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Systemic inflammation is associated with future risk of fatal infection: an observational cohort study

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Supplementary Table 1: Self-reported disease category definitions

NCD group	UK Biobank self-reported illnesses included
Hypertension	Hypertension Essential hypertension
Chronic cardiac disease	Angina Cardiomyopathy Heart attack/myocardial infarction heart failure/pulmonary oedema Hypertrophic cardiomyopathy Coronary angioplasty (ptca) +/- stent Coronary artery bypass grafts Triple heart bypass
Chronic respiratory disease	Asthma Bronchiectasis Chronic obstructive airways disease/COPD Emphysema Emphysema/chronic bronchitis Fibrosing alveolitis/unspecified alveolitis Interstitial lung disease Other chronic respiratory problems Pulmonary fibrosis
Diabetes	Diabetes Diabetic eye disease Diabetic nephropathy Diabetic neuropathy/ulcers Type 1 diabetes Type 2 diabetes
Cancer	Any cancer diagnosis during lifetime
Chronic liver disease	Liver failure/cirrhosis Non-infective hepatitis Oesophageal varices Primary biliary cirrhosis
Chronic kidney disease	Diabetic nephropathy Immunoglobulin A (IgA) nephropathy Kidney nephropathy Polycystic kidney Renal failure not requiring dialysis Renal failure requiring dialysis Renal/kidney failure
Prior stroke/TIA	Brain haemorrhage Ischaemic stroke Stroke Subarachnoid haemorrhage Transient ischaemic attack (TIA)
Other neurology disease	Cerebral palsy Epilepsy Motor neurone disease Multiple sclerosis Myasthenia gravis Parkinson's disease
Psychiatric disease	Depression Mania/bipolar disorder/manic depression Postnatal depression Schizophrenia
Chronic inflammatory and autoimmune rheumatic disease (Rheumatological disease)	Ankylosing spondylitis Dermatomyositis Dermatopolymyositis

	Giant cell/temporal arteritis Myositis/myopathy Polymyalgia rheumatica Polymyositis Psoriatic arthropathy Rheumatoid arthritis Sarcoidosis Scleroderma/systemic sclerosis Sjogren's syndrome/sicca syndrome Systemic lupus erythematosus Vasculitis
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All comorbidities are defined using self-reported illness at verbal nurse led interview (UK Biobank data fields 20002 and 20004). COPD, chronic obstructive pulmonary disease.

Supplementary Table 2: Non-steroidal anti-inflammatory and immunosuppressive medication definitions

Non-steroidal anti-inflammatory agents:

Code	Name
1140925806	aceclofenac
1141163014	acoflam 25mg e/c tablet
1140928656	advil 200mg tablet
1140871514	alrheumat 50mg capsule
1141180152	arcoxia 120mg tablet
1141180148	arcoxia 60mg tablet
1141180150	arcoxia 90mg tablet
1140871320	arthrofen 200 tablet
1140871492	arthrosin 250 tablet
1140927086	arthrotec 50 tablet
1140871266	arthrotec tablet
1140871556	arthroxen 250mg tablet
1140871344	artracin 25mg capsule
1141192804	bextra 10mg tablet
1141192808	bextra 20mg tablet
1141192812	bextra 40mg tablet
1141169530	brexidol 20mg tablet
1140871374	brufen 200mg tablet
1140871660	butacote 100mg e/c tablet
1140853022	butazolidin 100mg tablet
1140871662	butazone 100mg tablet
1141191742	calprofen 100mg/5ml s/f oral suspension
1141176668	celebrex 100mg capsule
1141176670	celebrex 200mg capsule
1141176662	celecoxib
1140856312	claradin 300mg tablet
1140871606	clinoril 100mg tablet
1141176886	closteril 100 m/r tablet
1140928844	clotam 200mg capsule
1141163126	condrotec tablet
1140871388	cuprofen 200mg tablet
1141190952	cuprofen plus tablet
1141181872	defanac 25mg e/c tablet
1140851754	defencin cp 40mg m/r capsule
1141164746	dexketoprofen
1141162950	dexomon sr 75mg m/r tablet
1140884488	diclofenac

1140921828 dicloflex 25mg e/c tablet
1140917394 diclomap sr 75mg m/r capsule
1141146404 diclotard 75 m/r tablet
1141157112 diclovol 25mg e/c tablet
1140871260 diclozip-25 e/c tablet
1141153330 difenor xl 100mg m/r tablet
1140871282 diflunisal
1141145626 digenac xl 100 m/r tablet
1140871284 dolobid 250mg tablet
1140871886 doloxene 65mg capsule
1140868262 doloxene compound capsule
1140871450 dysman-250 capsule
1141173776 ebretin 200mg capsule
1140871386 ebufac 200mg tablet
1141193170 eccoxolac 300mg capsule
1141191028 econac sr 75mg tablet
1140871188 etodolac
1141180140 etoricoxib
1140871672 feldene 10mg capsule
1141188522 feminax tablet
1141182674 fenactol 25mg e/c tablet
1140917074 fenoket 200mg m/r capsule
1140871226 fenoprofen
1140871228 fenopron 300mg tablet
1141182868 fenpaed 100mg/5ml s/f oral suspension
1141181112 feverfen 100mg/5ml s/f oral suspension
1141152674 flamatak mr 75mg m/r tablet
1140871590 flamatrol 10mg capsule
1140871276 flamrase 25mg e/c tablet
1141170824 flexin continus 25mg m/r tablet
1140871360 flexin-25 continus m/r tablet
1141146400 flexotard 100mg m/r tablet
1141156966 flexotard mr 100mg m/r tablet
1140871236 flurbiprofen
1140871238 froben 50mg tablet
1141165574 galprofen 100mg/5ml oral suspension
1140853090 ibular 200mg tablet
1140853094 ibumetin 200mg tablet
1140871310 ibuprofen
1141157412 ibuprofen product
1140878030 ibuprofen+codeine phosphate
1141164050 imazin xl 60mg/75mg m/r tablet
1140871348 imbrilon 25mg capsule

1140871354 indocid 25mg capsule
1140853108 indoflex 25mg capsule
1140853110 indolar 25mg capsule
1140871442 indomax 25 capsule
1140909936 indometacin
1141181656 indometacin product
1140871434 indomod 25mg m/r capsule
1140925868 inoven 200mg caplet
1140871392 isisfen 400mg tablet
1141150922 jomethid xl 200mg m/r capsule
1140871404 junifen 100mg/5ml s/f suspension
1141164750 keral 25mg tablet
1140916866 ketocid 200 m/r capsule
1140871532 ketonal 50mg capsule
1140871506 ketoprofen
1140884558 ketorolac
1140927756 ketotard 200 xl m/r capsule
1140871528 ketovail 100mg m/r capsule
1140917406 ketozip cr 200mg m/r capsule
1141168652 ketpron xl 100mg m/r capsule
1140856314 laboprin 300mg tablet
1140863514 laboprin dl 900mg sachet
1140888872 larafen cr 200mg m/r capsule
1140871396 lidifen 200mg tablet
1140871196 iodine 200mg tablet
1140921968 lofensaid 25 tablet
1141181752 mandafen 400mg tablet
1140871542 mefenamic acid
1140916806 meflam 250 capsule
1140926732 meloxicam
1140877864 migrafen 200mg tablet
1140926796 mobic 15mg tablet
1140926794 mobic 7.5mg tablet
1140875350 mobiflex 20mg tablet
1140853012 mobilan 25mg capsule
1140909354 motifene 75mg e/c+m/r capsule
1140871406 motrin 200mg tablet
1140875336 nabumetone
1140871472 naprosyn 250mg tablet
1140871462 naproxen
1140881612 naproxen+misoprostol
1141187776 nurofen 200mg tablet
1140871568 nycopren 250mg e/c tablet

1140922318 opustan 250mg capsule
1141182642 orbifen 100mg/5ml s/f oral suspension
1140871516 orudis 50mg capsule
1140871522 oruvail 100 m/r capsule
1140877862 pacifene 200mg tablet
1141153346 pardelprin mr 75mg m/r capsule
1141180126 parecoxib
1140853100 paxofen 200mg tablet
1140856212 paynocil 600mg tablet
1140871654 phenylbutazone product
1140921974 piroflam 10 capsule
1140871666 piroxicam
1140871582 pirozip 10 capsule
1140871546 ponstan 250mg capsule
1140871490 pranoxen continus 375mg m/r tablet
1140925808 preservex 100mg tablet
1140877856 proflex 200mg tablet
1140868330 progesic 200mg tablet
1140871628 prosaid 250mg tablet
1140853082 ramodar 200mg tablet
1140877858 relcofen 200mg tablet
1140875338 relifex 500mg tablet
1140871482 rheuflex-250 tablet
1140911098 rheumacin la 75mg m/r capsule
1141167426 rheumatac retard 75mg m/r tablet
1140871180 rhumalgan 25mg e/c tablet
1140868294 robaxisal forte tablet
1141165244 rofecoxib
1140856438 safapryn tablet
1140856440 safapryn-co tablet
1140853018 slo-indo 75mg m/r capsule
1141145722 slofenac sr 75mg m/r tablet
1140928266 solpaflex tablet
1140856214 solprin 300mg dispersible tablet
1140871604 sulindac
1140871616 surgam 200mg tablet
1140868336 synflex 275mg tablet
1140875346 tenoxicam
1140871614 tiaprofenic acid
1141199380 tiloket 50mg capsule
1141183944 tiloket cr 100mg m/r capsule
1140864412 timpron 250mg tablet
1140875270 tolectin 200mg capsule

1140853030 tolectin ds 400mg capsules
 1140928840 tolfenamic acid
 1140875268 tolmetin
 1140881118 toradol 10mg tablet
 1141192798 valdecoxib
 1141190644 valdic 75 retard 75mg m/r tablet
 1140871256 valenac 25mg e/c tablet
 1140871484 valrox 250mg tablet
 1141165252 vioxx 12.5mg tablet
 1141165312 vioxx 12.5mg/5ml oral suspension
 1141165254 vioxx 25mg tablet
 1141165314 vioxx 25mg/5ml oral suspension
 1141184290 vioxxacute 25mg tablet
 1141184292 vioxxacute 50mg tablet
 1140871248 volraman 25mg e/c tablet
 1140923920 volsaid retard 75mg m/r tablet
 1140871168 voltarol 25mg e/c tablet

Immunosuppressive agents (including glucocorticoids):

Code	Name
1140910598	5asa - mesalazine
1141188588	adalimumab
1141180066	anakinra
1141166306	arava 100mg tablet
1141166302	arava 10mg tablet
1141166304	arava 20mg tablet
1140865580	asacol 400mg e/c tablet
1141188658	asacol mr 400mg e/c tablet
1140875400	auranofin
1140874484	avloclor 250mg tablet
1140869930	azathioprine
1141153242	balsalazide disodium
1140874790	betamethasone
1140874792	betnelan 500mcg tablet
1140874794	betnesol 500mcg soluble tablet
1140862572	budesonide
1141157418	budesonide product
1141163032	calcort 1mg tablet
1140874482	chloroquine
1140912244	chloroquine 200mg tablet
1140912246	chloroquine 68mg/5ml syrup
1141153248	colazide 750mg capsule
1141173346	cortisone

1140884704 cortisone product
1140874810 cortistab 5mg tablet
1140874814 cortisyl 25mg tablet
1140874104 dapsone
1140874822 decadron 500micrograms tablet
1140868370 decortisyl 5mg tablet
1141145782 deflazacort
1140874936 deltacortril enteric 2.5mg e/c tablet
1140910634 deltahydrocortisone
1140874940 deltastab 1mg tablet
1140874816 dexamethasone
1141176842 dexsol 2mg/5ml oral solution
1140865742 dipentum 250mg capsule
1140926004 entocort cr 3mg m/r capsule
1140874784 florinef 100mcg tablet
1140884672 fludrocortisone
1140910424 hc - hydrocortisone
1141188594 humira 40mg injection solution 0.8ml prefilled syringe
1140874896 hydrocortisone
1141157294 hydrocortisone product
1140874954 hydrocortistab 20mg tablet
1140874956 hydrocortone 10mg tablet
1140884308 hydroxychloroquine
1141145996 imuran 10mg tablet
1141180070 kineret 100mg/0.67ml injection prefilled syringe
1140874978 medrone 2mg tablet
1140865578 mesalazine
1141189390 mesren mr 400mg m/r tablet
1140869848 methotrexate
1140874976 methylprednisolone
1140910036 mtx - methotrexate
1140879502 olsalazine
1140857534 oradexon 500micrograms tablet
1141156738 paludrine tablet+avloclor tablet 100mg/250mg travel pack
1140875316 penicillamine
1140865588 pentasa sr 250mg m/r tablet
1140875392 plaquenil 200mg tablet
1140874944 precortisyl 1mg tablet
1140874950 prednesol 5mg tablet
1140874930 prednisolone
1141157402 prednisolone product
1140868364 prednisone
1141156676 proguanil hydrochloride+chloroquine phosphate

1140875404 ridaura 3mg tablet
1141188196 ridaura tiltab 3mg tablet
1140865670 salazopyrin 500mg tablet
1140865598 salofalk 250mg e/c tablet
1140857672 sintisone 5mg tablet
1141188900 sulazine ec 500mg e/c tablet
1140909702 sulfasalazine
1140865668 sulphasalazine
1140868426 triamcinolone

Supplementary Table 3: Cardiovascular, infection and other causes of death definitions

Cardiovascular death:

I00-I99, excluding infection codes: [I32.0, I32.1, I33.0, I33.9, I38, I39, I40.0, I41.0-I41.2, I43.0, I52.0-I52.1, I68.1, I98.1]

Infection Death:

A00.0, A00.1, A00.9, A01.0-A01.4, A02.0-A02.2, A02.8, A02.9, A03.0-A03.3, A03.8, A03.9, A04.0-A04.9, A06.2, A06.4-A06.6, A07.0, A07.8, A07.9, A08.0-A08.4, A09.9, A15.0-A15.9, A16.0-A16.9, A17.0, A17.1, A17.8, A17.9, A18.0-A18.8, A19.0-A19.2, A19.8, A19.9, A20.0-A20.3, A20.7-A20.9, A21.0-A21.3, A21.7-A21.9, A22.0-A22.2, A22.7-A22.9, A23.0-A23.3, A23.8, A23.9, A24.0-A24.4, A25.0, A25.9, A26.7-A26.9, A27.0, A27.8, A27.9, A28.8, A28.9, A30.0-A30.5, A30.8, A30.9, A31.0, A31.1, A31.8, A31.9, A32.0, A32.1, A32.7-A32.9, A33.X, A34.X, A35.X, A36.0-A36.3, A36.8, A36.9, A37.0, A37.1, A37.8, A37.9, A39.0, A39.2-A39.5, A39.8, A39.9, A40.0-A40.3, A40.8, A40.9, A41.0, A41.0-A41.5, A41.8, A41.9, A42.0-A42.2, A42.7-A42.9, A46.X, A48.0, A48.8, A49.0-A49.3, A49.2, A49.8, A49.9, A54.0, A54.2-A54.4, A54.5, A54.6, A54.8, A54.9, A56.4, A57.X, A66.0-A66.4, A66.6-A66.9, A67.0-A67.3, A67.9, A68.0, A68.1, A68.9, A69.1, A70.X, A71.0, A71.1, A71.9, A74.0, A74.8, A74.9, A75.0-A75.3, A75.9, A77.0, A79.0, A79.8, A79.9, A80.9, A81.0, A81.8, A81.9, A82.0, A82.1, A82.9, A83.0, A83.6, A83.8, A83.9, A84.0, A84.8, A84.9, A85.0-A85.2, A85.8, A86.X, A87.0, A87.1, A87.2, A87.8, A87.9, A88.0, A88.8, A89.X, A90.X, A91.X, A92.0, A92.3, A92.8, A92.9, A93.0, A93.8, A94.X, A95.0, A95.1, A95.9, A96.0, A96.8, A96.9, A98.0, A98.3, A98.4, A98.8, A99.X, B00.0, B00.1, B00.2, B00.3-B00.5, B00.7-B00.9, B01.0, B01.1, B01.2, B01.8, B01.9, B02.0, B02.1, B02.2, B02.3, B02.7-B02.9, B03.X, B05.0, B05.1, B05.2, B05.3, B05.4, B05.8, B05.9, B06.0, B06.8, B06.9, B07.X, B08.0, B08.4, B08.5, B08.8, B09.X, B16.0-B16.2, B16.9, B17.0, B17.1, B17.8, B17.9, B18.0-B18.2, B18.8, B18.9, B19.0, B19.9, B25.0, B25.1, B25.2, B25.8, B25.9, B26.0, B26.1, B26.2, B26.3, B26.8, B26.9, B27.0, B27.1, B27.8, B27.9, B30.0-B30.2, B30.3, B30.8, B30.9, B33.0, B33.2-B33.4, B33.8, B34.0-B34.4 (exclude corona), B34.8, B34.9, B35.9, B36.8, B37.0-B37.9, B38.0-B38.4, B38.7-B38.9, B41.0, B41.7-B41.9, B43.1, B43.2, B44.0-B44.2, B44.7-B44.9, B45.0-B45.3, B45.7-B45.9, B46.8, B47.1, B48.7, B48.8, B50.0, B50.8,

B50.9, B51.0, B51.8, B51.9, B52.0, B52.8, B52.9, B53.0, B53.1, B53.8, B54.X, B55.0-
B55.2, B55.9, B56.0, B56.1, B56.9, B58.0-B58.3, B58.8, B58.9, B60.0, B60.8, B64.X,
B65.0-B65.2, B65.8, B65.9, B67.8, B67.9, B71.0, B71.8, B71.9, B76.1, B81.0, B81.4,
B81.8, B82.0, B82.9, B83.0, B83.8, B83.9, B85.0-B85.2, B85.4, B87.0-B87.4, B87.8,
B87.9, B88.0, B89.X, B91.X, B92.X, B94.0, B94.0, B94.1, B94.2, B94.8, B94.9, B95.0-
B95.8, B96.0-B96.2, B96.3, B96.4, B96.5, B96.7, B96.8, B97.0-B97.8, D47.5, D73.3,
E32.1, G00.0-G00.3, G00.8, G00.9, G01.X, G02.0, G02.1, G02.8, G03.0-G03.2,
G03.8, G03.9, G04.2, G05.0, G05.1, G05.2, G06.0-G06.2, G07X, G14.X, G53.0,
G53.1, G63.0, G73.1, G73.4, G93.3, G94.0, H03.0, H06.1, H10.0, H10.2, H10.3,
H10.4, H10.5, H10.8, H10.9, H13.0, H13.1, H13.2, H16.1, H16.2, H19.1, H19.2,
H19.3, H22.0, H32.0, H60.0, H60.1, H60.2, H60.3, H60.5, H60.8, H60.9, H62.0,
H62.1, H62.3, H62.4, H65.0, H65.1, H65.2-H65.4, H65.9, H66.0-H66.4, H66.9, H67.0,
H67.1, H67.8, H70.0, H70.1, H70.8, H70.9, H73.0, H73.1, H75.0, H94.0, I32.0, I32.1,
I41.0, I41.1, I41.2, I42.3, I43.0, I52.0, I52.1, I68.1, I98.1, J00.X, J01.0-J01.4, J01.8,
J01.9, J02.0, J02.8, J02.9, J03.0, J03.0, J03.8, J03.9, J06.0, J06.8, J06.9, J09.X,
J10.0, J10.0, J10.1, J10.8, J11.0, J11.1, J11.8, J12.0, J12.1, J12.2, J12.3, J12.8,
J12.9, J13X, J14X, J15.0- J15.9, J16.0, J16.8, J17.0, J17.1, J17.2, J17.3, J17.8,
J18.0-J18.2, J18.8, J18.9, J20.0, J20.1, J20.2, J20.3, J20.4, J20.5-J20.7, J21.0,
J21.1, J22.X, J31.0-J31.2, J32.0-J32.4, J32.8, J32.9, J34.0, J35.0, J36X, J39.0, J39.1,
J44.0, J65X, J85.0, J85.1, J85.2, J85.3, K04.6, K04.7, K11.3, K12.2, K23.0, K35.2,
K35.3, K35.8, K36.X, K37.X, K51.5, K52.3, K57.0, K57.1, K57.2, K57.3, K57.4, K57.5,
K57.8, K57.9, K61.0-K61.4, K63.0, K65.0, K65.8, K65.9, K67.0-K67.3, K75.0, K77.0,
K80.0-K80.5, K81.0, K81.1, K81.9, K83.0, K93.0, L00.X, L02.0-L02.4, L02.8, L02.9,
L03.0-L03.3, L03.8, L03.9, L05.0, L05.9, L92.2, L98.3, M00.0-M00.2, M00.8, M01,
M01.0, M01.1, M01.3, M01.4, M01.5, M01.6, M02.3, M03.0, M03.1, M35.4, M46.2,
M49.0-M49.2, M49.3, M63.0, M63.1, M65.0, M68.0, M71.0, M73.0, M86.0-M86.2,
M86.3-M86.6, M86.8, M86.9, M89.6, N08.0, N15.1, N16.0, N22.0, N29.1, N33.0,
N34.0, N35.1, N39.0, N41.2, N45.0, N45.9, N73.0, N73.1, N73.2, N73.3, N73.4,
N73.5, N74.0, N74.1, N75.1, N76.4, N77.0, N77.1, O26.4, O35.3, O75.3, O98.0,
O98.4, O98.5, O98.6, O98.8, O98.9, R57.2

Other

All other deaths not categorised as cardiovascular or infection

Supplementary Table 4: Characteristics of UK Biobank participants with missing CRP data

	CRP data available (461,052)	No CRP data available (32,200)
Age		
<45	47330 (10.3)	3364 (10.5)
45 to <50	60575 (13.1)	4276 (13.3)
50 to <55	70021 (15.2)	4918 (15.3)
55 to <60	83410 (18.1)	5845 (18.2)
60 to <65	111734 (24.2)	7631 (23.7)
65+	87982 (19.1)	6166 (19.2)
Sex		
Female	250435 (54.3)	18395 (57.1)
Male	210617 (45.7)	13805 (42.9)
Ethnicity		
White	437071 (94.8)	30091 (93.5)
Ethnic minority	23981 (5.2)	2109 (6.6)
SED quintile		
1 (least deprived)	92615 (20.1)	6074 (18.9)
2	92404 (20.0)	6209 (19.3)
3	92312 (20.0)	6341 (19.7)
4	92262 (20.0)	6387 (19.8)
5 (most deprived)	91459 (19.8)	7189 (22.3)
Smoking		
Never	252445 (54.8)	17763 (55.2)
Former	160153 (34.7)	10849 (33.7)
Current	48454 (10.5)	3588 (11.1)
Obesity		
Not obese	347843 (75.5)	23631 (73.4)
Class 1	81342 (17.6)	5867 (18.2)
Class 2	23015 (5.0)	1901 (5.9)
Class 3	8852 (1.9)	801 (2.5)
Hypertension	122101 (26.5)	8689 (27)
Chronic cardiac disease	21797 (4.7)	1668 (5.2)
Chronic respiratory disease	59587 (12.9)	4312 (13.4)
Diabetes	22992 (5.0)	1758 (5.5)
Cancer	37821 (8.2)	3185 (9.9)
Chronic liver disease	903 (0.2)	53 (0.2)
Chronic kidney disease	1175 (0.3)	96 (0.3)

Prior stroke/TIA	7979 (1.7)	613 (1.9)
Other neurological disease	6088 (1.3)	458 (1.4)
Psychiatric disorder	27759 (6.0)	1886 (5.9)
Rheumatological disease	10395 (2.3)	697 (2.2)

Legend: UKB recruited 502,505 participants and CRP data is available for 468,528 of these. Missing data for comorbidities (n=863), body mass index (n=3,106), smoking (n=2,949), ethnicity (n=2,777), and SED (n=624), and loss to follow-up or withdrawal of consent (n=1,343), resulted in exclusion of 7,476 participants from our analyses (some participants with more than one variable missing), resulting in a study cohort of 461,052 participants with available CRP data and 32,200 participants without CRP data for whom we have all of the other phenotyping data to present in this table. CRP – C-reactive protein; SED – socio-economic deprivation; TIA – transient ischaemic attack.

Supplementary Table 5: Characteristics of participants with CRP \geq 5mg/L

	CRP<5 n=407,584	CRP \geq5 n=53,468
Age		
<45	42,792 (10.5)	4,538 (8.5)
45 to <50	54,585 (13.4)	5,990 (11.2)
50 to <55	62,259 (15.3)	7,762 (14.5)
55 to <60	73,869 (18.1)	9,541 (17.8)
60 to <65	97,968 (24)	13,766 (25.7)
65+	76,111 (18.7)	11,871 (22.2)
Sex		
Female	217,953 (53.5)	32,482 (60.8)
Male	189,631 (46.5)	20,986 (39.2)
Ethnicity		
White	386,705 (94.9)	50,366 (94.2)
Non-white	20,879 (5.1)	3,102 (5.8)
SED quintile		
1 (least deprived)	83,400 (20.5)	8,889 (16.6)
2	82,828 (20.3)	9,306 (17.4)
3	82,260 (20.2)	9,959 (18.6)
4	81,111 (19.9)	11,090 (20.7)
5 (most deprived)	77,985 (19.1)	14,224 (26.6)
Smoking		
Never	226,697 (55.6)	25,748 (48.2)
Former	140,683 (34.5)	19,470 (36.4)
Current	40,204 (9.9)	8,250 (15.4)
Obesity		
Not obese	320,999 (78.8)	26,844 (50.2)
Class 1	66,687 (16.4)	14,655 (27.4)
Class 2	15,665 (3.8)	7,350 (13.7)
Class 3	4,233 (1)	4,619 (8.6)
Hypertension	102,357 (25.1)	19,744 (36.9)
Chronic cardiac disease	18,457 (4.5)	3,340 (6.2)
Chronic respiratory disease	49,662 (12.2)	9,925 (18.6)
Diabetes	18,818 (4.6)	4,174 (7.8)
Cancer	32,411 (8)	5,410 (10.1)
Chronic liver disease	720 (0.2)	183 (0.3)
Chronic kidney disease	930 (0.2)	245 (0.5)
Prior stroke/TIA	6,651 (1.6)	1,328 (2.5)

Other neurological disease	5,050 (1.2)	1,038 (1.9)
Psychiatric disorder	23,134 (5.7)	4,625 (8.7)
Rheumatological disease	7,499 (1.8)	2,896 (5.4)
NSAID use	63,966 (15.6)	11,207 (21.0)
Immunosuppressant use	9,097 (2.2)	3,084 (5.8)
Number of chronic diseases		
0	183,751 (45.1)	11,660 (21.8)
1	133,589 (32.8)	18,051 (33.8)
2	61,408 (15.1)	13,928 (26.0)
3+	28,836 (7.1)	9,829 (18.4)

Legend: CRP – C-reactive protein; NSAID – non-steroidal anti-inflammatory drug; SED – socio-economic deprivation; TIA – transient ischaemic attack.

Supplementary Table 6: Characteristics of participants with CRP ≥ 10 mg/L

	CRP<10 n=442,028	CRP ≥ 10 n=19,024
Age		
<45	45,702 (10.3)	1,628 (8.6)
45 to <50	58,506 (13.2)	2,069 (10.9)
50 to <55	67,290 (15.2)	2,731 (14.4)
55 to <60	80,060 (18.1)	3,350 (17.6)
60 to <65	106,814 (24.2)	4,920 (25.9)
65+	83,656 (18.9)	4,326 (22.7)
Sex		
Female	239,142 (54.1)	11,293 (59.4)
Male	202,886 (45.9)	7,731 (40.6)
Ethnicity		
White	419,125 (94.8)	17,946 (94.3)
Non-white	22,903 (5.2)	1,078 (5.7)
SED quintile		
1 (least deprived)	89,217 (20.2)	3,072 (16.1)
2	88,842 (20.1)	3,292 (17.3)
3	88,723 (20.1)	3,496 (18.4)
4	88,282 (20)	3,919 (20.6)
5 (most deprived)	86,964 (19.7)	5,245 (27.6)
Smoking		
Never	243,451 (55.1)	8,994 (47.3)
Former	153,080 (34.6)	7,073 (37.2)
Current	45,497 (10.3)	2,957 (15.5)
Obesity		
Not obese	337,916 (76.4)	9,927 (52.2)
Class 1	76,834 (17.4)	4,508 (23.7)
Class 2	20,552 (4.6)	2,463 (12.9)
Class 3	6,726 (1.5)	2,126 (11.2)
Hypertension	114,902 (26)	7,199 (37.8)
Chronic cardiac disease	20,509 (4.6)	1,288 (6.8)
Chronic respiratory disease	55,726 (12.6)	3,861 (20.3)
Diabetes	21,367 (4.8)	1,625 (8.5)
Cancer	35,757 (8.1)	2,064 (10.8)
Chronic liver disease	826 (0.2)	77 (0.4)
Chronic kidney disease	1,061 (0.2)	114 (0.6)

Prior stroke/TIA	7,476 (1.7)	503 (2.6)
Other neurological disease	5,653 (1.3)	435 (2.3)
Psychiatric disorder	26,049 (5.9)	1,710 (9)
Rheumatological disease	9,001 (2)	1,394 (7.3)
NSAID use	70,886 (16.0)	4,287 (22.5)
Immunosuppressant use	10,709 (2.4)	1,472 (7.7)
Number of chronic diseases		
0	191,331 (43.3)	4,080 (21.4)
1	145,499 (32.9)	6,141 (32.3)
2	70,351 (15.9)	4,985 (26.2)
3+	34,847 (7.9)	3,818 (20.1)

Legend: CRP – C-reactive protein; NSAID – non-steroidal anti-inflammatory drug; SED – socio-economic deprivation; TIA – transient ischaemic attack.

Supplementary Table 7: Association between CRP \geq 2mg/L and cause-specific mortality using partially and fully adjusted models

Model	CV death	IRR (95% CI)	
		Infection death	Other death
Age + sex			
CRP \geq 2 mg/L	1.95 (1.85-2.06)	2.33 (2.09-2.61)	1.62 (1.58-1.67)
As above + socio-demographic factors + co-morbidity			
CRP \geq 2 mg/L	1.48 (1.40-1.57)	1.72 (1.53-1.93)	1.41 (1.37-1.45)
As above + NSAID use			
CRP \geq 2 mg/L	1.48 (1.35-1.77)	1.71 (1.52-1.93)	1.41 (1.37-1.45)
As above + immuno-suppressant use ('fully adjusted')			
CRP \geq 2 mg/L	1.48 (1.40-1.57)	1.70 (1.51-1.92)	1.41 (1.37-1.45)

Legend: CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular; IRR – incidence rate ratio; NSAID – non-steroidal anti-inflammatory drug.

Supplementary Table 8: Association between CRP ≥ 2 mg/L, CRP ≥ 5 mg/L or CRP ≥ 10 mg/L and cause-specific mortality using fully adjusted models after exclusion of participants who died during the first 6-months of follow-up

	IRR (95% CI)		
	CV death	Infection death	Other death
CRP ≥ 2 mg/L	1.47 (1.39-1.56)	1.70 (1.51-1.91)	1.39 (1.35-1.43)
CRP ≥ 5 mg/L	1.55 (1.44-1.66)	1.91 (1.67-2.17)	1.51 (1.45-1.56)
CRP ≥ 10 mg/L	1.58 (1.43-1.74)	2.16 (1.82-2.55)	1.70 (1.62-1.80)

Legend: CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular; IRR – incidence rate ratio.

Supplementary Table 9: Absolute cause-specific mortality rates according to CRP category

	Rates per 1000 person years (95% CI)		
	Infection death	CV death	Other death
CRP ≥ 2	0.43 (0.40-0.46)	1.59 (1.53-1.65)	5.39 (5.28-5.50)
CRP ≥ 5	0.64 (0.58-0.71)	2.08 (1.96-2.20)	6.83 (6.62-7.05)
CRP ≥ 10	0.88 (0.76-1.02)	2.41 (2.20-2.64)	8.53 (8.14-8.95)

Legend: CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular

Supplementary Table 10: Association between CRP \geq 5 mg/L and cause-specific mortality stratified by individual comorbidity groups

Disease	IRR (95% CI)		
	CV death	Infection death	Other death
Obesity Class 1	1.44 (1.26-1.65)	1.93 (1.47 - 2.53)	1.51 (1.40-1.62)
Obesity Class 2	1.29 (1.06-1.57)	1.70 (1.10 - 2.63)	1.17 (1.04-1.32)
Obesity Class 3	1.36 (1.05-1.76)	2.51 (1.46 - 4.31)	1.08 (0.90-1.29)
Hypertension	1.55 (1.41-1.70)	1.71 (1.43 - 2.06)	1.47 (1.39-1.56)
Chronic cardiac disease	1.61 (1.41-1.84)	2.02 (1.49 - 2.73)	1.50 (1.34-1.67)
Chronic respiratory disease	1.42 (1.23-1.65)	2.27 (1.81 - 2.84)	1.58 (1.46-1.71)
Diabetes	1.80 (1.56-2.09)	1.73 (1.26 - 2.36)	1.31 (1.17-1.46)
Cancer	1.44 (1.16-1.79)	2.02 (1.43 - 2.87)	1.82 (1.68-1.96)
Chronic kidney disease	2.18 (1.29-3.68)	5.71 (2.49 - 13.07)	1.78 (1.24-2.56)
Prior stroke/TIA	1.35 (1.06-1.71)	1.86 (1.16 - 2.98)	1.62 (1.37-1.92)
Other neurological disease	1.57 (1.06-2.32)	1.18 (0.58 - 2.38)	1.29 (1.04-1.59)
Psychiatric disorder	1.49 (1.18-1.87)	2.06 (1.41 - 3.01)	1.55 (1.37-1.77)
Rheumatological disease	1.51 (1.15-1.99)	1.79 (1.16 - 2.75)	1.59 (1.35-1.86)

Legend: IRRs denote risk of cause-specific death associated with CRP \geq 5 mg/L versus CRP $<$ 5 mg/L in disease strata. CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular; IRR – incidence rate ratio; TIA – transient ischaemic attack.

Supplementary Table 11: Association between CRP ≥ 10 mg/L and cause-specific mortality stratified by individual comorbidity groups

Disease	IRR (95% CI)		
	CV death	Infection death	Other death
Obesity Class 1	1.59 (1.30 - 1.95)	2.36 (1.64 - 3.39)	1.83 (1.65 - 2.03)
Obesity Class 2	1.54 (1.19 - 2.01)	1.73 (0.98 - 3.06)	1.31 (1.11 - 1.55)
Obesity Class 3	1.42 (1.07 - 1.89)	2.05 (1.25 - 3.37)	1.16 (0.95 - 1.43)
Hypertension	1.58 (1.39 - 1.80)	1.98 (1.56 - 2.50)	1.67 (1.55 - 1.81)
Chronic cardiac disease	1.60 (1.33 - 1.92)	1.81 (1.20 - 2.73)	1.71 (1.48 - 1.99)
Chronic respiratory disease	1.37 (1.12 - 1.67)	2.45 (1.87 - 3.21)	1.71 (1.54 - 1.91)
Diabetes	1.71 (1.40 - 2.09)	1.84 (1.23 - 2.75)	1.42 (1.23 - 1.65)
Cancer	1.31 (0.96 - 1.79)	2.13 (1.37 - 3.34)	2.27 (2.05 - 2.50)
Chronic kidney disease	1.48 (0.72 - 3.06)	10.22 (4.32 - 24.19)	2.30 (1.51 - 3.52)
Prior stroke/TIA	1.17 (0.82 - 1.66)	3.23 (1.88 - 5.54)	1.82 (1.46 - 2.27)
Other neurological disease	1.14 (0.64 - 2.02)	1.47 (0.60 - 3.58)	1.60 (1.22 - 2.10)
Psychiatric disorder	1.53 (1.11 - 2.11)	1.88 (1.15 - 3.07)	1.77 (1.49 - 2.10)
Rheumatological disease	1.79 (1.31 - 2.45)	2.48 (1.56 - 3.95)	1.45 (1.20 - 1.76)

Legend: IRRs denote risk of cause-specific death associated with CRP ≥ 10 mg/L versus CRP < 10 mg/L in disease strata. CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular; IRR – incidence rate ratio; TIA – transient ischaemic attack.

Supplementary Table 12: Association between CRP ≥ 5 mg/L and cause-specific mortality stratified by number of morbidities

Number of comorbidities	IRR (95% CI)		
	CV death	Infection death	Other death
0	1.73 (1.42-2.11)	1.85 (1.26-2.72)	1.53 (1.40-1.67)
1	1.54 (1.34-1.77)	1.85 (1.43-2.40)	1.53 (1.43-1.63)
2	1.54 (1.36-1.74)	1.93 (1.53-2.43)	1.47 (1.37-1.57)
3+	1.48 (1.32-1.65)	1.89 (1.53-2.34)	1.42 (1.32-1.53)

Legend: IRRs denote risk of cause-specific death associated with CRP ≥ 5 mg/L versus CRP < 5 mg/L in multimorbidity strata. CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular; IRR – incidence rate ratio; TIA – transient ischaemic attack.

Supplementary Table 13: Association between CRP ≥ 10 mg/L and cause-specific mortality stratified by number of morbidities

Number of comorbidities	IRR (95% CI)		
	CV death	Infection death	Other death
0	1.90 (1.43-2.54)	2.19 (1.27-3.78)	1.76 (1.54-2.01)
1	1.78 (1.46-2.18)	1.87 (1.28-2.75)	1.85 (1.68-2.03)
2	1.49 (1.24-1.80)	3.10 (2.35-4.08)	1.68 (1.52-1.85)
3+	1.58 (1.36-1.84)	2.04 (1.56-2.67)	1.72 (1.57-1.89)

Legend: IRRs denote risk of cause-specific death associated with CRP ≥ 10 mg/L versus CRP < 10 mg/L in multimorbidity strata. CI – confidence interval; CRP – C-reactive protein; CV – cardiovascular; IRR – incidence rate ratio; TIA – transient ischaemic attack.