SUPPLEMENTARY DATA

Box S1

Operational definition of clinical trial and types of studies

Consistent with the World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE) for purposes of registration,[1,2] a clinical trial is defined here as any experimental or interventional study that prospectively assigns subjects (individually or clusters) to an intervention(s), with or without concurrent comparison or control groups, to evaluate the effects on biomedical outcomes (inflammatory biomarkers). The term "prospectively assigns" refers to a pre-defined process specified stipulating the assignment of research subjects to one or more arms of the clinical trial. To be prospectively assigned, there need not be randomisation or a control group. The term "intervention" is defined as a manipulation of the individual's home built environment (BE) for modifying the health-related endpoint (see Box S2).

Therefore, we will include all types of clinical trials, experimental studies (including randomised and pseudo-randomised, controlled and uncontrolled trials, etc.) We adhere to the Cochrane Handbook,[3] and we refer to non-randomised trials as a quantitative experimental study design in which individuals (or households) are prospectively assigned to an intervention(s) using methods that differ from the randomisation procedure. Randomised controlled trials (RCTs) are prospective, experimental study design involving random allocation of participants to interventions; that includes two-arm parallel, cluster, crossover, stepped-wedge RCTs, etc. The term "controlled" refers to the presence of a concurrent control or comparator group. We will include any clinical trial, regardless of whether the blind method is used or not (e.g., open-label, single-, double-blind, etc.). Mixed-methods studies employing quantitative data will be included if meeting the inclusion criteria.

Observational studies, that means non-experimental or non-interventional studies, including case reports, case series, cross-sectional, case–control, cohort, ecological, etc., will be excluded.[5] Other studies in which the intervention is not manipulated experimentally to change the home built environment (i.e., policy intervention) and provided or assigned by a research team will be excluded.[5] Pilot and feasibility studies of clinical trials will be considered if meeting eligibility criteria.

References

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Box S2

Home built environment definition and specification for eligibility criteria.

The umbrella term Home Built Environment and its acronym (H-BE) is used in this study protocol to refer to the BE of homes.

The H-BE as place of usual residency is defined as a housing facility for a person living on their own or with a family group or non-relative members –regardless of the dwelling type, tenure status and housing conditions– for an indefinite period. This broad definition will embrace private dwellings, public housing facilities, sheltered housing, retirement homes and recreated naturalistic home settings.

A residential healthcare facility provides a home-like atmosphere, spaces, and recreational activities, facilitate communal living spaces for long-term care, and provide overnight permanent accommodation. However, these facilities will not be considered in this study as they do not reflect typical domestic microenvironments in terms of resident's behaviour, activity-time-space patterns and spatial configuration. Health care environments which offer rehabilitations interventions in which the patient spent less than 24-hour period or short stays (i.e., day hospitals, day centres) will not be considered as H-BE and will be excluded. The same applies to studies carried out in institutional settings of medium- and long-term residence (i.e., hospitals, prisons). A BE that provides accommodation for a finite period (i.e., college student settings, campus dormitories) will be also excluded.

Studies carried out in experimental settings will be left out as we seek investigations evaluating household environmental conditions in naturalistic home settings. But those conducted in recreated naturalistic settings that simulate a conventional home space(s) will be considered for inclusion. Research carried out across several settings (i.e., college student settings and private homes) will be included if quantitative data is clearly differentiated between the settings.

Box S3

Strategy for involvement of non-academic GP and eligibility criteria.

A group of non-academic, English or Spanish speaking, practising GPs will be actively involved in conducting the screening process for study selection in cooperation with the first reviewer (EHG). Non-academic GPs have showed willingness to participate in research studies if these address topics of high relevance to their daily practice, specially caring for multimorbid patients at home.[6] The effectiveness of H-BE interventions on inflammatory status in community-dwelling adults is a topic of particular interest of GPs for caring patients with long-term and chronic conditions, and consequently, we expect a high level of GP's willingness to participate in this research study.

Involvement of GPs will be sought through different strategies. In a first round, they will be invited to participate through online cancer community and primary care networks. The use of Primary Care Networks has showed the highest recruitment rate (41%) with no financial and human resources, compared with published ads, personal visits in practice and calls.[7] Our involvement activity will be disseminated in regular newsletters and/or social media platforms from different cancer and primary care networks– e.g., Cancer and Primary Care Research International Network (Ca-PRI), Royal College of General Practitioners (RCGP), Doctors.net, Cancer Research UK (CRUK), Spanish Society of Primary Care Physicians (SEMERGEN), Spanish Society of Family and Community Medicine (semFYC), etc. If there is low initial response, we will use snowball sampling methods that are successful used to recruit hard-to-reach subjects in research studies.[8] Initial GPs involved in the first round that meet eligibility criteria will recruit others from their surgeries or social network who also meet the study inclusion criteria. This strategy will be supplemented by a third round, in which a convenience sample of GPs will be first approached and recruited if meeting the eligibility criteria. Primary care settings will be asked to gain permission to mail invitations to their clinician staff.

Once both GPs show their willingness to participate, a cooperation agreement accompanied by further material about the study and involvement activity will be provided. They will be provided with a complete list of the 287 biomarkers and H-BE interventions, including variants and abbreviations. The signed cooperation agreement will be considered as a successful inclusion.

Each GP group member involved in the research will screen no more than 300 titles and abstracts of the total number of identified papers in a first phase, in duplicate with the first reviewer (EHG). Then, they will be asked for supporting the screening process of the remaining studies.

Inclusion criteria

We will include a primary care physician defined as (1) currently practising as a GP, family practitioner or general internist, (2) being able to read, write and understand English language, (3) meeting technical requirements (internet connection), (4) willing to participate in a short session about the H-BE interventions and screening process in Rayyan software, and (5) signed cooperation agreement.

Quality control mechanisms into the screening process

The following mechanisms for quality controls into the screening process conducted by non-experienced GPs will be implemented:

- Before screening begins, GPs will (1) be provided of an abstract screening tool consisting of the set of eligibility criteria organised hierarchically across the PICO question; and (2) conduct a pilot screening 10 abstracts together with the first reviewer (EHG) in a training phase.[9]
- During abstract screening, (3) GPs will be monitored continuously as the agreement rates at individual level are visible in the Rayyan screening software by the first reviewer; this allows determining if any GP with high levels of disagreement (agreement rates < 75%) may require booster training;[9] (4) the text mining function in Rayyan screening tool will successfully assist GP reviewers to identify the relevant studies early in the process.[10]
- After screening ends, (5) a second experienced reviewer will independently be acting as a resolver to screen all records that received discordant assessments between the first reviewer and the crowd of GPs.[11] Following this partial replication of citation-screening task, the remaining disagreements between the first and second reviewers will be resolved by consensus. The same approach will be applied in the full-text article screening.

References

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Table S1

Environmental exposure categories within home built environments.

Category	Terms for environmental attributes[1]		
Air quality	Bioaerosols	Aerosols	Carbon monoxide
	Volatile organic compounds	Particulate matter	Nitrogen dioxide
	Fungi	Fine/ulftrafine particles	Nitrous acid
	Mold	Formaldehyde	Sulfur dioxide
	Ventilation	Polycyclic aromatic hydrocarbons	Ozone
	Air-conditioning	Phthalic acids	
	Air filtration	High-efficiency particulate air	
Thermal comfort	Temperature	Thermal insulation	warmth
	Heating		
Non-ionising radiation	Natural lighting	Artificial lighting	Illumination
	Daylight	Night lighting	Illuminance
	Sunlight	Light at night	Photoperiod
	Electromagnetic fields	Microwaves	VLF-EMFs
	Electric / Magnetic field	Radiofrequency	ELF-EMFs
	Electricity		
Noise	Sound	Acoustic	Noise
	Soundscape		
Nature	Green	Natural	Houseplant
	Greenspace	Garden	Vegetation
	Blue space	Plants	
Water	Drinking water	Water filtration	Water supply
	Water quality	Water purification	

VLF, very low frequency; ELF, extremely low frequency; EMFs, electromagnetic fields.
[1] A full list of variants terminology, synonyms, alternative topics, or spelling variations for each term is provided by requesting to the corresponding author. These variants are shown in the search strategy (Table S4).

Table S2

Potential home built environment interventions for improving or modifying quality of household environmental exposure.

Environmental attribute	*Description of some home-built environment interventions[1, 2]*
Warmth, indoor air and energy efficiency improvements	Heating installation/repair, electric storage heater, thermal insulation, reproofing, window replacement, provision of ventilation, air filter installations, delivery of portable ventilation devices, use of low volatile organic compound products and materials, provision of elements/devices for air ionisation, improvements for avoiding moisture exposure.
Artificial lighting and sunlighting[3]	Replacement of luminaries, space layout and re-configurations of surface area of window or internal space, terrace, patios. Home-based bright light therapy with devices will be included if these are integrated into domestic luminaries or other built environment elements.
Non-ionising radiation[3]	Installing protective panels, unplugging devices not in use to reduce field strengths in the home, increasing the distance or changing phase and neutral line (system upgrade), relocation from apartment building with new electric system.
Noise, soundscape	Installing soundproof windows/panels, acoustic insulation in party walls or building facades to block external noises, ventilation device replacement to mask unwanted sounds, supplying phono-acoustic material, indoor technological systems to release wanted soundscape.
Nature	Provision and improvement (e.g., accessibility and/or visibility) of natural elements to individual/community private gardens, incorporating greater number of houseplants, spatial re-design to provide domestic greenspaces, supplying devices to recreate digitally nature views.
Water	Installation of sustainable water systems, home treatment devices for production of water with ionisation characteristics and specific potential of hydrogen (pH).

[1]The proposed home built environment interventions do not pretend to represent a comprehensive list, but to serve as potential examples.

[2]Those studies where residents were rehoused or received housing refurbishment will be included if enough data about the specific home built environment intervention(s) are available.

[3]Although the artificial and natural lighting belong to the non-ionising radiation group, the former is dealt with separately because of the large number of research studies examining the health effects from these environmental attributes.

Table S3
Cancer-associated systemic inflammation biomarkers

Circulating individual inflammatory markers[1, 2]					
Group	[ID_i-ID_f]	ID	Single marker	ID	Single marker
G1-10	Inflammatory mediators				
G1	[1-99]	Cytokines			
	[1-41]	Interleukins			
	[1-9]	Interleukin-1 family			
		1	Interleukin-1 alpha	6	Interleukin-36 gamma
		2	Interleukin-1 beta	7	Interleukin-36 alpha
		3	Interleukin-1Ra	8	Interleukin-37
		4	Interleukin-18	9	Interleukin-38
		5	Interleukin-33		
	[10-15]	Interleukin-2 family			
		10	Interleukin-2	13	Interleukin-9
		11	Interleukin-4	14	Interleukin-15
		12	Interleukin-7	15	Interleukin-21
	[16-24]	Interleukin-6 family			
		16	Interleukin-6	21	Cardiotrophin-like cytokine factor 1
		17	Interleukin-11	22	Ciliary neurotrophic factor
		18	Leukemia inhibitory factor	23	Neuropoietin
		19	Oncostatin	24	Interleukin-31
		20	Cardiotrophin-1		
	[25-31]	Interleukin-10 family			
		25	Interleukin-10	29	Interleukin-24
		26	Interleukin-19	30	Interleukin-26
		27	Interleukin-20	31	Interleukin-29
		28	Interleukin-22		
	[32-35]	Interleukin-12 family			
		32	Interleukin-12	34	Interleukin-27
		33	Interleukin-23	35	Interleukin-35
	[36]	36	Interleukin-13		
	[37, 38]	37	Interleukin-17	38	Interleukin-25 (/-17E)
	[39, 40]	39	Interleukin-32	40	Interleukin-32 gamma
	[41]	41	Interleukin-34		
	[42-46]	Colony-stimulating factor			
		42	Granulocyte colony stimulating factor	45	Multipotential colony stimulating factor Interleukin-3
		43	Granulocyte-macrophage colony stimulating factor		
		44	Macrophage colony stimulating factor	46	Erythropoietin Hematopoietin
	[47-50]	Adipokines			
		47	Adiponectin	49	Resistin
		48	Leptin	50	Visfatin
	[51-86]	Chemokines			
		CC family			
	[51-58]	CC Receptors			
		51	CC Receptor 1	55	CC Receptor 6
		52	CC Receptor 2	56	CC Receptor 7
		53	CC Receptor 4	57	CC Receptor 9
		54	CC Receptor 5	58	CC Receptor 10
	[59-73]	CC Ligand			
		59	CC Ligand 2	66	CC Ligand 19
		60	CC Ligand 3	67	CC Ligand 20
		61	CC Ligand 4	68	CC Ligand 21
		62	CC Ligand 5 RANTES	69 70	CC Ligand 22 CC Ligand 24
		63	CC Ligand 7	71	CC Ligand 25

		64	CC Ligand 8	72	CC Ligand 27
		65	CC Ligand 18	73	CC Ligand 28
		CXC family			
	[74-79]	CXC Receptors			
		74	CXC Receptor 1	77	CXC Receptor 4
		75	CXC Receptor 2	78	CXC Receptor 6
		76	CXC Receptor 3	79	CXC Receptor 7
	[80-92]	CXC Ligand			
		80	CXC Ligand 1	87	CXC Ligand 9
		81	CXC Ligand 2	88	CXC Ligand 10
		82	CXC Ligand 3	89	CXC Ligand 11
		83	CXC Ligand 4	90	CXC Ligand 12
		84	CXC Ligand 5	91	CXC Ligand 14
		85	CXC Ligand 6	92	CXC Ligand 16
		86	Interleukin-8 CXC Ligand 8		
	[93-95]	Interferons			
		93	Interferon gamma	95	Interferon alpha
		94	Interferon beta		
	[96-98]	Tumor necrosis factor			
	[96]	96	Tumor necrosis factor alpha		
	[97, 98]	Tumor necrosis factor receptor			
		97	Tumor necrosis factor receptor 1	98	Tumor necrosis factor receptor 2
	[99]	99	Macrophage migration inhibitory factor		
G2	[100-129]	Growth factors			
	[100]	100	Transforming growth factor-beta		
	[101-103]	Vascular endothelial growth factor			
		101	Vascular endothelial growth factor		
	[102,104]	Vascular endothelial growth factor receptors			
		102	Vascular endothelial growth factor receptor 1	104	Vascular endothelial growth factor receptor 3
		103	Vascular endothelial growth factor receptor 2		
	[105]	105	Platelet-derived growth factor		
	[106-108]	Fibroblast growth factor			
		106	Fibroblast growth factor 1	108	Fibroblast growth factor receptor
		107	Basic fibroblast growth factor		
	[109, 110]	Epidermal growth factor			
		109	Epidermal growth factor	110	Epidermal growth factor receptor
	[111]	111	Placental growth factor		
	[112]	112	Hepatocyte growth factor		
	[113]	113	Nerve growth factor		
	[114, 115]	Insulin			
		114	Insulin	115	Insulin-like growth factor
	[116-118]	Endothelins			
		116	Endothelin 1	118	Endothelin 3
		117	Endothelin 2		
	[119, 120]	Renin-angiotensin system			
		119	Angiotensin 1	120	Angiotensin 2
	[121, 122]	Angiopoietins			
		121	Angiopoietin 1	122	Angiopoietin 2
	[123-129]	Angiopoietin-like protein family			
		123	Angiopoietin-like protein 1	128	Angiopoietin related growth factor
		124	Angiopoietin-like protein 2		Angiopoietin-like protein 6
		125	Angiopoietin-like protein 3	129	Cornea-derived transcript 6
		126	Angiopoietin-like protein 4		Angiopoietin-like protein 7
		127	Angiopoietin-like protein 5		
G3	[130-141]	Transcription factor family			
	[130]	130	Nuclear factor kappa-B		
	[131, 132]	Nuclear factor erythroid-2 related factor			

		131	Nuclear factor erythroid-2 related factor 1	132	Nuclear factor erythroid-2 related factor 2
	[133-138]	Signal transducers and activators of transcription			
		133	phosphorylated- Signal transducer and activator of transcription 1	136	phosphorylated- Signal transducer and activator of transcription 4
		134	phosphorylated- Signal transducer and activator of transcription 2	137	phosphorylated- Signal transducer and activator of transcription 5
		135	phosphorylated- Signal transducer and activator of transcription 3	138	phosphorylated- Signal transducer and activator of transcription 6
	[139-141]	Hypoxia-inducible factors			
		139	Hypoxia-inducible factor-1 alpha	141	Hypoxia-inducible factor-2α
		140	Hypoxia-inducible factor-1β		
G4	[142-152]	Immunoglobulins. *Gamma globulins*			
	[142-148]	Cell-adhesion molecules			
		142	Intercellular cell-adhesion molecules	145	Epithelial cell-adhesion molecules
		143	Vascular cell-adhesion molecules	146	Neural cell-adhesion molecules
		144	Platelet endothelial cell-adhesion molecules		
	[147-149]	Selectin family			
		147	E-selectin Endothelial-leukocyte adhesion molecule 1 Leukocyte-endothelial cell adhesion molecule 2	148 149	P-selectin L-selectin
	[150-152]	Programmed cell death protein			
	[150]	150	Programmed cell death protein 1		
	[151, 152]	Programmed cell death protein ligand			
		151	Programmed cell death protein ligand 1	152	Programmed cell death protein ligand 2
G5	[153-165]	Eicosanoids			
	[153-159]	Cyclooxygenase pathways			
	[153, 154]	Cyclooxygenases			
		153	Cyclooxygenase 1 Prostaglandin-endoperoxide synthase 1	154	Cyclooxygenase 2 Prostaglandin-endoperoxide synthase 2
	[155-158]	Prostaglandins			
		155	Prostaglandin D2	158	Prostaglandin I2 Prostacyclin
		156	Prostaglandin E2		
		157	Prostaglandin F2 alpha		
	[159]	Tromboxanes			
		159	Tromboxane A2		
	[160-165]	Lipoxygenase pathways			
		Lipoxygenases			
	[160]	160	5-lipoxygenase		
	[161-164]	Leukotrienes			
		161	Leukotriene A4	163	Leukotriene C4
		162	Leukotriene B4	164	Leukotriene D4
	[165]	Lipoxines			
		165	Lipoxine A4		
G6	[166-209]	Acute phase proteins			
	[166-205]	Up-regulation			
	[166-172]	Pentraxins family			
	[166-168]	C-reactive protein			
		166	C-reactive protein *Beta globulin*	168	Monomeric c-reactive protein Modified c-reactive protein
		167	Pentameric c-reactive protein Native c-reactive protein		

	[169-172]	Pentraxins			
		169	Pentraxin-3		
	[170,171]	Neuronal pentraxin			
		170	Neuronal pentraxin 1	171	Neuronal pentraxin 2
	[172]	172	Serum amyloid P		
	[173-175]	Serum amyloid A			
		173	Serum amyloid A1	175	Serum amyloid A3
		174	Serum amyloid A2		*Beta globulin*
	[176-178]	Alpha 1 globulins			
	[176,177]	Alpha 1acid-glycoprotein			
		176	Orosomucoid 1 Alpha 1acid-glycoprotein 1	177	Orosomucoid 2 Alpha 1acid-glycoprotein 2
	[178]	178	Alpha 1 antitrypsin		
	[179-184]	Extracellular matrix proteins			
		179	Fibronectin	183	Vitronectin
		180	Ferritin (L-ferrint, H-ferritin)	184	Lipopolysaccharide binding protein
		181	H-ferritin		
		182	Osteopontin Early T lymphocyte activation gene 1		
	[185-195]	Coagulation and fibrinolytic system			
	[185-187]	185	Fibrinogen	187	Thrombin
		186	D-dimer		
	[188-195]	Plasminogen activation system			
		188	Plasmin	192	Plasminogen activator inhibitory-1
		189	Plasminogen	193	Plasminogen activator inhibitory-2
		190	Urokinase-plasminogen activator	194	Neuroserpin
		191	Urokinase-plasminogen activator receptor	195	Tissue-type plasminogen activator
	[196-197]	Microglobulins			
		196	Beta 2 microglobulin	197	Alpha 1 microglobulin
	[198-201]	Transport proteins			
		198	Ceruloplasmin	200	Hemopexin
		199	Haptoglobin *Alpha 2 globulin*	201	Alpha 2 macroglobulin *Alpha 2 globulin*
	[202-205]	Complement system			
	[202, 203]	Complement 3			
		202	Complement 3a	203	Complement 3b
	[204,205]	Complement 5			
		204	Complement 5a	205	Complement 5b-9
	[206-209]	Down-regulation			
	[206, 207]	206	Pre-albumin Transthyretin	207	Albumin
	[208, 209]	Transferrin			
		208	Transferrin receptor 1 *Beta globulin*	209	Transferrin receptor 2 *Beta globulin*
G7	[210-225]	Matrix metalloproteinases			
		210	Matrix metalloprotenase 1	218	Matrix metalloprotenase 12
		211	Matrix metalloprotenase 2	219	Matrix metalloprotenase 13
		212	Matrix metalloprotenase 3	220	Matrix metalloprotenase 14
		213	Matrix metalloprotenase 7	221	Matrix metalloprotenase 16
		214	Matrix metalloprotenase 8	222	Matrix metalloprotenase 17
		215	Matrix metalloprotenase 9	223	Matrix metalloprotenase 19
		216	Matrix metalloprotenase 10	224	Matrix metalloprotenase 26
		217	Matrix metalloprotenase 11	225	Matrix metalloprotenase 28
G8	[226-235]	Redox active mediators			
	[226,227]	Metalloproteins			
		226	Hemoglobin Cell-free hemoglobin	227	Cell-free heme
	[228-233]	Vitamin D			

		228	25-hydroxyvitamin D	231	hydroxycholecalciferol
		229	25-hydroxyvitamin D3 1-alpha-hydroxylase	232	Calcidiol, 25-hydroxyvitamin D_3
		230	25-hydroxyvitamin D3 1-α-hydroxylase	233	Calcitriol, 1,25-dihydroxyvitamin D3
	[234-235]	Melatonin			
		234	Melatonin	235	6-sulfatoxymelatonin
G9	[236-242]	Lipoproteins			
		236	Very low density lipoprotein	240	Apolipoprotein
		237	Low density lipoprotein	241	Total cholesterol
		238	High density lipoprotein	242	Triglycerides
		239	Oxidized low density lipoprotein		
G10	[243-252]	Adrenal cortex hormones and neurotransmitters			
		Glucocorticoids			
		243	Cortisone	244	Cortisol
		245	Corticotropin-releasing hormone	248	Serotonin
		246	Adrenocorticotropic hormone	249	5-hydroxytryptamine
		247	Gamma aminobutyric acid		
		Catecholamines			
		250	Epinephrine, adrenaline	252	Dopamine
		251	Norepinephrine		
G11-13	[253-264]	Inflammatory effector cells			
G11	[253]	Platelets parameters			
		253	Platelets Platelet count		
G12	[254-257]	Erythrocytes parameters			
		254	Red blood cell count	256	Erythrocyte sedimentation rate*
		255	Red blood cell distribution width*	257	Plasma viscosity
G13	[258-264]	Leukocytes			
	[258-260]	258	White blood cell count	260	Neutrophil count
		259	Monocyte count Macrophages		
	[261-264]	261	Total lymphocyte count	263	Regulatory T lymphocytes
		262	Absolute lymphocyte count	264	Circulating plasma cells

Combining multiple inflammatory markers (into a score)[1, 2]					
Group	[ID_i-ID_f]	ID	Multiple markers		[calculated]
				ID	Combined single and/or multi-markers
cG11.13	[265-271]	Leukocytes-platelets parameters			
	[265-267]	Classical scores			
		265	Lymphocyte-to-monocyte ratio		[259:261]
				259	Monocyte count
				261	Total lymphocyte count
		266	Neutrophil-to-lymphocyte ratio		[260:261]
				260	Neutrophil count
				261	Total lymphocyte count
		267	Platelet-to-lymphocyte ratio		[253:261]
				253	Platelet count
				261	Total lymphocyte count
	[268-271]	Novel combining scores[3]			
		268	Derived neutrophil-to-lymphocyte ratio		[260:(258-262)]
				258	White blood cell count
				260	Neutrophil count
				262	Absolute lymphocyte count
		269	Systemic immune-inflammation index		[253x260:261]
				253	Platelet count
				260	Neutrophil count

				261	Total lymphocyte count
		270	Combination of platelet count and neutrophil-to-lymphocyte ratio		[253; (260:261)]
				253	Platelet count
				260	Neutrophil count and
				261	Total lymphocyte count
		271	Combined neutrophil/platelet/ lymphocyte / differentiation score		[tumor differentiation score x (260:261)-(253:261) score)]
				253	Platelet count
				260	Neutrophil count
				261	Total lymphocyte count
cG6	[272-279]	Acute phase proteins, combinations			
	[272-275]	Classical scores			
		272	Glasgow prognostic score		[165;206]
				165	C-reactive protein
				206	Albumin
		273	Modified glasgow prognostic score		[165;206]
				165	C-reactive protein
				206	Albumin
		274	Glasgow prognostic score:modified glasgow prognostic score		[165;206]
				165	C-reactive protein
				206	Albumin
		275	Prognostic inflammatory and nutritional index		[165x(175,176)x206x205]
				165	C-reactive protein
				175	Alpha 1 acid-glycoprotein
				176	Alpha 1 acid-glycoprotein
				205	Transthyretin
				206	Albumin
	[276-279]	Novel combined scoring system[3]			
		276	C-reactive protein-to-albumin ratio		[165:206]
				165	C-reactive protein
				206	Albumin
		277	Pre-albumin-to-C-reactive protein prognostic score		[205:165]
				165	C-reactive protein
				205	Pre-albumin
		278	Albumin-to-globulin ratio		[206:*globulins* (total proteins-206)]
				206	Albumin
					Globulins. *Alpha 1, alpha 2, beta and gamma globulins*
		279	Inflammation based index		[(253x260):261]
				253	Platelet count
				260	Neutrophil count
				261	Total lymphocyte count
cG11.6	[280-284]	Leukocytes-acute phase proteins, combinations[3]			
		280	c-reactive protein and neutrophil-lymphocyte ratio score		[165;(260:261)]
				165	C-reactive protein
				260	Neutrophil count
				261	Total lymphocyte count
		281	Derived neutrophil-lymphocyte ratio and prognostic nutritional index		[260:(258-262);206+0.005x261]
				206	Albumin
				258	White blood cell count
				260	Neutrophil count
				261	Total lymphocyte count
				262	Absolute lymphocyte count
		282	Combination of neutrophil-lymphocyte ratio and glasgow prognostic score		[(260:261); 165, 206]
				165	C-reactive protein
				206	Albumin
				260	Neutrophil count
				261	Total lymphocyte count
		283	Combination of fibrinogen and neutrophil-lymphocyte ratio		[184; (260:261)]
				184	Fibrinogen
				260	Neutrophil count

				261	Total lymphocyte count
		284	Inflammation-based cumulative prognostic score system		[165;206;(259:261);(260:261);(253:258);184]
				165	C-reactive protein
				184	Fibrinogen
				206	Albumin
				253	Platelet count
				259	Monocyte count
				260	Neutrophil count
				261	Total lymphocyte count
cG11.6.8	[285]	Leukocytes-acute phase proteins-redox active mediators, combinations[3]			
		285	Combined hemoglobin, albumin, lymphocyte, platelet		[206x225x253x261]
				206	Albumin
				225	Hemoglobin
				253	Platelet count
				261	Total lymphocyte count
cG9.6	[286]	Lipoprotein particle–derived measure of insulin resistance			
		286	Lipoprotein insulin resistance score		[L235sz+L235p+237sz+237p+S236sz+S236p]
				235	Very low-density lipoprotein
				236	Low-density lipoprotein
				237	High-density lipoprotein
		287	AC score		[165;240]
				240	Apolipoprotein A-1
				165	C-reactive protein

G, group; cG, combined group; ID, identifier; L, large; P, particle concentration; S, small; Sz, particle size.
Cursive, globulin group to which the marker belongs.
*Method of measuring the marker, clinical test.
[1]The proposed panel of 287 cancer-associated inflammatory biomarkers could be modified and upgraded over time in accordance with clinical efficacy tested and promising clinical results of novel candidates.
[2] Novel combined systemic inflammation-based scoring systems proposed in further research will be incorporated into the panel.

Table S4

Search strategy for Pubmed-Medline

Key:
mh = Medical Subject Heading (MeSH) terms
mh:noexp = MeSH terms:no explode
tiab = title/abstract
* = truncation

Search	Query
Home built environment	
#1	((((((((((((((((housing[mh])) OR (built environment[mh])) OR (home environment[mh])) OR (built environment[tiab])) OR (hous*[tiab])) OR (home[tiab])) OR (homes[tiab])) OR (domestic[tiab])) OR (indoor[tiab])) OR (interior[tiab])) OR (residential building*[tiab])) OR (apartment*[tiab])) OR (dwelling*[tiab])) OR (flat[tiab])) OR (flats[tiab])) OR (tower block*[tiab])) OR (high rise building*[tiab])) OR (residential[tiab])) OR (residence*[tiab])
Environmental parameters	
#2	((((((air pollution, indoor[mh]) OR (air pollutants[mh])) OR (air pollut*[tiab])) OR (air quality[tiab])) OR (air contamin*[tiab])) OR (aerosols[mh])) OR (aerosol*[tiab])
#3	((particulate matter[mh]) OR (particulate matter[tiab])) OR (particle*[tiab])
#4	((((((((((((((((carbon monoxide[mh]) OR (carbon monoxide[tiab])) OR (carbon dioxide[mh])) OR (carbon dioxide[tiab])) OR (nitrogen dioxide[mh])) OR (nitrogen dioxide[tiab])) OR (nitrogen oxides[mh])) OR (nitrogen oxides[tiab])) OR (nitrous acid[mh])) OR (nitrous acid[tiab])) OR (sulfur dioxide[mh])) OR (sulfur dioxide[tiab])) OR (sulphur dioxide[tiab])) OR (ozone[mh]) OR (ozone[tiab]) OR (radon[mh])) OR (radon[tiab])
#5	((((((((((((volatile organic compounds[mh]) OR (volatile organic compound*[tiab])) OR (semivolatile organic compound*[tiab])) OR (formaldehyde[mh])) OR (formaldehyde*[tiab])) OR (polycyclic aromatic hydrocarbons[mh])) OR (polycyclic aromatic hydrocarbon*[tiab])) OR (phthalic acids[mh])) OR (phthalic acid*[tiab])) OR (phthalate*[tiab])) OR (aldehydes[mh])) OR (aldehyde*[tiab])) OR (methamphetamine[mh])) OR (methamphetamine[tiab])
#6	((((((((((((((((air microbiology[mh]) OR (bioaerosol*[tiab])) OR (fungi[mh])) OR (fungi[tiab])) OR (microbiome*[tiab])) OR (microbial[tiab])) OR (microorganism*[tiab])) OR (allergens, house dust mites[mh])) OR (dust[tiab])) OR (organic contamin*[tiab])) OR (mold[tiab])) OR (mould[tiab])) OR (moldy[tiab])) OR (mouldy[tiab])) OR (moisture[tiab])) OR (bacteria[mh])) OR (bacteria[tiab])
#7	((((((((((((((ventilation[mh]) OR (ventilation[tiab])) OR (air conditioning[mh])) OR (air condition*[tiab])) OR (air filters[mh])) OR (air filter*[tiab])) OR (air filtration[tiab])) OR (air purifier*[tiab])) OR (high efficiency particulate air[tiab])) OR (HEPA[tiab])) OR (heating[mh])) OR (HVAC[tiab])) OR (insulat*[tiab])) OR (air-change*[tiab])) OR (air exchange*[tiab])
#8	((((((temperature[mh]) OR (temperature*[tiab])) OR (thermal comfort[tiab])) OR (thermal condition*[tiab])) OR (thermal insulation[tiab])) OR (warmth[tiab])) OR (heat*[tiab])
#9	(((((((((lighting[mh]) OR (light*[tiab])) OR (photoperiod[mh])) OR (photoperiod*[tiab])) OR (illumination[tiab])) OR (illuminance[tiab])) OR (daylight*[tiab])) OR (sunlight*[tiab])) OR (nightlight*[tiab])) OR (light at night[tiab])
#10	((((((((((((radiation, nonionizing[mh]) OR (electromagnetic fields[mh])) OR (electromagnetic field*[tiab])) OR (electromagnetic phenomena[mh:noexp])) OR (electromagnetic radiation[tiab])) OR (radiation monitoring[mh])) OR (radio-frequency*[tiab])) OR (radiofrequency*[tiab])) OR (microwave*[tiab])) OR (electric field*[tiab])) OR (magnetic field*[tiab])) OR (electricity[mh]) OR (electric*[tiab])
#11	((((acoustics[mh])) OR (acoustic*[tiab])) OR (sound[mh])) OR (sound*[tiab])) OR (noise[tiab])
#12	(((((((nature[tiab]) OR (natural[tiab])) OR (green*[tiab])) OR (greenspace*[tiab])) OR ("blue space*"[tiab])) OR (garden*[tiab])) OR (plant*[tiab])) OR (houseplant*[tiab])) OR (vegetation[tiab])
#13	(((water[mh]) OR (water[tiab])) OR (drinking water[mh])) OR (water quality[mh])
#14	#2 OR #3 OR #4 OR #5 OR #6 OR…#13
Biomarkers of systemic inflammatory response	
#15	(((((((biomarker*[tiab]) OR (marker*[tiab])) OR (indicator*[tiab])) OR (mediator*[tiab])) OR (profile*[tiab])) OR (score*[tiab])) OR (index*[tiab])) AND (((((inflammat*[tiab]) OR (immun*[tiab])) OR (lipid*[tiab])) OR (metabolic[tiab])) OR (endocrine[tiab])) OR (biomarkers[mh:noexp])) OR (inflammation[mh:noexp])

#16	((((((((cytokines[mh]) OR (cytokine*[tiab]) OR (interleukin*[tiab])) OR (leukemia inhibitory factor[tiab])) OR (oncostatin[tiab])) OR (cardiotrophin[tiab])) OR (ciliary neurotrophic factor[tiab])) OR (colony stimulating factor*[tiab])) OR (erythropoietin[tiab])) OR (hematopoietin[tiab])
#17	((((((((((adipokines[mh]) OR (adipokine*[tiab])) OR (adipocytokine*[tiab])) OR (adipocytes[mh])) OR (adipocyte*[tiab])) OR(adiponectin*[tiab])) OR (leptin[tiab])) OR (receptors, leptin[mh])) OR (resistin[tiab])) OR (adipose tissue-specific secretory factor[tiab])) OR (visfatin[tiab]))
#18	(((((((chemokine*[tiab])) OR (receptors, chemokine[mh])) OR (interferon*[tiab])) OR (tumor necrosis factor*[tiab])) OR (macrophage migration-inhibitory factor*[tiab])) OR (glycosylation-inhibiting factor[tiab])
#19	((((((((((((transforming growth factor beta[tiab])) OR (angiogenic proteins[mh])) OR (vascular endothelial growth factor*[tiab])) OR (platelet-derived growth factor[MeSH Terms:noexp])) OR (platelet-derived growth factor[tiab])) OR (fibroblast growth factors[mh])) OR (fibroblast growth factor*[tiab])) OR (epidermal growth factor[mh])) OR (epidermal growth factor[tiab])) OR (placenta growth factor[tiab])) OR(hepatocyte growth factor[tiab])) OR (nerve growth factor[mh])) OR (nerve growth factor[tiab])
#20	((((insulin[mh]) OR (insulin[tiab])) OR (endothelins[mh]) OR (endothelin*[tiab]) OR (angiotensins[mh])) OR (angiotensin*[tiab])) OR (angiopoietin*[tiab])
#21	(((((((NF-kappa B[mh])) OR (NF-kappa B[tiab])) OR (nuclear factor kappa B[tiab])) OR (nuclear factor erythroid[tiab])) OR (STAT transcription factors[mh])) OR (STAT[tiab]) OR(hypoxia-inducible factor[mh])) OR(hypoxia-inducible factor[tiab])
#22	((((((((serum globulins[MeSH Terms]) OR (globulin*[Title/Abstract])) OR (immunoglobulin*[Title/Abstract])) OR (cell adhesion molecules[MeSH Terms:noexp])) OR (cell adhesion molecule*[Title/Abstract])) OR (selectins[MeSH Terms])) (selectin*[Title/Abstract])) OR (endothelial-leukocyte adhesion molecule[Title/Abstract])) OR (programmed cell death protein*[Title/Abstract])
#23	((((((((((eicosanoids[mh]) OR (eicosanoid*[tiab])) OR (prostanoid*[tiab]) OR (cyclooxygenase*[tiab])) OR (cyclo-oxygenase*[tiab])) OR (prostaglandin-endoperoxide synthases[mh])) OR (prostaglandin[tiab]) OR (thromboxane*[tiab])) OR (lipoxygenases[mh])) OR (lipoxygenase*[tiab])) OR (lipo-oxygenase*[tiab])) OR (leukotriene*[tiab])) OR (lipoxin*[tiab])
#24	((((((((((((((((((((((((((((((((((((acute phase proteins[mh]) OR (acute-phase protein*[tiab])) OR (acute phase reactant*[tiab])) OR (C-reactive protein*[tiab])) OR (pentraxin*[tiab])) OR (serum amyloid[tiab])) OR (acid glycoprotein[tiab])) OR (orosomucoid[tiab])) OR (antitrypsin[tiab])) OR (serpin[tiab])) OR (extracellular matrix proteins[mh:noexp])) OR (extracellular matrix protein*[tiab])) OR (fibronectin[tiab])) OR (ferritins[mh:noexp])) OR (ferritin*[tiab])) OR (osteopontin[tiab])) OR (vitronectin[tiab])) OR (fibrinogen[tiab])) OR (D-dimer[tiab])) OR (thrombin[mh])) OR (thrombin[tiab])) OR (fibrinolysin[mh])) OR (fibrinolysin[tiab])) OR (plasmin[tiab])) OR (plasminogen[tiab])) OR (macroglobulin*[tiab]) OR (ceruloplasmin[tiab])) OR (caeruloplasmin[tiab])) OR (haptoglobin*[tiab])) OR (hemopexin[tiab])) OR (haemopexin[tiab])) OR (microglobulin*[tiab])) OR (complement system proteins[mh]) OR (complement system protein*[tiab])) OR (serum albumin[mh])) OR (albumin[tiab])) OR (transferrin*[tiab])) OR (prealbumin*[tiab])
#25	((((((((((((hemoglobins[mh]) OR (hemoglobin*[tiab])) OR (haemoglobin*[tiab])) OR (glycohemoglobin[tiab])) OR (cell-free heme[tiab])) OR (vitamin D[mh]) OR (vitamin D[tiab])) OR (25-hydroxyvitamin D[tiab])) OR (25-hydroxyvitamin D3 1-alpha-hydroxylase*[tiab])) OR (25-hydroxyvitamin D3 1-α-hydroxylase*[tiab])) OR (1,25-dihydroxyvitamin D[tiab])) OR (hydroxycholecalciferol[tiab])) OR (calcidiol[tiab])) OR (calcitriol[tiab])) OR (matrix metalloproteinases, secreted[mh]) OR (matrix metalloproteinase*[tiab])
#26	(((((lipoproteins[mh]) OR (lipoprotein*[tiab])) OR (apolipoprotein*[tiab])) OR (cholesterol[tiab])) OR (triglycerides[mh])) OR (triglyceride*[tiab])
#27	((((((((((((((((((glucocorticoids[mh]) OR (glucocorticoid*[tiab])) OR (cortisone[mh])) OR (cortisone[tiab])) OR (cortisol[tiab])) OR (corticotropin-releasing hormone[tiab])) OR (adrenocorticotropic hormone[tiab])) OR (gamma-aminobutyric acid[mh:noexpl])) OR (gamma aminobutyric acid[tiab])) OR (serotonin[mh])) OR (serotonin[tiab])) OR (5-hydroxytryptamine[tiab])) OR (dopamine[mh])) OR (epinephrine[mh])) OR (norepinephrine[mh])) OR (catecholamine*[tiab])) OR (epinephrine[tiab])) OR (adrenaline[tiab])) OR (norepinephrine[tiab])) OR (dopamine[tiab]) OR (melatonin[mh])) OR (melatonin[tiab])) OR (6-sulfatoxymelatonin[tiab])
#28	((((((((((blood cell count[mh]) OR (blood cell count[tiab])) OR (blood platelets[mh]) OR (thrombocyte*[tiab])) OR (platelet*[tiab])) OR (erythrocytes[mh]) OR (erythrocyte*[tiab])) OR (red blood cell*[tiab])) OR (red blood cell distribution width[tiab])) OR (red cell distribution

	width[tiab])) OR (blood sedimentation[tiab])) OR (erythrocyte sedimentation rate[tiab])) OR(hemorheology[mh])) OR (blood viscosity[tiab])) OR (plasma viscosity[tiab])
#29	((((((((((((leukocytes[mh]) OR (leukocyte*[tiab])) OR (white blood cell*[tiab])) OR (white cell count[tiab])) OR (macrophages[mh])) OR (macrophage*[tiab])) OR (monocyte*[tiab])) OR (neutrophil*[tiab])) OR (lymphocyte*[tiab])) OR (regulatory T-cell*[tiab]) OR (Tregs count[tiab])) OR (Treg count[tiab])) OR (CD4 count[tiab])) OR (T-cell count[tiab])) OR (circulating plasma cell*[tiab])
#30	#15 OR #16 OR #17 OR #18 OR #19 OR…#29
#31	#1 AND #14 AND #30
#32	#31 NOT (animals[mh] NOT humans[mh])

Table S5

Variables collected in pre-established data extraction template.

Construct	Variables
(A) Study information	• First author's last name, publication year • Study design • Journal name • Geographical region in which the study was conducted • Duration of follow-up or study period • Aims and/or purpose of the study
(B) participant, patient characteristics	• Sample size • Gender composition • Mean or median age • Ethnicity • Socio-economic status (if available)
(C) clinicopathological characteristics (if available)	• Comorbidities: medical classification topography code, collection method, measure of association[1] • Baseline clinical parameters • Body mass index • Prescribed medications
(D) Home built environment intervention	• Device(s), technology and/or architecture element(s) information • Technical specifications • Duration of treatment period • Timing, delivery • Co-interventions • Economic information
(E) improved/modified environmental factor	• Parameter type within categories (i.e., pollutants) • Sources • Exposure levels • Method(s) of measurement • Equipment • Measurements: dose, duration, intensity, frequency
(F) Housing characteristics and design (if reported)	• Study setting • Housing typology • Residence type • Building age • Material specification • Spatial characteristics • Engineering systems
(G) Inflammatory biomarker data	• Sample types • Laboratory assay methods • Cut-offs, midpoints to report up- or down-regulation and to distinguish marker levels from unresolved to resolving outcomes • Concentration level for each marker (pre- and post-intervention; repeated over intervention period).
(H) Outcomes	• Analysis models • Effect estimates • Adjusted potential confounders
(I) Plausible mechanistic pathways[2]	• Initiating event(s) • Key events (e.g., cellular/tissue/system responses) • Adverse outcome(s)

[1] International Classification of Diseases (ICD-11) to group reported medical conditions. However, adjust of terms to the International Classification of Primary Care, 3rd edition (ICPC-3) into WHO Family of Internationals Classifications (FIC) [https://browser.icpc-3.info/] will be performed to classify the clinicopathological characteristics and patient and clinical data in the domains of General/Family Practice and Primary Care. [2] The plausible mechanistic pathways will be organised and structured according to the Adverse Outcome Pathway (AOP) framework.