ISM skriftserie Nr. 101

Explaining risk reductions in medical practice: Prevention or postponement?

Ph.D. Thesis
Peder Andreas Halvorsen, MD, GP *2008*

THE RESEARCH UNIT
FOR GENERAL PRACTICE
Odense

Faculty of Health Sciences
University of Southern Denmark
2008

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ISBN 13: 978 - 82 - 90263 - 13 - 8
2008

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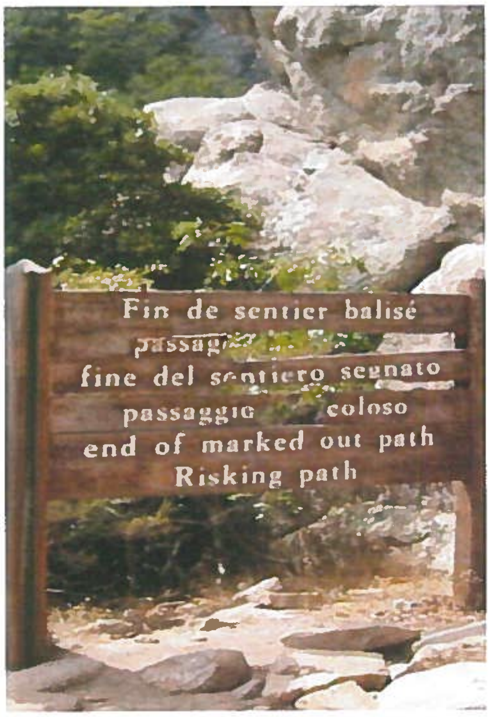

Ph.D. Thesis

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1. PREFACE AND ACKNOWLEDGMENTS

This thesis encompasses four scientific papers about risk communication in the context of preventive medicine. Apart from the fact that dealing with risk has been a daily task in my work as a general practitioner for a decade, I may not be able to explain the exact origins of this project. As for many other endeavours in my life, I am not sure why, or even if, I wanted to do it in the first place. Inspiration and motivation gradually emerged as the project evolved.

Dealing with risks involves decision making under uncertainty. Therefore, as this project commenced, I was quickly drawn to the Society for Medical Decision Making (SMDM), an international network for scientists with a special interest in decision related issues such as clinical decision analysis, decision psychology and risk communication. The opportunity to learn state of the art methodology in a friendly and supportive environment is probably the reason why many of its members speak of the SMDM as their intellectual home. All papers of this thesis have been presented and discussed at the annual meetings of SMDM, which has been a most rewarding experience. Going to these meetings has become a habit that I don't want to give up.

One of the members of SMDM is Ivar Sønbø Kristiansen, my scientific mentor and the main supervisor of this project. I first met him as a medical student at the University of Tromsø in the 1990ies, where he accepted to supervise a cost minimisation study of teleradiology in primary health care. At the time I didn't know that this was going to be a cost minimisation study and not much else about research either. Nevertheless, with his help the project was quite successful, and since then he has made most enjoyable efforts to keep me on track. Apart from his enduring supervision, I also acknowledge that he always seemed to understand and respect the time constraints and priorities of general practice. Without this approach to mentoring, I am not sure that I would have been able to enjoy general practice and research concomitantly for so many years. For his contributions I am very grateful.

Leaving Tromsø in 1995, Ivar made his southbound journey, eventually finding himself at the University of Southern Denmark in Odense. He was quickly surrounded by a network of researchers who took the name Odense Risk Group. Being a long distance member of this multidisciplinary group has been a privilege. Their generous sharing of knowledge and research ideas was pivotal to the works presented in this thesis. Dorte Gyrd-Hansen and Jørgen Nexøe were co-supervisors, whereas Arthur Elstein served as a co-mentor involving me in the Society for Medical Decision Making and the fascinating world of decision psychology. Their thoughtful comments and support are highly appreciated. Also, working with statisticians such as Henrik Støvring and Torbjørn Wisløff has been a pleasure.

Apart from the pivotal role of Odense Risk Group, I would like to acknowledge the collaboration and support from co-authors Randi Selmer, Olaf Gjerløw Aasland and Olav Helge Førde. Other supportive environments include the National Centre of Rural Medicine in Tromsø and the Nordic Risk Group. My fellow GPs in Alta made generous allowance for the time and effort I have allocated to this project. I realise that when I was not available, important tasks had to be taken care of by others. Last, but not least, this pertains to my closest family, *i.e.* my parents, my wife and my children. Their contribution was perhaps less visible, but certainly of utmost significance.

Financial support

The studies of this thesis were carried out during appointments with the Research Unit for General Practice in Odense and the Institute of Public Health, University of Southern Denmark from 2005 to 2008 funded by external grants. I am grateful for the generous contributions from the National Centre of Rural Medicine (Nasjonalt Senter for Distriktsmedisin), University of Tromsø, Norway. I also would like to thank Northern Norway Regional Health Authority (Helse Nord RHF), Finnmark Health Authority (Helse Finnmark HF), the Nowegian Medical Association (Den norske legeforening) and the municipality of Alta (Alta kommune) for research grants and other financial support.

2. SUMMARY

Background and aims: Diagnosis, treatment and follow up of risk conditions such as hypercholesterolemia and osteoporosis are prominent tasks of contemporary medical practice. The aim is to prevent, or at least postpone the onset of adverse health outcomes such as angina pectoris, heart attacks, strokes and fractures. Dealing with risks involves decision making under uncertainty. For patients to be able to engage meaningfully in shared decision making, benefits of risk reducing interventions must be communicated in easily comprehensible ways. From randomised controlled trials effectiveness of such interventions may be estimated and conveyed in traditional formats such as relative risk reduction, absolute risk reduction or number needed to treat (NNT). Alternatively, to account for the time dimension, prolongation of (disease free) life or, equivalently, postponement of adverse events may be used. There is ample evidence that the different formats for risk reductions yield different decisions, *i.e.* framing effects. The most consistent finding is that decision makers are more inclined to accept interventions when risk reductions are explained in relative rather than absolute terms. To some extent decisions on hypothetical drug therapies by NNT and postponement of adverse outcomes have been studied empirically. It appears that lay people are insensitive to effect size in terms of NNT but sensitive to the length of postponement. The aim of this Ph. D. study was to explore how physicians and lay people understand and respond to the concepts of NNT and postponement when making decisions about risk reducing interventions against cardiovascular diseases and osteoporosis. The thesis encompasses four scientific papers covering the following research questions:

- When considering risk reducing drug therapies, are lay people sensitive to effect size in terms of NNT for different diseases, treatment costs and interpretations of NNT?
- Are medical doctors sensitive to the magnitude of NNT when they consider recommending a cardioprotective drug therapy?
- Are lay people affected by personal risk information when considering how long they expect to live?
- Do lay people respond differently when risk reductions are explained in terms of NNT rather than postponement of adverse events?

Materials and methods: Attendees to a health study (n=2754), medical doctors (n=1616) and a sample of the general population (n=2000) were approached in three different surveys,

which shared a common design: Respondents were presented with hypothetical clinical scenarios or vignettes regarding long term preventive drug therapies. Important aspects of the therapies, in particular effect measures such as NNT or postponement of adverse outcomes, were varied across the scenarios. The respondents were randomly allocated to one version of the scenario and asked about their preferences for the intervention. Differences in responses to the different scenarios were analyzed using statistical methods as appropriate. In the fourth project a subset of the attendees to the health study (n=1748) were asked a simple question about their anticipated longevity; did they expect to live shorter, longer or about as long as the mean for Norwegians? Differences in anticipated longevity between respondents with high and low cardiovascular risk respectively, were analyzed.

Results: When lay people considered risk reducing drug therapies, the proportion consenting to therapy was fairly constant over a broad range of NNTs (50 to 1600). This pattern was consistent across different diseases to be prevented, different treatment costs and different interpretations of NNT. Among medical doctors the proportion recommending a cardioprotective drug therapy dropped by 20% when NNT increased from 50 to 200. Furthermore, lay people were more inclined to accept drug therapies explained as preventing interventions in terms of NNT compared to drugs conceptualized as postponing interventions. For example, in the context of heart attack prevention, 93% consented when informed in terms of NNT, 82% consented when informed in terms of a long postponement (8 months) of heart attack for one out of four of patients, whereas 69% consented when informed in terms of a short postponement (2 months) for all patients. Finally, lay people's anticipated longevity was moderately associated with personal cardiovascular risk information; odds ratio for high risk *versus* low risk individuals was 2.4 (95% CI 1.7 – 3.3) per level of anticipated longevity (shorter, about as long as, and longer than the mean, respectively).

Conclusion and implications: The major finding of this project was that lay people were more inclined to accept prophylactic drug therapies when risk reductions were explained in terms of number needed to treat to prevent one unfavourable outcome rather than postponement of adverse events. Second, it was confirmed that lay people are insensitive to the magnitude of NNT in complex decisions. Medical doctors, on the other hand, were sensitive to effect size in terms of NNT. Finally, there was a statistically significant but modest association between personal risk information and anticipated longevity. For clinical practice implications are that NNT as well as postponement should be used with caution when explaining risk reductions to patients, but that NNT may be suitable for communication between medical doctors. For further research the findings pose questions about how NNT and postponement would affect real life decisions. Second, if effect size does not really matter, what goals are important and what do patients expect to achieve when considering a risk reducing drug therapy? Finally, whether the link between personal risk information and anticipated longevity is emotional or cognitive in nature might be explored.

3. RESUMÉ (DANISH SUMMARY)

Baggrund og målsætning: Diagnose, behandling og opfølgning af risikotilstande som højt kolesterol og osteoporose er en central opgave i medicinsk praksis. Målet er at forhindre, eller i det mindste udskyde sygdom og skade som fx angina pectoris, blodprop i hjertet, apoplexi eller frakturer. Risikohåndtering indebærer at tage beslutninger under usikkerhed. Hvis patienterne skal involveres i beslutningsprocessen på en meningsfuld måde, kræves det, at gevinster af risikoreducerende interventioner kan forklares på forståelig vis. Gevinster af sådanne interventioner kan estimeres i randomiserede kontrollerede studier og formidles ved hjælp af traditionelle effektmål som relativ risikoreduktion, absolut risikoreduktion eller "number needed to treat" (NNT). For at tage højde for tidsdimensionen kan man alternativt anvende (sygdomsfri) overlevelse eller udskydelse af tidspunkt for indtræffen af uønskede udfald.

Der er solid dokumentation for, at forskellige effektmål for risikoreduktion medfører forskellige beslutninger. Det mest konsistente fund er, at beslutningstagere er mere tilbøjelige til at acceptere interventioner, når risikoreduktionen beskrives i relative termer frem for absolutte termer. Lægpersoners reaktioner på NNT og udskydelse af uønskede udfald er i nogen grad undersøgt i sammenhæng med risikoreducerende lægemidler. Når sådanne interventioner overvejes, viser undersøgelserne, at lægpersoner er insensitive for effektstørrelser forklaret som NNT, men sensitive for effektstørrelser formidlet som udskydelse af tidspunkt for indtræffen af uønsket udfald.

Hovedformålet med dette ph.d.- studie var at udforske nærmere, hvordan læger og lægfolk opfatter og reagerer på NNT og udskydelser i tid, når de overvejer interventioner mod kardiovaskulære sygdomme og osteoporose. Afhandlingen omfatter fire videnskabelige artikler, som belyser følgende problemstillinger:

- Er lægpersoner sensitive for størrelsen af NNT ved forskellige sygdomme, medicinudgifter og forskellige fortolkninger af NNT, når brug af risikoreducerende lægemidler overvejes?
- Er læger sensitive for størrelsen på NNT, når de overvejer at anbefale patienter lægemidler mhp. forebyggelse af kardiovaskulær sygdom?

- Bliver lægpersoner påvirket af personlig risikoinformation, når de vurderer, hvor længe de forventer at leve?
- Reagerer lægfolk forskelligt, når risikoreduktioner forklares ved hjælp af NNT sammenlignet med udskydelse af tidspunkt for indtræffen af uønskede udfald?

Materiale og metode: Deltagere i en helbredsundersøgelse (n=2754), læger (n=1616) og et repræsentativt udsnit af befolkningen (n=2000) blev inviteret til at deltage i tre spørgeundersøgelser med fælles design: Respondenterne fik information om hypotetiske forebyggende lægemidler til lang tids brug gennem kliniske scenarier eller vignetter. Vigtige attributter ved lægemidlene varierede i scenarierne, herunder effektmål som NNT og længde af udskydelse af uønskede hændelser. Respondenterne blev tilfældigt fordelt på forskellige versioner af scenariet og spurgt om præferencer for eller imod interventionen. Forskelle i respons på de forskellige scenarier blev analyseret ved hjælp af statistiske metoder. I det fjerde arbejde fik et udsnit af deltagerne i helbredsundersøgelsen (n=1748) et simpelt spørgsmål om forventet levealder: Forventede de at leve kortere, længere eller omtrent lige så længe som gennemsnittet for nordmænd? Forskelle mellem individer med høj og lav risiko for kardiovaskulære sygdomme blev analyseret.

Resultater: Når lægpersoner vurderede risikoreducerende lægemidler, var andelen som angav at ville acceptere behandlingen praktisk talt konstant over et bredt interval af værdier for NNT (50 – 1600). Dette mønster var konsistent for forskellige sygdomme, behandlingsudgifter og fortolkninger af NNT. Blandt læger faldt andelen, som ville anbefale et hjertebeskyttende medikament med 20% når NNT steg fra 50 til 200. Desuden var lægpersoner mere tilbøjelige til at acceptere lægemidler, når de blev fremstillet som *forebyggende* interventioner ved hjælp af NNT sammenlignet med *udskydende* interventioner. For eksempel var andelen, der accepterede et medikament til forebyggelse af blodprop i hjertet 93% når effekten blev forklaret ved hjælp af NNT, 82% når effekten blev fremstillet som en længere udskydelse (8 måneder) af tidspunkt for indtræffen af blodprop i hjertet for en af fire patienter, og 69% når effekten blev fremstillet som en kortvarig udskydelse (2 måneder) for alle patienter. Endelig var der en moderat association mellem lægfolks forventning om egen levealder og personlig information om kardiovaskulær risiko. Odds ratio for individer med høj versus lav risiko var 2.4 (95% CI 1.7 – 3.3) per kategori af subjektivt forventet levealder (kortere, omtrent lige længe eller længere end gennemsnittet).

Konklusion og implikationer: Det vigtigste fund i dette studie var, at lægpersoner var mere tilbøjelige til at acceptere profylaktiske lægemidler, når mulig risikoreduktion blev forklaret som "number needed to treat" for at forhindre et uønsket udfald sammenlignet med udskydelse i tid af uønskede udfald. Dernæst blev det bekræftet, at lægpersoner i forbindelse med komplekse beslutninger var insensitive for størrelsen på NNT. Læger var derimod sensitive for størrelsen på NNT. Endelig var der en statistisk signifikant men beskeden association mellem personlig risikoinformation og subjektivt forventet levealder. Resultaterne tyder på, at NNT så vel som udskydelse af uønskede hændelser bør anvendes med forsigtighed i patientsamtaler om risikoreduktion. NNT kan være bedre egnet til kommunikation mellem læger indbyrdes. Resultaterne giver anledning til at udforske hvorledes NNT og udskydelse af uønskede hændelser påvirker reelle beslutninger i klinisk praksis. Hvis effektstørrelser ikke er så vigtige for patienterne, som vi tror, hvilke mål er så væsentlige? Hvad forventer de at opnå gennem risikoreducerende interventioner? Endelig kan det være af interesse yderligere at undersøge om sammenhængen mellem personlig risikoinformation og subjektivt forventet levealder er af kognitiv eller emotionel natur.

4. INTRODUCTION

Would you consent to a drug therapy that 13 people would have to take every day to observe one less heart attack after five years of treatment? What about a drug that on average postpones the onset of heart attacks by two months if taken daily for five years? What if I told you that these are equivalent descriptions of the same drug – would you believe it? People's considerations about this kind of questions are main issues of this thesis.

Chronic diseases such as cancer and cardiovascular diseases, account for more than 60% of all mortality in Norway[1] and for a substantial burden of morbidity as well. Prevention of chronic diseases has been a major issue in medical research for decades, and there is ample evidence that interventions such as life style changes and drugs[2;3] may have benefits. At the societal level health authorities engage in campaigns to quit smoking, promotion of exercise and healthy food and setting priorities for reimbursement of risk reducing drugs. In medical practice much time is devoted to identification, medical treatment and follow up of individuals with symptom-free risk-conditions like hyperlipidemia, mild hypertension and osteoporosis.

Disease prevention and the concept of risk are closely connected. Dealing with risks involves decision making under uncertainty. For example doctors and their patients must decide whether to assess risks and - whenever a high risk condition is diagnosed – whether and how to intervene. Whatever they decide, however, the fate of the individual cannot be predicted for sure. According to Bernstein the mastery of risk is as a hallmark of modern societies,[4] and the risk concept is especially prominent in economics and health care. Being rooted in the Hindu-Arabic numbering system,[4] the modern concept of risk is a numerical one. In epidemiology risk means the probability of an undesirable event. More broadly risk may be defined as "a situation or an event where something of human value (including humans themselves) is at stake and where the outcome is uncertain".[5] In this thesis the epidemiologic risk definition is adopted.

The word "risk" stems from the Italian *risicare,* which means "to dare".[4] It is indicative of action and presupposes freedom to make choices. For patients to pursue this freedom in the context of disease prevention, two things may be important: Adequate information and support from a trusted other. These may be thought of as core elements of *shared decision making* in medicine. Although researchers may disagree about the exact definition,[6] shared decision making usually implies that doctors and patients share information, reach a joint decision based on that information and share the responsibility for the decision that is made.[6] In the context of disease prevention, the doctor's contribution typically would include information about risks, management options and possible outcomes. Patients, on the other hand, are expected to share information about values, preferences and goals they might wish to pursue when considering the management options. To build trust and facilitate shared decision making, doctors may need methods for explaining risks and outcomes of interventions in easily comprehensible ways.[7] For patients the rewards of effective risk communication include enhanced knowledge, better involvement in decisions, autonomy and empowerment.[8]

Several studies suggest that patient's preferred role in medical decision making is highly variable.[9-13] Furthermore, there is limited evidence regarding what goals patients and doctors want to pursue in context of disease prevention. It is often assumed, though, that people want to maximize quality and length of life. Expected utility theory[14] is a normative theory that prescribes how people should make decisions in order to maximize desirable outcomes such as quality adjusted life years.[15] A recent study indicates that people may hold life goals that do not fit well into quality adjusted life year models, but nevertheless may influence medical decisions.[16] Others claim that people do not,[17;18] or even should not,[19] aim for optimal decisions in terms of expected utility maximisation. Nevertheless, expected utility theory is a compelling normative basis for medical decisions. According to this theory, to arrive at optimal decisions, only two kinds of information are crucial: Probabilities of relevant outcomes and valuations (utilities) of these outcomes. It follows that in dealing with risks, doctors and patients need to evaluate probabilities of outcomes and integrate this information with values and preferences. Hopefully, open exchange of information and opinion about risk, will lead to better understanding and, ultimately, better decisions. The task is far from trivial, however. Assessment and integration of complex information may be cognitively demanding for doctors as well as patients. In this thesis different ways of explaining risks and risk reductions to medical doctors and lay people are tested empirically. The aim is two explore how medical decisions thereby might be affected.

4.1. Explaining risk reductions

How risk reductions should be explained to doctors, patients and health-policy makers, has been much debated. Survival- or mortality-curves,[20] gains in life expectancy,[21] relative risk reduction (RRR), absolute risk reduction (ARR) and number needed to treat (NNT)[22] are some of the measures that have been used to communicate the benefits of risk reducing interventions. During the 1990ies the issue was approached in several empirical studies. The main focus was on framing-effects,[18] *ie*. how decision-making may be affected by presenting study results or treatment effects in different frames (ARR, RRR, NNT, *etc*). From these studies it was well established that when treatment effects are presented in terms of relative risk reduction, decision makers are more likely to consent to therapy than when presented with absolute risk reduction and/or NNT. Such findings were made among doctors,[23;24] health policy makers[25] and patients.[26] Concomitant observations that the pharmaceutical industry tended to describe the effect of their drugs in terms of relative risk reductions made many doctors somewhat suspicious. It was felt that relative risk reductions overemphasize the effects of medical interventions and that people ought to be informed in absolute terms.

Since its introduction in 1988,[27] the number needed to treat (NNT) has gained wide acceptance as a cognitively simple effect measure for clinical practice.[28] Its popularity is based on the belief that the NNT conveys both clinical and statistical significance to doctors and their patients in one single, easily comprehensible - and absolute - measure.[29;30] Defined as the inverse of absolute risk reduction, NNT is usually given in whole numbers and is typically explained as the number of patients that must be treated for a specified time period to prevent one adverse outcome. Crudely, one could say that while ARR measures the number of treatment successes per, say, 100 people treated, the NNT measures the number of people treated per treatment success.

From a theoretical perspective NNT has been criticized because of unfavourable statistical properties and hence difficulties in estimation of valid confidence intervals.[31 32] Clinically more important, concerns have been raised that the NNT may in fact be difficult to understand.[33-35] If a treatment effect is presented as an NNT of 50, the interpretation is not as obvious as it might seem at a first glance. One possibility is that for every patient who benefits from therapy, there are 49 patients who don't.[27;36] This implies that the NNT provides a direct measure of the individual's likelihood of having benefit from the therapy; one patient wins the big prize of avoiding a bad outcome, while the others gain nothing. This interpretation is reasonable for lottery-like interventions in which the events to be prevented truly occur in a random fashion. Examples of lottery like interventions might be the use of seat belts and hip protectors. However, for interventions that postpone adverse events (*e.g.* death) rather that completely prevent them, an NNT of 50 may be consistent with the possibility that several or even all of the 50 patients will have some benefit in terms of a delay of the adverse events.[33] In that case, an NNT of 50 simply means that death is postponed to such an extent that on average, one fewer patient (out of 50) has had a fatal outcome at the specific point in time when NNT was measured.

Whether risk reducing therapies prevent or postpone *diseases* is a more complicated question. For example, it seems plausible that usual interventions for type II diabetes work by postponing the late complications of retinal, kidney and blood vessel diseases. Common risk reducing drug therapies such as antihypertensives, statins and bisphosphonates, however, are used for very different kinds and levels of risks. Whether they should be conceptualized as preventing or postponing interventions – or perhaps something in between - may vary accordingly. For slowly developing disease processes such as atherosclerosis and osteoporosis it might be argued that prophylactic drugs should be thought of as postponing interventions; in the long run we may all encounter their consequences provided that we live long enough.[37] The problem is, however, that many of us won't live that long. Thus the NNT may call for quite different interpretations depending on the clinical problem at hand. Since NNT and ARR are just different mathematical expressions of the risk difference between two groups, the same holds for ARR as well. The relationship between different risk reduction measures and postponement is illustrated in figure 1 (page 15) in which statin therapy for primary prevention of ischemic heart disease serves as an example. In this figure ARR and NNT is represented by the vertical distance between survival curves, whereas the average postponement of ischemic heart disease is represented by the area between the curves. The figure illustrates that the magnitude of NNT may depend on when it is measured. On the other hand NNT does not necessarily change much with increasing duration of therapy, even if the area between the curves does.

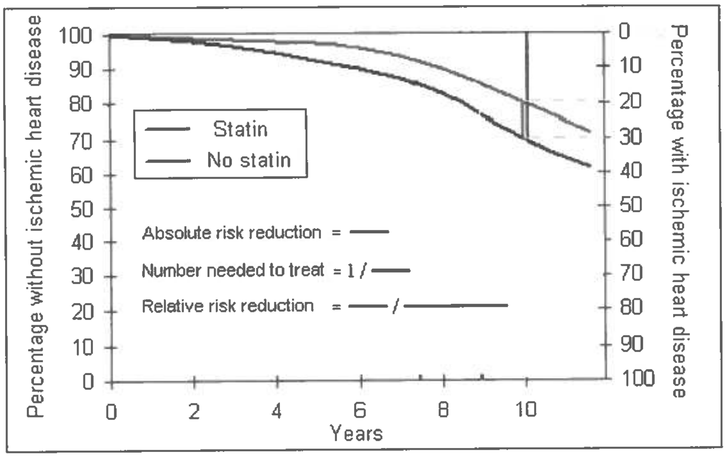

Figure 1. Hypothetical survival curves for patients with and without statin therapy to prevent ischemic heart disease. The relationship between ARR, RRR and NNT is represented by the short and long vertical bars, whereas the average prolongation of life without ischemic heart disease is represented by the area between the curves.

Given that interpretation of measures for absolute risk reduction is not always straight forward, informing decision makers about magnitudes of postponements might be an alternative strategy. The idea is not new;[38] for example it is a long standing tradition to present benefits of cancer therapy as gains in median survival. Whereas postponements as well as NNTs may be estimated from survival curves and conveyed to decision makers, others have presented people with the survival curves directly. Whether people are able to interpret such curves coherently is not clear. Cognitive biases such as framing effects,[39] insensitivity to the time span[40] and sensitivity to the order[41] of different survival curves have been observed. The idea of explaining benefits of risk reducing drug therapies as postponements of adverse events, however, has recently been explored.[34;42] These studies suggest that lay people may be able to discriminate between levels of effect and use this information in decisions regarding fracture and heart attack prevention.

4.2. Aims and research questions

Although people's responses to NNTs and postponements have been explored to some degree, empirical evidence to support the use of one or the other when explaining risk reductions is still sparse. This project aims at exploring further how people understand and respond to the concepts of NNT and postponement in the setting of cardiovascular risk and osteoporosis. The main research questions are the following:

4.2.1. Are decision makers sensitive to the NNT when considering risk reducing drug therapies?

Other things equal, one would expect people to respond differently to NNTs of different magnitudes, *i.e.* people should be sensitive to the effect size. This hypothesis has been investigated to some extent among lay people, but early works did not confirm it. On the contrary, lay people seemed to be insensitive to the NNT up to magnitudes of 400. The issue has not been studied among medical doctors. In the present project it was explored whether lay people's insensitivity might be reproduced for a broader range of NNTs, different diseases to be prevented, treatment costs, self reported risk factors and different interpretations of NNT. Furthermore, sensitivity to and interpretation of the NNT were studied among medical doctors.

4.2.2. Are lay people sensitive to risk information when considering how long they expect to live?

Previous work on how risk information might influence people has mainly focused on quality of life, particularly in terms distress, anxiety or depression. Personal risk information may, however, have cognitive effects beyond psychological harm. An interesting question is whether lay people adjust their personal anticipation of longevity in response to risk information. If they do, it supports the hypothesis that explaining *risk reductions* in terms of postponement may have intuitive meaning. This question was addressed among lay people in the context of cardiovascular risk.

4.2.3. Do lay people respond differently when risk reductions are explained in terms of NNT rather than postponement of adverse events?

Obviously, other things equal people will prefer complete avoidance over postponement of adverse outcomes when considering risk reducing drug therapies. However, other things are not likely to be equal. From randomized controlled trials it is not possible to infer how the benefits of prophylactic drugs are distributed among those in the treatment group. Whether all have some small benefit or a few have great benefits while others gain nothing, we may observe identical NNTs at a given point in time,[33] and even identical survival curves.[43] Explaining risk reductions in terms of NNT might create the impression that only a small fraction of those treated will achieve the great blessings of prevention, whereas using average postponements might suggest that everybody benefits, albeit to a smaller degree. Depending on the disease to be prevented, these different models of explanation may vary with respect to perceived plausibility. A hybrid model explicitly stating that a certain proportion of those treated will get the onset of a disease postponed, whereas the others don't benefit, might also be conceivable. In figure 1 the hybrid model would imply that the gain in disease free life years represented by the area between the curves is supposed to benefit only the proportion of patients that would get the disease without therapy. Responses to the different models were tested in the context of risk reducing drugs against heart attacks and hip fractures. Comparing magnitudes of NNT and postponement is not straight forward however; there is no simple conversion rule to derive one from the other. To make the numbers used in the models meaningfully comparable we derived them from renowned empirical studies.[2;3]

5. METHODS

Attendees to a health study, medical doctors and a sample of the general population were approached in three different surveys, which share a common design: Respondents were presented with hypothetical clinical scenarios or vignettes regarding long term preventive drug therapies. Important aspects of the therapies, such as effect measures, costs, and type of disease to be prevented were varied across the scenarios. The respondents were randomly allocated to one version of the scenario and asked about their preferences for or against the intervention. Differences in responses to the different scenarios were analyzed using statistical methods as appropriate. In a fourth project the attendees to the health study were asked a simple question about how long they expected to live. Differences in anticipated longevity between high and low risk individuals with respect to cardiovascular diseases were analyzed. In the following outlines of the individual studies are presented.

5.1. Medical doctors' perceptions of the number needed to treat[44] (paper 1)

A representative sample of medical doctors in Norway (n=1616) was mailed a questionnaire and asked whether they would prescribe a hypothetical drug as a strategy to prevent premature death. The benefit of the drug was described in terms of NNT, which was set at 50 for half of the respondents and at 200 for the other half. Doctors who would not prescribe the drug were asked to indicate their reasons. Differences in proportions recommending the drug between the two NNT-groups were assessed with χ^2-tests. Additionally, predictors of the doctors' stated willingness to prescribe the drug therapy was analysed using logistic regression. Independent variables were NNT, age, gender, medical speciality and number of years in current position.

5.2. Decisions on drug therapies by numbers needed to treat[45] (paper 2)

A representative sample of the general population in Norway (n=2000) was approached for a face-to-face or telephone interview. Respondents were allocated to clinical scenarios with random combinations of a disease to be prevented, treatment costs and effect size in terms of NNT. Upon presentation of the scenario they were interviewed about their hypothetical consent to a drug therapy aimed at preventing the disease in question. Subsequently, the respondents were randomised to receive different interpretations of NNT and asked to reconsider their initial responses. We tested the hypotheses that increasing the NNT would reduce the proportion consenting to therapy; that the association between the magnitude of

NNT and consent to therapy, if any, was dependent on the type of disease to be prevented, treatment costs or the presence of self-reported risk factors; and that change in preference for the drug therapy, if any, was dependent on the kind of NNT interpretation provided. Differences between proportions were assessed with χ^2-tests, including χ^2-tests for trend when appropriate. Other predictors of consent to therapy such as age, gender, education, income and place of residence were tested in multivariate logistic regression models.

5.3. Different ways to describe the benefits of risk-reducing treatments[46] (paper 3)

A sample of attendees to a general population health survey in Northern Norway (n=1754) was mailed a questionnaire and asked about preferences for a hypothetical drug therapy to prevent heart attacks. Based on results from the 4S study[26;47] treatment effect after 5 years was presented in three formats: "For every heart attack that is avoided, 13 patients must take the therapy" (NNT) or "for all patients taking therapy, heart attack is postponed by 2 months" or "for one out of four patients taking therapy, heart attack is postponed by 8 months, while the others don't benefit". Respondents were randomly allocated to one of these formats. Another sample (n=1000) was asked about preferences for a drug therapy against hip fractures. Based on the FIT study[3;48] benefit from 5 years of drug therapy was explained either as "for every hip fracture that is avoided, 57 patients must take the therapy" (NNT) or "for all patients taking therapy, hip fracture is postponed by 16 days" or "for three out of 100 patients who take the therapy, hip fracture is postponed by 16 months, while the others don't benefit". Again, allocation to one of the effect formats was random. Associations between consent to therapy and effect format were assessed with χ^2-tests. Other possible predictors of consent to therapy, such as age, sex, education and several health related variables were analysed using log-Poissoin regression.

5.4. Anticipated longevity among lay people screened for cardiovascular risk[49] (paper 4)

A subset of the participants described in paper 3 (n=1748) was classified according to cardiovascular risk to yield a high and a low risk sample. As part of the general health study they received comprehensive written information about their cardiovascular risk factors shortly after screening and risk assessment. High risk individuals were advised to see their GP for follow up. Four to six months after receipt of risk information they were mailed a questionnaire and first informed about the average life expectancy of Norwegian men and women. Subsequently they were asked whether they expected to live shorter, longer or about as long as to the average life expectancy. Possible predictors of anticipated longevity were tested in multinominal and ordinal regression models. Cardiovascular risk was the primary independent variable in the models which also included age, sex, education, marital status and several health related variables.

6. RESULTS

When considering risk reducing drug therapies, lay people were insensitive to effect size in terms of NNT (paper 2)[45] in the sense that the proportion consenting to therapy was fairly constant over a broad range of magnitudes of NNT. Among medical doctors, on the other hand, the proportion recommending a drug therapy dropped by 20% when NNT increased from 50 to 200 (paper 1).[44] Furhtermore, lay people were more inclined to accept drug therapies explained as preventing interventions in terms of NNT over drugs conceptualized as postponing interventions (paper 3).[46] Finally, lay people's anticipated longevity was moderately associated with personal cardiovascular risk information (paper 4).[49] Summarized in table 1 and figure 2, these were the key findings of this thesis. In the following each of the main findings is explained briefly.

Table 1: Consent to preventive drug therapies by different ways of explaining their benefits among lay people and medical doctors

Effect measure	Proportion of lay people consenting to therapy to prevent various diseases (n=1178)[1]	Proportion of MDs recommending therapy to prevent early death (n=1305)[2]
Number needed to treat		
50	76 %	72 %
100	71 %	
200	70 %	52 %
400	71 %	
800	68 %	
1600	67 %	

Effect measure	Proportion of lay people consenting to therapy to prevent heart attacks (n=1397)[3]	Proportion of lay people consenting to therapy to prevent hip fractures (n=831)[3]
Number needed to treat	93 %	74 %
Long postponement for some patients	82 %	56 %
Short postponement for all patients	69 %	34 %

1) From paper 2: Decisions on drug therapies by numbers needed to treat[45]
2) From paper 1: Medical doctors' perceptions of the number needed to treat[44]
3) From paper 3: Different ways to describe the benefits of risk-reducing treatments[46]

6.1. Medical doctors were sensitive to NNT

About three of four medical doctors indicated that they would recommend a drug aimed at preventing premature death when NNT was 50 after five years of therapy, whereas about half of the doctors would recommend it when NNT was set at 200 (table 1). Regression analysis indicated that age modified the effect of NNT on recommending the drug therapy; the difference between the two NNT groups was greater among the youngest doctors aged 26 – 35: 90 % with NNT set at 50 *versus* 57 % with NNT set at 200. Finally, the majority of doctors who would *not* recommend the drug (77 %) agreed with the statement that "only one out of NNT patients (50 or 200) would benefit from the drug therapy", an interpretation that was not inherent in the scenario presented to them.

6.2. Lay people were insensitive to NNT

Whereas medical doctors were sensitive to the magnitude of NNT in their decisions, lay people were not. The proportion consenting to different hypothetical drug therapies did not vary significantly by NNTs in the range of 50 to 1600 (table 1). This pattern was consistent across different diseases and different drug costs. For example 84%, 76%, 68% and 53% consented to the drug therapy when the disease to be prevented was a "lethal disease", stroke, heart attack and hip fracture, respectively, but within each disease group the proportion consenting was not dependent on the magnitude of NNT. When provided with an interpretation of NNT about one in five changed their mind and withdrew their initial consent. The kind of interpretation did not matter; people got more skeptical about the drug therapy whether NNT was explained as the likelihood of benefit (one out of NNT) or as compatible with benefit for everybody in terms of postponing the disease for awhile.

6.3. Lay people's anticipated longevity was associated with cardiovascular risk

Anticipated longevity and cardiovascular risk factors were associated, suggesting that being informed about an unfavorable risk profile translates into shorter anticipated longevity. In regression models high overall cardiovascular risk, use of lipid lowering drugs and a family history of heart attack before the age of 60 were independent predictors for anticipating to live shorter than the mean, whereas male sex, higher age, better education and perceived good health were predictors of anticipating to live longer than the mean. The associations were moderate, however, with odds ratios 2.4 or less. In fact, about 70% of lay people indicated that they expected to live about as long as the mean for Norwegians whether they belonged to a high risk or a low risk group (see figure 2).

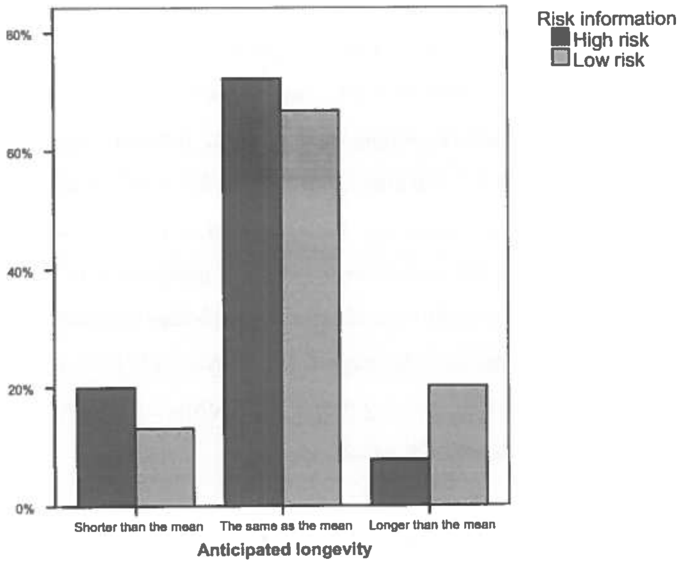

Figure 2. Distribution of anticipated longevity among high- and low CVD risk individuals. From paper 4: Anticipated longevity among lay people screened for cardiovascular risk factors

6.4. Lay people preferred drug therapies explained in terms of NNT

Conceptualizing drugs as postponing rather than preventing therapies had significant impact on lay people's decisions. Proportions consenting to hypothetical drug therapies were highest when benefits were explained in terms of NNT, intermediate when explained as a long postponement for a fraction of the patients and smallest when explained as a short postponement for all patients. This pattern was observed when the outcomes in question were hart attack as well as hip fracture (see table 1). Although those who said that it was easy to understand the benefits were more likely to consent to the therapy, perceived understanding did not vary significantly across the different conceptualizations.

7. DISCUSSION

7.1. Interpretation of findings

In the present studies we observed that lay people, when considering risk reducing drug therapies, were insensitive to effect size in terms of NNT (paper 2), whereas medical doctors were sensitive (paper 1). On the other hand, lay people were sensitive to treatment costs and the kind of disease to be prevented (paper 1). We also observed that lay people's anticipation for their own longevity was moderately associated with personal cardiovascular risk information (paper 4). Finally, explaining risk reductions in terms of postponement of adverse events rather than the equivalent NNT to prevent one adverse event yielded considerably lower consent rates to drug therapies (paper 3). This suggests that lay people have difficulties using NNT in their decisions, and that conceptualizing prophylactic drugs as postponing agents may have significant impact on people's decisions.

Expected utility theory[14] may serve as a starting point for interpreting these findings. Proposed as a normative theory for decisions under uncertainty it prescribes that people should aim to maximize desirable outcomes. In a medical context it follows that, other things equal (such as treatment costs and valuation of possible outcomes), the individual should pay more attention to common diseases than to rare diseases. Similarly, other things equal, individuals should be more concerned about serious diseases than trivial complaints, choose more effective drugs over less effective drugs, prefer cheap drugs to expensive drugs and so on. In this context, the observed results may be interpreted as true preferences for great but uncertain benefits over small but certain benefits. For example, why pay attention to the NNT if the possibility of avoiding a heart attack is at stake and the risk of a drug therapy is limited to rather small inconveniences? It might be argued that unless the NNT exceeds a threshold value, it will not get much weight in people's decisions. Similarly, if most people expect to live about as long as the average whatever their cardiovascular risk, they might not be much impressed by the prospect of postponing a heart attack unless the length of the postponement exceeds a certain threshold.

The idea of treatment threshold values for NNT has been explored to some extent theoretically,[50] but searches in Medline and Embase using the terms "number needed to treat" and "threshold" (April 1 2008) yielded no study of patient reported thresholds. In one of the present studies the majority of respondents indicated that they would accept an NNT of 1600, which is equivalent to an absolute risk reduction of 0.000625. If the threshold lies far beyond 1600 it is hardly meaningful as it would require unfeasibly large samples to detect such risk differences in clinical studies. Trewby *et al* asked patients and non-patients directly about threshold values for absolute risk reductions as well as average life extension to make preventive drugs worthwhile.[51] Median thresholds for absolute risk reduction were in the range of 20% – 30% which is not consistent with an NNT threshold beyond 1600. Median threshold values for life extension, on the other hand, were 12 to 18 months, *i.e.* way beyond the postponements presented to our respondents. Given a fixed 30% relative risk reduction for coronary disease, Marshall *et al* asked patients at what baseline risk they would accept drug treatment. 55% of the respondents would prefer treatment at a five year risk of 3%,[52] which would correspond to an NNT of about 100. In a related study the median treatment threshold among clinicians was a five year absolute risk of 15%,[53] which amounts to an NNT of about 20 given a relative risk reduction of 30%. Asking doctors and patients about their treatment thresholds is one thing; what exactly they expect to achieve from risk reducing interventions is another interesting issue that awaits empirical studies.

There are several descriptive theories explaining deviations from expected utility theory, among which prospect theory is perhaps the most prominent.[26] In prospect theory decisions are still supposed to be based on integration of probabilities and valuations of outcomes (*i.e.* utilities), but decisions are not supposed to be linear functions of probabilities. Within decision psychology, cognitive biases and heuristics[54] are emphasized as important determinants of people's choices. Heuristics are short cuts that people use to simplify complex decisions.[54] The results presented here may perhaps be better explained by descriptive theories. For example, insensitivity to NNT and different responses to empirically equivalent descriptions of drug benefits may be considered as potential violations of expected utility theory. Possible sources of such violations are accounted for below.

7.1.1. People may not understand risks and risk reductions

In the context of medical decision making, there may be several different senses of the term "understanding".[55] A complete discussion of this term is beyond the scope of this thesis. However, poor sensitivity for risk information and risk reductions explained in terms of NNT might be thought of as people having trouble with numbers. Numeracy – people's basic skills with numbers – is known to be associated with accuracy of risk perceptions, value assessments and comprehension of effect measures,[56-58] and numeracy seems to be surprisingly poor even among well educated people.[59] For example, less than 50% of patients were able to identify the best of two treatments when explained in terms of absolute risk reductions or NNT.[58] Medical students performed better, but the majority still made invalid quantitative interpretations of NNT.[57] Medical doctors may be no exception. In the first paper of this thesis[44] a significant proportion interpreted the NNT as a direct measure of the likelihood of benefit, which is not valid. A qualitative study by Lewis *et al* reports that physicians, nurses as well as lay people seemed to have difficulties with understanding the statistical concepts of risks and risk reductions,[60] whereas Yoon *et al* found poor ability to make basic probability calculations among physicians training to become specialists.[61]

7.1.2. People may understand, but can't evaluate

Imagine for awhile that your doctor informs you that your risk of heart attack is elevated. The doctor suggests that you take a drug to prevent heart attacks. The drug is to be taken daily, and you have to visit your doctor twice a year for follow up. Side effects are uncommon and trivial. The drug will cost you 100€ per year. The doctor explains that for every heart attack that is prevented, 50 patients will have to take the drug for five years. Would you choose to take this drug?

Hypothetical scenarios similar to this were used to elicit the findings in table 1. One might object that the scenario provides insufficient information, but still the decision-maker is exposed to complex information: A serious disease, the GPs advice, the term "prevention", 100€ a year, daily medication for five years and an NNT of 50. All the cues are more or less relevant for the decision at hand, but how will the different cues be weighted? Three closely related concepts from cognitive psychology – the recognition heuristic,[19] the availability heuristic[17;62] and the evaluability hypothesis[63] – all converge on the idea that cues that are easy to evaluate will be weighted heavily. Cues may be easy to evaluate because of recognition, ease of recall, knowledge, experience or available scales for comparison. Difficult cues, on the other hand, may be neglected, which may lead to low decision weights for unfamiliar numbers.

Is an NNT of 50 good or bad? People may have a basic understanding of the number "50", that 50 patients must be treated for a certain time to observe one less hart attack, and that 50 is different from, say, 100. In their assessment of NNT lay people may not, however, rely on recognition, recall or knowledge. This may result in poor sensitivity to effect measures such as NNT in complex decisions; people may instead put emphasis on the GP's advice, the prospect of preventing a serious disease or treatment costs. Interestingly, previous studies have shown that lay people are sensitive to effect size in terms of postponement of adverse events;[34;42] they may be expected to because they have natural experience with time. Furthermore, in paper 1 medical doctors, who *can* rely on experience and knowledge, were sensitive to NNT.[44]

From the evaluability hypothesis it may be inferred that if steps are taken to increase the evaluability of important, but difficult cues, they may get more emphasis in people's decisions. Several experiments have confirmed this hypothesis,[63] for example by providing decision makers with scales for comparison of unfamiliar numerical cues. Conversely, if cues are easy to evaluate as well as important, their decision weight may not change much by providing additional information. Recently, the Odense Risk Group tested the stability of lay people's decisions regarding a risk reducing drug against heart attacks based on one single effect format.[64] Respondents were randomly allocated to receive information in terms of either ARR, RRR, NNT or postponement of heart attacks and asked to indicate their preference for or against the drug therapy. Subsequently they received "complete information", *i.e.* all the effect formats and a pictogram, and were asked to reconsider their decision. Differences between the different effect formats were generally small, but interestingly, patients informed in terms of RRR and postponement were more inclined to change their decision after receiving the complete information. Those initially informed in terms of RRR got more skeptical whereas those informed in terms of postponement got more positive. What heuristics the respondents may have used when assessing this complex information remains elusive, but in line with the paper 3 of this thesis, it seems that people prefer the prospect of complete prevention, even if uncertain, to the prospect of postponing adverse outcomes. This begs the question which of these effect formats that is most truthful to reality. Unfortunately, whether prophylactic drug therapies should be conceptualized as preventing or postponing agents cannot be inferred from randomized controlled trails. This remains a matter of judgement that may better be based biomedical and epidemiological knowledge.

7.1.3. People's decisions are driven by emotions

There is ample evidence suggesting a significant impact of feelings on risk perception and decision making. The feelings need not be strong, not even conscious; Slovic *et al* talk about the "faint whisper of emotion".[65] For example, compared to a control group, medical doctors who received a small package of candy responded differently to questions regarding job satisfaction and creative problem solving.[66] Clinically more important, perhaps, physicians responding to clinical vignettes were more inclined to comply with patient wishes for referrals or hospital admittance when the vignette posed a threat (such as complaints to the health authorities or involvement of mass media) from the patient or a relative.[67] These may serve as examples of the *affect heuristic*[65] in medical decision making. Interestingly, when this heuristic is at work, evidence suggest that people attend to the *possibility* rather than the *probability* of affect laden outcomes;[68-70] small departures from certainty and impossibility have impact on risk perception and judgement, whereas people are relatively insensitive to a broad midrange of probabilities, as illustrated in figure 3:

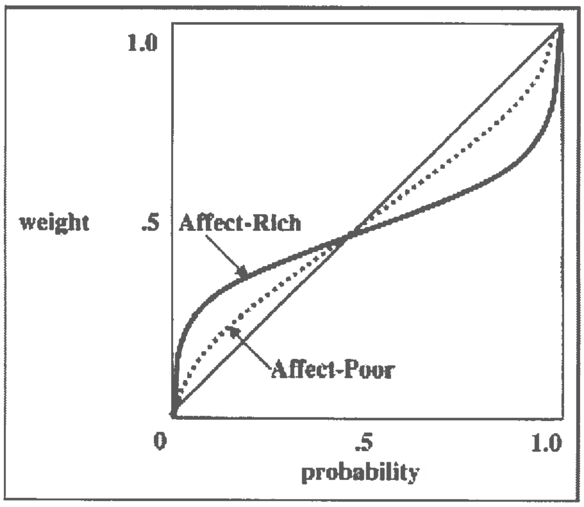

Figure 3: Hypothetical affect-rich and affect-poor probability weighting functions according to Rottenstreich and Hsee.[69] Used with permission.

Given the subtle nature of the affect heuristic, it is conceivable that affect was induced by cues used in scenarios of papers 1 - 3, *e.g.* the prospect of getting a heart attack. Insensitivity to the magnitude of NNT and preference for preventing over postponing drugs, at least partly, be explained as the affect heuristic being at work.

7.1.4. Optimism bias and the happiness gap

Insensitivity to the magnitude of NNT set aside, one might be struck by the high percentage (typically 70% or higher) of lay people consenting to preventive drug therapies given the NNT scenarios (paper 2 and 3). Also, one might wonder why personal risk information seemed to have such modest impact on people's anticipated longevity; after all the respondents were at the extremes of the risk scale (either high or low), but the majority nevertheless expected to live about as long as the average (paper 4). In other words lay people didn't seem to take much notice of risk information and they might have unrealistic expectations of what preventive drugs can do. Both observations may, at least partly, be attributed to optimism bias, *i.e.* a tendency to judge one self to be happy and hold inflated views about ones abilities, characteristics and prospects. Evidence suggests that optimism bias is pervasive in language, memory, perception and judgement, at least in the Western societies.[71] In a medical context it has been shown that people often underestimate their personal risks and tend to regard hazards as more risky to others than to themselves.[62] Furthermore, in a qualitative study Frich *et al* showed that among patients with familial hypercholesterolemia there was a tendency to portray candidates for coronary heart disease as different from oneself.[72]

Low impact of personal risk information on anticipated longevity might also be reflective of people's often remarkable ability to adapt to their present circumstances. Usually people underestimate this ability, however, leading to a bias in affective forecasting[73] sometimes referred to as the happiness gap or the disability paradox: People in good health overestimate the impact of diseases and their associated treatments on happiness and quality of life compared to people actually living with the disease in question.[74] If this holds for living with diseases, it may hold for living with knowledge of risks as well. To the extent that lay people's anticipations for their own longevity are affectively laden, and not just a cognitive adjustment of one's expectations, low impact of personal risk information may be attributed to the happiness gap. Asking people not yet aware of their risk about how they think they would react to a high risk label might then give different results.

7.2. Assessment of methods

Three of four papers in this project report decisions based on hypothetical scenarios or vignettes and variations in decisions consequent on varying information in these scenarios. With very few exceptions[75] similar designs have been used in previous studies regarding the

impact of information framing[25] on medical decisions. The methods of our studies can be veiwed in the light of social judgement theory and Brunswik's lens model.[62] This model emphasized that understanding judgement requires both understanding the environment for judgement and understanding what the person is trying to accomplish within that environment. In terms of Brunswik's lens model we are working on the right side of the lens, trying to capture which cues people respond to in their decisions. On the left side of the lens is the social environment in which decisions must be made, which is hopefully represented by the clinical scenarios. The fourth paper is basically an attempt at measuring the psychological impact of predicting individual's risk of disease in terms of anticipated longevity.
Use of statistical methods, sampling and randomization procedures, validity of individual vignettes and issues of external validity are further discussed in the individual papers. General aspects of vignette techniques and measurement of psychological impact of risk information are accounted for below.

7.2.1. Using vignette methodologies

Vignette methodologies are extensively used in studies of people's attitudes, perceptions, and judgements.[76;77] A vignette can be presented in different formats, such as video or audio tapes,[78] oral presentation by an interviewer,[79] computerized vignettes[80] or written case simulations ("paper people").[81;82] The main concern about studies of "paper patients" and other vignettes is that they are of questionable relevance to real world decisions, *i.e.* a problem of external validity. Several factors that may bias people's responses have been proposed. Lack relevant information or sufficient detail in the vignette may induce responses such as "it depends", or filling in missing information, perhaps based on personal experience with the issue at stake, before responding.[76;79]Also, people may respond in ways that they believe to be socially desirable.[76;79;83] Regarding strategy capturing studies Wigton observed that cue weights were sensitive to details of vignette design,[84] while others have observed that responses may depend on mode of presentation (e.g. videos *versus* equivalent written vignettes)[78;81] or response method.[85] Clearly, the design of vignettes and response methods (scales, forced choices or open ended questions) must depend on what one tries to measure.[76] Although some authors emphasise the use of open ended questions,[76;80] little is known about the relationship between vignette design and external validity. In a review Jones *et al* found no clear evidence about how well written case simulations predict physicians' behaviour,[82] whereas Gorman *et al* found that employers gave different judgments based on "paper people" compared to real interviews.[86]

In support of the external validity of written vignettes Lanza et al found similar judgements about actual cases of assault and written transcripts of these cases.[87] In a study on date rape Sleed *et al* showed that video vignettes did not differ from written transcripts regarding the extent to which the scenarios were perceived as believable or emotionally evocative.[78] Using the standardised patient technique[88] as a gold standard, clinical vignettes measured physician performance about equally well across different types of diseases and case complexities, and measures based on vignettes compared favourably to those based on patient chart abstracts.[80;83] However, the vignettes were found to overestimate the quality of physical examination and treatment plans.

Although the use of hypothetical scenarios probably cannot capture all relevant aspects of real world decisions, they can provide insights into important cognitive processes at work in people's choices.[15] The main advantages of hypothetical scenarios or vignettes are to ensure that information is given in a standardized manner to all the respondents and that the effect of varying information can be measured, which is hard to achieve in actual clinical practice. It can even be argued that vignettes should not mirror the complex real world too closely. Deliberately enhancing the "signal-to-noise ratio"[81] by using simple scenarios may actually help clarifying what factors that drive people's judgements.[89]

The main objective of the present project was to study how numerical effect formats influence physicians' and lay people's preferences for long term preventive drug therapies. Rather than using vignettes the issue might be approached using qualitative methods. Evidence from such studies is limited, but in a couple of studies these techniques were combined.[60;90] They suggest that factors other than numerical risk terms may influence decisions to accept preventive drug therapies; clinicians reported that in addition to risks and benefits, costs to patients and society[90] as well as the patient's preferred role in decision making[60] were important factors. Patients reported a general dislike of taking drugs and a preference for life style changes.[60] Such factors may be important for the face validity of vignettes, and some of them were indeed included in our scenarios. However, the qualitative approach is limited by the fact that what decision makers claim to be important factors may be different from the factors that actually drive their decisions.[84;91] As it is largely unknown to what extent numerical effect measures are actually used in clinical practice, the external validity of our scenarios is hard to assess.

7.2.2. Measuring anticipated longevity

The initial idea behind paper 4 was to use lay people's anticipated longevity as a proxy for "life optimism", which we proposed as an affectively laden psychological construct that might be adversely affected by cardiovascular risk information. The study was motivated by the fact that despite quite extensive research, there was little evidence of long lasting psychological harm from risk information, even for serious diseases such as HIV, Huntingtons disease or cancer.[92] To assess psychosocial consequences, previous studies typically used generic questionnaires designed for measuring health related quality of life or psychometric instruments otherwise used for clinical purposes. It seems unlikely, however, that these instruments may capture all relevant psychological consequences of risk information. In the context of cancer screening Brodersen *et al* argue against the use of diagnostic interviews and generic questionnaires[93] due to lack of content validity and methodological rigor regarding psychometric properties. They insist that measures should be condition specific and use patient reported outcomes, and they demonstrate how these principles and item response theory may be applied when measuring psychosocial consequences of false positive mammograms.[94] When it comes to psychosocial impact of cardiovascular risk information, the evidence is conflicting. Some studies indicate that such information may result in short term as well as long term distress,[95-97] whereas others do not.[98;99] However, rigorously tested and condition specific outcome measures have not been developed in this area, suggesting that any conclusions regarding psychological impact of cardiovascular risk information must remain tentative.

Given that it may be hard to assess psychological impact of risk information using quantitative measures, qualitative studies might again be an alternative approach. For example, Reventlow *et al*[100;101] and Hvas *et al*[102] have studied postmenopausal women's perception of osteoporosis. They report unspecific feelings of worry, but also that the women had mental images of brittle bones and, consequently, reduced their physical activity to protect themselves. Using qualitative techniques Frich *et al* explored feelings of guilt and shame[103] and sense of vulnerability to heart disease[104] among patients with familial hypercholesterolemia. It may be questioned whether these feelings and mental images result from information about risk in the epidemiological sense (*i.e.* probability of undesirable events) or from something else. Nevertheless, such findings lend support to the proposition that measures of psychological impact of risk information should be condition specific.

Thus, using anticipated longevity as a proxy for "psychological harm" or "life optimism" is at best tentative. When presenting the study to an audience of scientists with expertise in medical decision making, I labelled those who expected shorter longevity as pessimists. A psychologist stood up and suggested that perhaps these respondents were not pessimists; maybe they did nothing more than realistically adjusting their expectations. In other words he introduced the idea that there might be sort of a cognitive (rather than emotional) link between cardiovascular risk information and anticipated length of life. This hypothesis gives some support to the idea of explaining risk reductions in terms of postponement of bad outcomes, although others have observed that people don't necessarily link duration of treatment to increasing benefits.[60] Whether people respond cognitively or emotionally or both when asked about anticipated longevity remains elusive. However, since anticipated longevity and cardiovascular risk information was associated, this may deserve further inquiry.

8. CONCLUDING REMARKS

8.1. Conclusion

The major finding of this project was lay people were more inclined to accept drug therapies explained as preventing interventions in terms of NNT compared to drugs conceptualized as postponing interventions. Second, it was confirmed that lay people are insensitive to the magnitude of number needed to treat in complex decisions. Medical doctors, on the other hand, were sensitive to effect size in terms of NNT. Finally, a statistically significant but modest association between personal risk information and anticipated longevity was found among lay people.

8.2. Implications for practice

Unless efforts are made to educate the lay public about the meaning and magnitude of NNT, there are strong reasons to doubt that this effect measure is better suited for patient communication than other effect measures. NNT may, however, be suitable for communication between health professionals. Whether prophylactic drugs are conceptualized as postponing or preventing agents may matter to patients.[105] When explaining risk reductions, medical doctors should take care not to promise too much; *i.e.* complete prevention of adverse outcomes when postponement is all we reasonably can hope for. For example, we should not speak of statins and antihypertensive drugs as "life saving" agents; death may at best be postponed. On the other hand, physicians should also be careful so they don't promise too little; *i.e.* that there is only a small probability of benefit from an intervention when there is good reason to believe in postponement of adverse outcomes for all or most patients. An example might be interventions against hyperglycemia among high risk diabetics.

8.3. Implications for research

First, given that preventive drugs and other prophylactic interventions are wide spread in use already, it seems important to study how medical doctors and their patients conceptualize the benefits. What do they think they achieve – postponement or complete prevention of adverse outcomes – or something else? Furthermore, although research based on vignette techniques and hypothetical scenarios may give important insights, different ways of explaining risk reductions remain to be tested in clinical settings with doctors and patients facing real decisions.

Second, having observed that lay people were insensitive to effect size in their decisions, it might be worthwhile to take one step back and ask what goals patients wish to pursue when considering risk reducing interventions. Given the assumption that patients want to maximize length and quality of life we may insist that effect size should matter and, consequently, be explained properly. If patients have other goals, however, effect size may simply not be that important.

Finally, the association between personal risk information and anticipated longevity merits further study. If there is a cognitive link between risk perception and anticipated longevity, then explaining risk reductions in terms of postponements may be intuitively meaningful to patients. If there the link is emotional in nature, anticipated longevity may be considered for instruments measuring psychosocial consequences of risk information.

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Paper I

Taylor & Francis healthsciences

Medical doctors' perception of the "number needed to treat" (NNT)

A survey of doctors' recommendations for two therapies with different NNT

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Scand J Prim Health Care 2003;21:162–166. ISSN 0281-3432

Objective – While the number needed to treat (NNT) is in widespread use, empirical evidence that doctors or patients interpret the NNT adequately is sparse. The aim of our study was to explore the influence of the NNT on medical doctors' recommendation for or against a life-long preventive drug therapy.
Design – Cross-sectional study with randomisation to different scenarios.
Setting – Postal questionnaire presenting a clinical scenario about a hypothetical drug as a strategy towards preventing premature death among healthy people with a known risk factor. Benefit after 5 years of treatment was presented in terms of NNT, which was set at 50 for half of the respondents and 200 for the other half.
Subjects – Representative sample (n = 1616) of Norwegian medical doctors.
Main outcome measures – Proportion of doctors that would prescribe the drug. Reasons for recommending against the therapy.
Results – With NNT set at 50, 71.6% (99% CI 66.8–76.4) of the doctors would prescribe the drug, while the proportion was 52.3% (99% CI 47.5–57.1) with an NNT of 200 ($\chi^2 = 50.7$, $p < 0.001$). Multivariate logistic regression analysis indicated that the effect of NNT on the likelihood for recommending the therapy was age-dependent; young doctors (< 36 of age) were more sensitive to the difference in NNTs than older doctors. Thirty-six percent (n = 464) of the doctors would not prescribe the drug, and 77.4% (99% CI 68.5–86.2) of those agreed with an argument stating that only one out of NNT patients would benefit from the treatment.
Conclusion – Medical doctors appear to be sensitive to the magnitude of the NNT in their clinical recommendations. However, many doctors believe that only one out of NNT patients benefits from therapy. Clinical recommendations based on this assumption may be misleading.

Key words: number needed to treat, risk communication, risk management.

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How should the effects of preventive medical interventions be communicated to doctors, patients and policy-makers? This issue has been much debated (1). Advocates of evidence-based medicine claim that the number needed to treat (NNT) is a useful tool in clinical decision-making and in reporting treatment effects from medical trials (2). As opposed to relative risk reduction and absolute risk reduction, the NNT is said to convey both statistical and clinical significance (3). Furthermore, it is claimed that the concept of NNT is easier to understand for clinicians and patients (2,4,5). Critics, however, have pointed out that the NNT has undesirable statistical properties (1,6). The claim that NNT is easy to understand has little empirical support and has, in fact, been questioned (1,7). Recent evidence from Denmark indicates that neither lay people (8) nor medical doctors (9) readily grasp the concept of NNT.

The NNT is the inverse of absolute risk reduction. Usually, NNT is given in whole numbers (2), preferably with a confidence interval (10). The NNT is frequently interpreted as the number of patients that must be treated in order to prevent one adverse event (4). Expressed in these terms, the NNT may tend to direct the attention to "wasted effort" (11). Suppose

The "number needed to treat" is assumed to be readily understood, but empirical evidence to support this assumption is sparse.

- 72% of medical doctors recommended a preventive drug therapy when NNT was 50 compared to 52% when NNT was 200.
- 77% of doctors recommending against a preventive drug therapy thought that only one out of NNT patients benefits from therapy.
- Since this assumption may be misleading, we suggest that the NNT should be used with caution in clinical practice.

DOI 10.1080/02813430310001158

that a medical intervention after 5 years of therapy generates an absolute mortality reduction of 0.1 (10%); the corresponding figure for NNT is 10. A "wasted effort" argument can now be stated as: *One out of 10 individuals benefits from the intervention and avoids death. The other 9 either don't need the intervention or are non-responders, so they don't benefit.*

This interpretation of the NNT has been adopted by several authors (4,12) and is justified when the effect of an intervention is like a dichotomous lottery. This is the case when the adverse outcome to be prevented occurs in a random fashion, like fall trauma or road accidents. In the context of preventive therapies for chronic and slowly developing diseases, another interpretation of the NNT might be more appropriate: *Depending on the initial risk, some or most of the 10 individuals have some benefit in terms of delaying the adverse outcome, but after 5 years of treatment only one death has been avoided due to the intervention.*

Examples of such interventions would be medical treatment of hypertension and the use of lipid-lowering drugs. It seems biologically plausible that such interventions delay adverse outcomes (heart attack, stroke or death), rather than completely prevent them. When this is the case, it can be shown that an NNT of 10 is not incompatible with the possibility that all of the treated individuals will benefit (8). Thus interpretation of the NNT may not always be straightforward. We hypothesized that the concept of NNT might be difficult for medical doctors to comprehend, and we aimed to explore whether these doctors respond differently to NNTs of different magnitude. Secondly, we assessed their perception of NNT in terms of agreement with the aforementioned "wasted effort" argument.

MATERIALS AND METHODS

In 1993 the Research Institute of the Norwegian Medical Association mailed 2000 randomly selected doctors aged between 25 and 70 years and invited them to form a study panel. The purpose was to investigate their health and working conditions by repeated surveys of their attitudes and opinions. Initially, 1272 doctors consented, but owing to deaths and withdrawals the panel was reduced to 1251 members. In January 2000 another 795 randomly selected doctors authorized after 1993 were invited, and 365 consented. The panel therefore consists of 1616 doctors. ID numbers were consecutively assigned to each doctor in the order in which their written consent was received.

In February 2000, a comprehensive questionnaire was mailed to all current members of the panel. For our study, the doctors were presented with a clinical scenario as follows: "Imagine a disease which affects more than 20% of people more than 40 years old. The disease gives no symptoms, but increases the risk of premature death. A thoroughly tested and registered drug can prevent deaths from this disease. The medication is to be life-long and costs about NOK 4000 per individual treated per year. There are no serious side effects." The effect of the intervention was presented in terms of NNT after 5 years of treatment, and the doctors were allocated to an NNT of 50 or 200. Assuming that the ID numbers were randomly distributed among the doctors, the lower half of the ID numbers of both the 1993 part and the 2000 part of the panel were assigned to NNT = 50 and the upper halves to NNT = 200.

The doctors were asked if they would prescribe the hypothetical medication for patients with the risk factor in question. If they would not, they were asked to indicate one or more of several possible reasons specified in the questionnaire: reluctance to have people without any symptoms on medication, that the costs of the treatment were too high, that (NNT-1) of the treated persons would not benefit from the intervention (i.e. the "wasted effort" argument) or other reasons.

Differences between proportions were assessed by χ^2 tests and differences between means by Student's t-test. Logistic regression analysis was performed with the doctors' stated willingness to prescribe the medication as the dependent variable. This variable was dichotomised with doctors who would certainly or probably prescribe the medication grouped together and contrasted with doctors that responded "certainly not" or "probably not". In a second analysis among the non-prescribers, the dependent variable was agreement with the "wasted effort" argument (those who picked this argument versus those who did not). NNT, age, gender, medical speciality and time in current position were independent variables in both of the analyses, and we tested for first-order interactions between NNT and the other independent variables. Owing to multiple statistical testing, only p-values less than 0.01 were accepted as statistically significant.

RESULTS

Out of 1616 doctors, 1305 (81%) returned the questionnaire. The responders were representative of Norwegian doctors with respect to gender, while general practitioners were slightly over-represented (20.2% of the sample versus 15.9% of all Norwegian doctors, $p < 0.001$), the age group 35–54 years slightly under-represented (25.9% versus 30.8%, $p < 0.001$) and the age group 55+ slightly over-represented

(24.3% versus 20.3%, p < 0.01). Unfortunately, the two NNTs of 50 and 200 were not randomly distributed with respect to geographical distribution of the doctors (Table I). In addition, there were slight differences in the distribution of age and medical speciality between the two NNT groups.

While 71.6% (99% CI 66.8–76.4) of doctors presented with an NNT of 50 would recommend the intervention for their patients, the proportion was 52.3% (99% CI 47.5–57.1) when NNT was 200 (difference 19.3%, $\chi^2 = 50.7$, $p < 0.001$). The regression analysis indicated that NNT and age were independent predictors for recommending the therapy (Table II). Also, there was a statistically significant interaction between age and NNT ($p = 0.007$), which means that the effect of NNT on the likelihood for recommendation of the therapy was age-dependent.

Table I. The respondents' background variables by number needed to treat (NNT).

Variable	NNT = 50 (n = 592[1])	NNT = 200 (n = 713[2])	p-value
Age			
Mean,	47.8	45.4	< 0.001
95% CI	(46.8; 48.8)	(44.6; 46.2)	
Years since graduation			
Mean,	20.5	18.0	< 0.001
95% CI	(19.5; 21.5)	(17.2; 18.8)	
Years in current position			
Mean,	16.0	18.0	0.226
95% CI	(13.8; 18.2)	(15.7; 20.3)	
Gender			
Proportion female	33.0%	29.8%	0.207
Region of living			
South	19.9%	12.9%	< 0.001
West	0.9%	35.6%	
Middle	1.4%	25.4%	
North	1.0%	18.2%	
Central	76.9%	7.9%	
Current position			
General practitioner	22.3%	27.3%	0.001
Hospital physician	52.9%	56.1%	
Other	24.8%	16.6%	
Educational status			
Speciality approved	69.8%	64.9%	0.180
In speciality training	17.7%	20.8%	
None of the above	12.5%	14.3%	
Speciality			
Family medicine	17.6%	21.6%	0.017
Community medicine	3.5%	2.4%	
Surgery	13.0%	13.6%	
Internal medicine	21.5%	15.1%	
Psychiatry	7.8%	7.3%	
Laboratory	6.4%	4.8%	
None/missing	30.2%	35.2%	

[1]For individual variables, n may be less than 592 due to missing information.
[2]For individual variables, n may be less than 713 due to missing information.

With NNT set at 50, 90% of doctors in the youngest age group (26–35) would recommend the treatment, compared to 71% among older doctors ($\chi^2 = 17.0$, $p < 0.001$). With NNT set at 200, 57% of the youngest doctors and 52% of the older doctors would recommend the treatment ($\chi^2 = 2.0$, $p = 0.17$). Thus, the youngest doctors were most likely to recommend the therapy, but were the more sensitive to the difference in NNTs.

In total, 36% of the doctors would not recommend the treatment. The "wasted effort" argument ("i.e. (NNT-1) patients have no benefit") was the most frequent reason for recommending against the therapy (77%) followed by reluctance to have patients without symptoms on medication (56%) and high cost (50%). Logistic regression analysis showed that the magnitude of the NNT did not contribute significantly to predict agreement with the "wasted effort" argument (Table III).

DISCUSSION

Our study suggests that medical doctors are sensitive to the magnitude of NNT in their clinical recommendations, but that a substantial proportion may advise their patients against therapy in line with the "wasted effort" argument. Although the study sample differed from Norwegian doctors with respect to age and speciality, the differences were small, and we consider the sample fairly representative of Norwegian doctors. There was a considerable difference in place of living between the two groups of doctors presented with NNTs of 50 and 200, respectively (Table I). The reason turned out to be a mistaken assumption that ID numbers were randomly distributed in relation to postal codes. Unfortunately this was not the case, due to unexpected postal return routines. There was thus a strong correlation between ID number and place of living. The other slight differences between the two NNT groups may be due to this difference in place of living. Adjustment for place of living in the regression analysis did not significantly alter our findings with respect to NNT. It thus seems unlikely that these findings can be attributed to the imperfect randomisation procedure.

Empirical evidence on how the NNT affects decision-making is sparse and stems almost entirely from surveys of people's opinions. Several studies have focused on framing effects (13–15). A consistent finding in these studies is that when decision-makers are presented with relative risk reductions they are more likely to consent to therapy than when presented with absolute risk reduction and/or NNT. Kristiansen et al. investigated how the magnitude of NNT affects lay people's stated willingness to take medication to

Table II. Logistic regression analysis: Odds ratios (OR) with 99% confidence intervals for medical doctors' recommendation for a life-long drug therapy to prevent premature death (n = 1265).

Variable	Univariate OR	Multivariate OR
NNT		
200 (reference)	1.0	1.0
50	2.6 (1.9; 3.5)	2.7 (2.0; 3.8)
Age		
> 35 (reference)	1.0	1.0
26–35	1.6 (1.1; 2.4)	1.6 (1.0; 2.5)
Gender		
Female (reference)	1.0	1.0
Male	0.8 (0.6; 1.2)	0.9 (0.7; 1.3)
Speciality		
None (reference)	1.0	1.0
Family and community medicine	0.8 (0.5; 1.2)	0.9 (0.5; 1.5)
Other (hospital medicine)	0.7 (0.5; 1.0)	0.7 (0.5; 1.1)
Time since entry in current position		
0–10 years (ref.)	1.0	1.0
11–20 years	1.0 (0.7; 1.6)	1.1 (0.7; 1.9)
21–30 years	1.0 (0.6; 1.8)	1.1 (0.6; 2.1)
More than 30 years	1.2 (0.7; 1.9)	1.1 (0.7; 1.8)

prevent heart attacks (8). Interestingly, their main finding was that about 80% consented to therapy whether the NNT was 10 or 400. This apparent insensitivity to the magnitude of the NNT was not reproduced in our survey of medical doctors. The finding that the youngest age group showed the greatest sensitivity for the difference in NNTs could be due to the fact that the concept of NNT is relatively new compared to relative or absolute risk reduction. However, since the recommendation for or against life-long preventive therapy is a complex decision, experienced clinicians may hold many other factors, e.g. the patients' preferences, as equally or more important than the magnitude of the NNT in the decision process. The cost of the intervention might be of importance too, but these issues cannot be adequately assessed from our data.

On the issue of medical doctors' interpretation of the NNT, our data are incomplete and should be interpreted with caution. We only asked the doctors who recommended against the therapy, in a rather indirect way, about their interpretations of NNT.

Table III. Logistic regression analysis: Odds ratios (OR) with 99% confidence intervals for agreement with "the wasted effort" argument[1] among non-prescribers (n = 464).

Variable	Univariate OR	Multivariate OR
NNT		
200 (reference)	1.0	1.0
50	0.8 (0.4; 1.4)	0.7 (0.4; 1.3)
Age		
> 35 (reference)	1.0	1.0
26–35	1.3 (0.6; 2.9)	2.0 (0.7; 5.2)
Gender		
Female (reference)	1.0	1.0
Male	0.7 (0.4; 1.5)	0.6 (0.3; 1.3)
Speciality		
None (reference)	1.0	1.0
Family and community medicine	2.5 (1.1; 5.7)	4.4 (1.7; 11.5)
Other (hospital medicine)	1.6 (0.9; 3.1)	3.0 (1.4; 6.6)
Time since entry in current position		
0–10 years (ref.)	1.0	1.0
11–20 years	1.0 (0.5; 2.2)	0.8 (0.3; 1.9)
21–30 years	1.3 (0.4; 3.9)	1.1 (0.3; 3.7)
More than 30 years	1.3 (0.5; 3.7)	1.5 (0.5; 4.6)

[1] "(NNT-1) individuals will not benefit from treatment".

Furthermore, some features of the clinical scenario might be confusing. The condition to be treated was presented as a disease, while "risk factor" would have been a more proper term. The endpoint to be assessed was premature death, but the disease leading to death was not specified. It was not therefore obvious whether a "wasted effort" interpretation (no benefit for (NNT-1) of the treated individuals) was reasonable or not. Because of this, we cannot know for sure why a substantial proportion of the doctors agreed with the "wasted effort" statement. The agreement may be based on considerations about what diseases might be compatible with our scenario, or it may reflect the doctors' intuitive interpretation of the NNT irrespective of the clinical setting. When doctors have been asked more directly about how they interpret the NNT, the responses have been similar to our findings (9). Thus, it seems that without careful consideration, the "wasted effort" interpretation is intuitively appealing and can be adopted whether justified or not.

We conclude that medical doctors appear to be sensitive to the magnitude of the NNT in their clinical recommendations. However, many doctors seem to believe that only one out of NNT patients benefits from therapy. This interpretation is adequate in lottery-like interventions, such as treatment of acute ailments, but may be misleading in interventions that postpone adverse outcomes in chronic diseases.

ACKNOWLEDGEMENTS

The study was financially supported by governmental funds held by the University of Tromsø and dedicated to medical research in Northern Norway.

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Paper II

ORIGINAL INVESTIGATION

Decisions on Drug Therapies by Numbers Needed to Treat

A Randomized Trial

Peder Andreas Halvorsen, MD; Ivar Sønbø Kristiansen, PhD

Background: The number needed to treat (NNT) has been promoted as the preferred effect measure when patients and physicians share decision making. Our aim was to explore the impact of the NNT on laypeople's decisions about preventive drug therapies.

Methods: Two thousand subjects were selected for the survey; 1201 (60%) responded for a representative sample of the Norwegian population. Respondents were allocated to scenarios with random combinations of a disease to be prevented, drug treatment costs, and effect size in terms of NNT. They were interviewed about their hypothetical consent to the therapy, then randomized to different interpretations of NNT and asked to reconsider their initial responses.

Results: The proportions consenting varied from 76% when the NNT was 50 to 67% when the NNT was 1600 (P for trend=.06). When faced with the prospect of avoiding lethal disease, stroke, myocardial infarction, or hip fracture, the proportions consenting were 84%, 76%, 68%, and 53%, respectively ($P<.01$). Across different treatment costs ($37, $68, $162, and $589) the proportions consenting varied from 78% to 61% (P for trend <.01). Twenty-four percent of the respondents changed their decision when informed about how to interpret the NNT, and 93% of those switched from positive to negative decisions, regardless of the magnitude of NNT.

Conclusions: Respondents' decisions were influenced by the type of disease to be prevented and the cost of the intervention, but not by the effect size in terms of NNT. This suggests that NNT is difficult to understand and that other effect formats should be considered for shared decision making.

Arch Intern Med. 2005;165:1140-1146

Since its introduction in 1988,[1] the number needed to treat (NNT) has gained wide acceptance as a cognitively useful effect measure for clinical practice.[2] Its popularity is probably based on the belief that the NNT conveys both clinical and statistical significance to physicians and their patients in a single, easily comprehended measure.[3,4] Somewhat inconsistently with this belief, emerging empirical evidence suggests that laypeople are insensitive to the magnitude of NNT when making decisions about hypothetical interventions. When presented with different NNTs in the interval from 10 to 400, 80% of the respondents stated that they would accept a drug to prevent heart attacks,[5] whereas 60% would accept a drug therapy to protect against hip fracture,[6] in both cases irrespective of the magnitude of NNT. However, these previous studies have been criticized on the grounds that the scope of effectiveness was too narrow (NNT at a maximum of 400), that the study samples were not entirely representative, or that respondents were not properly randomized.

The NNT is defined as the inverse value of absolute risk reduction,[3] but what does an NNT of 50, for example, really mean? A possible answer is that for every patient who benefits from therapy, 49 patients do not.[1,7,8] This interpretation implies that the NNT provides a direct measure of the individual's likelihood of having benefit from a therapy. This is reasonable for lotterylike interventions in which the events to be prevented occur in a truly random fashion. However, for interventions that postpone adverse events rather than completely prevent them, an NNT of 50 may be consistent with the possibility that several or even all of the 50 patients will have some benefit.[5] In that case, an NNT of 50 simply means that adverse events are postponed to such an extent that 1 fewer patient (of 50) has had adverse outcomes at the specific point in

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Financial Disclosure: None.

time when the NNT was measured. Examples of lottery-like interventions might be the use of seat belts and hip protectors, whereas antihypertensives or lipid-lowering drug therapies seem more like postponing interventions. Somewhere between is the use of bisphosphonates or estrogens to protect against hip fractures. These can be regarded as postponing interventions to the extent that the process of osteoporosis is halted, but because hip fractures usually involve an accidental fall, the lottery aspect is also relevant. Unfortunately, we cannot know if or when an individual will experience an adverse event. Consequently, we can never know what would happen to an individual with and without a preventive drug therapy; therefore, postponements and proportions that benefit from an intervention cannot be observed directly.[5] Valid interpretations of NNTs for different types of interventions thus seem to be a matter of judgment.

Although it seems important that clinicians be aware of different interpretations of NNTs, the issue has attracted little attention in the medical literature and its significance for communicating the benefits of therapy to potential patients has hardly been studied empirically. The objective of this study was to explore whether the previously observed insensitivity to the magnitude of NNT could be extended to a broader range of NNTs and reproduced for different diseases to be prevented, treatment costs, self-reported risk factors, and different interpretations of the NNT.

METHODS

Statistics Norway, Oslo, regularly performs surveys of the Norwegian population to assess living conditions, demographic variables, and people's habits, attitudes, and opinions. Specific topics of interest are selected by Statistics Norway or chosen by external institutions (eg, research institutions, governmental departments, public or commercial organizations) that purchase survey questions. In addition, each survey collects information on a fixed set of background variables.

As part of their regular population surveys, Statistics Norway invited a random sample of 2000 individuals for a personal interview between May 6 and June 29, 2002. To ensure a representative sample, the Norwegian population was divided into 109 different strata based on geographic and demographic characteristics. One geographic area from each stratum was randomly selected, and individuals were drawn from these areas with a probability proportional to the size of the population within each area. Noninstitutionalized individuals in the group aged 16 to 79 years were eligible, but otherwise there were no eligibility criteria. Written invitations with general information about the survey were mailed a few weeks before the interview, and the respondents were subsequently contacted by telephone for consent. Face-to-face interviews at the respondents' homes were encouraged, but telephone interviews were allowed. Data were collected by 126 interviewers with special training. There was no pilot study, but a small proportion of the interviewers tested the questionnaire by simulated interviews, which resulted in minor adjustments of some of the questions. The interviewers used portable computers with preprogrammed questionnaires and registered responses electronically during the interview (ie, computer-assisted interviewing).

For our study, the respondents were presented with a hypothetical clinical scenario with the following wording:

> Suppose your physician tells you that you have an increased risk of getting disease *x*. The physician offers you a drug therapy to prevent it. The drug is to be taken daily and has no serious adverse effects. You need to visit your physician twice a year for follow-up, and the drug therapy will cost you $y per year. The physician informs you that to prevent 1 case of disease *x*, NNT patients must adhere to the drug therapy for 3 years.

The computer was programmed to assign random values to *x* (type of disease), *y* (treatment costs), and NNT, and these values were not known to the interviewer until each interview started. Possible values for disease *x* were hip fracture, myocardial infarction, stroke, or lethal disease. The diseases were chosen to reflect a spectrum of disease severity and diseases for which preventive drug therapies are offered in clinical practice. The yearly treatment costs were set to represent common preventive drug therapies such as aspirin, hydrochlorothiazide, metoprolol, and finally alendronate sodium or simvastatin and could thus take the values of 250, 460, 1100, or 4000 NKr, respectively ($37, $68, $162, or $589, respectively). The NNTs were set at 50, 100, 200, 400, 800, or 1600. Each respondent was thus presented with a random combination of a disease to be prevented, treatment cost, and NNT. They were then asked the following question: "How likely is it that you would choose to take such a drug?" Possible response categories were certainly, probably, probably not, and certainly not. After the initial response, the interviewer first emphasized that it might be difficult to comprehend the effectiveness of the drug and then offered 1 of the following 3 possible interpretations of the NNT: "(NNT − 1) of the treated patients would have no benefit from the treatment," "it is unknown whether (NNT − 1) would benefit or not," and finally "most of the treated patients would benefit in terms of a slight postponement of the disease, but after 3 years of therapy only 1 case of the disease would be prevented." The respondents were then asked the same question about consent to the drug therapy. The choice of the NNT interpretation was made randomly by the computer during the interview. Possible response categories were the same as for the initial question.

We tested the hypotheses that increasing the NNT will reduce the proportion consenting to therapy; that the association between the magnitude of NNT and consent to therapy, if any, is dependent on the type of disease to be prevented, treatment costs, or the presence of self-reported risk factors; and that change in preference for the drug therapy, if any, is dependent on the kind of NNT interpretation provided. The primary outcome was the individuals' stated consent to therapy. Consent was prespecified as present if respondents answered certainly or probably, and it was absent if the response was otherwise. The secondary outcome, change in decision about drug therapy, was considered to be present if an initial consent or refusal was withdrawn after an interpretation of NNT was provided. Age, sex, place of residence, educational status, and income were selected as secondary independent variables possibly associated with the outcomes of interest.

We assessed differences between proportions with χ^2 tests, including χ^2 tests for trend when appropriate. First-order interactions between NNT and the other independent variables were tested in multivariate logistic regression models, including NNT, one other variable, and their product term. Also, we used logistic regression analysis to explore the association between consent to therapy and the independent variables. All of these analyses were prespecified in the protocol. Because the number of planned interviews was predetermined by Statistics Norway, no formal power calculation was performed. We used SPSS version 10.0 software (SPSS Inc, Chicago, Ill) for data analysis.

Table 1. Characteristics of Respondents Randomly Allocated to Different NNT Groups

	Magnitude of NNT, No. (%) of Respondents					
Variable	**50 (n = 203)**	**100 (n = 182*)**	**200 (n = 216)**	**400 (n = 197)**	**800 (n = 229)**	**1600 (n = 174)**
Background						
Age group, y						
16-24	26 (13)	26 (14)	30 (14)	28 (14)	28 (12)	18 (10)
25-44	94 (46)	78 (43)	88 (41)	86 (44)	103 (45)	68 (39)
45-66	66 (33)	52 (29)	81 (38)	60 (30)	74 (32)	69 (40)
67-79	17 (8)	16 (9)	17 (8)	23 (12)	24 (10)	19 (11)
Female	97 (48)	86 (47)	114 (53)	95 (48)	109 (48)	78 (45)
Region of residence						
Central	95 (47)	86 (47)	89 (41)	94 (48)	100 (44)	87 (50)
Southwest	67 (33)	56 (31)	78 (36)	67 (34)	79 (34)	57 (33)
Middle	21 (10)	19 (10)	19 (9)	15 (8)	19 (8)	18 (10)
North	20 (10)	21 (12)	30 (14)	21 (11)	31 (14)	12 (7)
Self-reported risk factors						
Hypertension	13 (6)	15 (8)	25 (12)	28 (14)	25 (11)	25 (14)
Hypercholesterolemia	16 (8)	20 (11)	19 (9)	8 (4)	15 (7)	16 (9)
Diabetes mellitus	5 (2)	3 (2)	3 (1)	2 (1)	4 (2)	7 (4)
Osteoporosis	4 (2)	2 (1)	1 (<1)	2 (1)	4 (2)	2 (1)
Education >12 y	65 (32)	45 (25)	70 (32)	40 (20)	64 (28)	52 (30)
Annual income, US $						
<29 000	65 (32)	75 (41)	87 (40)	71 (36)	91 (40)	60 (34)
29 000-43 000	53 (26)	43 (24)	64 (30)	62 (31)	63 (28)	43 (25)
>43 000	75 (37)	51 (28)	57 (26)	50 (25)	68 (30)	64 (37)
Missing	10 (5)	13 (7)	8 (4)	14 (7)	7 (3)	7 (4)
Variables randomly assigned to each respondent						
Disease to be prevented						
Lethal disease	47 (23)	38 (21)	48 (22)	49 (25)	58 (25)	54 (31)
Heart attack	59 (29)	49 (27)	65 (30)	45 (23)	62 (27)	47 (27)
Stroke	52 (26)	46 (25)	52 (24)	61 (31)	53 (23)	40 (23)
Hip fracture	45 (22)	49 (27)	51 (24)	42 (21)	56 (24)	33 (19)
Annual treatment cost, US $						
37	46 (23)	48 (26)	59 (27)	46 (23)	61 (27)	47 (27)
68	48 (24)	46 (25)	45 (21)	46 (23)	57 (25)	43 (25)
162	55 (27)	44 (24)	62 (29)	51 (26)	56 (24)	44 (25)
589	54 (27)	44 (24)	50 (23)	54 (27)	55 (24)	40 (23)
Interpretation of NNT						
Only 1/NNT will benefit	71 (35)	52 (29)	76 (35)	66 (34)	80 (35)	60 (34)
Small postponement for all	75 (37)	66 (36)	77 (36)	82 (42)	63 (28)	47 (27)
Benefit for (NNT − 1) unknown	57 (28)	63 (35)	63 (29)	49 (25)	86 (38)	67 (39)

Abbreviation: NNT, number needed to treat.
*For interpretation of NNT, n = 181.

RESULTS

Of the initial study sample (n = 2000), 464 refused to participate before they had any knowledge about our study questions; 215 could not be reached during the field period (May 6 to June 29, 2002); 14 had emigrated or died; and 106 persons could not participate for other reasons. Thus, 1201 individuals (60%) were randomly assigned to the different NNT groups. Most of the respondents (66.6%) preferred to be interviewed by telephone rather than face-to-face. The proportion female was 48%. Compared with the general population aged 16 to 79 years, the group of individuals 67 years or older was underrepresented (9.6% in the net sample vs 11%), whereas the group aged 25 to 44 years was overrepresented (43% vs 39%).[9] Also, the central part of Norway, including the capital city of Oslo, was underrepresented (20% vs 22%), whereas the southwest part of Norway was slightly overrepresented (15% vs 14%).[9] Twenty-three respondents did not answer the initial question about consent to the drug therapy, whereas 28 refused to answer this question after an interpretation of NNT was provided. For unknown reasons, 1 respondent was not allocated to any of the interpretations of NNT after the initial question about consent to drug therapy. Participants with missing responses were excluded from the analysis. There were no major imbalances between the different NNT groups (**Table 1**).

The proportion consenting to the drug therapy was greater when the disease to be prevented was more serious, when the treatment costs were lower, or when at least 1 self-reported risk factor was present (**Table 2**). This was the case before and after an interpretation of the NNT was provided. A weak, nonsignificant trend to-

Table 2. Laypeople's Consent to Hypothetical Preventive Drug Therapies Before and After Explanation of NNT

Variable	Consent Before Interpretation of NNT		Consent After Interpretation of NNT	
	No. (%)	*P* Value	No. (%)	*P* Value
Magnitude of NNT				
50	151/200 (76)	.06*	106/200 (53)	.54*
100	127/178 (71)		82/177 (46)	
200	146/210 (70)		101/208 (49)	
400	139/195 (71)		106/194 (55)	
800	153/224 (68)		98/222 (44)	
1600	114/171 (67)		86/171 (50)	
Disease to be prevented				
Lethal disease	238/283 (84)	<.001	183/281 (65)	<.001
Stroke	230/301 (76)		162/299 (54)	
Heart attack	219/323 (68)		151/322 (47)	
Hip fracture	143/271 (53)		83/270 (31)	
Annual treatment cost, US $				
37	222/303 (73)	<.001*	159/302 (53)	.002*
68	218/280 (78)		148/280 (53)	
162	213/304 (70)		160/304 (53)	
589	177/291 (61)		112/286 (39)	
Self-reported risk factors				
≥1 Present	164/209 (78)	.005	121/207 (58)	.004
Absent	666/969 (69)		458/965 (47)	
Interpretation of NNT	NA			
Only 1/NNT will benefit			192/396 (48)	.43
Small postponement for all			196/376 (52)	
Benefit for NNT − 1 unknown			191/400 (48)	
Total	830/1178 (70)		579/1172 (49)	

Abbreviations: NA, not applicable; NNT, number needed to treat.
*Determined by χ^2 test for trend.

ward decreasing consent to therapy with increasing NNT was observed (76%, 71%, 70%, 71%, 68%, and 67% for NNTs of 50, 100, 200, 400, 800, and 1600, respectively; χ^2 test for trend, 3.5; $P=.06$). After the interpretation of NNT was given, the overall proportion consenting to therapy declined from 70% to 49%, and the trend toward lower consent with increasing NNT disappeared (χ^2 test for trend, 0.4; $P=.54$). Of 1172 respondents, 282 (24%) changed their opinion about the drug therapy when provided with an interpretation of the NNT. Two hundred sixty-three (93%) of 282 withdrew their initial consent, whereas 19 (7%) of 282 changed their decision in the opposite direction.

In logistic regression analysis, male sex was an additional significant predictor of consent to therapy (**Table 3**). No significant interactions between NNT and the other independent variables were detected; consent to therapy by NNT in different subgroups of treatment costs and diseases to be prevented is provided in **Table 4**. The magnitude and interpretation of the NNT were not significant predictors for changing opinion about the drug therapy (Table 3).

COMMENT

When considering long-term preventive drug therapies, respondents were insensitive to the magnitude of NNT, even after they were informed about its interpretation, whereas they were sensitive to the type of adverse events and treatment costs. These findings suggest that laypeople have difficulties in understanding the concept of NNT. Although the general population may not be entirely representative of patients, clinicians should probably observe that information about effect measures solely in terms of NNTs may have limited impact on patients' decisions.

The statistical[10-12] and clinical[1,3,4,13] properties of the NNT have been extensively described and debated on a theoretical basis, but empirical evidence from clinical practice is sparse. Fahey et al[14] compared the use of NNT to absolute risk reduction in a clinical guideline for cardiovascular risk management, but no effect on short-term patient surrogate end points was detected. Other empirical evidence stems from surveys of laypeople,[5] patients,[15] physicians,[7,16-18] and health administrators.[19] A consistent finding is the lower proportion of consent to therapy when treatment effects are presented as NNT or absolute risk reduction rather than relative risk reduction. Insensitivity to the magnitude of NNT is present among laypeople,[5] but not among physicians.[7] The present study adds to and extends the evidence of laypeople's low sensitivity to the magnitude of NNT, which is reproduced across different diseases, treatment costs, and interpretations of NNT. Similar findings have recently been demonstrated across different adverse effects of preventive drug therapies.[20] To our knowledge, there are no similar studies of patients facing real decisions.

Works in the field of cognitive psychology have emphasized heuristics, ie, techniques people use to simplify complex decisions. The availability heuristic im-

Table 3. Multivariate Logistic Regression Analysis

Variable	Consent to Therapy OR* (95% CI)	Consent to Therapy P Value	Changing Consent to Therapy OR* (95% CI)	Changing Consent to Therapy P Value
Magnitude of NNT				
50 (Reference)	1.00	.23	1.00	.63
100	0.79 (0.51-1.23)		1.02 (0.63-1.65)	
200	0.86 (0.57-1.31)		0.79 (0.49-1.27)	
400	1.09 (0.71-1.68)		0.85 (0.52-1.37)	
800	0.68 (0.45-1.03)		0.92 (0.58-1.46)	
1600	0.75 (0.48-1.16)		0.67 (0.39-1.13)	
Interpretation of NNT	NA			
Postponement for all (reference)			1.00	.32
Only 1/NNT will benefit			0.80 (0.57-1.13)	
Benefit for (NNT – 1) unknown			0.79 (0.56-1.12)	
Disease to be prevented				
Lethal disease (reference)	1.00	<.001	1.00	.18
Heart attack	0.46 (0.32-0.65)		1.33 (0.88-2.01)	
Stroke	0.60 (0.43-0.86)		1.34 (0.88-2.03)	
Hip fracture	0.22 (0.15-0.32)		1.62 (1.06-2.48)	
Annual treatment cost, US $				
37 (reference)	1.00	.001	1.00	.82
68	0.97 (0.68-1.38)		1.15 (0.77-1.72)	
162	1.01 (0.71-1.42)		0.95 (0.63-1.42)	
589	0.54 (0.38-0.77)		1.05 (0.70-1.57)	
Self-reported risk factors				
≥1 Present (reference)	1.00	.08	1.00	.77
Absent	0.73 (0.52-1.03)		0.94 (0.63-1.41)	
Age, y				
16-24 (Reference)	1.00	.26	1.00	.14
25-44	0.79 (0.51-1.22)		0.82 (0.52-1.31)	
45-66	1.06 (0.68-1.65)		0.61 (0.37-1.00)	
>66	0.91 (0.52-1.58)		0.97 (0.54-1.76)	
Sex				
Female (reference)	1.00	.01	1.00	.26
Male	1.41 (1.07-1.85)		0.84 (0.61-1.14)	
Region of residence				
North (reference)	1.00	.38	1.00	.005
Central, capital included	1.14 (0.75-1.73)		0.76 (0.47-1.23)	
Southwest	0.90 (0.59-1.38)		1.28 (0.79-2.07)	
Middle	0.89 (0.51-1.55)		1.48 (0.81-2.71)	
Length of education, y				
>12 (Reference)	1.00	.64	1.00	.52
0-12	0.93 (0.69-1.26)		1.13 (0.79-1.60)	
Annual income, US $				
<29 000 (Reference)	1.00	.11	1.00	.18
29 000-43 000	0.80 (0.57-1.12)		0.99 (0.69-1.44)	
>43 000	1.14 (0.79-1.65)		0.70 (0.45-1.09)	

Abbreviations: CI, confidence interval; NA, not applicable; NNT, number needed to treat; OR, odds ratio.
*Calculated as the odds for laypeople to consent to therapy and to change their decision after being informed about an interpretation of NNT.

plies that people tend to overemphasize issues that are easily brought to mind.[21] When exposed to affect-rich outcomes, people tend to be sensitive to deviations from probabilities of zero and one, but insensitive to nonzero probabilities,[22] ie, affect heuristic. Such heuristics might explain why our respondents were sensitive to diseases and costs but not to NNT.

Another important issue seems to be the basic skills of laypeople with numbers (numeracy), which may be quite poor even among well-educated people.[23] Positive correlation between numeracy and accuracy of risk perception has been shown.[23,24] A survey of medical students demonstrated a high proportion of good numeracy, yet only 25% of them interpreted the NNT correctly compared with 75% for other risk-reduction formats.[24] Among patients at a university internal medicine clinic, only 7% made accurate risk estimates on the basis of NNT.[25] These works represent a more direct approach to the assessment of people's understanding of NNTs.

We acknowledge that our study has several limitations. First, the study design did not directly address people's comprehension of the meaning of NNT, leaving open the possibility that people were unwilling rather than unable to make use of NNTs in their decisions. Unfortunately, we did not include measures of numeracy and literacy as possible covariates. Because respondents were randomized to different NNTs, it is unlikely that such

Table 4. Consent to a Hypothetical Drug Therapy by NNT in Different Subgroups of Disease to Be Prevented and Treatment Costs

	Disease to Be Prevented			
	Lethal Disease	Stroke	Heart Attack	Hip Fracture
NNT, No. (%)				
1600	35/52 (67)	23/40 (58)	19/47 (40)	9/32 (28)
800	27/53 (51)	26/51 (51)	32/62 (52)	13/56 (23)
400	33/48 (69)	34/61 (56)	21/45 (47)	18/40 (45)
200	32/45 (71)	27/50 (54)	28/64 (44)	14/49 (29)
100	23/37 (62)	25/46 (54)	25/46 (54)	9/48 (19)
50	33/46 (72)	27/51 (53)	26/58 (45)	20/45 (44)
OR* (95% CI)	1.08 (0.94-1.25)	0.99 (0.86-1.13)	1.02 (0.90-1.16)	1.08 (0.92-1.26)
	Cost of Treatment to Prevent Diseases			
	$37	$68	$162	$589
NNT, No. (%)				
1600	23/46 (50)	26/43 (60)	19/43 (44)	18/39 (46)
800	34/60 (57)	23/54 (43)	26/54 (48)	15/54 (28)
400	26/45 (58)	31/46 (67)	29/51 (57)	20/52 (38)
200	27/58 (47)	22/44 (50)	32/58 (55)	20/48 (42)
100	26/47 (55)	19/45 (42)	23/43 (53)	14/42 (33)
50	23/46 (50)	27/48 (56)	31/55 (56)	25/51 (49)
OR* (95% CI)	0.98 (0.85-1.12)	0.97 (0.84-1.11)	1.09 (0.95-1.25)	1.07 (0.92-1.23)

Abbreviations: CI, confidence interval; NNT, number needed to treat; OR, odds ratio.

*Based on univariate logistic regression analysis with consent to therapy as the dependent variable and NNT as the independent variable. The NNT was entered into the model as an ordinal variable with values from 1 to 6 for NNTs from 1600 to 50, respectively. Thus, the OR represents the likelihood for consenting to therapy for 1 magnitude of NNT (eg, 1600) relative to an NNT of half that magnitude (eg, 800).

factors confounded our results. Others have shown that, when asked directly, substantial proportions of laypeople are uncertain about how to interpret NNTs[20] and that their numerical understanding of NNTs is poor.[24,25] Our study added an attempt to explain NNTs to the respondents. In general they became more skeptical to the intervention in question but did not give more weight to the magnitude of NNTs in their decisions.

About 40% of the initial sample did not participate in this study. There were only minor differences, however, between the responders and the general Norwegian population regarding age, sex, and place of residence. Thus, we believe that our respondents are fairly representative of the general population. About 2 of every 3 respondents preferred to be interviewed by telephone. As a consequence, the interviewers could not rely on such factors as eye contact and facial expressions as possible cues to poor understanding of the questions. However, the decision to be interviewed by telephone or at home was made before randomization to the different scenarios. Therefore the mode of interview should not bias our results. Because our finding of insensitivity to NNTs essentially was a null result, formal calculation of sample size in advance would have been helpful in interpreting the results. The confidence intervals (Tables 3 and 4), however, indicate that NNTs had at most a very modest effect on the respondents' decisions. The scenarios we used were not extensively tested in pilot studies. Important cues present in all the scenarios might thus have influenced the responses so as to mask the real effect of NNT, eg, that the drug therapy was proposed by the physician or that adverse effects were not specified beyond the notion that they were not serious. The high proportion consenting could thus reflect laypeople's trust in their physicians[21] or the perception that there was not much to lose. However, because the respondents discriminated between different diseases and treatment costs, we find it unlikely that such factors can explain the insensitivity to the magnitude of NNT.

In our opinion, the body of empirical evidence suggests limited ability rather than limited willingness to make use of NNTs. Previous studies have shown that patients may be more able to understand risks in terms of natural frequencies or visual risk representations than in terms of probabilities or percentages such as absolute and relative risks.[26] Expressing treatment effects in terms of natural frequencies might thus be a better option. When the benefit of an intervention is judged to be in terms of postponement rather than complete prevention, informing people directly about these postponements might be a promising strategy. One might say, eg, "On average, this drug therapy postpones heart attacks by *x* months." Emerging empirical evidence indicates that laypeople are more sensitive to such effect measures than to NNTs.[6,27]

Notwithstanding the limitations, in this study laypeople gave almost no weight to effect size in terms of NNTs when considering long-term preventive drug therapies. In this context, the NNT may have limited value as a communication tool. Therefore, clinicians may do well to use NNT with caution when informing patients about the benefits of medical interventions.

Accepted for Publication: December 31, 2004.

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Funding/Support: This study was supported by governmental funds held by the University of Tromso, Tromso, Norway, and dedicated to medical research in Northern Norway.
Previous Presentation: This study was presented at the 13th Nordic Congress of General Practice; September 2, 2003; Helsinki, Finland; and at the 9th Biennial Conference of the European Society for Medical Decision Making; June 8, 2004; Rotterdam, the Netherlands.

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Paper III

ARTICLE | Annals of Internal Medicine

Different Ways to Describe the Benefits of Risk-Reducing Treatments

A Randomized Trial

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Background: How physicians communicate the risks and benefits of medical care may influence patients' choices. Ways to communicate the benefits of risk-reducing drug therapies include the number needed to treat (NNT) to prevent adverse events, such as heart attacks or hip fractures, and gains in disease-free life expectancy or postponement of adverse events. Previous studies suggest that the magnitude of the NNT does not affect a layperson's decision about risk-reducing interventions, but postponement of an adverse event does affect such decisions.

Objective: To examine laypersons' responses to scenarios that describe benefits as postponing an adverse event or the equivalent NNT.

Design: Cross-sectional survey with random allocation to different scenarios.

Setting: General community.

Participants: Respondents to a population-based health study.

Intervention: The survey presented scenarios regarding a hypothetical drug therapy to reduce the risk for heart attacks (1754 respondents) or hip fractures (1000 respondents). The data sources for both scenarios were clinical trials. Respondents were randomly assigned to a scenario with 1 of 3 outcomes after 5 years of treatment. For the drug to prevent heart attacks, the outcomes were postponement by 2 months for all patients, postponement by 8 months for 1 of 4 patients, or an NNT of 13 patients to prevent 1 heart attack. For the drug to prevent hip fractures, the outcomes were postponement by 16 days for all patients, postponement by 16 months for 3 of 100 patients, or an NNT of 57 patients to prevent 1 fracture.

Measurements: Consent to receive the intervention and perceived ease of understanding the treatment effect.

Results: The overall rate of response to the survey was 81%. In the heart attack scenarios, 93% of respondents who were presented with the NNT outcome consented to drug therapy, 82% who were presented with the outcome of large postponement for some patients consented to therapy, and 69% who were presented with the outcome of short postponement for all patients consented to therapy (chi-square, 89.6; $P < 0.001$). Corresponding consent rates for the hip fracture scenarios were 74%, 56%, and 34%, respectively (chi-square, 91.5, $P < 0.001$). Respondents who said that they understood the treatment effect were more likely to consent to therapy.

Limitation: Decisions were based on hypothetical scenarios, not real clinical encounters.

Conclusions: Treatment effects expressed in terms of NNT yielded higher consent rates than did those expressed as equivalent postponements. This result suggests that the description of the anticipated outcome may influence the patient's willingness to accept a recommended intervention.

Ann Intern Med. 2007;146:848-856. www.annals.org
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Considerable resources are devoted to drug therapies that are aimed at modifying risk factors, such as hypertension, elevated cholesterol levels (1), and osteoporosis. For individual patients, the choice to begin preventive drug therapy should be consistent with their values and preferences. Thus, to engage meaningfully in shared decision making and to provide truly informed consent, patients need to have a clear understanding of the benefits and harms of a treatment. Strong and consistent evidence shows that stated preferences for medical interventions may depend on how the treatment effects are described. For example, the likelihood of choosing a therapy may depend on whether its benefits are presented as absolute risk reductions or relative risk reductions (2) or as losses versus gains (3–5). These effects suggest the potential for influencing the patient's response by describing treatment effects in a certain way. We explore laypersons' responses to different ways of explaining possible outcomes of an intervention.

When informing decision makers about the benefit of risk-reducing drug therapies, several authors have advocated using the number needed to treat (NNT) to avoid 1 outcome (6–10), which is defined as the reciprocal of the absolute risk reduction. The NNT is the average number of patients in an intervention group who must be treated for a specific period to observe 1 fewer adverse outcome by the end of this period compared with those in a control group. Several authors believe that NNT provides an easily understood way to describe the effort needed to prevent adverse outcomes (9–11). However, for drug therapies aimed at disease processes that develop slowly, such as atherosclerosis and osteoporosis, the term *prevention* may be misleading. Rather than completely preventing adverse outcomes in a small fraction of patients, an intervention

See also:

Print

Web-Only

may postpone the event for many treated patients. Describing the outcome of treatment in terms of postponing an event may be a good alternative to using NNT for helping patients to understand the potential consequences of a decision.

We hypothesized that when laypersons consider preventive drug therapies, they will find the concept of time—and, hence, postponements—more useful than the concept of NNT. Specifically, we tested the hypotheses that laypersons perceive information about postponements as being easier to understand than the concept of NNT and that the rates at which a person consents to hypothetical drug therapies may depend on the measure that is used to describe the drugs' effects.

METHODS

Participants

In 2002, as part of regional health surveys in Norway (12, 13), the Norwegian Institute of Public Health invited all inhabitants born in 1925 to 1947, 1957, 1962, and 1972 and all persons born in 1948 to 1968 who had been invited to former screenings in Finnmark County, Norway, to participate in the Troms and Finnmark (TROFINN) health study (13). For each participant, blood pressure and body mass index were measured and a blood sample was drawn to measure lipids and glucose levels. The participants completed 2 comprehensive questionnaires that included sociodemographic data; health-related information; and habits regarding exercise, food and alcohol consumption, and smoking. Two weeks after screening, the participants received a letter with their results. Participants who were at high risk for cardiovascular disease were advised to contact their general practitioner for follow-up.

For our study, we surveyed a sample of participants from the TROFINN study (who lived in 10 municipalities along the coast of Finnmark) about their preferences for risk-reducing drug therapies. Figure 1 shows the formation of our study sample. Of the 11 284 persons invited to screening, 6854 (61%) participated, of whom 6445 were eligible for our study. Eligibility was based on the person's written consent to allow researchers to use data from the initial screening and his or her willingness to be approached about future surveys. We excluded persons who died or emigrated between the initial screening and the date of our survey and those with a missing address. For other study purposes (14), we ranked the participants according to their cardiovascular risk to identify high-risk (n = 754) and low-risk (n = 1000) persons. We surveyed these persons about whether they would use a hypothetical drug aimed at reducing the risk for a heart attack. We also surveyed a random sample of the remaining persons (n = 1000) about whether they would use a hypothetical drug to reduce the risk for hip fracture. To maximize the response rate, we mailed 1 reminder letter and a copy of the questionnaire to nonresponders. We planned to enroll approximately 1000 persons in each group, but the number of high-risk persons was lower than expected.

Context

In previous research, different ways of describing the outcomes of an intervention led to different health care decisions.

Contribution

Healthy people were randomly assigned to receive equal but different descriptions of the outcome of a hypothetical intervention to prevent myocardial infarction (MI). Responders were more likely to consent to treatment when the outcome was described as the number needed to treat to prevent 1 MI. They were less likely to consent when the intervention was described as not preventing but delaying an MI by 2 months for all persons or by 8 months for 25% of persons.

Caution

The scenarios were presented in a survey and were hypothetical.

Implication

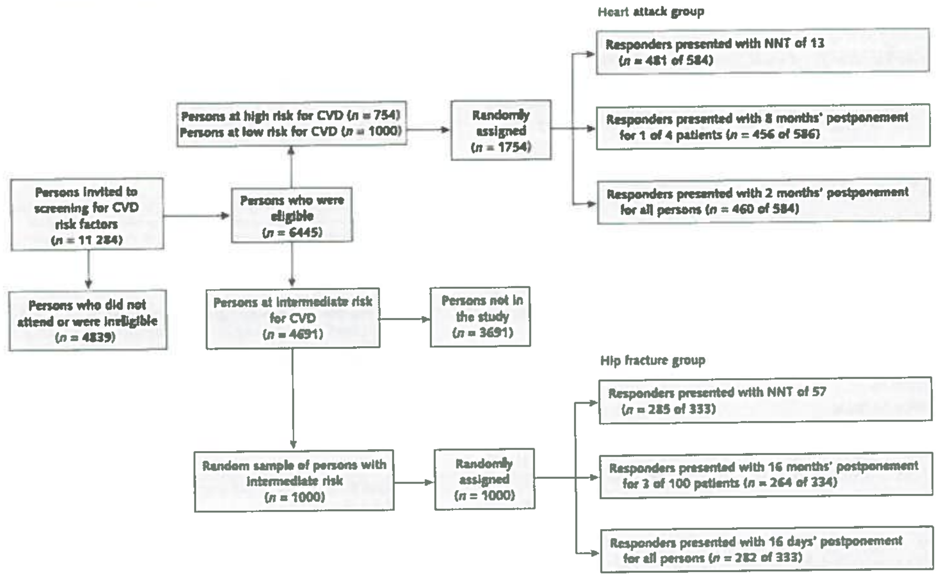
Quantitatively equal but differently worded outcomes elicit different health care decisions.

—The Editors

Procedures

We presented a scenario that described hypothetical drug therapy to prevent a heart attack to persons in 1 group and a scenario that described such therapy to prevent hip fracture to persons in the other group (**Figure 2**). Using data from the Scandinavian Simvastatin Survival Study (15, 16), we calculated the NNT to prevent 1 heart attack after 5 years of therapy (NNT, 13) and the number of participants for whom treatment would postpone a heart attack and the length of the disease-free interval (a 2-month average postponement for all patients and an 8-month postponement for 1 of 4 patients, with no benefit for 3 of 4 patients) (**Figure 2**; **Appendix** Tables 1 and 2, available at www.annals.org). We used a computerized random-sample function (SPPS, Chicago, Illinois) to randomly assign respondents in the high-risk and low-risk groups to 1 of the 3 scenarios (**Figure 1**). We also calculated the benefit of hip fracture prevention after 5 years of therapy using data from the Fracture Intervention Trial (17). The NNT to prevent 1 hip fracture was 57. Alternatively, as a result of treatment, all patients would have a hip fracture 16 days later than they would have without treatment or only 3 of 100 patients would have a hip fracture 16 months later than they would have without treatment, whereas the remaining patients would not benefit (**Figure 2**; **Appendix** Tables 1 and 2, available at www.annals.org). Again, allocation to the 3 scenarios was random. One survey question asked respondents whether they found it very easy, somewhat

Figure 1. **Study flow diagram.**



A total of 2754 attendees to a population-based health study were randomly assigned to hypothetical scenarios that presented the benefits of preventive drug therapies in terms of number needed to treat (*NNT*) or postponement of adverse events. Eligibility criteria were as follows: attended screening, consented to additional studies, were alive or did not emigrate between the time of the screening and the survey, and had a known address. Strategic allocation to the study groups by risk for cardiovascular disease (*CVD*) was done for other study purposes, and for similar reasons, the low-risk sample was selected so that the proportion of women was the same as that in the high-risk sample (14). We expected to enroll approximately 1000 persons in each risk group, but the number of high-risk persons was lower than expected.

easy, somewhat difficult, or very difficult to understand the treatment effect. Another question asked whether the respondent would consent to the hypothetical drug therapy because of the benefits described in the scenario. Possible response categories were "certainly," "probably," "probably not," or "certainly not." We linked each respondent's answers to his or her responses to the health survey given by the Norwegian Institute of Public Health.

Outcome Measures

We tested the hypotheses that more respondents would report difficulties in understanding the NNT effect format than the 2 postponement formats and that the proportion of respondents who consented to therapy would differ among the 3 scenarios. Therefore, the primary outcome measures were the rates of consent to therapy and the difficulty in understanding the effect format. Although the survey provided the respondent with several graded responses, we dichotomized these variables when we analyzed the survey data. Therefore, we defined difficulty as a response of "very difficult" or "quite difficult." We defined consent as a response of "certainly" or "probably" to the question regarding willingness to consent to the therapy. Analysis of these variables as 4-point responses instead of as dichotomous responses yielded similar results, but for ease of understanding, we present the results with the responses grouped as described. To test whether difficulty understanding the outcome measure had an effect on consent rates, we analyzed the perceived difficulty of understanding as a possible predictor of consent to therapy. We used age, sex, level of education, self-reported health state, smoking habits, and psychiatric symptoms as secondary independent variables in both study groups. In the heart attack group, history of cardiovascular diseases, use of lipid-lowering agents or antihypertensive medications, and premature coronary heart disease among close relatives were additional secondary variables. We used a history of fractures as a secondary variable in the hip fracture group.

Statistical Analysis

We evaluated differences between proportions by using chi-square tests. We used log–Poisson regression with robust SEs to explore possible associations (expressed as relative risks) between the dependent variables (primary outcome measures) and independent variables other than effect format. We tested for first-order interactions between effect format and other independent variables by adding product terms to the regression models. We also tested for interaction between level of education and perceived difficulty of understanding in predicting consent to therapy (dependent variable). We did not perform formal power calculations when we designed the study. We used SPSS, version 10.0 (SPSS), and Stata, version 9.2 (Stata Corp., College Station, Texas). The Norwegian Data Inspectorate approved the TROFINN study, and the regional committee for medical research ethics evaluated the study. We conducted the study in accordance with the Declaration of Helsinki.

Role of the Funding Source

The funding body had no involvement in the design of the study, data collection and interpretation, or decision to submit the manuscript for publication.

Results

Study Sample

In the heart attack group, 1397 of 1754 (80%) participants responded to the questionnaire, whereas 831 of 1000 (83%) participants in the hip fracture group responded. In the respective study groups, the mean age of the participants was 58 years (SD, 11) and 60 years (SD, 10) and the proportion of women was 34% and 60%. Nonresponders did not differ substantially from responders with respect to age and sex. In the heart attack group, responders were slightly better educated than were nonresponders (10.4 years [95% CI, 10.2 to 10.6 years] vs. 9.9 years [CI, 9.5 to 10.3 years]). In the hip fracture group, more responders than nonresponders (62% [CI, 59% to 65%] vs. 53% [CI, 45% to 61%]) reported good health. In

Figure 2. **The questionnaire for the heart attack group.**

Imagine that your doctor informs you that your risk for heart attack is elevated. The doctor suggests that you take a drug to prevent a heart attack. The drug must be taken daily, and you will have to visit your doctor twice a year for a check-up. Side effects are neither common nor dangerous. Drug costs are refunded according to the rules of the National Health Insurance.

Q1a. The doctor informs you that for every heart attack that is prevented, 13 patients have to take the drug for 5 years.

or

Q1b. The drug therapy may not completely prevent heart attacks. Rather, it postpones heart attacks for a while. The doctor informs you that all patients who take the drug therapy for 5 years will live about 2 months longer before they get a heart attack.

or

Q1c. The drug therapy may not completely prevent heart attacks. Rather, it postpones heart attacks for a while. The doctor informs you that 1 of 4 patients who take the drug for 5 years will live about 8 months longer before they get a heart attack, whereas the others will have no benefit from the drug therapy.

Would you choose to take this drug?

☐ Certainly ☐ Probably ☐ Probably not ☐ Certainly not

Q2. Did you find it easy or difficult to understand the magnitude of the effect of this drug therapy?

☐ Very easy ☐ Somewhat easy ☐ Somewhat difficult ☐ Very difficult

In each questionnaire, only 1 of the 3 versions of item Q1 (a, b, or c) was used. The respondents were randomly allocated to 1 version of the questionnaire only. We used similar scenarios with different numbers for the hip fracture questionnaire.

Table 1. **Characteristics of Respondents***

Variable	Scenario		
	NNT to Prevent 1 Outcome (95% CI)	Long Postponement of an Outcome for Some Patients (95% CI)	Short Postponement of an Outcome for All Patients (95% CI)
Heart attack group			
Mean age, y	58 (57–59)	58 (57–59)	57 (56–58)
Women, %	32 (28–36)	37 (32–41)	34 (30–38)
Education >12 y, %	22 (18–25)	23 (19–27)	24 (20–28)
Good self-reported health, %	61 (56–65)	62 (57–66)	63 (58–67)
History of cardiovascular diseases, %	21 (18–25)	20 (16–24)	21 (17–24)
Hip fracture group			
Mean age, y	60 (59–61)	60 (59–61)	60 (59–61)
Women, %	56 (50–62)	63 (57–69)	62 (57–68)
Education >12 y, %	19 (14–24)	20 (15–25)	20 (15–24)
Good self-reported health, %	61 (56–67)	60 (54–66)	65 (59–70)
History of fractures, %	15 (11–19)	11 (7–15)	13 (9–17)

* For the heart attack group, there were 481, 456, and 460 respondents in the NNT scenario, long postponement of an outcome scenario, and short postponement of an outcome scenario, respectively. For the hip fracture group, these numbers were 285, 264, and 282, respectively. Missing responses were 4% or less for all categories. For some categories, the number of respondents may therefore be slightly lower than indicated. NNT = number needed to treat.

Table 2. **Rates of Consent to Therapy and Difficulties with Understanding the Treatment Effect***

Variable	NNT to Prevent 1 Outcome	Long Postponement of Outcome for Some Patients	Short Postponement of Outcome for All Patients
Persons in the heart attack group, *n* (%)			
Would you choose to take this drug?			
Certainly	273 (47)	190 (32)	153 (26)
Probably	172 (29)	179 (31)	162 (28)
Probably not	24 (4)	66 (11)	94 (16)
Certainly not	10 (2)	17 (3)	49 (8)
Missing responses or nonresponders	105 (18)	134 (23)	126 (22)
Was it difficult or easy to understand the magnitude of the effect of this drug therapy?			
Very easy	96 (16)	80 (14)	85 (15)
Somewhat easy	226 (39)	219 (37)	189 (32)
Somewhat difficult	133 (23)	131 (22)	145 (25)
Very difficult	25 (4)	22 (4)	37 (6)
Missing responses or nonresponders	104 (18)	134 (23)	128 (22)
Persons in the hip fracture group, *n* (%)			
Would you choose to take this drug?			
Certainly	78 (23)	50 (15)	27 (8)
Probably	132 (40)	98 (29)	69 (21)
Probably not	48 (14)	77 (23)	89 (27)
Certainly not	25 (8)	39 (12)	96 (29)
Missing responses or nonresponders	50 (15)	70 (21)	52 (16)
Was it difficult or easy to understand the magnitude of the effect of this drug therapy?			
Very easy	36 (11)	50 (15)	58 (17)
Somewhat easy	81 (24)	81 (24)	76 (23)
Somewhat difficult	114 (34)	96 (29)	88 (26)
Very difficult	51 (15)	37 (11)	59 (18)
Missing responses or nonresponders	51 (15)	70 (21)	52 (16)

* For the heart attack group, there were 584, 586, and 584 participants in the NNT scenario, long postponement of an outcome scenario, and short postponement of an outcome scenario, respectively. For the hip fracture group, these numbers were 333, 334, and 333, respectively. NNT = number needed to treat.

both groups, participants in the 3 scenarios were fairly balanced in age, sex, education, self-assessed overall health, and history of cardiovascular diseases or fractures (Table 1).

Responses to the Scenarios

Table 2 shows the numbers of responses for each study group. In both groups, the proportion of respondents who consented to therapy was highest when the treatment effects were presented in terms of NNT, intermediate when treatment effects were presented as a long postponement of the outcome for a fraction of the patients, and lowest when treatment effects were presented as a short postponement of the outcome for all patients (Table 3). The differences were statistically significant in the heart attack group (93% [CI, 91% to 95%] vs. 82% [CI, 78% to 85%] vs. 69% [CI, 65% to 73%]; chi-square, 90; $P < 0.001$) and in the hip fracture group (74% [CI, 69% to 78%] vs. 56% [CI, 50% to 62%] vs. 34% [CI, 29% to 40%]; chi-square, 92; $P < 0.001$). In the regression analysis, greater perceived ease of understanding the effect measure and less education were additional independent predictors of consent to therapy (Table 3). Many persons in both study groups had difficulty understanding the treatment effect (Table 4), but differences among the scenarios were not statistically significant. Regression analysis of the hip fracture data—but not the heart attack data—indicated that difficulties were greater among older persons and those with less education (Table 4).

Discussion

In this population-based survey, laypersons were more inclined to accept therapy to reduce the risk for heart attack or hip fracture when the benefit was presented as the NNT to prevent 1 adverse outcome than when presented as postponements of the outcome. The benefits described in all 3 scenarios were equivalent because we used the same clinical study to calculate them. Many respondents reported difficulty understanding the description of treatment benefit regardless of how we presented it, and such persons were less likely to consent to therapy. These findings are intriguing when placed in the context of informed consent, patient-directed choices, and shared decision making. Because assisting patients in decision making is a core element of the physician's work, knowing that decisions may be influenced by the words used to describe benefits, and perhaps harms, is important for clinical practice. The main body of empirical knowledge, however, stems from the field of experimental cognitive psychology.

Seminal works in cognitive psychology (3) and medical decision making (4) have emphasized that a person's

Table 3. **Respondents' Consents to a Drug Therapy Aimed at Preventing Heart Attacks or Hip Fractures***

Variable	Heart Attack Group		Hip Fracture Group	
	Respondents Consenting to the Drug Therapy, *n/n (%)*	Relative Risk (95% CI)	Respondents Consenting to the Drug Therapy, *n/n (%)*	Relative Risk (95% CI)
Effect measure				
Postponement: same benefit for all persons (reference)	315/458 (69)	1.00	96/281 (34)	1.00
Postponement: greater benefit for some persons	369/452 (82)	1.17 (1.08–1.27)	148/264 (56)	1.60 (1.31–1.96)
NNT	445/479 (93)	1.34 (1.25–1.44)	210/283 (74)	2.16 (1.80–2.59)
Perception of effect measure				
Easy to understand	792/894 (89)	1.28 (1.20–1.37)	235/382 (62)	1.36 (1.21–1.54)
Difficult to understand (reference)	335/490 (68)	1.00	216/442 (49)	1.00
Age		1.03 (1.00–1.06)†		1.04 (0.96–1.11)†
<50 y (reference)	192/266 (72)		58/117 (50)	
50–59 y	398/485 (82)		150/281 (53)	
60–69 y	351/418 (84)		143/265 (54)	
≥70 y	188/220 (86)		103/165 (62)	
Sex				
Women (reference)	378/476 (79)	1.00	269/499 (54)	1.00
Men	751/913 (82)	1.00 (0.94–1.06)	185/329 (56)	1.00 (0.88–1.14)
Length of education		0.96 (0.93–1.00)†		0.85 (0.77–0.93)†
0–9 y (reference)	526/620 (85)		250/406 (62)	
10–12 y	347/428 (81)		123/241 (51)	
≥12 y	230/310 (74)		69/159 (43)	
Self-reported health condition				
Not good or bad	434/528 (82)	0.96 (0.91–1.02)	186/311 (60)	1.08 (0.95–1.23)
Good or excellent (reference)	687/853 (81)	1.00	268/515 (52)	1.00
Psychiatric symptoms				
Yes (reference)	611/761 (80)	1.00	288/508 (57)	1.00
No	452/551 (82)	1.02 (0.96–1.07)	145/282 (51)	0.95 (0.83–1.10)
Smoking habits				
Present smoker	318/375 (85)	1.09 (1.02–1.17)	162/281 (58)	1.15 (0.97–1.36)
Former smoker	469/566 (83)	1.06 (0.99–1.13)	173/302 (57)	1.08 (0.92–1.28)
Never smoked (reference)	336/441 (76)	1.00	116/242 (48)	1.00
Previous fractures				
Yes	–	–	53/104 (51)	0.86 (0.72–1.04)
No (reference)	–	–	386/701 (55)	1.00
Cardiovascular disease				
Yes	240/282 (85)	0.99 (0.92–1.07)	–	–
No (reference)	870/1087 (80)	1.00	–	–
Family history of premature cardiovascular disease				
Yes	367/426 (86)	1.05 (0.99–1.10)	–	–
No (reference)	762/963 (80)	1.00	–	–
Taking lipid-lowering drugs				
Yes	284/330 (86)	1.01 (0.94–1.08)	–	–
No (reference)	824/1035 (80)	1.00	–	–
Taking antihypertensive drugs				
Yes	349/406 (86)	1.05 (0.98–1.11)	–	–
No (reference)	774/976 (79)	1.00	–	–

* Multivariate Poisson regression analysis was used to estimate relative risks. Respondents were considered to have consented if they indicated that they would "certainly" or "probably" accept the therapy. Otherwise, consent was considered absent. NNT = number needed to treat.
† Trend analysis across the subgroups.

decisions may depend on how the outcomes of interventions are described. The 2 descriptions in each of the following pairs may evoke different choices: *losses versus gains* (see Glossary) (3, 4), gains in *life expectancy* (see Glossary) versus gains in *cumulative probability* (see Glossary) of survival (4), and *certain outcomes* (see Glossary) versus *uncer-*

tain outcomes (see Glossary) (18). For example, in the context of lung cancer treatment, McNeil and coworkers (4) found that surgery was more attractive to respondents when the benefits were described in terms of life expectancy than when they were expressed as cumulative probabilities of survival. Collectively, these differences are known as "framing effects". Several studies have shown that persons choose differently when the outcome is framed as an NNT or absolute risk reduction rather than as a relative risk reduction (19–22). In a recent study (23), laypersons considering a hypothetical drug therapy for osteoporosis discriminated between levels of effectiveness that were presented as degrees of postponement of hip fracture but not when presented in terms of different NNTs.

Why, then, did we observe higher consent rates when we expressed treatment effects as NNTs rather than as postponements of an outcome? First, the findings may reflect preferences for a large but uncertain benefit (an outcome avoided for only a few patients) over a smaller benefit enjoyed by all patients. Respondents may have perceived 2 of the effect formats as gambles (24): 1 with a "big prize" of completely avoiding the adverse outcome (the NNT format) and the other with a substantial, but not indefinite, postponement of the adverse outcome for a few patients. The hypothesis that persons perceive the NNT format as a gamble has empirical support from surveys of laypersons (23–25) and physicians (26). Tversky and Kahneman (3) observed that persons tend to be risk-averse (preferring a certain, intermediate outcome) when outcomes are described as gains, but risk-seeking (preferring a gamble to get a better outcome) when they perceive the outcomes as worsening their status (3). Eraker and Sox (18) replicated this finding with medical scenarios. By analogy, perhaps our respondents are risk-seeking because the risky effect formats (NNT and long postponement of an outcome for some patients) evoked the highest consent rates. We framed our scenarios as an imminent loss of health (Figure 2)—the prospect of a heart attack or a hip fracture—which may explain why treatment effects framed as gambles were attractive to our respondents.

A second explanation is that different consent rates with different outcome descriptions may reflect what cog-

Table 4. **Respondents Reporting Difficulties with Understanding the Benefits of a Preventive Drug Therapy***

Variable	Heart Attack Group		Hip Fracture Group	
	Respondents Reporting Difficulties, *n/n* (%)	Relative Risk (95% CI)	Respondents Reporting Difficulties, *n/n* (%)	Relative Risk (95% CI)
Effect measure				
Postponement: same benefit for all persons (reference)	182/456 (40)	1.00	147/281 (52)	1.00
Postponement: greater benefit for some persons	153/452 (34)	0.85 (0.71–1.01)	133/264 (50)	0.98 (0.83–1.15)
NNT	158/480 (33)	0.84 (0.70–1.00)	165/282 (59)	1.12 (0.96–1.31)
Age				
<50 y (reference)	94/266 (35)	1.00	45/117 (38)	1.00
50–59 y	171/484 (35)	0.99 (0.79–1.24)	150/282 (53)	1.35 (1.05–1.75)
60–69 y	140/420 (33)	0.91 (0.71–1.16)	150/265 (57)	1.44 (1.10–1.87)
≥70 y	88/218 (40)	1.06 (0.81–1.40)	100/163 (61)	1.57 (1.18–2.08)
Sex				
Women (reference)	175/474 (37)	1.00	267/500 (53)	1.00
Men	318/914 (35)	0.97 (0.83–1.14)	178/327 (54)	0.98 (0.86–1.13)
Length of education				
0–9 y (reference)	225/618 (36)	1.00	233/405 (58)	1.00
10–12 y	137/428 (32)	0.86 (0.71–1.03)	132/241 (55)	1.03 (0.89–1.20)
≥12 y	114/310 (37)	0.99 (0.80–1.23)	68/159 (43)	0.80 (0.65–1.00)†
Self-reported health condition				
Not good or bad	190/528 (36)	0.98 (0.83–1.17)	162/312 (52)	0.88 (0.76–1.02)
Good or excellent (reference)	300/582 (35)	1.00	282/513 (55)	1.00
Psychiatric symptoms				
Yes	182/551 (33)	1.15 (0.97–1.35)	273/507 (54)	1.05 (0.91–1.22)
No (reference)	285/761 (37)	1.00	148/282 (52)	1.00
Smoking habits				
Present smoker	124/375 (33)	0.92 (0.75–1.13)	151/280 (54)	1.02 (0.86–1.21)
Former smoker	202/566 (36)	1.00 (0.84–1.20)	159/301 (53)	0.94 (0.80–1.11)
Never smoked (reference)	164/439 (37)	1.00	133/243 (55)	1.00

* Multivariate Poisson regression analysis was used to estimate relative risks. NNT = number needed to treat.
† $P = 0.048$.

nitive psychology teaches us about the properties of *heuristics* (see Glossary). When using these shortcuts in making decisions, persons may put the most weight on cues that are easily recalled (*availability heuristics* [see Glossary] [27]), easily recognized (recognition heuristics [28]), or easily evaluated (the *evaluability hypothesis* [see Glossary] [29]). Our scenarios portrayed some cues that persons should easily recognize: a serious disease (heart attack or hip fracture), the word *prevention*, and the word *postponement*. Our scenarios also portrayed some outcomes as numbers: the NNT to prevent 1 event and the length of a postponement. One reason for using a written scenario is to standardize the stimulus to the respondent. Numbers can be a source of unwanted variability if they are evaluated differently. In fact, persons vary in their numeracy and may have difficulty evaluating a number, such as an NNT, without a reference point for comparison. Under such circumstances, the evaluability hypothesis (29) predicts that NNTs would have little impact on decisions, a finding that has considerable empirical support (23–25, 30). However, one would expect laypersons to be more familiar with the concept of time and thus to be better able to evaluate the extent of postponement of an adverse outcome. Perhaps some respondents simplified the scenarios to "complete prevention of heart attack" (in the NNT scenarios), "substantial postponement of heart attack," and "small postponement of heart attack." This heuristic simplifies the decision-making task by circumventing the need to interpret numbers. The rank ordering of these 3 simplified options according to their face value is the same as the observed rates of consent with the 3 scenarios (Table 3).

A third explanation is that the NNT and postponement scenarios have different face validity in representing the true treatment effect. The NNT is like a lottery—a few people win a "big prize" and the rest receive nothing. However, the NNT format leaves much unsaid. One cannot directly infer the proportion of patients who benefit from the intervention (24) or that the "lucky ones" will completely avoid an adverse outcome. Of the 2 postponement formats, the "greater postponement for a proportion of patients" format is similar to the outcomes of the studies on which we based the scenarios (16, 17) (Appendix Tables 1 and 2, available at www.annals.org). In these studies, most participants in the control groups did not experience the adverse event. Thus, only a minority of participants could benefit during the study period. In our hypothetical scenarios, we did not state the proportion of persons who would have an adverse event without the drug therapy. In the end, however, neither hip fractures nor heart attacks are inevitable. The NNT format reflects this uncertainty, albeit indirectly, whereas the short postponement for all patients do not. Thus, it is conceivable that the consent rates were higher in the NNT scenarios because they seemed more plausible to the participants.

This study has important strengths—proper randomization, a large community-based survey sample, and high response rates—and several limitations. First, although the participants were selected from respondents to a general health survey, only 61% of invited persons attended the screening, which means that our respondents may not be entirely representative of the general population. Second, the survey questionnaire did not probe deeply into respondents' understanding of the scenarios. Qualitative studies or more direct assessments of understanding (31) might teach us more about why persons report difficulty in understanding measures of the effect of preventive drug therapies. Third, whether responses to hypothetical scenarios reflect real-life decisions is a long-standing concern about studies such as ours (32, 33). We cannot rule out the possibility that the respondents' reactions to the outcomes described in the scenarios have little resemblance to real-life decisions. In particular, our scenarios did not include measures of the uncertainty in the effect estimates. Henderson and Keiding (34) have proposed methods for communicating uncertainty in effect estimates of survival, but to our knowledge, no studies have empirically tested these strategies. Fourth, our scenarios did not specify potential harms or represent the tradeoffs between benefits and harms. Finally, we did not tailor the scenarios to the individual respondents' level of risk. Therefore, the respondents were free to use assessment of their own risk, which may have introduced unwanted variability in their responses. Including measures of baseline risks, uncertainty, or harms to our scenarios would have added realism and complexity to the decision tasks. Respondents might have reacted by relying more on heuristics that focused on the salient attributes of the scenarios, such as the seriousness of the disease to be prevented (30).

Notwithstanding these limitations, we conclude that the NNT format and the 2 postponement formats, as dif-

Glossary

Availability heuristics: The process by which people judge an event as more likely if it is easily recalled. Judgment based on what comes easily to mind.

Certain outcomes: Outcomes that are inevitable (that is, $P = 1.0$) (for example, death, at least in the long run).

Cumulative probability: The probability that an event has occurred at a specific point in time (for example, 10 years after the onset of an intervention). A gain in cumulative probability may be presented in several ways, such as relative risk reduction, absolute risk reduction, or number needed to treat.

Evaluability hypothesis: This hypothesis states that when making complex choices, people tend to base their decisions on cues or factors that are easy to evaluate and put little or no weight on factors that are hard to evaluate.

Heuristics: Mental short cuts or "rules of thumb" that people use to simplify complex decision-making processes.

Life expectancy: The average statistical (expected) remaining lifetime for a group of people with similar characteristics (for example, 60-year-old men with localized prostate cancer). Gains in life expectancy is the extent to which a medical intervention, on average, extends (disease-free) life.

Losses versus gains: Logically equivalent ways of presenting the outcome of an intervention in terms of losses (for example, 1 of 100 people will die) or gains (99 of 100 people will survive).

Uncertain outcomes: Outcomes that may or may not occur (that is, $P < 1.0$) (for example, heart attack, stroke, or cancer).

ficult as they may be to understand, evoke very different choices when laypersons respond to hypothetical scenarios about risk-reducing drug therapies. Perhaps the same is true in real life.

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Acknowledgments: The authors thank Arthur Elstein, Dorte Gyrd-Hansen, Jorgen Nexoe, and Henrik Stovring for comments on the paper. The authors also thank the residents of Finnmark, Norway, for their willingness to contribute to the study and the Norwegian Institute of Public Health for conducting the practical part of the data collection.

Grant Support: By governmental funds held by the University of Tromso, Tromso, Norway.

Potential Financial Conflicts of Interest: None disclosed.

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Appendix Table 1. **Estimation of Corresponding Magnitudes of Number Needed to Treat and Postponement of Adverse Events after 5 Years of Drug Therapy in the Heart Attack Group***

Variable	Data	
	Placebo Group	Intervention Group
Data from the 4S study according to van Hout and Simoons (16)		
Participants, *n*	2223	2221
Events (stroke or heart attack), *n*	576	400
Mean event-free survival, *y*	4.32	4.48
Our estimations		
ARR	576/2223 – 400/2221 = 0.079	
Number needed to treat (1/ARR)	1/0.079 ~ 13	
Mean gain in event-free survival	4.48 – 4.32 = 0.16 y (~ 2 mo)	
Proportion with adverse event in placebo group	~ 576/2223 (~ 0.25 or 1 of 4)	
Gain in event-free survival distributed among the proportion of persons with adverse events in the placebo group	2 mo/0.25 = 8 mo	

* Estimations are based on the 4S study (16). 4S = Scandinavian Simvastatin Survival Study; ARR = absolute risk reduction.

Appendix Table 2. **Estimation of Corresponding Magnitudes of Number Needed to Treat and Postponements of Adverse Events after 5 Years of Drug Therapy in the Hip Fracture Group***

Variable	Vertebral Fracture Group		Clinical Fracture Group	
	Placebo	Intervention	Placebo	Intervention
Participants, *n*	1005	1022	812	819
Annual incidence of hip fractures	0.0077	0.0037	0.0053	0.0023
Our estimations				
Fractures in placebo groups, *n*	59			
Fractures in intervention groups, *n*	28			
ARR	59/(1005 + 812) – 28/(1022 + 819) = 0.0173			
Number needed to treat (1/ARR)	1/0.0173 ~ 57			
Fracture-free life-years in placebo groups	8935.7			
Fracture-free life-years in intervention groups	9015.4			
Fracture-free life-years gained	9015.4 – 8935.7 = 79.7			
Mean gain in fracture-free survival if the placebo group received the intervention	79.7/(1005 + 812) = 0.044 y (~ 16 d)			
Proportion with hip fractures in the placebo group	59/(1005 + 812) ~ 0.032 ~ 3 of 100			
Gain in fracture-free survival distributed among the proportion of persons with hip fractures in the placebo group	0.044 y/0.032 (~ 16 mo)			

* Estimations are based on the FIT (17). The FIT had 2 study groups: the vertebral fracture group, which included women who had vertebral fractures identified on radiographs at baseline, and the clinical fracture group, which included women without vertebral fracture but who had a femoral neck T-score less than −1.6 at baseline. We used the annual incidence of hip fractures in the different groups to calculate fracture-free life-years gained after 5 years of therapy. For each of the 5 years, we assumed that fractures occurred in the middle of the year. ARR = absolute risk reduction; FIT = Fracture Intervention Trial.

Paper IV

Submitted May 17, 2008:

Anticipated longevity among lay people screened for cardiovascular risk factors

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Running title: Impact of risk information on anticipated longevity

Abstract

Background: Whether informing people about their cardiovascular risk may have adverse psychological consequences, has been a long standing concern. In terms of mental health and quality of life previous studies have largely failed to show long term effects, but cardiovascular risk information may still have psychological impact of a more subtle nature.

Objective: Exploring the possible impact of cardiovascular screening and risk information on lay people's anticipations of their own longevity.

Design: Cross sectional survey.

Setting: General community

Participants: High risk (n=752) and low risk (n=996) individuals identified in a health study that included screening for cardiovascular risk factors.

Intervention: Participants received comprehensive written information about their personal risk factors. About six months later they were mailed a questionnaire and first informed about the life expectancy for women and men in Norway. Subsequently they were asked whether they expected to live longer, shorter than or approximately as long as the mean figures.

Main outcome measure: Personal anticipation of longevity.

Results: The response rate was 75% (n=1,314). Whereas 210 respondents (16%) expected to live shorter than the mean, 198 (15%) expected to live longer. In a multivariate regression model high risk of cardiovascular disease (CVD) was associated with lower anticipated longevity (OR 2.4, 95% CI 1.7 – 3.3). Other predictors of low anticipation were use of lipid lowering drugs and a family history of heart attack before the age of 60. Higher age, male sex, better education and good self reported health were associated with high anticipations.

Conclusions: A CVD risk label was moderately associated with lay people's anticipated longevity. Respondent characteristics may be as important as risk information *per se* when considering possible psychological reactions to a high risk label.

Keywords: Risk assessment, cardiovascular diseases/psychology, longevity

Introduction

Medical doctors in the industrial world devote time and effort to the identification, treatment and follow up of risk factors that may threaten the future health of their patients. Concerns that this pursuit may have adverse consequences are prevailing: Screening for and management of risk factors may be time consuming and involve large proportions of the population.[1] Resources in health care may potentially be diverted away from already sick patients to asymptomatic individuals with risk factors.[2] At the individual level risk labeling may cause adverse psychological effects such as uncertainty and worry as well as overt anxiety, depression and, ultimately, reduced quality of life. From empirical studies regarding the psychological impact of predicting individuals' risk of cardiovascular diseases (CVD), cancer and genetic diseases, a general picture emerges. First, the majority seems to cope well with risk information in terms of long term mental health and quality of life.[3-6] Second, although a significant minority may experience varying degrees of distress in response to risk information, adverse reactions tend to be transient and associated with emotional state prior to risk assessment rather than with the risk information *per se.* [3, 4]

Although the general picture may seem reassuring, measurements of adverse psychological impact have largely been limited to psychometric measures otherwise used for clinical purposes or generic measures of quality of life. It is conceivable that screening and subsequent risk information may have psychological consequences of emotional or cognitive nature that are not captured by these instruments.[7] Measures that capture more subtle effects of risk communication may therefore be desirable. Life optimism might be one such measure. For this study we hypothesized that lay people may adjust their expectations for their own longevity in accordance with cardiovascular risk information from screening. Because previous research suggests that most psychological reactions to risk information tend to be short lived, *i.e.* a couple of weeks only, we wanted to assess anticipated longevity several months after receipt of risk information.

Methods

In 2002 The Norwegian Institute of Public Health, as part of regional health surveys in Norway, invited all inhabitants born 1925-1947, 1957, 1962 and 1972 and all persons born 1948-1968 who had been invited to former screenings in Finnmark County, to the Troms and Finnmark (TROFINN) health study. For each participant blood pressure and body mass index were measured, and a non fasting blood sample was drawn for measurement of lipids and glucose. The participants filled in two comprehensive questionnaires covering sociodemographic data, health related variables and habits regarding exercise, food, alcohol and smoking. Two weeks after the screening the participants received a letter with their own results. The front page displayed numerical values for lipids, blood pressure, heart attack risk indices, body mass index and hip waist ratio (*fig. 1*). The following three pages provided comprehensive information about each risk factor or index, including normal ranges in the population. People with high CVD risk were recommended to contact their general practitioner for follow-up. The others were informed that follow up was not needed, but that most people nevertheless can reduce their risk through life style changes. High risk status was based on high levels of one or more of the following: Blood pressure, serum cholesterol, blood glucose, heart attack risk or Framingham risk score. This implies that respondents with established CVD but a favourable risk factor profile were classified as low risk individuals. The cut-off value for blood glucose was 8.5, whereas cut-off values for the other measures were age dependent (see appendix).

The present study was a sub project to the TROFINN health study. A sample of attendees from 10 municipalities along the coast of Finnmark was selected (*fig. 2*). Of 11,284 individuals invited to screening, 6,854 (61%) participated and 6,445 were eligible for our study. Eligibility was based on written consent to use their data for medical research and willingness to be offered further surveys in the future. From the eligible group of participants we selected a high risk and a low risk sample. To the high risk sample we allocated the individuals who were advised to see their GP due to high CVD risk as outlined above. The remaining participants were ranked according to heart attack risk. Separate ranking lists were made for women and men, and the low risk sample was selected bottom up from these lists to ensure similar proportions females and males in the high- and low risk groups. We planned to have 1,000 individuals in each group, but the number of high risk individuals turned out to be lower than expected (n=754). Four low risk and two high risk individuals died shortly after the initial screening, and these were excluded from further studies. Thus 752 high risk and 996 low risk participants were included in our study.

Four to six months after the initial screening our participants were mailed a questionnaire which informed them about the mean life expectancy for Norwegian women (81 years) and men (75 years).[8] For participants 60 years or older the figures were set at 84 years for women and 80 years for men, based on mean life expectancy given survival to 60 years.[8] The participants were then asked what they anticipated for their own longevity. Possible response categories were "shorter than the mean", "approximately the same as the mean" or "longer than the mean". Additionally they were asked whether they would like their GP to inform them about their risk of heart attack. For other study purposes (not reported here) the questionnaire also posed a hypothetical scenario asking the respondents to imagine that they were at increased risk of getting a heart attack. Subsequently they were asked whether they would consent to a drug therapy aimed at reducing that risk, and finally, whether it was easy or difficult to understand the benefit of this intervention.

We tested the hypothesis that expectations for one's own longevity would differ between high risk and low risk participants. Consequently our primary outcome variable was the respondent's anticipated longevity. The primary independent variable was cardiovascular risk group (high versus low) as defined by the information letter. Other independent variables were history of cardiovascular diseases, presence of diabetes mellitus, use of lipid lowering or antihypertensive drugs, smoking habits, exercise habits, self reported health condition, a family history of heart attack before the age of 60 and a family history of stroke. These variables were included to adjust for the fact that some respondents might be aware of their CVD risk already when the risk information was received. Age, sex, education, marital status and psychiatric symptoms reported at the initial screening were also included. These variables might be associated with CVD risk as well as how the respondents might deal with risk information.

Differences between proportions in different categories of anticipated longevity in the high – and low risk groups were assessed with χ^2-tests and logistic regression. The primary outcome variable had three possible response categories for anticipated longevity – shorter, longer or mean. These may be conceived of as a graded response or as qualitatively distinct responses. For this reason ordinal as well as multinomial regression analyses were used to explore associations between the independent variables and anticipated longevity. Univariate and multivariate analyses were performed. Because results of these analyses were similar, only the multivariate analyses are reported. Regression diagnostics indicated that the proportional odds assumption for ordered logit regression was violated. Consequently a partial proportional odds model[9] was fitted. No formal power calculation was performed. As multiple statistical tests were performed, we regarded *p*-values < 0.01 as statistically significant. SPSS version 14.0 (SPSS, Chicago, Illinois) and STATA version 9.2 (Stata Corp., College Station, Texas) were used for data analysis.

Results

Of the 1,748 individuals approached, 1,314 (75.0 %) gave valid responses to the anticipated longevity question. The non-responders smoked more, exercised less and had higher Framingham risk scores risk than the non-responders. Also, non-responders were slightly less educated, more of them were living alone and they regarded their health as worse compared to responders (table 1). The two risk groups turned out to be fairly balanced with respect to age, marital status, subjective overall health and psychiatric symptoms at the initial screening. They differed in expected ways with respect to smoking, exercise habits and education. Notably, more low risk individuals reported CVDs, and more of them used lipid lowering medication (table 1). The vast majority (n=1,230, 94%) indicated that they certainly or probably would like their GP to inform them about their heart attack risk.

Overall 16% (n=210) expected to live shorter than the mean, 69% expected to live about as long at the mean whereas 15% (n=198) expected to live longer. In the high risk group these figures were 20%, 72% and 8% respectively, compared to 13%, 67% and 20% in the low risk group ($\chi^2 = 41.8$, $df = 2$, $p<0.001$). Thus, in the high risk group the response pattern was slightly more pessimistic, and conversely, slightly more optimistic in the low risk group (*fig. 3*).

In the ordinal logistic regression model CVD risk remained a statistically significant predictor of low expectations for longevity (OR for high versus low CVD risk 2.4 per level of anticipated longevity, 95% CI 1.7 – 3.3, table 2). Other statistically significant predictors of low expectations were use of lipid lowering drugs (OR 2.0, 95% CI 1.2 – 3.1) and a family history of heart attack before the age of sixty (OR 1.8, 95% CI 1.3 – 2.5). Higher age, good self reported health and better education were associated with high expectations. Notably, diabetes mellitus and use of antihypertensive drugs were not associated with anticipated longevity. For those who would regard the multinominal model as more appropriate, some further nuances emerge: The primary effect of high CVD risk was to drive the responses away from the *highest* expectations of longevity, whereas family history of heart attack primarily drove the responses towards the *lowest* expectations. Male sex and high education were positively associated with the *highest* expectations, whereas people at high age less often expected shorter longevity than the average compared to younger people.

Discussion

In this population based survey a high CVD risk label was associated with lower expectations for one's own longevity four to six month after receiving the risk label. Some risk information (using lipid lowering drugs and a family history of heart attack) provided by the respondents before receiving the risk label showed similar associations with anticipated longevity. This suggests that CVD risk information may have long term psychological effects. The associations were modest, however, and the majority anticipated about mean longevity regardless of risk information. Furthermore, less than 7% in retrospect indicated that information about their heart attack risk would be unwanted. Use of antihypertensive drugs and diabetes were not associated with anticipated longevity, which may indicate that some risks are perceived as less dangerous or more easily modified than others.

Should these finding raise any concerns? It may seem reassuring that the majority have neutral or even optimistic expectations of longevity after receiving a CVD risk information letter and no more than an optional follow up by their GPs. In two other studies, of which one was conducted in the same geographical area as our study, no negative psychological effects of screening and risk interventions were detected after at least five years of follow up.[5, 6] Other studies, however, suggest that a high CVD risk label may evoke short term[10] as well as long term psychological distress.[11] The studies vary with respect to exactly what is measured (*e.g.* well-being, intrusive thoughts, preoccupation with health) and how it is measured. No study that we are aware of (including our) has used rigorously developed outcome measures with respect to content validity and psychometric properties.[7]

Rather than concerns about psychological harm, one might be concerned that the risk information seemed to have little impact on our respondents. After all, since they were either high or low risk individuals, shouldn't we expect greater proportions of pessimistic as well as optimistic responses? In a medical context it has been shown that people often underestimate their personal risks and tend to regard hazards as more risky to others than to themselves,[12] *i.e.* optimism bias. Furthermore, high risk individuals might be relatively optimistic about their longevity because they felt able to reduce their risk. Indeed, the high proportion of CVD and lipid-lowering drug use among the low risk individuals indicate extensive secondary prophylaxis at work. Some studies do indicate that high CVD risk information has impact[13] including efforts to reduce the risk.[11] Marteau et al., however, observed that a screening and intervention programme against CVD did not raise much concern and might even provide false reassurance.[14] Interestingly, in a study of osteoporotic women only those who were concerned were ready to take action to reduce their fracture risk.[15] Evidence from Denmark suggest that regular health screening may lead to an initial increase in GP consultations, but in the long run there was a decrease utilisation of primary as well as secondary care.[16, 17] This may indicate that to some degree the concern may lead to desirable consequences which ought to be weighed against the possibility of psychological harm.

We realise that this study has several limitations. Because of the cross-sectional non-randomised study design we could not measure change in anticipated longevity directly. Even if we adjusted for several factors in the analysis, the possibility remains that the association between risk information and anticipated longevity is confounded. High risk individuals were not asked whether they had followed the advice to see their GP. It is possible that their risk perception may have been modified by interaction with health care providers and others. Low risk individuals were not explicitly told that their risk profile was favourable. This had to be inferred by comparing their results to normal ranges provided in the letter. Furthermore, the questionnaire posed a scenario asking them to imagine being at risk of heart attack, which may have counteracted any tendency to optimism bias. Since only about 60% of the invited individuals showed up for screening, our study sample may not be completely representative of high- and low-risk individuals in the general population. On the other hand, they might be more representative of patients in general practice. The outcome measure was rather single minded, and the interpretation is not straight forward. Does a lower expectation of longevity represent an affectively laden and stressful experience or just a realistic adjustment of one's expectations based on the risk information? From our study design we cannot know. Or perhaps we measured some human trait of optimism versus pessimism? Evidence suggests that dispositional optimism might be a stable trait that is inversely associated with cardiovascular death.[18] It is not clear to what extent CVD screening and risk information might interfere with such a trait. Finally, we did not ask our respondents how much shorter or longer they expected to live compared to the average. Patients who underwent a stress-test for the evaluation of chest pain increased their anticipated longevity by 1.5 years on average.[19] Another study of patients indicates that prolongation of life must be of about this magnitude to make preventive drug therapies worthwhile.[20]

In our opinion the present study suggests that the majority cope well with CVD risk information. A significant minority, however, may have adverse psychological reactions that need special attention. Paraphrasing Hippocrates, it may be more important to know the person who has a risk factor than to know what risk factors a person has.

Funding: National Centre of Rural Medicine, University of Tromsø, Norway *and* Northern Norway Regional Health Authority *and* Finnmark Health Authority, Norway.

Ethical approval: The study was evaluated by the regional committee for medical research ethics and approved by the Norwegian Data Inspectorate. We conducted the study in accordance with the Declaration of Helsinki.

Conflicts of interests: None.

Acknowledgements: Per G Lund-Larsen assisted with coordinating the data collection and the Norwegian Institute of Public Health conducted the practical part of it. We would like to thank the population of Finnmark for their willingness to contribute to this study.

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Table 1. Characteristics of high- and low risk individuals, responders and non-responders to a questionnaire about their anticipated longevity

Variable	High risk group n = 752	Low risk group n = 996	Responders n = 1,314	Non-responders n = 434
Framingham risk score	20.1 (19.4 – 20.8)	8.8 (8.4 – 9.2)	13.3 (12.8 – 13.9)	14.6 (13.6 – 15.6)
Ever used lipid-lowering drugs	14% (11 – 16)	30% (27 – 33)	24% (21 – 26)	22% (18 – 26)
Ever used anti-hypertensive drugs	28% (25 – 31)	30% (27 – 32)	28% (26 -31)	30% (26 – 35)
Diabetes mellitus	8% (6 – 9)	6% (5 – 8)	7% (5 – 8)	8% (5 – 10)
Family history of heart attack < 60y	35% (32 – 39)	26% (23 – 29)	31% (28 – 33)	27% (23 – 31)
Family history of stroke	33% (29 – 36)	27% (25 – 30)	30% (28 – 33)	28% (24 – 33)
Current smoker	54% (50 – 57)	12% (10 – 14)	27% (25 – 30)	37% (33 – 42)
Exercise (hours per week) [1]				
None	38% (34 – 41)	29% (27 – 32)	31% (29 – 34)	39% (34 – 44)
< 1 hour	22% (19 – 25)	21% (18 – 23)	22% (20 – 24)	19% (16 – 23)
1 – 2 hours	17% (14 – 19)	21% (18 – 24)	20% (18 – 23)	15% (12 – 19)
3 hours +	8% (6 – 10)	13% (11 – 15)	11% (10 – 13)	9% (6 – 12)
Level of self-reported health [1]				
Poor	2% (1 – 3)	2% (1 – 3)	2% (1 – 3)	3% (1 – 5)
Not too good	38% (35 – 42)	35% (32 – 38)	35% (33 – 38)	40% (35 – 45)
Good	52% (49 – 56)	49% (46 – 53)	52% (49 – 54)	47% (43 – 52)
Excellent	7% (5 – 8)	13% (11 – 15)	11% (9 – 12)	9% (6 – 11)
Psychiatric symptoms	55% (52 – 59)	55% (52 – 59)	55% (53 – 58)	55% (50 – 60)
History of cardio-vascular disease	12% (10 – 14)	27% (24 – 30)	20% (17 – 22)	23% (19 – 27)
Age (yrs)	57 (57 – 58)	58 (57 – 58)	58 (57 – 58)	57 (56 – 58)
Male sex	66% (62 – 69)	66% (63 – 69)	66% (63 – 68)	66% (61 – 70)
Living with spouse	72% (68 – 75)	74% (71 – 77)	75% (73 – 78)	67% (62 – 71)
Education (yrs)	10.0 (9.8 – 10.3)	10.5 (10.2 – 10.7)	10.5 (10.3 – 10.7)	9.8 (9.4 -10.1)
Responders	72% (69 – 75)	79% (77 – 82)	NA	NA

1) Because of missing responses the sum of the categories does not add up to 100%

Table 2. Regression analyses of the respondent's anticipated longevity

Independent variable	Ordinal regression[1]		Multinominal regression[2]			
	Lower expectations		Shorter than the mean		Longer than the mean	
	OR	95% CI	OR	95% CI	OR	95% CI
High CVD risk	2.40**	1.73 – 3.33	1.48	0.96 – 2.28	0.31**	0.19 – 0.50
Ever used lipid-lowering drugs	1.95**	1.23 – 3.09	1.55	0.88 – 2.71	0.48	0.23 – 1.00
Ever used anti-hypertensive drugs	1.05	0.72 – 1.53	1.12	0.69 – 1.80	0.91	0.52 -1.58
Diabetes mellitus	1.11	0.61 – 2.03	0.60	0.26 – 1.40	0.31	0.09 – 1.06
Family history of heart attack < 60y	1.84**	1.34 – 2.53	2.23**	1.52 – 3.27	0.86	0.54 – 1.38
Family history of stroke	1.09	0.82 – 1.46	1.05	0.71 – 1.54	0.91	0.61 – 1.37
Current smoker	1.26	0.89 – 1.79	1.34	0.88 – 2.04	0.86	0.49 – 1.50
Level of regular exercise[3]	0.88*	0.77 – 1.00	0.88	0.74 – 1.06	1.10	0.92 – 1.31
Level of self-reported health[3]	0.73**	0.58 – 0.92	0.82	0.60- 1.11	1.41*	1.03 – 1.94
Psychiatric symptoms	1.15	0.86 – 1.53	1.54*	1.03 – 2.31	1.17	0.79 – 1.72
History of cardio-vascular disease	1.79*	1.11 – 2.90	1.87*	1.04 – 3.35	0.89	0.42 – 1.89
Age (per year)	0.96**	0.95 – 0.98	0.96**	0.94 – 0.98	1.02*	1.00 – 1.04
Male sex	0.74*	0.55 – 0.99	1.00	0.68 – 1.47	1.76**	1.16 – 2.68
Living with spouse	0.75	0.54 – 1.03	0.73	0.49 – 1.10	1.20	0.76 – 1.91
Education (per year)[4]			1.04	0.97 – 1.10	1.11**	1.05 – 1.18
Level 2 + 3 *vs* 1(ref)	0.90**	0.86 – 0.95				
Level 3 vs 1 + 2 (ref)	1.02	0.97 – 1.08				

1. A partial proportional odds model was fitted. The dependent variable – anticipated longevity - had three levels. Level 1: Longer than the mean. Level 2: About the same as the mean. Level 3: Shorter than the mean. OR>1.0 indicates increased likelihood of lower (more pessimistic) expectations for one's longevity. When the proportional odds assumption holds, a common odds ratio for levels 2+3 vs 1 and 3 vs 1 + 2 is estimated.
2. In the multinomial model low expectations (shorter than the mean) as well as high expectations (longer than the mean) is contrasted to "neutral" expectations (about the same as the mean) for one's longevity.
3. This variable was analyzed as a trend variable across the ordered groups indicated in table 1.
4. This variable violated the proportional odds assumption of ordered logistic regression. In the partial proportional odds model different odds ratios across the different levels of anticipated longevity (the dependent variable) is estimated.
OR: Odds ratio. CI: Confidence interval. CVD: Cardiovascular disease * $p<0.05$ ** $p<0.01$

The Norwegian Institute of Public Health **November 27 2003**

Dear Mr. NN,

Here are your results from the health study

Thank you for participation in the Finnmark Health Study on November 11 2003. Below you will find results of the most important measurements. If any of these results need to be followed up by your GP, you will find a message about this below. On the following pages of this letter you will find general information and explanations about the measurements.

Total cholesterol	8.7 mmol/l
HDL cholesterol	1.3 mmol/l
Triglycerides	2.4 mmol/l
Glucose (non-fasting)	4.7 mmol/l
Systolic blood pressure	130 mmHg
Diastolic blood pressure	80 mmHg
Heart attack risk (Framingham)	5.0 %
Heart attack risk (SHUS)	62 units
Body mass index (BMI)	28.3 kg/m^2
Waist/hip ratio (W/H-ratio)	1.0

Comment:

We recommend that you contact your GP for control/follow-up of the following findings:

Elevated blood levels of total cholesterol.

Figure 1. The front page of the information letter to attendees of the Troms and Finnmark Health Study

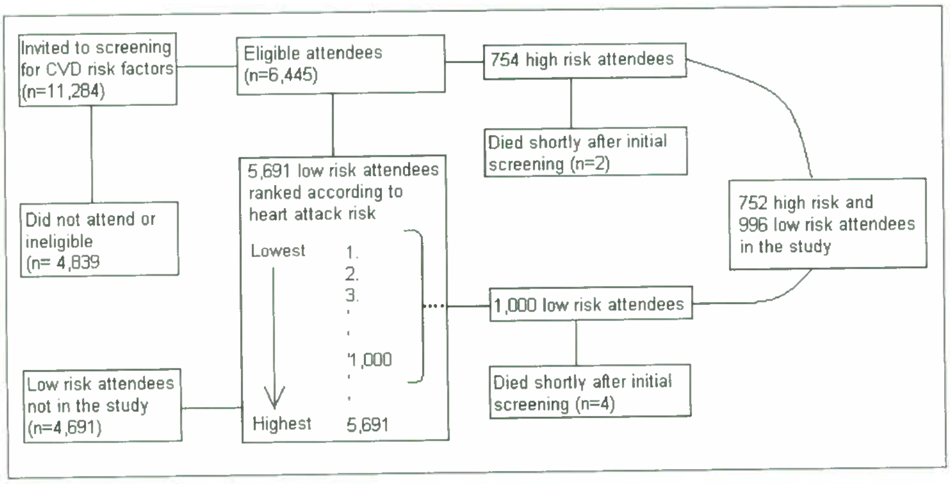

Figure 2. Study flow diagram. A total of 1748 attendees to a population-based health study were mailed a questionnaire and asked about their expectations for their own longevity. Eligibility criteria were as follows: attended screening, consented to additional studies, were alive or did not emigrate between the time of the screening and the survey, and had a known address. The low-risk sample was selected so that the proportion of women was the same as that in the high-risk sample. We expected to enroll approximately 1000 persons in each risk group, but the number of high-risk persons was lower than expected.

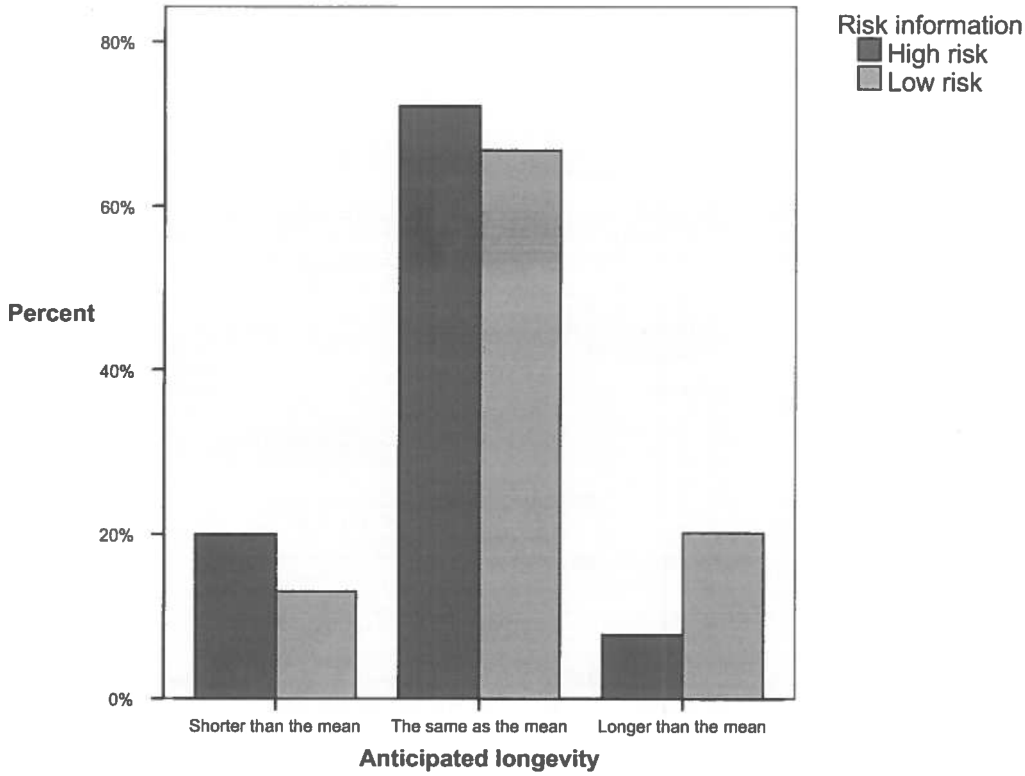

Figure 3. Distribution of anticipated longevity among high- and low CVD risk individuals

APPENDIX

HIGH RISK ATTENDEES TO THE TROFINN STUDY : CUT OFF VALUES FOR RECOMMENDING INDIVIDUALS TO CONSULT THEIR GP

Allocation to the high risk group of this study was determined by two sets of cut off values for risk factors and risk indices, *i.e.* the criteria of the Ullevål University Hospital and the criteria of the former Governmental Health Studies (Statens helseundersøkelser, SHUS) in Norway. The attendees were allocated to the high risk group is they fell for at least one of the criteria. High risk attendees were advices to see their GP for follow up.

<u>The Ullevål criteria</u>

Age <= 60 years

- Framingham risk score > 20%
- Non-fasting blood glucose >= 11.1 unless known to be a diabetic
- HDL cholesterol <= 0.99 and total cholesterol >= 6.00
- HDL cholesterol <= 0.99 and blood glucose >= 6.00 and triglycerides >= 3.50
- Systolic blood pressure >= 165 if not on antihypertensive drugs
- Diastolic blood pressure >= 100 if not on antihypertensive drugs

Age <= 40 years

- Total cholesterol >= 7.00

Age >= 41 and <= 60 years

- Total cholesterol >= 7.80 and HDL cholesterol < 2.00
- Total cholesterol >= 9.80

Age >= 61 years

- Diastolic blood pressure >= 125
- Systolic blood pressure >= 220
- Non-fasting blood glucose >= 11.1 unless known to be a diabetic
- Total cholesterol >= 9.80

The SHUS criteria

High blood pressure

The cut off values are according to the following formula for age < 80 years:

Systolic blood pressure: 145,8 + 0,68*age

Diastolic blood pressure: 94,2 + 0,32*age

For age>=80 the cut off values are

Systolic blood pressure: 240

Diastolic blood pressure:120

The SHUS-criteria apply irrespective of use of antihypertensive drugs.

Non-fasting blood glucose >= 8.50 unless known to be a diabetic

High cholesterol: See table 1

High risk of heart attack: See tables 1 and 2

Blood pressure

When the SHUS criteria and the Ullevål criteria differ, the lowest cut off value applies. Consequently, for people who are not on antihypertensive drugs, criteria apply according to age as follows:

Systolic blood pressure:	<= 28 years: SHUS criteria
	29 –60 years: Ullevål criteria
	61-79 years: SHUS criteria
	>=80+ years: Ullevål criteria
Diastolic blood pressure:	15-16 years: SHUS criteria
	17-60 years: Ullevål criteria
	>= 61+ years: SHUS criteria

Cholesterol

The Ullevål criteria and the SHUS criteria apply according to age and gender as follows:

Males:

HDL cholesterol < 2.00:	15 – 28 years: SHUS criteria
	29 – 60 years: Ullevål criteria
	>= 61 years: SHUS criteria
HDL cholesterol >= 2.00:	15 – 28 years: SHUS criteria
	29 – 40 years: Ullevål criteria
	>= 41 years: SHUS criteria

Females:

HDL cholesterol < 2.00:	15 – 21 years: SHUS criteria
	22 – 60 years: Ullevål criteria
	61 – 67 years: SHUS criteria
	>= 68 years: Ullevål criteria
HDL cholesterol >= 2.00:	15 – 21 years: SHUS criteria
	22 – 40 years: Ullevål criteria
	41 – 67 years: SHUS criteria
	>= 68 years: Ullevål criteria

Table 1. Cut off values for cholesterol and heart attack risk

Age	Cholesterol Males	Cholesterol Females	Age	Heart attack risk Males	Heart attack risk Females
15	5,5	6	15	70	70
16	5,65	6,15	16	70	70
17	5,79	6,31	17	70	70
18	5,95	6,47	18	70	70
19	6,1	6,62	19	70	70
20	6,26	6,78	20	70	70
21	6,41	6,93	21	70	70
22	6,57	7,09	22	70	70
23	6,62	7,14	23	70	70
24	6,67	7,19	24	70	70
25	6,75	7,27	25	70	70
26	6,8	7,32	26	70	70
27	6,85	7,37	27	70	70
28	6,98	7,5	28	70	70
29	7,11	7,63	29	70	70
30	7,29	7,81	30	70	70
31	7,42	7,94	31	70	70
32	7,55	8,07	32	70	70
33	7,6	8,12	33	70	70
34	7,66	8,17	34	70	70
35	7,68	8,2	35	70	70
36	7,73	8,25	36	72	72
37	7,78	8,3	37	74	74
38	7,81	8,33	38	76	76
39	7,84	8,35	39	78	78
40	7,89	8,4	40	80	80
41	7,91	8,43	41	82	82
42	7,94	8,46	42	84	84
43	8,02	8,53	43	86	86
44	8,09	8,61	44	88	88
45	8,15	8,66	45	90	90
46	8,2	8,72	46	92	92
47	8,28	8,79	47	94	94
48	8,33	8,84	48	96	96
49	8,38	8,9	49	98	98
50	8,43	8,95	50	100	100
51	8,48	9	51	102	102
52	8,53	9,05	52	104	104
53	8,59	9,1	53	106	106
54	8,64	9,16	54	108	108
55	8,69	9,21	55	110	110
56	8,74	9,26	56	112	112
57	8,79	9,31	57	114	114
58	8,84	9,36	58	116	116
59	8,9	9,41	59	118	118
60	8,95	9,45	60	120	120
61	9	9,5	61	122	122
62	9,05	9,55	62	124	124

Table 1 continued

Age	Cholesterol Males	Cholesterol Females	Age	Heart attack risk Males	Heart attack risk Females
63	9,1	9,6	63	126	126
64	9,15	9,65	64	128	128
65	9,2	9,7	65	130	130
66	9,25	9,75	66	132	132
67	9,3	9,8	67	134	134
68	9,35	9,85	68	136	136
69	9,4	9,9	69	138	138
70	9,45	9,95	70	140	140
71	9,5	10	71	142	142
72	9,5	10	72	144	144
73	9,5	10	73	146	146
74	9,5	10	74	148	148
75	9,5	10	75	150	150
76	9,5	10	76	150	150
77	9,5	10	77	150	150
78	9,5	10	78	150	150
79	9,5	10	79	150	150
80	9,5	10	80	150	150
81	9,5	10	81	150	150
82	9,5	10	82	150	150
83	9,5	10	83	150	150
84	9,5	10	84	150	150
85	9,5	10	85	150	150
86	9,5	10	86	150	150
87	9,5	10	87	150	150
88	9,5	10	88	150	150
89	9,5	10	89	150	150
90	9,5	10	90	150	150
91	9,5	10	91	150	150
92	9,5	10	92	150	150
93	9,5	10	93	150	150
94	9,5	10	94	150	150
95	9,5	10	95	150	150
96	9,5	10	96	150	150
97	9,5	10	97	150	150
98	9,5	10	98	150	150
99	9,5	10	99	150	150
100	9,5	10	100	150	150
101	9,5	10	101	150	150
102	9,5	10	102	150	150
103	9,5	10	103	150	150
104	9,5	10	104	150	150
105	9,5	10	105	150	150
106	9,5	10	106	150	150
107	9,5	10	107	150	150
108	9,5	10	108	150	150
109	9,5	10	109	150	150
110	9,5	10	110	150	150

Table 2. Table of factors for calculating relative risk of heart attack (SHUS-risk)

Cholesterol mmol/l *100	Factor	Cholesterol mol/l *100	Factor	Cholesterol mmol/l *100	Factor	Cholesterol mmol/l *100	Factor
490	1	779 - 784	5	890 - 891	9	981 - 982	13
491 - 515	1,1	785 - 789	5,1	892 - 894	9,1	983 - 984	13,1
516 - 525	1,2	790 - 793	5,2	895 - 896	9,2	985 - 986	13,2
526 - 533	1,3	794 - 795	5,3	897 - 899	9,3	987 - 988	13,3
534 - 543	1,4	796 - 798	5,4	900 - 902	9,4	989 - 990	13,4
544 - 551	1,5	799 - 801	5,5	903 - 904	9,5	991 - 992	13,5
552 - 561	1,6	802 - 803	5,6	905 - 906	9,6	993 - 995	13,6
562 - 569	1,7	804 - 806	5,7	907 - 908	9,7	996 - 997	13,7
570 - 579	1,8	807 - 808	5,8	909 - 910	9,8	998 - 1000	13,8
580 - 590	1,9	809 - 811	5,9	911 - 912	9,9	1001 - 1002	13,9
591 - 597	2	812 - 814	6	913 - 914	10	1003 - 1004	14
598 - 605	2,1	815 - 816	6,1	915 - 916	10,1	1005 - 1006	14,1
606 - 613	2,2	817 - 819	6,2	917 - 918	10,2	1007 - 1008	14,2
614 - 621	2,3	820 - 821	6,3	919 - 920	10,3	1009 - 1010	14,3
622 - 628	2,4	822 - 824	6,4	921 - 922	10,4	1011 - 1012	14,4
629 - 636	2,5	825 - 827	6,5	923 - 924	10,5	1013	14,5
637 - 644	2,6	828 - 829	6,6	925 - 926	10,6	1014 - 1015	14,6
645 - 652	2,7	830 - 832	6,7	927 - 928	10,7	1016 - 1017	14,7
653 - 657	2,8	833 - 834	6,8	929 - 930	10,8	1018 - 1019	14,8
658 - 665	2,9	835 - 837	6,9	931 - 932	10,9	1020	14,9
666 - 670	3	838 - 839	7	933 - 934	11	1021 - 1022	15
671 - 678	3,1	840 - 842	7,1	935 - 937	11,1	1023 - 1024	15,1
679 - 683	3,2	843 - 845	7,2	938 - 939	11,2	1025 - 1026	15,2
684 - 690	3,3	846 - 847	7,3	940 - 942	11,3	1027 - 1028	15,3
691 - 696	3,4	848 - 850	7,4	943 - 945	11,4	1029 - 1030	15,4
697 - 703	3,5	851 - 852	7,5	946 - 948	11,5	1031 - 1032	15,5
704 - 709	3,6	853 - 855	7,6	949 - 951	11,6	1033 - 1045	15,8
710 - 714	3,7	856 - 858	7,7	952 - 953	11,7	1046 - 1058	16,5
715 - 719	3,8	859 - 860	7,8	954 - 956	11,8	1059 - 1071	17,2
720 - 724	3,9	861 - 863	7,9	957 - 958	11,9	1072 - 1084	18
725 - 729	4	864 - 865	8	959 - 961	12	1085 - 1096	19
730 - 734	4,1	866 - 868	8,1	962 - 963	12,1	1097 - 1109	20
735 - 740	4,2	869 - 870	8,2	964 - 965	12,2	1110 - 1122	21
741 - 745	4,3	871 - 873	8,3	966 - 967	12,3	1123 - 1135	22
746 - 750	4,4	874 - 876	8,4	968 - 969	12,4	1136 - 1148	23
751 - 755	4,5	877 - 878	8,5	970 - 971	12,5	1149 - 1162	24
756 - 760	4,6	879 - 881	8,6	972 - 974	12,6	1163	25
761 - 765	4,7	882 - 883	8,7	975 - 976	12,7		
766 - 773	4,8	884 - 886	8,8	977 - 978	12,8		
774 - 778	4,9	887 - 889	8,9	979 - 980	12,9		

Cigarettes/day	Factor	Cigarettes/day	Factor	Cigarettes/day	Factor	Cigarettes/day	Factor
0	1	7	2	14	2,5	20	3,5
1	1,3	8	2	15	3	21	3,5
2	1,3	9	2	16	3	22	3,5
3	1,3	10	2,5	17	3	23	3,5
4	1,3	11	2,5	18	3	24	3,5
5	2	12	2,5	19	3	25	4
6	2	13	2,5				

Table 2 continued

Systolic Blood Pressure	Factor	Systolic Blood Pressure	Factor	Systolic Blood Pressure	Factor	Systolic Blood Pressure	Factor
134	1	146	1,8	158	3	170	4,5
135	1,1	147	1,9	159	3	171	4,5
136	1,1	148	2	160	3,5	172	4,5
137	1,2	149	2,1	161	3,5	173	4,5
138	1,2	150	2,5	162	3,5	174	4,5
139	1,3	151	2,5	163	3,5	175	4,5
140	1,3	152	2,5	164	3,5	176	4,5
141	1,4	153	2,5	165	4	177	4,5
142	1,4	154	2,5	166	4	178	4,5
143	1,5	155	3	167	4	179	4,5
144	1,6	156	3	168	4	180	5
145	1,7	157	3	169	4		

Family history of coronary heart disease	Factor	Sex	Factor
Yes	1,5	male	5
No	1	female	1
Don't know	1,5		

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1. Bidrag til belysning av medisinske og sosiale forhold i Finnmark fylke, med særlig vekt på forholdene blant finskættede i Sør-Varanger kommune.
Av Anders Forsdahl, 1976. (nytt opplag 1990)

2. Sunnhetstilstanden, hygieniske og sosiale forhold i Sør-Varanger kommune 1869-1975 belyst ved medisinal-beretningene.
Av Anders Forsdahl, 1977.

3. Hjerte-karundersøkelsen i Finnmark - et eksempel på en populasjonsundersøkelse rettet mot cardiovasculære sykdommer. Beskrivelse og analyse av etterundersøkelsesgruppen.
Av Jan-Ivar Kvamme og Trond Haider, 1979.

4. D. The Tromsø Heart Study: Population studies of coronary risk factors with special emphasis on high density lipoprotein and the family occurrence of myocardial infarction.
Av Olav Helge Førde og Dag Steinar Thelle, 1979.

5. D. Reformer i distriktshelsetjenesten III: Hypertensjon i distriktshelsetjenesten.
Av Jan-Ivar Kvamme, 1980.

6. Til professor Knut Westlund på hans 60-års dag, 1983.

7.* Blodtrykksovervåkning og blodtrykksmåling.
Av Jan-Ivar Kvamme, Bernt Nesje og Anders Forsdahl, 1983.

8.* Merkesteiner i norsk medisin reist av allmennpraktikere - og enkelte utdrag av medisinalberetninger av kulturhistorisk verdi.
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9. "Balsfjordsystemet." EDB-basert journal, arkiv og statistikksystem for primærhelsetjenesten.
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Av Georg Høyer, 1986.

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Av Bjarne Koster Jacobsen, 1988.

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Av Anne Johanne Søgaard, 1989.

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