The Rotterdam Cohort Study

The Rotterdam Study (RS) is a prospective cohort study of the community-dwelling population aged 55 years and older in Rotterdam, the Netherlands. The detailed study design has been described elsewhere.[1] Briefly, the baseline examination for the first cohort was completed between 1990 and 1993 (RS-I) with 10,215 participants aged 55 years or over; the response rate was 78%. The Rotterdam Study was extended in 2000 to include all inhabitants who became 55 years of age or moved into the research area after the start of the study (RS-II).

An overview of the study population is shown in **Figure 1**. We used the third center visit (1997-99, n=4,797) of RS-I and the first visit of RS-II (2000-01, n=3,011) as the baseline for current study. Among 7808 participants recruited, 2529 were excluded for the following reasons: i) no informed consent to access medical records (n=82), ii) prevalent type 2 diabetes (T2D) or unavailable data on baseline diabetes status (n=1733), iii) missing body mass index (BMI), waist-hip ratio (WHR), relative fat mass (RFM) values (n=568), iv) BMI < 18.5 kg/m^2 or waist circumference < 40 cm (n=42), and v) missing covariates (n=104), resulting in a total of 5279 participants finally included.

The Rotterdam Study has been approved by the Medical Ethics Committee of the Erasmus MC (registration number MEC 02.1015) and by the Dutch Ministry of Health, Welfare, and Sport (Population Screening Act WBO, license number 1071272-159521-PG). All participants provided written informed consent to participate in the study and to have their information obtained from their treating physicians.

Measurements

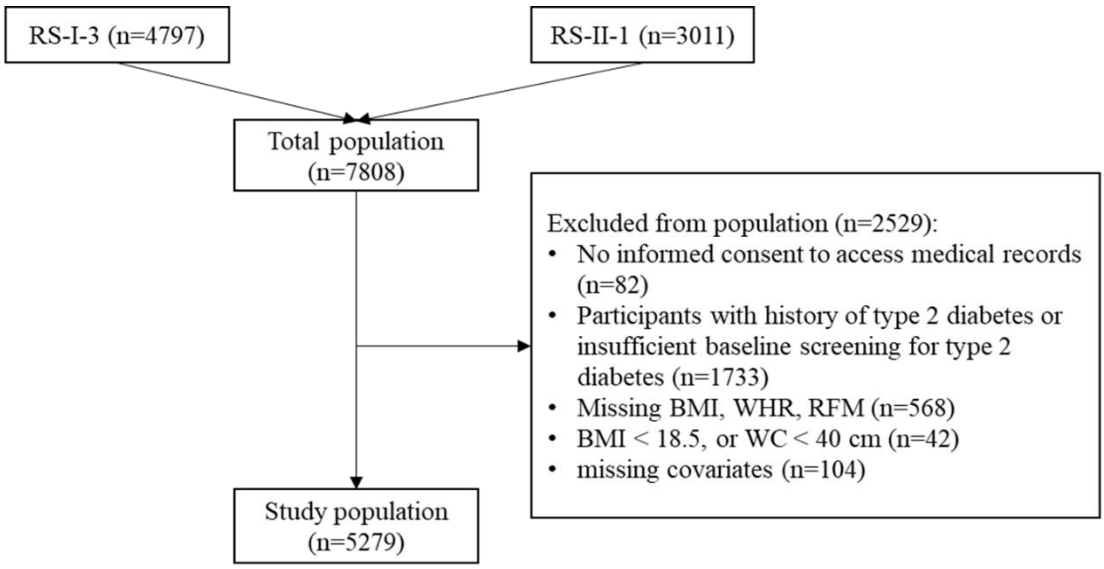
Anthropometrics were measured in the research center by trained staff. Height and weight were measured with the participants standing without shoes and heavy outer garments. BMI was calculated as body weight (in kg) divided by the square of height (in meters). Waist circumference was measured at the level midway between the lower rib margin and the iliac crest with participants in standing position without heavy outer garments and with emptied pockets, breathing out gently. Hip circumference was

recorded as the maximum circumference over the buttocks. WHR was calculated as the ratio of waist circumference over the hip circumference. RFM was calculated as: 64 – (20*Height/ Waist circumference) + (12*sex), with sex=0 (men), and sex=1 (women). Blood pressure was measured twice at the right brachial artery with a random-zero sphygmomanometer with the participant in a sitting position, of which the mean of 2 consecutive measurements was used. Hypertension was defined as a blood pressure ≥140/90 mmHg or use of blood pressure-lowering medications. Smoking behavior was assessed using a computerized questionnaire and classified as current smoking or others (former and never).

Ascertainment of type 2 diabetes

Participants were followed up from the date of attending baseline visit onwards. At baseline and during follow-up, cases of T2D were ascertained by the use of general practitioners' records, hospital discharge letters, and serum glucose measurements collected from center visits, which take place roughly every 4 years. T2D was defined as a fasting blood glucose concentration of 7.0 mmol/L (126 mg/dL) or higher, a non-fasting blood glucose concentration of 11.1 mmol/L (200 mg/dL) or higher (when fasting samples were unavailable), or the use of blood glucose-lowering medications. Information about blood glucose-lowering medications was obtained from both structured home interviews and pharmacy dispensing records. At baseline, more than 95% of the Rotterdam Study population was covered by the pharmacies in the study area. Two study physicians independently adjudicated all potential events of T2D. In the case of disagreement, a consensus was sought from an endocrinologist. Participants were followed until the occurrence of incident T2D, death, or the end of the study period (January 1st, 2015).

Figure 1. Flow chart of participant selection for the present study population



The LifeLines Cohort Study

The Lifelines Cohort Study has been extensively described elsewhere.[2,3] Briefly, Lifelines (www.lifelines.nl) is a multidisciplinary, prospective population-based cohort study examining the health and health-related behaviours of 167,729 participants living in the North of The Netherlands in a unique three generation design. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioural, physical and psychological factors which contribute to the health and disease of the general population, with a special focus on multi-morbidity and complex genetics. Participants were recruited from 2006 to 2013, initially by participating GPs, who invited all patients aged 25–50 from their own practices. Participants were then encouraged to invite family members to participate in Lifelines as well. People who were not invited could also participate by registering themselves through the Lifelines website. The Lifelines study was approved by Medical Ethical Committee of the University Medical Center Groningen and performed in agreement with the Declaration of Helsinki, and all participants provided written informed consent.

Participants were asked to complete extensive questionnaires about a wide range of health-related topics at home. Next, they were invited for a physical visit, which included anthropometry and blood pressure measurements, electrocardiography, pulmonary function testing, and collection of blood, urine, and genetics samples. Additionally, current medication use was recorded. With a planned follow-up of at least 30 years, the Lifelines study is currently still ongoing. Participants are sent follow-up questionnaires approximately every 1.5 years and are invited for physical follow-up visits approximately every 5 years. For the current study, we included 99,147 participants with available questionnaire data at baseline (1A) and follow-up (2A). The total follow-up duration was 3.8 (3.2-4.6) years.

From the initial sample (n = 99,147), we excluded individuals with prevalent diabetes (n = 3065) and missing diabetes status at baseline (n = 115). We also excluded participants with missing anthropometric data (n = 30), BMI < 18.5 (n = 679) and missing covariates (n = 1388), resulting in a final total of 93,870 individuals left for analysis.

References

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