

# Influence of number needed to treat, costs and outcome on preferences for a preventive drug

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Nexøe J, Kristiansen IS, Gyrd-Hansen D and Nielsen JB. Influence of number needed to treat, costs and outcome on preferences for a preventive drug. *Family Practice* 2005; **22**: 1–6.

**Background.** The number needed to treat (NNT) has been widely recommended for communicating benefits from risk reductions. It has been claimed that NNT is easily understood and that it has intuitive meaning. There are, however, only few studies of lay people's understanding of NNT.

**Objective.** The objective of this study was to explore whether lay people are sensitive to the magnitude of treatment effectiveness as expressed in terms of NNT, and whether the sensitivity is influenced by variation in the type of health outcome, variation in patients' payment for the treatment or variation in the type of side effects.

**Methods.** In total, 2326 non-institutionalized Danes aged 18–91 years were interviewed face to face and asked whether they would consent to a treatment against a somewhat increased risk of death or heart attack. The respondents were allocated to different levels of effectiveness of treatment expressed as NNT of 10, 100, 200 or 400, different costs and different descriptions of adverse effects.

**Results.** The odds for consenting to therapy were little influenced by the magnitude of NNT, but were greater among married respondents and among those who had side effects presented in terms of headache and constipation.

**Conclusion.** In this study, the respondents' choice of treatment was largely insensitive to the magnitude of NNT independently of variations in type of health outcome and costs. NNT may not be easily understood by lay people.

**Keywords.** General practice, number needed to treat, outcome type, randomized trial, risk communication.

## Introduction

Benefits from preventive interventions targeting chronic conditions such as atherosclerosis may be measured at a specific point in time [and expressed in terms of cross-sectional statistics such as absolute risk reduction (ARR), its reciprocal, the number needed to be treated (NNT), relative risk reduction (RRR) or odds ratio (OR)], across time in longitudinal measures (and expressed in terms of increased median survival time) or a combination of longitudinal and cross-sectional measures (and expressed as gain in mean survival or life expectancy).

While NNT is often used in medical publications and possibly also in clinical practice, there is little evidence

that patients or doctors make more appropriate decisions when they use NNT rather than other measures of benefit.<sup>1</sup> By 'appropriate' we mean decisions that are in line with those that patients and doctors would make when they have received and comprehended all relevant information. Previous studies indicate that lay people as well as doctors<sup>2–4</sup> have difficulties in understanding NNT in that they either are insensitive to the magnitude of NNT when making decisions or ascribe NNT characteristics that it does not have. These studies, however, may be criticised on the grounds that the respondents have been offered treatment with negligible side effects and costs and have consented to therapy even when the effectiveness was very small. The aim of this study was to explore whether variation in the type of health outcome, variation in patients' payment for the treatment or variation in the type of side effects would affect preferences for therapy when its treatment benefit was expressed in terms of NNT.

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Received 7 January 2004; Accepted 16 March 2004.

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## Methods

Four random samples, each of 562–610 respondents, of which three were subdivided further randomly into four subgroups, each of 139–164 respondents, were interviewed in person about preferences for a hypothetical therapy. In total, 2326 non-institutionalized Danes aged 18–91 years participated in ‘Computer Assisted Personal Interviewing’ by AC Nielsen Inc., Denmark. The interviews were performed by 128 trained professional interviewers (see Appendix for exact wording of interviews). All interviews took place during an 8 week period in August and September 2001. Questions were presented to respondents both verbally and in writing. Each interview took ~30 min. When sampled individuals were not at home, up to two repeat calls were made. Fifty percent of the subjects that were contacted agreed to be interviewed (Table 1). In addition to demographic variables such as age, gender, marital status, level of education and personal income, the respondents were asked to consider whether they would consent to a hypothetical treatment for a somewhat increased risk of heart attack. The treatment was described as taking a pill once a day and having a check-up twice a year in the GP’s office. Except for one group, the respondents were allocated to treatment effectiveness expressed as NNT of 10, 100, 200 or 400. The adverse event averted was either heart attack (myocardial infarction) or death. The out-of-pocket payment was either DKK 500 (€65) or DKK 5000 (€650) per year. Respondents were told that side effects were either mild and harmless or headache and constipation.

The 580 respondents in group 2 were asked how they understood the expression of effectiveness of treatment: “For each case of heart attack avoided NNT (NNT = 10, 100, 200 or 400) patients must take medication for 3 years”.

The group size was calculated on the assumption that 90% of the respondents would consent to treatment

TABLE 1 Persons invited for computer-assisted personal interviewing

	Number	% of gross sample	% of net sample
Gross sample	9093		
Drop-out because of age (<18 years)	142	2%	
Drop-out because of disease, foreign language, etc.	352	4%	
Not private address (institution)	122	1%	
Respondent not at home	3783	42%	
Net sample	4694	52%	
Refused to participate in interview	2368	26%	51%
Accepted to participate in interview	2326	26%	50%

when it was most effective (NNT = 10), and 75% when it was one step less effective (NNT = 100). In this case, we would need a sample size of 100 to achieve an 80% probability of detecting a difference of 15% between the groups with a significance level of 5% two-tailed tests.

Statistical analyses were performed in SPSS for Windows release 11.5. The odds for consenting to therapy (‘yes’ versus ‘no’, with ‘uncertain’ classified as ‘no’) were analysed in a logistic regression model using socio-demographic factors, out-of-pocket payment, description of adverse effects and magnitude of NNT as covariates. We tested for interaction between magnitude of NNT and the type of adverse effects and out-of-pocket payment. Two-tailed *P*-values are given throughout.

## Results

### Demographics

The respondents’ mean age was 47 years, and 56% were female compared with 47 years and 51% in the general population. Personal annual income was above DKK 300 000 in 15% of respondents compared with 7% of the general population, and the study population had a slightly better educational attainment (proportion of individuals with elementary school only was 26% compared with 37% in the general population) (Table 2).

### Consenting to treatment and sensitivity to magnitude of NNT

Among all 2326 respondents, 56% consented to the treatment, 36% rejected it and 8% were uncertain. For groups 2 and 4, there was no association between consent to treatment and the magnitude of the NNT (Table 3). A greater proportion of the respondents consented to treatment when the outcome measure was death instead of heart attack (64.8 versus 49.6%, chi-square = 3.14, *P* = 0.002). The proportion consenting was about the same whether the treatment cost was DKK 500 or DKK 5000 (47.9 versus 49.6%, chi-square = 0.27, *P* = 0.785). The odds for consenting to therapy were greater among married respondents (OR 1.210, 95% confidence interval 1.007–1.452) and those who had side effects presented in terms of headache and constipation [OR 1.812 (1.270–2.586)], while the effects of other covariates including NNT were not statistically significant (Table 4). We found no significant interaction between NNT and out-of-pocket payment or NNT and type of side effect. However, in group 3 (side effects presented as headache and constipation), there was a borderline statistically significant declining consent to treatment with increasing NNT (chi-square test for trend = 3.71, *P* = 0.054).

### Interpretation of NNT

When asked about interpretation of NNT, 30% of respondents thought that the likelihood of having

TABLE 2 Respondents' characteristics

Group	Subgroup (NNT)	No. of respondents	Mean age (years)	Percentage female	Percentage with personal income $\geq$ DKK 300 000	Percentage with elementary school only
Group 1: outcome heart attack; costs DKK 500/year; adverse effects mild and harmless	100	562	47	54	11	21
Group 2: outcome heart attack; costs DKK 5000/year; adverse effects mild and harmless	10	144	47	63	19	25
	100	146	45	57	14	25
	200	143	44	58	22	23
	400	147	45	55	19	25
	Total	580	45	58	18	24
Group 3: outcome heart attack; costs DKK 500/year; adverse effects headache and constipation	10	139	47	57	10	23
	100	154	47	55	20	22
	200	142	47	54	16	19
	400	139	47	50	16	23
	Total	574	47	54	16	22
Group 4: outcome death; costs DKK 500/year; adverse effects mild and harmless	10	157	47	60	16	25
	100	142	49	56	16	23
	200	147	45	56	18	19
	400	164	49	60	15	21
	Total	610	48	58	16	22

TABLE 3 Preferences for treatment according to description of outcome and adverse effects, out-of-pocket payment and its effectiveness in terms of number needed to treat

Group	NNT	No. (%) consenting to treatment	No. (%) rejecting treatment	No. (%) uncertain
Group 1: outcome heart attack; costs DKK 500/year; adverse effects mild and harmless	100	279 (49.6%)	244 (43.4%)	39 (6.9%)
Group 2: outcome heart attack; costs DKK 5000/year; adverse effects mild and harmless	10	68 (47.2%)	56 (38.9%)	20 (13.9%)
	100	70 (47.9%)	61 (41.8%)	15 (10.3%)
	200	84 (58.7%)	54 (37.8%)	5 (3.5%)
	400	60 (40.8%)	71 (48.3%)	16 (10.9%)
	Total	282 (48.6%)	242 (41.7%)	56 (9.7%)
Group 3: outcome heart attack; costs DKK 500/year; adverse effects headache and constipation	10	94 (67.6%)	32 (23.0%)	13 (9.4%)
	100	90 (58.4%)	54 (35.1%)	10 (6.5%)
	200	85 (59.9%)	47 (33.1%)	10 (7.0%)
	400	76 (54.7%)	58 (41.7%)	5 (3.6%)
	Total	345 (60.1%)	191 (33.3%)	38 (6.6%)
Group 4: outcome death; costs DKK 500/year; adverse effects mild and harmless	10	111 (70.7%)	32 (20.4%)	14 (8.9%)
	100	92 (64.8%)	44 (31.0%)	6 (4.2%)
	200	97 (66.0%)	40 (27.2%)	10 (6.8%)
	400	109 (66.5%)	42 (25.6%)	13 (7.9%)
	Total	409 (67.0%)	158 (25.9%)	43 (7.0%)

a treatment effect is one out of the NNT (Table 5). Thirty-six percent were uncertain about how to interpret the NNT concept.

#### *Classification of uncertain responses in dependent variable*

No major differences in results were found if the 'uncertain' responses were omitted from analysis instead of being classified together with the 'no' responses.

## Discussion

The findings of this study indicate that the magnitude of NNT has little or no impact on lay people's preferences for a therapy. When costs are not negligible, people, presumably, make trade-offs between costs and benefits when they decide on a treatment for themselves. The costs of the intervention may be the monetary expenses, loss of leisure or productive time, risk of potential

adverse effects or uneasiness about using drugs. In a Danish context, DKK 5000 per year is a considerable outlay for patients, and people would be expected to make trade-offs between costs and effects, but still their choices were not influenced by effectiveness when it was presented in terms of NNT. Adverse effects were described either as mild and harmless or as headache and constipation, a difference that may be considered marginal to the medical professional. If adverse effects

were described specifically as headache and constipation, more weight was put on the magnitude of NNT, but respondents seemed to be more willing to accept treatment. This may be explained as a general scepticism toward a treatment with mild and harmless side effects. Patients may suspect the GP of not knowing the medicine well enough if adverse effects cannot be described any better than as mild and harmless. When adverse effects were described in detail, patients, apparently, at the same time became more conscious about the magnitude of the NNT and consented to treatment to a significantly higher degree.

The logistic regression analysis suggested that being married or co-habiting was significantly associated with consenting to treatment. This result coincides with a recent Finnish study which shows that being married suppresses unhealthy behaviour.<sup>5</sup>

#### Study limitations

The results of this study should be interpreted within the context of the study limitations. The features of the drug used in this study, though hypothetical, are not unrealistic. The description compares well with the features of lipid-lowering drugs with regard to benefits and adverse effects.

The response rate was low compared with response rates in questionnaire studies. This was to be expected as the interviews were time-consuming and respondents might be busy doing other things when the interviewers called. Personal interviews were still chosen because of the complexity of the questions asked. Due to the low response rate, some caution should be taken in generalizing the results. The respondents were not fully representative of the general population in that their education was for longer and their personal income higher. This may indicate that the respondents in this study had higher levels of numeracy, were more qualified decision makers, and were supposedly even

TABLE 4 Logistic regression analysis of odds for consenting to therapy (consenting = 1, not consenting = 0)

Variables	Odds ratio	95% CI
Age (years)	0.999	0.994 to -1.004
Gender (0 = female, 1 = male)	0.923	0.768 to -1.109
Education (0 = elementary school only, 1 = higher education)	0.889	0.711 to -1.111
Personal income (0 = <DKK 300 000, 1 = ≥DKK 300 000)	0.989	0.763 to -1.282
Marital status (0 = single, 1 = married, cohabitant)	1.210*	1.007 to -1.452
Outcome (0 = heart attack, 1 = death)	2.042*	1.552 to -2.686
Out-of-pocket payment (0 = DKK 5000, 1 = DKK 500)	0.972	0.683 to -1.384
Description of adverse effects (0 = mild and harmless, 1 = headache and constipation)	1.812*	1.270 to -2.586
NNT (10–400)	0.999	0.998 to -1.001
NNT × description of adverse effects	0.999	0.998 to -1.001
NNT × out-of-pocket payment	1.000	0.999 to -1.002
Constant	1.068	

*n* = 2045. Those for whom information on income and/or education was missing (*n* = 281) were omitted from analysis.

\* *P* < 0.05.

TABLE 5 Interpretation of NNT

	Perception of NNT			Total
	Only one out of NNT patients benefit from treatment in 3 years	It is impossible from the expression to calculate how many patients benefit from treatment in three years	I am uncertain how to understand the expression	
Consenting to treatment	88 (31.2%)	95 (33.7%)	99 (35.1%)	282 (100%)
Rejecting treatment	73 (30.2%)	84 (34.7%)	85 (35.1%)	242 (100%)
Uncertain	13 (23.2%)	16 (28.6%)	27 (48.2%)	56 (100%)
Total	174 (30.0%)	195 (33.6%)	211 (36.4%)	580 (100%)

A total of 580 patients were asked how they understood the expression of effectiveness of treatment: “For each case of cardiac infarction avoided NNT patients must take medication for 3 years”.

more able than average to understand the NNT concept. Positive correlations between numeracy and accuracy of risk perception have been shown in a study among medical students; however, only 25% interpreted the NNT correctly.<sup>6</sup> If the low and slightly biased response rate had any effect, it most probably led us to underestimate the difficulties in understanding the NNT concept.

#### *Relation to findings in other studies*

Why were the respondents so insensitive to the magnitude of NNT and apparently not considering costs but adverse effects in decision making? We find it most likely that lay people do consider benefits and costs, but the concept of NNT is simply difficult to understand. This is in line with previous studies.<sup>2,3,7,8</sup> The facts that 30% agree that the likelihood of having an effect of the treatment is one out of the NNT and 36.4% express uncertainty as to how to understand NNT are further support that NNT is not an easily understandable concept. As we have pointed out in previous studies,<sup>2,3,9</sup> the NNT will in some cases mean that the probability of benefit for the individual patient really is one out of the NNT and the treatment is like a lottery in which a few win a prize. However, most often, many or even all treated patients gain a little from treatment. In general, the lottery-like interpretation of NNT may be warranted for acute diseases, while 'small benefits in many patients' may be more appropriate for chronic diseases.

#### *Conclusion*

The concept of NNT appears not to be easily understood by lay people. Insensitivity to the magnitude of NNT may be explained by lack of understanding, as information not understood cannot be used in decision making. Clinicians and health care policy makers should be cautious in using NNT as a decision-making tool.

## Declaration

Funding: Danish Medical Research Council  
Ethical approval: Not required for this kind of study according to Danish legislation.  
Conflicts of interest: None.

## References

- 1 Dowie J. The 'number needed to treat' and the 'adjusted NNT' in health care decision-making. *J Health Serv Res Policy* 1998; **3**: 44–49.
- 2 Kristiansen IS, Gyrd-Hansen D, Nexøe J, Nielsen JB. Number needed to treat: easily understood and intuitively meaningful?; theoretical considerations and a randomized trial. *J Clin Epidemiol* 2002; **55**: 888–892.
- 3 Nexøe J, Gyrd-Hansen D, Kragstrup J, Kristiansen IS, Nielsen JB. Danish GPs' perception of disease risk and benefit of prevention. *Fam Pract* 2002; **19**: 3–6.

- 4 Halvorsen PA, Kristiansen IS, Aasland OG, and Førde OH. Medical doctors' perception of the 'number needed to treat' (NNT). A survey of doctors' recommendations for two therapies with different NNT. *Scand J Prim Health Care* 2003; **21**: 162–166.
- 5 Laaksonen M, Prattala R, Lahelma E. Sociodemographic determinants of multiple unhealthy behaviours. *Scand J Public Health* 2003; **31**: 37–43.
- 6 Sheridan SL, Pignone M. Numeracy and the medical student's ability to interpret data. *Eff Clin Pract* 2002; **5**: 35–40.
- 7 Nexøe J, Oltarzewska AM, Sawicka-Powierza J, Kragstrup J, Kristiansen IS. Perception of risk information. Similarities and differences between Danish and Polish general practitioners. *Scand J Prim Health Care* 2002; **20**: 183–187.
- 8 Sheridan SL, Pignone M, Lewis CL. A randomized comparison of patients' understanding of number needed to treat and other common risk reduction formats. *J Gen Intern Med* 2003; **18**: 884–892.
- 9 Kristiansen IS, Nexøe J, Gyrd-Hansen D, Nielsen JB. NNT is not easily understood. *Fam Pract* 2002; **19**: 566.

## Appendix: exact wording (translated from Danish) of the interview in the four groups

### *Group 1*

Imagine that your doctor tells you that you have a slightly increased risk of having a heart attack. The doctor offers you a medicine to be taken as a pill once daily. The pill has mild and harmless side effects. A prerequisite for the treatment is that you see your doctor twice a year. You have to pay for the medicine yourself, approximately DKK 500 per year. The doctor tells you that when 100 patients have taken the medicine, after 3 years' treatment there will be one less case of heart attack than otherwise.

Q1: Would you choose to accept such a treatment?  
YES  
NO  
DON'T KNOW

### *Group 2. $X = 10 + 100 + 200 + 400$*

Imagine that your doctor tells you that you have a slightly increased risk of having a heart attack. The doctor offers you a medicine to be taken as a pill once daily. The pill has mild and harmless side effects. It is a prerequisite for the treatment that you see your doctor twice a year. You have to pay for the medicine yourself, approximately DKK 500 per year. The doctor tells you that for each case of heart attack avoided, X patients have to take the medicine for 3 years.

Q1: Would you choose to accept such a treatment?  
YES  
NO  
DON'T KNOW

Q2: It may be difficult to understand how great the effect of the medicine is. How do you perceive the statement: “for each case of heart attack avoided, X patients have to take the medicine for 3 years”?

Only 1 out of X patients would benefit from the medicine during the 3 years

One cannot say how many would benefit from the medicine in the 3 years

I am not quite sure how the statement should be understood

*Group 3.  $X = 10 + 100 + 200 + 400$*

Imagine that your doctor tells you that you have a slightly increased risk of having a heart attack. The doctor offers you a medicine to be taken as a pill once daily. The pill causes constipation or headache in three out of 100 patients. It is a prerequisite for the treatment that you see your doctor twice a year. You have to pay for the medicine yourself, approximately DKK 500 per year. The doctor tells you that for each case of heart attack avoided, X patients have to take the medicine for 3 years.

Q1: Would you choose to accept such a treatment?

YES

NO

DON'T KNOW

*Group 4.  $X = 10 + 100 + 200 + 400$*

Imagine that your doctor tells you that you have a slightly increased risk of having a heart attack. The doctor offers you a medicine to be taken as a pill once daily. The pill has mild and harmless side effects. It is a prerequisite for the treatment that you see your doctor twice a year. You have to pay for the medicine yourself, approximately DKK 500 per year. The doctor tells you that for each case of coronary death avoided, X patients have to take the medicine for 3 years.

Q1: Would you choose to accept such a treatment?

YES

NO

DON'T KNOW