Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Associations of cereal grains intake with cardiovascular disease and mortality

across 21 countries in Prospective Urban and Rural Epidemiology study: prospective cohort study
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PURE Project Office Staff, National Coordinators, Investigators and Key Staff

PURE Project Office Staff, National Coordinators, Investigators, and Key Staff:

Project office (Population Health Research Institute, Hamilton Health Sciences and McMaster University, Hamilton, Canada): S Yusuf* (Principal Investigator).
S Rangarajan (Program Manager); K K Teo, S S Anand, C K Chow, M O’Donnell, A Mente, D Leong, A Smyth, P Joseph, M Duong, R D’Souza, M Walli-Attaei, S Islam (Statistician), W Hu (Statistician), C Ramasundarahettige (Statistician), P Sheridan (Statistician), S Bangdiwala, L Dyal, B Liu (Biometric Programmer), C Tang (Biometric Programmer), X Yang (Biometric Programmer), R Zhao (Biometric Programmer), L Farago (ICT), M Zarate (ICT), J Godreault (ICT), M Haskins (ICT), M Jethva (ICT), G Rigitano (ICT), A Vaghela (ICT), M Dehghan (Nutrition Epidemiologist), A Aliberti, A Reyes, A Zaki, B Connolly, B Zhang, D Agapay, D Krol, E McNeice, E Ramezani, F Shifaly, G McAlpine, I Kay, J Rimac, J Swallow, M Di Marino, M Jakymyshyn, M(a) Mushtaha, M(o) Mushtaha, M Trotter, N Aoucheva, N Kandy, P Mackie, R Buthool, R Patel, R Solano, S Gopal, S Ramachan, S Trotter

Core Laboratories: G Pare, M McQueen, S Lamers, J Keys (Hamilton), X Wang (Beijing, China), A Devanath (Bangalore, India).

Argentina: R Diaz*, A Orlandini, P Lamelas, M L Diaz, A Pascual, M Salvador, C Chacon;
Bangladesh: O Rahman*, R Yusuf*, S A K S. Ahmed, T Choudhury, M Sintaha, A Khan, O Alam, N, Nayeem, S N Mitra, S Islam, F Pasha; Brazil: A Avezum*, C S Marcilio, A C Mattos, G B Oliveira; Canada: K Teo*, S Yusuf*, Sumathy Rangarajan, A Arshad, B Bideri, I Kay, J Rimac, R Buthool, S Trotter, G Dagenais, P Poirier, G Turbite, AS Bourlaud, A LeBlanc De Bluts, M Cayer, I Tardif, M Pettigrew, S Lear, V de Jong, A N Saidy, V Kandola, E Corber, I Vukmirovich, D Gasevic, A Wielgosz, A Pipe, A Lefebvre, A Pepe, A Auclair, A Prémont, A S Bourlaud; Chile: F Lanas*, P Serón, M J Oliveros, F Cazor, Y Palacios; China: Liu Lisheng*, Li Wei*, Chen Chunming*, Zhao Wenhua. Hu Bo, Yin Lu, Zhu Jun, Liang Yan, Sun Yi, Wang Yang, Deng Qing, Jia Xuan, He Xinye, Zhang Hongye, Bo Jian, Wang Xingyu, Liu Xu, Gao Nan, Bai Xiulin, Yao Chenrui, Cheng Xiaoru, Wang Chuangshi, Li Sidong, Liu Weida, Lang Xinyue, Liu Xiaoyun, Zhu Yiping, Su yuxuan, Han Guoliang, Song Rui, Cao Zhuangni, Sun Yaya, Li Xiangrong, Wang Jing, Wang Li, Peng Ya, Li Xiaoqing, Li Ling, Wang
Jia, Zou Jianmei, Gao Fan, Tian Shaofang, Liu Lifu, Li Yongmei, Bi Yanhui, Li Xin, Zhang Anran, Wu Dandan, Cheng ying, Xiao Yize, Lu Fanghong, Li Yindong, Hou Yan, Zhang Liangqiong, Guo Baoxia, Liao Xiaoyang, Chen Di, Zhang Peng, Li Ning, Ma Xiaolan, Lei Rensheng, Fu Minfan, Liu Yu, Xing Xiaojie, Yang Youzhu, Zhao Shenghu, Xiang Quanyong, Tang Jinhua, Liu Zhengrong, Qiang Deren, Li Xiaoxia, Xu Zhengting, Aideeraili.Ayoupu, Zhao Qian; Colombia: P Lopez-Jaramillo*, P A Camacho-Lopez, M Perez, J Otero-Wandurraga, D I Molina, C Cure-Cure, JL Accini, E Hernandez, E Arcos, C Narvaez, A Sotomayor, F Manzur, H Garcia, G Sanchez, F Cotes, A Rico, M Duran, C Torres; India: Bangalore - P Mony *, M Vaz*, S Swaminathan, AV Bharathi, K Shankar#, A V Kurpad, K G Jayachitra, H A L Hospital, AR Raju, S Niramala, V Hemalatha, K Murali, K Balaji, A Janaki, K Amaranad, P Vijayalakshmi, Chennai - V Mohan*, R M Anjana, M Deepa, K Parthiban, L Dhanasekaran, SK Sundaram, M Rajalakshmi, P Rajaneesh, K Munusamy, M Anitha, S Hemavathy, T Rahulashankiruthiyayan, D Anitha, R. Dhanasekhar, S. Sureshkumar, D Anitha, K Sridevi, Jaipur - R Gupta, R B Panwar, I Mohan, P Rastogi, S Rastogi, R Bhargava, M Sharma, D Sharma, Trivandrum - V Raman Kutty, K Vijayakumar, S Nair, Kamala R, Manu MS, Arunlal AR, Veena A, Sandeep P Kumar, Leena Kumari, Tessi R, Jith S, K Ajayan, G Rajasree, AR Renjini, A Deepu, B Sandhya, S Asha, H S Soumya, Chandigarh - R Kumar, M Kaur, P V M Lakshmi, V Sagar J S Thakur, B Patro, R Mahajan, A Joshi, G Singh, K Sharma, P Chaudary, Iran: R Kelishadi*, A Bahonar, N Mohammadifard, H Heidari, Kazakhstan: K Davletov*, B Assembekov, B Amirov; Kyrgyzstan: E Mirrakhimov*, S Abilova, U Zakirov, U Toktomamatov; Malaysia: UiTM - K Yusoff*, T S Ismail, K Ng, A Devi, N Mat-Nasir, AS Ramli, MNK Nor-Ashikin, R Dasiman, MY Mazapuspavina, F Ariffin, M Miskan, H Abdul-Hamid, S Abdul-Razak, N Baharudin, NMN Mohd-Nasir, SF Badlishah-Sham, MS Mohamed-Yassin, M Kaur, M Koshy, F A Majid, N A Bakar, N Zainon, R Salleh, SR Norlizan, NM Ghazali, M Baharom, H Zulkifli, R Razali, S Ali, CWJCW Hafar, F Basir; UKM - Noorhassim Ismail, M J Hasni, M T Azmi, M I Zaleha, R Ismail, K Y Hazdi, N Saian, A Jusoh, N Nasir, A Ayub, N Mohamed, A Jamaludin, Z Rahim; Occupied Palestinian Territory: R Khatib*, U Khammash, R Giacaman; Pakistan: R Iqbal*, R Khawaja, I Azam, K Kazmi; Peru: J Miranda*, A Bernabe Ortiz, W Checkley, R H Gilman, L Smeeth, R M Carrillo, M de los Angeles, C Tarazona Meza; Philippines: A Dans*, H U Co, J T Sanchez, L Pudol, C Zamora-Pudol, L A M Palileo-Villanueva, M R Aquino, C Abaquin, SL Pudol, K Manguiat, S Malayang; Poland: W Zatonski*, A Szuba, K Zatonska, R Ilow#, M Ferus, B Regulska-Ilow, D Różańska, M Wolyniec; Saudi Arabia: KF AlHabib*, M Alshamiri, HB Altaradi, O Alnobani, N Alkamel, M Ali, M Abdulrahman, R Nouri; South Africa: L Kruger*, A Kruger#, P Bestra, H Voster,
A E Schutte, E Wentzel-Viljoen, FC Eloff, H de Ridder, H Moss, J Potgieter, A Roux, M Watson, G de Wet, A Olckers, J C Jerling, M Pieters, T Hoekstra, T Puoane, R Swart*, E Igumbor, L Tsolekile, K Ndayi, D Sanders, P Naidoo, N Steyn, N Peer, B Mayosi#, B Rayner, V Lambert, N Levitt, T Kolbe-Alexander, L Ntyintyane, G Hughes, J Fourie, M Muzigaba, S Xapa, N Gobile, K Ndayi, B Jwili, K Ndibaza, B Egbuie; Sweden A Rosengren*, K Bengtsson Boström, A Rawshani, A Gustavsson, M Andreasson, L Wirdemann; Tanzania: K Yeates*, M Oresto, N West Turkey: A Oguz*, N Imeryuz, Y Altuntas, S Gulec, A Temizhan, K Karsidag, K B T Calik, A K Akalin, O T Caklili, M V Keskinler, K Yildiz; United Arab Emirates: A H Yusufali, F Hussain, M H S Abdelmotagali, D F Youssef, O Z S Ahmad, F H M Hashem, T M Mamdouh, F M AbdRabboou, S H Ahmed, M A AlOmairi, H M Swidan, M Omran, N A Monsef; Zimbabwe: J Chifamba*, T Ncube, B Ncube, C Chimhete, G K Neya, T Manenji, L Gwaunza, V Mapara, G Terera, C Mahachi, P Murambiwa, R Mapanga, A Chinhara

*National Coordinator
# Deceased
## PURE Country Institution Names

| Country       | Institution                                                                 |
|---------------|-----------------------------------------------------------------------------|
| **South Africa** | Faculty of Health Science  
North-West University  
Potchefstroom Campus  
University of the Western Cape  
Department of Dietetics and Nutrition  
Private Bag X17, 7535  
Bellville, South Africa |
| **Zimbabwe**   | University of Zimbabwe  
College of Health Sciences  
Physiology Department  
Harare, Zimbabwe |
| **Tanzania**   | Pamoja Tunaweza Health Research Centre, Moshi, Tanzania  
Division of Nephrology, Department of Medicine  
Queen's University |
| **China**      | National Centre for Cardiovascular Diseases  
Cardiovascular Institute & Fuwai Hospital  
Chinese Academy of Medical Sciences  
167, Bei Li Shi Lu, Beijing, China  
Fuwai Hospital  
167 Beilishi Rd. Xicheng District  
Beijing, 100037 China |
| **Philippines**| University of Philippines, Section of Adult Medicine & Medical Research Unit, Manila, Philippines |
| **Pakistan**   | Department of Community Health Sciences and Medicine  
Aga Khan University  
Stadium Road, P.O Box 3500  
Karachi Pakistan |
| **India, Bangalore** | St John's Medical College and Research Institute  
Bangalore 560034, India |
| **India, Chennai** | Madras Diabetes Research Foundation & Dr. Mohan’s Diabetes Specialities Centre, Chennai |
| **India Jaipur** | Eternal Heart Care Centre and Research Institute, Jaipur |
| **India, Trivandrum** | Health Action by People, Thiruvananthapuram, Kerala, 695011 INDIA |
| **India, Chandigarh** | School of Public Health, Post Graduate Institute of Medical Education & Research, Chandigarh (India) |
| **Bangladesh** | Independent University, Bangladesh  
Bashundhara, Dhaka  
Bangladesh |
| **Malaysia**   | Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia AND UCSI University, Cheras, Selangor, Malaysia  
Department of Community Health. Faculty of Medicine. University Kebangsaan Malaysia. Kuala Lumpur. Malaysia |
| **Poland** | Wroclaw Medical University  
Department of Internal Medicine; Department of Social Medicine  
Borowska 213 street; 50- 556 Wroclaw, Poland  
Department of Epidemiology,  
The Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology  
02-034 Warsaw, 15B Wawelska str.  
Poland |
| --- | --- |
| **Turkey** | Istanbul Medeniyet University  
Istanbul, Turkey |
| **Sweden** | Sahlgrenska Academy  
University of Gothenburg  
Sweden |
| **Iran** | Isfahan Cardiovascular Research Center, Isfahan Research Institute  
Isfahan University of Medical Sciences, Isfahan, Iran |
| **UAE** | Dubai Medical University, Hatta Hospital, Dubai Health Authority, Dubai, United Arab Emirates |
| **Saudi Arabia** | Department of Cardiac Sciences, King Fahad Cardiac Center  
College of Medicine  
King Saud University  
Riyadh, Saudi Arabia |
| **Palestine** | Institute of Community and Public Health, Birzeit University, Ramallah, occupied Palestinian territory |
| **Canada** | Université Laval Institut universitaire de cardiologie et de pneumologie de Québec, Quebec  
Canada G1V 4G5  
Simon Fraser University,  
Dept. of Biomedical Physiology & Kinesiology, BC, Canada  
Department of Medicine,  
University of Ottawa,  
Ottawa, Canada  
Population Health Research Institute, McMaster University, Hamilton  
Health Sciences, Hamilton, Ontario, Canada |
| **Argentina** | Estudios Clinicos Latinoamerica ECLA  
Rosario, Santa Fe  
Argentina  
Department of Chronic Diseases  
South American Center of Excellence for Cardiovascular Health (CESCAS)  
Institute for Clinical Effectiveness and Health Policy (IECS) |
| **Brazil** | Dante Pazzanese Institute of Cardiology;  
Hospital Alemao Oswaldo Cruz  
Sao Paulo, SP Brazil |
| **Colombia** | Facultad de Ciencias de la Salud, Universidad de Santander (UDES), Bucaramanga, Santander,  
Fundacion Oftalmologica de Santander (FOSCAL)  
Floridablanca-Santander, Colombia |
| Country     | Institution                                                                 |
|-------------|-----------------------------------------------------------------------------|
| Chile       | Universidad de La Frontera                                                  |
|             | Temuco, Chile                                                               |
| Ecuador     | DECANO                                                                      |
|             | Facultad de Ciencias de la Salud Eugenio Espejo                            |
|             | Universidad Tecnológica Equinoccial                                         |
|             | Dirección: Av. Mariscal Sucre s/n y Av. Mariana de Jesús, Quito Ecuador     |
| Peru        | CRONICAS Centro de Excelencia en Enfermedades Crónicas                     |
|             | www.cronicas-upch.pe                                                       |
|             | Universidad Peruana Cayetano Heredia | www.upch.edu.pe               |
|             | Av. Armendáriz 497, Miraflores, Lima                                        |
| Russia      | Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, |
|             | Russia                                                                       |
|             | Institute For Medical Education, Yaroslav-the-Wise Novgorod State University|
|             | Ministry of Education and Science of the Russian Federation                 |
|             | Russia, Saint-Petersburg, 197022, Karpovka river emb., Bld.13, office 28     |
| Kazakhstan  | Research Institute of Cardiology & Internal Diseases, Almaty, Kazakhstan    |
| Kyrgyzstan  | Kyrgyz Society of Cardiology, National Center of Cardiology and Internal    |
|             | Disease, Bishkek, Kyrgyzstan                                                |
Supplementary methods
The Prospective Urban Rural Epidemiology Study (PURE Study) Design

The Prospective Urban Rural Epidemiology Study (PURE Study) enrolled 186,790 individuals between 35 and 70 years of age from low, middle and high-income countries. The study includes population samples from 639 communities from 24 countries from 5 continents representing a broad range of economic and social circumstances (1). PURE includes countries in four income strata based on World Bank classification in 2006: five low-income countries (Bangladesh, India, Pakistan, Tanzania, and Zimbabwe), eleven middle-income countries (Argentina, Brazil, Chile, China, Colombia, Iran, Malaysia, Occupied Palestine Territory, Poland, South Africa, and Turkey), and four high-income countries (Canada, Saudi Arabia, Sweden, and United Arab Emirates). The study is coordinated by the Population Health Research Institute, Hamilton Health Sciences and McMaster University, Canada.

PURE Study Participant Selection Methodology as Excerpted from Teo et al

Selection of Countries
The choice and number of countries selected in PURE reflects a balance between involving a large number of communities in countries at different economic levels, with substantial heterogeneity in social and economic circumstances and policies, and the feasibility of centers to successfully achieve long-term follow-up. Thus, PURE included sites in which investigators are committed to collecting good-quality data for a low-budget study over the planned 10-year follow-up period and did not aim for a strict proportionate sampling of the entire world.

Selection of Communities
Within each country, urban and rural communities were selected based on broad guidelines. A common definition for “community” that is applicable globally is difficult to establish (2). In PURE, a community was defined as a group of people who have common characteristics and reside in a defined geographic area. A city or large town was not usually considered to be a single community, rather communities from low-, middle-, and high-income areas were selected from sections of the city and the community area defined according to a geographical measure (e.g., a set of contiguous postal code areas or a group of streets or a village). The primary sampling unit for rural areas in many countries was the village. The reason for inclusion of both urban and rural communities is that for many countries, urban and rural environments exhibit distinct characteristics in social and physical environment, and hence, by sampling both, we ensured considerable variation in societal factors across PURE communities. The number of communities selected in each country varied, with the aim to recruit communities with substantial heterogeneity in social and economic circumstances balanced against the capacity of local investigators to maintain follow-up. In some countries (e.g., India, China, Canada, and Colombia), communities from several states/provinces were included to capture regional diversity, in policy, socioeconomic status, culture, and physical environment. In other countries (e.g., Iran, Poland, Sweden, and Zimbabwe), fewer communities were selected.

Selections of Households and Individuals
Within each community, sampling was designed to achieve a broadly representative sample of that community of adults aged between 35 and 70 years. The choice of sampling frame within each center was based on both “representativeness” and feasibility of long-term follow-up, following broad study guidelines. Once a community was identified, where possible, common and standardized approaches were applied to the enumeration of households, identification of individuals, recruitment procedures, and data collection. The method of approaching households differed between regions. For example, in rural areas of India and China, a community announcement was made to the village through contact of a community leader, followed by in-person door-to-door visits of all households. In contrast in Canada, initial contact was by mail followed by telephone inviting members of the households to a central clinic. Households were eligible if at least 1 member of the household was between the 10 ages of 35 and 70 years and the household members intended to continue living in their current home for a further 4 years. For each approach, at least 3 attempts at contact
were made. All individuals within these households between 35 and 70 years providing written informed consent were enrolled. When an eligible household or eligible individual in a household refused to participate, demographics and self-reported data about CVD risk factors, education, and history of CVD, cancers and deaths in the households within the two previous years were recorded. To ensure standardization and high data quality, we used a comprehensive operation manual, training workshops, DVDs, regular communication with study personnel and standardized report forms. We entered all data in a customized database programmed with range and consistency checks which was transmitted electronically to the Population Health Research Institute in Hamilton (Ontario, Canada) where further quality checks were implemented.
Collection of Demographics, Risk Factors and Outcome Events

CVD risk factors (smoking, history of hypertension, diabetes, psychosocial factors and alcohol consumption, diet, use of tobacco, physical activity) are recorded using standardized questions.

| Urban and rural | In urban areas, communities from low-, middle- and high-income areas were selected based on known information of the geographical area such as a set of contiguous postal codes or groups of streets to obtain some representative population of each income area. Rural communities were villages at least 50 km from the cities. Many of these communities were remote with few health facilities. |
| Household wealth | Information on indicators of housing characteristics (e.g., type of windows and flooring, water and sanitation facilities) and assets (e.g., ownership of home, car, computer, and mobile phone) were weighted and combined with weights derived from a principal component analysis procedure. The resulting variable was standardized to a mean of 0 and standard deviation of 1 and using this index the household population was divided into thirds from poorest to richest. |
| Blood pressure measurements | Two BP readings are taken in the right arm in the sitting position and after a minimum of 5 minutes of rest by trained personnel with an Omron automatic digital blood pressure monitor (Omron HEM-757), using the mean of the 2 BP measures. High blood pressure was defined by SBP >140, DBP >100 mmHg. |
| Blood lipid measurements | Fasting blood samples were collected and stored between -20 and -70 degrees centigrade. Samples were analysed for total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, Apolipoprotein A (ApoA), Apolipoprotein B (ApoB) after being either shipped to Hamilton General Hospital (Hamilton, ON, Canada) or at the regional laboratories at Beijing (China), Bangalore (India), or Kocaeli (Turkey), with validated, standardized methods |
| Physical activity | One-week recall of physical activity (PA) and sitting time were assessed using the long-form International Physical Activity Questionnaire, with high PA defined as metabolic equivalent task (MET) score ≥ 3000, moderate as MET score 600–3000 and low as MET score o600 MET-minutes per week |
Prospective Follow-up for Cardiovascular Events and Total mortality

History of disease was collected at baseline from every participant with standardized questionnaires. Follow-up was initiated in all sites by 2008 and completed by March, 2017. Up to three attempts were made to interview all households to document events.

Information on specific events (death, myocardial infarction, stroke, heart failure, cancer, hospitalizations, new diabetes, injury, tuberculosis, human immunodeficiency viral infections, malaria, pneumonia, asthma, chronic obstructive pulmonary disease) were obtained from participants or their family members. This information was adjudicated centrally in each country by trained physicians using standardized definitions. Because the PURE study involves urban and rural areas from middle- and low-income countries, supporting documents to confirm cause of death and/or event varied in degrees of completion and availability. In most of middle- and low-income countries there was no central system of death or event registration. Therefore, information was obtained about prior medical illness and medically certified cause of death where available, and, second, best available information was captured from reliable sources in those instances where medical information was not available in order to be able to arrive at a probable diagnosis or cause of death. Event documentation was based on information from death certificates (available in 100% of deaths), medical records (MI: 49.4%, stroke 80.8% and heart failure: 76.2%), household interviews and other sources. Verbal Autopsies were also used to ascertain cause of death in addition to medical records which were reviewed by a health professional. This approach has been used in several studies conducted in middle- and low-income countries.

To ensure a standard approach and accuracy for classification of events across all countries and over time, the first 100 CVD events (deaths, MI, strokes, heart failure or cancers) for China and India, and 50 cases for other countries were adjudicated both locally and also by the adjudication chair, and if necessary further training was provided. Thereafter, every year, 50 cases for China and India and 25 cases for each of the remaining countries were adjudicated as above.
Event Definitions

FATAL EVENTS

Cardiovascular Death – Definitions
01.00 DEATH DUE TO CARDIOVASCULAR EVENTS
01.10 Sudden unexpected Cardiovascular Death (SCVD)

Without evidence of other cause of death, death that occurred suddenly and unexpectedly (examples: witnessed collapse, persons resuscitated from cardiac arrest who later died) or persons seen alive less than 12 hours prior to discovery of death (example persons found dead in his/her bed).

- SCVD is either definite, probable or possible according to the following characteristics:

| PURE Adjudication Code | Event Type | Acceptable ICD-10 codes |
|------------------------|------------|-------------------------|
| 01.11: Definite        | One of the following in persons with: |
|                        | • known cardiovascular disease, or |
|                        | • diabetes with an additional risk factor such as hypertension, smoking, dyslipidemia, microalbuminuria, serum creatinine 50% above upper limit of normal, or |
|                        | • 3 of the above risk factors, or |
|                        | • 2 of the above risk factors in men aged 60 and more and women aged 65 and more |
|                        | No ICD-10 Code |
| 01.12: Probable        | One of the following in persons with: |
|                        | • diabetes, or |
|                        | • 2 of the above risk factors in men aged less than 60 and in women less than 65, or |
|                        | • one of the above risk factor in men aged 60 and more and in women aged 65 and more, or |
|                        | • typical of chest pain or sudden severe dyspnea of less than 20-minute duration preceding the event |
| 01.13: Possible        | In persons without risk factor |

For SCVD, the patient was well or had a stable CVD (example stable angina) when last seen alive. The event of a sudden death occurring during the hospitalization of MI is considered a fatal MI and not sudden death.
01.30 Fatal Myocardial Infarction

**Symptoms of Myocardial Infarction:**
Typical symptoms or suggestive symptoms of MI according to physician are characterized by severe anterior chest pain as tightness, crushing, burning, lasting at least 20 minutes, occurring at rest, or on exertion, that may radiate to the arms or neck or jaw and may be associated with dyspnea, diaphoresis and nausea. However, death associated with nausea and vomiting with or without chest pain not due to another cause may be considered as possible MI if ECG and cardiac markers are not done. These symptoms may have occurred the last month before death.

Fatal myocardial infarction is either definite, probable or possible according to the following characteristics:

| PURE Adjudication Code | Event Type | Acceptable ICD-10 codes |
|------------------------|------------|------------------------|
| **01.31: Definite**    | 1. Autopsy demonstrating fresh myocardial infarction and/or recent coronary occlusion, **or**  
2. ECG showing new and definite sign of MI (Minnesota code 1-1-1) **or**  
3. Symptoms typical or atypical or inadequately described but attributed to cardiac origin lasting at least 20 minutes and by troponin or cardiac enzymes (CKMB, CK, SGOT, SLDH) above center laboratory ULN  
4. ECG with new ischemic changes (new ST elevation/depression or T wave inversion ≥ 2 mm) and by troponin or cardiac enzymes (CKMB, CK, SGOT, SLDH) above center laboratory ULN | I21- I22 |
| **01.32: Probable**    | 1. ECG with sign of probable MI (Minnesota code 1-2-1), **or**  
2. Typical symptoms lasting at least 20 minutes considered of cardiac origin, with only new ST-T changes (new ST elevation/depression or T wave inversion ≥ 1 but < 2mm) without documented increased cardiac markers or enzyme as in PURE definition 1.31 (above), **or**  
3. Increased cardiac enzymes as in PURE definition 1.31 (above) showing a typical pattern of MI as above without symptoms or significant ECG changes |  |
| **01.33: Possible**    | 1. ECG with sign of possible MI (Minnesota code 1-3-1) **or**  
2. Typical symptoms or symptoms suggestive of MI according to the physician lasting at least 20 minutes without documented ECG or cardiac marker. |  |

The Minnesota codes for MI is taken from Rose and Blackburn and published in their book “Evaluation Methods of Cardiovascular Disease WHO 1969”.

- **Definite MI** is Q/R ratio $\geq 1/3$ and Q duration $\geq 0.03$ second in one of the following leads: I, II, V2, 3, 4, 5, 6. (code 1-1-1)
- **Probable MI** is Q/R ratio $\geq 1/3$ and Q duration between 0.02 and 0.03 second in one of the following leads: I, II, V2, 3, 4, 5, 6. (code 1-2-1)
- **Possible MI** is Q/R ratio between 1/5 and 1/3 and Q duration between 0.02 and 0.03 second in one of the following leads: I, II, V2, 3, 4, 5, 6. (code 1-3-1)
**01.40 Fatal Stroke**

Fatal stroke is either definite or possible according to the following characteristics:

| PURE Adjudication Code | Event Type | Acceptable ICD-10 codes |
|------------------------|------------|------------------------|
| **01.41: Definite**    | Stroke death is defined as death within 30 days from an acute focal neurological deficit *diagnosed by a physician* and thought to be of vascular origin (without other cause such as brain tumor) with signs and symptoms lasting $\geq 24$ hrs. Stroke death is also considered if death occurred within 24 hrs. of onset of persisting signs and symptoms, or if there is evidence of a recent stroke on autopsy. | I60- I64, I69 |
|                        | N.B.       |                        |
|                        | *In a subject with a stroke $\leq 30$ days:* If death occurred with a pneumonia due to possible aspiration, death will be considered to be due to stroke. | |
|                        | *In a subject with a stroke $> 30$ days:* If death occurred with a pneumonia due to possible aspiration, the adjudicator will make a decision according to his/her clinical judgment if death is related to stroke or not. | |
|                        | Subarachnoid hemorrhage death manifested by sudden onset headache with/without focal signs and imaging (CT or MRI) evidence of bleeding primarily in the subarachnoid space is considered a fatal stroke in absence of trauma or brain tumor or malformation | |
|                        | Subdural hematoma death is not considered as a stroke death and may be related to previous trauma or other cause. | |
| **01.43: Possible**    | Death in a participant with a history of sudden onset of focal neurological deficit of one or more limbs, loss of vision or slurred speech lasting about 24 hours. | |
## 01.50 Fatal Congestive Heart Failure
Fatal congestive heart failure is either definite or possible according to the following characteristics:

| PURE Adjudication Code | Event Type                                                                 | Acceptable ICD-10 codes |
|------------------------|-----------------------------------------------------------------------------|-------------------------|
| 01.51: **Definite**    | The diagnosis of congestive heart failure may be an autopsy finding in absence of other cause or requires signs (rales, increased jugular venous pressure or ankle edema) or symptoms (nocturnal paroxysmal dyspnea, dyspnea at rest or ankle edema) of congestive heart failure **and** one or both of the following:  
  - radiological signs of pulmonary congestion,  
  - treatment of heart failure with diuretics  

*If sudden death occurred in a patient with chronic severe heart failure, it should be adjudicated as fatal congestive heart failure.* | I50 |
| 01.52: **Probable**    | Progressive shortness of breath on lying down or at night, improving on sitting up **and** any of the following signs or symptoms: swelling of feet, distension of abdomen, progressive cough in a person with known hypertension or a history of previous MI/angina or other heart disease |
| 01.53: **Possible**    | Progressive shortness of breath on lying down or at night, improving on sitting up **and** any of the following signs or symptoms: swelling of feet, distension of abdomen, progressive cough |
### 01.60 Death Due to Other Cardiovascular Deaths

*(other causes [1.10 to 1.50 above] having been excluded)*

| PURE Adjudication Code | Event Type                                                                 | Acceptable ICD-10 codes |
|------------------------|-----------------------------------------------------------------------------|-------------------------|
| 01.61                  | Arterial rupture of aneurysm                                                | I71- I72                |
| 01.62                  | Pulmonary embolism<br>Note: Death associated with pulmonary embolism occurring within 2 weeks after a fracture such as hip, femur should attributed to death due to injury. Refer to Injury, Section 6.0 | I26                     |
| 01.63                  | Arrhythmic death (A-V block, sustained ventricular tachycardia in absence of other causes) | I44- I45, I47- I49      |
| 01.64                  | Death after invasive cardiovascular intervention: a perioperative death extending to 30 days after coronary or arterial surgical revascularization and to 7 days after a coronary or arterial percutaneous dilatation (angioplasty) with or without a stent or an invasive diagnostic procedure. | I97                     |
| 01.65                  | Congenital heart disease                                                    | Q20-Q28                 |
| 01.66                  | Heart valve disease (including rheumatic heart disease)                     | I01, I05- I09, I34- I37 |
| 01.67                  | Endocarditis                                                                | I33, I38                |
| 01.68                  | Myocarditis                                                                 | I40                     |
| 01.69                  | Tamponade (pericarditis)                                                    | I30, I31, I32           |
| 01.70                  | Other cardiovascular events (Excluding 1.61 to 1.69 above) <br><br>Valid ICD-10 codes would include the following: I11, I12, I13, I23, I24, I25, I27, I28, I42, I51, I52, I65-I68, I73, I74, I96, I98, I99 (Refer to ICD-10 Listing for associated definitions for each code) | Any valid ‘I’ (Cardiovascular) ICD-10 code that can be classified as underlying Code, not specified above |
**NON-FATAL EVENTS**

Cardiovascular Events – Definitions

10.00 NON-FATAL CARDIOVASCULAR EVENTS

10.10 Non-Periprocedural Myocardial Infarction (MI)

MI is considered either definite, probable or possible according to the following characteristics:

| PURE Adjudication Code | Event Type | Acceptable ICD-10 codes |
|------------------------|------------|------------------------|
| **10.11: Definite**    | 5. ECG showing new and definite sign of MI (Minnesota code 1-1-1) **or**  
6. Symptoms typical or atypical or inadequately described but attributed to cardiac origin lasting at least 20 minutes and by troponin or cardiac enzymes (CKMB, CK, SGOT, SLDH) above center laboratory ULN  
7. ECG with new ischemic changes (new ST elevation/depression or T wave inversion ≥ 2 mm) and by troponin or cardiac enzymes (CKMB, CK, SGOT, SLDH) above center laboratory ULN  

Please note that increased markers may occur in trauma (CK, AST, myoglobin and CK MB to a lesser degree); renal insufficiency, heart failure, pulmonary embolism…. (troponin), cardioversion (all) |
| 121-122                |
| **10.12: Probable**    | 4. ECG with new and probable sign of MI (Minnesota code 1-2-1), **or**  
5. Typical symptoms lasting at least 20 minutes considered of cardiac origin, with only new ST-T changes (new ST elevation/depression or T wave inversion ≥ 1 but < 2mm) without documented increased cardiac markers as in PURE definition 10.11 (above), **or**  
6. Increased cardiac enzymes showing a typical pattern of MI as above without symptoms or significant ECG changes. |
| **10.13: Possible**    | 1. ECG with new and possible sign of MI (Minnesota code 1-3-1), **or**  
2. Typical symptoms lasting 20 minutes and more considered to be of cardiac origin without documented ECG or cardiac marker. |
10.20 Periprocedural Myocardial Infarction

| PURE Adjudication Code | Event Type | Acceptable ICD-10 codes |
|------------------------|------------|------------------------|
| 10.21: **Definite**    | 1. ECG showing new and definite sign of MI (Minnesota code 1-1-1), or 2. Increased cardiac markers within 48 hours of procedure:  
  - percutaneous coronary intervention: CKMB should be $\geq 5 \times$ ULN or troponin $\geq 5 \times$ above lower level of necrosis OR $> 20\%$ increase in cardiac markers if elevated at the beginning of the procedure in a patient with symptoms suggestive of myocardial ischemia  
  - Coronary surgery: Increased cardiac markers CKMB should be $\geq 10 \times$ ULN or troponin $\geq 10 \times$ above lower limit of necrosis. | I21-I22 |

The **Minnesota codes** for MI is taken from Rose and Blackburn and published in their book “Evaluation Methods of Cardiovascular Disease WHO 1969”.

- **Definite MI** is Q/R ratio $\geq 1/3$ and Q duration $\geq 0.03$ second in one of the following leads: I, II, V2, 3, 4, 5, 6. (code 1-1-1)
- **Probable MI** is Q/R ratio $\geq 1/3$ and Q duration between 0.02 and 0.03 second in one of the following leads: I, II, V2, 3, 4, 5, 6. (code 1-2-1)
- **Possible MI** is Q/R ratio between 1/5 and 1/3 and Q duration between 0.02 and 0.03 second in one of the following leads: I, II, V2, 3, 4, 5, 6. (code 1-3-1)
Classification of PURE Countries into Geographic Regions

South Asia: India, Bangladesh and Pakistan
China: China
South East Asia: Malaysia
Africa: South Africa, Zimbabwe, Tanzania
North America and Europe: Canada, Poland, Sweden, Turkey
Middle East: United Arab Emirates, Iran, Saudi Arabia, occupied Palestinian territory
South America: Argentina, Brazil, Colombia, Chile
### PURE food frequency questionnaire validation studies

| Country      | Validated | Reference dietary method | Reference                                      |
|--------------|-----------|--------------------------|------------------------------------------------|
| Argentina    | Yes       | Multiple dietary recalls  | Dehghan et al. PLoS One. 2012;7(5):e37958       |
| Brazil       | Yes       | Multiple dietary recalls  | Under preparation                               |
| Canada       | Yes       | Multiple dietary recalls  | Kelemen L et al. J Am Diet Assoc. 2003 103(9):1178-84 |
| Chile        | Yes       | Multiple dietary recalls  | Dehghan et al. Public Health Nutr. 2013;16 (10):1782-8. |
| China        | Yes       | Multiple dietary recalls  | Zhao WH et al. Biomedical and environmental sciences. 2010; 23(suppl.)to 1-38. |
| Colombia     | Yes       | Multiple dietary recalls  | Dehghan et al. J Nutr Educ Behav. 2012;44(6):609-13. |
| Iran         | Yes       | Multiple dietary recalls  | Under preparation                               |
| India        | Yes       | Multiple dietary recalls  | Iqbal R et al. Public Health Nutr. 2009; 12(1):12-18 |
|              |           |                          | Bharati A et al. Asia Pac J Clin Nutr 2008; 14(1):178-185. |
|              |           |                          | Mahajan R et al. The National Medical Journal of India vol. 26to no. 5to 2013 |
| Malaysia     | Yes       | Multiple dietary recalls  | Book chapter                                    |
| Palestine    | Yes       | Multiple dietary recalls  | Under preparation                               |
| Poland       | Yes       | Multiple dietary recalls  | Dehghan et al. J Hum Nutr Diet. 2012; 25(3):225-32 |
| Sweden       | Yes       | Multiple dietary recalls  | Khani B et al. J Nutr. 2004to 134:1541-1545      |
| South Africa | Yes       | Multiple dietary recalls  | MacIntyre UE et al. Public Health Nutr. 2000; 4(1): 63-71 |
| Turkey       | Yes       | Multiple dietary recalls  | Gunes eat al. J Pak Med Assoc. 2015; 65(7):756-63. |
| UAE          | Yes       | Multiple dietary recalls  | Dehghan et al. Nutr J. 2005;4:18                 |
| Kuwait/UAE   | Yes       | Multiple dietary recalls  | Dehghan et al. Saudi Med J 2009; Vol30(1)         |
| Zimbabwe     | No        | FFQ development          | Development of FFQ Merchant et al. Nutr J. 2005;4:37 |
PURE food frequency questionnaires - Regional list of food items and portion sizes for refined grains, whole grains and white rice

**North America/Europe**

**Refined grains:** Cold cereal breakfast, white bread, pasta, spaghetti, macaroni, crisp bread, bagels, bread made with corn flour, doughnuts, pancakes, cracker, muffins, pies and tarts, Danish, yeast cake, gingerbread cake, corn cereal, polish dumplings, shortcake, acma

*Portion size:* Cold cereal breakfast- 25g; Bread- one slice; Rice- one cup; Pasta, spaghetti, macaroni- one plate, Cookies and biscuit- one number; Dumpling- one plate; Pies- one slice; Cakes- one slice

**Whole grains:** whole wheat bread, rye brown bread, wheat bran, wheat germ, kajzerki, bread ekmek (whole grain esmer), wroclawskie, zurek sour rye soup, bran/granola cereals, bran/oat muffins, buckwheat groats (boiled), pearl barley groats, boiled, bulgur

*Portion size:* Breads - one slice; Kajzerki and ekmek- one piece; Bran/oat= one cup

**Rice:** Fried rice, boiled rice

*Portion size:* Fried rice, boiled rice - one cup

**South America**

**Refined grains:** Cold cereal breakfast, white bread, pasta, spaghetti, cracker, flour toast , ravioli, gnocci, noodle, budin, alfajor, dulce de leche, bizocho, bread with chicharron, factura, brownies, waffle, cakes, panqueques, doughnuts, manjar, empanada, corn pastel, ayaco, cookie

*Portion size:* Cold cereal breakfast- 25g; Bread-one slice; Pasta, spaghetti, macaroni- one plate; Cookies and biscuit- one number; Pies- one slice; Cake - one slice

**Whole grains:** Whole wheat bread, gluten bread, polenta/angu, rye bread, integral bread, other grains (cebada/avena)

*Portion size:* Breads - one slice; Polenta/angu - one plate

**Rice:** White rice

*Portion size:* White rice- one cup

**Africa**

**Refined grains:** Breakfast cereals, pasta, white bread, bread rolls, mealie, nophi, macaroni, dumpling, biscuits, cookies, crackers, scones, samosa, cake, scones, doughnut

*Portion size:* Cold cereal breakfast- 25g; Breads - one slice; Samosa - one medium piece; Macaroni - one plate; Dumpling - one plate
**Whole grains**: Sadza, mealie, maize meal porridge, mabella, samp, finger millet porridge, mahindi, provita, samp, dark bread

*Portion size*: Sadza - one plate; Samp - one cup; Porridge - one cup

**Rice**: White rice, spiced rice

*Portion size*: Rice - one cup

**Middle East**

**Refined grains**: Cold cereal breakfast, white bread, Irani bread, cheese croissant, khubz white, pasta, spaghetti, sambosa, lasangna, shabura, rahash, falodeh, ghotab, musakan, zaatar manakeesh, biscuits, crackers, baklava, knafeh, hareesh, cake, hallaweh, nekhee, khameer, chabab, rigag, pita, betheeth, kanafa, lagaimaat, mahlabiyyeh, mehaiwah, tarhana soup, lahmacun, manti, bread ekmek, yufka, acma, helva irmik, arayes, aaseedah

*Portion size*: Cold cereal breakfast - 25 g; Irani breads - one piece; Samosa - one medium piece; Spaghetti - one plate; Zaatar - one large; Pita one medium; All types of pastries - one piece

**Whole grains**: whole wheat bread, jareesh, hareese, fatayer zatar (whole), Chapati, Khubz brown, brown pita bread, Irani bread with sesame, balaleet, bread ekmek (whole grain esmer), managesh zatar whole

*Portion size*: Whole wheat breads - one piece; Irani bread (whole wheat) - one piece; Samosa - one medium; Spaghetti - one plate; Zaatar - one large; Brown pita - one medium

**Rice**: White rice, tahchin, shirbranj, kofteh sabzi, reshteh polo, kalam polo, mamowash rubian, mahamer

*Portion size*: All types of rice listed above - one plate

**South Asia**

**Refined grains**: Cold breakfast cereal, cornflakes, white bread, bun, pizza, burgers, pasta, spaghetti, noodles, sambosa/samosa, shingara, tandoori naan, mathri, vegetarian puff, non-vegetarian puff, salted biscuits, sweet biscuits, rusk, fuchka, chotpoti, sheermaal/taftan, mithai, kheer, firni, sheer, zarda, rabri, cake, jamun, jilebi, barfi, cake

*Portion size*: Cold cereal breakfast - 25g; Bread one slice; Pizza, burgers – one number; Pasta, spaghetti, noodles - one bowl; Sambosa/samosa, shingara, tandoori naan, mathri, vegetarian puff, non-vegetarian puff, salted biscuits, sweet biscuits, rusk, fuchka, chotpoti, sheermaal/taftan, mithai, zarda, cake, jamun, jilebi, barfi, cake - one number/slice; Kheer, firni, sheer, rabri./rabadi – one bowl/katori
**Whole grains**: Chapati (whole wheat/jowar/bajra), puri, mughlai paratha, paratha, puree, roti, phulka, mixed roti, ragi ball, rabri (bajra/jau/makka), oats porridge, dalia, upma, kesari bhath, halwa

*Portion size*: Chapati (whole wheat/jowar/bajra), puri, mughlai paratha, paratha, puree, roti, phulka, mixed roti, ragi ball- one number; Rabri (bajra/jau/makka), oats porridge, dalia, upma, kesari bhath- one bowl/katori; Halwa- one bowl/number

**Rice**: White polished and unpolished rice, parboiled rice, puffed rice (hand-pounded), water rice (hand-pounded), biryani/pulao/fried rice/jeera rice, lime rice, tomato rice, rice porridge/kanji, kitchree/khichdi, bhelpuri, all chaats, pongal, avalakki, poha, rice kheer, sweet pongal, rice pudding, idli, dosa, masala dosa, adai, puttu, appam, murukku, chakli, adhirasam, namkeen

*Portion size*: White polished and unpolished rice, parboiled rice, puffed rice (hand-pounded), water rice (hand-pounded), biryani/pulao/fried rice/jeera rice, lime rice, tomato rice, rice porridge/kanji, kitchree/khichdi, bhelpuri, all chaats, pongal, avalakki, poha, rice kheer, sweet pongal, rice pudding-one bowl; Idli, dosa, masala dosa, adai, puttu, appam, murukku, chakli, adhirasam- one number

**South East Asia**

**Refined grains**: Cold breakfast cereal, shite bread, roti canai, roti telur, dosai, bun, cracker, pasta, fried noodles, bandung, hailam, laksa, yong tau foo, kokodok pisang, curry puff, cucur udang, Sri muka, lopes, lapis, cake, pandesal, monay, biscuit, native kakanin, spaghetti/macaroni, pancit bihon, Instant noodles/canton, monay

*Portion size*: All types of bread - one slice; Pasta - one plate; Porridge - one bowl; yong tau foo, Laksa and other similar foods -one bowl; Biscuit - one piece; Cake - one slice; Noodles - one bowl

**Whole grains**: Oatmeal

*Portion size*: one bowl

**Rice**: White rice, fried rice, nasi lemak, nasi dagang, nasi kerabu

*Portion size*: All rice listed above- one plate

**China**

**Refined grains**: Bread, cakes, starch noodle, fried wheat flour

**Whole grains**: Corn, sorghum

**Rice**: White rice, sticky rice, rice noodle, Stick rice

*Portion size*: All portion sizes were based on one Liang
Figure 1: Flow chart of recruitment

- 149,573 households approached
  - 525,174 individuals
  - 21 countries
  - 47,633 (9.1%) declined to participate

- 477,521 (91.0%) individuals consented to participate
  - 253,747 (53.1%) met age eligibility of 35-70 years
  - 223,774 (46.9%) were <35 years or >70 years

- 185,635 (73.2%) consented to Core study with detailed baseline data collection
  - 66,112 (26.8%) consented to Surveillance study with only mortality collection

- 166,762 participants in 21 countries phase I+II eligible for follow-up
  - 14,509 Core study participants in phase III are still undergoing follow-up

- 164,007 participants with at least 1 follow-up in 21 countries

- 148,858 participants from 21 countries

- 137,130 participants in Final analysis from 21 countries

- 15,278 participants with implausible value of energy intake, missing value in age and sex excluded
- 11,728 participants with missing values on grains intake excluded
### Supplementary tables

Table S1: Classification of PURE Countries by country income level and follow up rates

| Low-income countries | No. of participants at the baseline (N) | Follow up rate (%) | Duration of follow up (Median (IQR)) |
|----------------------|----------------------------------------|--------------------|--------------------------------------|
| Bangladesh           | 2936                                   | 84.3               | 7.38 (7.25 - 7.55)                   |
| India                | 29259                                  | 85.8               | 11.85 (10.02 - 13.38)                |
| Pakistan             | 2721                                   | 95.2               | 5.59 (5.33 - 8.64)                   |
| Tanzania             | 2061                                   | 72.5               | 5.25 (3.27 - 5.88)                   |
| Zimbabwe             | 1263                                   | 80.3               | 9.32 (8.00 - 10.58)                  |
| **Total**            | **38 240**                             |                    |                                      |

| Middle-income countries | No. of participants at the baseline (N) | Follow up rate (%) | Duration of follow up (Median (IQR)) |
|-------------------------|----------------------------------------|--------------------|--------------------------------------|
| Argentina               | 7535                                   | 98.1               | 9.54 (9.09 - 10.08)                  |
| Brazil                  | 6081                                   | 97.5               | 9.57 (8.79 - 10.60)                  |
| Chile                   | 3590                                   | 97.0               | 9.08 (8.83 - 9.52)                   |
| China                   | 47935                                  | 98.5               | 9.68 (8.70 - 10.74)                  |
| Colombia                | 7542                                   | 95.3               | 9.78 (8.73 - 10.50)                  |
| Iran                    | 6013                                   | 98.0               | 9.68 (8.82 - 10.09)                  |
| Malaysia                | 15793                                  | 93.1               | 9.12 (8.68 - 9.52)                   |
| Palestine               | 1668                                   | 94.5               | 3.20 (3.10 - 3.26)                   |
| Philippines             | 5019                                   | 83.3               | 3.01 (2.93 - 3.10)                   |
| Poland                  | 2036                                   | 96.9               | 10.92 (9.97 - 10.99)                 |
| South Africa            | 4059                                   | 89.5               | 6.96 (5.62 - 10.33)                  |
| Turkey                  | 4056                                   | 99.2               | 9.01 (8.77 - 9.84)                   |
| **Total**               | **111 327**                            |                    |                                      |

| High-income countries   | No. of participants at the baseline (N) | Follow up rate (%) | Duration of follow up (Median (IQR)) |
|-------------------------|----------------------------------------|--------------------|--------------------------------------|
| Canada                  | 10462                                  | 98.5               | 9.44 (8.91 - 11.06)                  |
| Saudi Arabia            | 2046                                   | 91.1               | 3.38 (3.21 - 6.02)                   |
| Sweden                  | 4153                                   | 96.8               | 3.38 (3.21 - 6.02)                   |
| United Arab Emirates    | 1499                                   | 97.3               | 10.11 (9.39 - 10.43)                 |
| **Total**               | **18160**                              |                    |                                      |
| **Total from all regions** | **167 727**                         | **94.1**           | **9.49 (8.59 - 10.87)**              |
Table S2: Description of covariates by categories of refined grain intake

| Parameters | <50 | 50-150 | 150-250 | 250-350 | >=350 | P-Value |
|------------|-----|--------|---------|---------|-------|---------|
| Age       | 50.4±10.2 | 50.9±9.9 | 50.7±9.9 | 51.1±9.9 | 49.9±9.7 | <0.001 |
| Sex       |            |        |         |         |       | <0.001 |
| Male      | 22 841 (59.9) | 28 597 (59.8) | 16 523 (59.1) | 7686 (57.4) | 9858 (50.2) |  |
| Female    | 15 307 (40.1) | 19 219 (40.2) | 11 416 (40.9) | 5714 (42.6) | 9767 (49.8) |  |
| Education |            |        |         |         |       | <0.001 |
| None, Primary, or Unknown | 20 334 (53.5) | 17 418 (36.5) | 10 722 (38.4) | 5349 (40) | 8547 (43.6) |  |
| Secondary/High/Higher secondary | 11 921 (31.4) | 18 118 (38) | 11 000 (39.4) | 5599 (41.9) | 8817 (45) |  |
| Location  |            |        |         |         |       | <0.001 |
| Urban     | 17 450 (45.7) | 29 157 (61) | 17 082 (61.1) | 7526 (56.2) | 7896 (40.2) |  |
| Rural     | 20 698 (54.3) | 18 659 (39) | 10 857 (38.9) | 5874 (43.8) | 11 729 (59.8) |  |
| Level of Physical Activity |            |        |         |         |       | <0.001 |
| Low - Met score < 600 | 7411 (21.6) | 7807 (17.7) | 4303 (16.2) | 1941 (15) | 3355 (17.6) |  |
| Moderate - Met score in 600-3000 | 12 194 (35.5) | 16 892 (38.4) | 10 497 (39.6) | 4942 (38.3) | 7151 (37.4) |  |
| High - Met score >= 3000 | 14 743 (42.9) | 19 307 (43.9) | 11 729 (44.2) | 6025 (46.7) | 8605 (45) |  |
| History of tobacco use |            |        |         |         |       | <0.001 |
| Former    | 3447 (9.1) | 7364 (15.5) | 3576 (12.9) | 1558 (11.7) | 1476 (7.6) |  |
| Current   | 8368 (22.2) | 8524 (17.9) | 5483 (19.7) | 2913 (21.9) | 4657 (24.1) |  |
| Never     | 25 924 (68.7) | 31 668 (66.6) | 18 713 (67.4) | 8832 (66.4) | 13 194 (68.3) |  |
| Diagnosed with Diabetes |            |        |         |         |       | <0.001 |
| No        | 35 436 (93) | 42 962 (90) | 25 405 (91.1) | 12 364 (92.5) | 18 528 (94.6) |  |
| Yes       | 2658 (7) | 4777 (10) | 2493 (8.9) | 1008 (7.5) | 1059 (5.4) |  |
| Waist to hip ratio | 0.86±0.09 | 0.88±0.09 | 0.88±0.08 | 0.88±0.08 | 0.87±0.07 | <0.001 |
| Energy in kcal | 1844±711 | 2111±754 | 2283±830 | 2349±902 | 2537±842 | <0.001 |
| Global Wealth Index | -0.46±1.14 | 0.23±0.99 | 0.33±0.82 | 0.21±0.72 | -0.15±0.74 | <0.001 |
| Fruits & Vegetables (g/d) | 282.8 (129.6,466.3) | 451.2 (273.7,773.6) | 450.0 (301.2,700.2) | 391.4 (287.0,609.9) | 362.3 (292.7,476.1) | <0.001 |
| Red Meat (g/d) | 15.7 (7.8,51.0) | 40.7 (13.1,82.8) | 56.6 (21.0,113.1) | 53.6 (19.7,116.4) | 40.0 (14.3,100.0) | <0.001 |

¶ Mean±SD, One way ANOVA; § N(%), Chi-Square test; ¥ Median(IQR), Kruskal Wallis test
Table S3: Description of covariates by categories of whole grain intake

| Parameters                                      | 0       | <50     | 50-99   | >=100   | P-Value |
|------------------------------------------------|---------|---------|---------|---------|---------|
| Age[^]                                         | 50.6±9.7| 50.2±9.9| 50.8±9.9| 50.9±10.2| <0.001  |
| Sex[^]                                         |         |         |         |         |         |
| Male                                           | 19 768 (57.3) | 28 214 (58) | 11 085 (59.7) | 27 513 (58.4) | <0.001 |
| Female                                         | 14 708 (42.7) | 20 458 (42) | 7477 (40.3) | 19 635 (41.6) |         |
| Education[^] N(%)                              |         |         |         |         |         |
| None, Primary, or Unknown                      | 17 438 (50.7) | 22 104 (45.5) | 5757 (31.1) | 18 200 (38.7) |         |
| Secondary/High/Higher secondary                | 13 517 (39.3) | 17 630 (36.3) | 7571 (40.9) | 17 472 (37.1) | <0.001 |
| Trade or College/University                    | 3429 (10) | 8795 (18.1) | 7571 (40.9) | 17 472 (37.1) |         |
| Location[^]                                    |         |         |         |         |         |
| Urban                                          | 14 559 (42.2) | 24 809 (51) | 11 700 (63) | 28 046 (59.5) | <0.001 |
| Rural                                          | 19917 (57.8) | 23 863 (49) | 6862 (37) | 19 102 (40.5) |         |
| Level of Physical Activity[^]                  |         |         |         |         |         |
| Low - Met score < 600                          | 6445 (19.4) | 9186 (19.8) | 2812 (16) | 6773 (16.3) |         |
| Moderate - Met score in 600-3000               | 12 184 (36.6) | 17 007 (36.6) | 6884 (39.1) | 16 242 (39.2) | <0.001 |
| High - Met score >= 3000                       | 14 643 (44.0) | 20 292 (43.7) | 7925 (45.0) | 18 417 (44.5) |         |
| History of tobacco use[^]                      |         |         |         |         |         |
| Former                                         | 3303 (9.7) | 5653 (11.7) | 2783 (15.1) | 5793 (12.4) |         |
| Current                                        | 7741 (22.8)  | 10078 (20.8) | 3312 (17.9) | 9292 (19.9) |         |
| Never                                          | 22 948 (67.5) | 32 690 (67.5) | 12 359 (67.0) | 31 660 (67.7) | <0.001 |
| Diagnosed with Diabetes[^]                     |         |         |         |         |         |
| No                                             | 32 073 (93.2) | 44 416 (91.4) | 16 696 (90.1) | 43 260 (91.9) |         |
| Yes                                            | 2348 (6.8) | 4197 (8.6) | 1832 (9.9) | 3795 (8.1) | <0.001 |
| Waist to hip ratio[^]                           | 0.88±0.08 | 0.87±0.09 | 0.87±0.09 | 0.87±0.09 | <0.001 |
| Energy in kcal[^]                               | 2047±807 | 2091.8±800 | 2142±795 | 2279±833 | <0.001 |
| Global Wealth Index[^]                         | -0.04±0.82 | 0.02±1.1 | 0.26±0.98 | -0.08±1.03 | <0.001 |
| Fruits & Vegetables (g/d)[¥]                   | 338.4 (250.6,518.6) | 362.7 (230.8,605.7) | 439.4 (298.7,745.0) | 394.3 (248.3,685.9) | <0.001 |
| Red Meat (g/d)[¥]                              | 40.83 (13.19,100) | 31.9 (8.2,79.4) | 41.9 (13.1,83.8) | 35.2 (7.7,78.9) | <0.001 |

[^] Mean±SD, Oneway ANOVA; § N(%), Chi-Square test; ¥ Median(IQR), Kruskal Wallis test
Table S4: Description of covariates by categories of white rice intake

| Parameters                          | <50   | 50-150 | 150-300 | 300-450 | >=450 | P-Value |
|-------------------------------------|-------|--------|---------|---------|-------|---------|
| Age†                                | 51.7±10.0 | 50.1±9.9 | 50.9±9.8 | 51.5±9.8 | 49.3±9.9 | <0.001  |
| Sex†                                |        |        |         |         |       |         |
| Male                                | 24 751 (58.9) | 23 007 (59.7) | 10 718 (59.7) | 10 391 (59.2) | 17 713 (54.1) | <0.001  |
| Female                              | 17 304 (41.1) | 15 522 (40.3) | 7 227 (40.3) | 7 176 (40.8) | 15 049 (45.9) |         |
| Education‡                          |        |        |         |         |       |         |
| None, Primary, or Unknown           | 17 086 (40.7) | 17 406 (45.3) | 6 523 (36.4) | 7 389 (42.1) | 15 095 (46.3) | <0.001  |
| Secondary/High/Higher secondary     | 13 534 (32.2) | 13 958 (36.3) | 7 461 (41.6) | 6 953 (39.7) | 14 284 (43.8) |         |
| Trade or College/University         | 11 352 (27) | 7 094 (18.4) | 3 936 (22.0) | 3 193 (18.2) | 3 219 (9.9) |         |
| Location§                           |        |        |         |         |       |         |
| Urban                               | 23 499 (55.9) | 22 421 (58.2) | 10 990 (61.2) | 9 923 (56.5) | 12 281 (37.5) | <0.001  |
| Rural                               | 18 556 (44.1) | 16 108 (41.8) | 6 955 (38.8) | 7 644 (43.5) | 20 481 (62.5) |         |
| Level of Physical Activity§         |        |        |         |         |       |         |
| Low - Met score < 600               | 6451 (16.8) | 7 135 (20.2) | 3 179 (18.7) | 2 589 (15.4) | 5 862 (18.7) |         |
| Moderate - Met score in 600-3000    | 14 093 (36.7) | 13 817 (39.1) | 6 898 (40.6) | 6 412 (38.2) | 11 097 (35.5) | <0.001  |
| High - Met score >= 3000            | 17 868 (46.5) | 14 376 (40.7) | 6 926 (40.7) | 7 770 (46.3) | 14 337 (45.8) |         |
| History of tobacco use§             |        |        |         |         |       |         |
| Former                              | 7 711 (18.5) | 4 569 (12.0) | 1 604 (9.0) | 1 913 (11.0) | 1 735 (5.3) | <0.001  |
| Current                             | 8 651 (20.7) | 7 376 (19.3) | 3 126 (17.6) | 3 228 (18.5) | 8 042 (24.8) |         |
| Never                               | 25 359 (60.8) | 26 277 (68.7) | 13 073 (73.4) | 12 288 (70.5) | 22 660 (69.9) | <0.001  |
| Diagnosed with Diabetes§            |        |        |         |         |       |         |
| No                                  | 38 667 (92.1) | 35 122 (91.4) | 15 981 (89.2) | 15 936 (90.8) | 30 739 (93.9) | <0.001  |
| Yes                                 | 3 315 (7.9) | 3 321 (8.6) | 1 938 (10.8) | 1 617 (9.2) | 1 981 (6.1) |         |
| Waist to hip ratio§                 | 0.88±0.09 | 0.88±0.08 | 0.88±0.08 | 0.88±0.08 | 0.86±0.08 | <0.001  |
| Energy in kcal†                     | 2 001±782 | 2 157±828 | 2 157±820 | 2 174±822 | 2 299±814 | <0.001  |
| Global Wealth Index§                | 0.32±1.04 | 0.19±0.88 | 0.28±0.81 | -0.01±0.82 | -0.76±0.90 | <0.001  |
| Fruits & Vegetables (g/d)§          | 434.3 (268.2,734.0) | 429.4 (276.4,730.7) | 407.8 (285.1,645.1) | 396.5 (277.9,652.3) | 284.4 (154.0,377.3) | <0.001  |
| Red Meat (g/d)§                     | 37.0 (13.0,76.1) | 48.5 (16.4,100.4) | 48.6 (14.6,103.6) | 48.0 (15.3,109.7) | 14.8 (1.6,50.0) | <0.001  |

† Mean±SD, Oneway ANOVA; § N(%), Chi-Square test; ¥ Median(IQR), Kruskal Wallis test
### Table S5: Associations between refined grain intake and clinical outcomes among those with diabetes (DM) and without diabetes (WO DM)

| Hazard ratio (95 CI) | <50 g/d (n=35 665) | 50-150 g/d (n=44 015) | 150-250 g/d (n=25 507) | 250-350 g/d (n=12 133) | ≥350 g/d (n=17 940) | P trend |
|---------------------|-------------------|----------------------|------------------------|------------------------|---------------------|--------|
| DM                  |                   |                      |                        |                        |                     |        |
| Base model          | 1 (reference)     | 0.97 (0.91 to 1.02)  | 0.97 (0.91 to 1.02)    | 0.93 (0.87 to 0.99)    | 0.97 (0.89 to 1.05) | 0.97 (0.89 to 1.05) |
| Minimally adjusted  | 1 (reference)     | 1.07 (1.01 to 1.15)  | 1.09 (1.02 to 1.16)    | 1.11 (1.03 to 1.20)    | 1.12 (1.03 to 1.21) | 1.16 (1.05 to 1.28) |
| Fully adjusted      | 1 (reference)     | 1.07 (1.01 to 1.14)  | 1.09 (1.02 to 1.16)    | 1.11 (1.03 to 1.21)    | 1.12 (1.04 to 1.22) | 1.17 (1.05 to 1.29) |
| Fully adjusted with medications | 1 (reference) | 1.08 (1.01 to 1.15)  | 1.09 (1.02 to 1.16)    | 1.12 (1.03 to 1.21)    | 1.13 (1.04 to 1.23) | 1.18 (1.06 to 1.30) |
| **Total mortality** |                   |                      |                        |                        |                     |        |
| No (% events)       | 2703(7.6)         | 2289(5.2)            | 1122 (4.4)             | 532 (4.4)              | 878 (4.9)           |        |
| Base model          | 1 (reference)     | 0.91 (0.85 to 0.97)  | 0.91 (0.85 to 0.97)    | 0.87 (0.80 to 0.95)    | 0.87 (0.80 to 0.95) | 0.85 (0.76 to 0.96) |
| Minimally adjusted  | 1 (reference)     | 1.04 (0.96 to 1.13)  | 1.06 (0.98 to 1.15)    | 1.08 (0.97 to 1.20)    | 1.09 (0.98 to 1.21) | 1.04 (0.91 to 1.19) |
| Fully adjusted      | 1 (reference)     | 1.04 (0.96 to 1.13)  | 1.06 (0.98 to 1.15)    | 1.09 (0.98 to 1.21)    | 1.10 (0.99 to 1.22) | 1.05 (0.91 to 1.20) |
| Fully adjusted with medications | 1 (reference) | 1.05 (0.96 to 1.14)  | 1.06 (0.98 to 1.15)    | 1.09 (0.98 to 1.21)    | 1.10 (0.99 to 1.23) | 1.05 (0.92 to 1.21) |
| **Major CVD**       |                   |                      |                        |                        |                     |        |
| No (% events)       | 1,774(5.0)        | 2000(4.5)            | 1127(4.4)              | 654(5.4)               | 1233(6.9)          |        |
| Base model          | 1 (reference)     | 1.08 (1.00 to 1.17)  | 1.08 (1.00 to 1.17)    | 1.03 (0.94 to 1.13)    | 1.03 (0.94 to 1.13) | 1.12 (1.00 to 1.25) |
| Minimally adjusted  | 1 (reference)     | 1.11 (1.01 to 1.21)  | 1.12 (1.03 to 1.22)    | 1.13 (1.02 to 1.26)    | 1.14 (1.02 to 1.27) | 1.25 (1.10 to 1.42) |
| Fully adjusted      | 1 (reference)     | 1.11 (1.01 to 1.21)  | 1.12 (1.03 to 1.22)    | 1.13 (1.02 to 1.26)    | 1.14 (1.03 to 1.27) | 1.26 (1.10 to 1.43) |
| Fully adjusted with medications | 1 (reference) | 1.11 (1.02 to 1.21)  | 1.12 (1.03 to 1.22)    | 1.14 (1.03 to 1.27)    | 1.15 (1.03 to 1.28) | 1.27 (1.12 to 1.45) |

*Diabetes- as a covariate only in the DM model not in WO DM
IQR=interquartile range.

**Cox frailty model:** **Base Model:** adjusted for age and sex with centre as random effect; **Minimally adjusted:** adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes*, daily intakes of energy (kcal), vegetable and fruits, red meats with centre as random effect. **Fully adjusted:** Minimally adjusted + whole grains with centre as random effect. Fully adjusted with medications: Fully adjusted + medications (statins and blood pressure) with centre as a random effect.

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*IQR=interquartile range.*
**Table S6: Association between whole grain intake and clinical outcomes among those with diabetes (DM) and those without diabetes (WO DM)**

| Hazard ratio (95% CI) | P trend |
|-----------------------|---------|
|                       | 0 (n=45 380) | <50 g/d (n=46 234) | 50-100 g/d (n=14 581) | ≥100 g/d (n=28 901) |
| **DM** | **WO DM** | **DM** | **WO DM** | **DM** | **WO DM** |
| Composite events | | | | | |
| No (%) events | 2717(8.6) | 4484(9.9) | 1455(8.6) | 4012(9.3) |
| Base Model | 1.15 (1.08 to 1.23) | 1.15 (1.08 to 1.23) | 1.08 (1.02 to 1.14) | 1.08 (1.02 to 1.14) | 1.04 (0.97 to 1.11) | 1.04 (0.97 to 1.11) | 1 (reference) | <0.001 | <0.001 |
| Minimally Adjusted | 1.04 (0.97 to 1.12) | 1.00 (0.93 to 1.08) | 1.02 (0.96 to 1.09) | 0.99 (0.93 to 1.05) | 1.05 (0.98 to 1.13) | 1.03 (0.96 to 1.10) | 1 (reference) | 0.37 | 0.84 |
| Fully adjusted | 1.03 (0.96 to 1.10) | 0.99 (0.92 to 1.07) | 1.01 (0.95 to 1.08) | 0.98 (0.92 to 1.04) | 1.05 (0.98 to 1.13) | 1.03 (0.96 to 1.11) | 1 (reference) | 0.59 | 0.59 |
| Fully adjusted with medications | 1.03 (0.96 to 1.11) | 1.00 (0.93 to 1.07) | 1.01 (0.95 to 1.08) | 0.98 (0.92 to 1.05) | 1.05 (0.98 to 1.13) | 1.03 (0.96 to 1.11) | 1 (reference) | 0.57 | 0.70 |
| **Total Mortality** | | | | | |
| No (%) events | 1518(4.8) | 2892(6.4) | 840 (4.9) | 2571(5.9) |
| Base Model | 1.17 (1.07 to 1.28) | 1.17 (1.07 to 1.28) | 1.06 (0.99 to 1.14) | 1.06 (0.99 to 1.14) | 0.99 (0.91 to 1.08) | 0.99 (0.91 to 1.08) | 1 (reference) | <0.001 | <0.001 |
| Minimally Adjusted | 0.99 (0.90 to 1.09) | 0.94 (0.85 to 1.04) | 0.96 (0.88 to 1.04) | 0.91 (0.84 to 0.99) | 1.01 (0.92 to 1.11) | 0.98 (0.89 to 1.08) | 1 (reference) | 0.54 | 0.08 |
| Fully adjusted | 0.97 (0.88 to 1.07) | 0.93 (0.84 to 1.02) | 0.95 (0.87 to 1.03) | 0.91 (0.84 to 0.99) | 1.00 (0.91 to 1.11) | 0.98 (0.89 to 1.08) | 1 (reference) | 0.37 | 0.05 |
| Fully adjusted with medications | 0.97 (0.88 to 1.07) | 0.93 (0.84 to 1.03) | 0.95 (0.87 to 1.03) | 0.91 (0.84 to 0.99) | 1.00 (0.91 to 1.10) | 0.98 (0.89 to 1.08) | 1 (reference) | 0.37 | 0.06 |
| **Major CVD** | | | | | |
| No (%) events | 1618(5.1) | 2243(5.0) | 853(5.0) | 2184(5.0) |
| Base Model | 1.11 (1.02 to1.20) | 1.11 (1.02 to 1.2) | 1.05 (0.98 to 1.13) | 1.05 (0.98 to 1.13) | 1.06 (0.98 to 1.16) | 1.06 (0.98 to 1.16) | 1 (reference) | 0.03 | 0.03 |
| Minimally Adjusted | 1.04 (0.95 to 1.14) | 1.01 (0.92 to 1.11) | 1.04 (0.96 to 1.13) | 1.01 (0.93 to 1.10) | 1.07 (0.97 to 1.17) | 1.05 (0.96 to 1.15) | 1 (reference) | 0.37 | 0.95 |
| Fully adjusted | 1.04 (0.95 to 1.14) | 1.01 (0.92 to 1.11) | 1.04 (0.96 to 1.13) | 1.01 (0.93 to 1.10) | 1.07 (0.97 to 1.17) | 1.05 (0.96 to 1.15) | 1 (reference) | 0.41 | 0.98 |
| Fully adjusted with medications | 1.05 (0.95 to 1.15) | 1.02 (0.93 to 1.12) | 1.04 (0.96 to 1.12) | 1.01 (0.93 to 1.10) | 1.06 (0.97 to 1.17) | 1.05 (0.96 to 1.15) | 1 (reference) | 0.38 | 0.84 |

**Cox frailty model:**
- **Base model:** adjusted for age and sex with centre as a random effect;
- **Minimally adjusted:** adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes*, daily intakes of energy (kcal), vegetable and fruits, red meats with centre as a random effect;
- **Fully adjusted:** Minimally adjusted+ refined grains with centre as a random effect; Fully adjusted with medications: Fully adjusted +medications (statins and blood pressure) with centre as a random effect.

*Diabetes- as a covariate only in the DM model not in WO DM

IQR=interquartile range.
Table S7: Association between white rice intake and clinical outcomes among those with diabetes (DM) and those without diabetes (WO DM)

| Hazard ratio (95 CI) | P trend |
|----------------------|---------|
|                      | <50 g/d (n=38 022) | 50-150 g/d (n=35 617) | 150-300 g/d (n=16 230) | 300-450 g/d (n=16 045) | ≥450 g/d (n=31 216) |     |
|                      | DM       | WO DM    | DM       | WO DM    | DM       | WO DM    |
| Composite events     | 20.0 (8.2-28.0) | 84.6 (67.7-114.3) | 200 (171.4-214.3) | 395.0 (327.3-400.0) | 863.1 (608.2, 988.8) |     |
| No (% events)        | 3437 (9.0) | 2826 (7.9) | 1393 (8.6) | 1436 (9.0) | 3576 (11.5) |     |
| Base model           | 1 (reference) | 0.89 (0.85 to 0.95) | 0.89 (0.85 to 0.95) | 0.84 (0.78 to 0.90) | 0.84 (0.78 to 0.90) | 0.79 (0.72 to 0.86) | <0.001 | <0.001 |
| Minimally adjusted   | 1 (reference) | 1.00 (0.93 to 1.06) | 0.99 (0.92 to 1.05) | 0.97 (0.89 to 1.06) | 0.98 (0.90 to 1.07) | 0.95 (0.86 to 1.04) | 0.94 (0.86 to 1.03) | 0.87 (0.79 to 0.96) | 0.83 (0.75 to 0.92) | 0.01 | 0.001 |
| Fully adjusted       | 1 (reference) | 1.01 (0.94 to 1.07) | 1.00 (0.94 to 1.07) | 1.01 (0.93 to 1.11) | 1.03 (0.94 to 1.12) | 0.98 (0.89 to 1.08) | 0.98 (0.89 to 1.08) | 0.97 (0.86 to 1.08) | 0.93 (0.83 to 1.04) | 0.58 | 0.33 |
| Fully adjusted with medications | 1 (reference) | 1.01 (0.95 to 1.08) | 1.00 (0.94 to 1.07) | 1.01(0.92 to 1.11) | 1.02 (0.94 to 1.12) | 0.98 (0.89 to 1.08) | 0.98 (0.89 to 1.08) | 0.96 (0.86 to 1.08) | 0.93 (0.83 to 1.04) | 0.55 | 0.32 |
| Total mortality      | 2114 (5.6) | 1698 (4.8) | 784 (4.8) | 867 (5.4) | 2358 (7.6) |     |
| No (% events)        |               |                   |               |                   |               |     |
| Base model           | 1 (reference) | 0.85 (0.79 to 0.91) | 0.85 (0.79 to 0.91) | 0.77 (0.70 to 0.85) | 0.77 (0.70 to 0.85) | 0.81 (0.72 to 0.90) | 0.81 (0.72 to 0.90) | 0.77 (0.69 to 0.86) | 0.77 (0.69 to 0.86) | <0.001 | <0.001 |
| Minimally adjusted   | 1 (reference) | 0.95 (0.87 to 1.04) | 0.94 (0.87 to 1.03) | 0.89 (0.79 to 1.00) | 0.90 (0.80 to 1.02) | 0.91 (0.80 to 1.03) | 0.90 (0.80 to 1.02) | 0.81 (0.71 to 0.93) | 0.77 (0.68 to 0.88) | 0.004 | <0.001 |
| Fully adjusted       | 1 (reference) | 0.96 (0.88 to 1.05) | 0.96 (0.88 to 1.04) | 0.93 (0.82 to 1.05) | 0.95 (0.84 to 1.07) | 0.95 (0.83 to 1.08) | 0.95 (0.83 to 1.08) | 0.90 (0.78 to 1.04) | 0.87 (0.75 to 1.01) | 0.18 | 0.10 |
| Fully adjusted with medications | 1 (reference) | 0.96 (0.89 to 1.05) | 0.96 (0.88 to 1.04) | 0.93 (0.82 to 1.05) | 0.95 (0.84 to 1.07) | 0.94 (0.83 to 1.07) | 0.95 (0.83 to 1.07) | 0.90 (0.78 to 1.04) | 0.87 (0.75 to 1.01) | 0.17 | 0.01 |
| Major CVD            | 1925 (5.1) | 1598 (4.5) | 851 (5.2) | 824 (5.1) | 1700 (5.5) |     |
| No (% events)        |               |                   |               |                   |               |     |
| Base model           | 1 (reference) | 0.93 (0.86 to 1.00) | 0.93 (0.86 to 1.00) | 0.90 (0.81 to 0.99) | 0.90 (0.81 to 0.99) | 0.86 (0.77 to 0.95) | 0.86 (0.77 to 0.95) | 0.79 (0.70 to 0.89) | 0.79 (0.70 to 0.89) | <0.001 | <0.001 |
| Minimally adjusted   | 1 (reference) | 1.01 (0.93 to 1.10) | 1.00 (0.92 to 1.09) | 0.99 (0.89 to 1.11) | 1.01 (0.90 to 1.12) | 0.93 (0.82 to 1.05) | 0.93 (0.82 to 1.04) | 0.87 (0.76 to 0.99) | 0.83 (0.73 to 0.95) | 0.05 | 0.02 |
| Fully adjusted       | 1 (reference) | 1.02 (0.94 to 1.11) | 1.02 (0.94 to 1.10) | 1.04 (0.93 to 1.16) | 1.05 (0.94 to 1.18) | 0.98 (0.86 to 1.10) | 0.97 (0.86 to 1.10) | 0.97 (0.84 to 1.13) | 0.94 (0.81 to 1.08) | 0.70 | 0.48 |
| Fully adjusted with medications | 1 (reference) | 1.03 (0.95 to 1.12) | 1.02 (0.94 to 1.11) | 1.03 (0.92 to 1.15) | 1.04 (0.93 to 1.17) | 0.97 (0.86 to 1.10) | 0.97 (0.85 to 1.10) | 0.97 (0.83 to 1.12) | 0.93 (0.81 to 1.08) | 0.63 | 0.44 |

Cox frailty model: Base model: adjusted for age to sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes*, daily intakes of energy (kcal), vegetable and fruits, and red meats with centre as a random effect; Fully adjusted: Minimally adjusted + refined grains to whole grains with centre as a random effect; Fully adjusted with medications: Fully adjusted + medications (statins and blood pressure) with centre as a random effect.

*Diabetes- as a covariate only in the DM model not in WO DM

IQR=interquartile range.
Table S8a Association between refined grain intake and clinical outcomes in high intake countries (N= 102 075)

| Median (IQR) | Hazard ratio (95 % CI) |
|--------------|------------------------|
|              | <50 g/d (n=17 033)     | 50-150 g/d (n=32 805) | 150-250 g/d (n=22 775) | 250-350 g/d (n=11 701) | ≥350 g/d (n=17 761) |
| Composite events | 26.0 (13.6-38.0) | 94.4 (73.0-119.5) | 186.8 (165.8-214.6) | 300.0 (273.1-319.7) | 499.0 (450.0-675.0) |
| No (%) events | 1129(6.6) | 2259(6.9) | 620(7.1) | 966(8.3) | 755(9.9) |
| Base model | 1.00 (reference) | 1.06 (0.98 to 1.14) | 1.05 (0.96 to 1.14) | 1.09 (0.98 to 1.20) | 1.25 (1.14 to 1.38) |
| Minimally adjusted | 1.00 (reference) | 1.12 (1.04 to 1.22) | 1.19 (1.09 to 1.31) | 1.23 (1.10 to 1.38) | 1.33 (1.18 to 1.50) |
| Fully adjusted | 1.00 (reference) | 1.13 (1.04 to 1.22) | 1.20 (1.09 to 1.32) | 1.24 (1.11 to 1.39) | 1.35 (1.20 to 1.53) |
| Fully adjusted with medications | 1.00 (reference) | 1.13 (1.04 to 1.22) | 1.21 (1.10 to 1.32) | 1.25 (1.12 to 1.40) | 1.36 (1.21 to 1.53) |
| Total mortality |  |  |  |  |  |
| No (%) events | 613 (3.6) | 1282 (3.9) | 905 (4.0) | 495 (4.2) | 860 (4.8) |
| Base model | 1.00 (reference) | 1.00 (0.91 to 1.11) | 1.01 (0.90 to 1.13) | 0.97 (0.84 to 1.11) | 1.22 (1.07 to 1.39) |
| Minimally adjusted | 1.00 (reference) | 1.11 (0.99 to 1.24) | 1.17 (1.03 to 1.33) | 1.09 (0.94 to 1.28) | 1.28 (1.08 to 1.50) |
| Fully adjusted | 1.00 (reference) | 1.11 (0.99 to 1.24) | 1.17 (1.03 to 1.33) | 1.10 (0.94 to 1.28) | 1.28 (1.09 to 1.52) |
| Fully adjusted with medications | 1.00 (reference) | 1.11 (0.99 to 1.24) | 1.18 (1.04 to 1.34) | 1.11 (0.95 to 1.29) | 1.29 (1.09 to 1.52) |
| Major CVD |  |  |  |  |  |
| No (%) events | 654 (3.8) | 1332 (4.1) | 978 (4.3) | 636 (5.4) | 1223 (6.9) |
| Base model | 1.00 (reference) | 1.13 (1.02 to 1.25) | 1.11 (0.99 to 1.24) | 1.21 (1.07 to 1.37) | 1.33 (1.18 to 1.51) |
| Minimally adjusted | 1.00 (reference) | 1.18 (1.06 to 1.31) | 1.24 (1.10 to 1.40) | 1.39 (1.20 to 1.60) | 1.48 (1.28 to 1.72) |
| Fully adjusted | 1.00 (reference) | 1.18 (1.06 to 1.31) | 1.25 (1.11 to 1.41) | 1.40 (1.21 to 1.61) | 1.51 (1.30 to 1.76) |
| Fully adjusted with medications | 1.00 (reference) | 1.18 (1.06 to 1.31) | 1.26 (1.11 to 1.42) | 1.41 (1.23 to 1.63) | 1.52 (1.30 to 1.76) |

Cox frailty model: Base model: adjusted for age, sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; Fully adjusted: Minimally adjusted + whole grains with centre as a random effect; Fully adjusted with medications: Fully adjusted +medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range.
Table S8b Association between refined grain intake and clinical outcomes in low intake countries (N= 33 185)

| Hazard ratio (95 % CI) | <50 g/d (n=18632) | 50-150 g/d (n=11210) | 150-250 g/d (n=2732) | 250-350 g/d (n=432) | ≥350 g/d (n=179) |
|-----------------------|------------------|---------------------|---------------------|-------------------|------------------|
| Median (IQR)           | 11.6 (4.2, 25.4) | 89.4 (68.8, 115.3)  | 180.0 (162.9, 206.4)| 278.9 (262.1, 305.4)| 451.8 (386.0,582.8) |
| Composite events       |                  |                     |                     |                   |                  |
| No (%) events          | 2774 (14.9)      | 1427 (12.7)         | 318 (11.6)          | 50 (11.6)         | 23 (12.8)        |
| Base model             | 1.00 (reference) | 0.89 (0.82 to 0.96) | 0.77 (0.68 to 0.88) | 0.76 (0.57 to 1.01)| 0.90 (0.59 to 1.36) |
| Minimally adjusted     | 1.00 (reference) | 1.02 (0.91 to 1.14) | 0.95 (0.79 to 1.13) | 1.03 (0.69 to 1.53)| 1.31 (0.79 to 2.16) |
| Fully adjusted         | 1.00 (reference) | 1.02 (0.91 to 1.14) | 0.95 (0.79 to 1.13) | 1.03 (0.69 to 1.53)| 1.31 (0.79 to 2.16) |
| Fully adjusted with medications | 1.00 (reference) | 1.02 (0.91 to 1.14) | 0.95 (0.79 to 1.13) | 1.03 (0.69 to 1.53)| 1.31 (0.79 to 2.17) |
| Total mortality        |                  |                     |                     |                   |                  |
| No (%) events          | 2090 (11.2)      | 1007 (9.0)          | 217 (7.9)           | 37 (8.6)          | 18 (10.1)        |
| Base model             | 1.00 (reference) | 0.86 (0.78 to 0.94) | 0.73 (0.63 to 0.85) | 0.75 (0.54 to 1.05)| 0.93 (0.58 to 1.49) |
| Minimally adjusted     | 1.00 (reference) | 0.97 (0.85 to 1.11) | 0.93 (0.74 to 1.15) | 1.02 (0.63 to 1.65)| 1.53 (0.87 to 2.68) |
| Fully adjusted         | 1.00 (reference) | 0.97 (0.86 to 1.11) | 0.93 (0.75 to 1.16) | 1.03 (0.63 to 1.66)| 1.54 (0.88 to 2.7) |
| Fully adjusted with medications | 1.00 (reference) | 0.98 (0.86 to 1.11) | 0.93 (0.75 to 1.16) | 1.03 (0.64 to 1.67)| 1.54 (0.88 to 2.7) |
| Major CVD              |                  |                     |                     |                   |                  |
| No (%) events          | 1120 (6.0)       | 668 (6.0)           | 149 (5.5)           | 18 (4.2)          | 10 (5.6)         |
| Base model             | 1.00 (reference) | 1.02 (0.91 to 1.16) | 0.90 (0.74 to 1.09) | 0.73 (0.45 to 1.17)| 0.99 (0.53 to 1.87) |
| Minimally adjusted     | 1.00 (reference) | 0.92 (0.78 to 1.09) | 0.81 (0.63 to 1.05) | 0.78 (0.44 to 1.38)| 1.18 (0.58 to 2.42) |
| Fully adjusted         | 1.00 (reference) | 0.92 (0.78 to 1.09) | 0.81 (0.63 to 1.05) | 0.78 (0.44 to 1.38)| 1.18 (0.58 to 2.41) |
| Fully adjusted with medications | 1.00 (reference) | 0.93 (0.78 to 1.09) | 0.81 (0.63 to 1.05) | 0.78 (0.44 to 1.38)| 1.18 (0.58 to 2.42) |

Cox frailty model: Base model: adjusted for age, sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; Fully adjusted: Minimally adjusted + whole grains with centre as a random effect; Fully adjusted with medications: Fully adjusted +medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range
Table S9: Association between quantiles of refined grain intake and clinical outcomes (N=135 260) without baseline CVD

|                      | Q1 (n=27 493) | Q2 vs Q1 (n=26 870) | Q3 vs Q1 (n=26 832) | Q4 vs Q1 (n=26 899) | Q5 vs Q1 (n=27 166) | Hazard ratio (95% CI) | P trend |
|----------------------|---------------|---------------------|---------------------|---------------------|---------------------|----------------------|---------|
| **Median (IQR)**     | 22.1 (5.3-41.6) | 76.0 (49.2-118.0)   | 142.5 (75.3-204.3)  | 197.9 (107.5-325.7) | 325.3 (183.5-602.5) |                      |         |
| **Composite**        |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 2616 (9.5)    | 2401 (8.9)          | 2386 (8.9)          | 2403 (8.9)          | 2515 (9.3)          |                      | <0.001  |
| Fully adjusted       | 1.00 (reference) | 1.12 (1.05 to 1.19) | 1.13 (1.06 to 1.20) | 1.15 (1.08 to 1.23) | 1.19 (1.11 to 1.27) |                      |         |
| **Total Mortality**  |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 1746 (6.4)    | 1510 (5.6)          | 1421 (5.3)          | 1404 (5.2)          | 1443 (5.3)          |                      | 0.01    |
| Fully adjusted       | 1.00 (reference) | 1.11 (1.02 to 1.20) | 1.07 (0.99 to 1.17) | 1.11 (1.02 to 1.21) | 1.14 (1.04 to 1.25) |                      |         |
| **Non-CV mortality** |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 1266 (4.6)    | 1071 (4.0)          | 968 (3.6)           | 949 (3.5)           | 934 (3.4)           |                      | 0.50    |
| Fully adjusted       | 1.00 (reference) | 1.07 (0.97 to 1.17) | 1.02 (0.92 to 1.12) | 1.06 (0.96 to 1.17) | 1.04 (0.93 to 1.17) |                      |         |
| **CV mortality**     |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 544 (2)       | 511 (1.9)           | 523 (1.9)           | 522 (1.9)           | 576 (2.1)           |                      | <0.001  |
| Fully adjusted       | 1.00 (reference) | 1.26 (1.10 to 1.45) | 1.25 (1.08 to 1.44) | 1.30 (1.12 to 1.50) | 1.41 (1.21 to 1.64) |                      |         |
| **Major CVD**        |               |                     |                     |                     |                     |                      | <0.001  |
| No (%) events        | 1223 (4.4)    | 1264 (4.7)          | 1379 (5.1)          | 1418 (5.3)          | 1504 (5.5)          |                      |         |
| Fully adjusted       | 1.00 (reference) | 1.21 (1.11 to 1.32) | 1.27 (1.17 to 1.39) | 1.28 (1.18 to 1.40) | 1.37 (1.25 to 1.50) |                      | <0.001  |
| **MI**               |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 529 (1.9)     | 544 (2.0)           | 615 (2.3)           | 596 (2.2)           | 647 (2.4)           |                      | <0.001  |
| Fully adjusted       | 1.00 (reference) | 1.26 (1.10 to 1.44) | 1.35 (1.18 to 1.54) | 1.29 (1.13 to 1.48) | 1.40 (1.22 to 1.62) |                      |         |
| **Stroke**           |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 568 (2.1)     | 595 (2.2)           | 627 (2.3)           | 681 (2.5)           | 739 (2.7)           |                      |         |
| Fully adjusted       | 1.00 (reference) | 1.18 (1.04 to 1.34) | 1.19 (1.05 to 1.35) | 1.22 (1.08 to 1.38) | 1.34 (1.18 to 1.53) |                      | <0.001  |
| **Heart Failure**    |               |                     |                     |                     |                     |                      |         |
| No (%) events        | 115 (0.4)     | 116 (0.4)           | 146 (0.5)           | 138 (0.5)           | 137 (0.5)           |                      |         |
| Fully adjusted       | 1.00 (reference) | 1.09 (0.82 to 1.46) | 1.37 (1.03 to 1.81) | 1.32 (0.99 to 1.75) | 1.33 (0.98 to 1.81) |                      | 0.03    |

**Cox frailty model: Fully adjusted**: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits to red meats and whole grains with centre as a random effect.
IQR=interquartile range
### Table S10 Association between whole grain intake and clinical outcomes (N= 1313313) in all regions excluding Africa

|                      | Hazard ratio (95 %CI) | P trend |
|----------------------|-----------------------|---------|
|                      | 0 (n=31 646)          |         |
|                      | <50 g/d (n=44 951)    |         |
|                      | 50-100 g/d (n=16 648) |         |
|                      | ≥100 g/d (n=38 068)   |         |
| **Median (IQR)**     | 0 (0,0)               | 17.3 (9.1, 31.3) |
|                      | 73.6 (61.8, 84.1)     | 214.3 (147.8, 326.5) |
| **Composite**        |                       |         |
| No (% events)        | 2714 (8.6)            | 4470 (9.9) |
|                      | 1418 (8.5)            | 3266 (8.6) |
| Base model           | 1.18 (1.10 to 1.26)   | 1.09 (1.03 to 1.16) |
|                      | 1.05 (0.98 to 1.13)   | 1.00 (reference) |
|                      | <0.001                | 0.20     |
| Minimally adjusted   | 1.05 (0.98 to 1.13)   | 1.03 (0.97 to 1.10) |
|                      | 1.05 (0.98 to 1.13)   | 1.00 (reference) |
|                      | 0.0                  | 0.34     |
| Fully adjusted       | 1.04 (0.97 to 1.12)   | 1.03 (0.96 to 1.09) |
|                      | 1.06 (0.98 to 1.14)   | 1.00 (reference) |
|                      | 0.33                  |          |
| Fully adjusted with medications | 1.04 (0.97 to 1.12) | 1.02 (0.96 to 1.09) |
|                      | 1.05 (0.98 to 1.13)   | 1.00 (reference) |
| **Total mortality**  |                       |         |
| No (% events)        | 1515 (4.8)            | 2882 (6.4) |
|                      | 812 (4.9)             | 1992 (5.2) |
| Base model           | 1.20 (1.10 to 1.31)   | 1.08 (1.00 to 1.16) |
|                      | 1.01 (0.92 to 1.10)   | 1.00 (reference) |
|                      | <0.001                | 0.80     |
| Minimally adjusted   | 1.00 (0.91 to 1.10)   | 0.97 (0.89 to 1.05) |
|                      | 1.00 (0.91 to 1.11)   | 1.00 (reference) |
|                      | 0.80                  |          |
| Fully adjusted       | 0.99 (0.90 to 1.09)   | 0.96 (0.88 to 1.04) |
|                      | 1.00 (0.90 to 1.10)   | 1.00 (reference) |
|                      | 0.60                  |          |
| Fully adjusted with medications | 0.99 (0.89 to 1.09) | 0.96 (0.88 to 1.04) |
|                      | 1.00 (0.90 to 1.10)   | 1.00 (reference) |
|                      | 0.60                  |          |
| **Major CVD**        |                       |         |
| No (% events)        | 1617 (5.1)            | 2239 (5.0) |
|                      | 842 (5.1)             | 1955 (5.1) |
| Base model           | 1.11 (1.02 to 1.21)   | 1.05 (0.98 to 1.14) |
|                      | 1.07 (0.98 to 1.16)   | 1.00 (reference) |
|                      | 0.02                  |          |
| Minimally adjusted   | 1.05 (0.96 to 1.15)   | 1.04 (0.96 to 1.13) |
|                      | 1.06 (0.97 to 1.17)   | 1.00 (reference) |
|                      | 0.35                  |          |
| Fully adjusted       | 1.05 (0.95 to 1.15)   | 1.04 (0.96 to 1.13) |
|                      | 1.07 (0.97 to 1.17)   | 1.00 (reference) |
|                      | 0.38                  |          |
| Fully adjusted with medications | 1.05 (0.96 to 1.15) | 1.04 (0.96 to 1.13) |
|                      | 1.06 (0.97 to 1.17)   | 1.00 (reference) |
|                      | 0.35                  |          |

**Cox frailty model: Base model:** adjusted for age and sex with centre as a random effect; **Minimally adjusted:** adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; **Fully adjusted:** Minimally adjusted+ refined grains, with centre as a random effect; **Fully adjusted with medications:** Fully adjusted + medications (statins and blood pressure with centre as a random effect.

IQR=interquartile range
Table S11 Association between whole grain intakes estimated on dry weight basis and clinical outcomes (N= 137 130)

| Hazard ratio (95 CI) | 0 g/d (n=31 686) | <10 g/d (n=33 495) | 10-19.9 g/d (n=15 178) | 20-29.9 g/d (n=9775) | >=30 g/d (n=46 996) | P trend |
|---------------------|------------------|-------------------|------------------------|---------------------|---------------------|---------|
| **Composite events** |                  |                   |                        |                     |                     |         |
| No (% events)       | 2717 (8.6)       | 3440 (10.3)       | 1335 (8.8)             | 818 (8.4)           | 4358 (9.3)          |         |
| Base model          | 1.16 (1.09 to 1.23) | 1.10 (1.04 to 1.17) | 1.03 (0.97 to 1.11) | 1.02 (0.95 to 1.11) | 1.00 (reference)   | <0.001  |
| Minimally Adjusted  | 1.02 (0.96 to 1.10) | 1.01 (0.95 to 1.08) | 1.01 (0.94 to 1.09) | 0.99 (0.91 to 1.08) | 1.00 (reference)   | 0.47    |
| Fully adjusted      | 1.01 (0.94 to 1.09) | 1.00 (0.94 to 1.07) | 1.00 (0.93 to 1.08) | 1.00 (0.91 to 1.09) | 1.00 (reference)   | 0.75    |
| Fully adjusted with Medications | 1.01 (0.94 to 1.09) | 1.00 (0.94 to 1.07) | 1.01 (0.93 to 1.09) | 1.00 (0.91 to 1.09) | 1.00 (reference)   | 0.75    |
| **Total mortality** |                  |                   |                        |                     |                     |         |
| No (% events)       | 1518 (4.8)       | 2269 (6.8)        | 800 (5.3)              | 480 (4.9)           | 2754 (5.9)          |         |
| Base model          | 1.18 (1.09 to 1.29) | 1.10 (1.02 to 1.18) | 1.01 (0.93 to 1.11) | 0.98 (0.89 to 1.09) | 1.00 (reference)   | <0.001  |
| Minimally Adjusted  | 0.97 (0.89 to 1.07) | 0.94 (0.87 to 1.02) | 0.96 (0.87 to 1.06) | 0.95 (0.84 to 1.06) | 1.00 (reference)   | 0.42    |
| Fully adjusted      | 0.96 (0.87 to 1.06) | 0.93 (0.86 to 1.02) | 0.96 (0.87 to 1.06) | 0.94 (0.84 to 1.06) | 1.00 (reference)   | 0.27    |
| Fully adjusted with Medications | 0.96 (0.87 to 1.06) | 0.93 (0.85 to 1.01) | 0.96 (0.87 to 1.06) | 0.94 (0.83 to 1.06) | 1.00 (reference)   | 0.26    |
| **Non-CV mortality** |                 |                   |                        |                     |                     |         |
| No (% events)       | 1030 (3.3)       | 1614 (4.8)        | 535 (3.5)              | 325 (3.3)           | 1902 (4.1)          |         |
| Base Model          | 1.20 (1.08 to 1.33) | 1.09 (1.00 to 1.19) | 0.98 (0.88 to 1.09) | 0.94 (0.83 to 1.07) | 1.00 (reference)   | <0.001  |
| Minimally Adjusted  | 0.96 (0.85 to 1.07) | 0.91 (0.82 to 1.00) | 0.91 (0.81 to 1.02) | 0.93 (0.82 to 1.07) | 1.00 (reference)   | 0.22    |
| Fully adjusted      | 0.93 (0.83 to 1.05) | 0.88 (0.80 to 0.98) | 0.91 (0.80 to 1.02) | 0.92 (0.80 to 1.07) | 1.00 (reference)   | 0.08    |
| Fully adjusted with Medications | 0.93 (0.83 to 1.04) | 0.88 (0.80 to 0.98) | 0.91 (0.80 to 1.02) | 0.92 (0.80 to 1.06) | 1.00 (reference)   | 0.08    |
| **CV mortality**    |                  |                   |                        |                     |                     |         |
| No (% events)       | 557 (1.8)        | 764 (2.3)         | 301 (2.0)              | 170 (1.7)           | 985 (2.1)          |         |
| Base model          | 1.18 (1.03 to 1.35) | 1.10 (0.97 to 1.25) | 1.08 (0.93 to 1.25) | 1.03 (0.86 to 1.22) | 1.00 (reference)   | 0.02    |
| Minimally Adjusted  | 1.04 (0.89 to 1.21) | 1.02 (0.89 to 1.18) | 1.08 (0.92 to 1.26) | 0.92 (0.76 to 1.13) | 1.00 (reference)   | 0.51    |
| Fully adjusted      | 1.05 (0.89 to 1.22) | 1.03 (0.89 to 1.19) | 1.08 (0.91 to 1.27) | 0.94 (0.76 to 1.15) | 1.00 (reference)   | 0.46    |
| Fully adjusted with Medications | 1.05 (0.90 to 1.23) | 1.03 (0.89 to 1.19) | 1.08 (0.92 to 1.28) | 0.93 (0.76 to 1.15) | 1.00 (reference)   | 0.45    |

**Major CVD**

| Median (IQR) | 0 (0-0) | 4.2 (2.5-6.9) | 14.9 (12.5-17.3) | 25.0 (22.5-28.0) | 73.8 (48.4-131.8) |         |
| **Composite events** |         |              |               |                  |
| No (% events)       |         |              |               |                  |
| Base model          |         |              |               |                  |
| Minimally Adjusted  |         |              |               |                  |
| Fully adjusted      |         |              |               |                  |
| Fully adjusted with Medications |         |              |               |                  |
| **Total mortality** |         |              |               |                  |
| No (% events)       |         |              |               |                  |
| Base model          |         |              |               |                  |
| Minimally Adjusted  |         |              |               |                  |
| Fully adjusted      |         |              |               |                  |
| Fully adjusted with Medications |         |              |               |                  |
| **Non-CV mortality** |        |              |               |                  |
| No (% events)       |         |              |               |                  |
| Base Model          |         |              |               |                  |
| Minimally Adjusted  |         |              |               |                  |
| Fully adjusted      |         |              |               |                  |
| Fully adjusted with Medications |         |              |               |                  |
| **CV mortality**    |         |              |               |                  |
| No (% events)       |         |              |               |                  |
| Base model          |         |              |               |                  |
| Minimally Adjusted  |         |              |               |                  |
| Fully adjusted      |         |              |               |                  |
| Fully adjusted with Medications |         |              |               |                  |
| **Major CVD**       |         |              |               |                  |
| No (%) events | 1618 (5.1) | 1652 (4.9) | 753 (5.0) | 472 (4.8) | 2403 (5.1) |
|---------------|------------|------------|-----------|-----------|------------|
| Base model    | 1.11 (1.02 to 1.2) | 1.06 (0.98 to 1.15) | 1.04 (0.95 to 1.14) | 1.05 (0.95 to 1.17) | 1.00 (reference) |
| Minimally adjusted | 1.03 (0.94 to 1.12) | 1.03 (0.94 to 1.12) | 1.03 (0.94 to 1.13) | 0.99 (0.88 to 1.11) | 1.00 (reference) |
| Fully adjusted | 1.03 (0.94 to 1.12) | 1.03 (0.94 to 1.12) | 1.02 (0.93 to 1.13) | 0.99 (0.88 to 1.11) | 1.00 (reference) |
| Fully adjusted with medications | 1.03 (0.94 to 1.12) | 1.02 (0.94 to 1.12) | 1.03 (0.93 to 1.13) | 0.99 (0.88 to 1.11) | 1.00 (reference) |

**MI**

| No (%) events | 651 (2.1) | 772 (2.3) | 358 (2.4) | 224 (2.3) | 994 (2.1) |
|---------------|------------|------------|-----------|-----------|------------|
| Base model    | 1.11 (0.97 to 1.26) | 1.02 (0.91 to 1.15) | 1.08 (0.94 to 1.24) | 1.09 (0.94 to 1.28) | 1.00 (reference) |
| Minimally adjusted | 1.08 (0.94 to 1.25) | 1.03 (0.90 to 1.18) | 1.12 (0.97 to 1.30) | 1.02 (0.86 to 1.21) | 1.00 (reference) |
| Fully adjusted | 1.08 (0.93 to 1.25) | 1.03 (0.90 to 1.18) | 1.11 (0.95 to 1.29) | 1.01 (0.85 to 1.21) | 1.00 (reference) |
| Fully adjusted with medications | 1.08 (0.93 to 1.25) | 1.03 (0.90 to 1.17) | 1.11 (0.96 to 1.29) | 1.01 (0.85 to 1.21) | 1.00 (reference) |

**Stroke**

| No (%) events | 852 (2.7) | 669 (2.0) | 318 (2.1) | 211 (2.2) | 1177 (2.5) |
|---------------|------------|------------|-----------|-----------|------------|
| Base model    | 1.13 (1.01 to 1.26) | 1.04 (0.93 to 1.17) | 0.99 (0.87 to 1.13) | 1.06 (0.91 to 1.23) | 1.00 (reference) |
| Minimally adjusted | 1.04 (0.92 to 1.17) | 0.99 (0.87 to 1.12) | 0.95 (0.82 to 1.09) | 1.03 (0.87 to 1.21) | 1.00 (reference) |
| Fully adjusted | 1.03 (0.92 to 1.17) | 0.98 (0.86 to 1.11) | 0.94 (0.82 to 1.08) | 1.01 (0.86 to 1.19) | 1.00 (reference) |
| Fully adjusted with medications | 1.04 (0.92 to 1.17) | 0.98 (0.86 to 1.11) | 0.94 (0.82 to 1.09) | 1.01 (0.86 to 1.19) | 1.00 (reference) |

**Heart Failure**

| No (%) events | 109 (0.3) | 184 (0.6) | 93 (0.6) | 50 (0.5) | 220 (0.5) |
|---------------|------------|------------|-----------|-----------|------------|
| Base model    | 0.86 (0.66 to 1.14) | 1.18 (0.93 to 1.5) | 1.23 (0.94 to 1.61) | 1.05 (0.76 to 1.45) | 1.00 (reference) |
| Minimally adjusted | 0.77 (0.56 to 1.05) | 1.24 (0.95 to 1.61) | 1.27 (0.95 to 1.71) | 0.94 (0.65 to 1.36) | 1.00 (reference) |
| Fully adjusted | 0.75 (0.55 to 1.03) | 1.25 (0.96 to 1.63) | 1.29 (0.96 to 1.72) | 0.96 (0.67 to 1.39) | 1.00 (reference) |
| Fully adjusted with medications | 0.76 (0.55 to 1.03) | 1.24 (0.95 to 1.63) | 1.30 (0.97 to 1.74) | 0.96 (0.67 to 1.39) | 1.00 (reference) |

**Cox frailty model:** *Base model:* adjusted for age and sex with centre as a random effect; *Minimally adjusted:* adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), , vegetable and fruits, dairy and red meats with centre as a random effect; *Fully adjusted:* Minimally adjusted+ refined grains, with centre as a random effect; *Fully adjusted with medications:* Fully adjusted + medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range.
Table S12a Association between white rice intake and clinical outcomes in Asian countries (N=82 652)

| Hazard ratio (95 CI) | <50 g/d (n=13,953) | 50-<150 g/d (n=15 669) | 150-<300 g/d (n=10 887) | 300-<450 g/d (n=11 289) | ≥450 g/d (n=30 854) |
|----------------------|---------------------|-------------------------|-------------------------|-------------------------|----------------------|
| Median (IQR)         | 19.7 (6.6-30.2)     | 85.7 (64.3-143.3)       | 200.0 (186.6-214.3)     | 389.0 (321.9-400.6)     | 885.7 (609.8-989.5)  |
| Composite events     |                     |                         |                         |                         |                      |
| No (%) events        | 1550 (11.1)         | 1458 (9.3)              | 1083 (10.0)             | 1081 (9.6)              | 3561 (11.5)          |
| Base model           | 1.00 (reference)    | 0.86 (0.80 to 0.93)     | 0.79 (0.72 to 0.87)     | 0.78 (0.71 to 0.86)     | 0.74 (0.68 to 0.82)  |
| Minimally adjusted   | 1.00 (reference)    | 0.98 (0.90 to 1.07)     | 0.96 (0.86 to 1.06)     | 0.94 (0.84 to 1.05)     | 0.85 (0.76 to 0.95)  |
| Fully adjusted       | 1.00 (reference)    | 1.00 (0.92 to 1.10)     | 1.03 (0.92 to 1.15)     | 1.01 (0.90 to 1.13)     | 0.99 (0.87 to 1.13)  |
| Fully adjusted with medications | 1.00 (reference) | 1.01 (0.93 to 1.11) | 1.03 (0.92 to 1.14) | 1.01 (0.90 to 1.13) | 0.99 (0.87 to 1.13) |
| Total mortality      |                     |                         |                         |                         |                      |
| No (%) events        | 974 (7.0)           | 821 (5.2)               | 608 (5.6)               | 634 (5.6)               | 2352 (7.6)           |
| Base model           | 1.00 (reference)    | 0.77 (0.70 to 0.85)     | 0.70 (0.62 to 0.78)     | 0.72 (0.63 to 0.81)     | 0.70 (0.62 to 0.79)  |
| Minimally adjusted   | 1.00 (reference)    | 0.89 (0.79 to 1.01)     | 0.85 (0.74 to 0.98)     | 0.87 (0.75 to 1.01)     | 0.78 (0.67 to 0.90)  |
| Fully adjusted       | 1.00 (reference)    | 0.92 (0.81 to 1.03)     | 0.91 (0.79 to 1.05)     | 0.93 (0.79 to 1.09)     | 0.88 (0.74 to 1.05)  |
| Fully adjusted with medications | 1.00 (reference) | 0.92 (0.82 to 1.04) | 0.91 (0.79 to 1.05) | 0.93 (0.79 to 1.09) | 0.88 (0.75 to 1.05) |
| Major CVD            |                     |                         |                         |                         |                      |
| No (%) events        | 952 (6.8)           | 919 (5.9)               | 671 (6.2)               | 621 (5.5)               | 1691 (5.5)           |
| Base model           | 1.00 (reference)    | 0.91 (0.83 to 1.00)     | 0.86 (0.77 to 0.97)     | 0.82 (0.72 to 0.92)     | 0.75 (0.66 to 0.85)  |
| Minimally adjusted   | 1.00 (reference)    | 1.00 (0.90 to 1.12)     | 0.98 (0.86 to 1.11)     | 0.92 (0.79 to 1.05)     | 0.83 (0.72 to 0.97)  |
| Fully adjusted       | 1.00 (reference)    | 1.03 (0.92 to 1.14)     | 1.04 (0.91 to 1.19)     | 0.98 (0.85 to 1.14)     | 0.97 (0.82 to 1.15)  |
| Fully adjusted with medications | 1.00 (reference) | 1.04 (0.93 to 1.16) | 1.03 (0.90 to 1.18) | 0.98 (0.85 to 1.14) | 0.97 (0.82 to 1.15) |

Cox frailty model hazard ratios (HR) and 95% confidence intervals (CI): Base model: adjusted for age, sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal),...
vegetable and fruits, dairy and red meats with centre as a random effect; **Fully adjusted**: Minimally adjusted + refined grains, whole grains with centre as a random effect. Fully adjusted with medications: Fully adjusted + medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range.
Table S12b Association between consumption of white rice and clinical outcomes in Non-Asian countries (N=54,478)

| Consumption (g/d) | Hazard ratio (95 CI) | Median (IQR) | Composite events | Total mortality | Major CVD |
|-------------------|----------------------|--------------|------------------|----------------|-----------|
|                   |                      | <50 g/d (n=24,069) | 50-150 g/d (n=19,948) | 150-300 g/d (n=5,343) | 300-450 g/d (n=4,756) | ≥450 g/d (n=3,62) |
|                   |                      | n            | n               | n              | n         | n           |
| <50 g/d           | 1.00 (reference)     | 20.7 (8.2, 26.8) | 79.0 (67.7, 120.1) | 171.4 (158.0, 214.3) | 395.0 (327.5, 395.0) | 589.5 (503.4, 786.0) |
| 50-150 g/d        | 1.02 (0.92 to 1.12)  | 23.6 (13.6, 41.1) | 77.8 (65.5, 106.2) | 171.4 (158.0, 214.3) | 395.0 (327.5, 395.0) | 589.5 (503.4, 786.0) |
| 150-300 g/d       | 1.02 (0.91 to 1.12)  | 30.4 (18.5, 51.8) | 144.3 (120.8, 176.6) | 395.0 (327.5, 395.0) | 589.5 (503.4, 786.0) | 589.5 (503.4, 786.0) |
| 300-450 g/d       | 1.02 (0.92 to 1.12)  | 40.3 (20.5, 80.1) | 205.5 (181.1, 235.6) | 589.5 (503.4, 786.0) | 589.5 (503.4, 786.0) | 589.5 (503.4, 786.0) |
| ≥450 g/d          | 1.02 (0.92 to 1.12)  | 58.8 (21.5, 160.7) | 307.5 (235.0, 400.0) | 589.5 (503.4, 786.0) | 589.5 (503.4, 786.0) | 589.5 (503.4, 786.0) |

Composite events

| Events | Hazard ratio (95 CI) | Median (IQR) |
|--------|----------------------|--------------|
| No (%) |                      |              |
| Base model | 1.00 (reference)     | 20.7 (8.2, 26.8) |
| Minimally adjusted | 1.02 (0.92 to 1.12)  | 23.6 (13.6, 41.1) |
| Fully adjusted | 1.02 (0.92 to 1.12)  | 30.4 (18.5, 51.8) |
| Fully adjusted with medications | 1.02 (0.92 to 1.12)  | 40.3 (20.5, 80.1) |

Total mortality

| Events | Hazard ratio (95 CI) | Median (IQR) |
|--------|----------------------|--------------|
| No (%) |                      |              |
| Base model | 1.00 (reference)     | 20.7 (8.2, 26.8) |
| Minimally adjusted | 1.02 (0.91 to 1.16)  | 30.4 (18.5, 51.8) |
| Fully adjusted | 1.02 (0.91 to 1.16)  | 40.3 (20.5, 80.1) |
| Fully adjusted with medications | 1.02 (0.91 to 1.16)  | 58.8 (21.5, 160.7) |

Major CVD

| Events | Hazard ratio (95 CI) | Median (IQR) |
|--------|----------------------|--------------|
| No (%) |                      |              |
| Base model | 1.00 (reference)     | 20.7 (8.2, 26.8) |
| Minimally adjusted | 1.02 (0.90 to 1.16)  | 30.4 (18.5, 51.8) |
| Fully adjusted | 1.02 (0.90 to 1.16)  | 40.3 (20.5, 80.1) |
| Fully adjusted with medications | 1.02 (0.90 to 1.16)  | 58.8 (21.5, 160.7) |

Cox frailty model hazard ratios (HR) and 95% confidence intervals (CI): Base model: adjusted for age, sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; Fully adjusted: Minimally adjusted + refined grains, whole grains with centre as a random effect. Fully adjusted with medications: Fully adjusted + medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range.
Table S13: Association between refined grain intake and clinical outcomes (N=135 260) without baseline CVD adjusted for sodium and saturated fat

| Hazard ratio (95% CI) | Hazard ratio (95% CI) | Hazard ratio (95% CI) | Hazard ratio (95% CI) | Hazard ratio (95% CI) | Hazard ratio (95% CI) | P trend |
|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|---------|
|                        | <50 g/d (n=35 665)   | 50-150 g/d (n=44 015) | 150-250 g/d (n=25 507) | 250-350 g/d (n=12 133) | ≥350 g/d (n=17 940)   |         |
| Composite events       |                       |                       |                       |                       |                       |         |
| No (% events)          | 3903 (10.9)           | 3686 (8.4)            | 1938 (7.6)            | 1016 (8.4)            | 1778 (9.9)            | <0.001  |
| Fully adjusted         | 1.00 (reference)      | 1.07 (1.01 to 1.15)   | 1.11 (1.02 to 1.20)   | 1.15 (1.04 to 1.28)   | 1.26 (1.13 to 1.40)   | <0.001  |
| Total mortality        |                       |                       |                       |                       |                       |         |
| No (% events)          | 2703 (7.6)            | 2289 (5.2)            | 1122 (4.4)            | 532 (4.4)             | 878 (4.9)             |         |
| Fully adjusted         | 1.00 (reference)      | 1.04 (0.96 to 1.13)   | 1.08 (0.97 to 1.20)   | 1.03 (0.90 to 1.19)   | 1.24 (1.08 to 1.44)   | 0.01    |
| Non-CV mortality       |                       |                       |                       |                       |                       |         |
| No (% events)          | 1907 (5.4)            | 1564 (3.6)            | 812 (3.2)             | 375 (3.1)             | 530 (3.0)             | 0.004   |
| Fully adjusted         | 1.00 (reference)      | 1.08 (0.98 to 1.19)   | 1.20 (1.06 to 1.36)   | 1.12 (0.95 to 1.32)   | 1.32 (1.10 to 1.57)   | 0.01    |
| CV mortality           |                       |                       |                       |                       |                       |         |
| No (% events)          | 904 (2.5)             | 851 (1.9)             | 358 (1.4)             | 179 (1.5)             | 384 (2.1)             |         |
| Fully adjusted         | 1.00 (reference)      | 0.99 (0.86 to 1.14)   | 0.83 (0.70 to 1.00)   | 0.87 (0.69 to 1.09)   | 1.09 (0.86 to 1.37)   | 0.94    |
| Major CVD              |                       |                       |                       |                       |                       |         |
| No (% events)          | 1774 (5.0)            | 2000 (4.5)            | 1127 (4.4)            | 654 (5.4)             | 1233 (6.9)            | <0.001  |
| Fully adjusted         | 1.00 (reference)      | 1.10 (1.01 to 1.20)   | 1.12 (1.01 to 1.25)   | 1.23 (1.08 to 1.40)   | 1.30 (1.14 to 1.49)   | <0.001  |
| MI                     |                       |                       |                       |                       |                       |         |
| No (% events)          | 874(2.5)              | 983 (2.2)             | 485 (1.9)             | 229 (1.9)             | 360 (2.0)             | 0.37    |
| Fully adjusted         | 1.00 (reference)      | 1.08 (0.95 to 1.23)   | 1.05 (0.89 to 1.23)   | 1.09 (0.89 to 1.35)   | 1.12 (0.90 to 1.40)   | 0.37    |
| Stroke                 |                       |                       |                       |                       |                       |         |
| No (% events)          | 751 (2.1)             | 774 (1.8)             | 519 (2.0)             | 369 (3.0)             | 797 (4.4)             | <0.001  |
| Fully adjusted         | 1.00 (reference)      | 1.08 (0.95 to 1.24)   | 1.14 (0.97 to 1.33)   | 1.29 (1.07 to 1.55)   | 1.42 (1.18 to 1.72)   | <0.001  |
| Heart Failure          |                       |                       |                       |                       |                       |         |
| Events N (%)           | 129 (0.4)             | 244 (0.6)             | 150 (0.6)             | 57 (0.5)              | 72 (0.4)              |         |
| Fully adjusted         | 1.00 (reference)      | 1.23 (0.93 to 1.62)   | 1.61 (1.17 to 2.20)   | 1.48 (0.98 to 2.23)   | 1.23 (0.77 to 1.94)   | 0.13    |

Cox frailty model hazard ratios and 95% confidence intervals (CI): Fully adjusted: adjusted for age, sex, location (urban/rural, wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats and whole grains with centre as random effect.

IQR=interquartile range
Table S14: Association between whole grain intake and clinical outcomes (N=137 130) without baseline CVD adjusted for sodium and saturated fat

| Hazard ratio (95 %CI) | 0 (n=31 686) | <50 g/d (n=45 112) | 50-100 g/d (n=17 016) | ≥100 g/d (n=43 316) | P trend |
|----------------------|--------------|---------------------|-----------------------|---------------------|---------|
| Median (IQR)         | 0 (0-0)      | 17.3 (9.2-31.3)     | 73.6 (62.0-84.2)      | 226.8 (154.3-362.2) |         |
| **Composite**        |              |                     |                       |                     |         |
| No (% ) events       | 2717(8.6)    | 4484(9.9)           | 1455(8.6)             | 4012(9.3)           |         |
| Fully adjusted       | 1.03 (0.96 to 1.11) | 1.01 (0.95 to 1.08) | 1.05 (0.98 to 1.13)  | 1.00 (reference)    | 0.57    |
| **Total mortality**  |              |                     |                       |                     |         |
| No (% ) events       | 1518 (4.8)   | 2892 (6.4)          | 840 (4.9)             | 2571 (5.9)          |         |
| Fully adjusted       | 0.97 (0.88 to 1.08) | 0.95 (0.87 to 1.03) | 1.00 (0.91 to 1.11)  | 1.00 (reference)    | 0.38    |
| **Non-CV mortality** |              |                     |                       |                     |         |
| No (% ) events       | 1030 (3.3)   | 2023 (4.5)          | 570 (3.4)             | 1783 (4.1)          |         |
| Fully adjusted       | 0.94 (0.83 to 1.05) | 0.89 (0.81 to 0.98) | 0.97 (0.86 to 1.09)  | 1.00 (reference)    | 0.10    |
| **CV mortality**     |              |                     |                       |                     |         |
| No (% ) events       | 557 (1.8)    | 1008 (2.2)          | 300 (1.8)             | 912 (2.1)           |         |
| Fully adjusted       | 1.08 (0.92 to 1.26) | 1.06 (0.93 to 1.22) | 1.03 (0.87 to 1.22)  | 1.00 (reference)    | 0.33    |
| **Major CVD**        |              |                     |                       |                     |         |
| No (% ) events       | 1618 (5.1)   | 2243 (5.0)          | 853 (5.0)             | 2184 (5.0)          |         |
| Fully adjusted       | 1.04 (0.95 to 1.14) | 1.04 (0.96 to 1.12) | 1.07 (0.97 to 1.17)  | 1.00 (reference)    | 0.39    |
| **MI**               |              |                     |                       |                     |         |
| No (% ) events       | 651 (2.1)    | 1038 (2.3)          | 392 (2.3)             | 918 (2.1)           |         |
| Fully adjusted       | 1.11 (0.96 to 1.29) | 1.07 (0.94 to 1.21) | 1.13 (0.97 to 1.30)  | 1.00 (reference)    | 0.22    |
| **Stroke**           |              |                     |                       |                     |         |
| No (% ) events       | 852 (2.7)    | 950 (2.1)           | 383 (2.3)             | 1042 (2.4)          |         |
| Fully adjusted       | 1.06 (0.93 to 1.20) | 1.00 (0.89 to 1.12) | 1.02 (0.89 to 1.16)  | 1.00 (reference)    | 0.47    |
| **Heart Failure**    |              |                     |                       |                     |         |
| No (% ) events       | 109 (0.3)    | 243 (0.5)           | 99 (0.6)              | 205 (0.5)           |         |
| Fully adjusted       | 0.75 (0.54 to 1.04) | 1.19 (0.92 to 1.54) | 1.26 (0.95 to 1.68)  | 1.00 (reference)    | 0.24    |

Cox frailty model: Fully adjusted adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats, and refined grains with centre as a random effect.

IQR=interquartile range
Table S15: Association between white rice intake and clinical outcomes (N=137130) without baseline CVD adjusted for sodium and saturated fat

|                        | <50 g/d (n=38022) | 50-150 g/d (n=35617) | 150-300 g/d (n=16230) | 300-450 g/d (n=16045) | ≥450 g/d (n=31216) | P trend |
|------------------------|-------------------|----------------------|----------------------|----------------------|--------------------|---------|
| **Hazard ratio (95 CI)** |                   |                      |                      |                      |                    |         |
| Composite events       |                   |                      |                      |                      |                    |         |
| No (% events)          | 3437 (9.0)        | 2826 (7.9)           | 1393 (8.6)           | 1436 (9.0)           | 3576 (11.5)        |         |
| Fully adjusted         | 1.00 (reference)  | 1.00 (0.94 to 1.07)  | 1.01 (0.92 to 1.10)  | 0.97 (0.88 to 1.07)  | 0.95 (0.84 to 1.07) | 0.43    |
| Total mortality        |                   |                      |                      |                      |                    |         |
| No (% events)          | 2114 (5.6)        | 1698 (4.8)           | 784 (4.8)            | 867 (5.4)            | 2358 (7.6)         |         |
| Fully adjusted         | 1.00 (reference)  | 0.96 (0.88 to 1.05)  | 0.92 (0.82 to 1.04)  | 0.94 (0.82 to 1.06)  | 0.88 (0.76 to 1.03) | 0.12    |
| Non-CV mortality       |                   |                      |                      |                      |                    |         |
| No (% events)          | 1527 (4.0)        | 1191 (3.3)           | 513 (3.2)            | 570 (3.6)            | 1605 (5.1)         |         |
| Fully adjusted         | 1.00 (reference)  | 0.94 (0.85 to 1.04)  | 0.90 (0.77 to 1.04)  | 0.91 (0.78 to 1.06)  | 0.81 (0.68 to 0.98) | 0.04    |
| CV mortality           |                   |                      |                      |                      |                    |         |
| No (% events)          | 659 (1.7)         | 605 (1.7)            | 319 (2.0)            | 338 (2.1)            | 856 (2.7)          |         |
| Fully adjusted         | 1.00 (reference)  | 1.03 (0.89 to 1.20)  | 1.00 (0.82 to 1.22)  | 0.98(0.80 to 1.21)   | 1.02 (0.80 to 1.31) | 0.98    |
| Major CVD              |                   |                      |                      |                      |                    |         |
| CVD (%) events         | 1925 (5.1)        | 1598 (4.5)           | 851 (5.2)            | 824 (5.1)            | 1700 (5.5)         |         |
| Fully adjusted         | 1.00 (reference)  | 1.02 (0.94 to 1.11)  | 1.03 (0.92 to 1.16)  | 0.98 (0.86 to 1.11)  | 0.98 (0.84 to 1.15) | 0.80    |
| MI                     |                   |                      |                      |                      |                    |         |
| No (% events)          | 832 (2.2)         | 670 (2.0)            | 380 (2.3)            | 337 (2.1)            | 780 (2.5)          |         |
| Fully adjusted         | 1.00 (reference)  | 1.00 (0.87 to 1.14)  | 1.08 (0.91 to 1.29)  | 0.89 (0.73 to 1.08)  | 0.89 (0.70 to 1.13) | 0.32    |
| Stroke                 |                   |                      |                      |                      |                    |         |
| No (% events)          | 891 (2.3)         | 735 (2.1)            | 395 (2.4)            | 407 (2.5)            | 799 (2.6)          |         |
| Fully adjusted         | 1.00 (reference)  | 0.98 (0.87 to 1.10)  | 0.95 (0.81 to 1.11)  | 0.97 (0.81 to 1.16)  | 0.97 (0.78 to 1.21) | 0.71    |
| Heart Failure          |                   |                      |                      |                      |                    |         |
| No (% events)          | 193 (0.5)         | 198 (0.6)            | 75 (0.5)             | 79 (0.5)             | 111 (0.4)          |         |
| Fully adjusted         | 1.00 (reference)  | 1.47 (1.13 to 1.92)  | 1.34 (0.92 to 1.94)  | 1.37 (0.93 to 2.03)  | 1.21 (0.73 to 1.98) | 0.25    |

**Cox frailty model Fully adjusted**: adjusted for age, sex, location (urban/rural, wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats, whole grains, sodium and saturated fat with centre as random effect.

IQR=interquartile range
Table S16: Associations between refined grain intake and clinical outcomes excluding CVD events until 2 years of follow up

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| <50 g/d              | 18.5 (7.1-33.0) | 34018             | 34155            | 34017       | 1524      |
| 50 to <150 g/d       | 93.1 (72.1-119.0) | 42163             | 42369            | 42163       | 1668      |
| 150 to <250 g/d      | 186.0 (165.4-213.9) | 24666             | 24787            | 24666       | 952       |
| 250 to <350 g/d      | 300.0 (272.3-319.4) | 11739             | 11797            | 11739       | 574       |
| ≥350 g/d             | 500.9 (450.0-675.0) | 17567             | 17627            | 17567       | 1132      |

No, total included N

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| No (%) events        | 34018             | 42163             | 34155            | 34017       | 1524      |

Base model

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

Fully adjusted

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

Non-CV mortality

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| No (%) events        | 1759 (5.2) | 1371 (3.2) | 707 (1.7) | 786 (2.3) | 153 (1.3) | 1524 (4.5) |

Base model

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

Fully adjusted

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

CV mortality

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| No (%) events        | 786 (2.3) | 707 (1.7) | 301 (1.2) | 786 (2.3) | 153 (1.3) | 1524 (4.5) |

Base model

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

Fully adjusted

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

Major CVD

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| No (%) events        | 1524 (4.5) | 1668 (4.0) | 952 (3.9) | 1524 (4.5) | 574 (4.9) | 1132 (6.4) |

Base model

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |

Fully adjusted

| Hazard ratio (95 CI) | Median (IQR) | Composite events | Non-CV mortality | CV mortality | Major CVD |
|----------------------|--------------|------------------|------------------|-------------|-----------|
| Minimally adjusted  | 1.00 (reference) | 1.04 (0.95 to 1.13) | 1.06 (0.96 to 1.18) | 1.06 (0.96 to 1.18) | 1.00 (0.98 to 1.16) |
|                         | Fully adjusted | Fully adjusted with medications |
|-------------------------|----------------|---------------------------------|
|                         | 1.00 (reference) | 1.10 (1.00 to 1.21)             |
|                         | 1.13 (1.01 to 1.27) | 1.28 (1.11 to 1.47)            |
|                         | 1.35 (1.17 to 1.56) | <0.001                         |
| MI                      | 1.00 (reference) | 1.10 (1.00 to 1.21)             |
|                         | 1.14 (1.02 to 1.28) | 1.29 (1.12 to 1.48)            |
|                         | 1.36 (1.17 to 1.57) | <0.001                         |
| No, total included      | 34,082          | 42,280                          |
| No (%) events           | 740 (2.2)       | 822 (1.9)                       |
| Base model              | 1.00 (reference) | 1.07 (0.95 to 1.21)             |
| Minimally adjusted      | 1.10 (0.95 to 1.27) | 1.08 (0.91 to 1.29)            |
| Fully adjusted          | 1.00 (reference) | 1.10 (0.95 to 1.27)             |
| Fully adjusted with medications | 1.00 (reference) | 1.10 (0.96 to 1.27)             |
| MI                      | 1.00 (reference) | 1.10 (0.95 to 1.27)             |
| No, total included      | 34,093          | 42,274                          |
| No (%) events           | 650 (1.9)       | 639 (1.5)                       |
| Base model              | 1.00 (reference) | 1.03 (0.91 to 1.17)             |
| Minimally adjusted      | 1.00 (reference) | 1.07 (0.93 to 1.24)             |
| Fully adjusted          | 1.00 (reference) | 1.07 (0.93 to 1.23)             |
| Fully adjusted with medications | 1.00 (reference) | 1.07 (0.93 to 1.23)             |
| Stroke                  | 1.00 (reference) | 1.16 (0.98 to 1.37)             |
| Heart Failure           | 1.00 (reference) | 1.16 (0.98 to 1.37)             |
| No, total included      | 34,150          | 42,345                          |
| No (%) events           | 116 (0.3)       | 212 (0.5)                       |
| Base model              | 1.00 (reference) | 1.16 (0.91 to 1.50)             |
| Minimally adjusted      | 1.00 (reference) | 1.16 (0.87 to 1.55)             |
| Fully adjusted          | 1.00 (reference) | 1.17 (0.87 to 1.56)             |
| Fully adjusted with medications | 1.00 (reference) | 1.17 (0.87 to 1.56)             |

Cox frailty model: Base model: adjusted for age, sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; Fully adjusted: Minimally adjusted + whole grains with centre as a random effect; Fully adjusted with medications: Fully adjusted + medications (statins and blood pressure) with centre as a random effect. 

IQR=interquartile range
Table S17: Associations between whole grain intake and clinical outcomes excluding CVD events until 2 years of follow up

|                         | Hazard ratio (95 CI)                                                                 | P trend |
|-------------------------|--------------------------------------------------------------------------------------|---------|
|                         | 0 | <50 g/d | 50 to <100 g/d | ≥100 g/d |          |
| Median (IQR)            |   |         |              |          |          |
| Composite events        |          |          |              |          |          |
| No, total included      | 30 510 | 43 553  | 16 384          |
| No (%) events           | 2317 (7.6) | 3980 (9.1) | 1277 (7.8) | 3478 (8.4) |
| Base model              | 1.17 (1.09 to 1.25) | 1.09 (1.03 to 1.16) | 1.04 (0.97 to 1.12) | 1.00 (reference) | <0.001 |
| Minimally adjusted      | 1.06 (0.98 to 1.15) | 1.04 (0.97 to 1.11) | 1.06 (0.98 to 1.14) | 1.00 (reference) | 0.16 |
| Fully adjusted          | 1.05 (0.97 to 1.13) | 1.03 (0.96 to 1.10) | 1.06 (0.98 to 1.14) | 1.00 (reference) | 0.30 |
| Fully adjusted with medications | 1.05 (0.97 to 1.13) | 1.03 (0.96 to 1.10) | 1.05 (0.98 to 1.14) | 1.00 (reference) | 0.29 |
| Total mortality         |          |          |              |          |          |
| No, total included      | 30 653 | 43 762  | 16 457          |
| No (%) events           | 1310 (4.3) | 2636 (6.0) | 758 (4.6) | 2254 (5.4) |
| Base model              | 1.17 (1.07 to 1.28) | 1.06 (0.99 to 1.15) | 1.00 (0.91 to 1.09) | 1.00 (reference) | 0.001 |
| Minimally adjusted      | 0.99 (0.90 to 1.10) | 0.96 (0.88 to 1.04) | 1.01 (0.91 to 1.11) | 1.00 (reference) | 0.60 |
| Fully adjusted          | 0.97 (0.88 to 1.08) | 0.95 (0.87 to 1.03) | 0.99 (0.90 to 1.10) | 1.00 (reference) | 0.38 |
| Fully adjusted with medications | 0.97 (0.88 to 1.08) | 0.95 (0.87 to 1.03) | 0.99 (0.90 to 1.10) | 1.00 (reference) | 0.38 |
| Non-CV mortality        |          |          |              |          |          |
| No, total included      | 30 653 | 43 762  | 16 457          |
| No (%) events           | 899 (2.9) | 1870 (4.3) | 518 (3.2) | 1586 (3.8) |
| Base model              | 1.16 (1.04 to 1.29) | 1.04 (0.95 to 1.13) | 0.95 (0.85 to 1.06) | 1.00 (reference) | 0.01 |
| Minimally adjusted      | 0.95 (0.84 to 1.07) | 0.91 (0.82 to 1.01) | 0.97 (0.86 to 1.09) | 1.00 (reference) | 0.19 |
| Fully adjusted          | 0.91 (0.80 to 1.03) | 0.89 (0.80 to 0.98) | 0.95 (0.84 to 1.08) | 1.00 (reference) | 0.06 |
| Fully adjusted with medications | 0.91 (0.80 to 1.03) | 0.89 (0.80 to 0.98) | 0.95 (0.84 to 1.08) | 1.00 (reference) | 0.06 |
| CV mortality            |          |          |              |          |          |
| No, total included      | 30 653 | 43 762  | 16 457          |
| No (%) events           | 462 (1.5) | 888 (2.0) | 261 (1.6) | 767 (1.8) |
| Base model              | 1.23 (1.06 to 1.44) | 1.14 (1.00 to 1.29) | 1.06 (0.91 to 1.24) | 1.00 (reference) | 0.006 |
| Minimally adjusted      | 1.13 (0.95 to 1.34) | 1.09 (0.94 to 1.26) | 1.04 (0.87 to 1.24) | 1.00 (reference) | 0.14 |
| Fully adjusted          | 1.14 (0.96 to 1.35) | 1.10 (0.95 to 1.28) | 1.04 (0.87 to 1.25) | 1.00 (reference) | 0.12 |
| Fully adjusted with medications | 1.14 (0.96 to 1.36) | 1.10 (0.95 to 1.28) | 1.04 (0.87 to 1.24) | 1.00 (reference) | 0.11 |
| Major CVD               |          |          |              |          |          |
| No, total included      | 30 510 | 43 553  | 16 383          |
| No (%) events           | 1386 (4.5) | 1927 (4.4) | 746 (4.6) | 1891 (4.6) |
| Base model              | 1.14 (1.04 to 1.25) | 1.06 (0.98 to 1.15) | 1.08 (0.99 to 1.18) | 1.00 (reference) | 0.007 |
| Minimally adjusted      | 1.09 (0.99 to 1.20) | 1.05 (0.97 to 1.15) | 1.08 (0.98 to 1.20) | 1.00 (reference) | 0.11 |
| MI                | Fully adjusted | 1.09 (0.99 to 1.20) | 1.05 (0.96 to 1.15) | 1.08 (0.98 to 1.20) | 1.00 (reference) | 0.13 |
|-------------------|----------------|---------------------|---------------------|---------------------|-----------------|------|
|                   | Fully adjusted with medications | 1.09 (0.99 to 1.20) | 1.05 (0.96 to 1.15) | 1.08 (0.98 to 1.19) | 1.00 (reference) | 0.11 |
| No, total included| 30 593         | 43 664              | 16 423              | 41 590              |                 |      |
| No (%) events     | 537 (1.8)      | 880 (2.0)           | 339 (2.1)           | 787 (1.9)           |                 |      |
| Base model        | 1.15 (0.99 to 1.32) | 1.05 (0.93 to 1.19) | 1.14 (0.99 to 1.31) | 1.00 (reference)   | 0.16            |
| Minimally adjusted| 1.15 (0.98 to 1.35) | 1.08 (0.95 to 1.24) | 1.15 (0.99 to 1.34) | 1.00 (reference)   | 0.15            |
| Fully adjusted    | 1.15 (0.98 to 1.35) | 1.08 (0.94 to 1.24) | 1.15 (0.98 to 1.35) | 1.00 (reference)   | 0.15            |
| Fully adjusted with medications | 1.15 (0.98 to 1.35) | 1.08 (0.94 to 1.24) | 1.15 (0.98 to 1.35) | 1.00 (reference)   | 0.15            |
| Stroke            | 30 578         | 43 668              | 16 427              | 41 557              |                 |      |
| No (%) events     | 747 (2.4)      | 826 (1.9)           | 344 (2.1)           | 916 (2.2)           |                 |      |
| Base model        | 1.17 (1.04 to 1.32) | 1.06 (0.95 to 1.18) | 1.05 (0.92 to 1.20) | 1.00 (reference)   | 0.02            |
| Minimally adjusted| 1.11 (0.97 to 1.26) | 1.02 (0.90 to 1.15) | 1.05 (0.91 to 1.20) | 1.00 (reference)   | 0.19            |
| Fully adjusted    | 1.10 (0.97 to 1.25) | 1.01 (0.89 to 1.14) | 1.03 (0.90 to 1.19) | 1.00 (reference)   | 0.22            |
| Fully adjusted with medications | 1.10 (0.97 to 1.26) | 1.01 (0.89 to 1.14) | 1.03 (0.90 to 1.18) | 1.00 (reference)   | 0.20            |
| Heart Failure     | 30 645         | 43 739              | 16 447              | 41 632              |                 |      |
| No (%) events     | 98 (0.3)       | 218 (0.5)           | 85 (0.5)            | 172 (0.4)           |                 |      |
| Base model        | 0.93 (0.69 to 1.25) | 1.22 (0.96 to 1.56) | 1.23 (0.93 to 1.63) | 1.00 (reference)   | 0.10            |
| Minimally adjusted| 0.84 (0.60 to 1.18) | 1.30 (0.99 to 1.71) | 1.29 (0.95 to 1.75) | 1.00 (reference)   | 0.75            |
| Fully adjusted    | 0.81 (0.57 to 1.13) | 1.29 (0.98 to 1.70) | 1.29 (0.95 to 1.75) | 1.00 (reference)   | 0.59            |
| Fully adjusted with medications | 0.81 (0.58 to 1.14) | 1.29 (0.98 to 1.70) | 1.29 (0.95 to 1.75) | 1.00 (reference)   | 0.61            |

**Cox frailty model** : **Base model**: adjusted for age and sex with centre as a random effect; **Minimally adjusted**: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; **Fully adjusted**: Minimally adjusted+ refined grains, with centre as a random effect; **Fully adjusted with medications**: Fully adjusted +medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range
Table S18: Associations between white rice intake and clinical outcomes excluding CVD events until 2 years of follow up

| Median (IQR)                                    | <50 g/d          | 50 to <150 g/d | 150 to <300 g/d | 300 to <450 g/d | ≥450 g/d          | P trend |
|-------------------------------------------------|------------------|----------------|------------------|-----------------|------------------|---------|
| No (%) events included                          | 36 904           | 34 474         | 15 498           | 15 224          | 29834            |         |
| Base model (reference)                          | 1.00             | 0.90 (0.85 to 0.95) | 0.84 (0.78 to 0.92) | 0.86 (0.79 to 0.94) | 0.80 (0.73 to 0.87) | <0.001  |
| Minimally adjusted                              | 1.00             | 1.00 (0.93 to 1.07) | 0.97 (0.89 to 1.07) | 0.95 (0.86 to 1.05) | 0.86 (0.77 to 0.96) | 0.01    |
| Fully adjusted                                  | 1.00             | 1.01 (0.94 to 1.08) | 1.02 (0.93 to 1.12) | 0.99 (0.90 to 1.10) | 0.96 (0.86 to 1.09) | 0.65    |
| Fully adjusted with medications                 | 1.00             | 1.01 (0.94 to 1.08) | 1.02 (0.93 to 1.12) | 0.99 (0.89 to 1.10) | 0.96 (0.85 to 1.08) | 0.62    |

Total mortality

| No (%) events included                          | 37 079           | 34 618         | 15 563           | 15 285          | 29 974            |         |
| Base model (reference)                          | 1.00             | 0.85 (0.79 to 0.92) | 0.77 (0.69 to 0.86) | 0.83 (0.74 to 0.93) | 0.79 (0.71 to 0.89) | <0.001  |
| Minimally adjusted                              | 1.00             | 0.97 (0.88 to 1.06) | 0.89 (0.78 to 1.00) | 0.91 (0.80 to 1.04) | 0.82 (0.72 to 0.94) | 0.008   |
| Fully adjusted                                  | 1.00             | 0.98 (0.89 to 1.07) | 0.93 (0.81 to 1.05) | 0.95 (0.83 to 1.09) | 0.91 (0.78 to 1.06) | 0.26    |
| Fully adjusted with medications                 | 1.00             | 0.98 (0.89 to 1.07) | 0.92 (0.81 to 1.05) | 0.95 (0.83 to 1.09) | 0.91 (0.78 to 1.06) | 0.25    |

Non-CV mortality

| No (%) events included                          | 37 079           | 34 618         | 15 563           | 15 285          | 29 974            |         |
| Base model (reference)                          | 1.00             | 0.85 (0.78 to 0.94) | 0.75 (0.66 to 0.85) | 0.83 (0.72 to 0.95) | 0.74 (0.65 to 0.85) | <0.001  |
| Minimally adjusted                              | 1.00             | 0.95 (0.85 to 1.06) | 0.87 (0.75 to 1.01) | 0.90 (0.77 to 1.05) | 0.75 (0.64 to 0.89) | 0.002   |
| Fully adjusted                                  | 1.00             | 0.96 (0.86 to 1.07) | 0.91 (0.78 to 1.07) | 0.94 (0.80 to 1.11) | 0.85 (0.70 to 1.02) | 0.12    |
| Fully adjusted with medications                 | 1.00             | 0.96 (0.86 to 1.07) | 0.91 (0.78 to 1.06) | 0.94 (0.80 to 1.11) | 0.84 (0.70 to 1.02) | 0.12    |

CV mortality

| No (%) events included                          | 37 079           | 34 618         | 15 563           | 15 285          | 29 974            |         |
| Base model (reference)                          | 1.00             | 0.85 (0.75 to 0.98) | 0.85 (0.71 to 1.00) | 0.85 (0.70 to 1.02) | 0.93 (0.77 to 1.13) | 0.36    |
| Minimally adjusted                              | 1.00             | 1.03 (0.88 to 1.21) | 0.96 (0.78 to 1.18) | 0.96 (0.78 to 1.19) | 0.99 (0.78 to 1.24) | 0.79    |
| Fully adjusted                                  | 1.00             | 1.05 (0.90 to 1.23) | 1.00 (0.81 to 1.24) | 0.99 (0.79 to 1.24) | 1.07 (0.83 to 1.38) | 0.75    |
| Fully adjusted with medications                 | 1.00             | 1.06 (0.90 to 1.24) | 1.00 (0.81 to 1.24) | 0.99 (0.79 to 1.23) | 1.07 (0.83 to 1.39) | 0.77    |

Major CVD
Cox frailty model hazard ratios (HR) and 95% confidence intervals (CI): Base model: adjusted for age, sex with centre as random effect; Minimally adjusted: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, dairy and red meats with centre as a random effect; Fully adjusted: Minimally adjusted + refined grains, whole grains with centre as a random effect. Fully adjusted with medications: Fully adjusted + medications (statins and blood pressure) with centre as a random effect.

IQR=interquartile range

Table S19: Association between refined grain and whole grain intakes in servings per day* and clinical outcomes
| Outcomes          | Refined grains (servings/d) | Whole Grain (Servings/day) |
|-------------------|-----------------------------|---------------------------|
|                   | No (%) events | Hazard ratio (95% C.I) | P-Value | No (%) events | Hazard ratio (95% C.I) | P-Value |
| Composite events  |               |                         |         |               |                         |         |
| Fully adjusted    | 11 968 (9.15) | 1.02 (1.01 to 1.03)   | <0.001  | 12 526 (9.37) | 1.00 (0.98 to 1.01)   | 0.60    |
| Total mortality   |               |                         |         |               |                         |         |
| Fully adjusted    | 7264 (5.55)   | 1.02 (1.00 to 1.03)   | 0.01    | 7737 (5.79)   | 1.01 (0.98 to 1.03)   | 0.58    |
| Non-CV mortality  |               |                         |         |               |                         |         |
| Fully adjusted    | 4984 (3.81)   | 1.02 (1.00 to 1.04)   | 0.01    | 5359 (4.01)   | 1.01 (0.98 to 1.03)   | 0.65    |
| CV mortality      |               |                         |         |               |                         |         |
| Fully adjusted    | 2615 (2.00)   | 1.01 (0.99 to 1.03)   | 0.49    | 2740 (2.05)   | 1.00 (0.97 to 1.04)   | 0.81    |
| Major CVD         |               |                         |         |               |                         |         |
| Fully adjusted    | 6648 (5.08)   | 1.02 (1.01 to 1.03)   | 0.002   | 6799 (5.08)   | 0.99 (0.97 to 1.01)   | 0.45    |
| MI                |               |                         |         |               |                         |         |
| Fully adjusted    | 2840 (2.17)   | 1.01 (0.99 to 1.03)   | 0.56    | 2953 (2.21)   | 0.98 (0.95 to 1.01)   | 0.20    |
| Stroke            |               |                         |         |               |                         |         |
| Fully adjusted    | 3168 (2.42)   | 1.03 (1.01 to 1.05)   | <0.001  | 3179 (2.38)   | 1.02 (0.98 to 1.06)   | 0.34    |
| Heart Failure     |               |                         |         |               |                         |         |
| Fully adjusted    | 646 (0.49)    | 1.01 (0.97 to 1.05)   | 0.65    | 649 (0.49)    | 0.95 (0.88 to 1.02)   | 0.17    |

*Servings per day considered as a continuous variable

Cox frailty model: **Fully adjusted**: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats and whole grains for refined grains, refined grains for whole grains and refined and whole grains for rice to with centre as a random effect.
Table S20: Associations between refined grain intake and clinical outcomes in high, middle, and low income countries

|                      | Hazard ratio (95 %CI) |
|----------------------|-----------------------|
|                      | <50 g/d | 50-150 g/d | 150-250 g/d | 250-350 g/d | ≥350 g/d |
| **High-income countries** |          |           |            |             |          |
| Number               | 2961   | 8368     | 3299       | 821         | 357      |
| Median (IQR)         | 32.3 (20.4-41.6) | 92.8 (71.7-118.9) | 183.4 (165.7-208.2) | 283.1 (265.8-309.6) | 402.9 (370.8-447.4) |
| Composite events     |          |           |            |             |          |
| No (%) events        | 187 (6.3) | 462 (5.5) | 171 (5.2) | 37 (4.5) | 20 (5.6) |
| Fully adjusted       | 1.00 (reference) | 1.01 (0.83 to 1.22) | 1.07 (0.82 to 1.38) | 0.99 (0.64 to 1.52) | 1.44 (0.84 to 2.46) |
| Total mortality      |          |           |            |             |          |
| No (%) events        | 81 (2.7) | 217 (2.6) | 85 (2.6) | 16 (1.9) | 11 (3.1) |
| Fully adjusted       | 1.00 (reference) |          |           |           |          |
| **Middle-income countries** |          |           |            |             |          |
| Number               | 14 731  | 26 257  | 20 210    | 11 018    | 17 435   |
| Median (IQR)         | 24.6 (11.8-36.9) | 95.3 (73.4-120.0) | 187.3 (165.8-215.4) | 300.6 (273.8-320.0) | 506.1 (450.0-675.0) |
| Composite events     |          |           |            |             |          |
| No (%) events        | 1064 (7.2) | 2087 (7.9) | 1558 (7.7) | 946 (8.6) | 1741 (10.0) |
| Fully adjusted       | 1.00 (reference) | 1.16 (1.06 to 1.27) | 1.23 (1.12 to 1.37) | 1.28 (1.14 to 1.44) | 1.37 (1.21 to 1.56) |
| Total Mortality      |          |           |            |             |          |
| No (%) events        | 626 (4.2) | 1284 (4.9) | 898 (4.4) | 493 (4.5) | 854 (4.9) |
| Fully adjusted       | 1.00 (reference) | 1.09 (0.97 to 1.23) | 1.14 (1.00 to 1.31) | 1.08 (0.92 to 1.27) | 1.23 (1.03 to 1.46) |
| Major CVD            |          |           |            |             |          |
| No (%) events        | 569 (3.9) | 1129 (4.3) | 917 (4.5) | 612 (5.6) | 1214 (7.0) |
| Fully adjusted       | 1.00 (reference) | 1.23 (1.09 to 1.38) | 1.32 (1.16 to 1.51) | 1.47 (1.26 to 1.71) | 1.59 (1.35 to 1.86) |
| **Low-income countries** |          |           |            |             |          |
| Number               | 17 973  | 9390     | 1998  | 294    | 148     |
| Median (IQR)         | 11.4 (4.1-24.6) | 87.4 (68.1-112.6) | 179.6 (162.4, 205.3) | 279.1 (262.0, 306.8) | 464.9 (391.3, 625.3) |
| Composite events     |          |           |            |             |          |
| No (%) events        | 2652 (14.8) | 1137 (12.1) | 209 (10.5) | 33 (11.2) | 17 (11.5) |
| Fully adjusted       | 1.00 (reference) | 1.00 (0.89 to 1.12) | 0.91 (0.75 to 1.10) | 0.97 (0.63 to 1.49) | 1.23 (0.73 to 2.06) |
| Total Mortality | Events N (%) | 1996 (11.1) | 788 (8.4) | 139(7.0) | 23(7.8) | 13(8.8) |
|----------------|--------------|-------------|----------|----------|---------|---------|
| Fully adjusted | 1.00 (reference) | 0.95 (0.83 to 1.08) | 0.91 (0.72 to 1.14) | 0.94 (0.55 to 1.58) | 1.42 (0.79 to 2.54) |

| Major CVD | Events N (%) | 1090 (6.1) | 583 (6.2) | 110 (5.5) | 15 (5.1) | 8 (5.4) |
|-----------|--------------|------------|----------|----------|---------|--------|
| Fully adjusted | 1.00 (reference) | 0.93 (0.78 to 1.10) | 0.75 (0.57 to 0.99) | 0.77 (0.42 to 1.39) | 1.03 (0.48 to 2.22) |

*Insufficient events reported, hazard ratio not estimable

**Cox frailty model :Fully adjusted**: adjusted for age, sex, location (urban/rural, wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats and whole grains with centre as random effect.

IQR=interquartile range
Table S21: Associations between whole grain intake and clinical outcomes in high, middle, and low income countries

|                          | Hazard ratio (95%CI) | P trend |
|--------------------------|----------------------|---------|
|                          | 0    | <50 g/d | 50-100 g/d | ≥100 g/d |
| **High-income countries**|      |         |            |         |
| Number                   | 488  | 5069    | 4075       | 6174    |
| Median (IQR)             | 0 (0-0) | 26.0 (13.7-37.4) | 71.1 (60.8-75.0) | 177.8 (132.0-254.4) |
| **Composite events**     |      |         |            |         |
| No (%) events            | 27 (5.5) | 273 (5.4) | 215 (5.3) | 362 (5.9) |
| Fully adjusted           | 1.04 (0.66 to 1.62) | 1.01 (0.83 to 1.23) | 0.98 (0.81 to 1.19) | 1.00 (reference) |
| **Total mortality**      |      |         |            |         |
| No (%) events            | 12 (2.5) | 121 (2.4) | 99 (2.4) | 178 (2.9) |
| Fully adjusted*          | 1.00 (reference) |
| **Middle-income countries** |     |         |            |         |
| Number                   | 28 680 | 28 252 | 9210       | 23 509  |
| Median (IQR)             | 0 (0-0) | 16.6 (9.2-31.3) | 75.0 (65.3-84.2) | 218.8 (144.2-348.6) |
| **Composite events**     |      |         |            |         |
| No (%) events            | 2271 (7.9) | 2225 (7.9) | 765 (8.3) | 2135 (9.1) |
| Fully adjusted           | 1.00 (0.92 to 1.08) | 1.01 (0.93 to 1.09) | 1.06 (0.97 to 1.17) | 1.00 (reference) |
| **Total mortality**      |      |         |            |         |
| No (%) events            | 1263 (4.4) | 1291 (4.6) | 404 (4.4) | 1197 (5.1) |
| Fully adjusted           | 0.97 (0.87 to 1.09) | 0.97 (0.87 to 1.08) | 1.08 (0.95 to 1.23) | 1.00 (reference) |
| **Major CVD**            |      |         |            |         |
| No (%) events            | 1353 (4.7) | 1315 (4.7) | 493 (5.4) | 1280 (5.4) |
| Fully adjusted           | 1.02 (0.92 to 1.13) | 1.04 (0.94 to 1.14) | 1.05 (0.94 to 1.17) | 1.00 (reference) |
| **Low-income countries** |     |         |            |         |
| Number                   | 2518 | 11 791 | 3731       | 13 633  |
| Median (IQR)             | 0 (0-0) | 14.5 (5.9-28.9) | 70.4 (59.3-83.5) | 273.7 (190.0-426.7) |
| Composite events |  |  |  |  |
|------------------|-----------------|-----------------|-----------------|-----------------|
| No (%) events    | 419 (16.6)      | 1986 (16.8)     | 475 (12.7)      | 1515 (11.1)     |
| Fully adjusted   | 1.31 (1.08 to 1.59) | 1.11 (0.97 to 1.26) | 1.14 (0.98 to 1.33) | 1.00 (reference) |

| Total mortality |  |  |  |  |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| No (%) events   | 243 (9.7)       | 1480 (12.6)     | 337 (9.0)       | 1196 (8.8)      |
| Fully adjusted  | 1.25 (0.99 to 1.58) | 1.05 (0.90 to 1.22) | 1.01 (0.84 to 1.21) | 1.00 (reference) |

| Major CVD       |  |  |  |  |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| No (%) events   | 248 (9.8)       | 748 (6.3)       | 229 (6.1)       | 691 (5.1)       |
| Fully adjusted  | 1.11 (0.84 to 1.47) | 1.06 (0.86 to 1.30) | 1.19 (0.95 to 1.50) | 1.00 (reference) |

*Insufficient events reported, hazard ratio not estimable*

**Cox frailty model : Fully adjusted**: adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats, and refined grains with centre as a random effect.

IQR=interquartile range
Table S22: Associations between white rice intake and clinical outcomes in high-, middle- and low-income countries

|                      | <50 g/d | 50-150 g/d | 150-300 g/d | 300-450 g/d | ≥450 g/d | P trend |
|----------------------|---------|------------|-------------|-------------|---------|---------|
| **High-income countries** |         |            |             |             |         |         |
| Number               | 11 059  | 4315       | 420         | 12          | 0       |         |
| Median (IQR)         | 17.9 (8.2-26.8) | 79.0 (62.5-89.3) | 197.5 (187.5-210.5) | 374.3 (337.6-375.0) |         |         |
| **Composite events** |         |            |             |             |         |         |
| No (% events)        | 684 (6.2) | 180 (4.2)  | 12 (2.9)    | 1 (8.3)     |         | 0.083   |
| Fully adjusted       | 1.00 (reference) | 0.82 (0.67 to 1.02) | 0.73 (0.37 to 1.42) | 4.75 (0.64 to 35.08) |         |         |
| **Total mortality**  |         |            |             |             |         |         |
| No (% events)        | 319 (2.9)  | 85 (2.0)   | 5 (1.2)     | 1 (8.3)     |         |         |
| Fully adjusted*      | 1.00 (reference) |         |            |             |         |         |
| **Middle-income countries** |         |            |             |             |         |         |
| Number               | 20 280  | 27 867     | 13 678      | 13 451      | 14 375  |         |
| Median (IQR)         | 22.6 (6.6-28.6) | 85.7 (67.7-120.8) | 200.0 (171.4-214.3) | 395.0 (327.5-400.0) | 750.0 (600.0-904.1) |         |
| **Composite**        |         |            |             |             |         |         |
| No (% events)        | 1952 (9.6) | 2307 (8.3) | 1115 (8.2)  | 1057 (7.9)  | 965 (6.7) |         |
| Fully adjusted       | 1.00 (reference) | 1.02 (0.94 to 1.09) | 0.99 (0.89 to 1.09) | 0.98 (0.88 to 1.10) | 0.88 (0.75 to 1.02) | 0.239   |
| **Total Mortality**  |         |            |             |             |         |         |
| No (% events)        | 1130 (5.6) | 1358 (4.9) | 573 (4.2)   | 587 (4.4)   | 507 (3.5) |         |
| Fully adjusted       | 1.00 (reference) | 0.96 (0.87 to 1.06) | 0.86 (0.75 to 0.99) | 0.91 (0.78 to 1.05) | 0.79 (0.64 to 0.97) | 0.037   |
| **Major CVD**        |         |            |             |             |         |         |
| No (% events)        | 1170 (5.8) | 1303 (4.7) | 713 (5.2)   | 670 (5)     | 585 (4.1) |         |
| Fully adjusted       | 1.00 (reference) | 1.03 (0.94 to 1.13) | 1.03 (0.91 to 1.17) | 1.01 (0.88 to 1.16) | 0.92 (0.76 to 1.10) | 0.708   |
| **Low-income countries** |         |            |             |             |         |         |
| Number               | 6683    | 3435       | 2132        | 2582        | 16841   |         |
| Median (IQR)         | 19.54 (8.61-31.75) | 80.1 (67.1-103.56) | 192.83 (168.39-234.21) | 353.9 (325.39-395) | 948 (679.14-1083.99) |         |
| **Composite**        |         |            |             |             |         |         |
| No (% events)        | 801 (12)  | 339 (9.9)  | 266 (12.5)  | 378 (14.6)  | 2611 (15.5) |         |
| Fully adjusted       | 1.00 (reference) | 1.07 (0.88 to 1.29) | 1.18 (0.94 to 1.48) | 1.00 (0.79 to 1.27) | 1.09 (0.86 to 1.36) | 0.579   |
| **Total Mortality**  |         |            |             |             |         |         |
| No (%) events | 665 (10) | 255 (7.4) | 206 (9.7) | 279 (10.8) | 1851 (11) |
|---------------|----------|-----------|-----------|------------|-----------|
| Fully adjusted | 1.00 (reference) | 0.97 (0.78 to 1.22) | 1.11 (0.87 to 1.42) | 0.93 (0.73 to 1.19) | 0.97 (0.77 to 1.22) | 0.690 |
| **Major CVD** |          |           |           |            |           |         |
| No (%) events | 344 (5.1) | 175 (5.1) | 129 (6.1) | 153 (5.9)  | 1115 (6.6) |
| Fully adjusted | 1.00 (reference) | 1.13 (0.86 to 1.50) | 1.20 (0.85 to 1.70) | 0.93 (0.64 to 1.36) | 1.11 (0.78 to 1.58) | 0.520 |

* Insufficient events reported, hazard ratio not estimable

**Cox frailty model: Fully adjusted:** adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats, refined grains and whole grains with centre as a random effect.

IQR=interquartile range
Table S23: Association of refined grain intake with blood lipids and blood pressure

|                      | Refined grains |       |       |       |       |       |       |
|----------------------|----------------|-------|-------|-------|-------|-------|-------|
|                      | <50 g/d        | 50-150 g/d | 150-250 g/d | 250-350 g/d | ≥350 g/d | P trend |
|                      | (n=35665)      | (n=44015) | (n=25507) | (n=12133) | (n=17940) |
| Total cholesterol (mmol/l) | 4.68±1.04     | 5.02±1.05     | 5.00±1.02     | 4.90±1.02     | 4.64±0.95     | 0.38    |
| LDL-C (mmol/l)      | 2.93±0.95      | 3.21±0.98     | 3.14±0.93     | 3.01±0.90     | 2.82±0.83     | 0.19    |
| HDL-C (mmol/l)      | 1.19±0.36      | 1.24±0.35     | 1.21±0.32     | 1.20±0.31     | 1.14±0.30     | 0.05    |
| TC/HDL-C ratio      | 4.17±1.27      | 4.28±1.29     | 4.34±1.28     | 4.30±1.25     | 4.25±1.18     | 0.53    |
| Triglycerides (mmol/l) | 1.26±1.78     | 1.29±1.78     | 1.35±1.78     | 1.38±1.78     | 1.26±1.78     | 0.001   |
| ApoA (mmol/l)       | 1.40±0.33      | 1.52±0.31     | 1.51±0.29     | 1.51±0.29     | 1.50±0.29     | 0.04    |
| ApoB (mmol/l)       | 1.01±0.26      | 1.03±0.25     | 1.02±0.25     | 0.98±0.25     | 0.93±0.25     | 0.008   |
| ApoB/ApoA (mmol/l)  | 0.75±0.24      | 0.70±0.23     | 0.70±0.21     | 0.67±0.21     | 0.64±0.21     | 0.46    |
| Systolic blood pressure (mm Hg) | 128.5±22.8   | 131.2±22.3   | 131.7±21.8   | 133.9±22.4   | 135.5±22.5   | <0.001 |
| Diastolic blood pressure (mm Hg) | 81.1±14.6    | 82.0±17.5    | 81.7±14.4    | 82.7±14.1    | 83.5±13.1    | 0.001  |

All values of lipids and blood pressure are represented as mean ±SD. Analysis done using multilevel linear regression with random effect adjusted for age, sex, location (urban/rural), wealth index, education, smoking status, waist-hip ratio (WHR), physical activity, history of diabetes, intakes of energy (kcal), fruit and vegetable intake, red meat and whole grain intake.
Table S24: Association of whole grain intake with blood lipids and blood pressure

|                        | Whole grains | P trend |
|------------------------|--------------|---------|
|                        | 0 (n=31686)  | <50 g/d (n=45112) | 50-100 g/d (n=17016) | ≥100 g/d (n=43316) |         |
| Total cholesterol (mmol/l) | 4.86±1.03    | 4.93±1.06 | 4.94±1.02 | 4.75±1.01 | 0.54   |
| LDL-C (mmol/l)          | 3.02±0.92    | 3.13±0.99 | 3.13±0.94 | 2.95±0.92 | 0.15   |
| HDL-C (mmol/l)          | 1.18±0.32    | 1.21±0.34 | 1.24±0.35 | 1.21±0.35 | 0.001  |
| TC/HDL-C ratio          | 4.36±1.29    | 4.31±1.31 | 4.21±1.21 | 4.14±1.2  | 0.003  |
| Triglycerides (mmol/l)  | 1.32±1.82    | 1.32±1.78 | 1.26±1.78 | 1.26±1.78 | <0.001 |
| ApoA (mmol/l)           | 1.46±0.32    | 1.48±0.33 | 1.55±0.3  | 1.47±0.3  | 0.62   |
| ApoB (mmol/l)           | 1.00±0.24    | 1.04±0.25 | 1.03±0.25 | 0.97±0.26 | 0.09   |
| ApoB/ApoA (mmol/l)      | 0.72±0.23    | 0.73±0.24 | 0.69±0.21 | 0.68±0.21 | 0.25   |
| Systolic blood pressure (mm Hg) | 132.1±22.5 | 128.6±22.0 | 130.6±21.3 | 132.1±22.3 | 0.001  |
| Diastolic blood pressure (mm Hg) | 82.0±16.1 | 80.7±16.6 | 81.9±13.0 | 82.5±13.7 | 0.51   |

All values of lipids and blood pressure are represented as mean ±SD. Analysis done using multilevel linear regression with random effect adjusted for age, sex, location (urban/rural), wealth index, education, smoking status, waist-hip ratio (WHR), physical activity, history of diabetes, intakes of energy (kcal), fruit and vegetable intake, red meat and refined grain intake.
Table S25: Association of white rice intake with blood lipids and blood pressure

|                               | <50 g/d (n=38 022) | 50-150 g/d (n=35 617) | 150-300 g/d (n=16 230) | 300-450 g/d (n=16 045) | ≥450 g/d (n=31 216) | P trend |
|-------------------------------|-------------------|-----------------------|------------------------|------------------------|---------------------|---------|
| Total cholesterol (mmol/l)    | 4.96±1.07         | 4.85±1.03             | 4.88±1                  | 4.96±1.02              | 4.66±1.01           | 0.001   |
| LDL-C (mmol/l)                | 3.07±0.93         | 3.01±0.9              | 3.05±0.9                | 3.12±0.94              | 3.02±1.05           | 0.01    |
| HDL-C (mmol/l)                | 1.26±0.36         | 1.17±0.32             | 1.18±0.31               | 1.2±0.31               | 1.17±0.34           | <0.001  |
| TC/HDL-C ratio                | 4.18±1.31         | 4.36±1.28             | 4.33±1.21               | 4.32±1.2               | 4.19±1.24           | <0.001  |
| Triglycerides (mmol/l)        | 1.26±1.82         | 1.35±1.82             | 1.35±1.74               | 1.38±1.78              | 1.20±1.74           | <0.001  |
| ApoA (mmol/l)                 | 1.52±0.3          | 1.48±0.3              | 1.5±0.31                | 1.5±0.32               | 1.36±0.34           | <0.001  |
| ApoB (mmol/l)                 | 1.01±0.25         | 0.98±0.26             | 1.02±0.24               | 1.03±0.25              | 1.01±0.26           | 0.09    |
| ApoB/ApoA (mmol/l)            | 0.68±0.2          | 0.69±0.22             | 0.71±0.23               | 0.71±0.23              | 0.79±0.26           | <0.001  |
| Systolic blood pressure (mm Hg)| 133.5±22.4        | 131.8±22.3            | 131.8±21.9              | 132.0±23.3             | 127.6±22.2          | 0.02    |
| Diastolic blood pressure (mm Hg)| 82.9±13.8        | 82.15±13.82           | 82.33±15.64             | 82.2±22.85             | 80.08±13.3          | 0.03    |

All values of lipids and blood pressure are represented as mean ±SD. Analysis done using multilevel linear regression with random effect adjusted for age to sex to location (urban/rural) to wealth index to education to smoking status to waist-hip ratio (WHR) to physical activity to history of diabetes to intakes of energy (kcal) fruit and vegetable intake to nuts to refined and whole grain intake.
Table S26: Intake of food groups by categories of refined grain intake

| Dietary Intake (g/d) | <50          | 50-150       | 150-250      | 250-350      | >=350        |
|----------------------|--------------|--------------|--------------|--------------|--------------|
| Fruits               | 72.2 (25.2,195.5) | 189.7 (76.1,392.2) | 210.9 (93.1,383.9) | 166.6 (70.9,337.8) | 126.2 (59.4,235.3) |
| Vegetables           | 194.0 (72.7,262.4) | 250.2 (140.0,378.1) | 250.0 (158.2,290.6) | 250.0 (155.8,264.3) | 250.0 (200.0,262.1) |
| Dairy                | 64.7 (0.0,240.0) | 131.4 (21.5,291.3) | 153.6 (26.6,298.6) | 102.9 (6.6,243.0)  | 38.2 (0.0,240.0)  |
| Red Meat             | 15.7 (0.8,51.0)  | 40.7 (13.1,82.8)  | 56.6 (21.0,113.1) | 53.6 (19.7,116.4) | 40.0 (14.3,100.0) |
| Nuts                 | 3.4 (0.0,17.1)   | 6.4 (0.2,21.8)    | 11.1 (1.3,37.5)   | 21.8 (2.7,64.2)   | 21.8 (4.9,57.1)   |
| Sweets               | 16.8 (2.9,56.6)  | 60.4 (14.5,204.0) | 74.9 (14.8,204.0) | 50.5 (7.1,193.2)  | 19.2 (0.8,85.7)   |
| Eggs                 | 7.1 (0.8,22.9)   | 19.6 (7.8,33.6)   | 25.5 (14.1,46.8)  | 31.4 (16.5,51.3)  | 50.0 (21.4,58.6)  |
| Fish                 | 2.9 (0.0,20.3)   | 16.9 (3.3,41.1)   | 14.2 (3.9,40.5)   | 12.0 (2.6,36.7)   | 9.4 (0.0,26.3)    |
| Legumes              | 47.7 (17.3,104.0) | 42.5 (18.2,90.1)  | 34.4 (14.5,66.6)  | 28.6 (13.0,59.3)  | 21.4 (5.3,49.4)   |

Values presented as median (interquartile range (IQR) intake)
Table S27: Intake of food groups by categories of whole grain intake

| Dietary Intake (g/d) | 0          | <50        | 50-99      | >=100      |
|----------------------|------------|------------|------------|------------|
| Fruits               | 115.5 (44.4,257.4) | 143.4 (48.4,305.1) | 186.4 (75.0,393.2) | 154.1 (57.8,345.4) |
| Vegetables           | 249.3 (137.4,260.8) | 225.9 (115.7,279.8) | 251.4 (172.3,329.3) | 250.0 (119.2,307.0) |
| Dairy                | 34.1 (0.0,240.0) | 70.5 (9.5,243.9) | 160.9 (36.0,293.9) | 168.4 (32.2,300.1) |
| Red Meat             | 40.8 (13.2,100.0) | 31.9 (8.2,79.5) | 41.9 (13.1,83.8) | 35.2 (7.7,78.9) |
| Nuts                 | 6.6 (0.0,28.6) | 6.4 (0.0,21.8) | 10.0 (1.0,38.3) | 10.4 (0.2,43.2) |
| Sweets               | 30.8 (4.2,112.6) | 45.4 (6.2,151.6) | 35.7 (6.1,183.3) | 35.6 (7.9,129.6) |
| Eggs                 | 22.9 (9.1,46.0) | 18.1 (7.0,35.1) | 22.3 (8.7,46.8) | 21.4 (4.6,50.0) |
| Fish                 | 11.8 (0.0,36.7) | 12.9 (1.3,38.2) | 14.7 (2.2,35.4) | 8.2 (0.0,25.8) |
| Legumes              | 23.4 (6.6,48.2) | 42.4 (18.0,86.0) | 41.6 (18.5,81.8) | 45.9 (18.6,95.8) |

Values presented as Median (interquartile range (IQR) intake)
Supplementary figures

**Figure S1:** Association between refined grain intake and clinical outcomes (<25 kg/m² N=62 033, ≥ 25 kg/m² N=65 756). Cox frailty model hazard ratios (HR) and 95% confidence intervals (CI) performed in a model fully adjusted for age, sex, location (urban/rural), education, wealth index, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats and whole grains with centre as a random effect.

**Figure S2:** Association between whole grain intake and clinical outcomes (<25 kg/m² N=63 330, ≥ 25 kg/m² N=66 295). Cox frailty model hazard ratios (HR) and 95% confidence intervals (CI) performed in a model fully adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats and refined grains with centre as a random effect.

**Figure S3:** Association between white rice intake and clinical outcomes (<25 kg/m² N=63 330, ≥ 25 kg/m² N=66 295). Cox frailty model hazard ratios (HR) and 95% confidence intervals (CI) performed in a model fully adjusted for age, sex, location (urban/rural), wealth index, education, smoking, waist-hip ratio, physical activity, history of diabetes, daily intakes of energy (kcal), vegetable and fruits, red meats, refined grains and whole grains with centre as a random effect.

**Figure S4:** Meta-analysis of the association of grain intake with clinical outcomes by regions. (A) Analysis of refined grains intake with clinical events of composite events, total mortality and major CVD (B) Analysis of refined grains intake for 50 g increase on a continuous scale with clinical events of composite events, total mortality and major CVD (C) Analysis of whole grains intake with clinical events of composite events, total mortality and major CVD (D) Analysis of white rice intake with clinical events of composite events, total mortality and major CVD. Africa region has been excluded from all regional analysis due to the very small sample size. An estimate for total mortality with refined grain intake could not be obtained for South East Asia region.
Figure S1: Meta-analysis of the association of grain intake with clinical outcomes by regions
Figure S2: Association between refined grain intake and clinical outcomes (<25 kg/m² N=62,033, ≥ 25 kg/m² N=65,756)

|          | BMI<25 |         | BMI≥25 |         |
|----------|--------|---------|--------|---------|
|          |        | Composite events |        | Composite events |  
|          |        | Grains g/d |        | Grains g/d |  
| Outcome and Refined | HR (95% CI) |  | HR (95% CI) |  
| Composite events  |  
| <50 (Ref)         | 1.00 (1.00 to 1.00) |  | 1.00 (1.00 to 1.00) |  
| 50 to <150        | 1.07 (0.93 to 1.21) |  | 1.03 (0.91 to 1.21) |  
| 150 to <250       | 1.07 (0.95 to 1.26) |  | 1.10 (0.94 to 1.27) |  
| 250 to <350       | 1.15 (0.99 to 1.33) |  | 1.08 (0.87 to 1.30) |  
| ≥350              | 1.28 (1.11 to 1.49) |  | 1.33 (1.10 to 1.62) |  
| Total Mortality   |  
| <50 (Ref)         | 1.00 (1.00 to 1.00) |  | 1.00 (1.00 to 1.00) |  
| 50 to <150        | 1.02 (0.91 to 1.14) |  | 1.05 (0.91 to 1.23) |  
| 150 to <250       | 1.10 (0.94 to 1.26) |  | 0.99 (0.82 to 1.20) |  
| 250 to <350       | 1.08 (0.87 to 1.30) |  | 1.20 (0.94 to 1.53) |  
| ≥350              | 1.33 (1.10 to 1.62) |  | 1.42 (1.18 to 1.71) |  
| Major CVD         |  
| <50 (Ref)         | 1.00 (1.00 to 1.00) |  | 1.00 (1.00 to 1.03) |  
| 50 to <150        | 1.12 (0.99 to 1.27) |  | 1.09 (0.96 to 1.23) |  
| 150 to <250       | 1.08 (0.92 to 1.27) |  | 1.18 (1.02 to 1.38) |  
| 250 to <350       | 1.27 (1.05 to 1.54) |  | 1.24 (1.04 to 1.47) |  
| ≥350              | 1.20 (1.04 to 1.53) |  | 1.42 (1.18 to 1.71) |  


Figure S3: Association between whole grain intake and clinical outcomes (<25 kg/m$^2$ N=63 330, ≥ 25 kg/m$^2$ N=66 295)
Figure S4: Association between white rice intake and clinical outcomes (<25 kg/m² N=63 330, ≥ 25 kg/m² N=66 295).