

Data analysis is performed using RStudio (<https://posit.co/products/open-source/rstudio/>) and R, version 4.4.1. No imputing of missing values is applied.

Main study

The Shapiro-Wilk normality test is applied to continuous variables in order to test the normality of their distributions. Log transformation is applied when the normality assumption is not satisfied. Univariable and penalized multivariable logistic regression analysis are applied to identify features associated with PCa diagnosis, using the entire cohort. Samples with complete information on the mostly associated variables are retained for subsequent analyses. On the resulting samples, two approaches (step1) are followed. Step1a: least absolute shrinkage and selection operator (LASSO) penalized logistic regression, with 10-fold cross-validation, is applied to retrieve the variables selected by at least 9/10 models (in each dataset partition, the same proportion of cases and non-cases as in the original dataset is maintained). Step1b: the entire cohort is divided into a training test used to build a LASSO model, which is then applied on the test set. In Step2, circulating molecule levels are included in the analysis and combined with anamnestic/lifestyle variables by LASSO regression with the 10-fold cross-validation approach. Area under the Receiver Operator Curve (ROC AUC) is used to assess the discriminatory ability of single variables or logistic regression models, with reported 95% confidence intervals (C.I.). Paired DeLong test is used to compare the discrimination among different variables/models and Student paired t-test to compare the average AUCs between the LASSO models and PSA or PSA plus age.

Prostate tissue transcriptomic profiles are associated with early relapse using penalized Cox regression analysis.

PBMC transcriptomic profiles are associated with outcome using penalized regression analysis.

Ancillary study

Improvements in physical fitness, anthropometric measures, cardiometabolic risk factors, mental well-being, and PSA levels over 6-12 months of NW activity are measured in the NW and the control group. We hypothesize that greater adherence to NW sessions is associated with larger health benefits. Correlation analysis with the number of NW sessions within 6 or 12 months is done to assess the adherence dependent benefits. Linear regression analysis adjusted for confounding factors (age, BMI, agexBMI and the baseline of each variable) is done to compare the two groups in terms of variable differences (T1-T0; T2-T0).

The Wilcoxon unpaired test is used to compare the two study groups (NW and controls) in terms of baseline variables or variable changes after 6 months (deltaT1-T0). The Wilcoxon paired test is used to assess the changes within each group after 6 or 12 months. Fisher's exact test is applied to test any baseline differences between the two groups in terms of blood pressure and anamnestic variables (concurrent diseases and family history of (prostate)

cancer). Pearson's correlation test is used to assess any correlation between the variable changes (at 6 or 12 months) and adherence to the NW program (number of training sessions completed by each participant in the tested period). The Friedman test is used to evaluate changes in the variables tested at three time points. Linear regression adjusted for confounding factors (baseline variable values, age, BMI, and age $\times$ BMI interaction) is also applied to assess variable changes at 6 months in the NW group versus the control group.