What if we change something?... a Cardiovascular risk analysis of a population.

Patrícia Silva[1] (MD, MSc), Ana Vieira[2] (MD, MSc), Pedro Damião[3] (MD)
[1]Resident physician of Primary Healthcare at USF Aveiro/Aradas, Invited assistant at Health Sciences Department of Aveiro University; [2] Resident physician of Public Health at ACeS Baixo Vouga; [3]Attending physician of Primary Healthcare at USF Aveiro/Aradas - ACeS Baixo Vouga

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Corresponding author: Patrícia Silva, patricialex87@gmail.com

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Introduction*:* Cardiovascular diseases (CVDs) are the leading cause of death in the world, accounting for 31% of all causes. Of these 85% are due to heart attack and stroke[1]. Most CVDs can be prevented by addressing behavioural risk factors such as tobacco use, unhealthy diet, obesity and physical inactivity[2].
The presence of major non-modifiable risk factors such as age and sex and modifiable ones such as high blood pressure, smoking, dyslipidemia and diabetes in the development of target organ damage (TOD) are widely accepted in the literature and by scientific societies[2].
Currently, physical activity is seen as a crucial factor in the control of several cardiovascular (CV) risk factors. There are several studies in the literature that prove the CV protective effect of physical activity[2,3]. The traditional CVD risk prediction models in use in clinical practice (SCORE) determine the probability of fatal events and are used in the discussion of scenarios with the patients, namely to visualize changes in the concretization of modifiable risk factors[3].
Traditionally, CV risk assessments characterize a population in terms of the prevalence of these factors but not of the expected impact in relation to the realistic modification of them[4,5].
We hypothesise that statistical simulation based on the estimated effect of physical activity prescribed to a primary health care population may assume a similar role to that achieved in individualized care delivered on real world clinical practice. On such basis, the physician may predict realistic effects of modifying a risk factor, in order to support the therapeutic strategic definition.
Primarily, we aimed to estimate the risk of TOD in an adult population of one Unidade de Saúde Familiar (USF) according to the main CV risk predictors using a statistical model. Then, we consider pertinent to simulate a non-pharmacological intervention in a population and estimate its impact on TOD reduction.

Methods: This is a retrospective study with an exploratory multivariate analysis of a convenience anonymized sample (n=3358), from patients with appointments conducted in 2018 at one USF of Aveiro district. The variables under study are TOD (i.e., coronary heart disease (CHD), stroke, peripheral artery disease (PAD) or heart failure (HF)); age; sex; total cholesterol; HDL cholesterol; systolic blood pressure (SBP); antihypertensive drugs (1/0); tobacco (1/0); Diabetes (1/0).

After data collection using the Sistema de Informação e Monitorização das Unidades Funcionais (MIM@UF), a subpopulation analysis was performed excluding patients less than 30 years and older than 74 years and patients with CHD, stroke, PAD or HF. The TOD risk assessment formula (developed by Ralph B. D 'Agostino et al, 2007, based on the Framingham Heart Study data for the following TOD: CHD, stroke, PAD, HF)[2,5] was applied to estimate in each case the probability of developing TOD after 10 years. Thus, using software R 3.4.2, multivariate distribution charts were created to visualize the distribution of CV risk factors and the estimated 10-year probability of TOD (see **Figure 1**).

Selecting the subpopulation with age greater than or equal to 55 years, a Monte Carlo simulation was conducted using uniform distributions to select randomly 0.669 of all cases (i.e. sedentary assumptions based on Eurostat data). With P1 defined as the probability of prescribing physical activity of 2.5h per week to a sedentary patient and P2 as the probability of success (patient adherence to this prescription).

The effect of physical activity in the reduction of SBP (-3.84 mmHg) and total cholesterol (-1.1%) and HDL increase (+5.6%) already described in meta-analysis was applied with probability (P1*P2) to occur. This process was repeated 1000 times for each pair (P1, P2). The results of each simulation were used to obtain the associated E(TOD) stored in a vector E_TOD. Then, $q_{0.025}$(E_TOD), $q_{0.975}$(E_TOD) were calculated for each pair (P1, P2).

Results: The sample size is 3358 patients, 1390 are male. The median age is 53 years, interquartile age range is 19 years and there are 1439 patients with ≥55 years old. 1130 are hypertensive under medication, 425 are diabetic and 658 tobacco smokers.

The expected E(TOD) of the original sample is 423.9 with 95%CI=[410.7,438.4]. The distribution of calculated risk is given in **Figure 1**.

The results of Monte Carlo simulation for each pair (P1, P2) are summarized in **Table 1**.

Discussion and conclusions*:* Estimating the 10-year risk of TOD is useful in determining the resources needed in a population of a primary care unit and in defining intervention strategies.

Thus, this non-pharmacological prescription should be considered in this subpopulation. The degree of success, if implemented, will be translated into a decrease in the baseline values of SBP and total cholesterol and increase in HDL of adherent patients, as well as the eventual decrease in the total TOD diagnoses performed versus predicted. The similar distribution of the ages of the sample and the study population does not allow to exclude the potential utility of the simulation thus obtained, because it´s a non-randomized sample.

Future studies are needed to evaluate the real success of this intervention if this prescription occurs.

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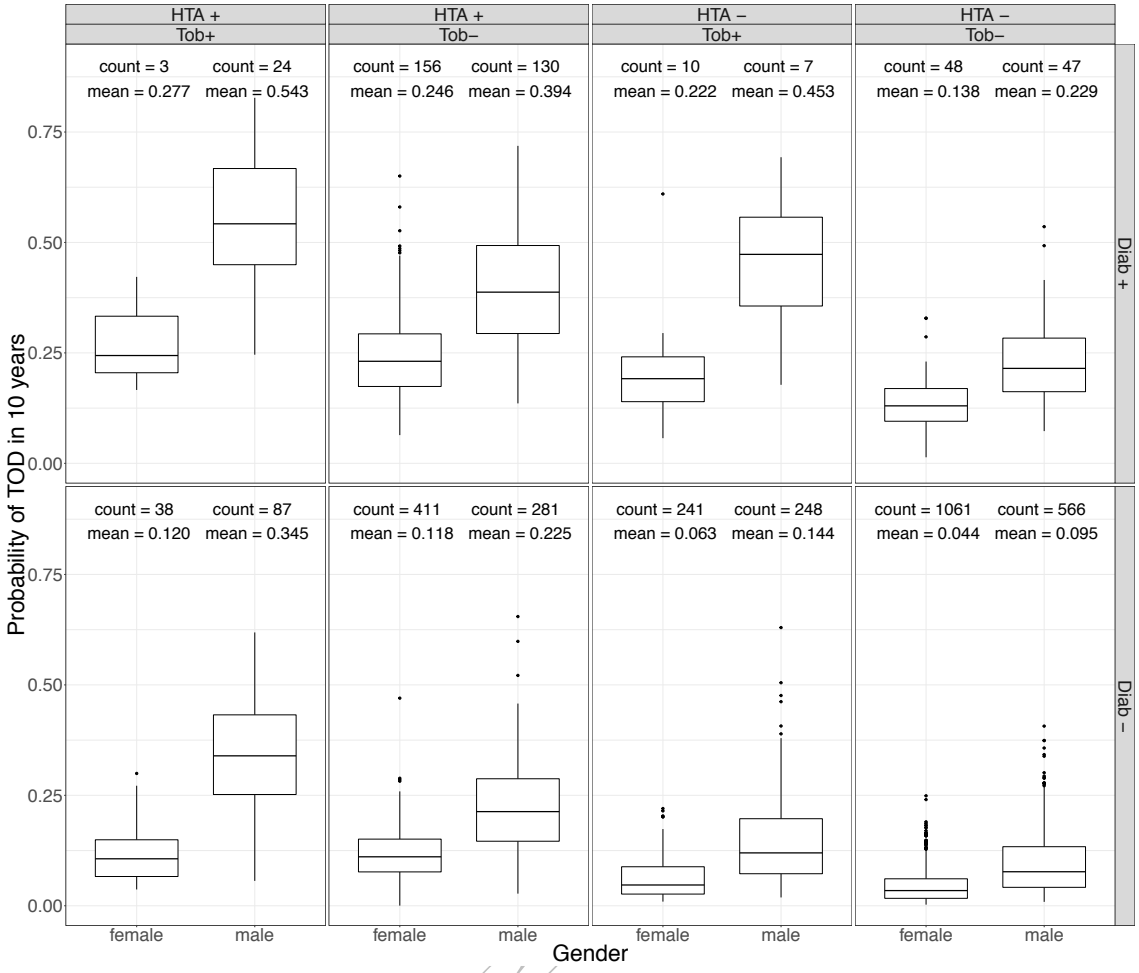

Figure 1: 10-Year Risk of TOD by cardiovascular predictor's distribution.
HTA: arterial hypertension, Tob: tobacco, Diab: Diabetes.

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Probability				
Prescription (P1)	Adherence (P2)	E(TOD)	95%CI	∆=423.9 - E(TOD|P1,P2)
0.6	0.2	421.5	[421.1,422.0]	2.1
0.6	0.4	419.1	[418.5,419.7]	4.8
0.8	0.2	420.7	[420.2,420.7]	3.2
0.8	0.4	417.5	[416.8,418.1]	6.4
1.0	1.0	403.8	[402.9,404.6]	20.1

Table 1: Monte Carlo simulation. Probability of non-pharmacological Prescription (P1) and Adherence (P2) by the patients. Expected value of TOD, E(TOD) depending on Probability (P1, P2) with 95%IC and the difference between the expectance of TOD before and after the intervention, ∆=423.9-E(TOD|P1,P2).