Supplementary information

Supplementary Methods

Data collection and processing

Asthma, atopic dermatitis (AD), and maternal hypertensive disorder (MHD) disease burden data was downloaded from Global Burden of Disease Study 2019 (GBD2019, https://vizhub.healthdata.org/gbd-results/). Crude birth rate (birth per 1000 people) and population data was from the World Bank databank (https://databank.worldbank.org/source/gender-statistics#). The gross domestic product (GDP) per capita data was obtained from the Maddison project[1]. GBD reported data from 1990 to 2019 and analyses were therefore based on this period of time. After collating disease and GDP data and excluding countries or timepoints with no data record, final data spanning 1990-2019 across about 150 countries were generated for analysis.

Pregnancy data per year was calculated based on crude birth rate and population data of each country. Crude birth rate data was from GBD2019, and population data was from the World Bank databank.

Percentages of pregnancies affected by MHD (MHD%) were calculated as the ratios of MHD cases per year and the pregnancies per year of the same country. As the peaks of incidences of asthma and AD are about 1-4 years old[2], this age group was focused for our analysis. Ratios of 1-4 years old asthma and AD cases per year versus the pregnancies 2 years prior of the same country were calculated as proxies of the percentages of pregnancies with offsprings developing asthma (asthma%) and AD (AD%) at 2 years of age. AD% and asthma% was compared with MHD% at the 2 years prior timepoint to decipher the link between MHD and offspring AD and asthma. Percentage data was all logit transformed before analysis.

Generalized additive models (GAMs)

Generalized additive models (GAMs)[3-5] feature in their capacity to interrogate multiple parameters simultaneously, as well as their potential interactions and non-linear effects, through the introduction of nonparametric smoothed functions. These functions are usually in forms of splines and provide flexible manners to evaluate non-linear associations.

Here, GAMs were run for AD% or asthma% using MHD% 2 years prior, GDP 2 years prior and time as predictors with the *mgcv* package and the "*gam*" function within[5,6]. In all models, countries from which the data originated were considered as random effects.

GAMs with aforementioned predictors and their different combinations, as well as a null model in which only the random effects of countries were considered were run. Using *mgcv* package[5,6], individual

parameters were modelled as smooth terms using the "s()" function, while their interactions were modelled utilizing the "ti()" or "te()" function, given their different scales, like MHD% and GDP.

Modelling results were compared according to their Akaike information criterion (AIC)[7] and the one with the lowest AIC was selected.

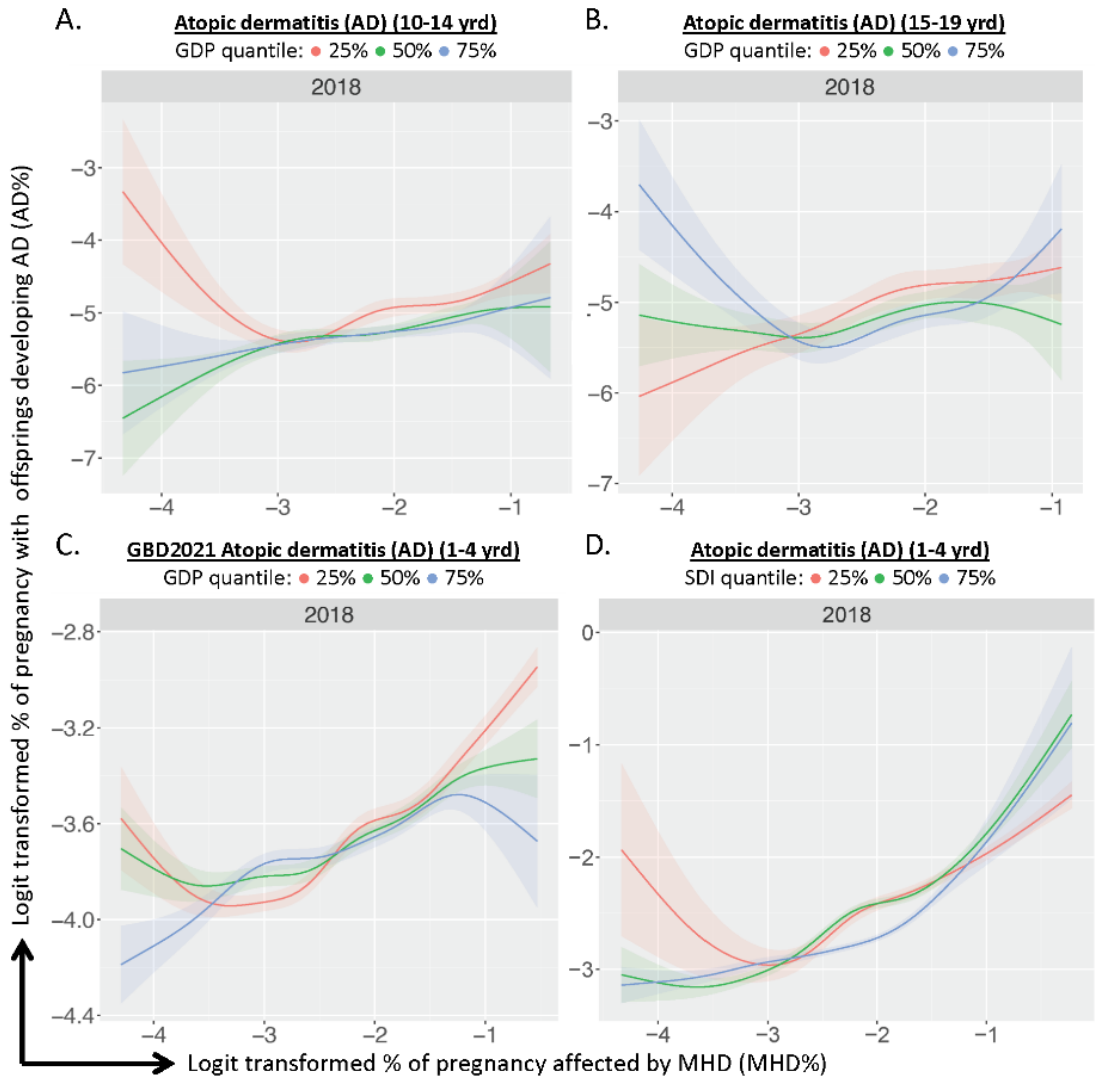

Figure S1. A. Predicted effects of logit transformed percentages of maternal hypertensive disorders-affected pregnancies (MHD%) 12 years prior, GDP and time on the logit transformed percentages of pregnancies with offspring developing atopic dermatitis (AD%) in 10-14 years old age group. **B.** Predicted effects of logit transformed percentages of maternal hypertensive disorders-affected pregnancies (MHD%) 17 years prior, GDP and time on the logit transformed percentages of pregnancies

with offspring developing atopic dermatitis (AD%) in 15-19 years old age group. **C.** Predicted effects of logit transformed percentages of maternal hypertensive disorders-affected pregnancies (MHD%) 2 years prior, GDP and time on the logit transformed percentages of pregnancies with offspring developing atopic dermatitis (AD%) in 1-4 years old age group based on data from GBD2021. **D.** Predicted effects of logit transformed percentages of maternal hypertensive disorders-affected pregnancies (MHD%) 2 years prior, socio-demographic index (SDI) and time on the logit transformed percentages of pregnancies with offspring developing atopic dermatitis (AD%) in 1-4 years old age group.

Supplementary Tables

Table S1-4 are GAM estimates and statistical outputs. The model estimates and related standard errors (Std.Error) were shown for parametric terms. For non-parametric smooth terms, their estimated and reference degrees of freedom (i.e. edf, sumEDF, Ref.df) and their test statistics were shown.

Table S1. Relative fit of GAM analyzing the predictors for AD%. AIC = Akaike information criterion. sumEDF indicates the degrees of freedom of the models. Model 16 was selected as the best model because of the lowest AIC. (related to Figure 1B)

GAM	AIC	sumEDF	Formula
0	-11055.96	157.91	gam(AD% ~ 1 + s(Country, bs = "re"))
1	-11292.71	166.47	gam(AD% ~ s(Country, bs = "re") + s(GDP))
2	-11144.48	162.09	gam(AD% ~ s(Country, bs = "re") + s(Year))
3	-11545.51	169.48	gam(AD% ~ s(Year) + s(GDP) + s(Country, bs = "re"))
4	-11579.22	176.77	gam(AD% ~ te(Year, GDP) + s(Country, bs = "re"))
5	-12320.01	166.78	gam(AD% ~ s(MHD%) + s(Country, bs = "re"))
6	-12372.69	171.04	gam(AD% ~ s(MHD%) + s(Year) + s(Country, bs = "re"))
7	-12645.50	175.48	gam(AD% ~ s(MHD%) + s(GDP) + s(Country, bs = "re"))
8	-12905.60	178.51	gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + s(Country, bs = "re"))
9	-12966.20	187.01	gam(AD% ~ s(MHD%) + te(Year, GDP) + s(Country, bs = "re"))
10	-13094.57	182.37	gam(AD% ~ te(MHD%, GDP) + s(Year) + s(Country, bs = "re"))
11	-12924.92	187.87	gam(AD% ~ te(MHD%, Year) + s(GDP) + s(Country, bs = "re"))
12	-13523.58	263.55	gam(AD% ~ te(MHD%, Year, GDP) + s(Country, bs = "re"))
13	-12523.69	178.17	gam(AD% ~ te(MHD%, Year) + s(Country, bs = "re"))
14	-12883.89	180.03	gam(AD% ~ te(MHD%, GDP) + s(Country, bs = "re"))
15	-13395.86	241.13	gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + s(Country, bs = "re"), data = complete
16	**-13674.22**	**274.60**	**gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, Year) + ti(MHD%, GDP) + ti(GDP, Year) + s(Country, bs = "re"))**
17	-13352.09	217.49	gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year) + ti(MHD%, GDP) + ti(GDP, Year) + s(Country, bs = "re"))
18	-1359260	267.85	gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, GDP) + ti(GDP, Year) + s(Country, bs = "re"))
19	-13496.98	255.39	gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, Year) + ti(GDP, Year) + s(Country, bs = "re"))
20	-13667.62	258.97	gam(AD% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, Year) + ti(MHD%, GDP) + s(Country, bs = "re"))

Table S2. Estimated effects of MHD%, GDP per capita and year on AD%. (related to Figure 1B)

Parametric coefficients				
	Estimate	**Std.Error**	**t value**	**Pr(>|t|)**
(Intercept)	-2.9621	0.1505	-19.68	<2e-16
Approximate significance of smooth terms				
	edf	**Ref.df**	**F**	**P value**
s(MHD%)	8.345	8.853	71.963	<2e-16
s(Year)	3.181	4.101	1.055	0.377
s(GDP)	8.496	8.922	23.766	<2e-16
ti(MHD%, Year, GDP)	60.240	62.297	6.848	<2e-16
ti(MHD%, Year)	12.943	13.939	6.873	<2e-16
ti(MHD%, GDP)	12.343	13.472	14.821	<2e-16
ti(Year, GDP)	11.061	11.999	1.533	0.105
s(Country)	156.986	158.000	1555.377	<2e-16
R-sq.(adj) = 0.994 Deviance explained = 99.4%				
GCV = 0.0024044 Scale est. = 0.0022501 n = 4278				

Table S3. Relative fit of GAM analyzing the predictors for asthma%. AIC = Akaike information criterion. sumEDF indicates the degrees of freedom of the models. Model 16 was selected as the best model because of the lowest AIC. (related to Figure 1C)

GAM	**AIC**	**sumEDF**	**Formula**
0	-6005.396	163.74	gam(Asthma% ~ 1 + s(Country, bs = "re"))
1	-6046.657	167.44	gam(Asthma% ~ s(Country, bs = "re") + s(GDP))
2	-6084.177	168.63	gam(Asthma% ~ s(Country, bs = "re") + s(Year))
3	-6182.928	177.04	gam(Asthma% ~ s(Year) + s(GDP) + s(Country, bs = "re"))
4	-6221.603	185.02	gam(Asthma% ~ te(Year, GDP) + s(Country, bs = "re"))
5	-6372.593	172.60	gam(Asthma% ~ s(MHD%) + s(Country, bs = "re"))

6	-6498.153	177.68	gam(Asthma% ~ s(MHD%) + s(Year) + s(Country, bs = "re"))
7	-6466.578	181.16	gam(Asthma% ~ s(MHD%) + s(GDP) + s(Country, bs = "re"))
8	-6629.696	186.90	gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + s(Country, bs = "re"))
9	-6683.406	194.13	gam(Asthma% ~ s(MHD%) + te(Year, GDP) + s(Country, bs = "re"))
10	-6600.789	192.65	gam(Asthma% ~ te(MHD%, GDP) + s(Year) + s(Country, bs = "re"))
11	-6577.306	195.48	gam(Asthma% ~ te(MHD%, Year) + s(GDP) + s(Country, bs = "re"))
12	-7170.909	279.89	gam(Asthma% ~ te(MHD%, Year, GDP) + s(Country, bs = "re"))
13	-6472.943	187.27	gam(Asthma% ~ te(MHD%, Year) + s(Country, bs = "re"))
14	-6414.504	187	gam(Asthma% ~ te(MHD%, GDP) + s(Country, bs = "re"))
15	-7067.771	240.75	gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + s(Country, bs = "re"), data = complete
16	**-7392.585**	**283.31**	**gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, Year) + ti(MHD%, GDP) + ti(GDP, Year) + s(Country, bs = "re"))**
17	-6882.094	225.35	gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year) + ti(MHD%, GDP) + ti(GDP, Year) + s(Country, bs = "re"))
18	-7338.786	276.73	gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, GDP) + ti(GDP, Year) + s(Country, bs = "re"))
19	-7288.454	272.75	gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, Year) + ti(GDP, Year) + s(Country, bs = "re"))
20	-7300.799	270.62	gam(Asthma% ~ s(MHD%) + s(Year) + s(GDP) + ti(MHD%, Year, GDP) + ti(MHD%, Year) + ti(MHD%, GDP) + s(Country, bs = "re"))

Table S4. Estimated effects of MHD%, GDP per capita and year on asthma%. (related to Figure 1C)

Parametric coefficients				
	Estimate	**Std.Error**	**t value**	**Pr(>|t|)**
(Intercept)	-2.5808	0.3884	-6.644	3.43e-11
Approximate significance of smooth terms				
	edf	**Ref.df**	**F**	**P value**
s(MHD%)	8.843	8.988	41.649	<2e-16
s(Year)	6.572	7.790	10.306	<2e-16
s(GDP)	8.611	8.955	13.542	<2e-16
ti(MHD%, Year, GDP)	61.876	62.917	10.092	<2e-16

ti(MHD%, Year)	15.244	15.697	7.572	<2e-16
ti(MHD%, GDP)	7.423	8.617	12.316	<2e-16
ti(Year, GDP)	10.745	11.955	7.951	<2e-16
s(Country)	162.993	164.000	639.022	<2e-16
R-sq.(adj) = 0.97 Deviance explained = 97.2%				
GCV = 0.011746 Scale est. = 0.011022 n = 4592				

References

1. Jutta Bolt RI, Herman de Jong, and Jan Luiten van Zanden. Rebasing 'Maddison': New income comparisons and the shape of long-run economic development. In. Vol GD-174. GGDC Research Memorandum: Groningen Growth and Development Center; 2018.
2. Shin YH, Hwang J, Kwon R, et al. Global, regional, and national burden of allergic disorders and their risk factors in 204 countries and territories, from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019. *Allergy.* 2023;78(8):2232-2254.
3. Diederich A. Generalized additive models.: An introduction with. *J Math Psychol.* 2007;51(5):339-339.
4. Lane PW, Wood S, Jones MC, et al. Generalized additive models for location, scale and shape - Discussion. *J Roy Stat Soc C.* 2005;54:544-554.
5. Verbeke T. Generalized additive models: an introduction with R. *J Roy Stat Soc A.* 2007;170:262-262.
6. Wood SN. *Generalized Additive Models: An Introduction with R.* Chapman and Hall/CRC; 2017.
7. Akaike H. Information theory and an extension of the maximum likelihood principle Second International Symposium on Information Theory; 1973; Budapest.