

1 **Understanding the rise of cardiometabolic diseases in low- and**
2 **middle-income countries**

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36 **Abstract**

37 Increases in the prevalence of non-communicable diseases (NCDs), but in particular
38 cardiometabolic diseases such as cardiovascular disease, stroke and diabetes, and their
39 major risk factors, have not been uniform across settings; for example, cardiovascular
40 disease mortality has declined over recent decades in high-income countries but increased
41 in low- and middle-income countries (LMICs). The factors contributing to this rise are varied
42 and are contributed to by the environmental, social, political and commercial determinants of
43 health, among other factors. This Review focuses on understanding the rise of
44 cardiometabolic diseases in LMICs, with particular emphasis on obesity and its drivers,
45 together with broader environmental and macro determinants of health, and the LMIC-based
46 responses to counteract cardiometabolic diseases.

47 Introduction

48 In the academic and political community, non-communicable diseases (NCDs) have been
49 framed as a global emergency.^{1,2} The economic burden that non-communicable diseases
50 (NCDs) impose to low- and middle-income countries (LMICs) has contributed to the visibility
51 of NCDs within the broader global health policy environment,³ and the projected economic
52 losses worldwide by 2030 associated with NCDs have been calculated to be \$47 trillion.^{4,5}
53 Furthermore, health is considered one of the key Sustainable Development Goals (SDGs)
54 proposed by the UN (**Box 1**).

55 NCDs involve a variety of conditions including cardiovascular and pulmonary disease,
56 diabetes and cancer; our focus here is on those considered cardiometabolic NCDs —
57 cardiovascular disease, stroke and diabetes. In high-income countries (HICs), such NCDs
58 are heavily clustered among people with low socioeconomic status, and NCDs are an
59 important cause of medical impoverishment.^{6–9} However, the highest chances of dying from
60 NCDs are observed in low-income and middle-income countries (LMICs),^{6,10} and in these
61 countries, while they remain most common among wealthier groups, the fastest rates of
62 increase are again among poorer socio-economic groups.¹¹

63 Changes in the prevalence of cardiometabolic diseases and their major risk factors have not
64 been uniform across settings. Over recent decades, cardiovascular disease mortality has
65 declined in HICs^{12–16} and increased in LMICs,^{12,13} and diabetes prevalence has increased
66 worldwide but at a faster rate in LMICs.^{17,18} Moreover, NCD mortality occurs on average at
67 earlier ages in LMICs, and the increasing number of years spent living with such conditions,
68 their complications and multimorbidities, have major consequences at individual, community,
69 societal and country levels.

70 Cardiometabolic diseases are linked to several risk factors, namely obesity, hypertension,
71 diet, tobacco, air pollution and physical inactivity.^{19,20} Hypertension and low education are
72 key contributors to cardiovascular events and mortality worldwide, yet the contribution of
73 other risks, e.g. household air pollution and poor diet, vary by a country's economic level.²¹
74 Despite the overall risk-factor burden appearing lower in LMICs relative to HICs,²² rates of
75 major cardiovascular events such as death from cardiovascular causes, myocardial
76 infarction, stroke, or heart failure, are lower in HICs than in LMICs, an observation that could
77 reflect poor management and weak health systems infrastructure.²² Many of the
78 achievements in NCD control in HICs are closely related to better healthcare delivery and
79 management of risk factors¹²

80 The epidemiology and management of NCDs in LMICs have received detailed
81 attention,^{10,11,23} and roadmaps to address specific diseases have been devised.²⁴ Hence,
82 rather than focusing on the epidemiology and treatment of these diseases and their risk
83 factors, in this Review we aim to provide a broader and more nuanced understanding of why
84 the epidemic of cardiometabolic NCD has exploded in LMIC settings. We address this by
85 focusing on the complex exposures faced by individuals raised in LMICs, in particular as
86 their environments become more toxic and obesogenic. In this Review we also explore the
87 commercial determinants of health, particularly in urban populations, together with
88 population-wide responses arising from LMIC settings. As an overarching conceptual
89 approach, we draw on the ‘capacity-load’ model of NCD (**Figure 1**).^{25,26} Below, we consider
90 how the epidemiology of NCDs in LMICs is shaped by the particular exposure of individuals
91 in these countries to factors affecting both metabolic capacity and load.

92 **The social and environmental determinants of cardiometabolic** 93 **disease in LMICs**

94 ***Nutrition***

95 The rise of cardiometabolic diseases has been strongly linked to rises in obesity. For
96 example in Africa, a study found that the age-standardized mean body mass index (BMI)
97 increased from 21.9 to 24.9 in women and from 21 to 23 in men, and a positive association
98 was observed between diabetes prevalence and BMI in 1980 and 2014.²⁷ Globally, much of
99 the increases in BMI has recently been linked to a predominant rise of BMI in rural areas.²⁸
100 Between 1975 and 2016, the global prevalence of obesity increased from 3% to 11% among
101 men and from 6% to 15% among women,²⁹ with different patterns of change across different
102 world regions. The rise in obesity varies between countries in association with
103 socioeconomic status and gender.³⁰ It is notable that the increase in obesity is not just
104 focused on adults, but has also increased in children and adolescents worldwide, from below
105 1% in 1975 to 6-8% in 2016.²⁹ Results from a Norwegian longitudinal studies with an
106 average follow-up of 45 years showed that obesogenic environments are major contributors
107 to the epidemics of obesity and NCDs and contribute more than genetic predisposition.³¹
108 This suggests that the environment is the primary determinant of the metabolic load (**Figure**
109 **1**) that humans accommodate to in their daily lives, particularly in terms of food and physical
110 activity.

111 Much of the rise in the burden of cardiometabolic conditions in LMICs is closely linked to the
112 recent epidemiological transition observed in these countries, that is the change in the
113 pattern of causes of mortality from a predominance of infectious disease to NCDs,^{32–34} a

114 change that is occurring in the context of persisting or recent under-nutrition.^{25,35} It is notable,
115 however, that the obesogenic environment might also influence different populations
116 differently with respect to disease development. For example, Asian populations develop
117 diabetes at relatively low levels of BMI.^{23,36,37} The capacity-load model (**Figure 1**) suggests
118 that exposures in early life such as a large burden of infections and chronic undernutrition
119 that were experienced decades ago by today's adults in LMICs still has negative effects on
120 their health.³⁸⁻⁴¹ Importantly, with respect to the present day, in the 1970s-1980s more than
121 50% of the population in LMICs were stunted⁴², thus introducing in these populations long-
122 term deficits in metabolic capacity.⁴³ Adults in LMICs tend to experience cardiovascular and
123 metabolic conditions much earlier in their adulthood than those born and raised in HICs,
124 which may be due to such different population penalties from hardship earlier in life.^{44,45}

125 Whilst undernutrition has not disappeared in LMICs, over the last four decades we have
126 observed a rise in BMI in children and adolescents worldwide.²⁹ Within one or two
127 generations, as in the cases of Mexico⁴⁶ and Chile,⁴⁷ this transition has resulted in what is
128 known as the “double burden of malnutrition” at the individual, household and community
129 level.^{48,49} Children exposed to the double burden will not develop to reach their full potential
130 when transitioning into adulthood,^{40,50-52} and it is likely that today's children in LMICs will also
131 have higher exposures, to ever more common obesogenic environments, at higher doses
132 and for longer durations than in the past.

133 Much of the world's rise in BMI and thus, increases in obesity, has recently been attributed
134 to changes in BMI in rural settings,²⁸ and understanding the contribution of the rural and
135 urban environments to obesity is important. When compared to those exposed to rural or
136 urban environments only, migrants serve as tracers of how exposure to different
137 environments affect cardiometabolic adaptations and responses.⁵³ For example, in the
138 PERU MIGRANT study, it was observed that among rural-to-urban migrants, those who
139 migrated when aged older than 12 years had higher probability of developing diabetes,
140 impaired fasting glucose and metabolic syndrome compared to people who migrated at
141 younger ages.⁵⁴ These observations indicate different reactions to the exposure to urban
142 environments depending on age, with those migrating at younger ages having greater
143 plasticity to adapt to their new environments.

144 ***The nutrition environment***

145 Sustainable food systems are essential to achieve the SDGs.⁵⁵ Economic improvement,
146 trade liberalization and increasing urbanization have resulted in important changes in the

147 LMIC food environment, defined as the composition, promotion, availability, accessibility and
148 affordability of foods.⁵⁶

149 In recent years, LMIC settings have experienced an increased availability of foods produced
150 by large international food corporations, as well as an important expansion of supermarkets
151 and fast-food chains which in part is driven by the Commercial Determinants of Health (see
152 below).^{57,58} As a result, people living in urban areas have rapid and cheap access to more
153 packaged, ready-to-eat or ready-to-heat foods manufactured by multinational food
154 corporations, compared to local foods that could be obtained in traditional open-air markets,
155 such as fruits, vegetables, and cereals.^{59,60} In the case of children, this scenario is worsened
156 by the presence of street-vendors in the surroundings of daycares and schools who now
157 offer snacks and industrialized beverages to children instead of natural foods, as shown in
158 examples from Brazil, Guatemala and Mexico.⁶¹⁻⁶³ Compounding this, an important
159 proportion of children do not have access to clean water during long periods in the day, and
160 some prefer to offer them sugar sweetened beverages.⁶⁴ Similarly, over the past two
161 decades, away-from-home food intake has had a large increase, with for example fast-food
162 chains now spread all over the Latin American continent.⁵⁷

163 The increased availability of packaged and ready-to-eat foods is worrisome because these
164 foods tend to be higher in nutrients of concern such as added sugars, sodium, saturated fat,
165 and trans-fat compared to unpackaged foods, whilst also being deficient in key
166 micronutrients.⁶⁵⁻⁶⁸ Moreover, recent evidence indicates that the nutrient composition of
167 packaged food products varies importantly around the world, being considerably less healthy
168 in LMICs such as Chile and Mexico.⁶⁹ No age group is unexposed to these dietary trends,
169 and even infants are at risk of receiving energy-dense micronutrient-poor complementary
170 foods.⁷⁰

171 Importantly, food prices have also evolved in recent years in LMICs. Large-scale sells have
172 allowed lower prices for packaged food products, so that it is now relatively cheaper to buy
173 foods high in sugar, fat, and sodium such as sugary sodas or salty snacks than healthy
174 foods such as fruits, vegetables, and dairy products; although this association may vary
175 depending on the income and development level of the country.⁷¹ The result is that these
176 products have become accessible to, and marketed at, the poorer socio-economic groups.
177 The consumption of ultra-processed foods has increased, for example throughout the Latin
178 American and Caribbean region, while consumption of healthy foods has remained low.⁷²
179 Consumption of ultra-processed foods is a key factor driving the epidemic of NCDs currently
180 imposing the greatest health and economic burden in LMICs, such as diabetes,
181 cardiovascular disease, and some types of cancer.^{59,73-75}

182 It is important to note that the penetration of ultra-processed foods have also reached rural
183 settings, in which women increasingly work more in non-farm occupations, which in turn
184 increases the demand for convenience food.^{57,76} Supermarkets initially opened in large cities
185 but have progressively expanded to small towns in rural areas through convenience stores
186 and small supermarkets. Marketing strategies of unhealthy food products have also spread
187 into rural areas. Therefore, not surprisingly, recent reports indicate that is precisely in rural
188 areas where obesity is increasing faster in LMICs.²⁸

189 ***Air pollution***

190 Another key source of metabolic load in LMICs is air pollution. This contributes to adult
191 morbidity and mortality through chronic obstructive pulmonary disease (COPD), stroke and
192 ischaemic heart disease, but also affects young children through acute lower respiratory
193 infections,⁷⁷ thus undermining metabolic capacity in early life (**Figure 1**). Already, air
194 pollution is suggested to account for 19% of all cardiovascular deaths and 21% of all stroke
195 deaths globally,⁷⁸ and 87% of this burden occurs in LMICs, concentrated in particular in sub-
196 Saharan Africa and south and east Asia⁷⁹ (**Box 2**).

197 Burning biomass for household fuel has long been a key source of air pollution in LMICs,^{80,81}
198 and more recently there has been rapid increases in the volume of vehicle traffic in many
199 cities which are an additional burden on human health and in urban areas where road
200 vehicle emissions are further concentrated.⁸²⁻⁸⁵ As reported by the International Energy
201 Agency, transport accounted for one quarter of total global CO2 emissions in 2016, a level
202 71% higher than in 1990.⁸⁶ The highest absolute increase was in road transport, and while
203 the Americas historically had the highest transport emission levels of all regions, and this has
204 continued over recent years, Asia is quickly closing the gap with annual growth rates in
205 emissions five times larger than the Americas.⁸⁶ Importantly, urban planning in LMICs has
206 lagged behind the rapidly rising traffic volumes,^{87,88} and the typical vehicles in LMICs are
207 more polluting than those in HICs.^{77,89}

208 There is increasing recognition that air pollution damages almost every organ in the body,
209 and is for example linked with heart disease, dementia and diabetes morbidity and
210 mortality.⁷⁸ Air pollution shows a dose-response association with ill-health, but beyond that,
211 those already affected by NCDs are also more susceptible to the harmful effects of air
212 pollution.⁹⁰ Clearly, exposure to air pollution lies largely outside individual control and
213 represents a generic toxic environment (**Box 2**).

214 **Urbanisation**

215 Urbanisation is one of the most important demographic shifts worldwide during the past
216 century. Today, more than half of the world's population resides in urban areas, representing
217 more than the world's total population in 1960.⁹¹ Between 2015 and 2030 the world will add
218 1.1 billion new city dwellers, growing the global urban population by 28 per cent, from 4.0
219 billion to 5.1 billion.^{92,93} Furthermore, the majority of projected urban population growth will
220 be in Africa and Asia, followed by the Latin America and the Caribbean region.^{92,93}

221 Within cities in LMICs, the majority of individuals simultaneously experience political,
222 economic, housing, and ecological vulnerability.⁹⁴ Given the large number of individuals
223 residing in urban areas, these vulnerabilities translate into the majority of the population
224 being exposed to an environment that directly impacts their risk of cardiometabolic disease
225 and furthermore, within this environment there is inequitable access to opportunities for
226 healthy eating, active living and unpolluted environments; an inequity that exists both within
227 countries and compared to the same context within HICs.

228 The historical contexts around which cities in LMICs have developed have influenced the
229 vulnerabilities that persist, and continue to influence the nature of urbanisation in LMICs and
230 hence the risk of cardiometabolic disease development (**Box 3**). First, the urban centres of
231 many cities in Africa, Asia and Latin America are rooted in colonial legacies of sociopolitical
232 exclusion that manifest today as spatial inequalities that become evident in terms of
233 proximity to aspects of the city that are meant to confer an urban advantage, e.g.
234 infrastructure and amenities, and are consequently closely linked to health inequities.⁹⁵
235 Second, unplanned and unmanaged growth in rapidly growing LMIC cities creates
236 opportunities to live exceeding the opportunities for employment, along with high rates of
237 poverty, resulting in an urban form overwhelmingly characterised by conditions of informality,
238 for example, 62% of urban dwellers live in slum conditions in Africa.⁹⁶ Last, the population
239 pyramids of LMICs highlight a distortion in urban versus rural populations with an increasing
240 proportion of adolescents and young people residing in cities, exposed to environments that
241 are not conducive to health-promoting behaviour.⁹⁷

242 Despite being largely unplanned and illegal, informal settlements are persistent features of
243 the urban landscape of LMIC cities, with a growing proportion of the population living in such
244 settlements.⁹⁸ In response, the New Urban Agenda⁹⁹ adopted by the United Nations
245 Conference on Housing and Sustainable Urban Development and endorsed by the UN
246 General Assembly and the SDGs¹⁰⁰ (**Box 1**) advocate for a shift away from eradication to
247 upgrading of informal settlements for inclusive human settlements (SDG 11), and health and

248 wellbeing (SDG 3). Such healthy city interventions have primarily focused on improving
249 access to water and sanitation,¹⁰¹ with little or no focus on primary NCD prevention through
250 improving active living and healthy eating environments or reducing air pollution. One
251 example of a city in Africa taking the initiative to address unhealthy environments associated
252 with NCD risk is the collaboration between the city government of Accra, Ghana and the
253 World Health Organization (WHO) on an air pollution campaign.¹⁰² The poor urban
254 environment affects particularly the urban poor.

255 The WHO's Health-in-All-Policies approach¹⁰³ aims to increase access to healthy, affordable
256 foods, opportunities for human interaction, and opportunities for physical activity;¹⁰⁴ all of
257 which are driven by sectors outside of health or healthcare. These obesogenic elements of
258 the urban built environment that influence obesity and NCDs —high prevalence of energy
259 dense foods, marketing of unhealthy foods, lack of or limited footpaths/cycle infrastructure
260 and safe places to play, exposure to air pollution— are multiple, entangled, and
261 interconnected, and those living in informality are particularly vulnerable as they are least
262 equipped to compensate for the inextricable obesogenic conditions that epidemiological,
263 nutritional, and urban transitions generate. Informal built environments add complexity to
264 addressing the causes and complications of cardiometabolic disease as, for example,
265 interventions to address obesity may not be implemented through formal regulated
266 structures.⁹⁷

267 Nonetheless, cities can play a vital role in addressing health and social inequity,^{97,101,105} and
268 greater coordination across sectors could contribute to improving health outcomes. This
269 would require connection between relevant health indicators and urban infrastructure
270 initiatives, such as monitoring changes in the urban food environment and the impact of
271 these changes on healthy eating behaviour and cardiometabolic disease outcomes in the
272 long-term. For example, case studies have demonstrated how integrated urban planning can
273 support the development of equitable access to healthy food systems, and prevent food
274 deserts, where fresh food is unavailable, and only unhealthy, heavily processed foods high
275 in sugar, fat and carbohydrates are readily available and affordable.¹⁰⁶

276 **Commercial determinants of health**

277 The etiology of cardiometabolic diseases is complex and influenced by different individual,
278 social, environmental and private sector determinants.¹⁰⁷ The recent increased risks of
279 developing many of the major cardiometabolic diseases are associated with the production,
280 marketing, and consumption of commercially produced products, food and drinks —such as
281 those containing sugar, salt and trans-fats—, alcohol and tobacco.¹⁰⁸ For example, the

282 global adult per-capita consumption of alcohol per year increased from 5.9L to 6.5L between
283 1990-2017 and is projected to reach 7.6L by 2030;¹⁰⁹ this includes a 104% increase in the
284 South-East Asian and a 54% increase in the Western Pacific, regions as defined by the
285 WHO. This increase in alcohol use is especially high in upper middle-income countries such
286 as China, India and Vietnam where levels of alcohol consumption are higher than in some
287 European countries (**Box 4**). The growth of snacks, soft drinks and processed foods is also
288 fastest in LMICs compared to HICs and is projected to grow by 20% in the next 5 years; on
289 the other hand, little or no growth is expected in HICs.¹¹⁰

290 Commercial determinants of health are “strategies and approaches used by the private
291 sector to promote products and choices that are detrimental to health”.¹¹¹ This single
292 concept includes consumer and health behavior, individual choice at the micro level, global
293 risks to society, the global consumer society and the global economy at the macro level. In
294 fact, reaching any set target to reduce cardiometabolic disease will be challenging as long as
295 strategies and policies are not designed to govern the commercial drivers contributing to the
296 rising burden of cardiometabolic disease worldwide. As internationalization of trade, capital
297 and information in the food, beverage, and tobacco industries have substantially increased,
298 progress on preventing and controlling cardiometabolic diseases will require the public
299 health community to address industry responsibility in relation to the burden of
300 cardiometabolic diseases.^{110,112–114}

301 The rise in consumption of unhealthy commodities reflects the fact that multinational
302 companies are increasingly targeting LMICs not only for their huge collective population size,
303 but also because governmental legislation protecting LMIC populations from unhealthy
304 commodities remains much weaker than in HICs, where the impacts on health are already
305 well recognised and supported by a strong scientific evidence base.²⁶ The role of
306 commercial interests in negative health effects is highlighted by the promotion of private
307 vehicle ownership, which simultaneously increases air pollution whilst also undermining
308 physical activity patterns.^{115,116}

309 Commercial influences may have both direct and indirect influences on cardiometabolic
310 diseases and contributory factors such as smoking, inactivity, and obesity; and these
311 influences often operate through long and complex causal pathways. The commercial
312 influences can also interact with one another, their contexts and society which has
313 implications for interventions at different levels.¹⁰⁷ For example, researchers have identified
314 practices from industry-funded charities, such as the International Life Science Institute
315 (ILSI), an institute with the purported mission “to provide science that improves human
316 health and well being”¹¹⁷ that was founded and funded by Coca-cola and supported by

317 McDonalds, Nestle and other corporate entities, against their purported objectives. Studies
318 found instances of ILSI seeking to influence research, conferences, public messages and
319 policy, including instances of punishments for related-bodies failing to promote industry-
320 favorable messaging.¹¹⁸

321 Similarly, children are important to industry marketers for many reasons: they often have
322 access to their own money to spend, they influence parental selection of products, and they
323 will grow up to be life-long consumers.¹¹⁹ Most families have televisions at home and
324 simultaneously, exposure to food advertisements has increased across all socioeconomic
325 groups.^{120–123} With the higher penetration of the Internet, new forms of food promotion are
326 being developed, particularly for children and adolescents.^{124,125} There is robust evidence
327 showing that unhealthy food products are more heavily advertised than healthier food
328 options; therefore, higher exposure to food marketing is likely promoting or sustaining
329 unhealthy dietary behaviors in LMICs, especially among children.¹²⁶ Moreover, increasing
330 evidence indicates that food marketing has been changing its potential audience, now
331 targeting socio-economic and ethnic minorities and hence increasing the risk of widening
332 existing health and nutrition disparities.¹²⁷

333 This generation of social collective harm is only one strategy being used to open new
334 markets in LMICs and promote the consumption of products linked to increased risk of
335 cardiometabolic disease. Industry also engages with and markets to stakeholders —people
336 with influence in the health policy and health investment world; as well as donors, policy
337 influencers, staffers, legislative aides, etc.— and politicians to influence the policy agenda
338 and undermine public health legislation.¹¹⁹ This has been quite effective for their work to
339 prevent industry regulation at national level (Box 4).

340 **Countering cardiometabolic diseases in LMICs**

341 ***Population-based efforts***

342 Strategies to address cardiometabolic diseases in the majority of LMICs to date have
343 predominantly focused on the identification of risk factors as well as screening to detect and
344 treat diseases.¹²⁸ Whilst these are important, there is a need for a greater focus on
345 prevention strategies that act on the upstream determinants. As NCDs have risen up the
346 global agenda, population-wide interventions merit attention.¹²⁹ Population-wide preventive
347 strategies focus on intervening upon the determinants of health in large groups, with the aim
348 of shifting the whole population's distribution of a given risk factor.^{130–132} For example,
349 reducing sodium intake and eliminating the intake of artificial trans fatty acids has been

350 proposed to delay 94 million deaths worldwide within 25 years.¹³³ This has been recently
351 applied in Peru, where a pragmatic population-based approach using a salt substitution
352 strategy has shown community-wide reductions in levels of blood pressure as well as
353 reductions in the incidence of hypertension.^{134,135}

354 Until recently, few examples of population-level interventions targeting cardiometabolic risk
355 factors in LMICs were available. As an example, the Framework Convention for Tobacco
356 Control (FCTC) provided a clear and systematic effort to include population-wide
357 interventions as a critical step to change the tide of tobacco consumption. The FCTC
358 proposed structural interventions, such as banning indoor smoking, increasing tobacco
359 prices, and restricting marketing channels to promote smoking, along with individual-level
360 interventions such as the provision of smoking cessation programs, to reduce tobacco-
361 related health problems.¹³⁶ It is now recognized that these strategies have been key to
362 stabilizing and reducing tobacco consumption globally,¹³⁷ and in particular in LMICs such as
363 Mexico,¹³⁸ Brazil,¹³⁶ or Thailand.¹³⁹

364 Similar strategies to that of the FCTC are being implemented to reduce obesity and
365 metabolic diseases. Latin America has been at the forefront of the implementation of
366 interventions aimed at reducing the consumption of sugar sweetened beverages (SSBs) and
367 low-nutritional high-energy foods (junk food). The SSBs tax in Mexico was one of the first
368 nationwide taxes aimed at reducing the consumption of sugary drinks in the country; two
369 years after implementation, consumption decreased on average 8.2%, while untaxed
370 beverages, such as water, increased 2.1%.¹⁴⁰ These changes, along with the projections of
371 the potential impact of the tax in deaths, health care costs, and obesity and diabetes cases,
372 created momentum for the implementation of similar taxes in other countries, and to
373 consider doubling the current 1-peso-per-liter-tax in Mexico.¹⁴¹

374 More recently, Chile has set a global example in the implementation of a complete package
375 of structural interventions to curb obesity.^{142,143} In 2014, Chile modified its previous sugar-
376 sweetened beverage tax, increasing the rate from 13% to 18% tax on industrialized
377 beverages with high levels of sugar (>6.25 g sugar/100 ml) and decreasing the rate from
378 13% to 10% tax on industrialized beverages with low or no sugar. By 2016, the country
379 implemented food labels to clearly identify foods and beverages high in sugars, calories,
380 sodium or saturated fats (now called “high-in” products). Simultaneously, the food
381 environment was regulated, banning the sales of these foods in schools and the marketing
382 of products in the media for children under 14 years of age.^{142–144} While the overarching
383 impact of these changes is still under analysis, recent studies have shown that people
384 understand well the labeling and that after implementation they improve food healthiness

385 classification and decrease the purchases of “high-in” products of some food categories
386 such as sweet-sugared beverages and breakfast cereals. Similarly, food-ad exposure on
387 television decreased among preschoolers and adolescents and the exposure to
388 unhealthy food products at the school also decreased substantially. Interestingly, it also
389 seems that the food industry is responding to the onset of regulation by decreasing the
390 amount of sugar and sodium in some food categories. Other countries in the Latin
391 American and Caribbean region have approved similar policies, such as Uruguay and
392 Peru.^{145,146}

393 Efforts to regulate the obesogenic environment are closely linked with the urban health
394 agenda in Latin America,^{147,148} and also to include the redesign of urban space and to
395 provide better infrastructure to increase active transportation, reduce car use, provide green
396 areas and increase public safety to incentivize utilitarian and leisure-time physical activity.¹⁴⁹
397 Combating obesity requires integrated governmental and societal action to protect
398 population health.^{150,151}

399 ***Improving healthcare***

400 LMICs have been facing major challenges regarding treating cardiometabolic diseases.
401 Usually, health systems, especially the primary healthcare care level, are better prepared to
402 respond to acute conditions, to provide maternal and child care, or to target prevention and
403 control efforts oriented to infectious diseases. However, the response to chronic conditions is
404 poorer mainly because, to combat these, people need frequent access to the health care
405 system, have a good and long-term adherence to pharmacological and non-pharmacological
406 treatment, and good coordination of care across levels of specialized treatment. In this
407 context, different solutions have been proposed to strengthen the current health system, to
408 implement different strategies to promote disease self-management or to identify
409 stakeholders that can support the health system.¹⁵² Here we briefly mention the role of
410 technologies and health (mHealth), integration of care, and task shifting, whose application
411 has been highly innovative in LMIC settings.

412 mHealth has been applied in LMICs by different actors and with a diversity of purposes. For
413 example, in terms of prevention of disease, particularly in weight reduction, patients and
414 caregivers have been offered different types of technological support to promote behavioural
415 change such as mobile phone apps, Web pages, and short messaging services (SMS)^{153–156}
416 as reminders to increase adherence to lifestyle changes through improving knowledge and
417 enhance motivation to change behaviour.¹⁵⁷ On the other hand, health workers have been
418 receiving training in the diagnosis and management of cardiometabolic diseases through

419 eHealth, whereas in other cases, both in HIC and LMICs, health professionals in remote
420 areas have received support through telemedicine.^{23,158–161}

421 Given the limitations and shortcomings of existing healthcare systems and infrastructure in
422 LMICs, be it in terms of budget, services and human resources, compounded with the
423 challenges of chronic conditions and multimorbidity,¹⁶² moving away from addressing single
424 diseases towards the integration of care seems to be a suitable response in LMICs.^{163–169}
425 Different projects have been working towards improving the health system, at all levels
426 (primary care, hospitals or specialized institutes) and working with all stakeholders (health
427 workers, managers, regional health directors) to improve access to care, increase availability
428 and affordability of medicines, improve coordination of care or improve patient
429 satisfaction.^{170–173} Given the comorbidity between mental health and cardiometabolic
430 conditions, some projects have promoted the opportunistic screening of mental health
431 disorders in this group of patients and their referral using existing resources.¹⁷⁴ Other
432 ongoing initiatives are using mHealth technologies to treat mild to moderate depressive
433 symptoms among patients with cardiometabolic conditions.¹⁷⁵

434 It is well known and commonly reported that health workers are overwhelmed by their daily
435 activities, and this is also true in LMICs. To overcome this, some initiatives have targeted the
436 transfer of some of the work of health workers to other key actors, i.e. community health
437 workers, caregivers, and others.^{176–180} Also, to address the shortage of physicians, task
438 shifting has been moved to other healthcare professionals, for example nurses to manage
439 hypertension.¹⁸¹ These strategies have usually been accompanied by training and
440 technological support, leveraging mobile technology, and have been used mostly to
441 diagnose or identify patients at risk.^{152,182,183}

442 **Future directions**

443 ***Intersectoral strategies***

444 Whilst both LMICs and HICs have rising trends of obesity and diabetes, cardiovascular
445 disease mortality is decreasing in HICs but not in LMICs. Strategies to reduce the increasing
446 burden of cardiometabolic diseases in LMICs are desperately needed. Recognizing the links
447 between NCDs and the wider development and economic agendas within LMICs policy
448 environments is crucial to counter NCDs. Among them, promoting leadership to champion
449 health issues in non-health sectors, such as agriculture, economics or trade is an urgent task
450 to ensure a health perspective in all policies. Long-term exposure to obesogenic and toxic
451 environments, including fundamental drivers such as the commercial determinants of health,

452 will require comprehensive responses going well beyond the health sector. Industry is
453 wealthy, complex and heterogeneous, so public health organizations will need more than
454 simple facts to confront it. Addressing the role of industry in NCDs raises discomfort for
455 many institutions and policy makers, due to potential conflicts of interest and distrust towards
456 some companies. This does not mean that there is no potential to engage and partner with
457 industry, but such partnerships are complicated and raise potential ethical issues, especially
458 for those who generate evidence or policy around cardiometabolic diseases.

459 LMICs have historically suffered the double burden of malnutrition, leaving a long lasting
460 metabolic mark in their population. Understanding the role of the biological penalties
461 suffered by LMIC populations in early life may provide additional information to develop
462 population-wide prevention initiatives that complement existing individual high-risk
463 approaches. LMICs also host areas of conflict and are fragile states, introducing another
464 example of rapid changes that will affect the development and control of NCDs.^{184–186} LMIC
465 populations are also those most vulnerable to wider planetary injuries, including climate
466 change.^{2,187,188} Efforts to prevent NCDs should not be considered as competing with other
467 health and development agendas, but can rather serve as a unifying force, ultimately driving
468 the common goal of improving peoples' wellbeing across the lifecourse.

469 We think that there is a need for multi-stakeholder—involving public, private, and civil
470 society sectors—dialogue platforms and mechanisms to support intersectoral policy action
471 plans that bring together sectors that influence NCDs and its risk factors, to ensure policies
472 are aligned to prevent cardiometabolic diseases. Such spaces are vital to bridge the gap
473 between those working to address the knowledge gaps such as researchers, actors
474 responsible for implementation at scale, such as policymakers and practitioners, and the
475 potential beneficiaries and advocates, which involves the wider society.

476 ***Improved disease surveillance***

477 In addition to the intersectoral governance mechanism required, there is a need for
478 integrated surveillance of cardiometabolic disease risk that incorporates both individual-level
479 health outcomes and community-level health-determinant exposures. Whilst surveillance of
480 this nature using traditional survey methodologies is resource-intensive, ongoing advances
481 in technologies to capture area-level data on health determinants are noteworthy and should
482 be incorporated into NCD prevention efforts. For example, advances in earth observation
483 data derived from satellite imagery which are increasingly available at neighbourhood
484 scales¹⁸⁹ could be harnessed to monitor relevant changes in the urban environment and the
485 health impact of built-environment interventions on healthy eating behaviour and NCD risk.

486 ***Prioritizing adolescents and youth***

487 There must also be a focus on reducing the exposure of adolescents and young people to
488 risk factors for cardiometabolic disease. Multi-faceted intersectoral efforts that seek to
489 intervene appropriately over a long-time period are crucial to reduce NCDs in children and
490 adolescents. This is particularly vital in considering strategies that target young people for
491 cardiometabolic disease prevention. Introducing healthier behaviours and protective factors
492 during childhood and adolescence can significantly change an individual's health trajectory
493 into adulthood.^{190,191} However, besides sexual and reproductive health, the majority of
494 adolescents do not perceive a need for NCD prevention, nor do they routinely access health
495 care.¹⁹²⁻¹⁹⁴ Therefore, there is a need for strategies that seek to identify ways to improve the
496 health of younger populations, which are not purely within the context of either the health
497 sector, or the household, or educational establishments.^{192,194} Such strategies would need to
498 be multisectoral, recognizing the interactions between environmental and economic factors,
499 social norms and personal choice.¹⁹⁵

500 ***Improving our understanding of complex systems***

501 Investing in the long-term understanding of NCD-related outcomes produced by LMIC
502 environments will be needed. Scientific research is a fundamental resource for informing
503 policy and decision making. The LMIC scientific community must seek to understand the rise
504 in cardiometabolic diseases in their regions to identify successful interventions to control
505 cardiometabolic diseases. This will require, at least, capacity in key and emergent disciplines
506 such as complex systems thinking,¹⁹⁶ implementation science,^{197,198} and decision-based
507 models.^{199,200}

508 It is now clear that the key risk factors for cardiometabolic diseases arise in a heavily
509 interrelated physical, biological, social, and economic space. Given this complexity, we will
510 need to find creative solutions that generate the benefits we expect, without producing
511 negative reverberations in the rest of the system. Complex systems thinking provides an
512 appropriate conceptual and methodological framework to pose and solve some of these
513 issues; however, its use remains limited, even in HICs.²⁰¹ Similarly, research in LMICs
514 remains mainly directed to simple etiological studies that try to uncover the causes of
515 diseases or their complications. For cardiometabolic diseases, a lot is already known about
516 prevention and treatment, but the implementation of these solutions is painfully slow.
517 Implementation science tries to close the gap between knowledge and practice, by
518 proposing specific frameworks and methods to translate, adapt, and facilitate the
519 implementation of proven interventions.²⁰² As yet, few examples of implementation science

520 departments in LMICs are available.²⁰³ Finally, mathematical models are increasingly being
521 used in the public health arena to help overcome data limitations, understand the dynamics
522 of complex problems, simulate different intervention scenarios, and provide long term
523 estimates of potential interventions. While some examples of these efforts produced in
524 LMICs exist, their use is still rare and is not fully embraced by the academic community.²⁰⁴
525 While imperfect, mathematical models can be informative for policy decision making and
526 extremely cost-effective for understanding the potential impacts of decisions at the
527 population level. However, such modeling requires strong interdisciplinary teams, capable of
528 bridging across methodological and conceptual differences, that are sorely lacking in LMIC
529 settings.

530 ***Funding***

531 LMICs need to drive their research agenda and thrive on it, in order to achieve and secure
532 population gains given the large burden imposed by cardiometabolic diseases. Yet, sufficient
533 funding remains a challenge. Health priorities in LMICs are often different from those in
534 HICs. Local funding for the development of structural interventions to solve population health
535 issues remains scarce and new models of funding will be necessary.²⁰⁵ Maternal and child
536 health agendas have achieved significant advances, that the NCD agenda has yet to
537 replicate, in terms of the alignment of political will and development agendas accompanied
538 by adequate funding.²⁰⁶ To harness large population gains given the widespread nature of
539 NCDs, funding will likely not need to target cellular or molecular biology, but rather the
540 complexity of the interrelationships between humans, private capital, public interest, the role
541 of governments, and the ability of the civil society to collectively work towards a more
542 humane, equitable and sustainable world. Increasing the funding for population health
543 interventions is also needed. This funding would be needed to study the development and
544 evaluation of interventions, acknowledging their complexity, and how best to implement
545 them. Funding for the actual implementation and scaling-up of proven interventions will also
546 be necessary to guarantee advancements in cardiometabolic diseases, and NCDs in
547 general, in LMICs.

548 **Figures**

549 ***Figure 1. The capacity-load model***

550 The capacity-load model considers that NCDs arise through the inability to maintain
551 metabolic homeostasis (healthy blood pressure, glycemic control, arterial health), resulting in
552 the development of pathophysiological traits that eventually lead to overt disease. NCD risk
553 is directly shaped by many components of physiology and behaviour (shown in red). A wide
554 range of factors manifesting in the body, impose a 'metabolic load' that challenges
555 homeostasis, examples being obesity, sedentary behaviour, diets high in sugar or fat,
556 psychosocial stress, smoking and the response to infection. High load elevates NCD risk,
557 whereas low load reduces it. However, the 'metabolic capacity' for homeostasis is also
558 strongly shaped by patterns of growth and development during 'critical windows' in early life,
559 when many physiological traits relevant to homeostasis are determined. High capacity
560 protects against NCDs, whereas insults to metabolic capacity elevate risk. The primary
561 environmental influence during early critical windows is maternal phenotype. NCD risk thus
562 emerges through the interaction of metabolic capacity and load (red arrow). Beyond the
563 body, numerous components of the environment also shape NCD risk. Harsh environmental
564 factors (shown in orange) drive elevations in metabolic load, and deplete metabolic capacity.
565 Public health efforts (shown in green) aim to counter these effects, by promoting metabolic
566 capacity in early life (promoting maternal and infant health) and reducing metabolic load in
567 children, adolescents and adults (promoting healthy lifestyles). This integrative model serves
568 to understand how NCD risk is shaped both by developmental experience and by exposure
569 to many aspects of today's unhealthy environments. Simply put, 'the higher the load, and the
570 lower the capacity, the greater the NCD risk.'²⁰⁷

571 **Boxes**

572 ***Box 1. Sustainable Development Goals***

573 The Sustainable Development Goals (SDGs) were proposed by the United Nations as the
574 blueprint to achieve a better and more sustainable future for all by 2030.¹⁰⁰ There are 17
575 SDGs and 169 SDG targets. Whilst all SDGs are interconnected, SDG 3 is specifically
576 devoted ensure healthy lives and promote well-being for all at all ages, and its target 3.4
577 commits countries to reducing by one third premature mortality from NCDs.²⁰⁸

578 Because health is an integral part of human capital and a precondition, driver and outcome
579 of sustainable development, SDG 3 is linked to around 50 health-related targets across the
580 SDGs and the pledge to leave no one behind.²⁰⁹

581

582 ***Box 2. Air pollution and cardiometabolic disease in India***

583 South Asia has the worst air pollution worldwide, being home to 17 of the top 30 cities with
584 the highest levels.²¹⁰ Although a global problem, the manifestation of air pollution in
585 countries such as India has some unique features that exacerbate cardiometabolic
586 disorders. These include the large numbers of two-stroke vehicles, the combustion of lower-
587 quality fuels, the open burning of solid fuel in residential cooking stoves, and poorly
588 regulated industrial processes.²¹¹ One of the most widely investigated markers of air
589 pollution is particulate matter of size ≤ 2.5 micrometers (PM2.5). Over the last three decades,
590 PM2.5 concentrations are estimated to have increased by ~25% in the South Asian region,
591 exacerbated by rapid rates of unregulated urbanisation and industrialisation,^{210,211} while the
592 high density of urban settlements results in substantial population exposure to this stress.
593 Even in rural areas, indoor air pollution remains substantial. Over 80% of the rural Indian
594 population continues to burn biomass for home cooking and heating,²¹² though efforts are
595 underway to reduce this practice. Poorer households are least likely to have access to
596 cleaner fuels, and typically lack a separate kitchen area, resulting in high levels of household
597 air pollution to which women and children are especially exposed.²¹² The consequence is
598 that average daily exposure to concentrations of PM 2.5 in India consistently and
599 substantially exceeds the World Health Organization (WHO) recommendations, primarily
600 through household exposure in rural populations, and through outdoor exposure in urban
601 areas.²¹⁰

602 Epidemiological studies identify air pollution exposure as the third most important risk factor
603 for ill health in India,²¹³ with higher levels of particulate matter associated in cross-sectional
604 studies with the risk of hypertension, diabetes and cardiovascular disease, and with
605 biomarkers of inflammation.²¹⁴ In the city of Chennai, for example, the prevalence of
606 diabetes was 77.5% higher (34.8% vs 19.6%) in areas of high versus low levels of PM2.5
607 exposure,²¹⁵ while in Delhi, higher daily levels of air pollution were associated with a 24%
608 increase in emergency room visits for acute coronary events.²¹⁶ Using long-term data from
609 satellite records, premature deaths in India attributable to PM2.5 exposure increased by
610 ~40% between 1999 and 2014. These trends were driven primarily by increases in
611 ischaemic heart disease and stroke, which increased by 40% and 48% respectively.²¹⁷

612 At a mechanistic level, there is increasing evidence that air pollution impacts directly on
613 cardio-metabolic risk markers, such as blood pressure and insulin resistance. In the Andhra
614 Pradesh Children and Parents Study, exposure to PM2.5 was positively correlated with
615 blood pressure and hypertension in women, though the associations were weaker in men.²¹⁸
616 Another study in rural West Bengal found that cooking with biomass exacerbated systemic
617 inflammation, oxidative stress, hypertension and tachycardia.²¹⁹

618 In those who already have cardio-metabolic conditions, representing a large proportion of
619 the Indian population, air pollution may worsen the progression of disease. For example,
620 among diabetic patients studied in the city of Pune, exposure to air pollution was associated
621 with poorer glycemic control and systemic inflammation, indicating the exacerbation of
622 diabetes complications.^{220,221}

623 Beyond its adverse metabolic impacts in adulthood, air pollution also generates detrimental
624 effects on early growth and development, thus undermining the long-term metabolic capacity
625 for homeostasis. For example, household air pollution has been associated with an
626 increased risk of low birth weight and intrauterine growth delay in India,^{222,223} which
627 propagates to shorter child height.²²⁴

628 Trends in air pollution in India are complex, and driven by many different factors associated
629 with economic development. However, the resulting health problems clearly have
630 commercial determinants. The decentralization that is characteristic of Indian cities has
631 increased travel distances and encouraged a shift to motorized transportation, largely
632 through private transport. Between 1981 and 2002 the number of motorized two-wheelers
633 increased 14-fold, and the country currently has the largest sales of such vehicles
634 worldwide.²²⁵ These sales overwhelm urban infrastructure, and persistent traffic congestion
635 substantially elevates emissions.

637

Box 3. Slum conditions and cardiometabolic diseases in Africa

638 Khayelitsha is the largest informal township in Cape Town, South Africa. Home to almost
639 half a million, predominantly black residents, the history of the establishment of Khayelitsha,
640 which means “our new home” in isiXhosa language, dates back to the apartheid policies of
641 racial segregation in South Africa.

642 Following the first racially segregated settlements established in the early 1900s,
643 Khayelitsha was established in the mid-1980s as the legal residence for black Africans in
644 Cape Town.⁹⁵ Located on low-lying sand dunes beyond the urban boundaries of Cape Town,
645 the settlement was planned to be isolated from the rest of the city. Whilst these segregation
646 laws have since been abolished, with transition to democracy in the 1990s, the spatial
647 marginalisation of Khayelitsha means that whilst there has been a growth of commercial
648 formal and informal activity, the settlement remains characterised by high levels of
649 unemployment, poverty and health outcomes significantly poorer than the national and city
650 average. Of note, mortality from stroke, hypertensive disease and diabetes is higher than the
651 average for Cape Town.²²⁶

652 These diseases are influenced by dietary and physical activity habits which are in turn
653 enabled or impeded by the respective food and activity environments. In Khayelitsha, the
654 food environment is characterised by food insecurity and poor dietary diversity with
655 insufficient access to healthy food.²²⁷ The geographical inaccessibility, with many
656 households having to travel long distances for food shopping,²²⁸ is exacerbated by
657 inadequate access to electricity and inability to store perishable fresh foods like fruits and
658 vegetables, even where market or non-market sources of these foods exist, and an
659 environment unconducive for urban agriculture. These challenges mean that even when
660 residents are aware of the health impact of high salt, high fat, processed foods, the agency
661 to make health food choices is significantly diminished. A study exploring food insecurity in
662 patients with hypertension or diabetes residing in Masiphumelele, another low-income
663 informal township in Cape Town demonstrated that patients with cardiometabolic disease
664 had a good understanding of the importance of a healthy diet in particular fruit and
665 vegetables.²²⁹ In this study, patients describe receiving nutritional advice from clinic as part
666 of their diabetes or hypertension clinical management which implied a level of choice that did
667 not exist in reality, and a lack of acknowledgement on the part of clinicians of the lack of food
668 choices in patients’ contexts. Barriers to accessing these foods expressed included the cost,
669 short shelf-life, and poor quality of available fresh foods in their neighbourhoods.

670 Similar barriers to physical activity are experienced in these informal settlements. In other
671 words, whilst residents recognise the value of taking walks and exercise, the perceived and
672 experienced threat of violence, lack of access to well-maintained open public spaces and
673 playgrounds, and the lack of opportunity for active travel due to the remoteness of the
674 location²²⁸ conspire to result in insufficient levels of physical activity to reduce the risk of
675 cardiometabolic disease.

676 These examples highlight the influence of the built environment, particularly in the context of
677 informal settlements, on cardiometabolic risk. As the proportion of urban residents residing in
678 conditions of informality continues to increase in Africa's rapidly growing cities, a recognition
679 by clinicians of the importance of this urban exposure and a willingness to engage with
680 urban design and planning sectors, which play a critical role, is vital to reduce these
681 population health inequities.

682

683

Box 4. Alcohol, a strong commercial determinant of health

684 One of the leading risk factors of deaths worldwide is the harmful use of alcohol, which is
685 linked to over 200 diseases and injuries and can have social and economic implications for a
686 country.^{230,231} In 2016, almost 5.3% (3 million deaths) of all deaths worldwide were caused
687 by harmful use of alcohol.²³² According to recent statistics, alcohol is consumed by some 2.3
688 billion people worldwide, and the total per capita consumption has risen from 5.5 liters in
689 2005 to almost 6.4 liters in 2016.²³² In 2016, an estimated 1.7 million NCD deaths and 65.5
690 million NCD DALYs were caused by alcohol consumption.²³² Additionally, an estimated 0.9
691 million injury deaths and 52.4 million injury DALYs are attributed to alcohol.²³²

692 The risk from alcohol is associated with the production, marketing, and consumption of such
693 products by commercial entities.¹⁰⁸ Alcohol industry, similar to tobacco, exerts influence
694 through four main channels: marketing, lobbying, corporate social responsibility strategies
695 and extensive supply chains worldwide.¹¹¹ One of the most impactful factors associated with
696 alcohol consumption is alcohol marketing and its regulation has been identified by WHO as a
697 "Best Buy" policy for reduction of harmful use of alcohol.²³³ While limited in number, existing
698 studies show that the alcohol industry uses policy-influencing direct and indirect strategies;
699 these include extensive lobbying, and attempts to shape public perceptions of alcohol and
700 the scientific content of regulatory debates.²³⁴ For example, 23 grants were given to
701 researchers by the industry in 13 countries over 6 years²³⁵ that is why calls for researchers

702 to sever financial ties with the alcohol industry and warnings about engaging with the alcohol
703 industry altogether have been issued.^{236,237}

704 The alcohol industry also uses corporate social responsibility activities to define themselves
705 as corporate citizens who are part of the policy solution; and organizations such as the
706 International Alliance for Responsible Drinking, previously International Center for Alcohol
707 Policies, are one of the main components of this strategy.^{234,238} For example, the alcohol
708 industry has been promoting weak interventions to control drunk driving; a 2016 study
709 showed that less than 1% of the industry's actions to reduce drunk driving aligned with
710 evidence-based recommendations,²³⁹ and at the same time the industry increased its
711 involvement in policymaking and scientific research.²⁴⁰

712 India in recent years, has seen a staggering increase in alcohol consumption, where the
713 average adult per capita alcohol consumption increased by 19% between 2005 and 2010.²³⁹
714 Diageo, a London based multinational alcohol corporation, is one of the largest sellers of
715 alcohol spirits in India and has over \$1.1 billion of investment in the country.²⁴⁰ Diageo has
716 employed various tactics to speed its growth in emerging markets like India. However, some
717 of this growth involved contentious activities; for example, in 2011 Diageo was charged with
718 major violations of the Foreign Corrupt Practices Act by the U.S. Securities and Exchange
719 Commission; Diageo had paid over \$1.7 million to hundreds of Indian government officials.
720 Diageo also uses strategic marketing to attract new, young consumers; for example, sale of
721 alcohol in small sachets ("tetrapacks") or mini-bottles. Diageo also recognized a trend of
722 growing alcohol consumption by Indian women and launched "a community investment
723 program that aims to empower women through learning".²⁴¹ These programs promote
724 individual level, voluntary, behavior change strategies diverting investment and attention
725 from effective public health strategies that modify the alcohol environment to reduce the
726 misuse of alcohol.²³⁹

727

728 **Acknowledgements**

729 JJM conceived the idea of linking child survival and adult population handicaps that will
730 affect responses to NCDs and climate change whilst supported through an Erasmus Mundus
731 Scholar at KIT Royal Tropical Institute, Amsterdam, in 2013. This idea was further
732 elaborated through interactions with William Pan, David Beran, and Fernando Maldonado,
733 among others.

734 JJM acknowledges having received support from the Alliance for Health Policy and Systems
735 Research (HQHSR1206660), the Bernard Lown Scholars in Cardiovascular Health Program
736 at Harvard T.H. Chan School of Public Health (BLSCHP-1902), Bloomberg Philanthropies,
737 FONDECYT via CIENCIACTIVA/CONCYTEC, British Council, British Embassy and the
738 Newton-Paulet Fund (223-2018, 224-2018), DFID/MRC/Wellcome Global Health Trials
739 (MR/M007405/1), Fogarty International Center (R21TW009982, D71TW010877), Grand
740 Challenges Canada (0335-04), International Development Research Center Canada (IDRC
741 106887, 108167), Inter-American Institute for Global Change Research (IAI CRN3036),
742 Medical Research Council (MR/P008984/1, MR/P024408/1, MR/P02386X/1), National
743 Cancer Institute (1P20CA217231), National Heart, Lung and Blood Institute
744 (HHSN268200900033C, 5U01HL114180, 1UM1HL134590), National Institute of Mental
745 Health (1U19MH098780), Swiss National Science Foundation (40P740-160366), Wellcome
746 (074833/Z/04/Z, 093541/Z/10/Z, 107435/Z/15/Z, 103994/Z/14/Z, 205177/Z/16/Z,
747 214185/Z/18/Z) and the World Diabetes Foundation (WDF15-1224).

748 TB-G was supported by Bloomberg Philanthropies, the Bernard Lown Scholars in
749 Cardiovascular Health Program at Harvard T.H. Chan School of Public Health, the “Fondo
750 Sectorial en Investigación en Salud y Seguridad Social” from the National Council for
751 Science and Technology of Mexico (CONACYT-FOSSIS-202671), and Wellcome
752 (205177/Z/16/Z).

753 CC receives a salary as Assistant Professor of INTA, University of Chile.

754 AAH did not receive external funding for this work but has internal support as Director,
755 Center on Commercial Determinants of Health, Milken Institute School of Public Health,
756 George Washington University. He has received support from numerous agencies including
757 current funding from the National Institutes of Health, Fogarty International Center, USA.

758 ML-P receives funding from the Swiss Excellence Government Scholarship (2018.0698).

759 TO is supported by the National Institute for Health Research (NIHR) Global Health
760 Research Group and Network on Diet and Activity. The views expressed in this publication
761 are those of the author and not necessarily those of the NHS, the National Institute for
762 Health Research or the Department of Health. Funding from NIHR (16/137/34) is gratefully
763 acknowledged. TO is also supported by the Stellenbosch Institute for Advanced Study Iso
764 Lomso Fellowship, and LIRA 2030 Africa Programme (LIRA2030-GR06/18), implemented by
765 the International Science Council (ISC) in partnership with the Network of African Science
766 Academies (NASAC) with support from the Swedish International Development Cooperation
767 Agency (Sida).

768 JCKW receives a salary as Professor of University College London's Great Ormond Street
769 Institute of Child Health.

770 We acknowledge the support of Dr. Nino Paichadze and Dr. Imran Bari from the Milken
771 Institute School of Public Health, George Washington University, for their support with the
772 case study on alcohol.

773

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1391 **Conflict of interest**

1392 The authors declare no competing interests

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