Justyna Kowalska
Copenhagen HIV Program
University of Copenhagen
Faculty of Health Sciences
The Panum Institute
Blegdamsvej 3B, 2200 Cph N, DK
Tel: +45 35 45 57 57
E-mail: jko@cphiv.dk

The relationship between an adverse effect of antiretroviral treatment and underlying risk illustrated by number needed to treat to harm (NNTH). Risk of myocardial infarction and abacavir use.

JD Kowalska [1], O Kirk [1], A Mocroft [2], L Høj[1], N Friis-Møller[1], P Reiss[3], JD Lundgren [1,4]

[1]Copenhagen HIV Programme, University of Copenhagen, Denmark; [2] University College London Medical School, Royal Free Campus, United Kingdom; [3]Academic Medical Center, Amsterdam, Netherlands; [4] Centre for Viral Diseases/KMA, Rigshospitalet, Copenhagen, Denmark

BACKGROUND

- With potentially life-long treatment of patients with HIV it is crucial to ensure antiretroviral treatment is used in such a way that adverse effects are reduced as much as possible

METHODS

- We illustrated the methodology of the number needed to treat to harm (NNTH) using the recent findings from the DAD study (90% increased relative risk, RR=1.90, of myocardial infarction (MI) in patients on abacavir compared with patients not receiving abacavir)(1). We assumed this RR remains constant across the range of underlying risk of MI

- NNTH was calculated as *1/[(underlying risk of MI x 1.90) – underlying risk of MI]*. The underlying risk of MI was calculated for 5 years using Framingham score (2)

- All NNTH values represent the number of patients who need to be treated with abacavir for 5 years to observe an MI in one additional patient as a consequence of this treatment

RESULTS

- The relationship between absolute risk increase and underlying risk of MI is linear (**figure 1, green line**) whereas the relationship between NNTH and underlying risk of MI is exponential (**figure 1, red line**). The NNTH decreases from 185 to 5 when the underlying risk of MI increases from 0.6% to 20%

- For the medium and high risk group (underlying risk of MI >5%) decrease in underlying risk is accompanied by a small increase in NNTH relative to the large increase in low risk group (underlying risk of MI <5%)

- These trends are not possible to observe when absolute risk increase (ARI) is related to underlying risk of MI

- NNTHs were calculated with different risk assumptions and for two different time periods. A low risk profile representing underlying risk of MI of 0.1% and NNTH=1111 was chosen. The NNTH drops from 1111 to 7 with different risk components of 5-year risk of MI combined and from 370 to as low as 4 for 10-year risk of MI (**table 1**)

- **Figure 2** presents a series of 3D graphs relating NNTH to any possible age and systolic blood pressure, and categorizes it according to smoking status and two chosen lipid profiles. Colours reflect ranges of NNTH (as described in the figure) and enables quick identification of high or low NNTH

- For example, **red** (Graph D) shifts to **orange** and **yellow** if the risk factor of smoking is removed (Graph C) and further to **green** and **blue** if lipids change to normal (Graph A)

- Exploring the graphs in this way helps to understand the relation between the NNTH and particular risk components modified in a way that reflects possible clinical interventions e.g. smoking cessation or lipid lowering intervention

CONCLUSIONS

- It is possible to increase NNTH values for any group of patients on abacavir by decreasing the underlying risk of MI
- Individual assessment of underlying risk may play an important role in decreasing the risk of adverse effect of cART

References:
1. Sabin C et al. Lancet 2008;371 (9622):1417-26 2. Anderson KM et al. Am Heart J 1991;121: 293-298

Figure 1

The relation between NNTH (red line), absolute risk increase (green line) and underlying risk of MI estimated for 5 years period for a drug associated with an increased risk of MI by 90%
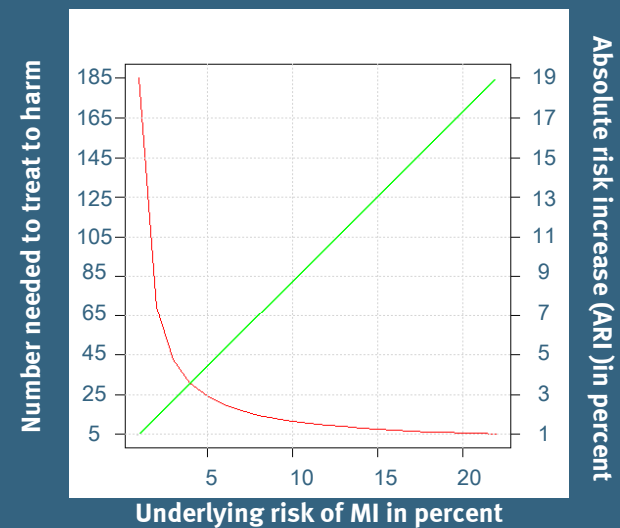

Table 1

NNTH for a drug associated with increased risk of MI by 90% calculated for different time period and risk components (one at a time)
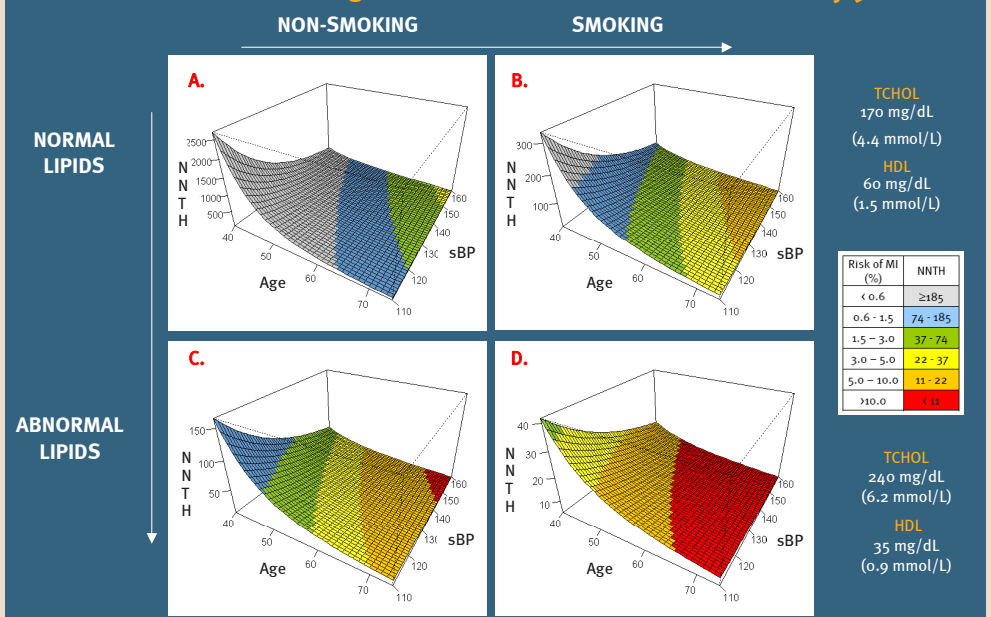
Factors contributing to the underlying risk	MI underlying risk (5 years)	NNTH	MI underlying risk (10 years)	NNTH
Low risk profile*	0.1%	1111	0.3%	370
↑TCHOL or diabetes or ECG-LVH	0.2%	555	0.7	158
↓ HDL 35	0.3%	370	1.2	92
Smoking	0.4%	277	1.5	74
↓ HDL and ↑ TCHOL	0.8%	138	2.6	42
Smoking and ↑ TCHOL	1.0%	111	3.0	37
Smoking and diabetes	1.1%	101	3.1	35
Smoking and ↑ sBP	1.3%	85	3.7	30
Smoking and ↓ HDL	1.6%	69	4.3	25
Smoking , ↓ HDL and ↑ TCHOL	3.1%	35	7.5	14
All unfavourable	15%	7	25.2	4

* 40-years- old male, non-smoking, non diabetic, no ECG-LVH, sBP 120 mmHg, total cholesterol 170 mg/dL (4.4mmol/L), HDL 60 mg/dL (1.5 mmol/L)

↑TCHOL = 240 mg/dl (6.2 mmol/l), ↓HDL=35mg/dl (0.9 mmol/L), ECG_LVH = ECG-left ventricle hypertrophy, ↑ sBP=160 mmHg

Figure 2

NNTH related to age and systolic blood pressure as components of underlying risk of MI for the drug associated with increased risk of MI by 90%

Risk of MI (%)	NNTH
< 0.6	≥185
0.6 - 1.5	74 - 185
1.5 - 3.0	37 - 74
3.0 - 5.0	22 - 37
5.0 - 10.0	11 - 22
>10.0	<11

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