Original article

Randomized trial of a computerized coronary heart disease risk assessment tool in HIV-infected patients receiving combination antiretroviral therapy

Heiner C Bucher[1,2], Martin Rickenbach[3], Jim Young[1], Tracy R Glass[1], Yannick Vallet[3], Enos Bernasconi[4], Matthias Cavassini[5], Christoph Fux[6], Véronique Schiffer[7], Pietro Vernazza[8], Rainer Weber[9], Manuel Battegay[2], the Swiss HIV Cohort Study[†]*

[1]Basel Institute for Clinical Epidemiology & Biostatistics, Basel, Switzerland
[2]Division of Infectious Diseases & Hospital Hygiene, University Hospital Basel, Basel, Switzerland
[3]Swiss HIV Cohort Data Centre, CHUV, Lausanne, Switzerland
[4]Regional Hospital Lugano, Lugano, Switzerland
[5]Division of Infectious Diseases, CHUV, Lausanne, Switzerland
[6]Division of Infectious Diseases, Inselspital and University of Bern, Bern, Switzerland
[7]Division of Infectious Diseases, University Hospital Geneva, Geneva, Switzerland
[8]Division of Infectious Diseases, Kantonsspital St Gallen, St Gallen, Switzerland
[9]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zurich, Switzerland

*Corresponding author e-mail: hbucher@uhbs.ch
[†]See Additional file 1 for a list of study group participants

Background: Exposure to combination antiretroviral therapy (cART) can lead to important metabolic changes and increased risk of coronary heart disease (CHD). Computerized clinical decision support systems have been advocated to improve the management of patients at risk for CHD but it is unclear whether such systems reduce patients' risk for CHD.
Methods: We conducted a cluster trial within the Swiss HIV Cohort Study (SHCS) of HIV-infected patients, aged 18 years or older, not pregnant and receiving cART for >3 months. We randomized 165 physicians to either guidelines for CHD risk factor management alone or guidelines plus CHD risk profiles. Risk profiles included the Framingham risk score, CHD drug prescriptions and CHD events based on biannual assessments, and were continuously updated by the SHCS data centre and integrated into patient charts by study nurses. Outcome measures were total cholesterol, systolic and diastolic blood pressure and Framingham risk score.
Results: A total of 3,266 patients (80% of those eligible) had a final assessment of the primary outcome at least 12 months after the start of the trial. Mean (95% confidence interval) patient differences where physicians received CHD risk profiles and guidelines, rather than guidelines alone, were total cholesterol -0.02 mmol/l (-0.09–0.06), systolic blood pressure -0.4 mmHg (-1.6–0.8), diastolic blood pressure -0.4 mmHg (-1.5–0.7) and Framingham 10-year risk score -0.2% (-0.5–0.1).
Conclusions: Systemic computerized routine provision of CHD risk profiles in addition to guidelines does not significantly improve risk factors for CHD in patients on cART.

Introduction

HIV-infected individuals are at considerable risk of coronary heart disease (CHD) and have a greater risk of CHD than HIV-negative individuals of the same age and gender. Exposure to combination antiretroviral therapy (cART) can lead to important metabolic changes in HIV-infected individuals, including insulin resistance, impaired glucose tolerance, type II diabetes, hyperlipidaemia, and visceral and body fat redistribution [1,2]. Data from large observational studies show an increased risk of myocardial infarction in patients treated with protease inhibitors and under current treatment with abacavir [3,4]. There is growing evidence from recent pathophysiological and epidemiological studies that HIV infection promotes a proinflammatory state that leads to an increased risk of myocardial infarction in patients interrupting cART [5–7]. In addition, lifestyle

factors, such as a higher prevalence of smoking among HIV-infected individuals relative to the general population, indicate the need for aggressive cardiovascular risk management in HIV-infected cART recipients [8,9].

A large body of evidence from clinical trials and meta-analyses indicates that pharmacological and lifestyle-related interventions targeting CHD risk factors reduce CHD death in non-HIV-infected populations [10–12]. As a consequence, evidence-based guidelines emphasize the importance of considering the overall risk of cardiovascular disease and of taking a holistic approach to cardiovascular risk factor management [13,14]. Guidelines that reflect these principles have been adapted to the needs of HIV patients and their physicians [15,16]. However, these interventions have not proved as successful in clinical practice as anticipated, in both HIV-infected and HIV-uninfected populations [17,18]. Therefore, computerized CHD risk evaluation and risk factor intervention programmes have been suggested and introduced to assist physicians with risk assessment and management of patients at risk of CHD. There is, however, conflicting evidence from randomized controlled trials, regarding whether such programmes actually reduce CHD risk. Relevant trials used different approaches and have methodological limitations, and evidence is completely lacking for HIV-infected populations [19].

We carried out a randomized controlled trial nested within the Swiss HIV Cohort Study (SHCS) to evaluate whether the regular provision of computerized CHD risk information reduces CHD risk factors in HIV-infected cART recipients.

Methods

Study design and setting

This randomized controlled cluster trial was nested within the SHCS, a prospective cohort with continuing enrolment of HIV-infected adults. The trial was conducted at the 7 SHCS centres, and at the hospitals and private practices associated with each centre that specialize in the care of HIV-infected individuals in Switzerland. The SHCS has been approved by the ethics committee of each participating centre, as was the protocol of this trial. All individuals participating in the SHCS have provided written informed consent. Informed consent for this trial was provided by the head of the Division of Infectious Diseases at each centre; these individuals were appointed guardians for this cluster trial [20].

Inclusion criteria

The SHCS data centre keeps a continuously updated list of all physicians caring for patients within the SHCS; all physicians on this list were eligible for the trial. Eligible patients were those registered with the SHCS, not pregnant, aged 18 years or older, with continuous cART for 90 days prior to baseline and with complete data on CHD risks factors at baseline.

Interventions

Since April 2000, when the SHCS joined the Data Collection on Adverse Events of Anti-HIV Drugs Study (D:A:D) [1], the family history of CHD has been recorded when a patient enrols in the SHCS and a CHD risk assessment has been made at follow-up visits scheduled 6 months apart. Smoking status, body weight, waist-to-hip ratio, systolic and diastolic blood pressure, and clinically judged lipodystrophy are recorded at each CHD risk assessment and a blood sample taken to measure serum glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides. In addition, use of lipid, blood pressure and blood glucose lowering drugs, and the use of insulin, are also recorded in the SHCS database.

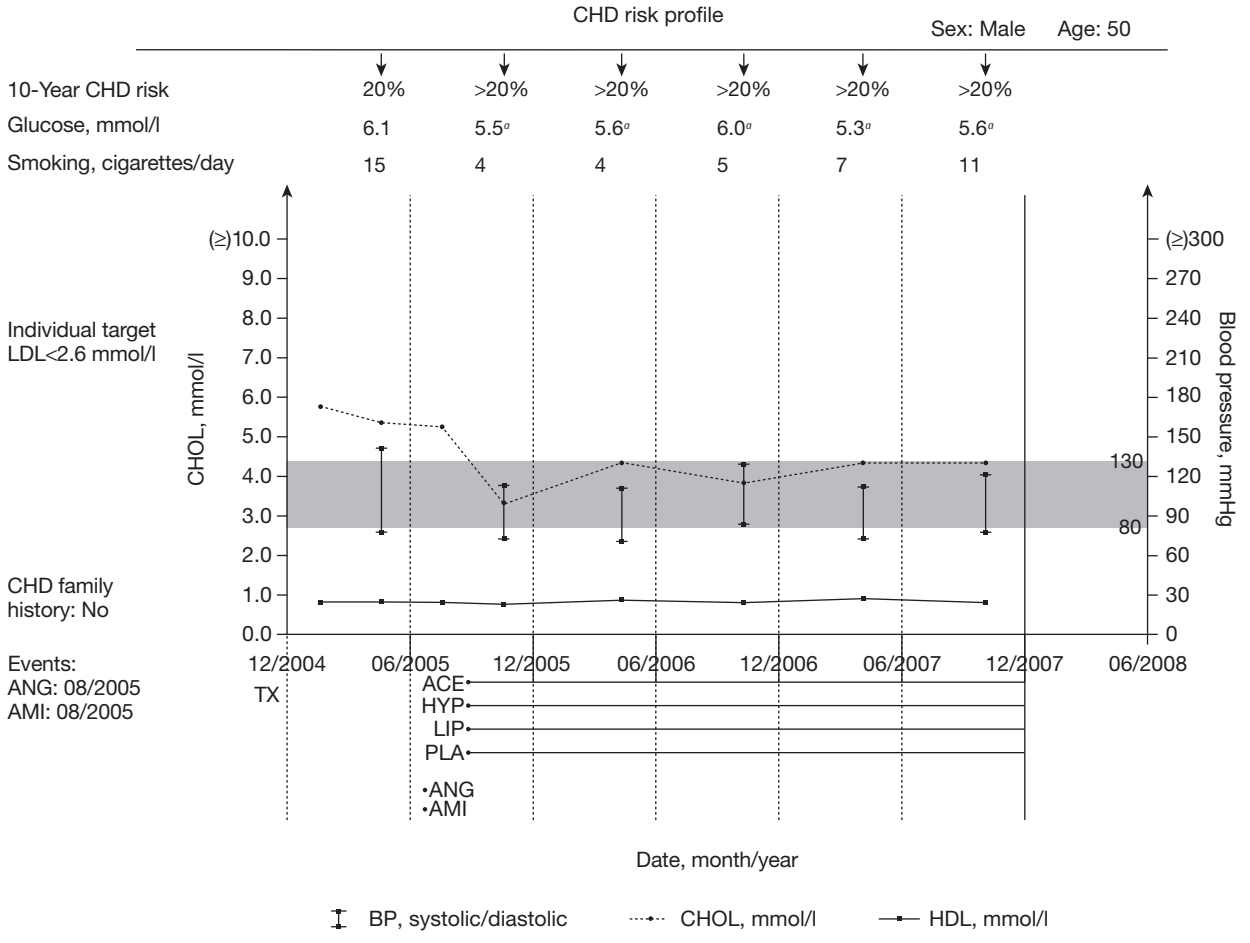
On the basis of this routinely collected data, a risk profile was programmed by the data centre for each patient seen by a physician randomized to the intervention (Figure 1 is an example). These risk profiles were sent to the relevant centre, and study nurses at each centre were responsible for adding these profiles to patient charts. The baseline risk profile contained data on CHD risk for a period of up to 3 years prior to the start of the trial. During the intervention period, CHD risk profiles were continuously updated and added to patient charts.

Each risk profile displayed the predicted 10-year risk of CHD at past risk assessments based on the Framingham risk score [21]. A previous CHD event or the presence of diabetes was considered equivalent to a 10-year risk of CHD of >20%. Because only 20% of blood samples in the SHCS are taken in the fasting state, we defined diabetes as a plasma fasting glucose of ≥7.0 mmol/l, an occasional plasma glucose >11.0 mmol/l, or the use of blood glucose lowering medication or insulin. The risk profile displayed the number of cigarettes smoked, blood glucose, total cholesterol and HDL cholesterol, systolic and diastolic blood pressure at past risk assessments, and whether there was a family history of CHD. Low-density lipoprotein (LDL) cholesterol was not estimated and displayed in risk profiles because blood samples were typically not taken in the fasting state. A family history of CHD was defined as CHD in any first-degree relative (genetic mother, father, brother or sister) experiencing a myocardial infarction or stroke before 50 years of age. Each risk profile provided individualized target values for LDL cholesterol, and systolic and diastolic blood pressure based on an individual's predicted risk of CHD. In the presence of a CHD risk equivalent of manifest CHD, these target values were based on Swiss

national guidelines [22]. Use of medication relevant to reducing CHD risk (blood pressure, lipid and blood glucose lowering drugs, and the use of antiplatelets) was also displayed, with start and stop dates shown for each drug class. For patients who had a CHD event (such as a non-fatal myocardial infarction, percutaneous coronary angioplasty or coronary bypass graft surgery), the dates of such events were shown.

For this trial we developed a booklet of evidence-based guidelines for the management of CHD risk factors in HIV-infected patients receiving cART [23]. Physicians in the control group did not receive CHD risk profiles (Figure 1) but were advised in this booklet to access a website for CHD risk assessment. Each physician in both groups received a booklet. Our guidelines reflect the recommendations of the International AIDS Society [15], and the American and Swiss guidelines for the management of dyslipidaemia, and were reviewed by national experts [13,14,22]. In the booklet, we recommended that physicians take action if they believed a patient's LDL cholesterol was in excess of the target value or if any of the following cutoffs were exceeded: office blood pressure of ≥140 mmHg for systolic or ≥90 mmHg for diastolic blood pressure, or systolic/diastolic blood pressure of >130/85 mmHg for diabetic patients. Guidelines also gave directions on how to approach and motivate smoking patients to quit, and physicians were asked to encourage patients who smoked to quit.

Figure 1. Example of a CHD risk profile for a patient in the Swiss HIV Cohort Study



The risk profile given to physicians in the intervention group shows the predicted 10-year risk of coronary heart disease (CHD) based on the Framingham risk score, the number of cigarettes smoked, blood glucose, total cholesterol (CHOL) and high-density lipoprotein (HDL) cholesterol, systolic and diastolic blood pressure and whether a patient has a family history of CHD. The profile also provides individualized target values for low-density lipoprotein (LDL) cholesterol and the target range for systolic and diastolic blood pressure (grey area) based on the predicted 10-year risk of CHD and on recommendations from Swiss national guidelines. Use of medication relevant to reducing CHD risk is also displayed, with start and stop dates shown for each drug class (represented by the solid lines below the time scale). For patients who have had a previous CHD event, the dates of such events are shown. [a]Fasting state. ACE, angiotensin converting enzyme inhibitor; AMI, acute myocardial infarction; ANG, angioplasty; HYP, antihypertensive drug, LIP, lipid-lowering drug; PLA, antiplatelet drug; TX, treatment of CHD risk factors.

The trial started on 1 July 2006, when physicians were informed about the trial and CHD risk profiles were distributed to each centre. The guardian at each centre was responsible for the distribution of guidelines and trial information leaflets to physicians at their centre and its associated clinics and private practices, and for overseeing the integration of CHD risk profiles into patient charts. The intervention started with a baseline CHD risk assessment by an eligible physician of an eligible patient at the patient's first follow-up visit within 6 months after 1 July 2006. The intervention ended with a final CHD risk assessment of an eligible patient at the patient's first follow-up visit at least 12 months, but no more than 18 months, after the baseline assessment. Outcomes were assessed at each visit by evaluating routinely collected data from the SHCS.

Randomization

Physicians were randomized in strata according to patient volume in the last 6 months prior to randomization (<20 patients, 20–79 patients or ≥80 patients) and the type of setting (at a SHCS centre, or at an affiliated hospital or private practice). Randomized groups were assigned according to a computerized list for each strata generated by a biostatistician not otherwise involved in the trial. This was an open intervention trial, that is, physicians knew whether they received the intervention or not but were not told what outcomes would be measured (although this information was available from a registry of clinical trials).

Measurements

The primary outcome in this trial was total cholesterol. Secondary outcomes were systolic and diastolic blood pressure and Framingham risk score.

Statistical analyses

Based on the results of a trial in non-HIV-infected patients, we aimed to reduce total cholesterol through this intervention by at least 7% [24]. This decrease could be expected to reduce the incidence of CHD by 8% over 2 years and by 15% over 10 years if the lower cholesterol level was maintained [25]. When the trial was designed, patients in the SHCS with a visit in the previous 9 months had a mean ±SD cholesterol level of 5.0 ±1.3 mmol/l. A total sample of 816 patients seen by 55 physicians was needed, given a calculated intraclass correlation coefficient of 0.048, and assuming a cluster size of 15 patients per physician, power of 80%, type I error rate of 5%, and dropout rates of 10% for patients and 2% for physicians [26]. In the SHCS database, we identified >55 physicians seeing at least 15 eligible patients, thus ensuring sufficient power to detect a 7% decrease in total cholesterol.

Analysis for this trial was conducted according to the intention-to-treat principle. For each outcome, we fit a linear model with predictors representing the randomized group plus either two or three covariates, all measured at baseline: the respective outcome variable at baseline plus either concomitant treatment with lipid-lowering drugs (for total cholesterol) or with antihypertensive drugs (for blood pressure), or with both concomitant treatment variables (for the Framingham risk score). We also fit a weighted version of each model with weights calculated as the inverse of the probability that an outcome was available for a patient. These probabilities were found by logistic regression with an indicator representing whether a final outcome was available for each patient in the trial as the response, and with the following predictors: randomized group, gender, intravenous drug use as the most likely mode of transmission, age at baseline, the most recent $CD4^+$ T-cell count, viral load and Framingham risk score within 12 months after baseline, any interval >9 months between visits prior to the trial, and the number of intermediate visits between baseline and 12 months. If this model for the probability of responding is correct, then the weighted analysis estimates the effect of the intervention in all trial patients as if non-response had not occurred [27].

We also carried out a subgroup analysis suggested by a reviewer to assess whether the intervention was of more benefit to patients at greater risk of CHD. Subgroup analyses are best carried out by adding an interaction term to a multivariate model [28]. We first centred each outcome variable at baseline around its mean (to minimize the correlation between each interaction and its components [29]) and then rescaled each centred variable so that each interaction term would be expressed in clinically meaningful units (per 0.5 mmol/l for total cholesterol, per 10 mmHg for blood pressure and per 10% for the Framingham risk score). Finally we included the centred rescaled outcome at baseline and its interaction with randomized group in the weighted version of each model. A negative estimate for this interaction would imply that the intervention leads to greater decreases in an outcome for patients at greater risk of CHD.

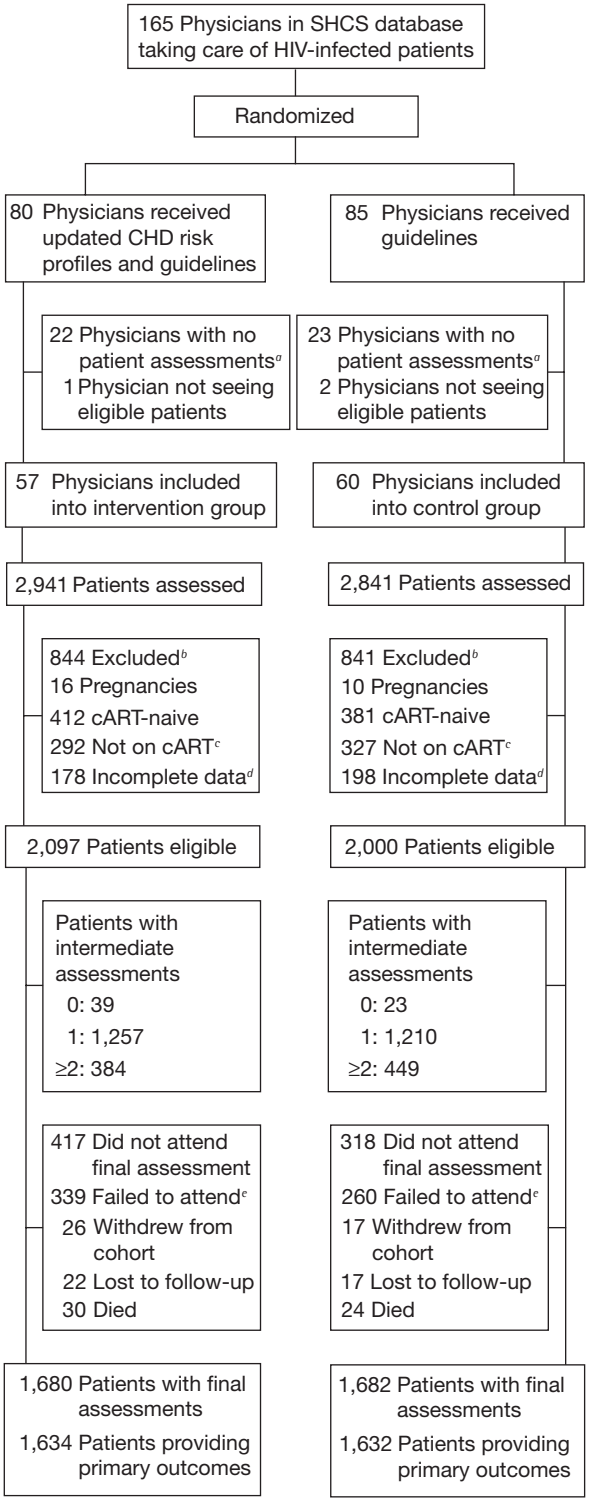
We report 95% confidence intervals based on robust standard errors, where these were calculated using generalized estimating equations with each physician as a cluster and assuming independent clusters. All analyses were carried out in SAS version 9.1.3 (SAS Institute, Inc., Cary, NC, USA).

Results

Physician and patient flow

There were 165 physicians in the SHCS database randomized, but 48 physicians did not assess any

Figure 2. Study flow diagram



[a]During the baseline period (for details see *Methods*). [b]Patients could have multiple reasons. [c]During a period of 90 days prior to the baseline assessment. [d]Incomplete data for cardiovascular risk assessment. [e]Failed to attend during the final assessment period (for details see *Methods*). cART, combination antiretroviral therapy; CHD, coronary heart disease; SHCS, Swiss HIV Cohort Study.

eligible patients within the first 6 months after 1 July 2006 (Figure 2). Randomized physicians assessed 5,782 patients: 26 women were pregnant, 1,412 patients were not on cART over the full 90 days prior to baseline and 376 patients had missing CHD risk information at baseline, leaving 4,097 patients eligible for this trial. Of these, 3,266 (80%) patients had a final assessment with data recorded for the primary outcome, 82 (2.0%) patients were lost to follow-up or withdrew from the SHCS, 54 (1.3%) patients died and 599 (15%) patients failed to attend a final assessment.

Physician and patient characteristics

Among randomized physicians, those who assessed eligible patients were both more experienced and more likely to be male (117 physicians, median of 15 years since graduation and 34% female) than those who did not assess eligible patients (48 physicians, median of 6 years since graduation and 48% female). The physicians who assessed eligible patients were similar in both randomized groups with respect to gender, years since graduation, and the median number of screened and eligible patients (Table 1). Baseline characteristics of eligible patients seen by randomized physicians were well balanced between groups (Table 1). Median age was 44 years, 30% of patients were females, 46% were smokers, 5% had diabetes, 12% had a family history of CHD and 26% had an estimated 10-year risk of CHD disease ≥10%.

Outcome measures

In unweighted analyses, mean (95% confidence interval) patient differences where physicians received CHD risk profiles and guidelines rather than guidelines alone (Table 2) were total cholesterol -0.01 mmol/l (-0.08–0.07), systolic blood pressure -0.5 mmHg (-1.7–0.8), diastolic blood pressure -0.5 mmHg (-1.6–0.6), and Framingham risk score -0.2% (-0.5–0.1). These results were not materially different in weighted analyses that estimate the effect of the intervention in all trial patients as if non-response had not occurred. In subgroup analyses (Table 2), there was no evidence that the intervention offered additional benefit for patients at higher risk of CHD. For example, the effect of the intervention on total cholesterol would change by 0.01 mmol/l (-0.02–0.04) for each 0.5 mmol/l increase in total cholesterol at baseline.

Table 3 summarizes changes to cART components and new prescriptions of antihypertensive, antilipidaemic and antidiabetic drugs cross-classified by randomized group, detectable viral load and Framingham risk score. There was no obvious difference between the intervention and control groups in the discontinuation of any protease inhibitor or in the initiation of drugs with more favourable lipid profiles (abacavir or

atazanavir) in either patients with low or intermediate to high estimated CHD risk. In both randomized groups, patients with a 10-year Framingham CHD risk score of ≥10% more frequently started drugs that reduce cardiovascular risk than those with a lower CHD risk score, but with no significant differences between groups.

Discussion

In this nested randomized controlled cluster trial, providing physicians with updated CHD risk assessments and information on current treatment status of CHD risk factors did not improve total cholesterol, blood pressure or Framingham risk scores in patients receiving cART. This suggests that simply giving physicians risk profiles and guidelines is not enough to change their management of CHD risk factors in HIV-infected cART recipients.

Several factors and limitations of this trial could explain these negative findings. First, particularly in the seven large centres, contamination between physicians might have reduced the effect of the intervention. The number of clusters needed meant that we could not randomize entire centres. Physicians in the control group,

Table 1. Baseline characteristics of trial physicians and of eligible patients seen by randomized physicians

Characteristic	Randomized group	
	Intervention	Control
Trial physicians at baseline		
Physicians with eligible patients, *n*	57	60
Female gender, %[a]	32	36
Median time since graduation, years (IQR)[a]	16 (9–25)	14 (7–23)
Median patients assessed by physicians, *n* (IQR)	36 (19–64)	31 (11–59)
Median eligible patients seen by physicians, *n* (IQR)	27 (11–41)	23 (7–43)
Eligible patients seen by randomized physicians[b]		
Eligible patients, *n*	2,097	2,000
Median age, years (IQR)[b]	44 (39–51)	44 (39–50)
Female gender, %	29	30
IV drug use as likely mode of transmission, %	19	21
CDC group C, %	30	29
Undetectable RNA, %[c]	83	83
Median $CD4^+$ T-cell count, µl (IQR)[c]	490 (340–690)	480 (330–670)
Median time since starting antiretroviral therapy, years (IQR)	8.2 (4.2–10.4)	8.2 (4.2–10.3)
Median time on current antiretroviral therapy, years (IQR)	1.8 (0.8–3.4)	1.8 (0.8–3.4)
Current antiretroviral therapy		
Protease inhibitor based, %	44	45
Non-nucleoside reverse transcriptase inhibitor based, %	35	37
Protease inhibitor and non-nucleoside reverse transcriptase inhibitor based, %	7	7
Triple nucleoside reverse transcriptase inhibitor, %	12	7
Other therapies, %	3	4
Past smoker, %	64	66
Current smoker at screening, %	45	47
Median systolic blood pressure, mmHg (IQR)	125 (115–135)	121 (112–133)
Median diastolic blood pressure, mmHg (IQR)	80 (72–85)	78 (70–85)
On antihypertensive medication, %	14	13
Median total cholesterol, mmol/l (IQR)	4.9 (4.2–5.7)	5.0 (4.3–5.7)
Median HDL cholesterol, mmol/l (IQR)	1.25 (1.00–1.56)	1.29 (1.04–1.59)
Diagnosed as diabetic, %	5	5
Family history of CVD, %	12	12
Median Framingham risk score (IQR)	4 (1–10)	3 (1–8)
Framingham risk ≥10%, %	26	25
Framingham risk group		
Low (<10%), %	74	75
Moderate (10–20%), %	23	23
High (>20%), %	4	2

[a]Data missing for two physicians (one in each group). [b]Eligible patients are those aged 18 years or older, not pregnant, on continuous antiretroviral therapy for 90 days prior to baseline and with all risk factors for cardiovascular disease (CVD) recorded at baseline. [c]Most recent measurement when the baseline risk assessment was made. HDL, high-density lipoprotein; IQR, interquartile range; IV, intravenous.

knowing that they were being scrutinized for their management of CHD risk, might have been more diligent than physicians in the intervention group. Second, the management of HIV-infected patients is challenging and physicians need to consider and manage many other issues, including side effects from cART, the risk of interactions between lipid-lowering drugs and cART, concomitant illegal drug use, methadone substitution, chronic coinfection with hepatitis B and C and psychosocial problems related to sexuality, reproductive health, depression, migration or discrimination. Therefore, the management of CHD risk factors in the context of cART-induced metabolic changes might still be seen by the majority of HIV physicians as a minor problem given the small increase in absolute risk of CHD resulting from exposure to cART. However, patients with moderate to high CHD risk in both groups were more likely to receive treatment for CHD risk factors although those in the intervention group had no better CHD risk factor control. This indicates that physicians were generally aware of the increased risk of CHD in these patients irrespective of the randomization to the intervention or control group. Finally, data collection and follow-up of patients in this trial was not strictly endorsed but continued within the routine data collection procedure of the SHCS. For this reason an appreciable number of patients did not have a final assessment during a window of 6 months, although these patients were not known to have withdrawn from the SHCS.

This trial also has a number of strengths. First, the study included the majority of physicians in Switzerland who treat patients with HIV and a large patient

Table 2. Primary and secondary outcome measures

		Estimates for the effect of the intervention on outcome (95% CI)[a]		
		Unweighted analysis[b]	Weighted analysis[c]	
Outcome	*n* (%)[d]	Intervention	Intervention	Interaction[e]
Primary outcome				
Total cholesterol	3,266 (80)	-0.01 (-0.08–0.07)	-0.02 (-0.09–0.06)	0.01 (-0.02–0.04)
Secondary outcome				
Systolic blood pressure	3,326 (81)	-0.5 (-1.7–0.8)	-0.4 (-1.6–0.8)	-0.2 (-0.8–0.5)
Diastolic blood pressure	3,326 (81)	-0.5 (-1.6–0.6)	-0.4 (-1.5–0.7)	0.1 (-0.6–0.8)
Framingham risk score	3,213 (78)	-0.2 (-0.5–0.1)	-0.2 (-0.5–0.1)	-0.3 (-1.0–0.4)

[a]Confidence intervals (CIs) calculated using robust standard errors from generalized estimating equations with each randomized physician as a cluster and assuming independent clusters. [b]Analysis by linear regression with outcome measured at baseline and concomitant lipid lowering or antihypertensive medication as covariates. [c]Each patient's outcome weighted by the inverse probability of the patient being included in the analysis, where this probability was found by logistic regression. [d]Number and percentage of eligible patients included in the analysis. [e]Analysis by linear regression as before, except with a centred rescaled outcome at baseline and an interaction added between this and randomized group.

Table 3. Changes in components of combination antiretroviral therapy and drugs initiated to reduce cardiovascular risk in patients with a final assessment cross-classified by viral load, Framingham risk and intervention group

	Framingham risk at baseline							
	<10%[a]		≥10%[a]		<10%[b]		≥10%[b]	
Variable	I	C	I	C	I	C	I	C
Patients with a final assessment, *n*[c]	794	769	262	266	450	488	174	159
Started a new component of antiretroviral therapy, %	33	41	34	33	50	47	47	53
Started abacavir, %	4	8	4	7	8	8	7	16
Started atazanavir, %	5	4	5	6	12	11	11	16
Started a drug that reduces cardiovascular risk, %	10	7	19	16	9	9	17	17
Started an antihypertensive drug, %	5	3	10	7	6	4	6	8
Started an antidiabetic drug, %	1	0	1	1	1	1	1	1
Started a lipid-lowering drug, %	4	3	9	9	2	4	11	8
Stopped an existing component of antiretroviral therapy, %	35	41	35	36	54	52	52	54
Stopped an existing component because of increased risk of cardiovascular disease, %	2	0	2	3	1	1	2	2
Stopped any protease inhibitor, %	10	13	9	10	28	25	26	28
Experienced a cardiovascular event during the trial, %[d]	1	1	3	2	0	1	6	2

[a]No detectable viral load at baseline or during trial. [b]Detectable viral load at baseline or during trial. [c]Total *n*=3,362. [d]Definite or possible myocardial infarction, unstable angina, cerebral infarction or haemorrhagia, coronary artery bypass grafting, angioplasty or stenting, carotid endarterectomy or procedures on other arteries. C, control; I, intervention.

sample representative of those patients with HIV that receive care in Switzerland. Second, the trial was sufficiently powered to detect a clinically relevant difference in the primary outcome. Third, the duration of the trial was sufficient to allow for the sort of behaviour and treatment changes that would reduce CHD risk. Fourth, physicians were not told how their management of CHD risk would be assessed. Fifth, the trial was nested into an ongoing prospective cohort study with no additional data collection or patient interviews, leading to minimal disruption of daily clinical routine. Finally, although end-of-trial assessments were missing in an appreciable number of patients, we found no difference in results when using a weighted analysis to account for non-response.

We took a patient and public health perspective when assessing the outcome of our intervention. From a public health perspective, it is not enough to show that suitable treatment has been provided by the physician; rather, any treatment must be shown to have had benefit for the patient. Results showing changes in treatment provided by the physician are important (and are shown in Table 3), but ultimately these must lead to an improvement in patient outcomes (such as the measures reported in Table 2). In fact, the information in these two tables is quite consistent. In Table 3, there is no major difference between the two randomized groups in the proportion of patients starting drugs that reduce cardiovascular risk. And in Table 2, there is no clinically relevant difference between the two randomized groups in any of the four patient outcomes. We chose measures of patient outcome that would not add to or alter daily clinical routine so that the trial would have high external validity. The problem with the Framingham risk score is that it is highly sensitive to smoking status; yet this is very difficult to measure reliably. Patients might give the answer they think their physician wants to hear, or they might stop smoking only temporarily. Blood pressure is often taken by a variety of clinical staff, is sometimes measured in different ways in different settings and is subject to the 'white coat' effect. We therefore chose total cholesterol as the primary outcome because it is routinely and reliably measured and high cholesterol is a common metabolic abnormality associated with cART and known to increase the risk of CHD.

To our knowledge no similar trial has been conducted to date to examine the effectiveness of a systemically used risk assessment instrument for CHD risk factor management in HIV-infected cART recipients. Several trials in patients without HIV have investigated the effectiveness of computerized risk assessment systems for modifiable CHD risk factors compared with standard care without systematic risk information or assessment, although all these trials have methodological limitations [19]. Some trials have used systematic risk assessment tools as just one component of an intervention. In a primary care trial in the UK, hypertensive patients cared by physicians with access to an internet platform for CHD risk calculation had worse blood pressure control and were less likely to achieve target blood pressure values [30]. In a Canadian trial, the provision of CHD risk profiles to general practitioners led to a small reduction in their patients' total and LDL cholesterol and CHD risk score [24]. The duration of the intervention in this trial was only 3 months and patients were not consecutively enrolled, factors that limit the external validity of these results. In an international cluster trial, handhold touch screen computers for CHD risk assessment were given to all physicians. Physicians in the intervention group received training both in risk communication and how to use the risk assessment tool. In addition, their patients received personalized information on their CHD risk and educational sessions with reminder phone calls to enhance behaviour change [31]. This led to a moderate 1.4% decrease in the predicted 10-year Framingham CHD risk in the intervention group. This difference was mainly driven by better blood pressure control and a higher rate of smokers quitting in the intervention group during the 6 month intervention. However, findings from this trial are limited because of the short duration of the intervention. In a multidisciplinary trial where nursing staff used similar risk assessment tools, individuals at high risk for CHD assigned to care facilities providing intensive CHD risk factor management were more likely to achieve blood pressure but not cholesterol targets [32]. Findings from these last two trials and from one other trial [33] suggest that CHD risk assessment and improved physician communication skills might be more likely to reduce risk factors for CHD when combined with an active multifaceted outreach programme that involves both physicians and patients.

The lifetime risk of CHD in HIV-infected patients in the SHCS is substantial given the median age, high prevalence of smoking and the considerable metabolic changes seen in cART recipients, and is comparable to the risk in other cohorts of HIV-infected individuals [9]. A growing body of evidence indicates that HIV *per se* could promote a proinflammatory state leading to increased risk of CHD, and this underlines the need for long-term treatment with antiretroviral drugs with fewer metabolic side effects [5]. With the remarkable success of cART, management of HIV-infected patients has advanced to chronic disease management requiring aggressive management of CHD risk factors and outreach programmes for behaviour change, in particular smoking cessation programmes. Such intervention strategies are of additional importance because recent findings suggest that HIV-infected individuals might be

at increased risk of non-HIV-related malignancies that are, in part, smoking related [34]. Thus, there is an additional excess risk of death for HIV-infected individuals from non-HIV-related conditions like CHD and cancer that are amenable to prevention. Findings from this trial show that the provision of CHD risk assessment tools and guidelines are insufficient to achieve this goal. More effective programmes directed, not only to HIV physicians, but with active patient involvement are needed for sustained management of CHD risk factor management. Such programmes must be appropriately evaluated in trials of sufficient duration.

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Additional file

Additional file 1: Members of the Swiss HIV Cohort Study and Swiss Mother and Child HIV Study can be found at www.intmedpress.com/uploads/documents/1319_Bucher_Additional_file.pdf

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