

## Assessments

Data on the following variables were collected by using a self-administered standardized questionnaire: age, sex, medical history, medication usage, relevant comorbidities, lifestyle factors (alcohol intake, sleep duration, and weight gain since age 20), and readiness to modify lifestyle. Health-related data including measurements of height, weight, and blood pressure of the study subjects were collected at an annual medical health checkup. Biochemical measurements of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), and uric acid (UA) were included for those who were over 40 years old. Hypertension was defined as systolic blood pressure  $\geq 140$  mm Hg, diastolic blood pressure  $\geq 90$  mm Hg, or receiving treatment for hypertension. Diabetes mellitus was defined according to the American Diabetes Association criteria of glycated hemoglobin  $\geq 6.5\%$ , fasting plasma glucose  $\geq 126$  mg/dl, or receiving treatment for diabetes. Dyslipidemia was defined as triglyceride  $\geq 150$  mg/dl, low-density lipoprotein cholesterol  $\geq 140$  mg/dl, high-density lipoprotein cholesterol  $< 40$  mg/dl, or receiving lipid-specific treatment. Hyperuricemia was defined as uric acid  $\geq 7.0$  mg/dl or receiving treatment for hyperuricemia.

### Tobacco use status

Data on tobacco use were collected with questions about current and previous tobacco use, prior attempts to quit, and interest in tobacco cessation. Regarding HTPs, we asked about the products used (IQOS®, glo®, and Ploom Tech®) and the current and past use of each product. We defined HTP users as those who currently used at least one brand of HTP, including dual users and exclusive HTP users. Dual users used both HTPs and cigarettes, while exclusive HTP users used only HTPs.

We asked the participants, via a questionnaire, 1) Are HTPs as harmful as cigarettes? 2) Are HTPs useful for tobacco cessation? English translations of the question options were as follows: 1) “HTPs are as harmful as cigarettes”, “HTPs are less harmful than cigarettes”, “HTPs are more harmful than cigarettes”, and “I have no idea”. 2) “HTPs are useful for smoking cessation”, “I have no idea” and “HTPs are not useful for smoking cessation”. We also asked if they lived with cohabitants.

### Questionnaire

Nicotine dependence was assessed by the Tobacco Dependence Screener (TDS).[1] All subjects completed a Japanese version of the chronic obstructive pulmonary disease (COPD) assessment test (CAT) for screening of respiratory health and the Patient Health

Questionnaire (PHQ-9) for screening for depression.[2]

### Statistical Analyses

Subjects' characteristics were summarized as numbers (percentage) for categorical variables and means (standard deviation) for continuous variables. Comparisons between groups were examined using Fisher's exact tests for categorical variables and t-tests for continuous variables. A P value of less than 0.05 was considered statistically significant, and the confidence intervals (CI) were 95%.

### Propensity Score Weighting

We conducted propensity score (PS) analyses to evaluate the association between HTP use and successful quitting. Because HTP use was not randomly assigned, PS weightings were used to account for differences.

Propensity scores were calculated for each subject using a logistic regression model with potential determinants included as independent variables and HTP use as the dependent variable. The model included the following covariates: age, body mass index, living with cohabitants, logarithm of Brinkman index (the number of tobacco used per day multiplied by the number of years of tobacco use), comorbidities (hypertension,

diabetes mellitus, hyperlipidemia, and hyperuricemia), previous attempt to quit smoking, interest in smoking cessation, consideration of HTPs as less harmful, consideration of HTPs as useful for smoking cessation, logarithm TDS, logarithm CAT, logarithm PHQ-9, weight gain more than 10 kg since age 20, daily drinking, sleep duration and readiness to modify lifestyle.

When assessing the effect of a treatment on an outcome, we estimated the average treatment effect (ATE). The ATE estimate is valid under the assumption that all participants are originally untreated and then treated.[3] To estimate the ATE, the HTP users' answers were weighted  $1/PS$ , while the non-HTP users' answers were weighted  $1/(1-PS)$ . To account for potential selection bias, differences in baseline characteristics between HTP users and non-HTP users were controlled for using an inverse probability of treatment weighting (IPW) adjusted analysis. Covariate balance between the groups before and after IPW adjustment was assessed using the standardized difference approach. After PS weighting created an acceptable balance, Poisson regressions with PS weighting were used to investigate the factors that affected successful quitting.

Statistical analyses were performed using R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

**References:**

- 1 Kawakami N, Takatsuka N, Inaba S, *et al.* Development of a screening questionnaire for tobacco/nicotine dependence according to ICD-10, DSM-III-R, and DSM-IV. *Addict Behav* 1999;**24**:155–66. doi:10.1016/S0306-4603(98)00127-0
- 2 Spitzer RL, Kroenke K, Williams JBW. Validation and Utility of a Self-report Version of PRIME-MD The PHQ Primary Care Study. <https://jamanetwork.com/>
- 3 Dugoff EH, Schuler M, Stuart EA. Generalizing observational study results: Applying propensity score methods to complex surveys. *Health Serv Res* 2014;**49**:284–303. doi:10.1111/1475-6773.12090