Implementing the number needed to harm in clinical practice: risk of myocardial infarction in HIV-1-infected patients treated with abacavir

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Objectives
The D:A:D study group reported a 1.9-fold increased relative risk (RR) of myocardial infarction (MI) associated with current or recent use of abacavir. The number needed to harm (NNH) incorporates information about the underlying risk of MI and the increased RR of MI in patients taking abacavir.

Methods
NNH was calculated as the reciprocal of the difference between the underlying risks of MI with and without abacavir use. A parametric statistical model was used to calculate the underlying risk of MI over 5 years.

Results
The relationship between NNH and underlying risk of MI is reciprocal, resulting in wide variation in the NNH with small changes in underlying risk of MI. The smallest changes in NNH are in the medium- and high-risk groups of MI. The NNH changes as risk components are modified; for example, for a patient who smokes and has a systolic blood pressure (sBP) of 160 mmHg and a 5-year risk of MI of 1.3% the NNH is 85, but the NNH increases to 277 if the patient is a nonsmoker and to 370 if sBP is within the normal range (120 mmHg).

Conclusions
We have illustrated that the impact of abacavir use on risk of MI varies according to the underlying risk and it may be possible to increase considerably the NNH by decreasing the underlying risk of MI using standard of care interventions, such as smoking cessation or control of hypertension.

Keywords: abacavir, antiretroviral treatment, myocardial infarction, number needed to harm

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Introduction
Abacavir is a common antiretroviral used in the treatment of HIV-1 infection and is currently recommended as one of the possible components of initial combination antiretroviral treatment [1–3]. The D:A:D study group recently reported an increased risk of myocardial infarction (MI) related to current or recent use of abacavir [4,5]. Some of the HIV-1 treatment guidelines have already taken into account the clinical implications of the D:A:D findings by emphasizing that clinicians should consider careful assessment of patients who are on abacavir and at high risk of MI [2,6,7]. It is therefore of great importance to ensure that the risk of MI attributed to abacavir use, together with the underlying risk of MI, is correctly interpreted and understood.

Presenting results as relative risks (RRs) is standard in observational studies [8], but may be difficult to translate into clinical practice. The number needed to treat (NNT) and absolute risk reduction may be more clinically relevant, when assessing the beneficial effect of treatment [9–11], and the number needed to harm (NNH), together with absolute risk increase (ARI), will better reflect any adverse effect of treatment than RR in clinical terms [12]. Both NNH and RR are measures that attempt to summarize two numbers (the risks of MI with and without abacavir). RR summarizes the relative increase in the underlying risk
of an event according to whether the patient receives a
given treatment or not and the NNH indicates the number
of patients that need to be treated to observe the adverse
effect of a treatment in one additional patient. This
approach was first proposed in 1988 [13], but it is still
infrequently used to describe risk of adverse events of
medicines [14–17].

NNH is a tool that can be used in different settings [18].
Currently it is calculated mostly for the results of
randomized controlled trials (RCTs) and presented in
summary papers as a single number describing the
difference in adverse treatment effect between treatment
and control groups [19–21]. However, if used in this way it
does not capture the effect of underlying risk variation in a
trial population [22]. Although that approach has been
strongly suggested by CONSORT [9] we rarely see NNH
recalculated for subpopulations with higher underlying risk
in RCTs [23,24].

The aims of this paper were to apply NNH for an adverse
event associated with HIV therapy and relate it to the
underlying risk of this event. As an example of an adverse
event, we used the recently reported association between
current or recent exposure to abacavir and increased rate
of MI [4,5]. The NNH and ARI from using the drug over a
5-year period were estimated in populations of HIV-1-
infected patients with varying underlying risk of MI.

Methods

The NNH was calculated as the reciprocal of ARI (1/ARI) in
accordance with standard methodology [12,13]. The ARI
was calculated as the difference between the risks of MI
with and without treatment with abacavir (the latter being
the underlying risk). The D:A:D study reported an increased
risk of MI, of RR = 1.90, in patients on abacavir, which
remained unchanged with longer exposure [4,5]. The NNH
was therefore calculated as NNH = 1/[(underlying risk of
MI × 1.9) – underlying risk of MI]. The underlying risk of
MI was calculated with a parametric statistical model based
on the Framingham equation [25] incorporated into the R
statistical program (www.r-project.org/) to calculate the
NNH for each underlying risk of MI and to create two- and
three-dimensional graphs relating NNH values to different
risk components. The RR of MI in patients on abacavir was
assumed not to vary with increasing exposure to abacavir
or according to the underlying risk of MI in our
calculations.

Assumptions about the time of exposure

The Framingham equation is limited to predicting cardio-
vascular risk in 30–74-year-old patients over 4–12 years
reflecting the characteristics of the Framingham Heart
Study population [25]. As the median follow-up in the
D:A:D study was 5.1 years per person [4], we calculated the
probability of an MI occurring within the next 5 years.

Relating NNH to underlying risk of MI and its
components

To relate NNH to different components contributing to the
underlying risk of MI, we performed a series of calculations
with different cardiovascular risk equation modifications,
and profiles reflecting possible clinical interventions were
presented with graphs. All graphs were created for male
gender and stratified into four groups according to
smoking status and lipid profile. Using National Cholesterol
Education Program (NCEP) Adult Treatment Panel (ATP) III
guidelines [26] and the first and third quartile lipid values
from the D:A:D study, we defined thresholds for favourable
profiles as a total cholesterol value of 170 mg/dL
(4.4 mmol/L) and a high-density lipoprotein (HDL) choles-
terol value of 60 mg/dL (1.5 mmol/L), and thresholds for
unfavourable profiles as a total cholesterol value of
240 mg/dL (6.2 mmol/L) and an HDL cholesterol value of
35 mg/dL (0.9 mmol/L). Within these groups, the NNH
was plotted against age and systolic blood pressure (sBP), and
for the latter a value of 120 mmHg, which represents the
median observed in the D:A:D study, was chosen [27,28].

Assumptions about the prior history of cardiovascular
disease

The applied Framingham equation was developed for a
population with no prior coronary heart disease (CHD) and
thus does not reflect the risk of developing an MI in that
patient group. According to the NCEP/ATP III guidelines, a
history of CHD is considered to confer a 10-year CHD risk
in excess of 20% [26], roughly corresponding to a 10-year
risk of MI of 10% and a 5-year risk of MI of 5%.

Estimating uncertainty for NNH

To summarize the uncertainty associated with NNH, the
95% confidence interval (CI) for the relative rate of MI
(1.47, 2.45) reported by Sabin et al. [4] is incorporated in
the calculations, as described below.

Interpreting the results

All NNH values represent the number of patients who need
to be treated with abacavir for 5 years to observe MI in one
additional patient as a consequence of this treatment.
Using the 10 and 20% cut-offs proposed in the NCEP/ATP III guidelines for assessing 10-year CHD risk [26] we defined low-, medium- and high-risk groups with absolute risks of MI of <5, 5–10 and >10% over 5 years, respectively. Therefore, in patients who are not on abacavir this risk will reflect the underlying risk of MI alone, while in patients on abacavir the absolute risk will consist of both the underlying risk of MI and the additional risk attributed to use of abacavir.

Results

Relation between NNH and underlying risk of MI for an adverse drug effect that is associated with increased risk of MI over a 5-year period

The relationship between NNH and underlying risk of MI is reciprocal (Fig. 1; dashed line), whereas the relationship between ARI and underlying risk of MI is linear (Fig. 1; continuous line). The NNH decreases quickly from 185 to 5 as the underlying risk of MI increases from 0.6 to >20%. If the underlying risk of MI is 5%, the ARI will be 4.5% (i.e. a 90% increase) and the NNH with abacavir will be 22. An ARI of 4.5% implies that using the drug over the next 5 years will increase this patient’s risk of having an MI from 5 to 9.5%. An NNH of 22 implies that if 22 patients with an estimated underlying risk of MI of 5% use abacavir over this same 5-year period, one additional patient may be expected to develop an MI which would not have occurred had this group of patients not used abacavir.

As the relationship is reciprocal, the same absolute change in the underlying risk of MI results in a small change in NNH for patients with a high MI risk and a large change for patients with a small underlying risk of MI. For example, a 5% decrease in the underlying risk of MI for an underlying risk of 15% reflects NNH changing from 7 to 11, while the same decrease for an underlying risk of 6% changes the NNH value from 18 to 111. Relating ARI to the underlying risk of MI is not capturing this relationship.

Estimating uncertainty for NNH

In order to determine the level of uncertainty we estimated the 95% CI for all NNH values presented in Table 1. For example, if the underlying risk of MI is 0.1% over 5 years the 95% CI is from 689 to 2127, representing the NNH for the upper (RR = 2.45) and lower (RR = 1.47) ranges of the 95% confidence interval for the relative rate of MI for patients on abacavir reported by the D:A:D study, respectively.

NNH in relation to underlying risk components

To determine how different risk components contribute to the change in the underlying risk of MI and NNH variability, we performed a series of analyses using different risk assumptions over two different time periods (Table 1), choosing a patient profile that reflects D:A:D patients’ characteristics as described in the Methods section: male, aged 40 years, nonsmoking with no diagnosis of diabetes, no changes in electrocardiogram (ECG), an sBP of 120 mmHg, a total cholesterol value of 170 mg/dL (4.4 mmol/L) and an HDL cholesterol value of 60 mg/dL (1.5 mmol/L). The NNH drops from 1111 to 555 for such a patient when the patient is diagnosed with diabetes, and by the same amount when the patient develops hypercholesterolaemia (total cholesterol value of 240 mg/dL; 6.2 mmol/L) or left ventricular hypertrophy is present on ECG. The NNH drops further to 370 if the patient’s sBP increases to 160 mmHg or his HDL cholesterol value decreases to 35 mg/dL (0.9 mmol/L) and to 277 if the patient starts smoking.

When two risk components with unfavourable levels coexist at the same time and in the same patient, the NNH
drops from 1111 to around 100 for most pairs of risk factors, except smoking combined with unfavourable HDL cholesterol, for which the NNH decreases even further to 69. The NNH decreases to 7 when all risk factors are defined as unfavourable at the same time and the underlying 5-year risk of an MI is 15%.

The NNH was further calculated after adjusting for the presence of a history of CVD, as defined in the Methods section, and was found to drop from 1111 to 22 and from 370 to 11, for 5- and 10-year risks of MI, respectively.

Figure 2 presents a series of graphs relating NNH to any possible age and sBP, and categorizes it according to smoking status and two chosen lipid profiles. In these graphs it is also possible to observe the change in NNH while different risk components are modified separately or consecutively. These graphs illustrate the impact on NNH of the introduction of an additional risk factor, here smoking and unfavourable lipid profile. Comparison of graphs A and B demonstrates that smoking produces a marked decrease in NNH, which means that you would need to treat considerably fewer smokers to observe one additional MI, and comparison of graphs C and D demonstrates that a further decrease in NNH is seen with an additional risk of an unfavourable lipid profile.

To give a specific example, a 50-year-old, nonsmoking patient with favourable lipid profiles and sBP of 120 mmHg will have an NNH in the range of 200–500 (graph A), while a patient of the same age who smokes (but who also has favourable lipid profiles and sBP of 120 mmHg) will have an NNH in the range of 50–100 (graph B). For these patients, an increase in sBP from 120 to 150 mmHg will lead to an NNH of 100–200 for the nonsmoking patient and an NNH of 30–50 for the patient who smokes (graph B), and unfavourable lipid profiles will change the NNH values of these patients to 30–50 (graph C) and 20–30 (graph D), respectively.

Coloured three-dimensional illustrations of these results (Fig. 3) enable easy identification of high or low NNH and help one to understand the dynamics of NNH change when particular risk components are modified in a way that reflects possible clinical interventions. For example, it is readily apparent that red, reflecting the lowest NNH (graph D), shifts to orange and yellow if the risk factor of smoking is removed (graph C). Therefore, introducing smoking cessation in this group of patients will eventually increase the NNH from $\frac{10}{11}$ to $\frac{42}{22}$.

Discussion

In this paper we combine estimates of the underlying risk of MI with the increased risk of MI associated with abacavir reported by the D:A:D study, and present the data not only in terms of ARI but also as NNH. Using this approach we show it is possible to increase NNH values for patients that

### Table 1

<table>
<thead>
<tr>
<th>Change in factors contributing to underlying risk</th>
<th>Estimated for 5 years</th>
<th>Estimated for 10 years</th>
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<tbody>
<tr>
<td></td>
<td>Underlying risk of MI (%)</td>
<td>NNH (95% CI)*</td>
</tr>
<tr>
<td>Example low-risk profile7</td>
<td>0.1</td>
<td>1111 (689–2127)</td>
</tr>
<tr>
<td>If total cholesterol unfavourable (240 mg/dL, 6.2 mmol/L)</td>
<td>0.2</td>
<td>555 (344–1063)</td>
</tr>
<tr>
<td>If diabetic</td>
<td>0.2</td>
<td>555 (344–1063)</td>
</tr>
<tr>
<td>If left ventricular hypertrophy present on ECG (ECG-LVH)</td>
<td>0.2</td>
<td>555 (344–1063)</td>
</tr>
<tr>
<td>If sBP = 160 mmHg</td>
<td>0.3</td>
<td>370 (229–709)</td>
</tr>
<tr>
<td>If HDL unfavourable (35 mg/dL, 0.9 mmol/L)</td>
<td>0.3</td>
<td>370 (229–709)</td>
</tr>
<tr>
<td>If smoker</td>
<td>0.4</td>
<td>277 (172–531)</td>
</tr>
<tr>
<td>If HDL and total cholesterol unfavourable</td>
<td>0.8</td>
<td>138 (86–265)</td>
</tr>
<tr>
<td>If smoker and total cholesterol unfavourable</td>
<td>1.0</td>
<td>111 (68–212)</td>
</tr>
<tr>
<td>If smoker and diabetes</td>
<td>1.1</td>
<td>101 (62–193)</td>
</tr>
<tr>
<td>If smoker and sBP = 160 mmHg</td>
<td>1.3</td>
<td>85 (53–163)</td>
</tr>
<tr>
<td>If smoker and HDL unfavourable</td>
<td>1.6</td>
<td>69 (43–132)</td>
</tr>
<tr>
<td>If smoker and HDL unfavourable</td>
<td>1.6</td>
<td>69 (43–132)</td>
</tr>
<tr>
<td>If any previous CVD (as defined in Methods section)</td>
<td>3.1</td>
<td>35 (22–68)</td>
</tr>
<tr>
<td>If all unfavourable combined (excluding ECG-LVH)</td>
<td>5.0</td>
<td>22 (13–42)</td>
</tr>
<tr>
<td>If all unfavourable combined (including ECG-LVH)</td>
<td>10.1</td>
<td>11 (6–21)</td>
</tr>
<tr>
<td></td>
<td>15.0</td>
<td>7 (4–14)</td>
</tr>
</tbody>
</table>

* Ninety-five per cent confidence interval (CI) of NNH calculated based on the upper and lower estimates of 95% CI for relative rate of myocardial infarction for patients on abacavir reported in the D:A:D study.

1 Forty-year-old man, nonsmoking, non-diabetic, left ventricular hypertrophy not present on ECG, normal systolic blood pressure (120 mmHg), desirable total cholesterol (170 mg/dL; 4.4 mmol/L), and favourable high-density lipoprotein (HDL) cholesterol (60 mg/dL; 1.6 mmol/L).

The NNH was calculated using the underlying risk of myocardial infarction (MI) estimated with rounding to one decimal. CVD, cardiovascular disease.
might use or start this drug by decreasing their underlying risk of MI. The clinical implication of this finding is simple – through regular screening for and proper management of established modifiable cardiovascular risk factors which determine the underlying risk of MI in HIV-1-infected patients, it may be possible to increase the number of patients who may be safely treated with a drug that is potentially associated with the development of a serious adverse event.

The adjusted RR of an MI of 1.90 reported in the D:A:D study [4] indicates a substantial increase in the underlying risk of MI, if already existing, underlying pretreatment risk is considered medium or high. It is therefore essential that this risk is put into context and appropriate consideration given to whether patients should be maintained on abacavir or whether the drug should be discontinued. For many patients, discontinuation might not be the most appropriate decision; the patient may be stable and satisfied with the current abacavir-containing regimen, or may have resistance to other antiretrovirals or a history of serious combination antiretroviral therapy (cART) adverse events, both of which could reduce options for switching to other antiretrovirals. Reducing the underlying risk of MI by stopping antiretrovirals is not an acceptable option, as it is known to increase the risk of HIV disease progression [29]. Our results may therefore help to identify the best possible interventions that could be introduced even if the drug cannot be switched or stopped.

Of note, if all 50-year-old patients with no other risk factors for MI except smoking ceased smoking, our

### NON SMOKING NON DIABETES

<table>
<thead>
<tr>
<th>Favourable lipid profiles total cholesterol 170 mg/dL (4.4 mmol/L) HDL 60 mg/dL (1.5 mmol/L)</th>
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<tbody>
<tr>
<td><strong>Graph A</strong></td>
</tr>
<tr>
<td><img src="image1.png" alt="Graph A" /></td>
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<tr>
<td><strong>Graph B</strong></td>
</tr>
<tr>
<td><img src="image2.png" alt="Graph B" /></td>
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### SMOKING NON DIABETES

<table>
<thead>
<tr>
<th>Unfavourable lipid profiles total cholesterol 240 mg/dL (6.2 mmol/L) HDL 35 mg/dL (0.9 mmol/L)</th>
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<tbody>
<tr>
<td><strong>Graph C</strong></td>
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<tr>
<td><img src="image3.png" alt="Graph C" /></td>
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<tr>
<td><strong>Graph D</strong></td>
</tr>
<tr>
<td><img src="image4.png" alt="Graph D" /></td>
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</table>

**Fig. 2** The graphs presenting age and systolic blood pressure as changing components of underlying risk of myocardial infarction (MI) estimated for 5 years in relation to number needed to harm (presented in defined ranges) for a drug associated with increased risk of MI. Numbers on the gridlines represent number needed to harm (NNH) values. Using the gridlines it is possible to relate the patient’s systolic blood pressure (x-axis) and age (y-axis) to a specific NNH or its range (e.g. 100–50). HDL, high-density lipoprotein.
calculation would predict that the number of MIs attributed to abacavir use would decline with time by 80%.

Interestingly, the NNT, as a measure of positive treatment effect, has been used far more frequently [30–33]. The approach taken in this paper, of illustrating the NNH and how it changes with modification of the underlying risk, has been less commonly described in the literature and, to our knowledge, has not been previously reported for adverse events associated with antiretroviral treatment in HIV-1-infected patients.

We have not investigated further the validity of the results of the D:A:D study or the possible causal mechanism. The example we chose served as a useful illustration, because the reported increased risk of MI occurred quickly after initiation of the drug, the increase was maintained and was stable irrespective of duration of use of the drug, and the increased risk ceased 6 months after drug cessation [4,5]. The presented approach can also be used for a drug that has a cumulative risk, for example the RR of MI of 1.16 per additional year of exposure to protease inhibitors (PIs) reported by the D:A:D group [27]. Applying both risks over a 5-year exposure period in a patient with a 5% underlying risk of MI results in an increase in the underlying risk of 1.9 for

**Fig. 3** The graphs presenting age and systolic blood pressure (SBP) as changing components of underlying risk of myocardial infarction (MI) estimated for 5 years in relation to the number needed to harm (NNH) presented in three-dimensional graphs with ranges defined by different colours for a drug associated with increased risk of MI. The y-, x- and z-axes present NNH, age and SBP values, while colours on the plane reflect NNH ranges as described in the key. Graphs A and B present NNH for nonsmoking and smoking patients with favourable lipid profiles. Graphs C and D present NNH for nonsmoking and smoking patients with unfavourable lipid profiles. HDL, high-density lipoprotein.
abacavir (RR = 1.9) and of 2.1 for PIs (RR = 1.16) and NNH values of 22 and 18, respectively.

We have presented the measure of uncertainty for NNH with the 95% CI reported in the D:A:D study for the RR of MI [4], which indicates the precision of the estimate for the relative rate of MI for patients on abacavir observed in the D:A:D study. For simplicity we have not incorporated additional uncertainty for NNH resulting from uncertainty in the assessment of the underlying risk. It is also important to note that the risk of MI is unlikely to disappear as soon as a risk factor is modified or removed, and therefore that the NNH will not change immediately when a risk factor is modified. For example, smoking cessation may completely reverse the cardiovascular risk attributable to smoking [34], and the observed time from stopping smoking to decrease in mortality from CHD has been reported to be between 5 and 10 years [35,36]. It is important to note, however, that these effects were observed in non-HIV-infected populations and it is unknown whether they can be applied similarly to HIV-infected patients.

NNH values cannot be addressed with commonly defined limits for what represents an acceptable risk or not [37]. The general approach is: the higher the NNH, the better. One possible solution is to relate NNH to already recognized high- or low-risk values [24,33,38]. It is also important to relate treatment harm and benefit to the size of the effect that treatment has. For interventions preventing death we are able to accept lower NNH than for those preventing nonfatal diseases [39]. In the same way, if the size of a positive treatment effect is large and therefore NNT low, we are more willing to accept lower NNH [12]. Furthermore, as the NNH values can be calculated for any chosen outcome they should always be interpreted in relation to this specific context [40]. For example, NNH to cause any bleeding requiring hospitalization in stroke survivors [37] was 467 for aspirin and 126 for warfarin, but for central nervous system bleeding alone NNH was 534 and 301, respectively.

The underlying risk of MI is continuously changing as a result of many factors influencing particular risk components (e.g. lipid-lowering treatment, diagnosis of diabetes or smoking cessation) and NNH values should not be considered as constant [23,24]. In addition, a delay in the onset of an adverse event may occur after exposure and NNH is not able to capture this effect [41]. Therefore, the most appropriate approach would be to assess patients’ risk on a regular basis, according to current guidelines for care of HIV-1-infected patients [42], along with repeated adjustments for the NNH. Risk assessment should also be made available for patients’ use in terms of communicating risk and increasing adherence to risk-lowering interventions. To facilitate this, an appropriate tool will be made available publicly at the Copenhagen HIV Programme webpage (www.cphiv.dk/TOOLS.aspx).

With increasing duration of antiretroviral treatment and aging of the HIV-1-infected population, more adverse effects can be observed. It is therefore of great importance to develop methods that incorporate this information into daily practice. The use of NNH, as presented in this paper, could have a positive impact on patients’ health, as we describe an increase in the NNH with simple lifestyle and/or medical interventions [43–45]. Conclusions regarding the long-term safety and efficacy of antiretrovirals should be drawn based on both clinical trials, typically of a shorter duration, and observational studies, with many years of follow-up [30,46,47]. The development of understandable methods for patients also applies the principles of good clinical practice in terms of delivering informed consent with regard to the treatment offered [48,49].

There are a number of limitations of our study which should be taken into consideration. Firstly, the potential harm of the treatment must be weighed against its benefit, which has not been presented here [12,23]. For the majority of HIV-infected patients, the benefits of antiretroviral treatment far outweigh the potential harm [50,51], which should be taken into account in clinical decision-making [46]. Secondly, the parametric model developed by Anderson et al. [25] used here to determine the underlying risk of MI reflected the Framingham study characteristics, which may be different from those of HIV-1-infected patients. Comparisons of predicted and observed rates of MI in HIV-infected populations suggest that the Anderson equation may overestimate the rate of MI in patients unexposed to antiretrovirals and underestimate it in those exposed to antiretrovirals [52]. Work is ongoing to develop a cardiovascular risk equation for HIV-infected persons, which will address this issue [53]. The RR of MI in patients on abacavir was assumed not to vary with increasing exposure to abacavir or according to the underlying risk of MI in our calculations. However, the D:A:D study reported a marginally significant interaction between moderate/high risk of MI and recent use of abacavir, but adjusted RRs for different categories of underlying risk have not yet been published [4]. Also, it is outside the scope of the present study to incorporate different RRs according to the underlying risk for CVD. Recent findings from a joint analysis of SMART/INSIGHT and D:A:D led to the recommendation that this relationship be further clarified before being taken into consideration in clinical practice [5]. Finally, recent results suggest that there might be an additional very small cumulative effect of the risk of MI with abacavir exposure [54,55]. This effect, in our opinion, will not change the principal relationship between NNH and the underlying risk of MI.
In conclusion, using NNH, we have illustrated that it is possible to increase the number of patients that may safely be treated with a drug that is associated with an increased risk of MI by appropriate management of underlying modifiable traditional cardiovascular risk factors. The NNH, along with underlying risk, may also serve to identify patients who are at a high risk of an MI and where risk-lowering methods are either not relevant or insufficient.

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References


6 DHIS Adults and Adolescents Antiretroviral Treatment Guidelines Panel’s Communication Regarding Abacavir, April 4, 2008.


11 Moriarty PM. Relative risk reduction versus number needed to treat as measures of lipid-lowering trial results. *Am J Cardiol* 1998; 82: 505–507.

12 Sierra F. Evidence-Based Medicine (EBM) in practice: applying number needed to treat and number needed to harm. *Am J Gastroenterol* 2005; 100: 1661–1663.


18 Moore A, McQuay H. Numbers needed to treat derived from meta analysis. NNT is a tool, to be used appropriately. *BMJ* 1999; 319: 1200.


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9

40 Altman DG, Andersen PK. Calculating the number needed to treat for trials where the outcome is time to an event. BMJ 1999; 319: 1492–1495.
47 Carr A. Improvement of the study, analysis, and reporting of adverse events associated with antiretroviral therapy. Lancet 2002; 360: 81–85.