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Supplemental Information

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vaccine-preventable diseases in China: 1950–2018**

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Impact of immunization programs on 11 childhood vaccine-preventable diseases in China:

1950-2018

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Supplemental Materials and Methods

Quasi-Poisson

We used the year during which each vaccine was introduced into the EPI as a cutoff year to define the pre-vaccination period (ten years prior to and including the cutoff year) and post-vaccination period (ten years after the cutoff year). The total number of years included in the analysis for each disease ranged from eight to twenty years, depending on the data availability and cutoff year. By assuming that any changes to the incidence rates of the examined VPDs were entirely attributable to immunization, we estimated the effectiveness of the EPI by using quasi-Poisson regression models to estimate the change in the incidence rate for each disease from the pre- to post-vaccination period. Diseases without available data prior to integration of the vaccine in the EPI (i.e., the pre-vaccination period) could not be included in these analyses.

Life table

The abbreviated life table method was used to calculate the decrease of life expectancy caused by infectious diseases from 1978 to 2018, and the distribution of these reductions in different age groups in 2010 and 2016. We were unable to obtain the incidence data for each age group from 1978 to 2003, and thus used the incidence ratio of each age group in 2004 for our calculation. The incidence ratio of each age group in 2017-2018 was calculated according to the incidence ratio in 2016. The potential years of life lost (PYLL) and potential working years lost caused by premature death from infectious diseases from 2004 to 2016 were estimated. Premature death was defined as death caused by not living to the expected lifespan, and was calculated based on the natural mortality rate of the Chinese census.

Supplemental Results

Impact of vaccination coverage on morbidity rates of VPDs

Figure S1. shows the relationship between the vaccination coverages and incidence rates of the VPDs. Focusing on diphtheria and pertussis, we see that after the combined DTP vaccine became available free for all children across the country in 1978, the transmission of the two diseases declined significantly. Similarly, the incidence of measles rapidly declined shortly after the measles-rubella vaccine and the measles-mumps-rubella vaccine were integrated into the EPI program in 1978 and 2007, respectively, and also following the initiation of supplementary immunization activity in 2008. Conversely, even though effective vaccines against tuberculosis and hepatitis B were integrated into the EPI in the 2000s, the incidences of these diseases have continued to rise. The incidence trends of the other nine diseases were basically consistent with those of the corresponding vaccination coverages. In 1982, the Ministry of Health set EPI targets (to be reached by 1990) of 80%-90% coverage for DPT and 90%-95% coverage for OPV and measles by the time a child reached school age. Therefore, the coverage of these vaccines increased during the 1980s. By 2003, however, central government funds accounted for only 1% of total immunization expenditures and more than 50% of expenditures were being made at the village and township levels, with the result that the coverage of vaccines was on the decline. In 2004, the central government for the first time allocated funds for vaccine delivery and administration at the village and township levels. In 2004–2005, the State Council passed the Law on the Prevention and Treatment of Infectious Diseases, reaffirming the requirements for all children to be fully vaccinated. Together, these measures strengthened the financing for vaccines and vaccination services, resulting in increased and more equitable coverage and a historically low VPD burden. From 1978 to 2018, the incidence of pertussis fell 98% from 126.35 to 1.58 per million; measles fell 99% from 249.76 to 0.28 per 100,000; meningococcal meningitis fell 99% from 32.23 to 0.01 per million; and JE fell 98% from

5.39 to 0.13 per million. The last case of diphtheria was reported in 2006.

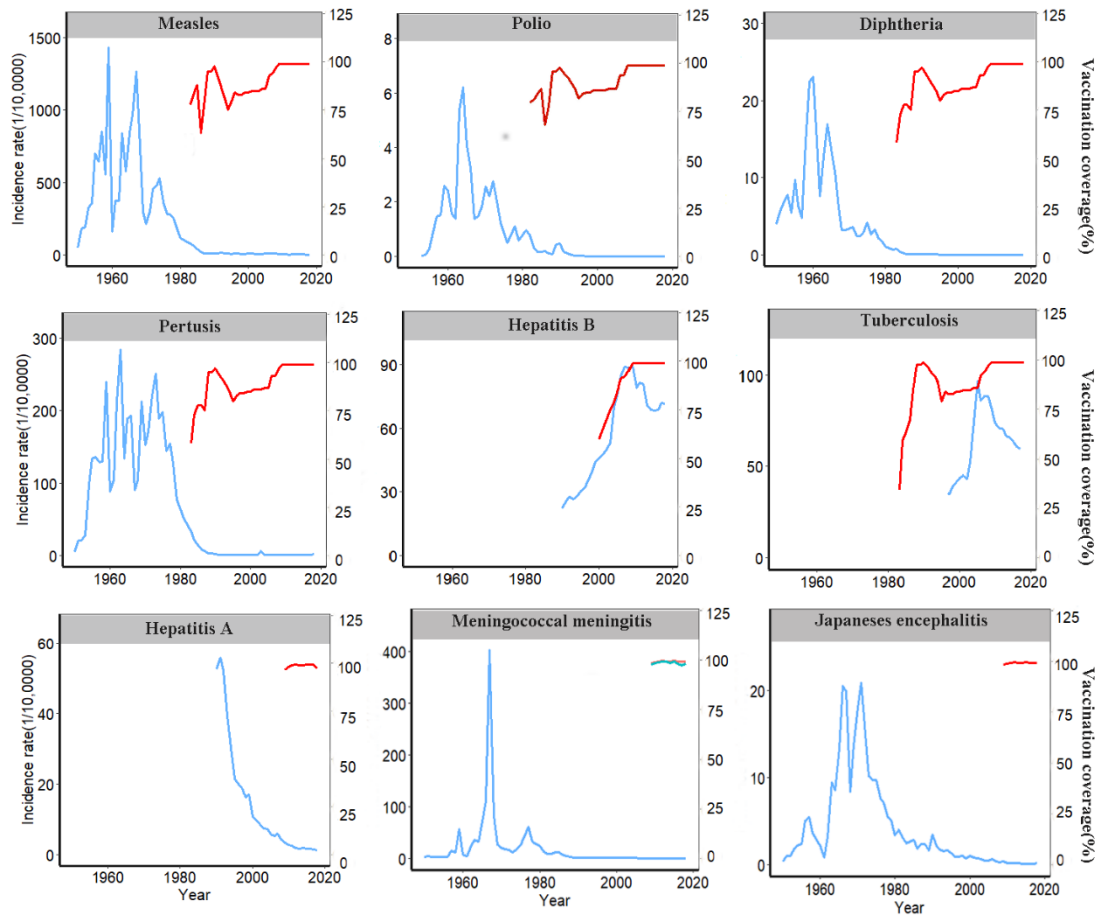


Figure S1. Annual incidence rates of selected VPDs and vaccination coverage

The gray background indicates the period in which the vaccination for a given disease was integrated into the national Expanded Program on Immunizations (EPI). The blue line indicates the morbidity rate of the disease; the red line represents the vaccination rate of the disease; and the green line represents the vaccination rate for the group A + C vaccine. Data on vaccination coverage of Japanese encephalitis, meningococcal meningitis and hepatitis A were collected from national vaccination coverage surveys. Data on vaccination rates for other diseases were obtained from the WHO website (<http://apps.who.int/gho/data/node.main.A824?lang=en>)

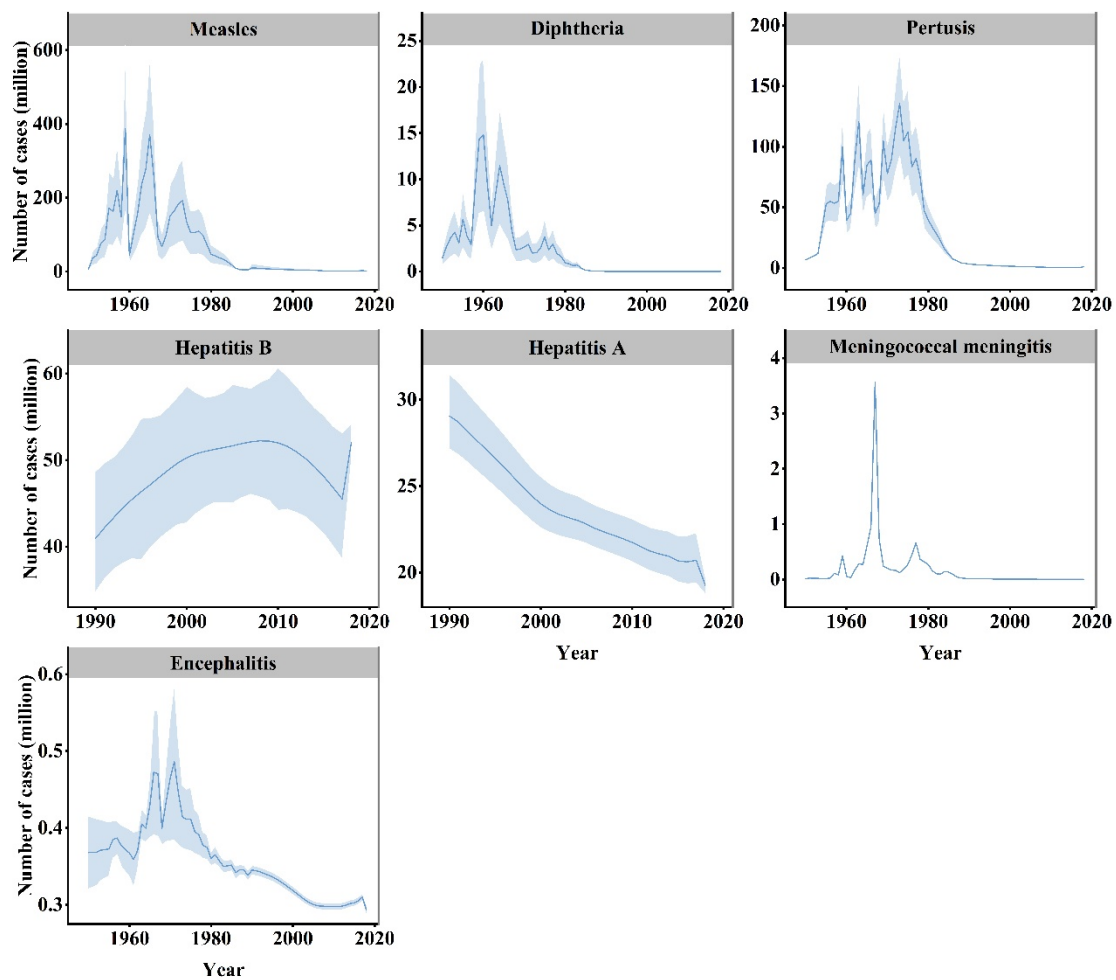


Figure S2. Number of infectious cases adjusted for underreported and under-ascertainment. The solid line represents the number of infectious cases and the dash area are 95% confidence interval. Cases between 1990 and 2017 were from GBD websites, cases between 1950 and 1989 and the year of 2018 were estimate from polynomial regression model

The burden of the 11 VPDs

For hepatitis A and hepatitis B, which were not included in the EPI in 1978, the impact on life expectancy has been calculated since 1990, when these vaccines were introduced. When the hepatitis B vaccine was first introduced in 1990, the impact of hepatitis B-related death on the life expectancy of newborns was 0.023 months; in 2018, when the hepatitis B vaccination rate reached more than 95%, the impact of hepatitis B-related death on the life expectancy of newborns dropped to 0.007 months. Compared with the value in 1990, the contribution of the hepatitis B vaccine to the life expectancy of

newborns in 2018 was 0.16 months. Similarly, the 1990 introduction of the hepatitis A vaccine increased the life expectancy of newborns in 2018 by 0.015 months. By 2018, the life expectancy of neonates for meningococcal and Japanese encephalitis increased by 0.53 months and 0.23 months, respectively, relative to the 1978 levels (Table S1).

When the measles vaccine was first added to the EPI in 1978, the impact of measles death on the life expectancy of newborns was 0.40 months. In 2018, when the measles vaccine vaccination rate was above 95%, the death rate impact was 0.00002 months. The impact of several other VPDS on life expectancy in 1978-2018 is presented in the supplementary information. Overall, the impact of these 11 diseases on life expectancy decreased during the study period.

Similar results were obtained for the loss of healthy life years and loss of work years due to early deaths from these infectious diseases. Table S2 show the loss of healthy life years and loss of work years due to 11 VPDs. From 2004 to 2016, the total loss of healthy life years due to early death caused by the 11 VPDs was 1,182,322 person-years, except for an increase seen in 2012, the loss of healthy life showed a downward trend over time. In 2016, the loss of healthy life years due to early death from the infectious diseases was 53,136.77 person-years, which was significantly lower than the 81,592.79 person-years in 2004 (a decrease of 37.5%).

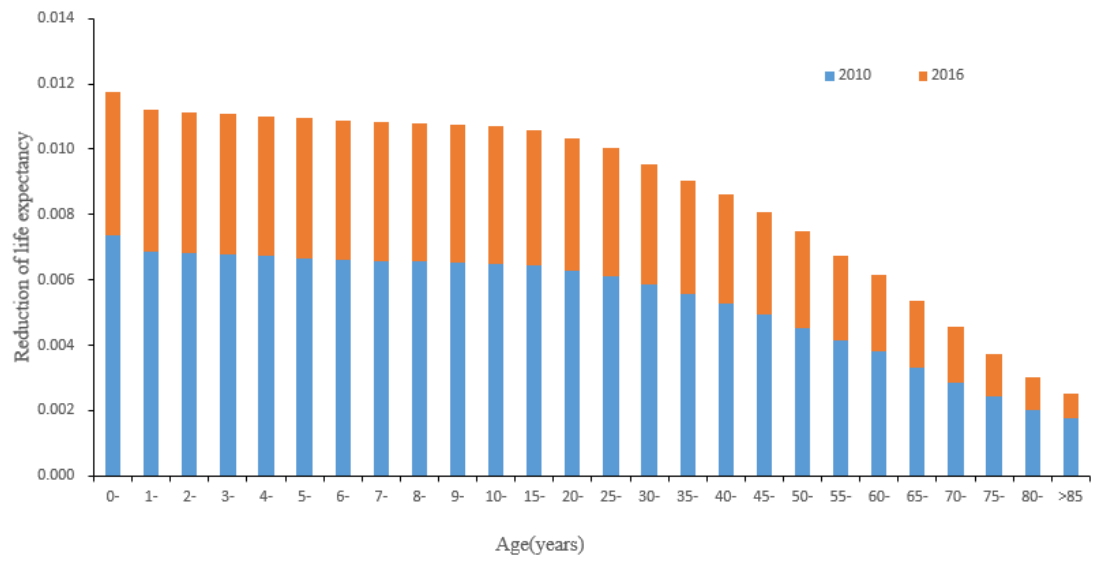


Figure S3. The impacts of the 11 diseases on life expectancy for different age groups

Table S1. The effect of vaccine-preventable diseases on life expectancy in 1978-2018

Year	Hepatitis A		Meningococcal Meningitis		Measles		Hepatitis B		Japanese encephalitis		Total of eleven diseases	
	years	months	years	months	years	months	years	months	years	months	years	months
1978			0.044470	0.533636	0.033021	0.396253			0.019287	0.231439	0.108308	1.299693
1979			0.035311	0.423727	0.025826	0.309916			0.016017	0.192205	0.084726	1.016715
1980			0.029751	0.357007	0.016344	0.196129			0.010460	0.125514	0.130526	1.566311
1981			0.017652	0.211822	0.013729	0.164743			0.013729	0.164743	0.050359	0.604304
1982			0.014056	0.168666	0.016671	0.200052			0.012748	0.152974	0.048068	0.576821
1983			0.012748	0.152974	0.013075	0.156897			0.007844	0.094133	0.037273	0.447277
1984			0.018917	0.227006	0.009260	0.111118			0.007537	0.090446	0.038133	0.457600
1985			0.019300	0.231596	0.008374	0.100487			0.019300	0.231596	0.036982	0.443784
1986			0.014513	0.174159	0.002615	0.031376			0.004935	0.059223	0.023341	0.280093
1987			0.006962	0.083542	0.000654	0.007844			0.007027	0.084327	0.015331	0.183967
1988			0.005001	0.060008	0.001601	0.019217			0.006373	0.076482	0.013313	0.159753
1989			0.003105	0.037259	0.001046	0.012550			0.004020	0.048241	0.008825	0.105901
1990	0.001209	0.014511	0.002222	0.026669	0.000556	0.006667	0.001928	0.023139	0.007714	0.092564	0.014219	0.170628
1991	0.001079	0.012942	0.001536	0.018433	0.001003	0.012040	0.001928	0.023139	0.003432	0.041181	0.009351	0.112216
1992	0.000882	0.010589	0.001405	0.016864	0.001128	0.013531	0.001732	0.020786	0.002092	0.025101	0.007439	0.089269
1993	0.000686	0.008236	0.000915	0.010981	0.001049	0.012589	0.001896	0.022747	0.001961	0.023532	0.006677	0.080130
1994	0.000546	0.006550	0.001039	0.012472	0.000690	0.008275	0.001696	0.020355	0.002186	0.026238	0.006338	0.076050
1995	0.000428	0.005138	0.001023	0.012276	0.000297	0.003569	0.001758	0.021100	0.001526	0.018315	0.005105	0.061263
1996	0.000363	0.004353	0.000945	0.011334	0.000428	0.005138	0.001700	0.020394	0.001039	0.012472	0.004523	0.054281
1997	0.000458	0.005491	0.000788	0.009452	0.000677	0.008118	0.001889	0.022669	0.001003	0.01204	0.007086	0.085033
1998	0.000353	0.004236	0.000641	0.007687	0.000346	0.004157	0.001575	0.018904	0.001330	0.015962	0.006697	0.080365
1999	0.000291	0.003490	0.000448	0.005373	0.000402	0.004824	0.001291	0.015492	0.000915	0.010981	0.005749	0.068990
2000	0.000196	0.002353	0.000350	0.004196	0.000431	0.005177	0.001530	0.018355	0.000431	0.005177	0.005766	0.069186

2001	0-000190	0-002275	0-000291	0-003490	0-000412	0-004942	0-001405	0-016864	0-000634	0-007608	0-005439	0-065264
2002	0-000206	0-002471	0-000314	0-003765	0-000337	0-004040	0-001902	0-022826	0-000559	0-006706	0-005952	0-071422
2003	0-000170	0-002039	0-000337	0-004040	0-000193	0-002314	0-001863	0-022355	0-000886	0-010628	0-006324	0-075893
2004	0-000099	0-001186	0-000701	0-008415	0-000128	0-001533	0-001568	0-018819	0-000828	0-009932	0-006357	0-076283
2005	0-000093	0-001120	0-000792	0-009506	0-000220	0-002645	0-001678	0-020142	0-000942	0-011306	0-010257	0-123090
2006	0-000092	0-001101	0-000604	0-007253	0-000155	0-001860	0-001824	0-021885	0-001805	0-021664	0-010719	0-128623
2007	0-000073	0-000876	0-000502	0-006029	0-000301	0-003613	0-00152	0-018245	0-000929	0-011151	0-010082	0-120985
2008	0-000021	0-000251	0-000444	0-005328	0-000459	0-005505	0-001471	0-017648	0-000576	0-006911	0-008077	0-096924
2009	0-000043	0-000512	0-000270	0-003246	0-000170	0-002034	0-001362	0-016349	0-000645	0-007735	0-009238	0-110856
2010	0-000012	0-000146	0-000123	0-001474	0-000111	0-001335	0-001158	0-013900	0-000343	0-004113	0-007376	0-088513
2011	0-000027	0-000321	0-000199	0-002393	0-000043	0-000514	0-001042	0-012505	0-000273	0-003280	0-006255	0-075056
2012	0-000019	0-000224	0-000199	0-002393	0-000085	0-001020	0-001829	0-021944	0-000446	0-005355	0-010952	0-131424
2013	0-000003	0-000040	0-000091	0-001093	0-000126	0-001511	0-000863	0-010350	0-000201	0-002415	0-005293	0-063516
2014	0-000011	0-000133	0-000052	0-000623	0-000131	0-001575	0-000562	0-006748	0-000102	0-001224	0-00426	0-051121
2015	0-000021	0-00025	0-000060	0-000722	0-000154	0-001846	0-000542	0-006505	0-000074	0-000888	0-004274	0-051293
2016	0-000006	0-000075	0-000042	0-000507	0-000076	0-000912	0-000600	0-007204	0-000128	0-001533	0-004394	0-052732
2017	0-000006	0-000070	0-000028	0-000335	0-000007	0-000088	0-000624	0-007488	0-000116	0-001392	0-000781	0-009373
2018	0-000004	0-000053	0-000015	0-000176	0-000001	0-000018	0-000604	0-007249	0-000197	0-002369	0-000825	0-009899

Table S2. Loss of healthy life and work years due to early death from the 11 vaccine-preventable diseases

Year	Loss of healthy life years (person years)	Total population	Early mortality rate	Loss of work years (person years)
2004	81592.79	1299880000	0.00006277	47410
2005	126949.6	1307560000	0.00009709	71137.5
2006	136593.4	1314480000	0.00010391	76960
2007	120585.1	1321290000	0.00009126	66375
2008	97181.57	1328020000	0.00007318	53487.5
2009	104323.7	1334500000	0.00007817	55740
2010	81033.93	1340910000	0.00006043	42905
2011	76899.41	1347350000	0.00005707	41262.5
2012	133739.4	1354040000	0.00009877	70355
2013	66203.94	1360720000	0.00004865	35052.5
2014	52293.87	1367820000	0.00003823	27477.5
2015	51788.21	1274620000	0.00004063	26907.5
2016	53136.77	1382710000	0.00003843	26955
Total	1182322	17333900000	0.00006821	642025