøkelse ☐ Under sykdom
☐ Under svangerskap ☐ Annet

SKADER

13 Har du noen gang hatt:

Hvis ja, hvor gammel var du **første** gang?

Eksempel: 3 4 *år gammel*

	Ja	Nei	Alder
Lårhalsbrudd	☐	☐	*år gammel*
Brudd i handledd/underarm	☐	☐	*år gammel*
Brudd/sammenfall av ryggvirvler	☐	☐	*år gammel*
Nakkesleng (whiplash)	☐	☐	*år gammel*

14 Har du foreldre, søsken eller barn som har, eller har hatt, følgende sykdommer?
(Sett ett kryss pr. linje)

	Ja	Nei	Vet ikke
Hjerneslag eller hjerneblødning før 60 års alder	☐	☐	☐
Hjerteinfarkt før 60-års alder	☐	☐	☐
Astma	☐	☐	☐
Allergi/høysnue/neseallergi	☐	☐	☐
Kronisk bronkitt/emfysem/KOLS	☐	☐	☐
Kreftsykdom	☐	☐	☐
Psykiske plager	☐	☐	☐
Beinskjørhet (osteoporose)	☐	☐	☐
Nyresykdom (ikke nyresten, urinveisinfeksjon, urinlekkasje)	☐	☐	☐
Diabetes (sukkersyke)	☐	☐	☐

15 Har noen av dine besteforeldre, dine foreldres søsken eller dine søskenbarn fått diagnosen diabetes (type 1 eller type 2)? Ja ☐ Nei ☐

HVORDAN FØLER DU DEG?

16 Har du de to siste uker følt deg:
(Sett ett kryss pr. linje)

	Nei	Litt	En god del	Svært mye
Trygg og rolig?	☐	☐	☐	☐
Glad og optimistisk?	☐	☐	☐	☐
Nervøs og urolig?	☐	☐	☐	☐
Plaget av angst?	☐	☐	☐	☐
Irritabel?	☐	☐	☐	☐
Nedfor/deprimert?	☐	☐	☐	☐
Ensom?	☐	☐	☐	☐

17 Har du noen gang i livet opplevd at noen over lengre tid har forsøkt å kue, fornedre eller ydmyke deg? Ja ☐ Nei ☐

TOBAKK

18 Røykte noen av de voksne innendørs da du vokste opp? Ja ☐ Nei ☐

19 Røykte mora di da du vokste opp? Ja ☐ Nei ☐

20 Røyker du selv?

- **Nei**, jeg har aldri røykt ☐

Hvis du aldri har røykt, hopp til spørsmål 22.

- **Nei**, jeg har sluttet å røyke ☐
- **Ja**, sigaretter av og til (fest/ferie, ikke daglig) ☐
- **Ja**, sigarer/sigarillos/pipe av og til ☐
- **Ja**, sigaretter daglig ☐
- **Ja**, sigarer/sigarillos/pipe daglig ☐

21 A Svar på dette hvis du nå røyker **daglig** eller tidligere har røykt **daglig**:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? ☐ *sigaretter pr. dag*

Hvor gammel var du da du begynte å røyke daglig? ☐ *år gammel*

Hvis du tidligere har røykt daglig, hvor gammel var du da du sluttet? ☐ *år gammel*

21 B Svar på dette hvis du røyker eller har røykt **av og til**, men ikke daglig:

Hvor mange sigaretter røyker eller røykte du vanligvis i måneden? ☐ *sigaretter pr. mnd*

Hvor gammel var du da du begynte å røyke av og til? ☐ *år gammel*

Hvis du tidligere har røykt av og til, hvor gammel var du da du sluttet? ☐ *år gammel*

22 Bruker du, eller har du brukt, snus?

Nei, aldri ☐ Ja, av og til ☐
Ja, men jeg har sluttet ☐ Ja, daglig ☐

Hvis du aldri har brukt snus, hopp til spørsmål 23.

Hvis ja:

Hvor gammel var du da du begynte med snus? ☐ *år gammel*

Hvor mange esker snus bruker/brukte du pr. måned? ☐ *esker snus pr. måned*

Hvis du bruker eller har brukt både sigaretter og snus, hva begynte du med først?

Snus	☐	Sigaretter	☐
Omtrent samtidig (innenfor 3 måneder)	☐	Husker ikke	☐

Da du begynte å bruke snus, var det for å prøve å slutte å røyke eller for å redusere røykinga?

Nei	☐	Ja, for å redusere røykinga	☐
Ja, for å slutte å røyke	☐		

MATVARER

23 Hvor ofte spiser du vanligvis disse matvarene?
(Sett ett kryss pr. linje)

	0-3 ganger pr. mnd	1-3 ganger pr. uke	4-6 ganger pr. uke	1 gang pr. dag	2 ggr el mer pr. dag
Frukt/bær	☐	☐	☐	☐	☐
Grønnsaker	☐	☐	☐	☐	☐
Sjokolade/smågodt	☐	☐	☐	☐	☐
Kokte poteter	☐	☐	☐	☐	☐
Pasta/ris	☐	☐	☐	☐	☐
Pølser/hamburgere	☐	☐	☐	☐	☐
Fet fisk (laks, ørret, sild, makrell, uer som pålegg/middag)	☐	☐	☐	☐	☐

24 Bruker du følgende kosttilskudd?
(Sett ett kryss for hvert kosttilskudd)

	Ja, daglig	Av og til	Nei
Tran	☐	☐	☐
Omega-3-kapsler	☐	☐	☐
Vitamin- og/eller mineraltilskudd	☐	☐	☐

25 Hvor mange glass drikker du vanligvis av følgende?
1/2 liter = 3 glass *(Sett ett kryss pr. linje)*

	Sjelden eller aldri	1-6 gl. pr uke	1 gl. pr. dag	2-3 gl. pr. dag	4 gl. eller mer pr. dag
Vann, farris o.l	☐	☐	☐	☐	☐
Helmelk (søt/sur)	☐	☐	☐	☐	☐
Annen melk (søt/sur)	☐	☐	☐	☐	☐
Brus/saft med sukker	☐	☐	☐	☐	☐
Brus/saft uten sukker	☐	☐	☐	☐	☐
Juice eller nektar	☐	☐	☐	☐	☐

26 Hvor mange kopper kaffe/te drikker du pr. døgn?
(Sett 0 dersom du ikke drikker kaffe/te daglig)

	Kokekaffe	Annen kaffe	Te
Antall kopper			

27 Hvor mange kopper kaffe drikker du om kvelden (etter kl 18)?

Antall kopper ☐

ALKOHOLBRUK

28 Omtrent hvor ofte har du i løpet av de siste 12 måneder drukket alkohol? *(Regn ikke med lettøl)*

4-7 ganger pr. uke	☐	Ca 1 gang pr. måned	☐
2-3 ganger pr. uke	☐	Noen få ganger pr. år	☐
ca 1 gang pr. uke	☐	Ingen ganger siste år	☐
2-3 ganger pr. måned	☐	Aldri drukket alkohol	☐

29 Har du drukket alkohol i løpet av de siste 4 uker?

Ja ☐ Nei ☐

Hvis ja:
Har du drukket så mye at du har kjent deg sterkt beruset (full)?

Nei	☐
Ja, 1-2 ganger	☐
Ja, 3 ganger eller mer	☐

30 Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av 2 uker? *(Regn ikke med lettøl)*
(Sett 0 hvis du ikke drikker alkohol)

	Øl	Vin	Brennevin
Antall glass			

31 Hvor ofte drikker du 5 glass eller mer av øl, vin eller brennevin ved samme anledning?

Aldri	☐	Ukentlig	☐
Månedlig	☐	Daglig	☐

MOSJON/FYSISK AKTIVITET

Med mosjon mener vi at du f.eks går tur, går på ski, svømmer eller driver trening/idrett.

32 Hvor ofte driver du mosjon? *(Ta et gjennomsnitt)*

Aldri	☐
Sjeldnere enn en gang i uka	☐
En gang i uka	☐
2-3 ganger i uka	☐
Omtrent hver dag	☐

33 Dersom du driver slik mosjon, så ofte som en eller flere ganger i uka; hvor hardt mosjonerer du?
(Ta et gjennomsnitt)

Tar det rolig uten å bli andpusten eller svett	☐
Tar det så hardt at jeg blir andpusten og svett	☐
Tar meg nesten helt ut	☐

34 Hvor lenge holder du på hver gang?
(Ta et gjennomsnitt)

Mindre enn 15 minutter	☐	30 minutter – 1 time	☐
15-29 minutter	☐	Mer enn 1 time	☐

35 Har du vanligvis minst 30 minutter fysisk aktivitet daglig på arbeid og/eller i fritida? Ja ☐ Nei ☐

36 Omtrent hvor mange timer sitter du i ro på en vanlig hverdag? *(Regn med både jobb og fritid)* Antall timer ☐

ARBEID

37 Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive arbeidet ditt? *(Sett ett kryss)*

- For det meste stillesittende arbeid *(f.eks skrivebordsarbeid, montering)* ☐
- Arbeid som krever at du går mye *(f.eks ekspeditørarbeid, lett industriarb.,undervisning)* ☐
- Arbeid hvor du går og løfter mye *(f.eks postbud, pleier, bygningsarbeid)* ☐
- Tungt kroppsarbeid *(f.eks skogsarbeid, tungt jordbruksarbeid, tungt bygningsarbeid)* ☐

HØYDE/VEKT

38 Omtrent hva var din høyde da du var 18 år?

☐ cm Husker ikke ☐

39 Omtrent hva var din kroppsvekt da du var 18 år?

☐ kg Husker ikke ☐

40 Er du fornøyd med vekta di nå?

Ja ☐ Nei, for lett ☐ Nei, for tung ☐

41 Har du forsøkt å slanke deg i løpet av de siste 10 år?

Nei ☐ Ja, noen ganger ☐ Ja, mange ganger ☐

42 Er din kroppsvekt minst 2 kg lavere nå enn for 1 år siden? Ja ☐ Nei ☐

Hvis ja:

Hva er grunnen til dette?

Slanking ☐ Sykdom/stress ☐ Vet ikke ☐

ALVORLIGE LIVSHENDELSER SISTE 12 MÅNEDER

43 Har det vært dødsfall i nær familie? *(barn, ektefelle/samboer, søsken eller foreldre)* Ja ☐ Nei ☐

44 Har du vært i overhengende livsfare pga. alvorlig ulykke, katastrofe, voldssituasjon eller krig? Ja ☐ Nei ☐

45 Har du hatt samlivsbrudd i ekteskap eller i lengre samboerforhold? Ja ☐ Nei ☐

46 Hvis du har svart ja på et eller flere av spm 43, 44 eller 45; i hvilken grad har du hatt reaksjoner på dette de siste 7 dager?

- Ikke i det hele tatt ☐
- Litt ☐
- I moderat grad ☐
- I høy grad ☐

OPPVEKST - DA DU VAR 0-18 ÅR

47 Hvem vokste du opp sammen med?

- Mor ☐
- Far ☐
- Stemor/stefar ☐
- Andre slektninger ☐
- Adoptivforeldre ☐
- Foster-/pleieforeldre ☐

48 Ble dine foreldre skilt, eller flyttet de fra hverandre, da du var barn?

- Nei ☐
- Ja, før jeg var 7 år ☐
- Ja, da jeg var 7-18 år ☐

49 Døde noen av dine foreldre da du var barn?

- Nei ☐
- Ja, før jeg var 7 år ☐
- Ja, da jeg var 7-18 år ☐

50 Vokste du opp med kjæledyr?

- Nei ☐
- Ja, katt ☐
- Ja, hest ☐
- Ja, hund ☐
- Ja, annet levende dyr ☐

51 Hvor mye melk eller yoghurt drakk du vanligvis?

Sjelden/ aldri	1-6 gl. pr. uke	1 glass pr. dag	2-3 gl. pr. dag	Mer enn 3 glass pr. dag
☐	☐	☐	☐	☐

52 Vokste du opp på gård med husdyr? Ja ☐ Nei ☐

53 Når du tenker på barndommen/oppveksten din, vil du beskrive den som:

- Svært god ☐
- God ☐
- Middels ☐
- Vanskelig ☐
- Svært vanskelig ☐

ALT I ALT

54 Når du tenker på hvordan du har det for tida, er du stort sett fornøyd med tilværelsen eller er du stort sett misfornøyd? *(Sett ett kryss)*

- Svært fornøyd ☐
- Meget fornøyd ☐
- Ganske fornøyd ☐
- Både/og ☐
- Nokså misfornøyd ☐
- Meget misfornøyd ☐
- Svært misfornøyd ☐

hunt 3
Helseundersøkelsen i Nord-Trøndelag

Kjære HUNT-deltaker

Takk for at du møtte til Helseundersøkelsen. Vi vil også be deg om å fylle ut dette spørreskjemaet. Noen av spørsmålene likner de som du har svart på før, men det er viktig at du allikevel besvarer alt. Opplysningene blir brukt til forskning og forebyggende helsearbeid. Forskere vil kun ha tilgang til avidentifiserte data, det vil si at opplysningene ikke kan spores tilbake til en enkelt person.

Slik fyller du ut skjemaet

Skjemaet vil bli lest maskinelt.

Det er derfor viktig at du krysser av riktig: Rett ☒ Galt

Krysser du feil et sted, retter du ved å fylle boksen slik: ■

Bruk svart eller blå penn. Ikke bruk blyant eller tusj.

Dato for utfylling: ☐☐.☐☐.☐☐☐☐ dd.mm.åååå

Mosjon/fysisk aktivitet

1. Under arbeid (lønnet eller ulønnet) eller vanlige daglige gjøremål- Hvordan vil du beskrive aktivitetsnivået ditt?

- ☐ For det meste stillesittende aktiviteter
- ☐ Aktiviteter som krever at du går mye
- ☐ Aktiviteter hvor du går og løfter mye
- ☐ Tungt kroppsarbeid

Med mosjon mener vi at du f.eks går tur, går på ski, svømmer eller driver trening/idrett.

2. Hvor ofte driver du mosjon? *(ta et gjennomsnitt):*

- ☐ Aldri
- ☐ Sjeldnere enn en gang i uka
- ☐ En gang i uka
- ☐ 2-3 ganger i uka
- ☐ Omtrent hver dag

3. **Hvor lenge holder du på hver gang?** *(ta et gjennomsnitt)*

- ☐ Mindre enn 15 minutter
- ☐ 15-29 minutter
- ☐ 30 minutter – 1 time
- ☐ Mer enn 1 time

4. **På en skala fra 6-20, hvor hard er aktivitetene du vanligvis utfører når du mosjonerer/trener?**

- ☐ 6
- ☐ 7 Meget, meget lett
- ☐ 8
- ☐ 9 Meget lett
- ☐ 10
- ☐ 11 Ganske lett
- ☐ 12
- ☐ 13 Litt anstrengende
- ☐ 14
- ☐ 15 Anstrengende
- ☐ 16
- ☐ 17 Meget anstrengende
- ☐ 18
- ☐ 19 Svært anstrengende
- ☐ 20

Smerte

5. Har du kroppslige smerter <u>nå</u>? ☐ Ja ☐ Nei
Hvis nei, gå til spørsmål 8.

6. Vennligst sett ring rundt det tallet som best angir hvor sterke smerter du har akkurat nå. Skriv tydelig ring rundt tallet: ⑥

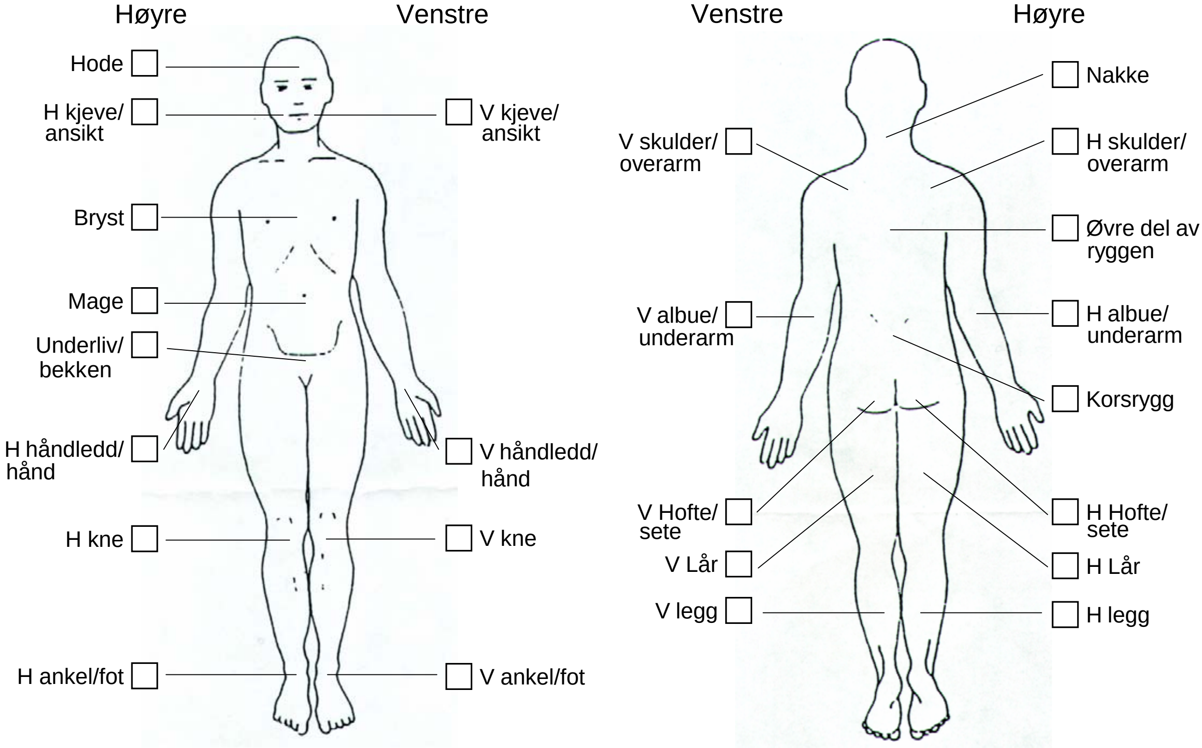
0	1	2	3	4	5	6	7	8	9	10

Ingen smerter — Verst tenkelige smerter

7. Vennligst sett kryss der du har smerte nå. *Du kan krysse av flere steder.*

FORAN — BAK

Høyre — Venstre — Venstre — Høyre



Generell helse

8. Hvordan vil du stort sett vurdere din helsetilstand i løpet av <u>den siste uka</u>?

Utmerket	Meget god	God	Nokså god	Dårlig	Svært dårlig
☐	☐	☐	☐	☐	☐

9. I løpet av <u>den siste uka</u>, i hvilken grad begrenset fysiske helseproblemer dine vanlige fysiske aktiviteter (spasere, gå opp trapper)?

Ikke i det hele tatt	Svært lite	En del	Mye	Kunne ikke utføre fysiske aktiviteter
☐	☐	☐	☐	☐

10. I løpet av <u>den siste uka</u>, hvor vanskelig var det for deg å utføre ditt vanlige arbeid (både i og utenfor hjemmet) på grunn av din fysiske helse?

Ikke i det hele tatt	Litt	Nokså	Meget	Kunne ikke utføre daglig arbeid
☐	☐	☐	☐	☐

11. Hvor sterke kroppslige smerter har du hatt i løpet av <u>den siste uka</u>?

Ingen	Meget svake	Svake	Moderate	Sterke	Meget sterke
☐	☐	☐	☐	☐	☐

12. I løpet av <u>den siste uka</u>, hvor mye overskudd hadde du?

Svært mye	Ganske mye	En del	Litt	Ikke noe
☐	☐	☐	☐	☐

13. I løpet av <u>den siste uka</u>, i hvilken grad begrenset din fysiske helse eller følelsesmessige problemer din vanlige sosiale omgang med familie eller venner?

Ikke i det hele tatt	Svært lite	En del	Mye	Kunne ikke ha sosial omgang
☐	☐	☐	☐	☐

14. I løpet av <u>den siste uka</u>, i hvilken grad har du vært plaget av følelsesmessige problemer (som f. eks. å være engstelig, deprimert eller irritabel)?

Ikke i det hele tatt	Litt	En del	Mye	Svært mye
☐	☐	☐	☐	☐

15. I løpet av <u>den siste uka</u>, i hvilken grad hindret personlige eller følelsesmessige problemer deg fra å utføre ditt vanlige arbeid, skolegang eller andre gjøremål?

Ikke i det hele tatt	Svært lite	En del	Mye	Kunne ikke utføre daglige gjøremål
☐	☐	☐	☐	☐

Vi vil gjerne vite når du fylte ut skjemaet i forhold til kondisjonstesten.

Var det: ☐ Før ☐ Etter ☐ Både før og etter

40101

Kondisprosjektet

hunt 3 Helseundersøkelsen i Nord-Trøndelag

Kode: ☐☐☐☐☐

Dato: ☐☐.☐☐.☐☐☐☐

Personnummmer: ☐☐☐☐☐☐ - ☐☐☐☐☐

☐ Mann ☐ Kvinne Menopause: ☐ Før ☐ Under ☐ Etter Dag i MS-syklus: ☐☐

Hormoner: ☐ Ja ☐ Nei P-piller/spiral: ☐ Ja ☐ Nei

Kommentar: ____________________

Blodtrykk: ☐☐☐ / ☐☐☐ Vekt: ☐☐☐.☐ kg Høyde: ☐☐☐.☐ cm

systolisk diastolisk

Diabetes ☐ Nei ☐ Ja, type ☐ 1 ☐ 2 Midjemål: ☐☐☐.☐ cm

Find-risk ☐☐ Medisiner: ☐ Nei ☐ Ja, hvilke? ____________________

Spørsmål fra lege

Pipende eller tung pust siste 12 mnd, astma, kronisk bronkitt, KOLS eller sarkoidose, hjertesykdom, angina eller medisin mot høyt blodtrykk, hjerneslag/-blødning, kreftsykdom, gravid, blind:... ☐ Nei ☐ Ja, eksl.

Medisinsk kontraindikasjon mot fysisk aktivitet:.................................. ☐ Nei ☐ Ja, eksl.

Klarer du gå i motbakke eller trapper:... ☐ Ja ☐ Nei, eksl.

Info (for legen): ____________________

Fysisk arbeid og fysisk aktivitet

"Hvor mange av de siste 7 dagene har du utført fysisk arbeide eller fysisk aktivitet som varte minst 10 minutter sammenhengende?" ☐ dager

"Hvor lenge holdt du gjennomsnittlig på med slike aktiviteter på de dagene du har nevnt?/Hvor lenge holdt du på med slike aktiviteter denne dagen?" ☐☐ timer ☐☐ min

"Jeg skal nå spørre deg om hvor hardt du har tatt i under aktiviteten eller arbeidet de siste 7 dagene. I den sammenheng har vi delt inn aktiviteten i følgende tidsintervaller: (1) 61 minutter eller mer, (2) 31-60 minutter, (3) 10-30 minutter." La gjennomsnittet bestemme hvilken varighet du spør om først. *"For å beskrive intensiteten bruker vi Borg skala som du ser her.* (Intervjuer peker på Borg skala). *Du kan velge alle tallene. Da spør jeg: Hvor hardt tok du i under aktiviteten/arbeidet ...?"* Spør om alle tidsintervallene.

☐☐ 10-30 minutter ☐☐ 31-60 minutter ☐☐ 61 minutter eller mer

Hvilket tidsintervall har du tilbrakt mest tid i den siste uka? ☐ 10-30 ☐ 31-60 ☐ 61 eller mer

Kondisprosjektet

hunt 3 Helseundersøkelsen i Nord-Trøndelag

Kode: ☐☐☐☐☐

Endotelfunksjon

Stimulans i dag: ☐ Nei ☐ Røyketobakk ☐ Snus/skrå ☐ Alkohol Forrige: ☐☐ timer ☐☐ min

Kaffe: ☐ Nei ☐ Ja, for ☐☐ timer ☐☐ min

Forrige næringsinntak (alt unntatt vann): ☐☐ timer ☐☐ min

Har du trent i dag? ☐ Nei ☐ Ja, for ☐☐ timer ☐☐ min

Medisiner i dag? ☐ Nei ☐ Ja, hvilke? ____________________

Faste medisiner? ☐ Nei ☐ Ja, hvilke? ____________________

Baseline: ☐☐☐ flow ☐.☐☐ diameter ☐☐☐ laveste puls

Post: ☐☐☐ flow(10 sek) ☐.☐☐ diameter(1 min)

Oksygenopptak

	km/t	% stigning	hjertefrekvens	VO2 (L/min)	Borg
Startbelastning:	☐☐.☐	☐☐	☐☐☐	☐.☐☐	☐☐
Trinn 2:	☐☐.☐	☐☐	☐☐☐	☐.☐☐	☐☐
VO2max ☐ / VO2peak ☐:	☐☐.☐	☐☐	☐☐☐	☐.☐☐	☐☐

RER ☐.☐☐ ventilasjon ☐☐☐

Tilbakemelding: VO2max:__________ mL/kg/min Makspuls:__________ slag/min

Kommentar endotel eller VO2:

____

____

____

Ikke gjennomført: ☐ Kondis ☐ Endotel ☐ Spørreskjema

30488

Vi takker for frammøtet til undersøkelsen.

Vi vil også be deg være vennlig å fylle ut dette spørreskjemaet. Opplysninger vil bli brukt i et større forskningsarbeid om forhold som har betydning for helsen.

Svar etter beste skjønn. Kryss av for bare en av svar-mulighetene (dersom det ikke står nevnt noe annet). Det utfylte skjema returneres i vedlagte svarkonvolutt. Porto er betalt.

Alle opplysningene er underlagt streng taushetsplikt.

Med hilsen

Statens skjermbildefotografering
Fylkeslegen ● Helserådet ● Statens Institutt For Folkehelse
Institutt for anvendt sosialvitenskapelig forskning/
Institutt for samfunnsforskning

Til etikett

Navn: ____________________

Adr. : ____________________

____

Postnr. Postkontor

F.nr. : ____________________

MOSJON

Med mosjon mener vi at du f.eks. går tur, går på ski, svømmer eller driver trening/idrett.

Hvor ofte driver du mosjon?
(Ta et gjennomsnitt)

- Aldri .... 12 ☐ 1
- Sjeldnere enn en gang i uka .... ☐ 2
- En gang i uka .... ☐ 3
- 2–3 ganger i uka .... ☐ 4
- Omtrent hver dag .... ☐ 5

Dersom du driver slik mosjon så ofte som en eller flere ganger i uka:
Hvor hardt mosjonerer du?
(Ta et gjennomsnitt)

- Tar det rolig uten å bli andpusten eller svett .... 13 ☐ 1
- Tar det så hardt at jeg blir andpusten og svett .... ☐ 2
- Tar meg nesten helt ut .... ☐ 3

Hvor lenge holder du på hver gang?
(Ta et gjennomsnitt)

- Mindre enn 15 minutter .... 14 ☐ 1
- 16–30 minutter .... ☐ 2
- 30 minutter–1 time .... ☐ 3
- Mer enn 1 time .... ☐ 4

SALT

Hvor ofte bruker du salt kjøtt eller salt fisk/sild til middag?

- Aldri, eller sjeldnere enn en gang i måneden .... 15 ☐ 1
- 1–2 ganger i måneden .... ☐ 2
- Opptil en gang i uka .... ☐ 3
- Opptil to ganger i uka .... ☐ 4
- Mer enn to ganger i uka .... ☐ 5

Hvor ofte pleier du å strø ekstra salt på middagsmaten?

- Sjelden eller aldri .... 16 ☐ 1
- Av og til .... ☐ 2
- Ofte .... ☐ 3
- Alltid eller nesten alltid .... ☐ 4

RØYKEVANER

		JA	NEI
Røyker du daglig for tiden?	17	☐	☐

Hvis du svarte «JA», røyker du DAGLIG for tiden:

		JA	NEI
Sigaretter?	18	☐	☐
Pipe?	19	☐	☐
Sigarer (eller serutter/sigarillos)?	20	☐	☐

		JA	NEI
Hvis du IKKE røyker SIGARETTER daglig for tiden: Har du røykt SIGARETTER daglig tidligere?	21	☐	☐

Hvis du svarte «JA», hvor lenge er det siden du sluttet å røyke sigaretter daglig?

- Mindre enn 3 måneder .... 22 ☐ 1
- 3 måneder– 1 år .... ☐ 2
- 1–5 år .... ☐ 3
- Mer enn 5 år .... ☐ 4

Hvis du røyker SIGARETTER daglig nå, eller har gjort det tidligere:

Hvor mange sigaretter røyker eller røykte du pr. dag? (Oppgi antall pr. dag medregnet håndrullede) .... 23 ____ Antall

Besvares av dem som røyker daglig nå eller har røykt daglig tidligere:
(Gjelder både sigarett-, pipe- og sigar-røykere)

Hvor gammel var du da du begynte å røyke daglig? .... 25 ____ år

Hvor mange år tilsammen har du røykt daglig? 27 ____ år

ALKOHOLBRUK

Hvor ofte har du drukket alkohol (øl, vin eller brennevin) de SISTE 14 DAGENE?

- Jeg har ikke drukket alkohol, men er ikke totalavholdende .... 29 ☐ 1
- Jeg har drukket 1–4 ganger .... ☐ 2
- Jeg har drukket 5–10 ganger .... ☐ 3
- Jeg har drukket mer enn 10 ganger .... ☐ 4
- Jeg er totalavholdende, drikker aldri alkohol .... ☐ 5

		JA	NEI
Dersom du har drukket alkohol de siste 14 dagene, har det ført til at du noen gang har følt deg beruset?	30	☐	☐

Har det vært perioder i livet ditt da du har drukket for mye, eller i hvert fall i meste laget?

- Nei .... 31 ☐ 1
- I tvil, kanskje .... ☐ 2
- Ja .... ☐ 3

BOSITUASJONEN

Bor du alene eller sammen med andre?
Kryss av for de du bor sammen med. (Her kan du sette flere kryss.)

- Bor alene ... 32
- Ektefelle eller samboer ... 33
- Foreldre eller svigerforeldre ... 34
- Andre voksne personer ... 35
- Barn under 5 år ... 36
- Barn 6–15 år ... 37
- Barn over 15 år ... 38

Bor du fast i institusjon?
(sykehjem, aldershjem eller liknende) ... 39 JA / NEI

UTDANNINGEN

Hvilken utdanning har du fullført?
Oppgi bare høyest fullførte utdanning.

- 7-årig folkeskole eller kortere ... 40 — 1
- Framhalds- eller fortsettelsesskole ... 2
- 9-årig grunnskole ... 3
- Real- eller middelskole, grunnskolens 10. år ... 4
- Ett- eller to-årig videregående skole ... 5
- Artium, økonomisk gymnas eller almenfaglig retning i videregående skoler ... 6
- Høyskole eller universitet, mindre enn 4 år ... 7
- Høyskole eller universitet, 4 år eller mer ... 8

Har du fullført annen heldags utdanning, og i tilfelle i hvor mange år?

Skriv antall år her .... 41 år

ARBEID

Hvis du er eller har vært i inntektsgivende arbeid, kan du angi hvilken av disse yrkesgruppene ditt yrke faller innenfor? (Hvis du ikke er i arbeid nå, svarer du ut fra det yrket du hadde sist.)

Hvis du har en ektefelle (eller samboer) som er i inntektsgivende arbeid nå, eller har vært det tidligere, angi tilsvarende hvilken yrkesgruppe han/hun tilhører. (Evt. angi om han/hun *ikke* har hatt inntektsgivende arbeid.)

Deg selv / Ektefellen

- Spesialarbeider, ufaglært arbeider ... 43. 44 — 1
- Fagarbeider, håndverker, formann ... 2
- Underordnet funksjonær (butikk, kontor, offentlige tjenester) ... 3
- Fagfunksjonær (f.eks. sykepleier, tekniker, lærer) ... 4
- Overordnet stilling i offentlig eller privat virksomhet ... 5
- Gårdbruker eller skogeier ... 6
- Fisker ... 7
- Selvstendig i akademisk erverv (f.eks. tannlege, advokat) ... 8
- Selvstendig næringsdrivende (Industi, transport, handel) ... 9
- Har *ikke* hatt inntektsgivende arbeid (f.eks. pga. heltids husarbeid, studier, trygd) ... 0

Hvis du er i arbeid (gjelder også heltids husarbeid), **ber vi deg fylle ut de neste spørsmålene:**

Er arbeidet ditt så fysisk anstrengende at du ofte er sliten i kroppen etter en arbeidsdag?

- Ja, nesten alltid ... 45 — 1
- Ganske ofte ... 2
- Ganske sjelden ... 3
- Aldri, eller nesten aldri ... 4

Krever arbeidet ditt så mye konsentrasjon og oppmerksomhet at du ofte føler deg utslitt etter en arbeidsdag?

- Ja, nesten alltid ... 46 — 1
- Ganske ofte ... 2
- Ganske sjelden ... 3
- Aldri, eller nesten aldri ... 4

Hvordan trives du alt i alt med arbeidet ditt?

- Veldig godt ... 47 — 1
- Ganske godt ... 2
- Godt ... 3
- Ikke særlig godt ... 4
- Dårlig ... 5

Hvis du er gårdbruker eller annen selvstendig næringsdrivende, har du noen ansatte som arbeider fast for deg?

- Ingen fast ansatte ... 48 — 1
- 1–2 fast ansatte ... 2
- 3–10 fast ansatte ... 3
- Mer enn 10 fast ansatte ... 4

HVORDAN HAR DU DET?

Når du tenker på hvordan du har det for tida, er du stort sett fornøyd med tilværelsen, eller er du stort sett misfornøyd?

- Svært fornøyd ... 49 — 1
- Meget fornøyd ... 2
- Nokså fornøyd ... 3
- Både - og ... 4
- Nokså misfornøyd ... 5
- Meget misfornøyd ... 6
- Svært misfornøyd ... 7

Føler du deg stort sett sterk og opplagt, eller trett og sliten?

- Meget sterk og opplagt ... 50 — 1
- Sterk og opplagt ... 2
- Ganske sterk og opplagt ... 3
- Både - og ... 4
- Ganske trett og sliten ... 5
- Trett og sliten ... 6
- Svært trett og sliten ... 7

MEDISIN/PLAGER

Har du vanligvis:

		JA	NEI
Hoste om morgenen?	51		
Oppspytt fra brystet om morgenen?	52		

Hvor ofte har du brukt smertestillende medisin den siste måneden?

- Daglig ... 53 — 1
- Hver uke, men ikke hver dag ... 2
- Sjeldnere enn hver uke ... 3
- Aldri ... 4

Hvor ofte har du brukt avslappende/beroligende medisin eller sovemedisin den siste måneden?

- Daglig ... 54 — 1
- Hver uke, men ikke hver dag ... 2
- Sjeldnere enn hver uke ... 3
- Aldri ... 4

Har du i løpet av siste måned vært plaget av nervøsitet (irritabel, urolig, anspent eller rastløs)**?**

- Nesten hele tida ... 55 — 1
- Ofte ... 2
- Av og til ... 3
- Aldri ... 4

Har du i løpet av siste måned hatt innsoving- eller søvnproblemer?

- Nesten hver natt ... 56 — 1
- Ofte ... 2
- Av og til ... 3
- Aldri ... 4

Har du i det store og hele en rolig og god følelse inne i deg?

- Nesten hele tida ... 57 — 1
- Ofte ... 2
- Av og til ... 3
- Aldri ... 4

VENNER/HJELP

Dersom du ble syk og måtte holde senga i lengre tid, hvor sannsynlig tror du det er at du kunne få nødvendig hjelp og støtte av familie, venner eller naboer?

- Svært sannsynlig ... 58 — 1
- Nokså sannsynlig ... 2
- Usikkert ... 3
- Usannsynlig ... 4
- Helt usannsynlig ... 5

Hender det ofte at du føler deg ensom?

- Meget ofte ... 59 — 1
- Ofte ... 2
- Av og til ... 3
- Meget sjelden ... 4
- Aldri ... 5

HVORDAN ER DU?

Har du tendens til å ta dine oppgaver mer alvorlig enn folk flest?

- Ja, nettopp slik er jeg ... 60 — 1
- Ja, stort sett ... 2
- Både - og ... 3
- Nei, stort sett ikke ... 4
- Nei, tvert imot ... 5

		JA	NEI	VET IKKE
Har du i løpet av det siste året ofte følt at du har presset deg, eller stadig drevet deg selv framover?	61			

Føler du deg alltid under tidspress, også når det gjelder daglige gjøremål?

- Alltid, eller nesten alltid ... 62 — 1
- Noen ganger ... 2
- Aldri ... 3

Er du vanligvis glad eller nedstemt?

- Svært nedstemt ... 63 — 1
- Nedstemt ... 2
- Nokså nedstemt ... 3
- Både - og ... 4
- Nokså glad ... 5
- Glad ... 6
- Svært glad ... 7

HVA ER VIKTIG?

Synes du det er viktig at man prøver å være fornøyd med det man har?

- Dette er særlig viktig ... 64 — 1
- Dette er viktig ... 2
- Både - og ... 3
- Dette er mindre viktig ... 4
- Dette er overhodet ikke viktig ... 5

Synes du det er viktig at man kan slå av på kravene?

- Dette er særlig viktig ... 65 — 1
- Dette er viktig ... 2
- Både - og ... 3
- Dette er mindre viktig ... 4
- Dette er overhodet ikke viktig ... 5

Synes du det er viktig at man alltid er i godt humør?

- Dette er særlig viktig ... 66 — 1
- Dette er viktig ... 2
- Både - og ... 3
- Dette er mindre viktig ... 4
- Dette er overhodet ikke viktig ... 5

Tusen takk for den hjelp du har gitt oss ved å fylle ut dette skjema.

TILLEGGS-SKJEMA OM BLODTRYKK

På skjemaet du leverte ved helseundersøkelsen, svarte du at du har, eller har brukt, medisin for høyt blodtrykk.

I Nord-Trøndelag har det siden 1980 pågått en undersøkelse om blodtrykksbehandling. Formålet ved undersøkelsen er å gjøre behandlingen bedre. En viktig del av undersøkelsen er å få opplysninger om hvordan du og alle andre med høyt blodtrykk har det, og hvilke erfaringer dere har gjort.

Det er derfor meget viktig at du fyller ut dette skjemaet så nøye som mulig.

Enkelte spørsmål kan være vanskelig å svare på. Prøv likevel å svare etter beste skjønn, og legg vekt på det som er vanlig eller gjennomsnittlig for deg.

Alle opplysninger blir behandlet av oss med streng taushetsplikt.

På forhånd takk!

Når ble det påvist at du hadde høyt blodtrykk første gang? (Skriv årstallet i ruta)

19

Vet ikke ... 67

Hvor ble det påvist?
(Sett kryss i bare *en* av rutene)

- Hos almenpraktiserende lege (distriktslege, privatpraktiserende lege, turnuskandidat) .... 69 — 1
- Hos militærlege 2
- På sykehus 3
- Vet ikke 4

JA | NEI

Bruker du medisin for blodtrykk nå? 70
Hvis «NEI»: Gå til de to siste spm. nederst til venstre.

Hvis «JA»: Når begynte du med medisiner for blodtrykket? (Skriv årstallet i ruta)

19

Vet ikke ... 71

JA | NEI

Bruker du doserings-eske for tabletter? 220

Har du medisinkort som viser hva slags medisin du skal ta? 221

Hender det at du glemmer å ta medisinene?
(Sett kryss i bare *en* av rutene)

- Aldri .... 73 — 1
- Sjelden (ca. en gang i mnd.) 2
- Oftere 3

Hvor viktig mener du at det er for deg at du tar blodtrykksmedisinen(e) akkurat som foreskrevet?
(Sett kryss i bare *en* av rutene)

- Ikke så viktig .... 74 — 1
- Viktig 2
- Meget viktig 3

Vet du hva blodtrykket ditt var ved siste kontroll?
(Sett kryss i bare *en* rute)

- Nei .... 75 — 1
- Ja 2
- Usikker 3

Hvis «JA» eller «USIKKER», skriv hvor mye du tror det var: 76

Ikke skriv her

Skriv her ________ 79

Hvis du har brukt medisin for blodtrykket før, men ikke nå: Når slutta du med medisiner?
(Skriv årstallet i ruta)

19

Vet ikke ... 82

Hvorfor slutta du med medisinene?
(Sett ett eller flere kryss)

- Legen bestemte det 84
- Jeg fikk plager av medisinene 85
- Jeg mente det ikke var nødvendig med medisiner 86
- Jeg var redd medisinene var skadelige 87
- Annen årsak (skriv hvilken nedenfor) 88

Ikke skriv her

________ 89
Skriv hvilken årsak det evt. var

Har legen gitt deg andre råd i forbindelse med at du har for høyt blodtrykk?
(Sett kryss i bare *en* av rutene)

- Nei .... 91 — 1
- Ja 2
- Husker ikke 3

Hvis «JA»; Hvilke råd?

________ 92

Ikke skriv her

________ 94

Hvordan opplever du behandlingen for blodtrykket? Gir det deg:
(Sett ett eller flere kryss)

- Lettelse, ro, trygghet 96
- Anspenthet, engstelse, redsel, uro 97
- Dårlig humør, depresjon 98
- Ingen spesielle følelser 99

Synes du at det er noen ulemper ved det at du må ha behandling for høyt blodtrykk?

- Nei, ingen ulemper 100
- Ja ....

Hvis «JA»: Hva synes du er mest plagsomt?
(Sett ett eller flere kryss)

- At du må bruke medisiner hver dag 101
- At du må gå til legekontroll 102
- At du må følge de råd som legen har gitt 103
- At du har ubehag av medisinene 104
- At du er engstelig for at det er noe alvorlig som feiler deg 105
- At du synes det er leit å bli betraktet som «pasient» 106
- Annet 107

TILLEGGS-SKJEMA FOR SUKKERSYKE

Du har opplyst at du har sukkersyke. Et viktig mål for helseundersøkelsen er å finne ut hvordan sukkersyke best kan behandles for å gi minst mulig plager.

Alle som har eller har hatt sukkersyke, bes derfor om å svare så godt som mulig på disse spørsmålene om sukkersyke.

Noen har svart på et lignende skjema høsten 1982. Det er likevel av stor betydning at disse fyller ut dette skjemaet.

Alle opplysninger blir behandlet av oss med streng taushetsplikt.

På forhånd takk!

Når ble sukkersyken din oppdaget? ... 19 108
(Skriv årstallet i ruta)

Hvordan ble sukkersyken din oppdaget?

- Jeg søkte lege på grunn av symptomer .... 110 ☐ 1
- Ble oppdaget uten at jeg hadde symptomer (ved legeattest, bedriftskontroll, undersøkelse for annen sykdom i eller utenfor sykehus) .... ☐ 2

Hva slags plager hadde du i tilfelle da sukkersyken ble oppdaget? (kryss evt. i flere ruter).

- Ingen plager .... 111 ☐
- Unormal tørste .... 112 ☐
- Stor vannlating .... 113 ☐
- Slapphet .... 114 ☐
- Vekttap .... 115 ☐
- Underlivskløe .... 116 ☐
- Andre plager .... 117 ☐

Hvis «ANDRE PLAGER», skriv hvilke:

________________ 118 Ikke skriv her

________________ 120

JA | NEI

Har noen av dine foreldre, søsken eller barn hatt sukkersyke? 122

Hvis «JA», bruker eller brukte noen av disse insulinsprøyter? 123

BEHANDLING

JA | NEI

Bruker du insulinsprøyter mot sukkersyken? 124

Hvis «JA», bruker du sprøyter daglig?

- Sprøyte en gang daglig .... 125 ☐ 1
- Sprøyte to eller flere ganger daglig .... ☐ 2

Om du bruker sprøyter, hvor mye insulin tar du tilsammen hver dag?
(Skriv antall ml i ruta – 1 «strek» svarer til 0,1 ml) .... 126 ☐, ☐ ml

Om du bruker sprøyter, hva heter den insulinen du bruker?
(Skriv navnet som står på glasset, begge dersom du bruker to sorter).

________________ 128 Ikke skriv her

________________ 130

JA | NEI

Bruker du tabletter mot sukkersyken? 132

Om du bruker tabletter mot sukkersyken, skriv nedenfor hva de heter, antall mg. som står på glasset/pakningen og hvor mange slike tabletter du tar hver dag:
(Skriv om begge sorter dersom du bruker mer enn en type tabletter mot sukkersyke)

Skriv navn på tabletten her	133 mg. pr. tabl.	138 antall pr. dag	
________________	☐,	☐	139

Skriv navn på tabletten her	140 mg. pr. tabl.	145 antall pr. dag	
________________	☐,	☐	146

Ikke skriv her

Hvor mange måltider spiser du hver dag? .... 147 Antall

JA | NEI

Føler du at du vet nok om hva slags mat du kan spise? 148

Hvis du skal svare på hva du virkelig spiser, og ikke hva legen din har sagt du bør spise, vil du da si at du: (Kryss av bare i den ruta som kommer nærmest det du virkelig gjør)

- Spiser stort sett det samme som de som ikke har sukkersyke .... 149 ☐ 1
- Spiser hva jeg vil unntatt sukker og søtsaker .... ☐ 2
- Bruker på øyemål bestemt mengde brød, potet, melk og frukt .... ☐ 3
- Veier/måler bestemt mengde brød, potet, melk og evt. frukt en eller flere dager i uka .... ☐ 4

JA | NEI

Kontrollerer du hjemme hvor mye sukker du har i urinen? (Kryss av også om noen hjelper deg eller gjør det for deg) 150

Hva heter den metoden du i tilfelle bruker til å måle sukker i urinen?

________________ 151 Ikke skriv her
Skriv navnet som står på pakningen her

JA | NEI

Kontrollerer du noen gang hjemme hvor mye sukker du har i blod (blodsukker)?
(Kryss av også om noen hjelper deg eller gjør det for deg) 152

Hva heter den metoden du i tilfelle bruker til å måle blodsukker?

________________ 153 Ikke skriv her
Skriv navnet på pakningen og navn på evt. apparat du måler med.

Hvis du selv kontrollerer sukker i urin eller blod, hvor ofte gjør du det?
(Kryss av også om noen hjelper deg eller gjør det for deg)

- Hver dag .... 154 ☐ 1
- 2-3 dager i uka .... ☐ 2
- En dag i uka .... ☐ 3
- En dag hver 14. dag .... ☐ 4
- En dag i måneden .... ☐ 5
- Sjeldnere enn en dag i måneden .... ☐ 6

VEND!

Hvis du selv kontrollerer sukker i urin eller blod: måler du flere ganger om dagen de dagene du gjør det? .... 155 JA / NEI

Dersom du tar urin- eller blodprøve selv, tar du resultatene med til legen ved kontroll?
(kryss av i den ruta som passer best)

- Aldri............ 156 — 1
- Av og til............ 2
- Oftest............ 3
- Alltid............ 4

Går du til regelmessig kontroll hos lege for sukkersyken din?............ 157 JA / NEI

Hvis «JA», hvor lenge var det mellom de to siste gangene du var hos legen din til kontroll for sukkersyken?

Antall måneder (skriv i ruta).... 158 mndr.

Hva slags lege går du til kontroll hos for sukkersyken?
(Sett kryss i bare *en* rute)

- Vanlig lege (distriktslege, almenpraktiserende lege, bedriftslege osv.)............ 160 — 1
- Sykehuslege (poliklinikk på sykehus)............ 2
- Er innlagt i sykehjem eller annen institusjon og får kontroll der............ 3
- Andre............ 4

Ikke skriv her

Hvis «andre», skriv hva slags lege på linja over 161

ANNEN SYKDOM

Bruker du regelmessig medisin for annet enn sukkersyken?............ 162 JA / NEI

Dersom «JA», skriv hva disse medisinene heter
(Skriv det navnet som står på glasset eller pakningen. Ta med alle sortene du bruker regelmessig. Skriv x bak navnet om du brukte dette også *før* du fikk sukkersyke).

Ikke skriv her

163
166
169
172
175
178
181

Tror du man er mer utsatt for å få enkelte andre sykdommer dersom man har dårlig kontrollert sukkersyke? .... 184 JA / NEI

Hvis «JA», nevn navnet på 3 slike sykdommer:
(Du behøver ikke å ha hatt disse sykdommene selv).

Ikke skriv her

185
187
189

Har du selv hatt noen vedvarende (kroniske) plager etter at du fikk sukkersyke?
(Skriv hva slags sykdom/plager på linjene under).

Ikke skriv her

191
193
195
197
199
201

UNDERVISNING - STØTTE

	JA	NEI
Er du medlem av Norges Landsforbund for Sukkersyke? 203		
Har du noen gang deltatt på kurs eller møte om sukkersyke? 204		
Får du grunnstønad gjennom trygdekontoret for sukkersyken? 205		
Har du søkt om og fått særfradrag i skattelikninga fordi du har sukkersyke? 206		

HVORDAN HAR DU DET?

Synes du det er vanskelig å ha sukkersyke?
(kryss av i den ruta som passer best).

- Ja, jeg føler det er som en plage hver dag .... 207 — 1
- Ja, jeg tenker ofte på det............ 2
- Ja, av og til 3
- Nei, sjelden............ 4
- Nei, jeg tenker nesten aldri på det 5
- Føler meg akkurat som alle som ikke har sukkersyke .. 6

Dersom du synes det er vanskelig å ha sukkersyke, hva synes du er verst?
(Skriv det du mener på linja nedenfor).

Ikke skriv her

Skriv her

Forteller du til andre at du har sukkersyke?
(kryss av i den ruta som passer best).

- Ja, alltid når jeg mener de bør vite det............ 210 — 1
- Ja, men bare om de spør............ 2
- Nei, helst ikke............ 3
- Jeg er redd for at andre skal få greie på det 4

Har du noen gang hatt for lavt blodsukker?
(«føling», «insulinsjokk») .... 211 JA / NEI

Hvis «JA», hvor mange ganger har du hatt det den siste uka? (Skriv antall ganger i ruta)............ 212

Hvor mange ganger har du vært innlagt i sykehus de siste 5 årene? (Skriv antall ganger i ruta)...... 213

Dersom du har ligget i sykehus de siste 5 årene, hva har du ligget der for?
(Skriv på linjene nedenfor)

Ikke skriv her

214
216
218