

Supporting Materials

S1 Sensitivity of DAAP and DAAO to parameters

In addition to GEMM, we estimated DAAP (Table S3) by Integrated Exposure Response (IER) function used in GBD 2017 study (GBD 2016 Risk Factors Collaborators, 2017) to investigate the difference of DAAP caused by C-R functions. DAAP from 5-COD estimated by GEMM function is 45%–50% (vary with years) larger than those based on IER function. We also summarized estimates of DAAP in recent literatures and found that C-R function difference was the controlling factor of the difference among studies (Fig. S8 and Table S4). The difference of DAAP estimated by GEMM and IER functions is 77%, larger than our estimate due to the difference of other parameters. When accounting for other NCD besides the 5-COD, DAAP is 10%–22% larger, with larger difference at higher PM_{2.5} concentrations. The change rates of DAAP in 2013–2019 estimated by recent literature is 55 ± 33 thousand yr^{-1} (70% of these estimates are in 2013–2017, Table S3). Our estimates of deaths avoided from NCD + LRI (56 thousand yr^{-1}) and 5-COD (25 thousand yr^{-1}) in 2013–2017 are within the range of previous estimates.

We also did a sensitivity test of using linear C-R function to estimate DAAO and find that in the peak season mean O₃ concentration range in 2013–2020, the difference of estimated DAAO using linear and log-linear C-R function is within 5% (Fig. S9 and Table S5).

S2 Age-standardized death ratio

Age-standardized rates are used to make comparison between two time periods or two geographical areas, accounting for the differences in the age structure of the population being compared. Age-standardized death rates are estimates as follows (Eq. (S1)):

$$Rate = \sum_a^n Rate_a AgeS_{standard} \quad (S1)$$

where *Rate* is the Age-standardized death rate, *Rate_a* is the age-specific death rate, and *AgeS_{standard}* is the proportion of population with age *a* in the standard population. We adjust population in each year and calculate the age-standardized rate according to the WHO standard population (Ahmad et al., 2001).

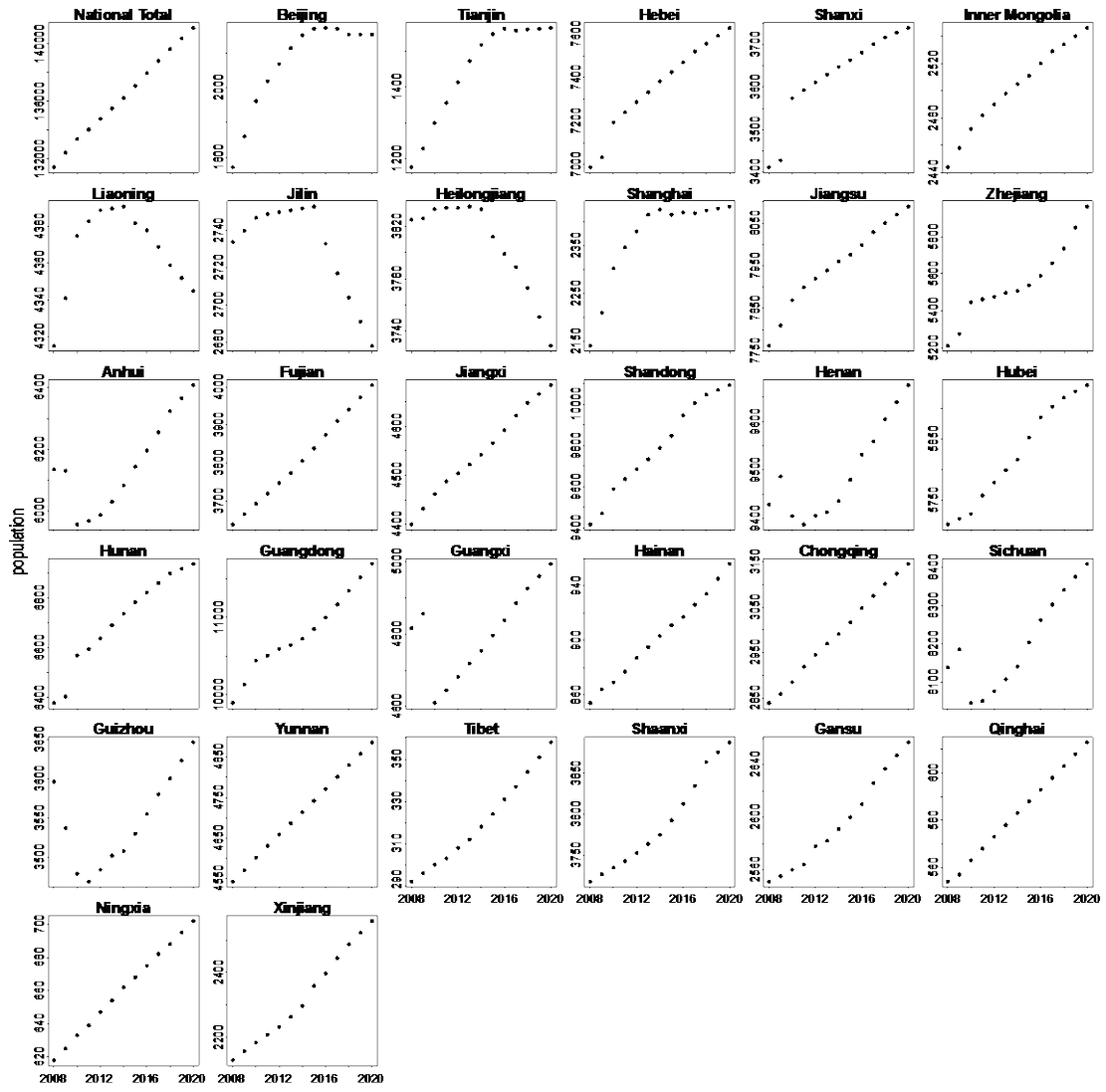


Fig. S1 Population in China and its provinces in 2008–2020.

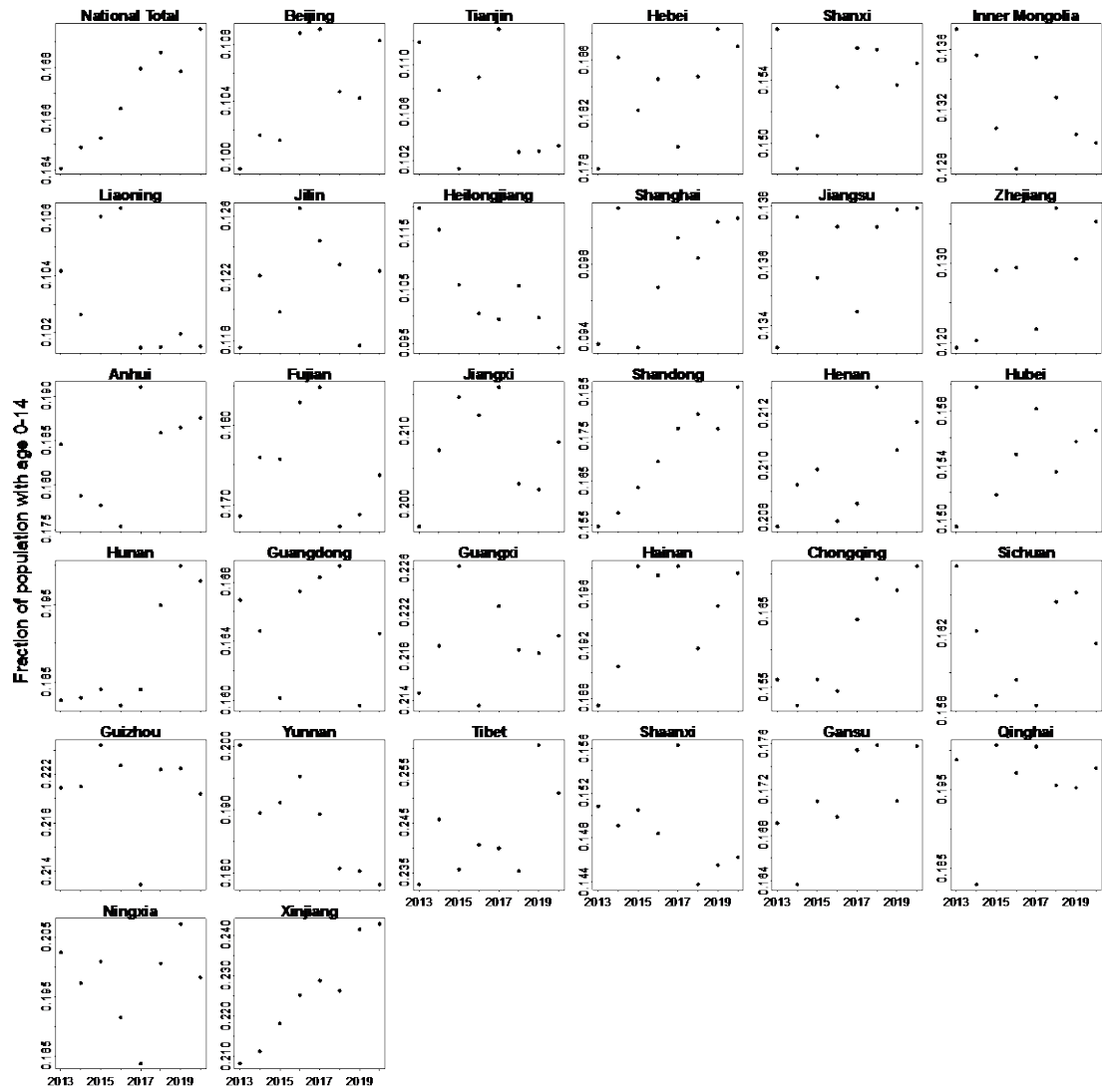


Fig. S2 Fraction of population with age 0–14 in 2013–2020.

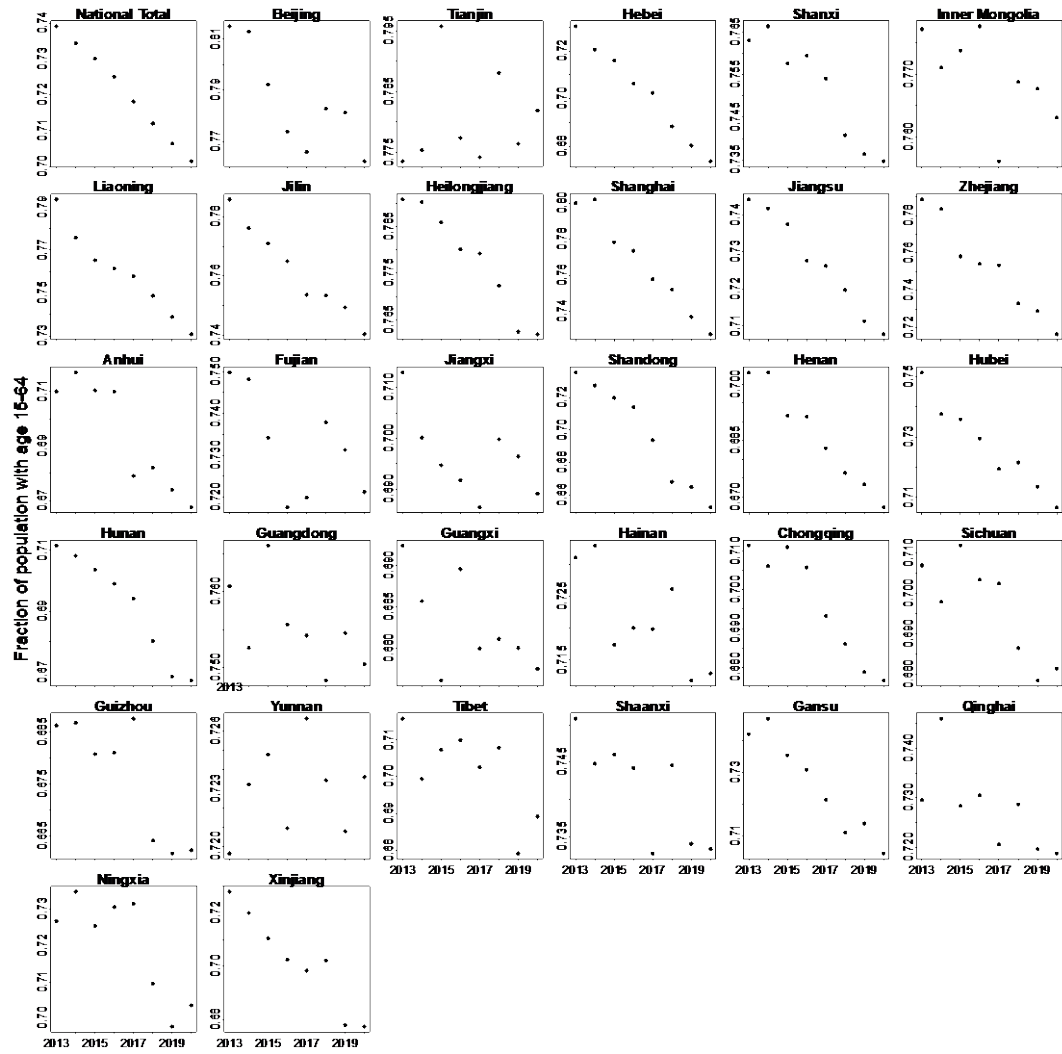


Fig. S3 Similar as Fig. S2, but for age 15–64.

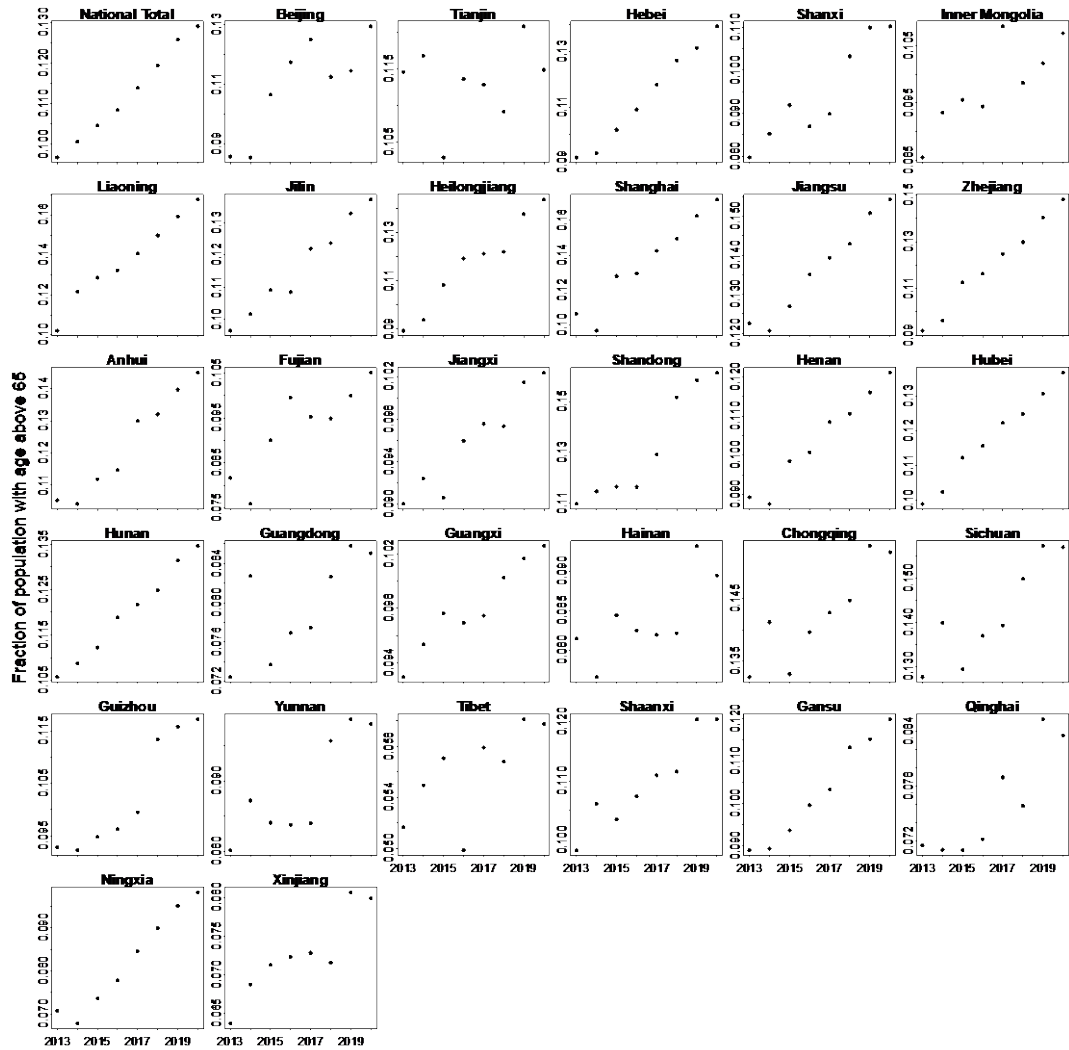


Fig. S4 Similar as Fig. S2, but for age above 65.

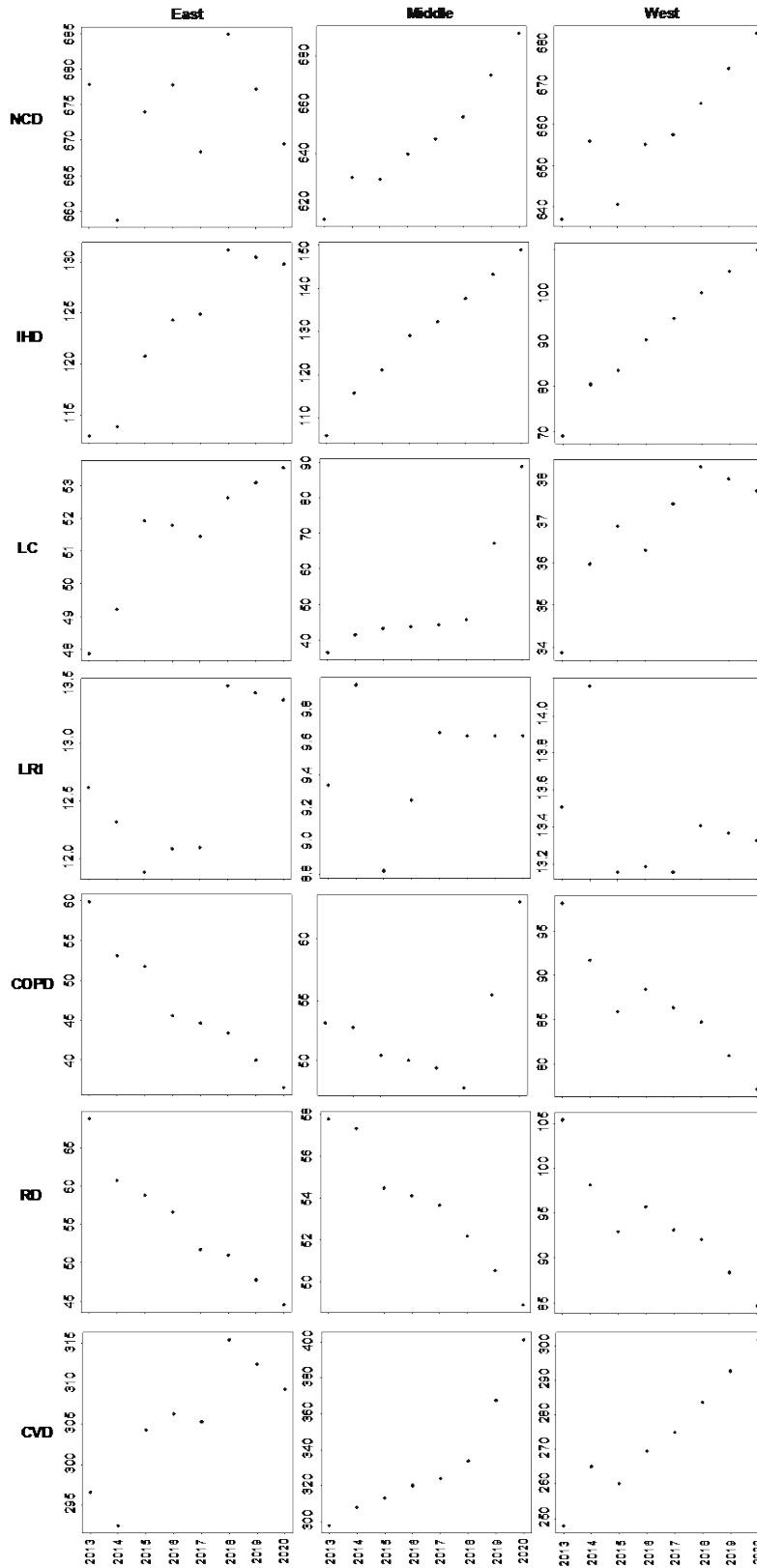


Fig. S5 Baseline mortality in the East, Middle and West region for all ages in China in 2013–2020.

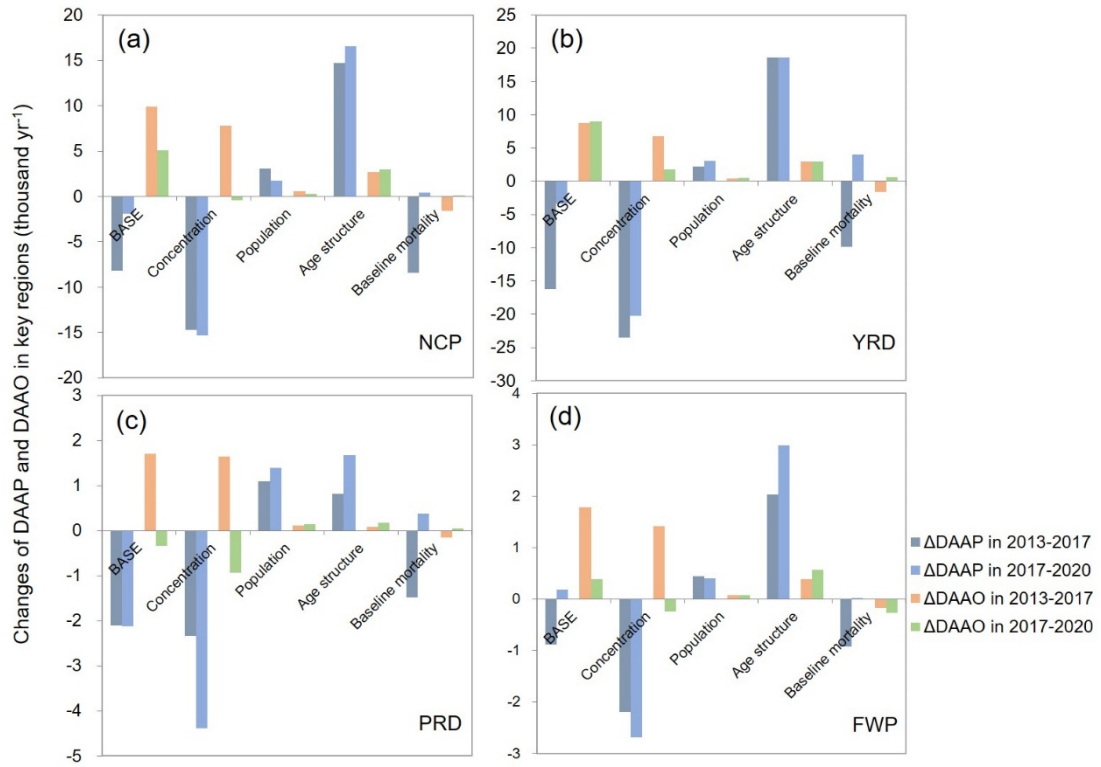


Fig. S6 Factors controlling changes of DAAP and DAAO in APPCAP (2017–2013) and TAPFAP (2020–2017) in key regions (NCP (a), YRD (b), PRD (c) and FWP (d)) in China.

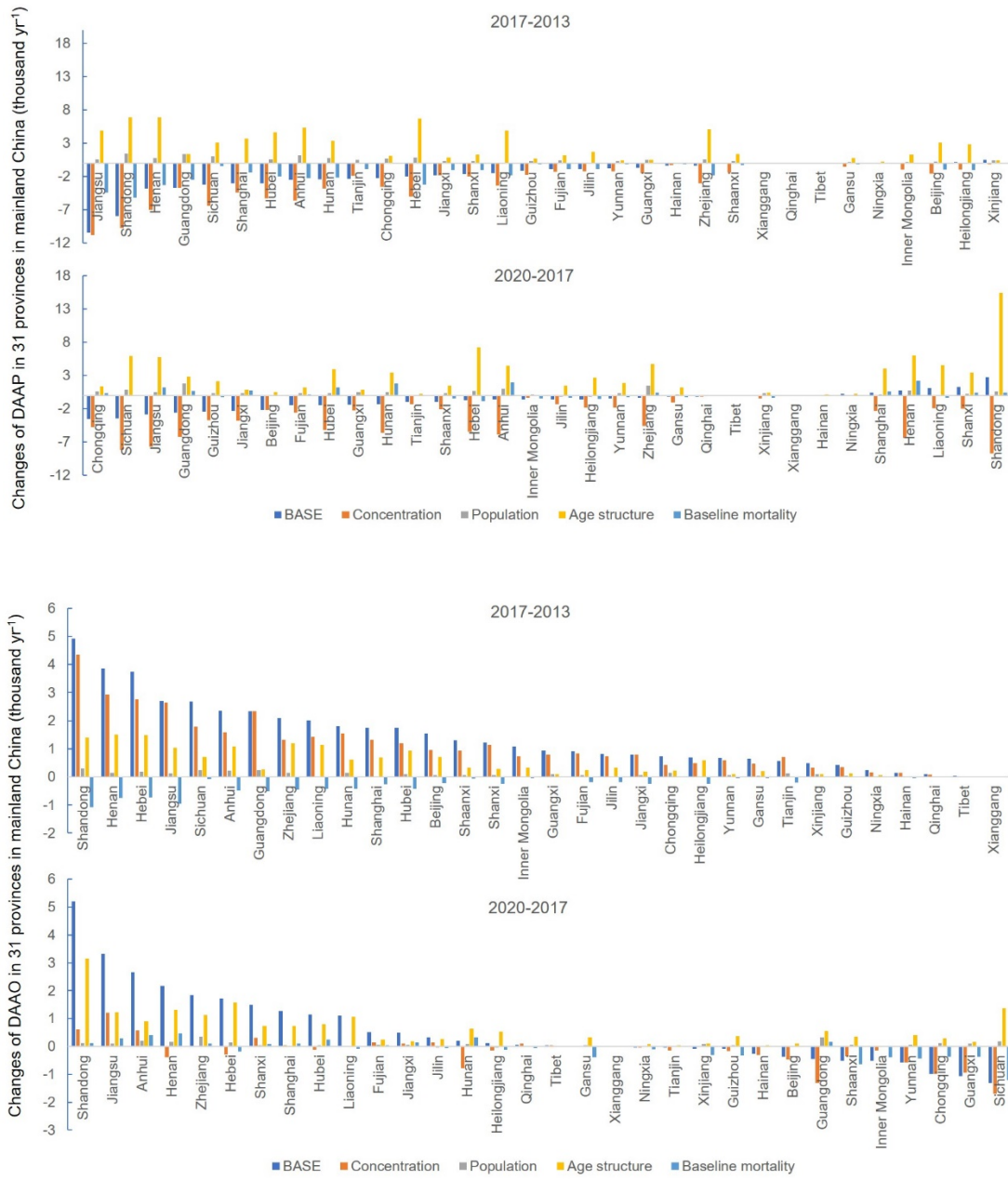


Fig. S7 Similar as in Fig. S6, but for the 31 provinces in China.

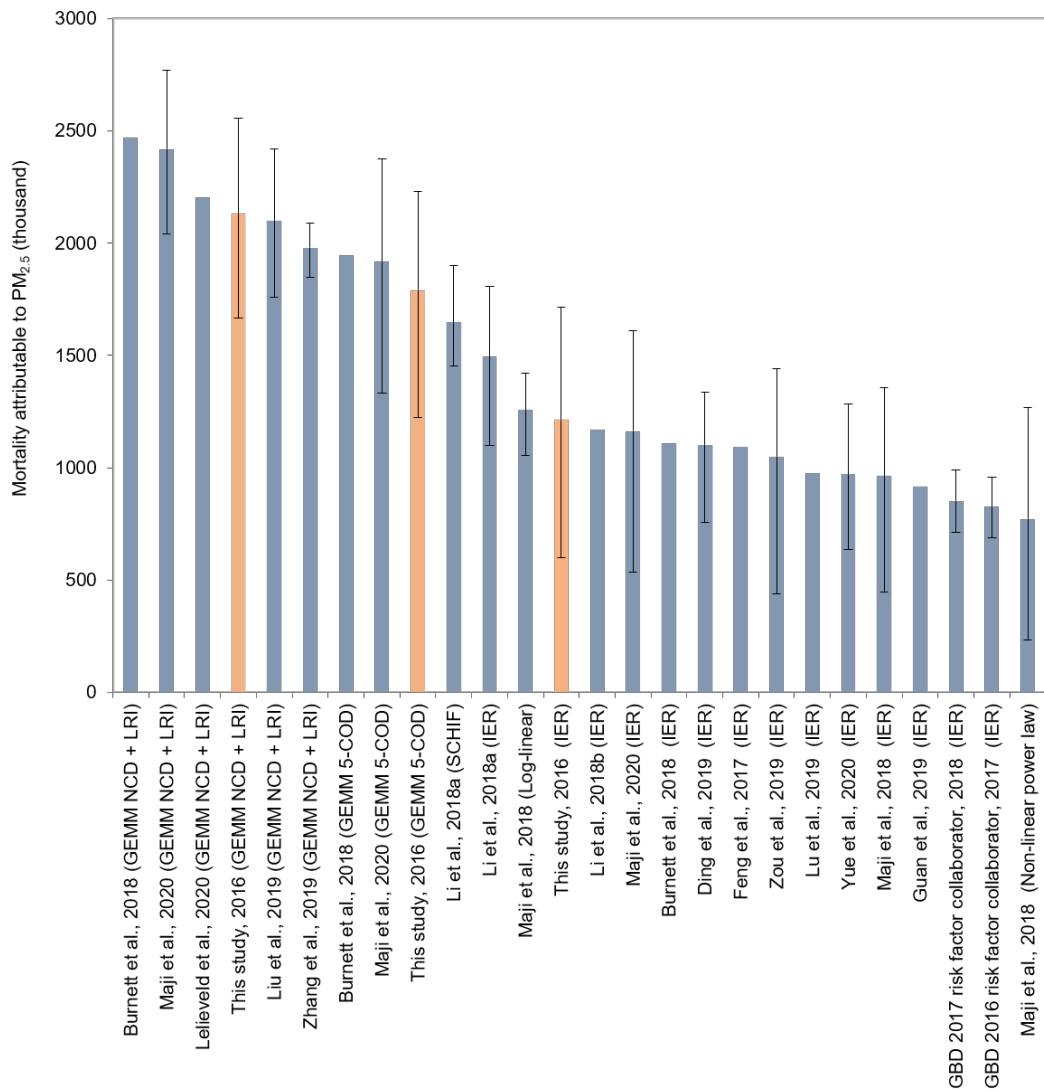


Fig. S8 DAAP in this study and recent literatures in 2013–2020. Also shown are C-R functions used in the respective study (Feng et al., 2017; Burnett et al., 2018; GBD 2016 Risk Factors Collaborators, 2017; GBD 2017 Risk Factors Collaborators, 2018; Li et al., 2018a; Li et al., 2018b; Maji et al., 2018; Ding et al., 2019; Guan et al., 2019; Liu et al., 2019; Lu et al., 2019; Zhang et al., 2019; Zou et al., 2019; Lelieveld et al., 2020; Maji, 2020; Yue et al., 2020).

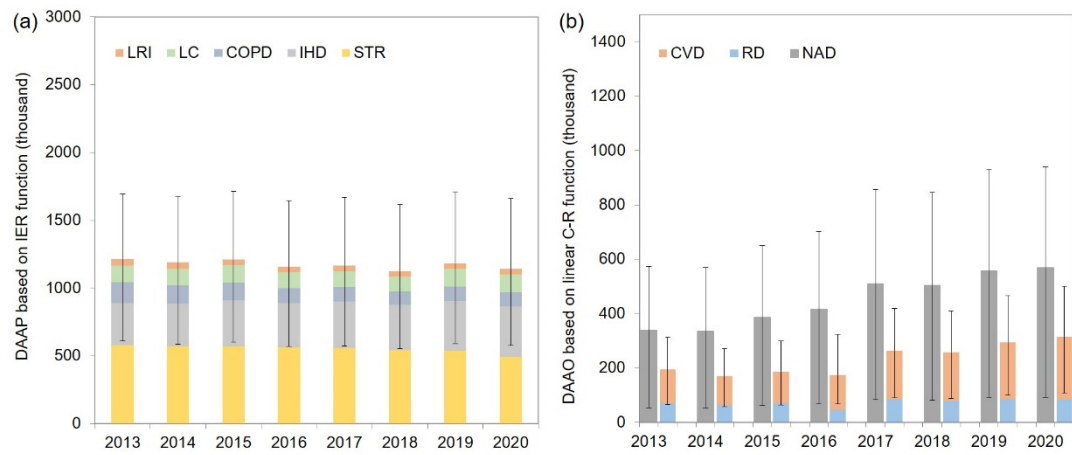


Fig. S9 DAAAP based on Integrated Exposure Response function (a) and DAAO based on linear concentration-response function (b). Error bars are 95% confidence intervals.

Table S1 DAAP, DAAO, population-weighted annual mean PM_{2.5} concentrations (μg/m³) and population-weighted peak season O₃ concentrations (μg/m³) in 2013, 2017 and 2020 in the 31 provinces in China

Provinces	DAAP			DAAO			Population-weighted annual mean PM _{2.5} (μg/m ³)			Population-weighted peak season mean O ₃ (μg/m ³)		
	2013	2017	2020	2013	2017	2020	2013	2017	2020	2013	2017	2020
Shandong	207976	176311	184423	34831	54510	70130	96.0	61.8	45.7	110.2	136.5	139.4
Jiangsu	178840	136907	128221	30698	41489	51474	79.4	47.6	34.8	107.4	124.3	130.7
Henan	172666	157232	159365	32143	47561	54084	89.4	62.3	48.3	114.8	136.1	133.9
Sichuan	170482	157508	147076	30775	41507	37585	62.0	45.9	33.3	103.4	114.2	106.9
Hebei	130291	122181	120126	24884	39808	44949	97.8	67.1	49.9	117.5	144.6	142.3
Anhui	120775	110797	108791	18965	28403	36382	78.3	52.6	37.6	102.9	117.8	121.9
Hunan	114886	104946	101066	13498	20694	21326	57.2	44.2	32.3	86.8	99.7	95.1
Hubei	109524	97406	93034	16801	23766	27184	75.1	49.8	35.8	100.7	113.0	112.3
Guangdong	102229	87136	79256	10069	19434	18111	40.7	31.4	21.0	78.6	96.5	89.0
Chongqing	73826	64655	53831	12055	14998	12022	72.2	47.9	30.2	102.8	109.0	98.2
Zhejiang	73624	72247	71031	12235	20625	26177	45.7	33.8	22.4	93.7	109.0	108.9
Liaoning	72799	66723	69893	12817	20878	24208	56.8	39.2	33.1	100.1	118.7	118.7
Shaanxi	60127	59523	56597	11573	16789	15258	58.5	48.9	39.6	105.1	120.3	116.1
Jiangxi	60068	52765	45572	7696	10861	12315	44.5	35.8	23.9	85.5	96.4	97.4
Shanghai	57536	45242	46488	7522	14492	18274	77.5	40.1	29.2	95.4	121.2	121.8
Guangxi	56600	53658	49438	6029	9777	6604	36.2	30.2	23.8	78.8	89.0	79.9

Shanxi	56445	49755	53608	9753	14593	19087	74.9	55.8	44.3	106.3	128.8	133.6
Guizhou	47122	42438	35032	4044	5778	5539	48.6	36.6	21.4	77.9	84.2	82.1
Heilongjiang	45550	46170	44360	5511	8243	8635	43.9	37.4	29.5	83.4	91.9	90.1
Yunnan	43076	39891	38548	4482	7186	5469	30.0	24.5	19.0	76.3	85.1	78.7
Jilin	37968	34570	32655	4020	7286	8279	49.8	38.8	31.7	82.1	98.8	101.2
Beijing	37548	37887	31356	7321	13514	12415	88.6	60.2	40.1	117.1	148.4	136.7
Fujian	37000	33329	28849	3471	7119	8674	34.9	27.3	17.5	76.1	91.9	94.0
Tianjin	36391	27033	24007	7198	9435	9282	108.3	63.9	49.3	122.8	149.1	145.0
Inner Mongolia	28632	28968	27038	4991	9281	7732	40.9	31.7	29.8	92.8	112.8	110.2
Gansu	28550	28838	28107	5730	8363	8440	38.5	33.6	27.2	97.1	109.6	109.7
Xinjiang	19502	21421	21108	3508	5481	5260	40.7	38.5	34.1	93.9	106.9	107.7
Hainan	6847	5202	5380	646	1180	352	24.4	17.5	15.2	72.9	85.7	66.6
Ningxia	6712	7034	7608	1387	2368	2269	45.8	39.0	37.2	102.7	124.0	120.9
Qinghai	4867	4996	4387	708	1127	1304	34.5	31.9	25.3	84.6	96.9	107.8
Tibet	1244	1531	1121	119	265	381	17.1	19.6	11.7	70.7	81.1	93.2
Hong Kong	23	22	22	3	7	4	34.5	24.8	16.7	79.8	107.3	80.7

Table S2 Estimates of DAAO in this study and recent literatures

Diseases	References	DAAO (thousand)	Year	threshold value ($\mu\text{g}/\text{m}^3$)	HR per 10 $\mu\text{g}/\text{m}^3$ per 10ppb	Risk factor references
RD	Malley et al., 2017	316	2010	53.4	1.12 (1.08, 1.16)	Turner et al., 2016
	Chowdhury et al., 2020	230	2015	53.4	1.12 (1.08, 1.16)	Turner et al., 2016
	Seltzer et al., 2018	200	2015	53.4	1.12 (1.08, 1.16)	Turner et al., 2016
	Malley et al., 2017	154	2010	53.4	1.04 (1.013, 1.067)	Jerrett et al., 2009
	Seltzer et al., 2018	135	2015	53.4	1.04 (1.013, 1.067)	Jerrett et al., 2009
	Maji and Namdeo, 2021	82.8	average 2015- 2019	53.4	1.04 (1.00, 1.09)	Lim et al., 2019
	This study	73–89	2013–2020	60	1.023 (1.007, 1.038)	WHO guidelines (WHO, 2021)
CVD	Seltzer et al., 2018	129	2015	53.6	1.03 (1.01, 1.05)	Turner et al., 2016
	Maji and Namdeo, 2021	112	2019	53.6	1.03 (1.01, 1.06)	Lim et al., 2019
	This study	125–233	2013–2020	60	1.03 (1.01, 1.06)	Lim et al., 2019
COPD	Liu et al., 2021	137.8	2018	29.1–35.7 ppb	1.06 (1.02, 1.10)	GBD 2017 (GBD 2016 Risk Factors Collaborators, 2018)
	Xiao et al., 2021	147.7	2020	29.1–35.7 ppb	1.061 (1.029, 1.093)	GBD 2019 (GBD 2019 Risk Factors Collaborators, 2020)

NAD	Maji and Namdeo, 2021	181	2019	53.4	1.02 (1.01, 1.04)	Turner et al., 2016
	This study	345–579	2013–2020	60	1.013 (1.002, 1.023)	WHO guidelines (WHO, 2021)

Table S3 Region- and disease-specific deaths attributable to long-term exposure to PM_{2.5} in China based on Integrated Exposure Response (IER) function

Disease/Region	Deaths (thousand)			Age-standardized death rate (deaths per 100000 people)		
	Net Changes in 2013–2020	average annual rate of change (%/yr)		Net Changes in 2013–2020	average annual rate of change (%/yr)	
		2013–2017	2017–2020		2013–2017	2017–2020
5-COD	-76 (-88, -50)	-1.0 (-1.4, -0.4)	-0.2 (-0.4, 0.2)	-14 (-19, -10)	-2.2 (-2.7, -1.8)	-3.8 (-3.9, -3.3)
NCP	-5 (-10, 15)	-0.3 (-1.8, 0.5)	1.2 (0.9, 2.0)	-15(-23, -11)	-2.7 (-4.4, -2.1)	-1.5(-2.3, -0.8)
YRD	-16 (-31, -5)	-1.9 (-2.7, -1.4)	0.1 (0, 0.8)	-20 (-25, -17)	-4.0 (-4.8, -3.6)	-3.8 (-4.0, -3.5)
PRD	-9 (-12, -7)	-1.7 (-1.9, -1.4)	-6.2 (-6.3, -3.6)	-21 (-25, -19)	-4.0 (-4.1, -4.0)	-7.9 (-5.8, -8.1)
FWP	5 (1, 8)	0.6 (0.3, 1.1)	2.8 (2.6, 3.5)	-4 (-10, 1)	-1.4 (-1.8, -1.0)	0.4 (0, 0.9)
LC	9 (5, 12)	-1.4 (-4.8, -0.1)	4.5 (0.4, 6.2)	-1 (-2, -1)	-3.1 (-6.0, -2.3)	-1.6 (-4.5, -0.6)
Stroke	-86 (-94, -72)	-0.9 (-1.6, 0.5)	-3.1 (-3.9, -1.9)	-6 (-9, -5)	-0.9 (-1.4, -0.2)	-5.3 (-4.0, -3.6)
LRI	-11 (-11, -11)	-4.5 (-4.5, -4.4)	-1.9 (-1.9, -1.9)	-1 (-1, -1)	-6.4 (-6.4, -6.4)	-6.1 (-6.1, -6.1)
IHD	61(58, 69)	2.6 (1.6, 2.8)	2.9 (0.4, 3.7)	-1 (-2, 0)	-0.2 (-1.4, 0)	-1.5 (-4.5, -1.3)
COPD	-50 (-53, -47)	-7.5 (-8.8, -6.7)	-1.2 (-3.2, 0.0)	-4 (-5, -4)	-8.8 (-10, -8.4)	-5.8 (-7.3, -5.1)

Table S4 DAAP (million) and change rate of DAAP (thousand/yr) in 2013–2020 in recent literatures

Refs	C-R	2013	2014	2015	2016	2017	2018	2019	change rate of DAAP (thousand/yr)
Zheng et al., 2017	IER	1.22 (1.05, 1.37)		1.10 (0.95, 1.25)					-60
Zou et al., 2019	IER	1.2 (0.57, 1.71)				1.05 (0.44, 1.44)			-37.5
Ding et al., 2019	IER	1.39 (1.01, 1.63)				1.10 (0.76, 1.34)			-71.75
Lu et al., 2019	IER	1.078				0.963			-28.75
Maji, 2020	IER			1.001 (458, 1402)				0.88 (0.39, 1.26)	-31.25
Yue et al., 2020	IER	936				974			+ 9.5
Li et al., 2021	IER		1.15		0.96				-94
Liu et al., 2021	GEMM NCD + LRI	2.51					2.12		-78
Maji, 2020	GEMM NCD + LRI			2.14 (1.80, 2.45)				1.76 (1.47, 2.03)	-95.75
Liu et al., 2021	GEMM 5-COD	2.02					1.69		-66
Maji, 2020	GEMM 5-COD			1.70 (1.18, 2.11)				1.38 (0.95, 1.74)	-79

Table S5 Region- and disease-specific deaths attributable to long-term exposure to O₃ in China based on linear concentration-response function

Disease/Region	Deaths (thousand)			Age-standardized death rate (deaths per 100000 people)		
	Net Changes in 2013–2020	average annual rate of change (%/yr)		Net Changes in 2013–2020	average annual rate of change (%/yr)	
		2013–2017	2017–2020		2013–2017	2017–2020
NAD	230 (174, 274)	12.7 (12.2, 13.4)	3.6 (3.3, 3.8)	6 (3, 8)	8.5 (8.1, 9.1)	−0.8 (−0.8, −0.9)
NCP	52 (41, 60)	14.6 (13.7, 15.7)	4.9 (4.8, 4.9)	10 (6, 14)	7.8 (7.1, 8.6)	0.7 (0.7, 0.7)
YRD	60 (47, 69)	12.4 (11.0, 13.0)	8.6 (8.5, 8.7)	8 (4, 10)	6.3 (5.9, 6.8)	2.5 (2.4, 2.6)
PRD	6 (5, 7)	27.1 (26, 28.4)	−2.5 (−2.3, −2.7)	3 (2, 5)	15.9 (15.3, 16.7)	−6.5 (−6.3, −6.5)
FWP	8 (6, 10)	11.4 (10.8, 12.1)	1.8 (1.7, 1.9)	7 (4, 10)	6.8 (6.3, 7.3)	0.1 (0, 0.2)
RD	14 (6, 20)	4.8 (4.3, 5.5)	0.1 (0, 0.1)	0 (0, 0)	1.3 (0.9, 1.9)	−2.4 (−2.4, −2.4)
CVD	105 (88, 122)	10.9 (10.7, 11.3)	9.5 (9.5, 9.5)	3 (2, 4)	6.8 (6.6, 7.0)	4.3 (4.3, 4.3)

References

- Ahmad O B, Boschi-Pinto C, Lopez A D, Murray C J, Lozano R, Inoue M (2001). Age Standardization of Rates: A New WHO Standard. Geneva, Switzerland: World Health Organization 2001
- Burnett R, Chen H, Szyszkowicz M, Fann N, Hubbell B, Pope C A III, Apte J S, Brauer M, Cohen A, Weichenthal S, Coggins J, Di Q, Brunekreef B, Frostad J, Lim S S, Kan H, Walker K D, Thurston G D, Hayes R B, Lim C C, Turner M C, Jerrett M, Krewski D, Gapstur S M, Diver W R, Ostro B, Goldberg D, Crouse D L, Martin R V, Peters P, Pinault L, Tjepkema M, Van Donkelaar A, Villeneuve P J, Miller A B, Yin P, Zhou M, Wang L, Janssen N A H, Marra M, Atkinson R W, Tsang H, Quoc Thach T, Cannon J B, Allen R T, Hart J E, Laden F, Cesaroni G, Forastiere F, Weinmayr G, Jaensch A, Nagel G, Concin H, Spadaro J V (2018). Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. *Proceedings of the National Academy of Sciences of the United States of America*, 115(38): 9592–9597
- Chowdhury S, Pozzer A, Dey S, Klingmueller K, Lelieveld J (2020). Changing risk factors that contribute to premature mortality from ambient air pollution between 2000 and 2015. *Environmental Research Letters*, 15(7): 074010
- Ding D, Xing J, Wang S, Liu K, Hao J (2019). Estimated contributions of emissions controls, meteorological factors, population growth, and changes in baseline mortality to reductions in ambient PM_{2.5} and O₃-related mortality in China, 2013–2017. *Environmental Health Perspectives*, 127(6): 67009
- Feng L, Ye B, Feng H, Ren F, Huang S, Zhang X, Zhang Y, Du Q, Ma L (2017). Spatiotemporal changes in fine particulate matter pollution and the associated mortality burden in China between 2015 and 2016. *International Journal of Environmental Research and Public Health*, 14(11): 1321
- GBD 2016 Risk Factors Collaborators (2017). Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, 390(10100): 1345–1422
- GBD 2017 Risk Factors Collaborators (2018). Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, 392(10159): 1923–1994
- GBD 2019 Risk Factors Collaborators (2020). Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*, 396(10258): 1223–1249
- Guan Y, Kang L, Wang Y, Zhang N N, Ju M T (2019). Health loss attributed to PM_{2.5} pollution in China's cities: Economic impact, annual change and reduction potential. *Journal of Cleaner Production*, 217: 284–294
- Jerrett M, Burnett R T, Pope C A III, Ito K, Thurston G, Krewski D, Shi Y, Calle E, Thun M (2009). Long-term ozone exposure and mortality. *New England Journal of Medicine*, 360(11): 1085–1095
- Lelieveld J, Pozzer A, Poschl U, Fnais M, Haines A, Munzel T (2020). Loss of life expectancy from air pollution compared to other risk factors: a worldwide perspective. *Cardiovascular Research*, 116(11): 1910–1917
- Li J, Liu H, Lv Z, Zhao R, Deng F, Wang C, Qin A, Yang X (2018a). Estimation of PM_{2.5} mortality burden in China with new exposure estimation and local concentration-response function. *Environmental Pollution*, 243(Pt B): 1710–1718
- Li S, Zou B, You J, Fang X, Zhao X, Yao X (2018b). Satellite-based China's PM_{2.5} pollution and associated premature mortality measurement over past two decades. *The International Archives of the Photogrammetry Remote Sensing and Spatial Information Sciences*, XLII-3/W5: 39–45

- Li Y, Liao Q, Zhao X, Tao Y, Bai Y, Peng L (2021). Premature mortality attributable to PM_{2.5} pollution in China during 2008–2016: Underlying causes and responses to emission reductions. *Chemosphere*, 263: 127925
- Lim C C, Hayes R B, Ahn J, Shao Y, Silverman D T, Jones R R, Garcia C, Bell M L, Thurston G D (2019). Long-term exposure to ozone and cause-specific mortality risk in the United States. *American Journal of Respiratory and Critical Care Medicine*, 200(8): 1022–1031
- Liu C, Chen R, Sera F, Vicedo-Cabrera A M, Guo Y, Tong S, Coelho M, Saldiva P H N, Lavigne E, Matus P, Valdes Ortega N, Osorio Garcia S, Pascal M, Stafoggia M, Scortichini M, Hashizume M, Honda Y, Hurtado-Diaz M, Cruz J, Nunes B, Teixeira J P, Kim H, Tobias A, Iniguez C, Forsberg B, Astrom C, Ragettli M S, Guo Y L, Chen B Y, Bell M L, Wright C Y, Scovronick N, Garland R M, Milojevic A, Kysely J, Urban A, Orru H, Indermitte E, Jaakkola J J K, Rytty N R I, Katsouyanni K, Analitis A, Zanobetti A, Schwartz J, Chen J, Wu T, Cohen A, Gasparini A, Kan H (2019). Ambient particulate air pollution and daily mortality in 652 cities. *New England Journal of Medicine*, 381(8): 705–715
- Liu J, Yin H, Tang X, Zhu T, Zhang Q, Liu Z, Tang X, Yi H (2021). Transition in air pollution, disease burden and health cost in China: A comparative study of long-term and short-term exposure. *Environmental Pollution*, 277: 116770
- Lu X, Lin C, Li W, Chen Y, Huang Y, Fung J C H, Lau A K H (2019). Analysis of the adverse health effects of PM_{2.5} from 2001 to 2017 in China and the role of urbanization in aggravating the health burden. *Science of the Total Environment*, 652: 683–695
- Maji K J (2020). Substantial changes in PM_{2.5} pollution and corresponding premature deaths across China during 2015–2019: A model prospective. *Science of the Total Environment*, 729: 138838
- Maji K J, Namdeo A (2021). Continuous increases of surface ozone and associated premature mortality growth in China during 2015–2019. *Environmental Pollution*, 269: 116183
- Maji K J, Ye W F, Arora M, Shiva Nagendra S M (2018). PM_{2.5}-related health and economic loss assessment for 338 Chinese cities. *Environment International*, 121(Pt 1): 392–403
- Malley C S, Henze D K, Kuylensstierna J C, Vallack H W, Davila Y, Anenberg S C, Turner M C, Ashmore M R (2017). Updated global estimates of respiratory mortality in adults ≥ 30 years of age attributable to long-term ozone exposure. *Environmental Health Perspectives*, 125(8): 087021
- Seltzer K M, Shindell D T, Malley C S (2018). Measurement-based assessment of health burdens from long-term ozone exposure in the United States, Europe, and China. *Environmental Research Letters*, 13(10): 104018
- Turner M C, Jerrett M, Pope C A 3rd, Krewski D, Gapstur S M, Diver W R, Beckerman B S, Marshall J D, Su J, Crouse D L, Burnett R T (2016). Long-term ozone exposure and mortality in a large prospective study. *American Journal of Respiratory and Critical Care Medicine*, 193(10): 1134–1142
- WHO (2021). WHO Air Quality Guidelines. Particulate matter (PM₁₀ and PM_{2.5}), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Geneva: World Health Organization. Licence: CCBY-NC-SA3.0IGO
- Xiao Q, Geng G, Xue T, Liu S, Cai C, He K, Zhang Q (2021). Tracking PM_{2.5} and O₃ pollution and the related health burden in China 2013–2020. *Environmental Science & Technology*, 56(11): 6922–6932
- Yue H, He C, Huang Q, Yin D, Bryan B A (2020). Stronger policy required to substantially reduce deaths from PM_{2.5} pollution in China. *Nature Communications*, 11(1): 1462
- Zhang Q, Zheng Y, Tong D, Shao M, Wang S, Zhang Y, Xu X, Wang J, He H, Liu W, Ding Y, Lei Y, Li J, Wang Z, Zhang X, Wang Y, Cheng J, Liu Y, Shi Q, Yan L, Geng G, Hong C, Li M, Liu F, Zheng B, Cao J, Ding A, Gao J, Fu Q,

Huo J, Liu B, Liu Z, Yang F, He K, Hao J (2019). Drivers of improved PM_{2.5} air quality in China from 2013 to 2017. *Proceedings of the National Academy of Sciences of the United States of America*, 116(49): 24463–24469

Zheng Y, Xue T, Zhang Q, Geng G, Tong D, Li X, He K (2017). Air quality improvements and health benefits from China's clean air action since 2013. *Environmental Research Letters*, 12(11): 114020

Zou B, You J, Lin Y, Duan X, Zhao X, Fang X, Campen M J, Li S (2019). Air pollution intervention and life-saving effect in China. *Environment International*, 125: 529–541