nature cardiovascular research

Article

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Cardiometabolic and renal phenotypes and transitions in the United States population

In the format provided by the authors and unedited

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STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies.

Supplementary Fig. 1. Cluster characteristics as the number of clusters changes from 5 to 12.

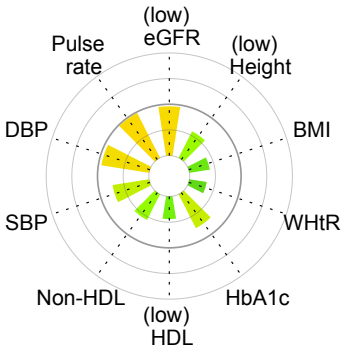
Each panel corresponds to a cluster, each bar shows the median value of one risk factor for all participants in the cluster. The number next to the cluster name represents the percentage of the participants grouped in this cluster.

The concentric circles show the minimum, 25^{th}, 50^{th}, 75^{th} percentiles and maximum in the whole sample, with the median shown in darker color. The height and color of the bar represent the median level of each risk factor, positioned relative to the distribution in the whole population so that the scale is common across all clusters. The scale is reversed for height, eGFR and HDL because lower values indicate higher risk.

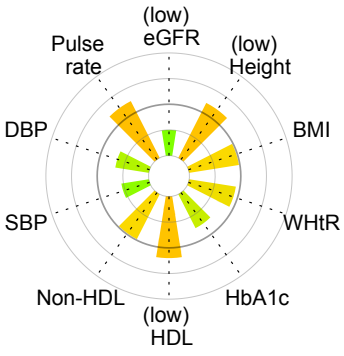
eGFR: estimated glomerular filtration rate; BMI: body-mass index; WHtR: waist-to-height ratio; HbA1c: glycated hemoglobin; HDL: high-density lipoprotein cholesterol; non-HDL: non-high-density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Women (5 clusters)

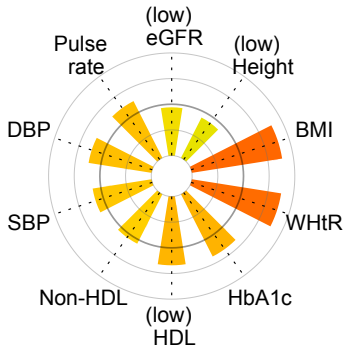
Low risk (26%)



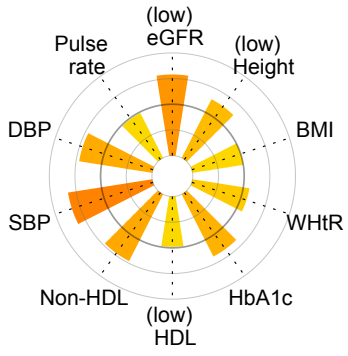
Mid-risk (26%)



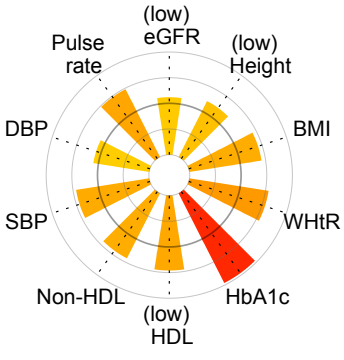
Severe obesity (19%)



High blood pressure (25%)

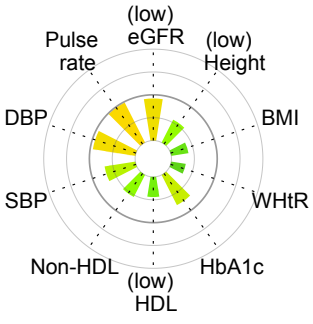


Severe hyperglycemia (4%)

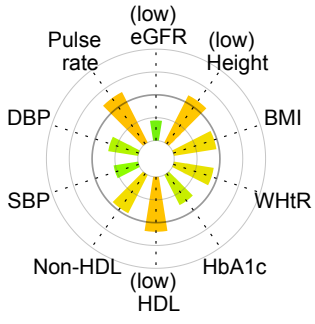


Women (6 clusters)

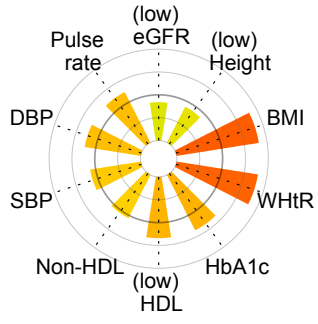
Low risk (24%)



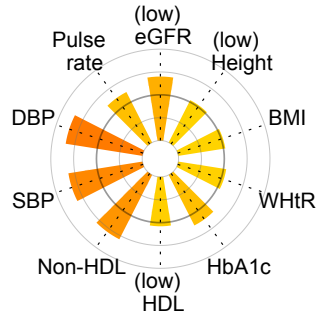
Mid-risk (24%)



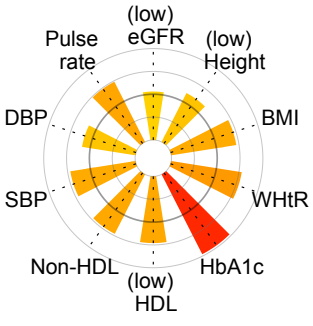
Severe obesity (16%)



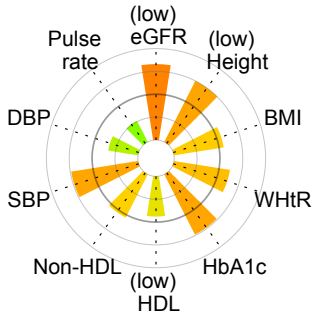
High blood pressure (18%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (15%)

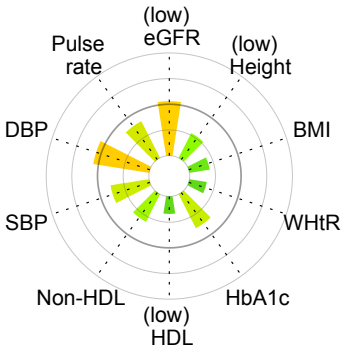


Risk factor percentile

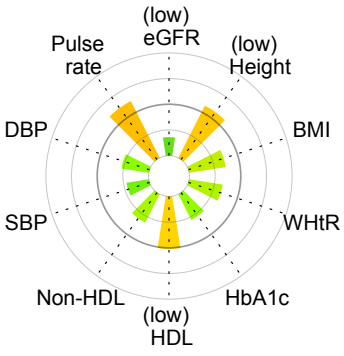
← more optimal more hazardous →

Women (7 clusters)

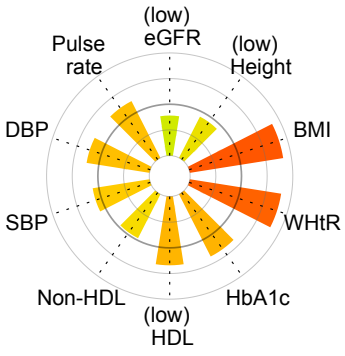
Low risk (20%)



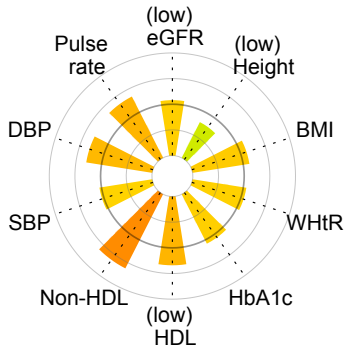
Mid-risk (21%)



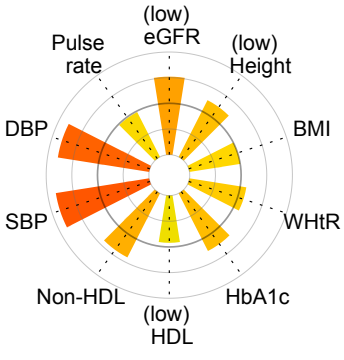
Severe obesity (14%)



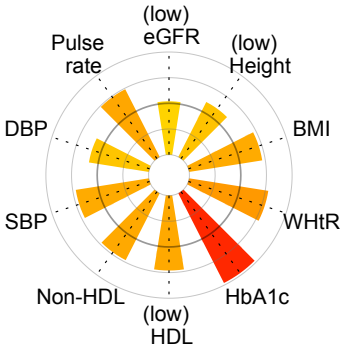
High cholesterol (17%)



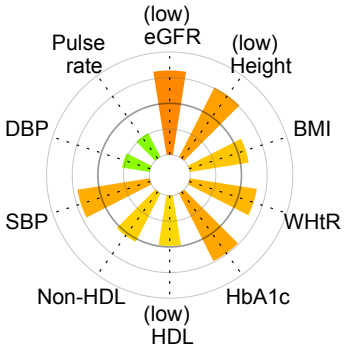
High blood pressure (11%)



Severe hyperglycemia (3%)

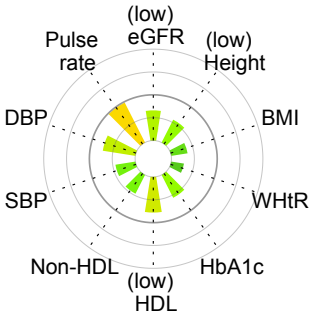


Low DBP, low eGFR (14%)

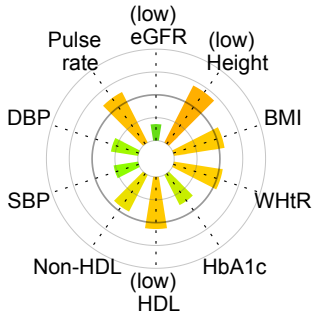


Women (8 clusters)

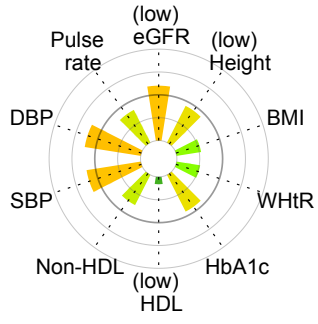
Low risk (19%)



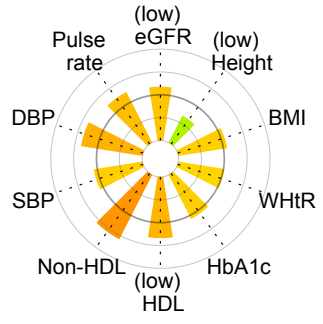
Mid-risk short (16%)



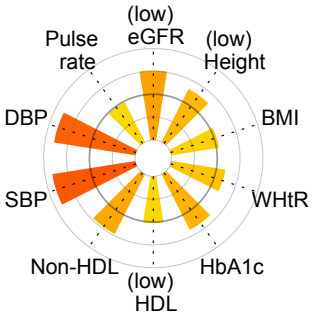
Low BMI, high HDL (12%)



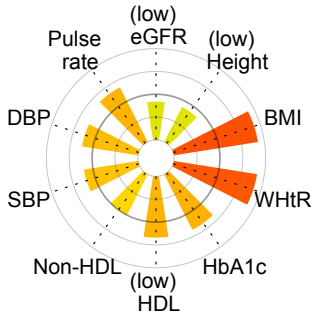
High cholesterol (16%)



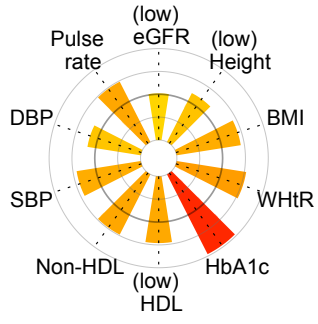
High blood pressure (10%)



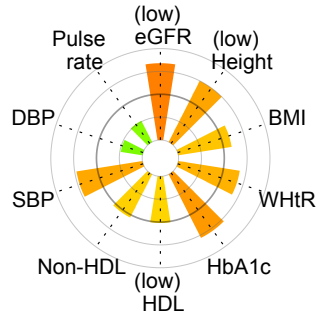
Severe obesity (13%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (12%)

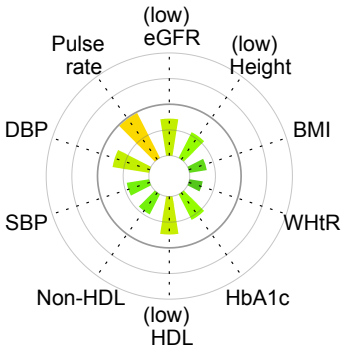


Risk factor percentile

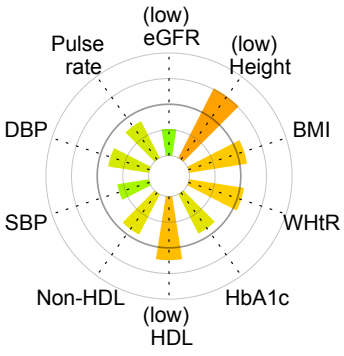
← more optimal more hazardous →

Women (9 clusters)

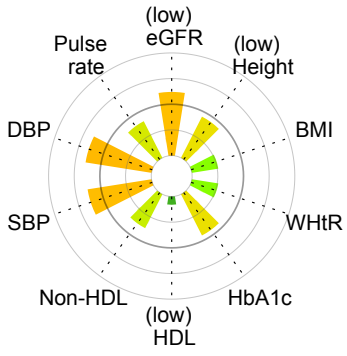
Low risk (17%)



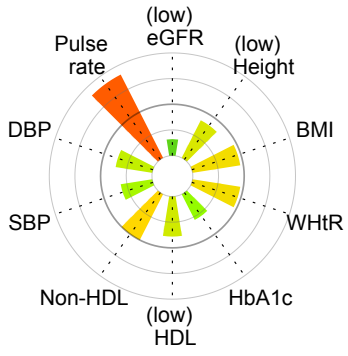
Mid-risk short (14%)



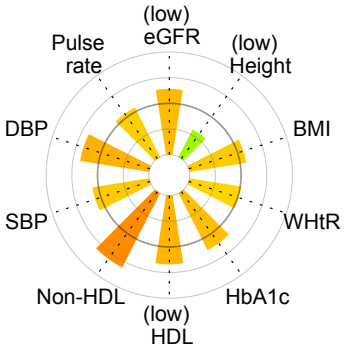
Low BMI, high HDL (11%)



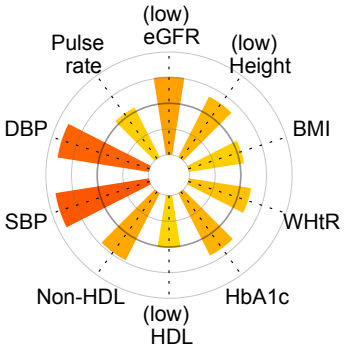
High heart rate (9%)



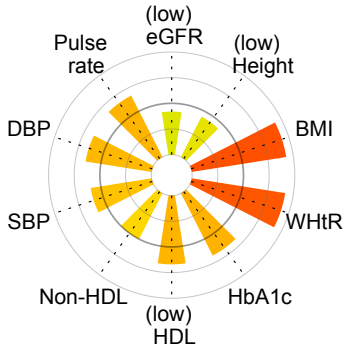
High cholesterol (14%)



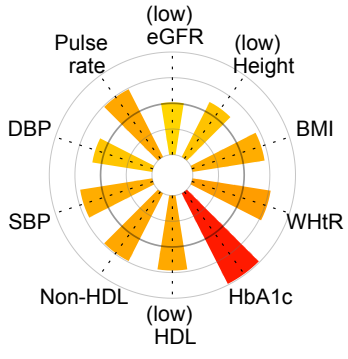
High blood pressure (10%)



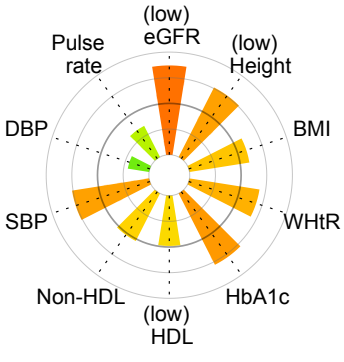
Severe obesity (12%)



Severe hyperglycemia (3%)

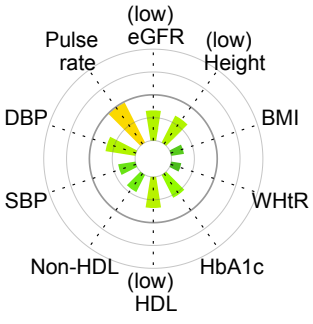


Low DBP, low eGFR (10%)

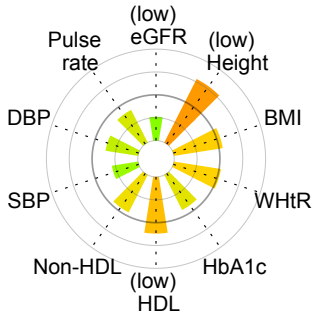


Women (10 clusters)

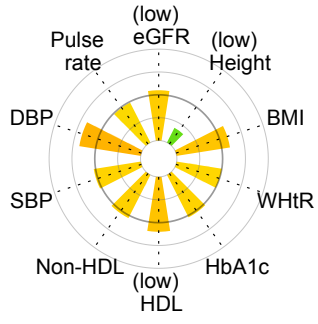
Low risk (15%)



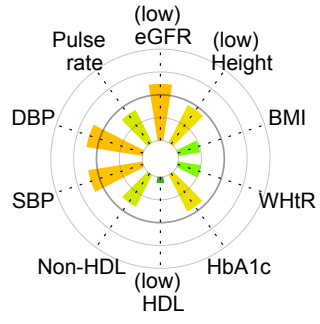
Mid-risk short (13%)



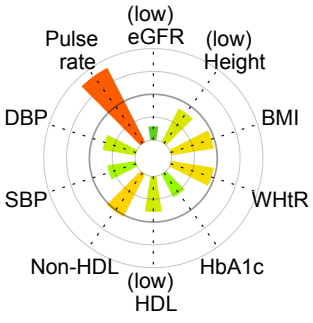
Mid-risk tall (12%)



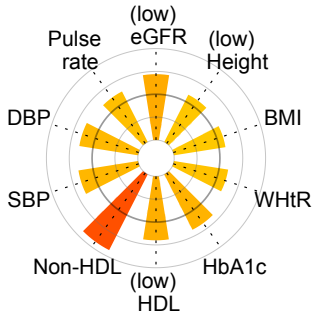
Low BMI, high HDL (10%)



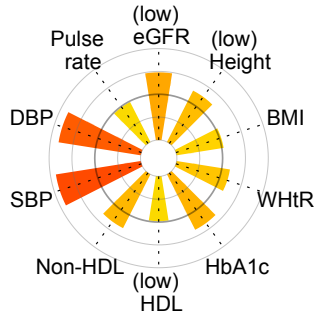
High heart rate (9%)



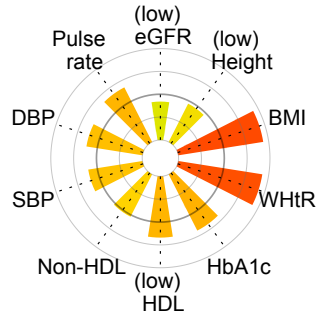
High cholesterol (9%)



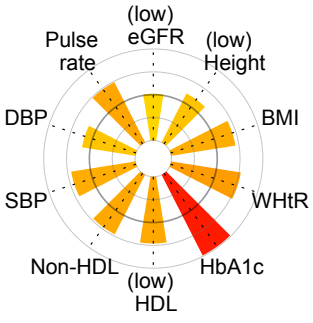
High blood pressure (8%)



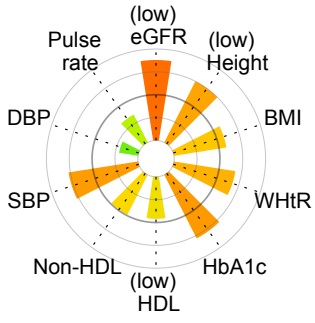
Severe obesity (11%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (9%)

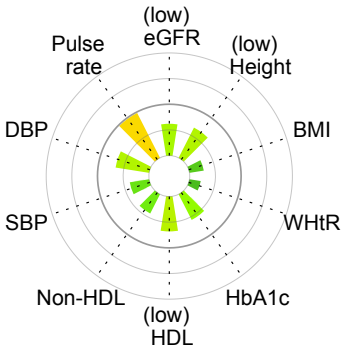


Risk factor percentile

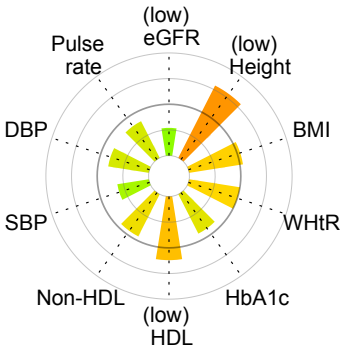
← more optimal more hazardous →

Women (11 clusters)

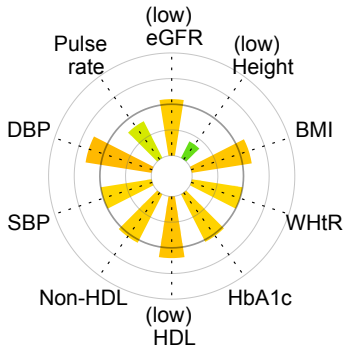
Low risk (15%)



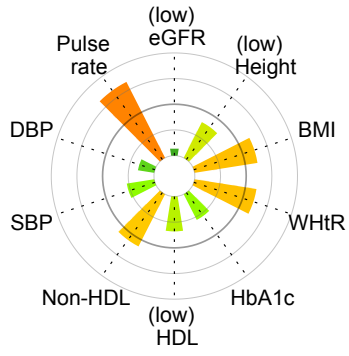
Mid-risk short (12%)



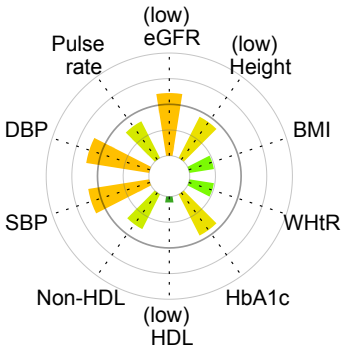
Mid-risk tall (11%)



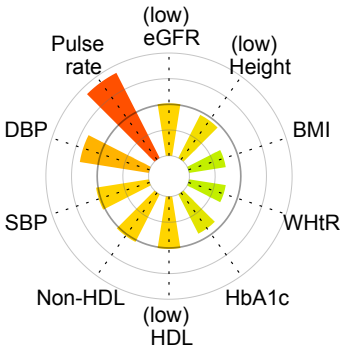
Low BP, high heart rate (6%)



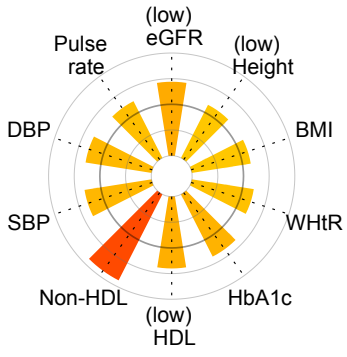
Low BMI, high HDL (9%)



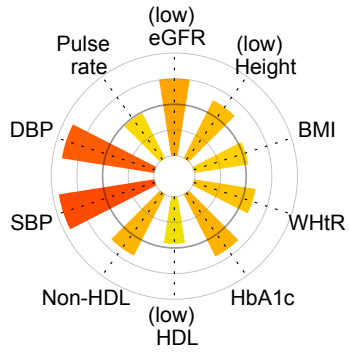
High heart rate (8%)



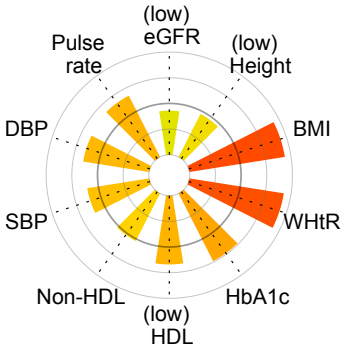
High cholesterol (8%)



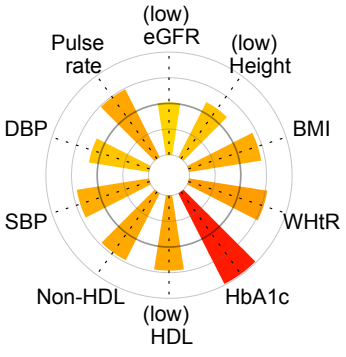
High blood pressure (8%)



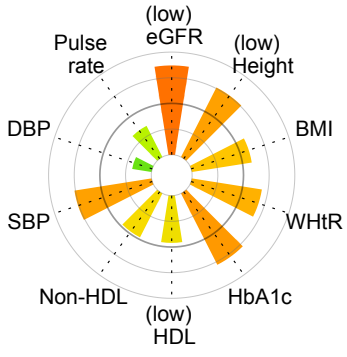
Severe obesity (10%)



Severe hyperglycemia (3%)

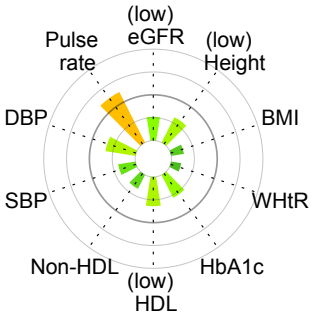


Low DBP, low eGFR (9%)

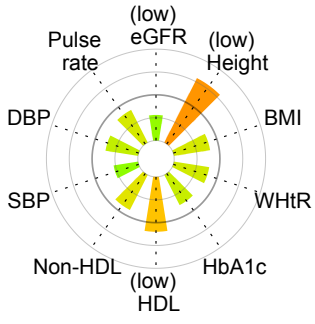


Women (12 clusters)

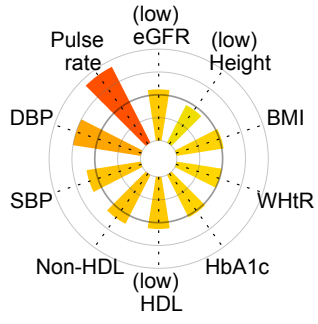
Low risk (13%)



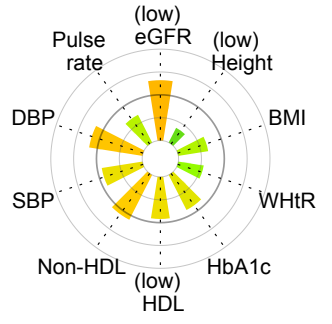
Low risk short (12%)



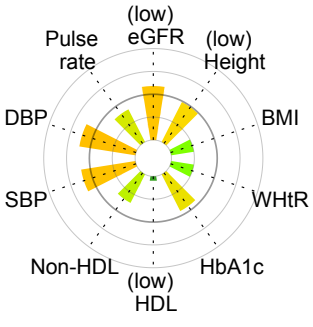
High heart rate (7%)



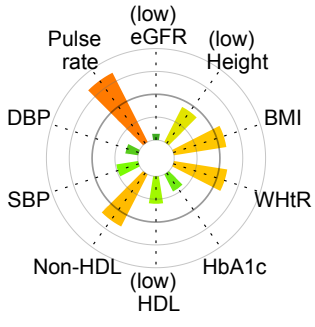
Low anthropometrics (10%)



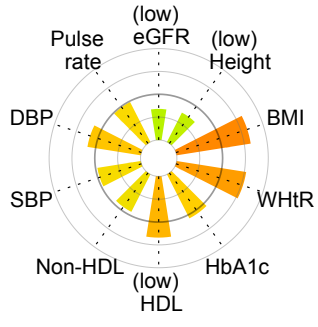
Low BMI, high HDL (8%)



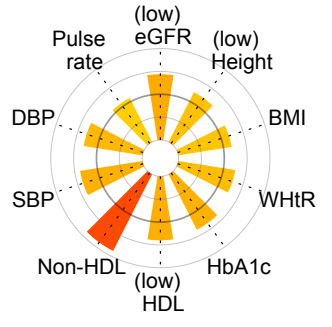
Low BP, high heart rate (5%)



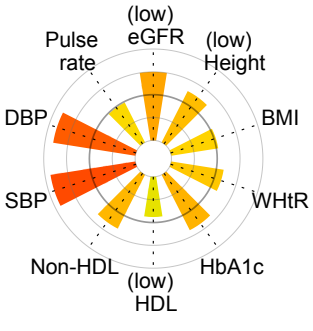
Overweight (11%)



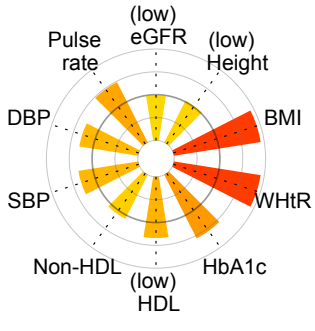
High cholesterol (8%)



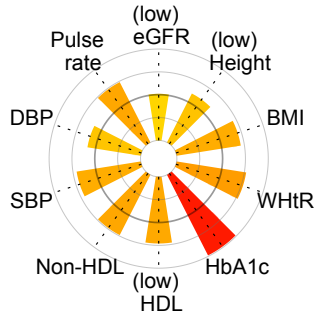
High blood pressure (8%)



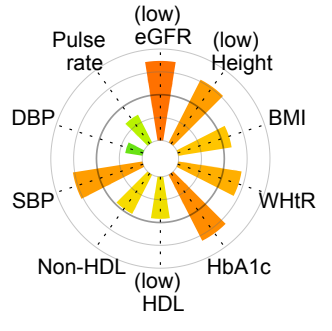
Severe obesity (7%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (9%)

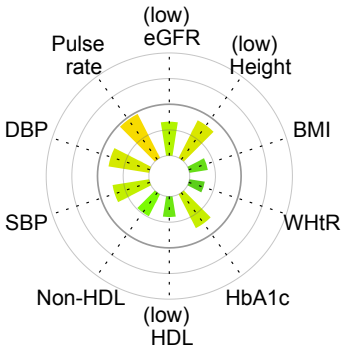


Risk factor percentile

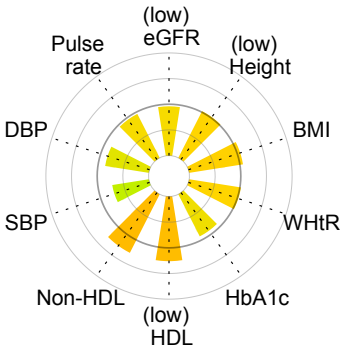
← more optimal more hazardous →

Men (5 clusters)

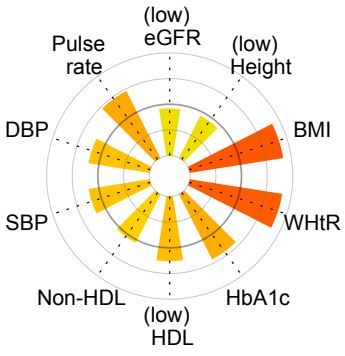
Low risk (26%)



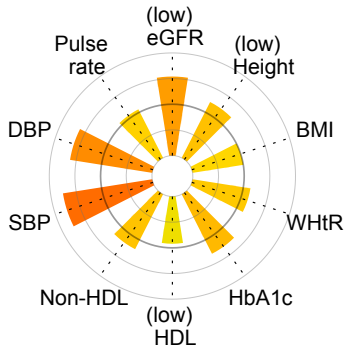
Mid-risk (35%)



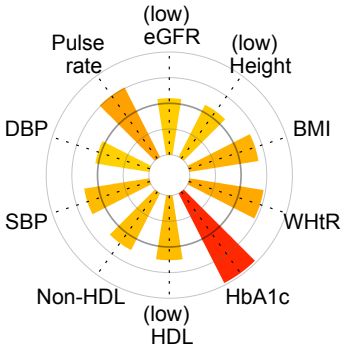
Severe obesity (15%)



High blood pressure (19%)

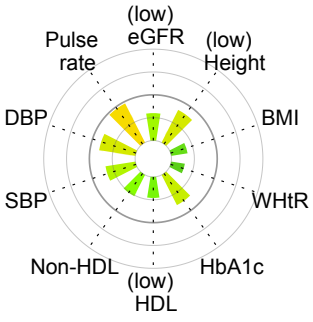


Severe hyperglycemia (4%)

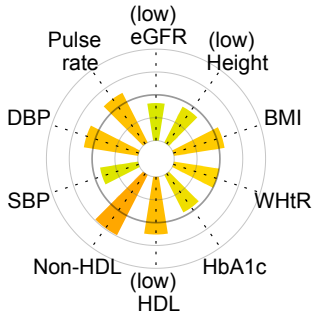


Men (6 clusters)

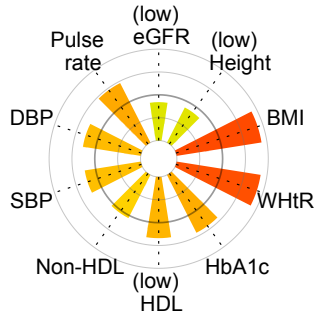
Low risk (25%)



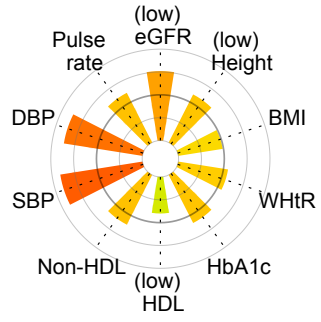
Mid-risk (28%)



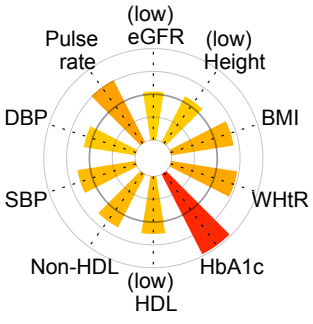
Severe obesity (12%)



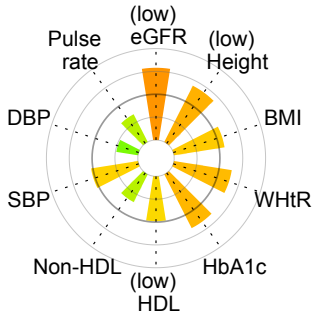
High blood pressure (14%)



Severe hyperglycemia (4%)



Low DBP, low eGFR (17%)

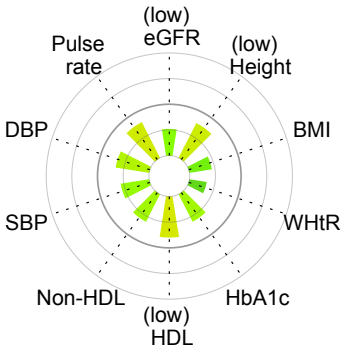


Risk factor percentile

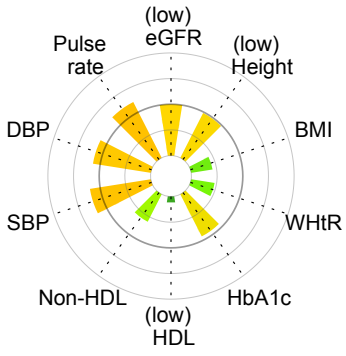
← more optimal more hazardous →

Men (7 clusters)

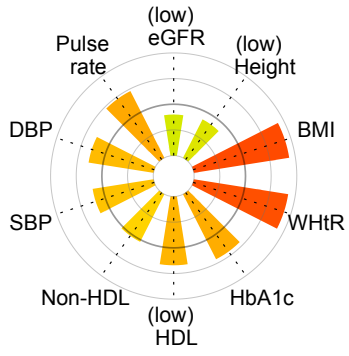
Low risk (22%)



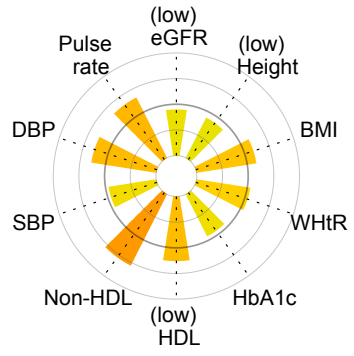
Low BMI, high HDL (10%)



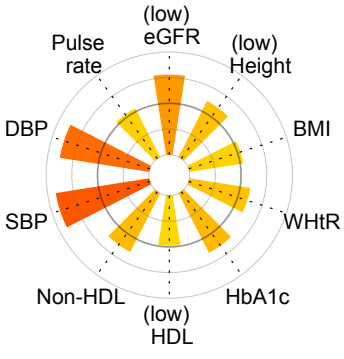
Severe obesity (11%)



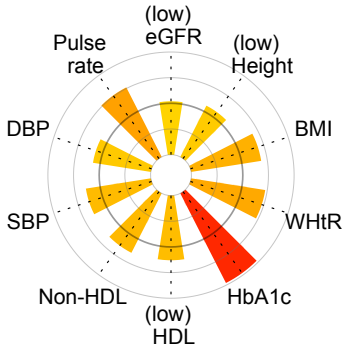
Mid-risk (25%)



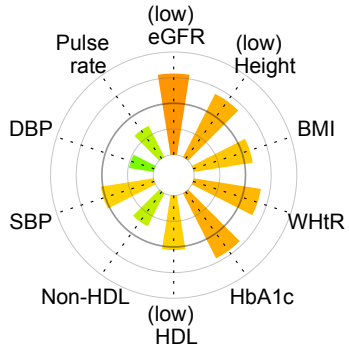
High blood pressure (11%)



Severe hyperglycemia (4%)

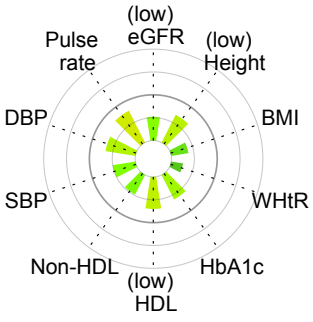


Low DBP, low eGFR (16%)

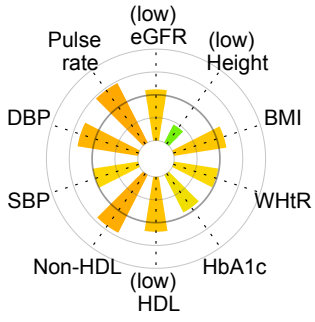


Men (8 clusters)

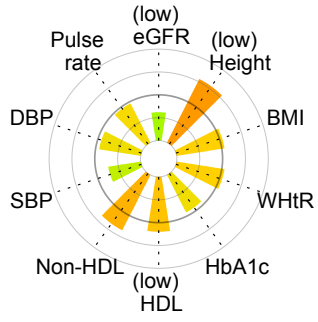
Low risk (18%)



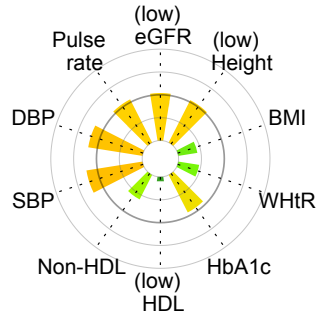
Mid-risk tall (18%)



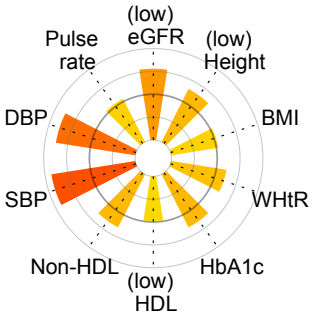
Mid-risk short (17%)



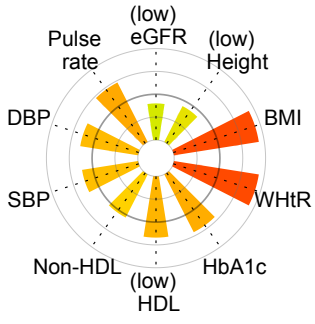
Low BMI, high HDL (9%)



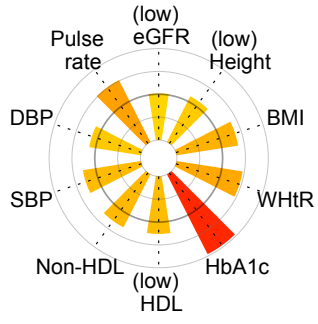
High blood pressure (11%)



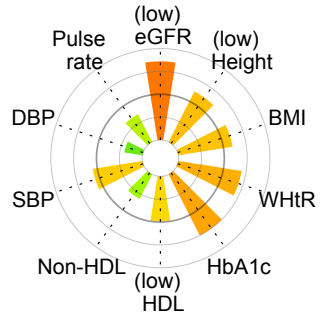
Severe obesity (10%)



Severe hyperglycemia (4%)



Low DBP, low eGFR (13%)

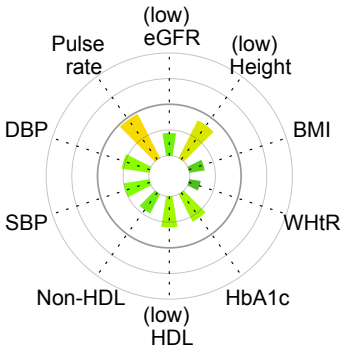


Risk factor percentile

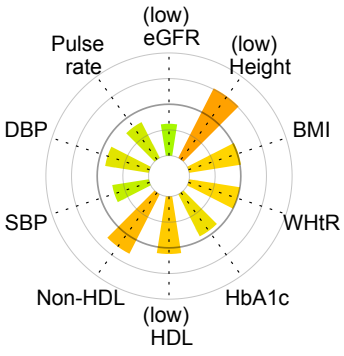
← more optimal more hazardous →

Men (9 clusters)

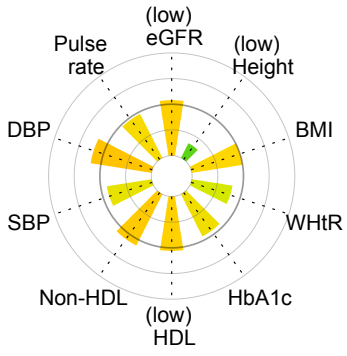
Low risk (15%)



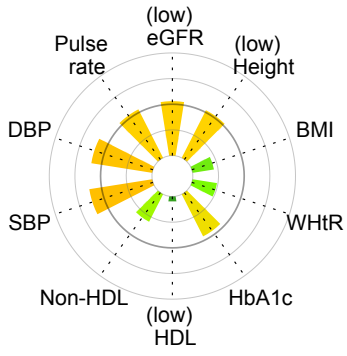
Mid-risk short (16%)



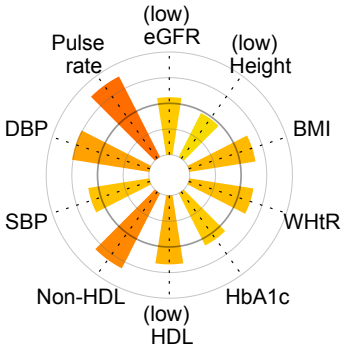
Mid-risk tall (16%)



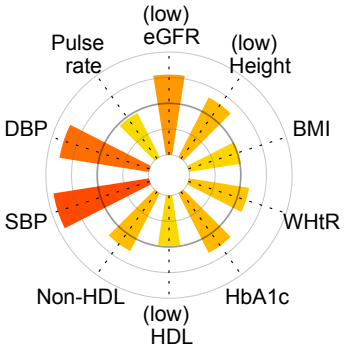
Low BMI, high HDL (8%)



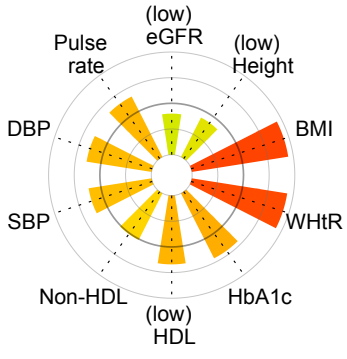
High cholesterol (12%)



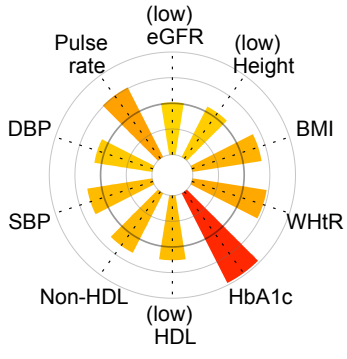
High blood pressure (9%)



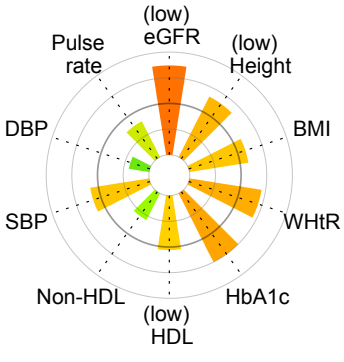
Severe obesity (9%)



Severe hyperglycemia (4%)

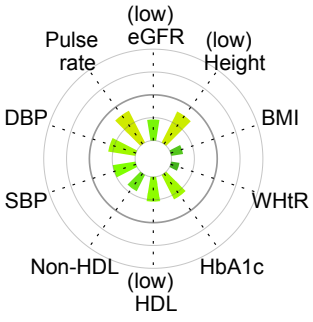


Low DBP, low eGFR (12%)

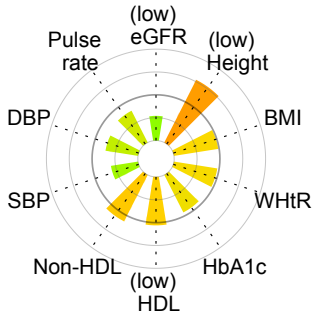


Men (10 clusters)

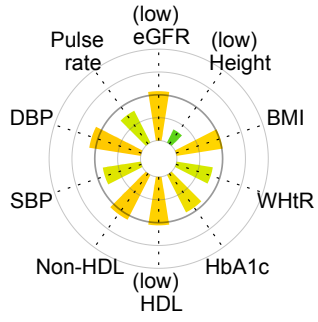
Low risk (13%)



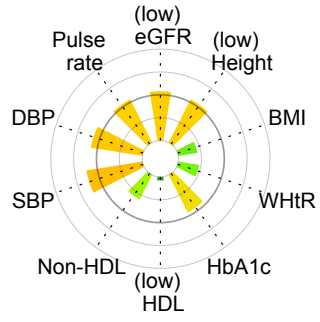
Mid-risk short (14%)



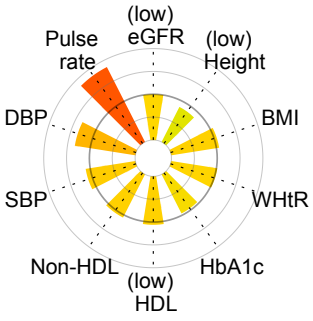
Mid-risk tall (14%)



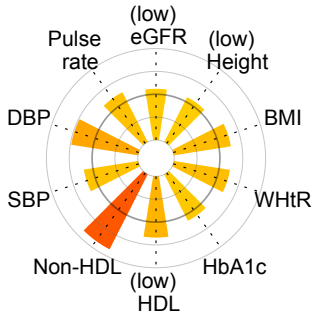
Low BMI, high HDL (8%)



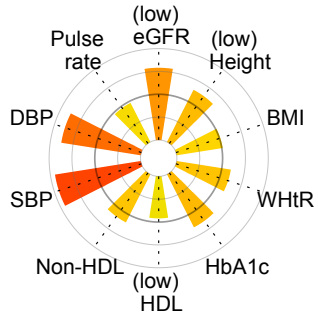
High heart rate (8%)



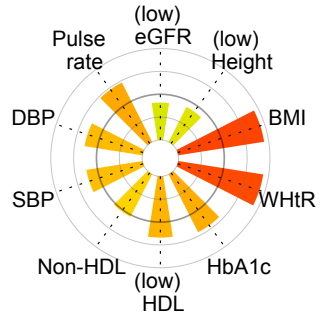
High cholesterol (10%)



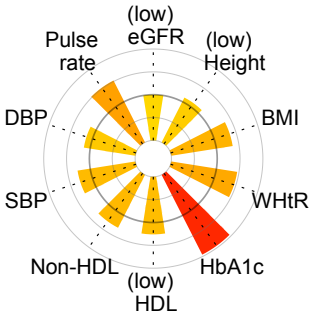
High blood pressure (8%)



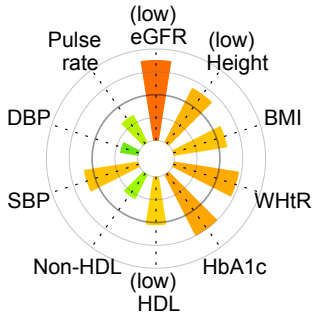
Severe obesity (9%)



Severe hyperglycemia (3%)



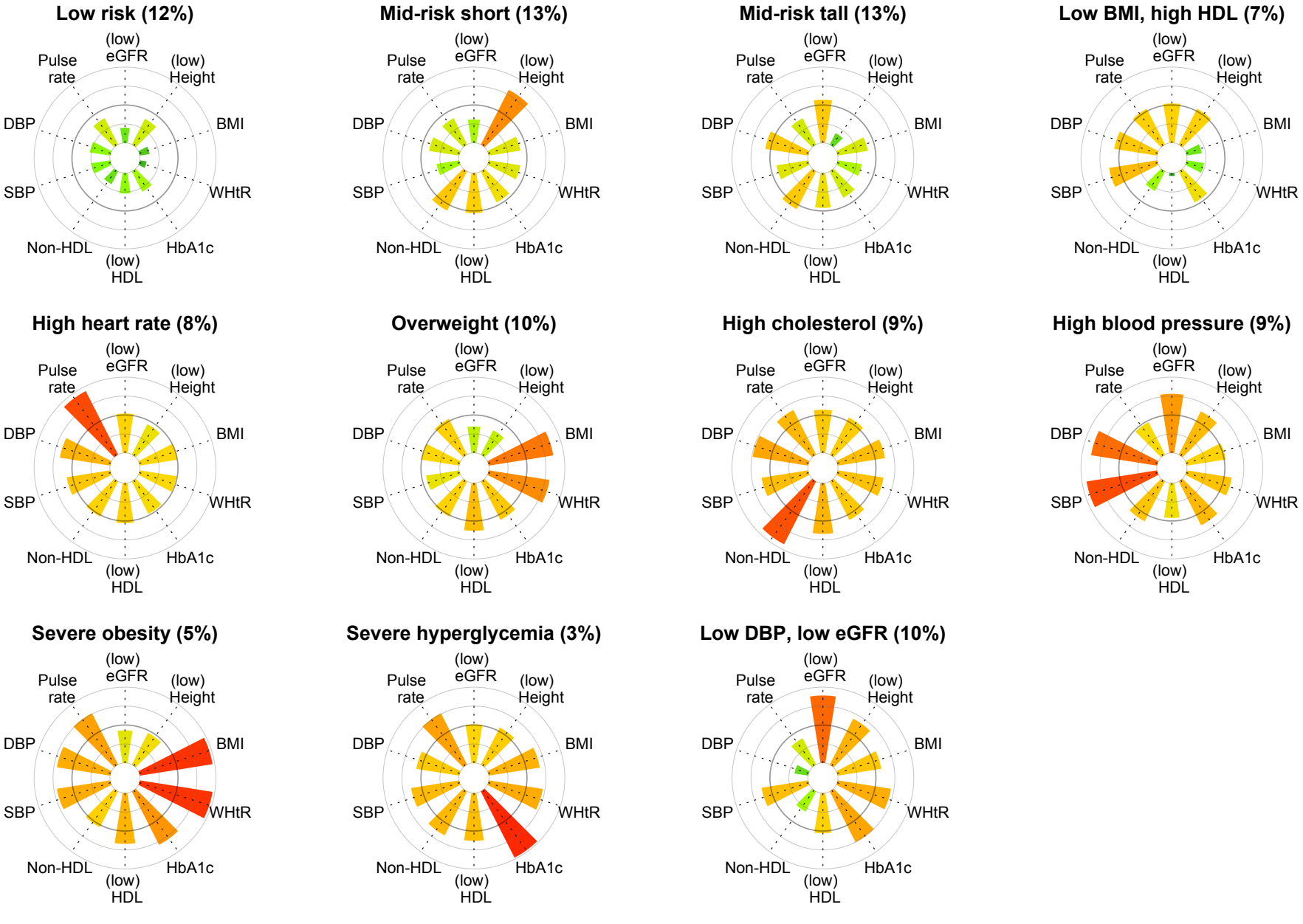
Low DBP, low eGFR (11%)



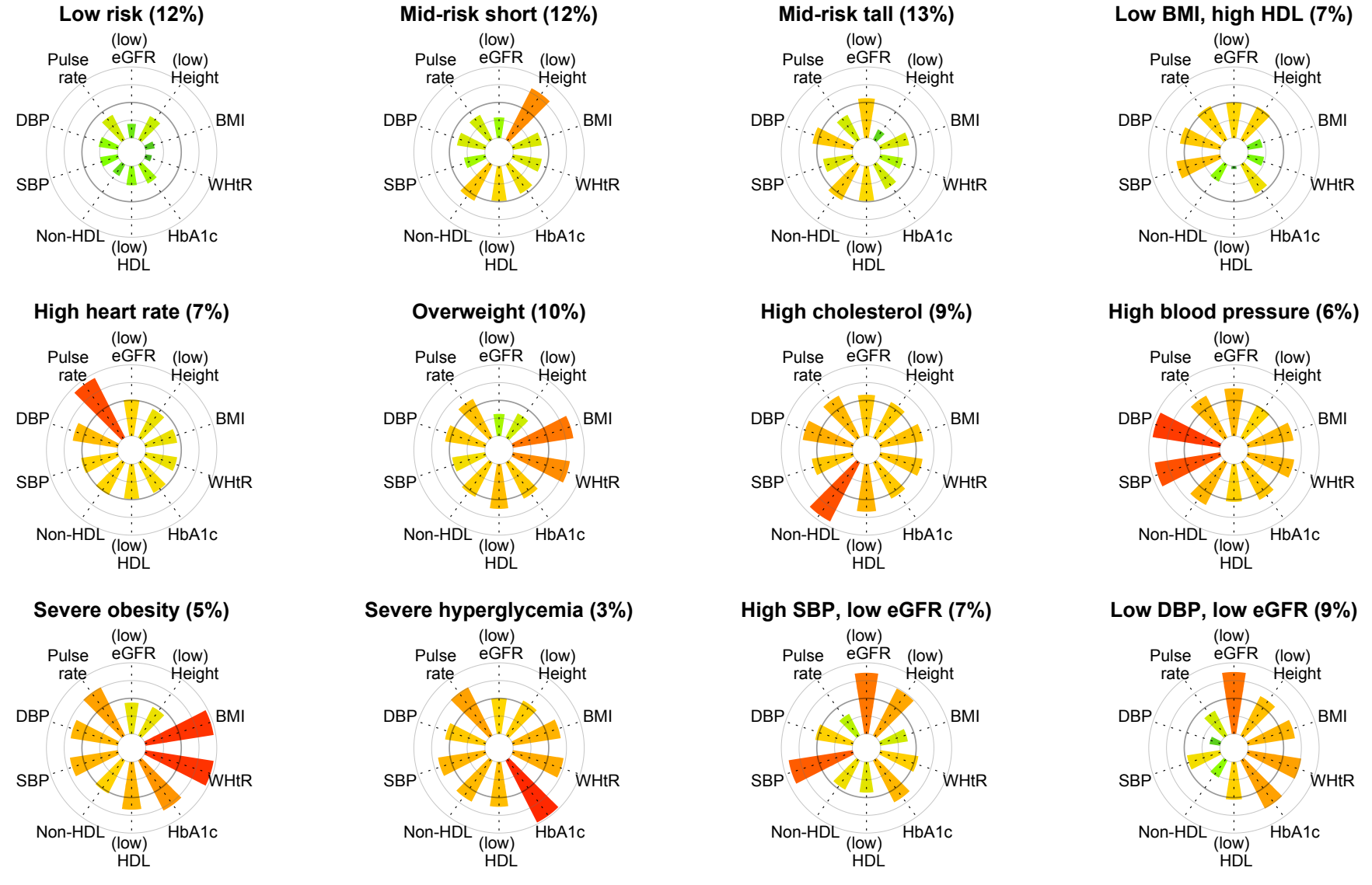
Risk factor percentile

← more optimal more hazardous →

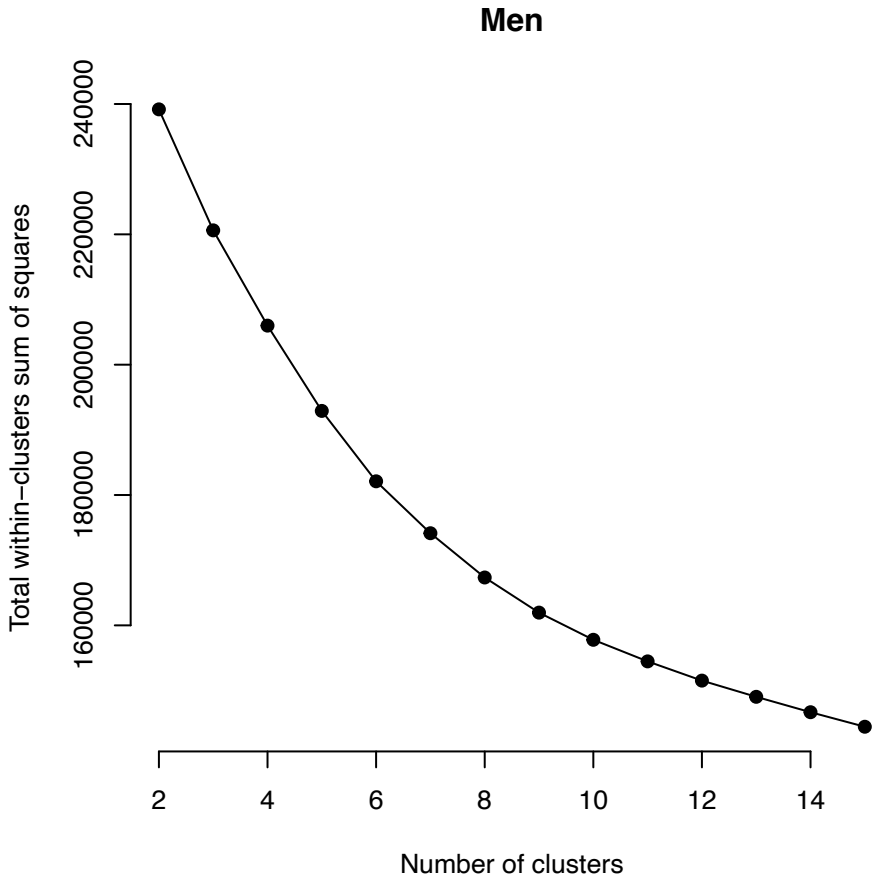
Men (11 clusters)

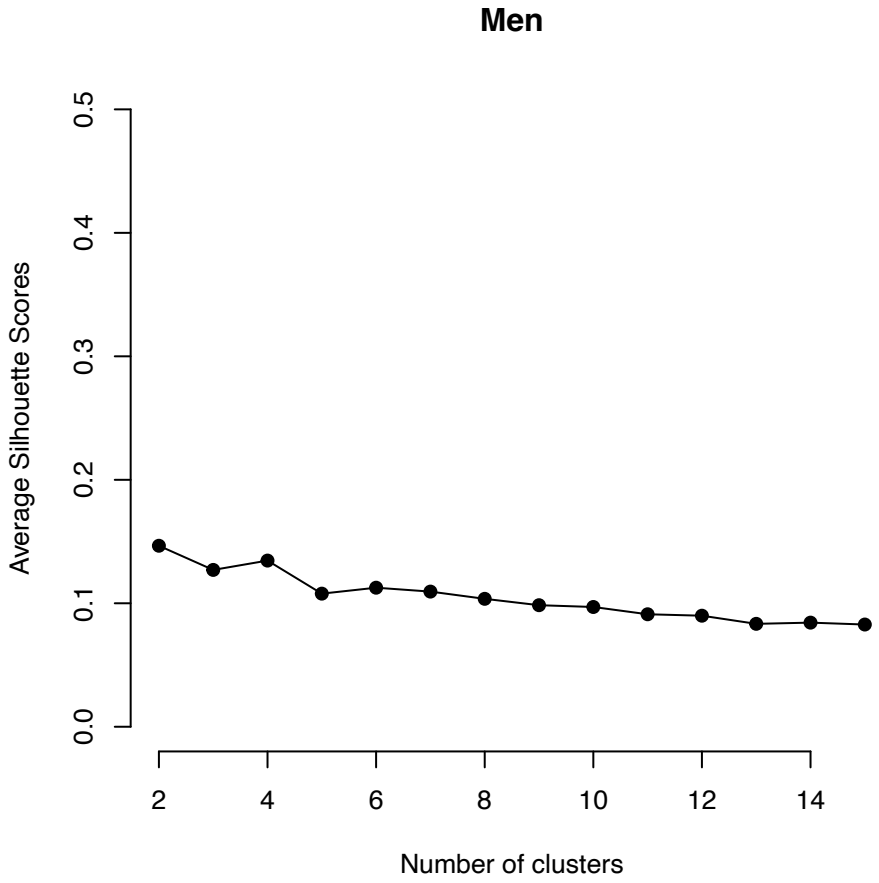


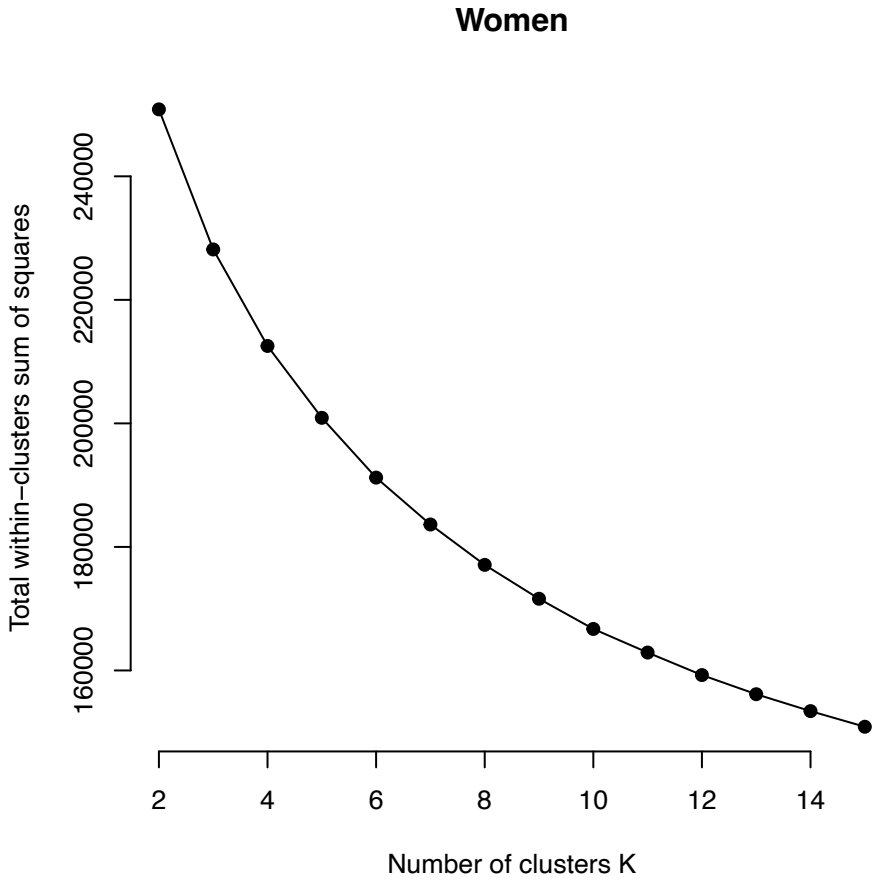
Men (12 clusters)

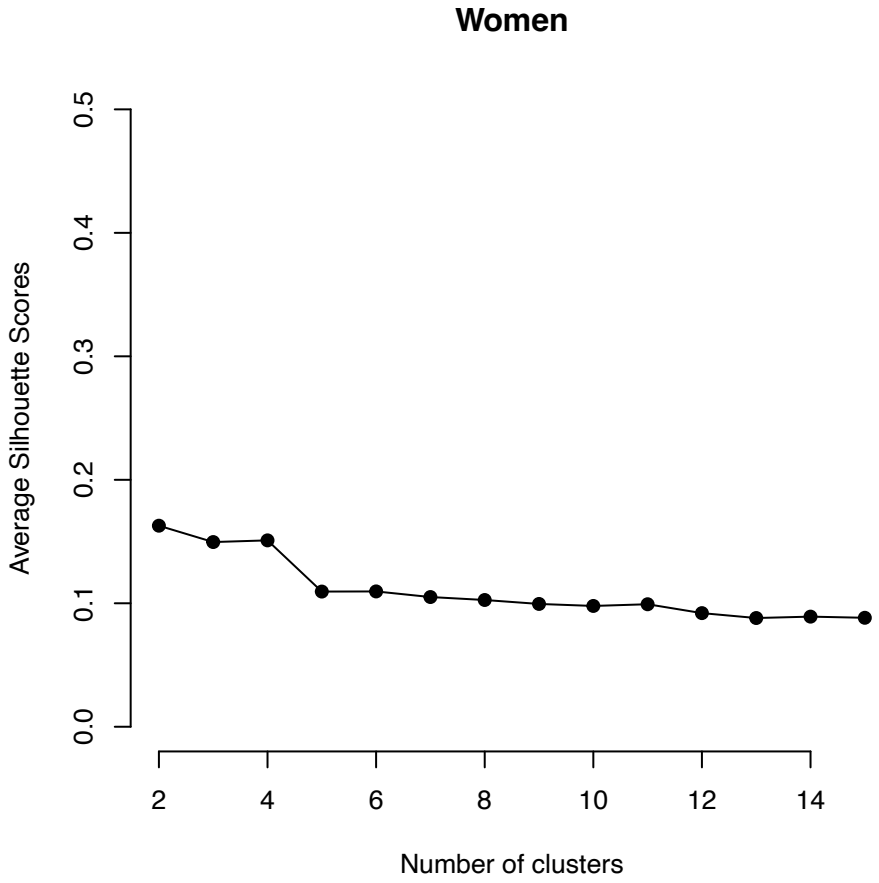


Supplementary Fig. 2. Elbow and silhouette plot when the number of clusters varies from 2 to 15 for (A) women and (B) men.


Men
Total within−clusters sum of squares
160000
180000
200000
220000
240000
2
4
6
8
10
12
14
Number of clusters


Men
Average Silhouette Scores
0.0
0.1
0.2
0.3
0.4
0.5
2
4
6
8
10
12
14
Number of clusters


Women
Total within−clusters sum of squares
160000
180000
200000
220000
240000
2
4
6
8
10
12
14
Number of clusters K


Women
Average Silhouette Scores
0.0
0.1
0.2
0.3
0.4
0.5
2
4
6
8
10
12
14
Number of clusters

Supplementary Fig. 3. Phenotypes identified by clustering NHANES III, NHANES 1999-2008 and NHANES 2009-2018 separately.

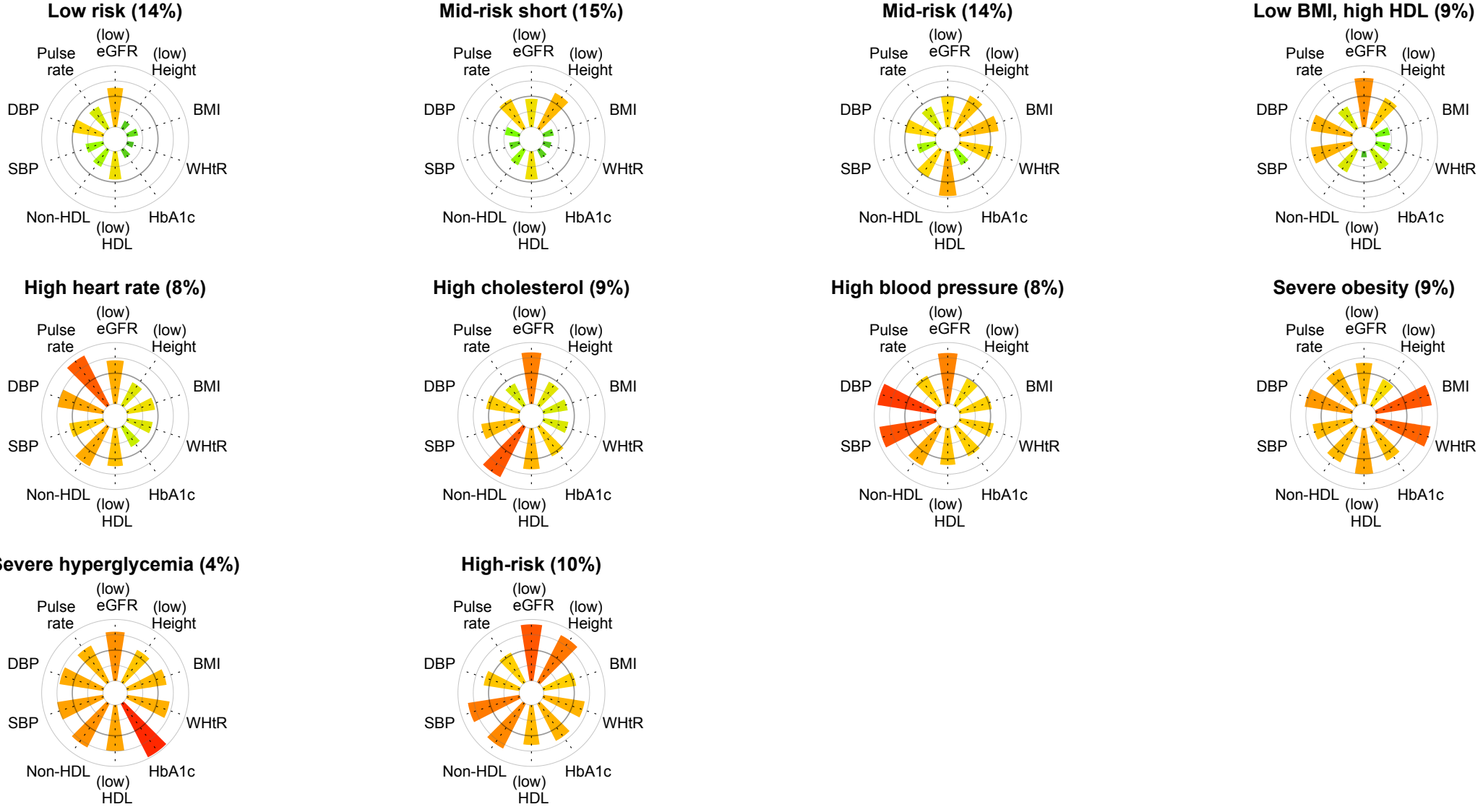
For each cluster in each subperiod, each bar shows the median value of one risk factor for all participants in the cluster. The number next to the cluster name represents the percentage of the participants grouped in this cluster.

The concentric circles show the minimum, 25^{th}, 50^{th}, 75^{th} percentiles and maximum in the whole sample, with the median shown in darker color. The height and color of the bar represent the median level of each risk factor, positioned relative to the distribution in the population of all periods combined so that the scale is common across all clusters and subperiods. The scale is reversed for height, eGFR and HDL because lower values indicate higher risk.

eGFR: estimated glomerular filtration rate; BMI: body-mass index; WHtR: waist-to-height ratio; HbA1c: glycated hemoglobin; HDL: high-density lipoprotein cholesterol; non-HDL: non-high-density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Women

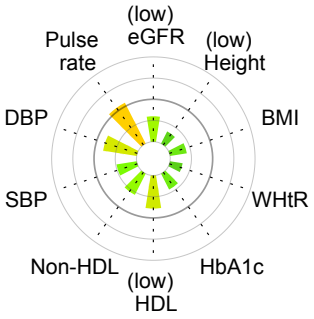
NHANES III



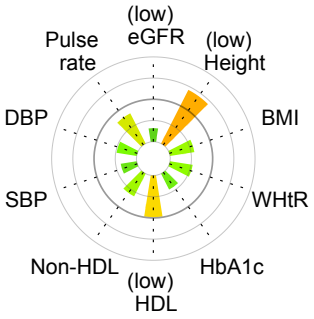
Women

NHANES 1999-2008

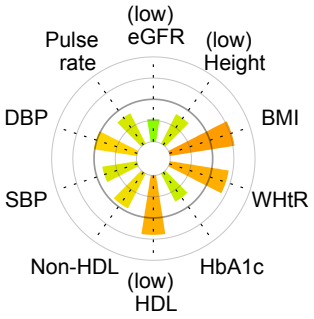
Low risk (14%)



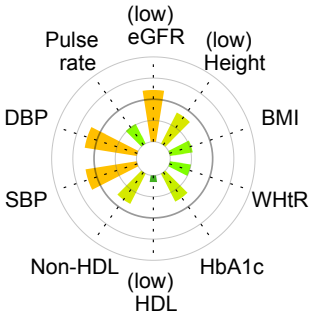
Mid-risk short (12%)



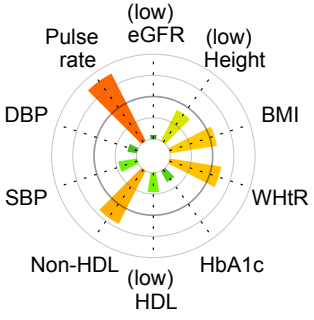
Obesity (14%)



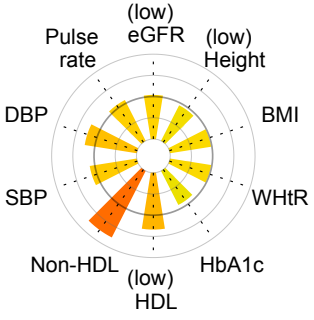
Low BMI, high HDL (11%)



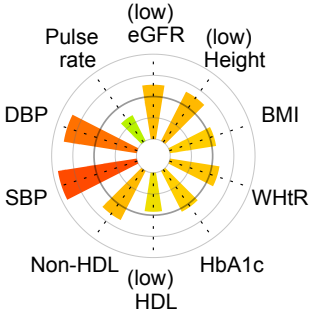
High heart rate (7%)



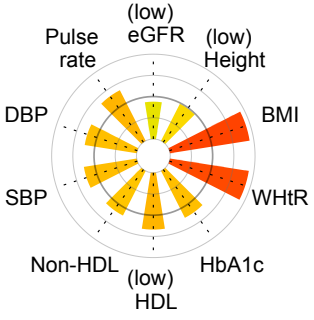
High cholesterol (12%)



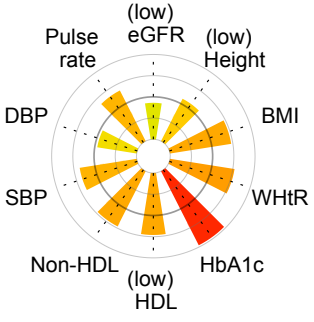
High blood pressure (9%)



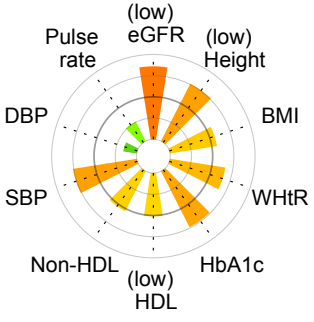
Severe obesity (8%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (10%)



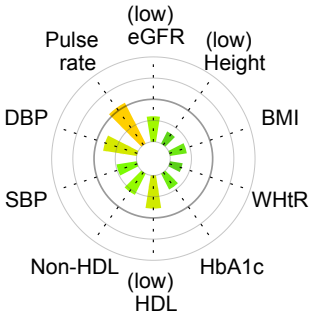
Risk factor percentile

more optimal ← → more hazardous

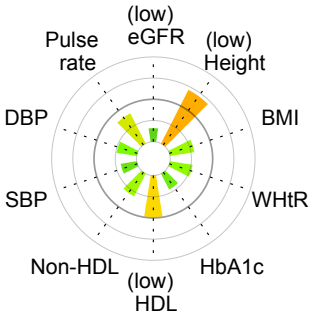
Women

NHANES 2009-2018

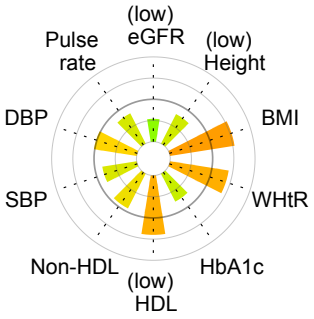
Low risk (14%)



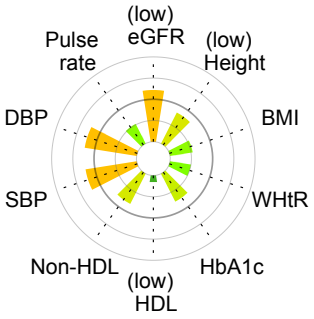
Mid-risk short (12%)



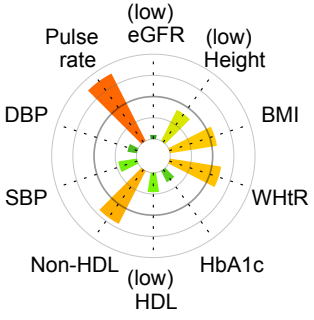
Obesity (14%)



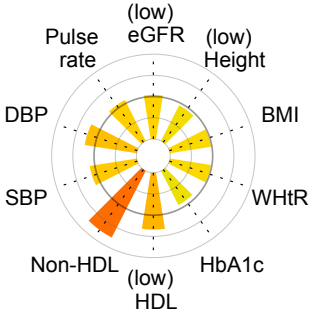
Low BMI, high HDL (11%)



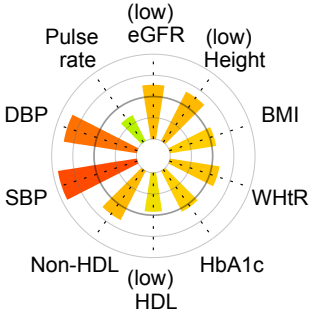
High heart rate (7%)



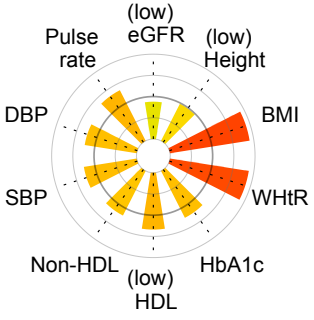
High cholesterol (12%)



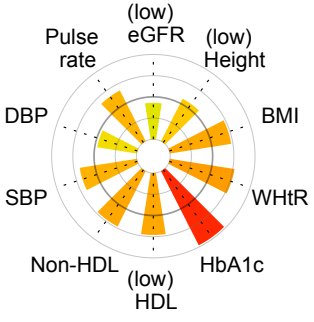
High blood pressure (9%)



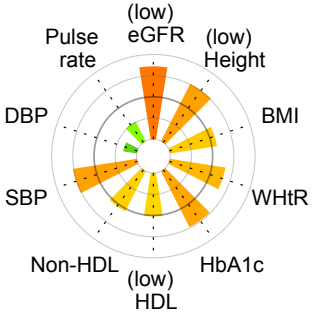
Severe obesity (8%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (10%)



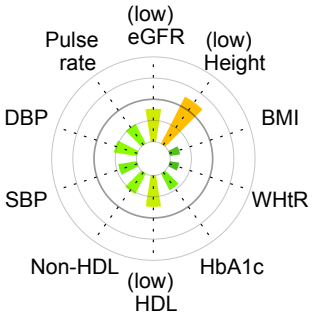
Risk factor percentile

more optimal ← → more hazardous

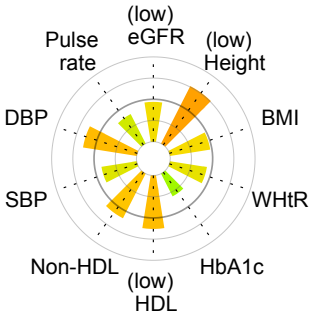
Men

NHANES III

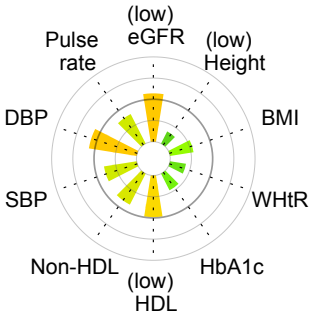
Low risk (13%)



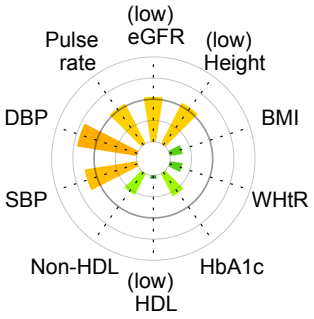
Mid-risk short (14%)



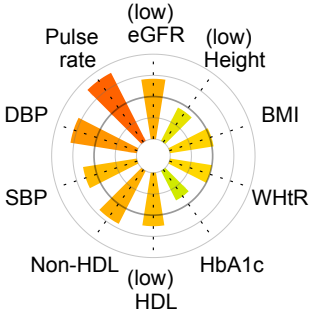
Mid-risk tall (14%)



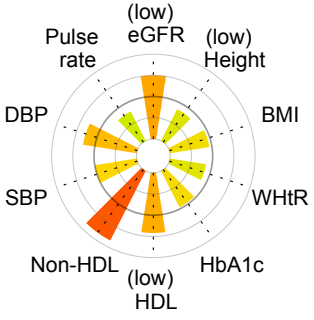
Low BMI, high HDL (7%)



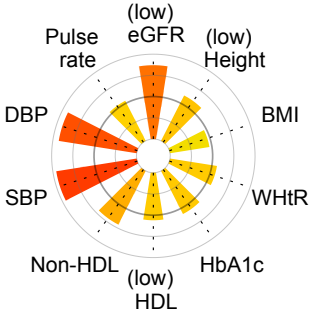
High heart rate (10%)



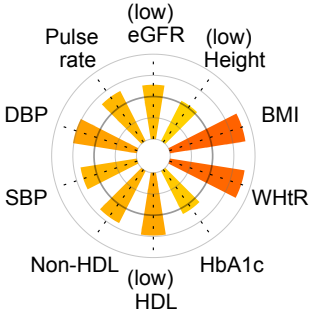
High cholesterol (11%)



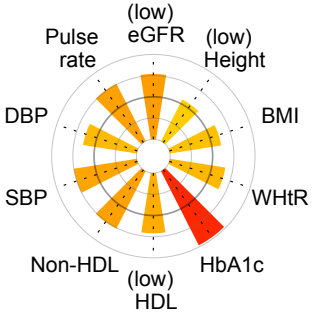
High blood pressure (9%)



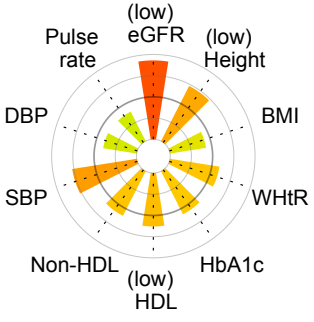
Severe obesity (9%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (10%)



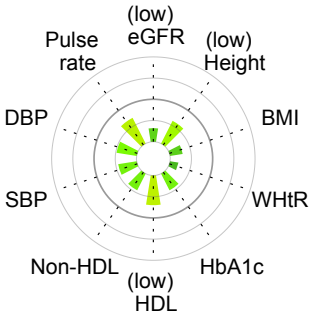
Risk factor percentile

more optimal ← → more hazardous

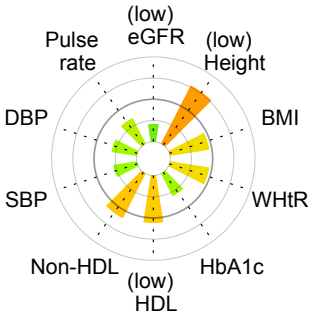
Men

NHANES 1999-2008

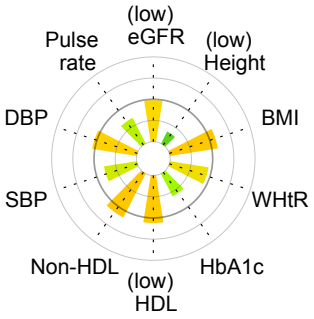
Low risk (12%)



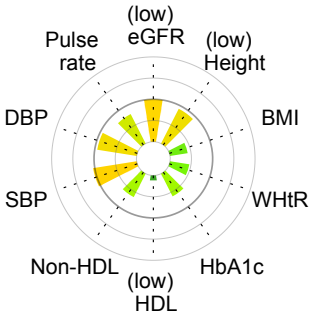
Mid-risk short (14%)



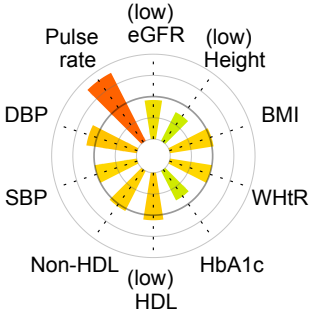
Mid-risk tall (15%)



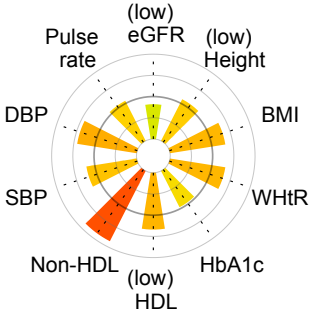
Low BMI, high HDL (8%)



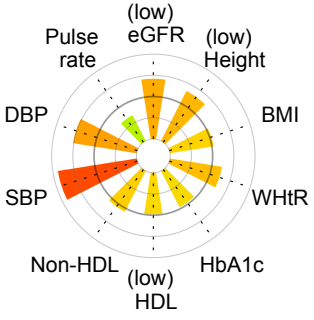
High heart rate (8%)



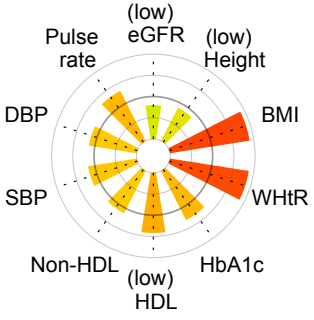
High cholesterol (10%)



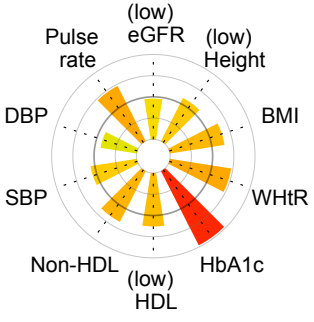
High blood pressure (8%)



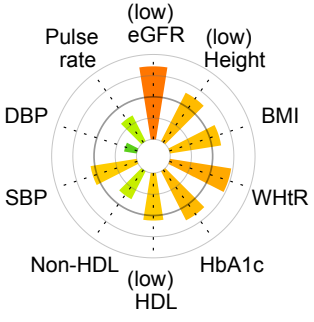
Severe obesity (9%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (11%)



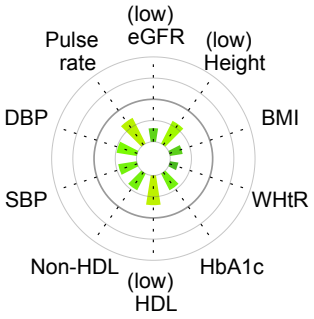
Risk factor percentile

more optimal ← → more hazardous

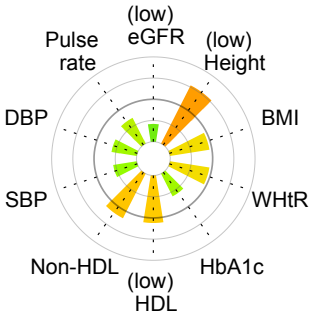
Men

NHANES 2009-2018

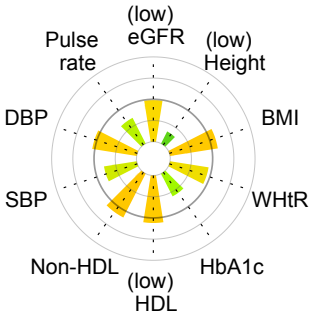
Low risk (12%)



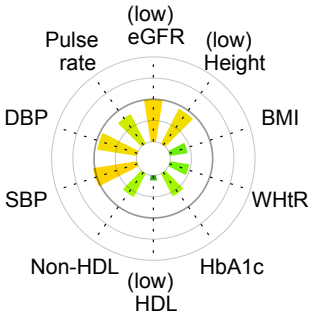
Mid-risk short (14%)



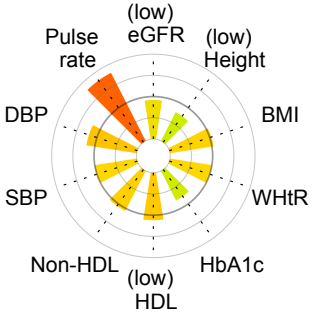
Mid-risk tall (15%)



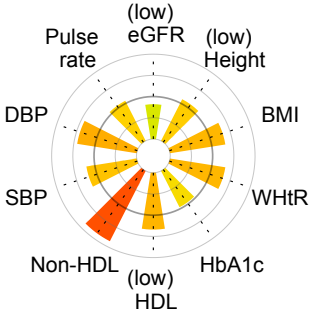
Low BMI, high HDL (8%)



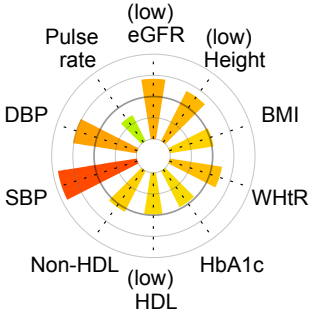
High heart rate (8%)



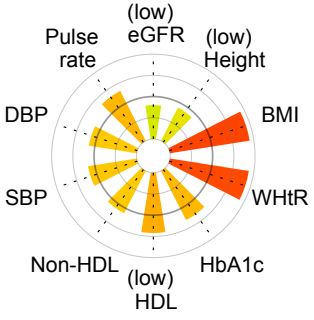
High cholesterol (10%)



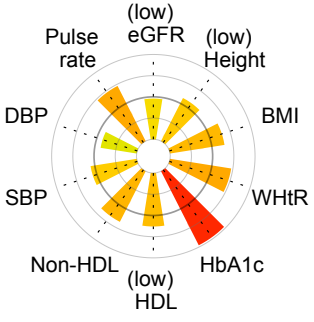
High blood pressure (8%)



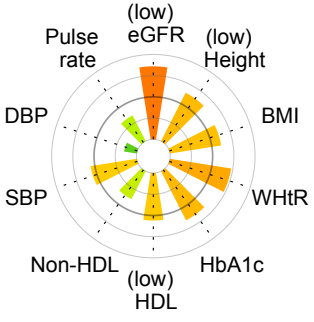
Severe obesity (9%)



Severe hyperglycemia (3%)



Low DBP, low eGFR (11%)



Risk factor percentile

more optimal ← → more hazardous

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page Number (page numbers refer to the clean manuscript)
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4, 15
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	15, 17-18
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	15-17
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	16-17
Bias	9	Describe any efforts to address potential sources of bias	19-21
Study size	10	Explain how the study size was arrived at	17-18, Extended Data Figure 4, Supplementary Table 2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	17, 20-21
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	18-21
		(*b*) Describe any methods used to examine subgroups and interactions	20-21
		(*c*) Explain how missing data were addressed	15, Extended Data Figure 4
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	21
		(*e*) Describe any sensitivity analyses	19-20
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg	17-18, Extended

		numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Data Figure 4
		(b) Give reasons for non-participation at each stage	17-18, Extended Data Figure 4
		(c) Consider use of a flow diagram	Extended Data Figure 4
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, Fig. 3, Extended Data Table 1, Extended Data Table 2
		(b) Indicate number of participants with missing data for each variable of interest	Extended Data Figure 4, Supplementary Table 2
Outcome data	15*	Report numbers of outcome events or summary measures	Fig. 1, Table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Not applicable
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not relevant
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-10, Fig 2-5
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22-23

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.