

Forecasting time-series trends in vaccination coverage and their links with socio-economic factors: A global analysis over 30 years

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Background Incomplete immunisation coverage causes preventable illness and death in both the developing and developed world. Identifying factors that may modulate coverage can inform effective immunisation programmes and policies.

Methods We perform a data-driven analysis of unprecedented scale, examining time-varying trends in Diphtheria-tetanus-pertussis coverage across 190 countries over the past three decades. Gaussian process regression is employed to forecast future coverage rates and provide a Vaccine Performance Index: a summary measure of the strength of immunisation coverage in a country.

Findings Overall vaccine coverage has increased in all five world regions between 1980 and 2010, with marked variation in volatility and trends. Our Vaccine Performance Index identifies 53 countries with a less than 50% chance of missing the Global Vaccine Action Plan (GVAP) target of 90% worldwide DTP3 coverage by 2015, in agreement with recent immunisation data. These countries are mostly sub-Saharan and South Asian, but Austria and Ukraine in Europe also feature. Factors associated with DTP3 immunisation coverage vary by world-region: personal income ($\rho = 0.66, p < 0.001$) and government health spending ($\rho = 0.66, p < 0.01$) are particularly informative in the Eastern Mediterranean between 1980 and 2010, whilst primary school completion is informative in Africa ($\rho = 0.56, p < 0.001$) over the same time. The fraction of births attended by skilled health staff is significantly informative across many world regions

Interpretation A Vaccine Performance Index can highlight countries at risk identifying the strength and resilience of immunisation programmes. Weakening correlations with socio-economic factors indicate a need to tackle vaccine confidence whereas strengthening correlations points to clear factors to address.

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Introduction

Vaccine-preventable disease rates have decreased in many parts of the world over recent decades, but there are still large numbers of unvaccinated children. In 2013, UNICEF reported that there were 21.8 million children under one year who had not completed the DTP (diphtheria-tetanus-pertussis) immunisation series (with a similar number not receiving a single measles vaccination) [1]. While access to vaccinations is the primary barrier in many settings, there appear to be growing numbers of parents who do not immunise their children due to their own personal attitudes [2,3].

The recent literature has identified both socio-economic and attitudinal barriers to vaccination coverage for a number of countries. A set of recurring socio-economic and demographic correlates of coverage have been found, with parental education level [4-8], age [6,9,10], employment status and workplace [4,6,7], religion [11], ethnicity [12], child gender

[13], poverty [14-18], and distance to healthcare facilities [4,6,11,14,17,18] (among others) all linked to vaccine uptake (though there are often marked differences between countries [11]). Similarly, repeating themes are found when examining personal reasons for vaccine acceptance or delay which range from perceived risks around potential adverse events to religious or political beliefs external to, albeit influencing, vaccination [9, 19-27]. Trust in healthcare professionals [19,20,23,24] and the government [19,23,26] also feature highly.

Recommendations to address gaps in vaccine coverage are context dependent. It has been suggested that targeting mothers with low education [28], low health literacy [29], and disseminating more information to communicate vaccine benefits and risks transparently [2] can aid in improving vaccine hesitancy. As can the customisation of messages and engagement efforts for specific groups [30]. Efficient identification of clusters of non-vaccinators through monitoring of local immunisation rates has been identified as a key public health challenge for the prevention of outbreaks when local groups adopt non-vaccination status (as was the case in the recent measles outbreak at Disneyworld, California) [31]. Monitoring trust in immunisation programmes [32] through a variety of indices [32] in order to understand best understand where these areas might occur, have also been proposed.

Our objectives in this paper are to introduce a summary measure -- based on forecasted coverage using Gaussian process regression -- which may be used to describe the variability and trends in vaccine coverage induced by confidence and access issues and allows for an inter-country analysis of trends. We term this measure the Vaccine Performance Index and we interpret the values in light of the Global Vaccine Action Plan's target of attaining 90% coverage in all countries by 2015 [34]. We discuss implications of both the correlative study and performance index on immunisation strategies. Further, we perform a large-scale, worldwide correlative analysis between a range of socio-economic factors and vaccine coverage, identifying differences between world regions as defined by the World Health Organization (WHO) and identifying temporal trends.

Methods

Data

A broad range of quantitative data on 190 descriptive socio-economic factors (SEFs) for 190 countries are considered from 1980 to 2010. Factors span (among others) the fields of economics, healthcare, industry, demographics, communications, infrastructure, physical geography, trade, and education; in addition to vaccination coverage. This breadth of SEFs is an attempt to expose, in an unbiased fashion, which indicators might be related to immunisation coverage. World regions are categorised by WHO region according to the definitions at www.who.int/about/regions/en (accessed 08/08/2013): AFR (Africa); AMR (Americas); EMR (Eastern Mediterranean); EUR (Europe); SEAR (South-East Asia); and WPR (Western Pacific). (See Figure 1F.) Data is obtained from the website Gapminder (www.gapminder.org) which draws from sources including the World Bank, the International Labour Organization, and the World Health Organization (WHO). A data curation approach involving filtering and imputation to reduce the missing data fractions is deployed and described in the Supplementary Materials (SM) [35], wherein we show that correlations estimated in the following section are robust to our imputation procedure.

Vaccine coverage data -- represented as a percentage of a target group immunised -- for BCG (Bacillus Calmette-Guérin vaccination against tuberculosis), DTP1, DTP3 (representing the first and third doses of the Diphtheria, Tetanus, and Pertussis vaccine and typically scheduled for six months after birth), MCV (measles-containing vaccine), and POL3 (the third dose of the polio vaccination programme) are obtained from the 2011 WHO-UNICEF estimates of vaccine coverage (www.childinfo.org/tables/Immunization/coverage/1980-2011.xls -- accessed 08/08/2013) for the same countries and across the same time period (though we use the latest estimates for use in our Vaccine Performance Index). Immunisation rates have increased across all WHO regions over the last three decades: coverage in Europe and the Americas leads the world, with other regions achieving less complete coverage (Figure 1A). Joint investigation of all vaccine time-series reveals strong mutual correlations between the DTP1, DTP3, MCV, and POL3 vaccines, but reveals that BCG falls outside this grouping (Figure 1B). Time-series of coverage in individual countries differ markedly in magnitude, variability, and trends (Figure 1C). We henceforth focus on DTP3 coverage both because of this high correlation and in accordance with previous literature which considers DTP3 as a marker of the strength of a country's immunisation programmes (as it requires three different administrations) [36]. We provide repeats of our correlative analysis for the other vaccines in the SM.

We illustrate time-series of SEF data with two examples, rural access to water and female education, in Figure 1 D

and E (respectively). An example scatter plot of average DTP3 coverage against female education levels for three regions is shown in Figure 1G. We further explore the SEF dataset by using t-distributed stochastic neighbour embedding (t-SNE) -- a local structure-preserving clustering technique which can improve visualisation quality of high-dimensional data over other clustering algorithms [37] -- on a similarity matrix S constructed by taking correlations between all pairs of SEFs and vaccines in a single year x_{it} (for SEF -- or vaccine -- i in year t), and averaging the correlation across all 31 years: $S_{ij} = 1 - \frac{1}{T} |\sum_t \rho(x_{jt}, x_{it})|$, where T is the total number of years and ρ is Spearman's rank correlation between two SEFs (or vaccines). Application of t-SNE reveals strong links between SEFs in similar categories, in addition to revealing a separation of the BCG vaccine -- which is closer in t-SNE space to factors relating to health spending -- from the other four vaccines which appear to be more correlated with schooling variables (Figure 1H). The WHO regions are shown in Figure 1F.

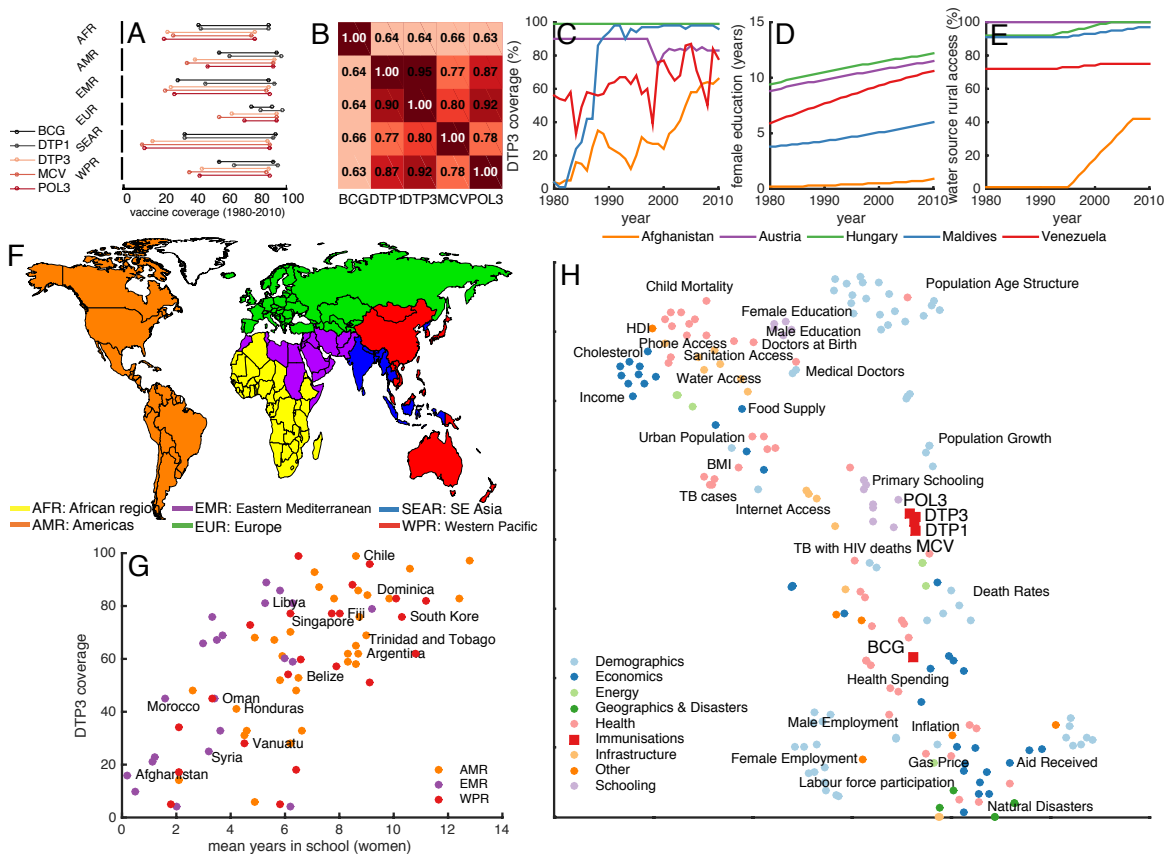


Figure 1 Exploration of socio-economic factors and illustrative dynamics of SEFs and DTP3 coverage. **A** Increasing trends in vaccine coverage across WHO regions with time. Leftmost circle represents 1980 coverage levels; rightmost is 2010, averaged across all countries in a region. **B** Spearman correlation between all vaccines across all countries and years. **C** Diversity of behaviours in vaccine coverage with time: countries show markedly different behaviours of DTP3 coverage with time. **D**, **E** Time-series of rural water access (**D**) and female education (**E**). **F** World regions as defined by the WHO. **G** Scatter plot illustrating the link between DTP3 coverage and female education in 1982, coloured by WHO-region. **H** Visualisation of similarity matrix between all pairs of SEFs using t-SNE (as described in text) reveals pronounced structure throughout the set of SEFs considered. Heuristic categories are assigned before using t-SNE.

Method for correlative analysis

Spearman's rank correlation is used to explore links between coverage and SEFs (Figure 1G) as coverage data is confined to the $[0,100]$ interval and often non-linear relationships between coverage and SEFs arise (which may be ordinal). To investigate the strengths of SEF correlations with coverage over time, we compute a time-averaged correlation between each factor x_t and coverage y_t (in a given year t) for all countries in a particular region, $\rho(x_t, y_t)$. The time-average of this value is then taken,

$$\rho = \frac{1}{t_2 - t_1} \sum_{t=t_1}^{t_2} \rho(\mathbf{x}_t, \mathbf{y}_t) \quad \text{Equation 1}$$

where t_1, t_2 are the most distant and recent years, respectively. For historic trends, we consider $t_1 = 1980$ and $t_2 = 2010$ and, to observe recent ones, we consider $t_1 = 2001$. To focus on the strongest signals, the top-ten correlating SEFs in each region across both time ranges are agglomerated for a cross-comparison of informative correlates between regions and we restrict these SEFs to those with a Bonferroni-corrected meta p-value (against the null hypothesis that the set of correlations are uninformative) of under 0.01. Included with these factors are others which are related and are useful for a comparison: primary school completion rate (male), improved sanitation access (overall and rural), and improved urban water access (see SM [35] for further details).

Method for forecasting

Vaccine coverage data is first transformed using the logistic transform $y' = -\log(\frac{100}{y} - 1)$, where y is vaccine coverage, to map the coverage values to the real line, so that Gaussian distributions over data points are not truncated at $y = 0$ or $y = 100$. Gaussian processes -- with a squared-exponential covariance function and linear mean function (to account for the broadly linear increases in trend observed in this transformed space) -- are used to forecast vaccine coverage data, based on previous coverage values. (Please consult the SM for prediction accuracy of this method, which is quantified by forecasting on a test data set [35]). The predictive distribution over forecasted values is used to define a summary measure -- the Vaccine Performance Index -- which balances the (desirable) probability of attaining high future coverage against the (undesirable) probability of experiencing a future negative perturbation to coverage, informed by preceding trends and variability. The VPI is defined as the probability of achieving coverage in excess of a threshold value v , less the probability of a drop in coverage of size at least d ,

$$VPI_{v,\tau,d}(t_*) = P[y(t_*) > v] - P[y(t_*) < y(t_N) - d], \quad \text{Equation 2}$$

where t_N is the most recent point for which coverage exists, $t_* = t_N + \tau$ is the forecasted point, $y'(t_*) = f(t_*) + \epsilon$, where ϵ is normal noise (so that, for example, $t_N = 1999$ and $t_* = 2000$ for a country's 2000 VPI value), and where we map the predictive distributions back to the range $[0,100]$. This expression is reweightable if the reader or policymaker wishes to focus on a different combination of strategic properties. There are natural alternative forms to this index: for example, to assess the GVAP goal of achieving 90% coverage in all countries by 2015, we set $\tau = 2$ years, $v = 90$, and $d = \infty$ above, thus using our model to forecast the probability that coverage in 2015 will exceed 90%.

MATLAB version 2015a is used for all analyses.

Role of the funding source

The funding bodies had no role in the study design nor in any subsequent part of the data collection, analysis, interpretations, writing of the report, or decision to submit the paper for publication. The corresponding authors confirm that they had full access to the data in the study and have final responsibility for the decision to submit for publication.

Results

Vaccine Performance Index

We assess countries' trends and variability by considering the probability of coverage exceeding 95% minus the probability of coverage dropping by over 2% one year in the future (that is, $v = 95$, $d = 2$, and $\tau = 1$ in Equation 2). (Please consult the SM [35] for justification of these parameter values and alternative forms of this index, which may be natural alternatives that address different policymaking goals.) Figure 2A shows worldwide VPI values for these parameters in 2001, 2005, 2009, and 2013; trends and low index values are readily identified. We display DTP3 coverage time-series and Gaussian process fits for the five countries with highest increases and decreases in VPI from 2009-2013 (Figure 2B and C). Malta has the most improved VPI between 2009 and 2013, since in 2009 Malta has sharply decreasing coverage rates, which have since fully recovered. Romania has the most deteriorated VPI value, since high and steady coverage values have gradually worsened. (VPI values are listed in the SM Table 3 [35].)

The consistently high-performing countries include Saudi Arabia, Russia, Hungary, and Slovakia which have had

consistent DTP3 coverage rates in the high 90s since at least 2000. The UK, US, Canada, Australia, and New Zealand have historically lower VPIs, which have improved in the UK, US, and Canada, but a notable disparity is that they remain low in Australia and New Zealand.

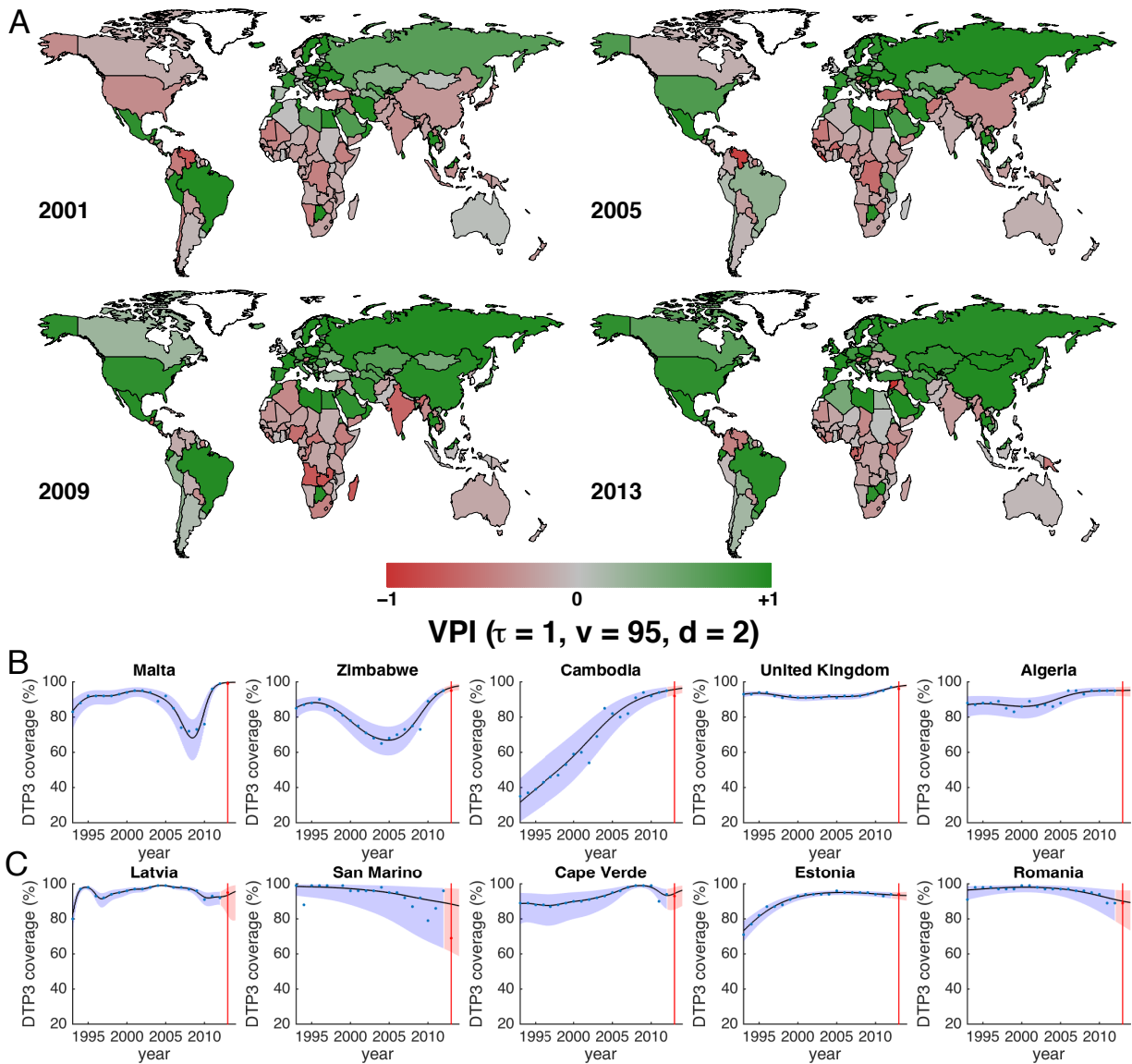


Figure 2 *A Vaccine Performance Index highlights regions with a large probability of variable coverage below the 95% threshold. A* The performance index (VPI; Equation 2) for all countries $t_N = 2001, 2005, 2009$ and 2013. Sub-Saharan Africa, parts of Southern and South-East Asia and some European countries have low VPI. White represents missing data. *B* Countries with the largest improvement in VPI between 2009 and 2013 (Malta is most improved). *C* Countries with the largest decrease in VPI over the same period (Romania has the most deteriorated performance). WHO-UNICEF coverage estimates are in blue with the observed (test) value in 2013 in red; the mean of the Gaussian process in black, and shaded 95% confidence intervals for training (blue) and forecasted (red) data. We show 2013 as the red vertical line.

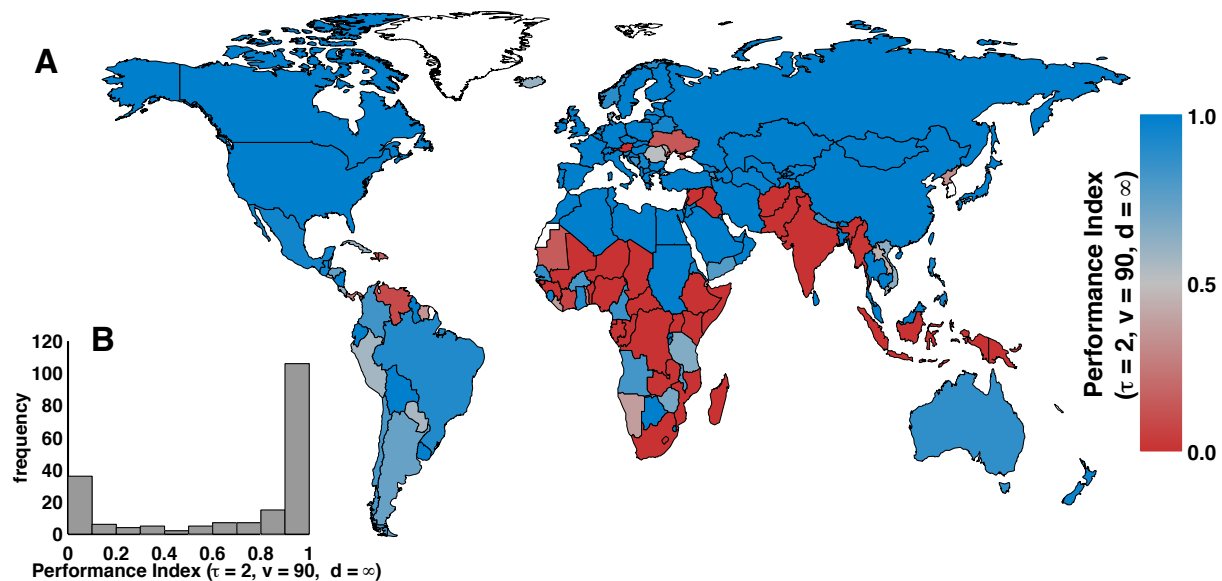
More generally, Europe, North and Central America, and much of Asia has shown steady progress since 2005; in contrast, South America, the Indian subcontinent and sub-Saharan Africa have shown little signs of improvement. Perhaps surprisingly, there are many European countries struggling to increase coverage to top levels: Norway, Iceland, Ukraine, and Romania — despite reasonably high 2013 DTP3 coverage rates (83%, 91%, 94%, and 89% respectively) — all have VPI values far from +1 signifying coverage rates which are below 95% and show little sign

of improvement beyond this threshold. Africa is mixed: North African countries show high VPI levels, whereas sub-Saharan Africa generally shows low VPI values due to high variability and low coverage, with some exceptions, notably Rwanda, Burundi, Botswana, and Zimbabwe. These low and volatile coverage rates are a likely sign of the vast number of people in sub-Saharan Africa with poor continued access to latter doses in the DTP programme.

South East Asia generally performs poorly; many countries have VPI values close to -1, indicating high chances of a drop in coverage in the following year. Many Eastern Mediterranean countries show clear improvement over the past decade: with countries here typically presenting high, sustained coverage rates, although there are notable exceptions in Syria, Iraq, Pakistan, Afghanistan, and Yemen.

Forecasting vaccine coverage with respect to Global Vaccine Action Plan goals

To assess the GVAP's goal of achieving 90% coverage in all countries by 2015, we use our Vaccine Performance Index in Equation 2 with $\tau = 2$ years, $v = 90$, and $d = \infty$; hence, we use our simple Gaussian process model to forecast the probability that coverage in 2015 (2 years after the most recent available datapoints, in 2013) will exceed 90%.



$0.5 \leq \text{VPI} < 0.9$: Angola, Argentina, Armenia, Australia, Bosnia and Herzegovina, Brunei Darussalam, Burkina Faso, Cameroon, Chile, Colombia, Costa Rica, Cuba, Denmark, El Salvador, Honduras, Iceland, Jamaica, Kiribati, Malawi, Nauru, Nepal, Norway, Palau, Paraguay, Peru, Romania, Samoa, Senegal, Trinidad and Tobago, Tuvalu, United Republic of Tanzania, Viet Nam, Yemen, Zimbabwe.

$0.1 \leq \text{VPI} < 0.5$: Barbados, Comoros, Korea, Democratic People's Republic of, Djibouti, Dominican Republic, Lao People's Democratic Republic, Liberia, Mauritania, Micronesia, Federated States of, Namibia, Panama, Republic of Moldova, San Marino, Solomon Islands, Suriname, Togo, Ukraine.

$\text{VPI} < 0.1$: Afghanistan, Austria, Benin, Central African Republic, Chad, Congo, Cote d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Ethiopia, Gabon, Guinea, Guinea-Bissau, Haiti, India, Indonesia, Iraq, Kenya, Lebanon, Madagascar, Mali, Marshall Islands, Mozambique, Burma, Niger, Nigeria, Pakistan, Papua New Guinea, Somalia, South Africa, Syrian Arab Republic, Timor Leste, Uganda, Vanuatu, Venezuela, Zambia.

Figure 3 Extrapolation of current trends based on our Gaussian process model reveal countries which may fail to reach GVAP targets. **A** 53 countries have more than a 50% chance of failing to meet GVAP 2015 targets if current DTP3 trends continue. **B** Histogram of index values.

Figure 3 shows values of this index (GVAP marker). This analysis yields a bimodal distribution (Figure 3B), where countries are set to either comfortably reach this goal or to fall rather short of it (with the exception of South America, which has many borderline countries). We find that European countries generally perform better than other regions

(with the notable exceptions of Denmark, Iceland, Romania, Austria, Moldova, San Marino, and Ukraine) with an almost certain chance of reaching the GVAP goal (based on their recent trend). Countries from sub-Saharan Africa and the Indian subcontinent (with only few exceptions) seem likely to drastically miss the GVAP target. We note that this inference and forecasting approach highlights both regions that require stronger action and those borderline countries where comparatively minor action may realise the GVAP goal.

Socio-economic correlations with vaccine coverage over time

The most consistently correlating historic (1980-2010) and recent (2001-2010) socio-economic underpinnings of vaccine coverage are displayed in Figure 4A. From the broad range of 190 socio-economic factors (SEFs) considered, those in Figure 4A can be interpreted as those most likely to have a genuine (and consistent) link with DTP3 coverage.

The strength of correlation between SEFs and DTP3 coverage varies between region, over time, and across factors. Births attended by skilled health staff and access to sanitation are the two factors which have mean-averaged p -values below 0.05 across the largest number of regions. In Africa, the Americas, and Europe, the magnitude of correlations are high historically but have decreased recently and show behaviours which are broadly comparable: the importance of access to water and sanitation, births attended by skilled health staff, and economic factors in determining coverage is historically high but diminishing (and decreasing particularly strongly in the Americas). An exception to this is the correlation with the service industry (the service SEF is the net output of the service industry, defined as wholesale and retail trade, transport, and other governmental services such as education and healthcare. See <http://data.worldbank.org/indicator/NV.SRV.TETC.ZS> for a comprehensive definition), which is reasonably high and increasing in Africa and the Americas. By contrast in the Eastern Mediterranean and the West Pacific we see that SEFs have remained correlated over time. South East Asia has a more mixed pattern of recent changes in socio-economic connections, with, for example, a decreasing link to primary school completion rates and an increasing link to water access and sanitation.

In Africa and the Eastern Mediterranean, educational variables and access to water are particularly informative of DTP3 coverage; whilst in the Eastern Mediterranean government health spending, income metrics, access to sanitation, phone users, and CO2 emissions are also strongly linked with coverage. Socio-economic correlates are generally low (recently and historically) in Europe, and are reasonably low in the Americas. In South East Asia, education ratio and access to water are notably high correlates, and ones that have not decreased in importance. In the Western Pacific region, births attended by skilled health staff is the strongest correlate (and one that appears to be becoming more informative of DTP3 coverage).

The association between public health spending and coverage varies globally, with a strong link in the Eastern Mediterranean and rather weaker links in South East Asia, Africa, and the West Pacific (where the link is increasing), and the Americas (where it is decreasing). Only in the Eastern Mediterranean is GDP per capita the strongest correlate of vaccine coverage; in all other regions the strongest links are with less directly economic factors.

We observe a significant difference between the correlation strength between DTP3 coverage and male and female education (Figure 4B) in Africa and South East Asia ($p \leq 0.001$ for both using a t-test for paired samples). (There is no significance at $p \leq 0.05$ for the other regions, though we note that paternal education is more informative in the West Pacific $p = 0.07$).

In Figures S10 and S11, we plot these correlations for the other vaccinations we examine. Some notable observations arise from the comparison of these other vaccines with DTP3. One regional trend is that the influence of public health spending and access to sanitation in South East Asia, moderate for DTP3, is very high and often increasing for other vaccines. Another striking observation is that the Eastern Mediterranean, which displays stable or decreasing correlations with several socio-economic factors for DTP3, instead shows increasing links with all factors (except investments) for BCG. The Americas, which show decreasing correlations for most factors with DTP3, show decreases to almost Europe-like absences of coverage correlation in DTP1 and MCV, though all other regions and factors show similar behaviours between DTP3 and MCV coverage. Europe is broadly the same across all vaccines except BCG, where there appear to be negative relationships between factors such as government health spending, sanitation access, and income and BCG coverage.

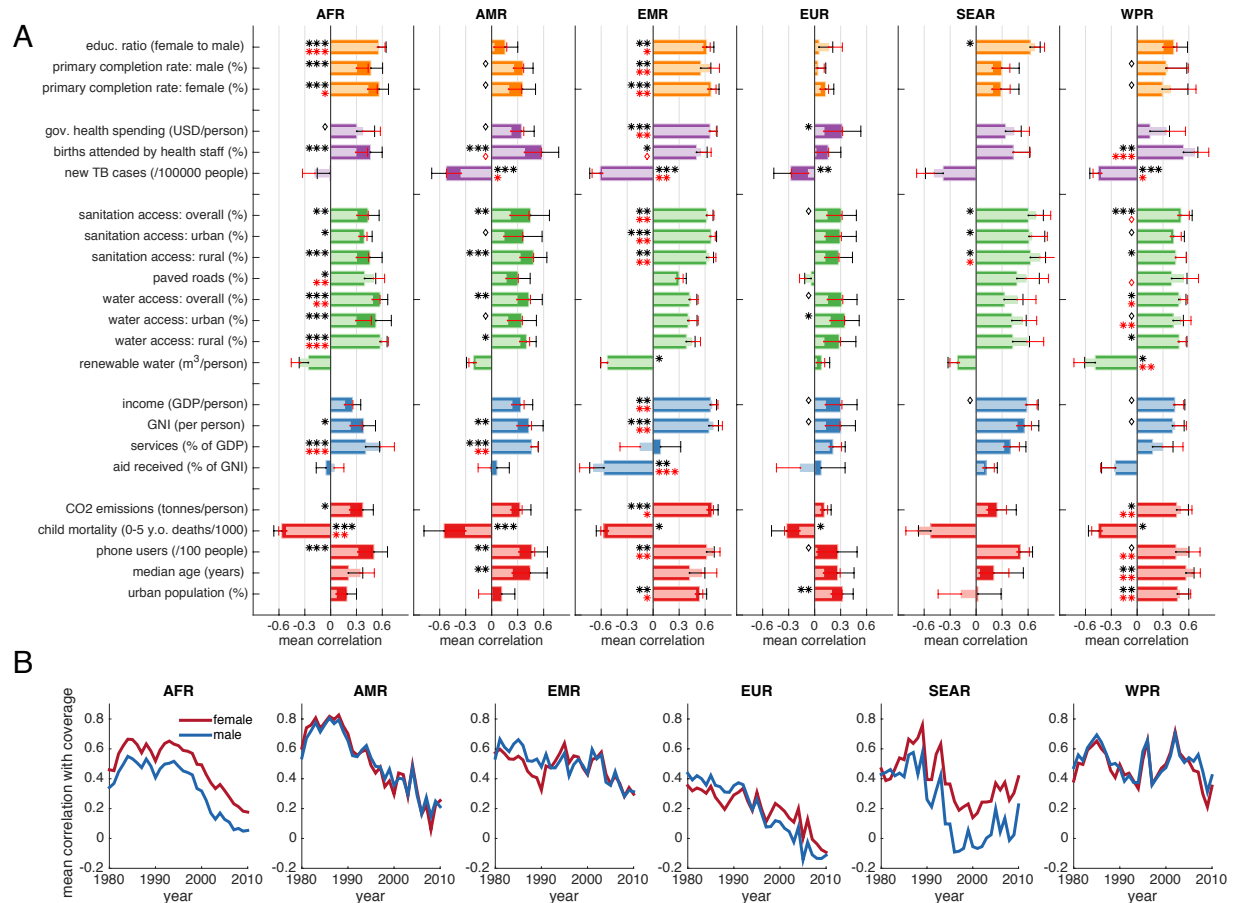


Figure 4 *Historic and recent best-performing correlates with DTP3 coverage include factors relating to education, health, access to water and sanitation, and economics. A* Groups of key SEFs, obtained by collecting the top correlating SEFs in each region across the time-periods 1980-2010 and 2001-2010. Only factors displaying the most consistent nonzero correlations with coverage are presented. Spearman's ρ is represented for 1980-2010 in thick dark bars, whilst for 2001-2010 it is represented in thin light bars. Mean p -values are displayed in black for 1980-2010 and red for 2001-2010: *** denotes $p < 0.001$, ** denotes $p < 0.01$; * denotes $p < 0.05$; and \diamond denotes $p < 0.10$. *B* Time-series of the Spearman's ρ between DTP3 coverage and female (blue) and male (red) education.

Discussion

We have performed a large-scale, data-driven study of links between socio-economic factors and vaccine coverage, and have constructed a performance indicator that can quantitatively approximate measures of the susceptibility of immunisation programmes to coverage losses. In keeping with these earlier studies, we have found a number of socio-economic factors informative of immunisation levels, such as healthcare facilities [3] and educational variables [4-8]. The recent literature has indeed identified numerous socio-economic and attitudinal barriers to vaccination coverage for a number of countries, such as parental education level [4-8], age [6,9,10], employment status and workplace [4,6,7], poverty [14-18], inequity [38], and distance to healthcare facilities [4,6,11,14,17,18]. A recent review has emphasised the link between out-of-hospital birth and lower immunisation rates in countries with a medium or low Human Development Index, and has associated the use of private health care services, and no health insurance with low immunisation levels in countries with very high HDI [39]. In keeping with these findings, we also find a link between income and births attended by skilled health staff and immunisation levels. We believe we are the first to identify several other potential barriers to immunisation coverage; for example, the link between governmental health spending and primary completion levels (in addition to income) across Eastern Mediterranean countries and access to water and primary completion rates in Africa.

We suggest that having a set of low-magnitude socio-economic correlations with vaccine coverage corresponds to an

encouraging state where vaccine access is available to most of the population. Conversely, where strong socio-economic correlations exist, they signal potential limiting factors in vaccine access, though further analyses would need to be employed to infer causation between these factors and coverage. Hence, Europe, displaying consistently low socio-economic correlations, enjoys high access to all vaccines; however, it suffers from non-infrastructural barriers to vaccination that centre on religious or philosophical beliefs and perceived risks rather than access, which we suspect is in contrast to other regions in which access is the primary barrier [3,40]. The Americas, interestingly, show low (and decreasing) socio-economic correlations with DTP1, MCV, and BCG, but higher correlations (though currently decreasing) associated with DTP3. This pattern suggests a transitional stage wherein vaccines in the region are broadly accessible, but where certain factors (including medical staff present at births) are limiting uptake of DTP3. This seems to be supported in the literature, which cites a range of socio-economic determinants (including refusal from groups with higher socio-economic status [41,42], personal beliefs, and lack of access to healthcare facilities) as barriers to vaccination [3]. We note the strength and consistency of births attended by skilled health staff as an informer of DTP3 coverage rates, and we suggest its potential as a proxy indicator of the condition of a healthcare system.

We speculate that regions where correlations are strengthening can be interpreted as more pressing targets for intervention. For example, primary education sex ratio, public health spending, and sanitation in South East Asia and the Eastern Mediterranean; rural access to clean water (which is widely believed to be able to prevent polio in some parts of Nigeria [27]) and the presence of skilled health staff in Africa, where a potential surrogate, children born in a public or private healthcare facility, is consistently linked to completion of routine vaccinations [11].

Although an aim of the present study is to provide a global overview of correlates of immunisation coverage, we note a number of limitations. Regional variability will likely exist within countries and also between other sets of countries grouped by region other than that defined by the WHO. A large-scale global analysis investigating regional trends and identifying factors associated both within and between countries may therefore uncover more nuanced trends. Higher-frequency data from social media sources may be able to more accurately predict trends in vaccination uptake behaviour than lower frequency national coverage data. The Vaccine Performance Index (VPI) methodology can be naturally integrated with models incorporating high frequency time-series predictive variables to more accurately forecast immunisation levels, as high-frequency data on vaccine sentiments becomes increasingly available. These more fine-grained analyses could facilitate the use of time-lags in exploring predictive models of vaccine coverage using combinations of high-frequency social media data and low-frequency socio-economic factors.

Review of historical trends and variability in vaccination rates can aid policy makers' assessment of the strength and resilience of immunisation programmes. The GVAP's 2014 report notes one-third of 194 countries considered which have failed to reach 90% coverage in 2013 [43], but these static summaries conceal both the vaccination track-record and the likely future immunisation levels. A recent World Health Organization report notes that 65 countries have failed to achieve either "90% coverage globally or 80% coverage in every district or equivalent administrative unit against diphtheria, tetanus and whooping cough by 2015" [44], which is in line with predictions from our Vaccine Performance Index.

We thus highlight our VPI as a tool for future research, which can enhance GVAP's assessment reports for future targets by providing predictive measures accounting for coverage trends and variability.

Author contributions

All authors conceived and designed the study, contributed to the data interpretation, and wrote the manuscript. AF and HL performed a literature search. AF collected the data, and AF and DMDS created the figures. AF and IGJ performed the data analysis.

Declaration of interests Dr. Larson reports personal fees from GSK, other from Merck Vaccines, grants from NIHR (UK), grants from EU Innovative Medicines Initiative, grants from Novartis, grants from Centre for Strategic & International Studies, grants from WHO, outside the submitted work. The other authors have nothing to disclose.

Panel: Research in context

Systematic Review:

Evidence before this study Google Scholar was used to search for related literature on socio-economic correlates of vaccine coverage using search terms such as "socio-economic demographic correlates vaccine coverage", where each

individual term is allowed to vary. For instance, we allow “vaccine” to be replaced with “vaccination”, “immunise”, “immunisation” etc, in addition to specific names of vaccine-preventable diseases such as “DTP” and “MMR” and allowing for alternative spellings such as “immunize”, etc. Publications were searched up to a publication date of 1 January 2015. For attitudinal correlates of vaccine coverage, search terms such as “vaccine hesitancy”, “vaccine acceptance” and “vaccine delay” were used. There were relatively few publications that examined differences in both attitudinal and socio-economic correlates between countries, although there were recent reviews which looked at differing attitudes towards vaccination uptake across Europe [3,36], and differing socio-economic correlates in East African countries [11]. Both attitudinal and socio-economic surveys found numerous correlates of vaccine uptake. Attitudes range from personal, religious, and political beliefs, to trust in healthcare and the government. Socio-economic correlates vary between countries, but education level, religion, ethnicity, and distance to healthcare facility are all recurring themes.

Interpretation:

Added Value of this study We perform a correlative study of unprecedented scale between 190 socio-economic factors and immunisation coverage in 190 countries and reveal variations in the strength of socio-economic correlates between world regions and across time. To our knowledge, this work represents the broadest analysis of socio-economic links to vaccine coverage yet available, allowing insights into how socio-economic correlates modulate coverage and how these vary by world region. Forecasting of vaccine coverage time-series allows us to summarise the recent trend and variability in uptake rates and form a Vaccine Performance Index (VPI) which is, as far as we know, the first quantitatively derived marker of vaccine performance. Our predictive performance index represents a distinctive, interpretable measure to assess likely future vaccine coverage behaviour and resilience of immunisation programmes to volatile changes triggered by external shocks, whether political rumour driven or natural disaster.

Implications of all the available evidence By using a probabilistic forecast of future vaccination levels, we can provide a world-map of a Vaccine Performance Index that is informative of both the likelihood of stagnated or substandard coverage levels and the chance coverage levels will decline. These forecasts can easily single-out countries which are likely to fail to achieve the Global Vaccine Action Plan's target of 90% DTP coverage by 2015. We speculate that regions of strengthening socio-economic ties to vaccination coverage can be interpreted as targets for intervention (as socio-economic factors present barriers to vaccination), but that some regions (namely, Europe and the Americas), with low ties to socio-economic factors, show increased attitudinal barriers to vaccination.

- [1] Weekly epidemiological record. World Health Organization, 44: 421-436, 2012.
- [2] S. Black and R.A. Rappuoli. A crisis of public confidence in vaccines. *Sci. Trans. Med.*, 2(61):61mr1, 2010.
- [3] H. J. Larson, C. Jarrett, E. Eckersberger, D.M.D. Smith, P. Paterson. Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: a systematic review of the published literature, 2007-2012. *Vaccine*, 32(19): 2150–2159, 2014.
- [4] B. A. Ushie, O.A. Fayehun, and D.B. Ugal. Trends and patterns of under-5 vaccination in Nigeria, 1990–2008: what manner of progress? *Child: Care, Health and Development*, 40(2):267–274, 2013.
- [5] L. M. Calhoun, A.M. van Eijk, K.A. Lindblade, et al. Determinants and coverage of vaccination in children in western Kenya from a 2003 cross-sectional survey. *Am. J. Trop. Med. Hyg.*, 90(2): 234–241, 2003.
- [6] Y. Hu, Y. Chen, J. Guo, X. Tang, and L. Shen. Completeness and timeliness of vaccination and determinants for low and late uptake among young children in eastern China. *Human Vaccines & Immunotherapeutics*, 10(5):1408–1415, 2014.
- [7] M. Ueda, N. Kondo, M. Takada, and H. Hashimoto. Maternal work conditions, socioeconomic and educational status, and vaccination of children: A community-based household survey in Japan. *Preventable Medicine*, 66:17–21, 2014.
- [8] S. Desai and S. Alva. Maternal education and child health: Is there a strong causal relationship? *Demography*, 35(1): 71–78, 1998.
- [9] N.A. Otieno, B.O. Nyawanda, A. Audi, et al. Demographic, socio-economic and geographic determinants of seasonal influenza vaccine uptake in rural western Kenya, 2011. *Vaccine*, 32(49):6699–6704, 2014.
- [10] K. Danis, T. Georgakopoulou, T. Stavrou, D. Laggas, and T. Panagiotopoulos. Socioeconomic factors play a more important role in childhood vaccination coverage than parental perceptions: a cross-sectional study in Greece. *Vaccine*, 28(7):1861–1869, 2010.
- [11] M.E. Canavan, H.L. Sipsma, G.M. Kassie, and E.H. Bradley. Correlates of complete childhood vaccination in East African countries. *PLoS One*, 9(4):e95709, 2014.

- [12] K. S. Wagner, J.C.J van Wijgerden, N. Andrews, K. Goulden, and J.M. White. Childhood vaccination coverage by ethnicity within London between 2006/2007 and 2010/2011. *Arch. Dis. Child*, 99:348–353, 2014.
- [13] R. P. Pande and A. S. Yazbeck. What’s in a country average? Wealth, gender and regional inequalities in immunization in India. *Social Science & Medicine*, 57(11):2075–2088, 2003.
- [14] E.M. Galarce, S. Minsky, and K. Viswanath. Socioeconomic status, demographics, beliefs and A(H1N1) vaccine uptake in the United States. *Vaccine*, 29(32):5284–5289, 2011.
- [15] V. Friederichs, J.C. Cameron, and C. Robertson. Impact of adverse publicity on MMR vaccine uptake: a population based analysis of vaccine uptake records for one million children, born 1987–2004. *Arch. Dis. Child*, 91:465–468, 2006.
- [16] R. Reading, A. Colver, S. Openshaw, and S. Jarvis. Do interventions that improve immunisation uptake also reduce social inequalities in uptake? *BMJ*, 308(6379):1142–1144, 1994.
- [17] S. Mitchell, N. Andersson, N.M. Ansari, K. Omer, J.L. Soberanis, and A. Cockcroft. Equity and vaccine uptake: a cross-sectional study of measles vaccination in Lasbela district, Pakistan. *BMC Int. Health Hum. Rights*, 9(suppl. 1): S7, 2009.
- [18] O.T. Le Polain de Waroux, J.R. Armstrong Schellenberg, F. Manzi, et al. Timeliness and completeness of vaccination and risk factors for low and late vaccine uptake in young children living in rural southern Tanzania. *int. Health*, 5(2):139–147, 2013.
- [19] J. E. Atwell and D. A. Salmon. Pertussis resurgence and vaccine uptake: Implications for reducing vaccine hesitancy. *Pediatrics*, 134:602–604, 2014.
- [20] A. Benin, D.J. Wisler-Scher, E. Colson, E.D. Shapiro, and E.S. Holmboe. Qualitative analysis of mothers’ decision- making about vaccines for infants: The importance of trust. *Pediatrics*, 117(5):1532–1541, 2006.
- [21] N.E. MacDonald, J. Smith, and M. Appleton. Risk perception, risk management and safety assessment: What can governments do to increase public confidence in their vaccine system? *Biologicals*, 40(5):384–388, 2012.
- [22] E. Hak, Y. Schönbeck, H. De Melker, G.A. Van Essen, and E.A.M Sanders. Negative attitude of highly educated parents and health care workers towards future vaccinations in the Dutch childhood vaccination program. *Vaccine*, 23(24):3103–3107, 2005.
- [23] L.A.V. Marlow, J. Waller and J. Wardle. Trust and experience as predictors of hpv vaccine acceptance. *Human Vaccines*, 3(5):171–175, 2007.
- [24] R. McMurray, F.M. Cheater, A. Weighall, C. Nelson, M. Schweiger, and S. Mukherjee. Managing controversy through consultation: a qualitative study of communication and trust around MMR vaccination decisions. *British Journal of General Practice*, 54(504):520–525, 2004.
- [25] J.D. Allen, M.K.D. Othus, R.C. Shelton, et al. Parental decision making about the HPV vaccine. *Cancer Epidemiol. Biomarkers Prev.*, 19:2187–2198, 2010.
- [26] V.S. Freimuth, D. Musa, K. Hilyard, S. Crouse Quinn, and K. Kim. Trust during the early stages of the 2009 H1N1 pandemic. *Journal of Health Communication*, 19(3):321– 339, 2014.
- [27] B. Murele, R. Vaz, A. Gasasira, P. Mkanda, T. Erbetto, J. Okeibunor. Vaccine perception among acceptors and non- acceptors in Sokoto state, Nigeria. *Vaccine*, 32(26):3323– 3327, 2014.
- [28] V. Nankabirwa, T. Tylleskär, J.K. Tumwine, and H. Sommerfelt. Maternal education is associated with vaccination status of infants less than 6 months in eastern Uganda: a cohort study. *BMC Pediatrics*, 10:92–101, 2010.
- [29] J. Mira, S.V. Subramanian, M.P Sylvestre, et al. Association between maternal health literacy and child vaccination in India: a cross-sectional study. *Journal of epidemiology and community health* (2015): jech-2014.
- [30] M.T. Keane, M.V. Walter, B.I. Patel, et al. Confidence in vaccination: a parent model. *Vaccine*, 19(31):2486–2493, 2005.
- [31] E. Wolf, A. Rowhani-Rahbar, J. Duchin et. al. The Challenges in Measuring Local Immunization Coverage: A Statewide Case Study *Pediatrics* 137.5: e20153755, 2016.
- [32] S. Ozawa and M. L. Stack. Public trust and vaccine acceptance-international perspectives. *Human Vaccines and Immunotherapeutics*, 9(8):1774–1778, 2013.
- [33] H. Larson, W. Schulz, et. al. The State of Vaccine Confidence. *The Vaccine Confidence Project, London School of Hygiene and Tropical Medicine*, 2015. <http://www.vaccineconfidence.org/The-State-of-Vaccine-Confidence-2015.pdf> (accessed 29 April 2016).
- [34] Global Vaccine Action Plan 2011–2020. Annex 1., <http://www.unicef.org/immunization/files/GVAP.pdf>.
- [35] Materials and methods are available as online supplementary materials.
- [36] L. Arevshatyan, C.J. Clements, S.K. Lwanga et al. An evaluation of infant immunization in Africa: is a transformation in progress? *Bulletin of the World Health Organization*, 85(6):449–457, 2007.

- [37] L. J. P. van der Maaten and G. E. Hinton. Visualizing high-dimensional data using t-SNE. *Journal of Machine Learning Research*, 9(Nov):2579–2605, 2008.
- [38] A. R. Hinman, and M. A. McKinlay. Immunization equity. *Am J Prev Med*: published online Aug 14, doi: 10.1016/j.amepre.2015.04.018
- [39] T. M. De Cantuária Tauil, A. P. S. Sato, and E. A. Waldman. Factors associated with incomplete or delayed vaccination across countries: A systematic review. *Vaccine*, 34(24), 2635-2643, 2016.
- [40] O. Yaqub, S. Castle-Clark, N. Sevdalis, and J. Chataway. Attitudes to vaccination: A critical review. *Social Science & Medicine*, 112:1–11, 2014.
- [41] R.B. Barata, M.C.S. de Almeida Ribeiro, J.C. de Moraes, and B. Flannery. Socioeconomic inequalities and vaccination coverage: results of an immunisation coverage survey in 27 Brazilian capitals, 2007-2008. *J. Epidemiol. Community Health*, 66(10):934–941, 2012.
- [42] S.S. Kim, J.A. Frimpong, P. A. Rivers, and J.J. Kronenfeld. Effects of maternal and provider characteristics on up-to-date immunization status of children aged 19 to 35 months. *Am. J. Public Health*, 97(2):259–266, 2007.
- [43] Strategic Advisory Group of Experts on Immunization Assessment Report 2014. *World Health Organization*. http://www.who.int/immunization/global_vaccine_action_plan/SAGE_DoV_GVAP_Assessment_report_2014_English.pdf?ua=1 (accessed 11 July 2015).
- [44] World Immunization Week 2016: Immunization game-changers should be the norm worldwide. *World Health Organization. news release* <http://www.who.int/mediacentre/news/releases/2016/world-immunization-week/en/> (accessed 29 April 2016).

Forecasting time-series trends in vaccination coverage and their links with socio-economic factors: A global analysis over 30 years

Supplementary Material

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1 Materials and Methods

1.1 Data Cleaning and Imputation

1.1.1 Introduction

Missing data is a feature of the Gapminder dataset and, to a much lesser extent, vaccine coverage data. The full Gapminder dataset contains a total of 513 socio-economic factors (SEFs) for 196 countries. We downloaded all data from between 1980 and 2010. Of this data, a total of 67.7% is missing: this percentage varies substantially across SEFs and between country-years. Those SEFs which remain in our data set after the filtering process are tabulated in Supplementary Table 2 and given a numeric reference for convenience.

We presently describe the process by which we filter and impute missing data. We begin this approach by filtering the full data set, omitting SEFs which have large quantities of missing data and removing SEFs which contain occasional values which are many orders of magnitude higher than median values (an example of is a country’s population, which is removed in favour of the population density (383)) and thus may introduce outliers which may bias correlation estimates. A number of imputation methods are considered and their performance is evaluated on a test matrix. The statistic of interest, the time-averaged Spearman’s rank between a given socio-economic factor \mathbf{x}_t and vaccination coverage \mathbf{y}_t for all countries in a given region¹ is given by,

$$\bar{\rho} = \frac{1}{t_2 - t_1 + 1} \sum_{t=t_1}^{t_2} \rho(\mathbf{x}_{i,t}, \mathbf{y}_{i,t}) \quad (1)$$

where i is the SEF, and the sum is calculated between years t_1 and t_2 , and where $\rho(\cdot, \cdot)$ denotes the Spearman’s rank correlation coefficient. This statistic is then assessed for robustness to the selected imputation method by comparing values of $\bar{\rho}$ obtained using imputed data to true values obtained using clean data. We receive further support for our imputation procedure by comparing these true values to those obtained from pairwise deletion, which are less ably predicted than those obtained through imputation, providing further vindication for the imputation of missing data in this context.

1.1.2 Filtering

A total of 513 of SEFs are downloaded from the website Gapminder and examined for data quality. A total of 219 SEFs have fewer than three data points for at least 136 countries (representing about 70% of the full set of countries) and are stripped from the data set because of their very high missing data proportions. We then remove SEFs which may contain outlying values, but keep any normalised version which may be present; for example, raw population is removed, but population density (383) is kept and electricity use total is removed in favour of electricity use per person (98). A total of 104 of these outlier-prone SEFs are removed, but – to increase the number of SEFs in our filtered data set – maintain a further five by manually normalising by population: children out

¹Regions are defined by the World Health Organization: AFR (Africa), AMR (Americas), EMR (Eastern Mediterranean), EUR (Europe), SEAR (South-East Asia), and WPR (Western Pacific) according to the definitions at <http://www.who.int/about/regions/en/>

of school primary (total, male, female) (82-84), yearly CO2 emissions (143), and total sulphur emissions (144). These final SEFs are displayed in Supplementary Table 2 where we summarise, for each SEF, the number of countries with at least three data points, $N_C(\geq 3)$, the number of countries with no data $N_C(0)$, the average number of data points per country (av. data) and the percentage of missing data for each region. The matrix X contains a total of 190 SEFs across 196 countries.

1.1.3 Imputation

A number of imputation methods are considered to replace missing data values. For the purposes of testing these methods, it is instructive to form a data matrix X , where $X_{i,j,t}$ denotes data from country i , socio-economic factor j , and at time t (and where we use similar notation for all similar matrices henceforth). To test imputation methods, we first generate a clean data matrix C from X , and artificially insert missing values in C (to arrive at C') according to the structure of missing data in X . We impute values in C' to obtain I and test the accuracy of our imputation methods. This method has the shortcoming that not all SEFs in the original filtered matrix X appear in the cleaned matrix C ; however, since the missing data structure for all SEFs in X is considered in C , and since the above procedure is repeated a number of times, we expect that the effect of imputing missing values in SEFs with high missing data fractions is captured.

The clean data matrix C is created from the raw data X by removing columns (SEFs) in X with above a specified missing data fraction and then removing any row (country-year) containing at least one missing data entry. We repeat this procedure varying the missing data fraction and selecting the matrix C which has both a large number of data points and socio-economic factors. (To maximise the number of SEFs we consider in X , we forego the data matrix C which has been maximised solely for the number of clean data points). The resulting clean data matrix has 72 SEFs across 87 countries with an average of 19.2 data points per country (1730 country-years in total). There is more data for AFR (370 country-years), AMR (400), EUR (524), than EMR (111), SEAR (126), and WPR (189).

The mechanism by which missing data is present in X is likely to vary between socio-economic factors and between countries. For many countries, missing data might be due to a lack of reporting of this variable in a particular year (in which case the data would be *missing not at random*, MNAR); or, when missing data is related to the value of another variable (such as GDP), the data is said to be *missing at random*, MAR. If the data is neither MNAR nor MAR, the data could be *missing completely at random*, MCAR (see [43, 44], for example, for a fuller description of the types of missing data). Given the large volume of data and the various possible missing data mechanisms, we consider an imputation strategy which is not explicitly model dependent. We attempt to model the missing data structure in X in our clean matrix by forming the 196 by 190 matrix P whose entries are given by

$$P_{ij} = \frac{1}{31} \sum_{t=1}^{31} M_{ij,t}^X, \quad (2)$$

where M^X is a missing data indicator matrix for X (that is, $M_{ij,t} = 1$ if $X_{ij,t}$ is missing and 0 otherwise), and which correspond of the fraction of missing data for country i and factor j . (We assume here that each data point in a socio-economic factor time-series is equally likely to be missing). We then, to align with the size of C , sample 87 countries (rows) and 72 SEFs (columns) uniformly at random and without replacement from P and call this matrix P' and form the missing data indicator for C' as follows

$$M_{ij,t}^{C'} = \begin{cases} 1 & \text{if } U_{ij,t} < P'_{i,j} \\ 0 & \text{otherwise} \end{cases}$$

where $U_{ij,t} \sim \mathcal{U}(0,1)$, and where U has the same dimension as C . This method allows us to recover an instance of the missing data structure in X as the sampling will induce a correlation structure between missing data values between SEFs and country-years. Many countries have missing data across a number of SEFs; furthermore, many SEFs are more likely to have missing data for certain countries: this procedure allows us to capture this.

The following imputation methods are considered:

mean replacement (MR): Mean replacement replaces all missing points in a time-series with the mean value across all points that are present.

linear interpolation and 2-point/6-point/all-point extrapolation (L2,L6,LA): the linear interpolant is used between any two points which contain missing data between them. Extrapolation is based on a linear fit to the most recent two (2-point), six (6-point), or all (all-point) data points. Interpolation is performed first such that the extrapolation may use interpolated points.

KNN imputation (KNN): KNN imputation replaces missing values in a given row (country-year) with an average of K corresponding values across the K nearest-neighbour rows. A common implementation of KNN imputation is to only allow missing values to be replaced from rows with no missing values (for example, as described in [45] and as implemented using MATLAB's `knnimpute` function); however, only a small fraction of rows are complete cases in the Gapminder dataset, and so we allow any country-year (row) to be utilised in the distance calculation between two rows, so long as it contains a corresponding value for the target. We account for distances calculated between rows with large missing data fractions by adding a small penalisation term to the (Euclidean) distance between rows by multiplying the Euclidean distance by $\sqrt{(p/p^*)}$, where p is the total number of socio-economic factors (rows) and p^* is the number of non-missing instances in each row. Data across each SEF is linearly scaled to the $[0,1]$ interval before applying KNN imputation.

We pursue an imputation strategy which has two stages: we first find the optimal imputation method when there are at least five (from the 31 possible time-series points – or the fractional equivalent, in the case when there are fewer than 31 points per time-series) data points; we then consider all methods again on all time-series after having imputed those with at least five points per time-series. This allows us to evaluate methods as the missing data fraction varies (and when, for example, the linear methods above cannot be applied

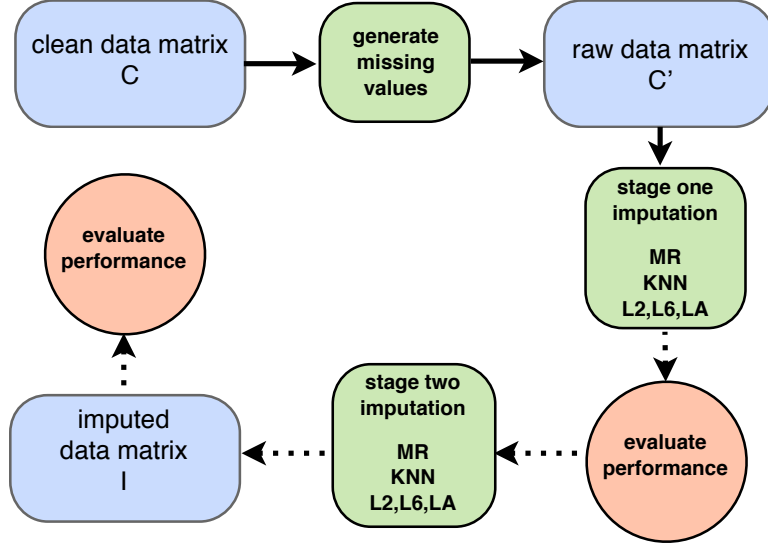


Figure S1: **The testing procedure for imputation methods involves two stages.** The flow chart illustrates the process by which imputation methods are tested on an artificial clean data matrix C . Missing data values are first generated in C to obtain a raw data matrix C' , we then impute all time-series with at least five data points using all methods and apply these methods again when there are fewer than five data points to obtain the fully imputed matrix I . Imputation performance is evaluated after each of the imputation stages.

as there are too few data points). (All methods, except for KNN , are applied to individual time-series case-by-case). In the case of KNN for the second stage of imputations we allow already imputed values to be used to replace missing data). We summarise our method in Figure S1. For a given SEF, we evaluate the performance of the imputation procedures on a data point using the normalised absolute error (NAE)

$$\epsilon_{ij,t} = \frac{|C_{ij,t} - I_{ij,t}|}{|\frac{1}{n_j} \sum_{i,t} C'_{ij,t}|}, \quad (3)$$

where n_j is the number of non-missing data points for SEF j . This error metric allows us to compare errors both between socio-economic factors (which may have different scales) and within scales (which might also vary between several orders of magnitude). The procedure outlined above is repeated 20 times to ensure we obtain fair estimates of errors, since the mechanism above may result in a high fraction of missing data for a given SEF which will increase the error estimates for this factor.

1.1.4 Results

Linear interpolation with 2-point extrapolation is found to be the optimal imputation strategy when the number of missing data points is at least two and mean imputation is preferred to KNN when there is only one data point (in this case, mean replacement refers to replacing all missing data with the value of data point present). The median NAE errors for these methods are displayed in Figure S2A as a function of the fraction f of non-missing

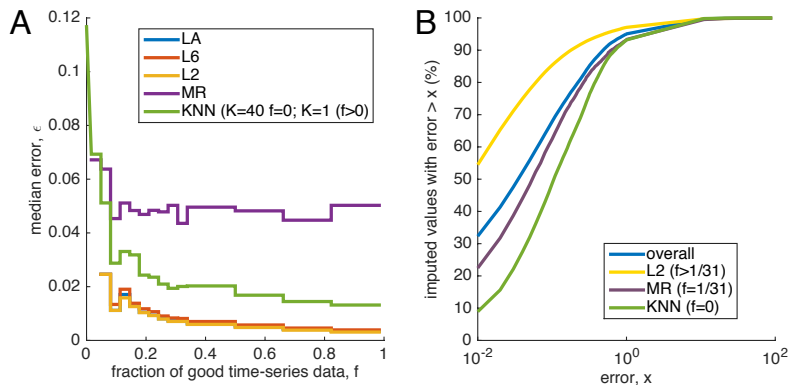


Figure S2: **A combination of imputation methods is necessary to impute data in the Gapminder dataset.** A – Linear interpolation with extrapolation using the two most recent data points outperforms all other methods when the fraction of non-missing time-series data is greater than $1/31$. Mean replacement outperforms the optimal KNN method when $f = 1/31$ and KNN is the only method considered when $f = 0$. B – Error distributions for the optimal method (which combines L2, MR, KNN at varying fractions) are highly skewed.

time-series data (we plot the optimal value of K for each stage: we find that $K = 1$ is optimal for $f \geq 1/31$, but $K = 40$ optimal when $f = 0$). (We display the mean-averaged median error in given ranges of f). The median error is used since error distributions are highly skewed across imputation methods (Figure S2B).

Large errors are induced by time-series with less smoothly-varying values and also, in the case of KNN imputation, the number of missing elements in a country-year. There often exist many orders of magnitude between the observed and imputed values (Figure S3A); however, these large errors often arise from a handful of SEFs whose time-series are prone to sudden, large jumps (for example, factors relating to natural disasters (127,128,136,137), inflation (43), and GDP growth (30)). Factors which vary more smoothly over time such blood pressure or education levels have much lower errors (Figure S3B). In addition to the type of SEF which may contribute to larger errors, country-years which contain many missing data values are subject to high KNN error, since there are fewer values used in the calculation of the euclidean distance between country-years (Figure S3C). Example KNN imputed time-series for income per person (2) and example L2 interpolations for food supply (282) are displayed in Figure S4A and B respectively. For both instances, we display the NAE error and the country which has had data imputed.

1.1.5 Test correlation study

The effect of imputation and pairwise deletion [44] – wherein each missing data element is simply removed from the correlative study – on our statistic of interest (given in Equation 1) is considered. To investigate the effect that imputation has on the value of this statistic, we calculate its values for all regions for a given imputed data set I , and compare these values to the true values calculated from C . Similarly, to explore the effect pairwise deletion has, the values of the statistic are calculated using C' , where the individual missing values are removed. The statistic is then calculated over the years 1980-2010 (to observe historic

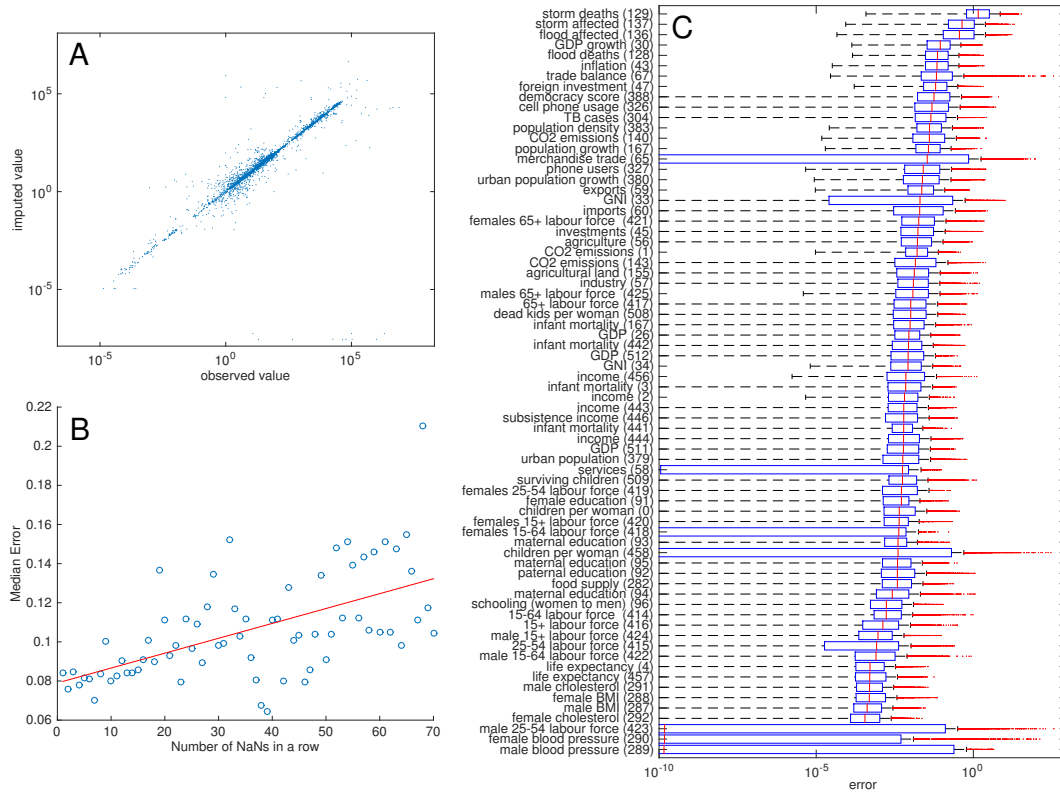


Figure S3: **Overall imputation error varies by SEF and KNN-imputation error increases with fraction of missing data in a country-year.** A – scatter plot of imputed values versus real values for our clean matrix *C* B – Median error increases with the number of missing data values in a country-year. C – Box and whisker plots for all errors across all SEFs in our test matrix *C*: factors prone to sudden jumps in value have larger median errors. (x-axis has been cut off at 10⁻¹⁰ for clarity.) Numbers refer to the SEFs referenced in Supplementary Table 2.

trends) and 2001-2010 (to observe recent ones). As in the main text, the statistic is only calculated when there exist at least eight data points (in our test data set *C*, this means that only three WHO regions have data available).

In comparing the true value of $\bar{\rho}$ to the imputation-predicted value, we report absolute mean differences (and standard deviations) in statistic values of $.03 \pm .06$ for AFRO, $.05 \pm .04$ for AMRO, and $.06 \pm .06$ for EURO for data between 1980 and 2010 and $.05 \pm .09$ for AFRO, $.08 \pm .07$ for AMRO, and $.06 \pm .06$ for EURO for data between 2001 and 2010.

In comparing the true value of $\bar{\rho}$ to the pairwise deletion-predicted value, we report absolute mean differences (and standard deviations) in statistic values of $.06 \pm .07$ for AFRO, $.08 \pm .07$ for AMRO, and $.12 \pm .11$ for EURO for data between 1980 and 2010 and $.06 \pm .09$ for AFRO, $.11 \pm .10$ for AMRO, and $.09 \pm .11$ for EURO for data between 2001 and 2010.

To observe the difference between the accuracy of our imputation method and pairwise deletion we display scatterplots between the true statistic value and the value obtained

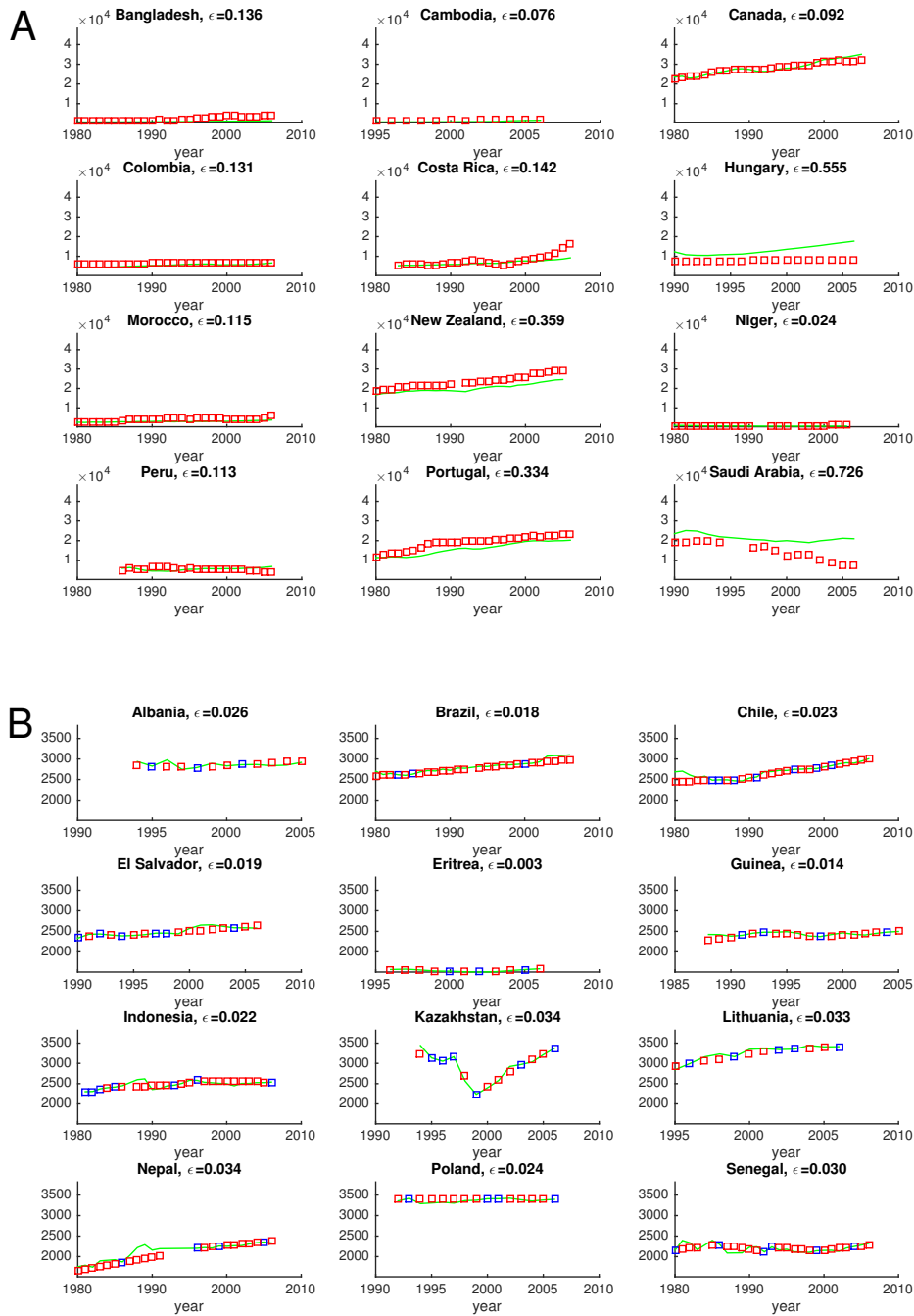


Figure S4: **Example imputations** Time-series from the clean data matrix C (green) have missing values generated to generate the test matrix C' (with non-missing values represented by blue squares). A – KNN imputed values (red squares) for the SEF income per person (3). B – Values imputed by L2 interpolation (red squares) for food supply (282). Mean NAE error for each time-series is shown.

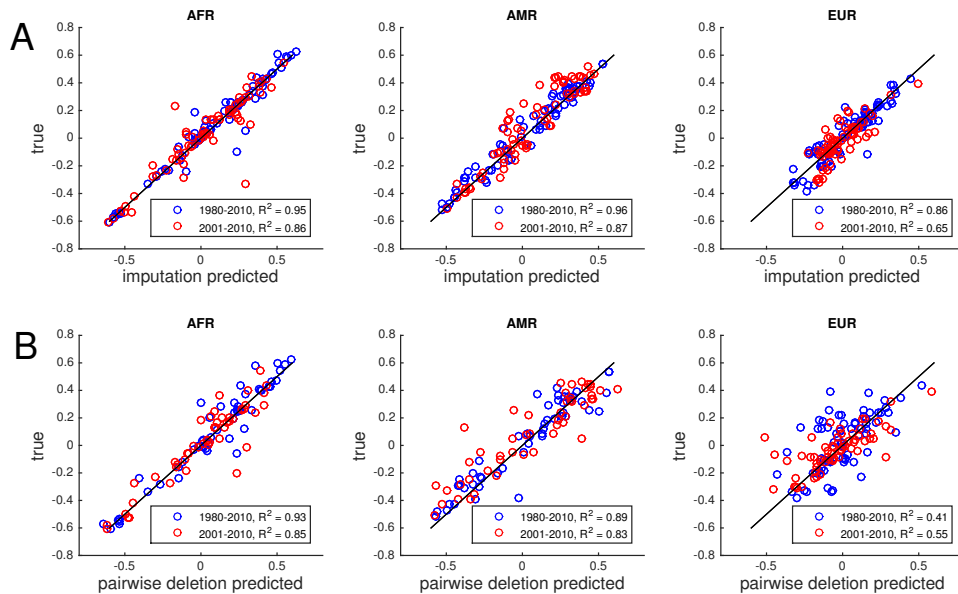


Figure S5: **Calculation of time-averaged Spearman’s rank values are robust to imputation of large numbers of missing data values** A – For each WHO-region present in our imputed data matrix I (with at least eight data points used for a single time correlation) we display our statistic of interest $\bar{\rho}$ calculated on the clean data C against values from imputed data. B – The true value of the statistic is also plotted against values obtained from the data set C' where missing data values are removed from the analysis.

from an imputed data set (Figure S5A) and between the true statistic value and the value obtained from pairwise deletion (Figure S5 B). These results highlight the problematic approach of pairwise deletion and underlines the robustness of our statistic of interest to our imputation method.

1.1.6 Imputing the original Gapminder data set, X

Many SEFs with large prediction error were identified in the imputation testing process. The raw dataset X contains many more SEFs, some of which we expect to behave in a similar way. These SEFs are not removed from our analysis, but rather we make a note of these SEFs in the case that they correlate strongly (and significantly) with vaccine coverage. However, this isn’t the case (see Figure 3A main text). Since KNN error increases with the fraction of missing data in a given country-year, data is not imputed (by KNN) when there exists more than 50% missing data values in a given country-year. The optimal value of K ($K = 40$) when $f = 0$ is in keeping with the recommendation of using $K = \sqrt{n_{obs}}$ [46], where $n_{obs} = 1669$ is the number of cases (rows) used in the imputation method C . We thus increase this value to $K = 80$ for KNN imputation of the matrix X as we have 6076 rows.

The Gapminder data has a missing data fraction of 48.4%, which is reduced to 9.5% after we apply the combination imputation method. Of the data that is imputed, most of it

(87.9%) is by linear interpolation (and of which a very large proportion – 91.0% – have greater than five data points per time series, so we can expect a very small imputation error); a very small amount of time-series have one data point and are thus imputed by mean-replacement (0.02% of the total imputed); and the remainder (12.1%) is *KNN* imputed. After imputation, there are a total of 23 countries which have no time-series data for at least one socio-economic factor (the mean number of socio-economic factors missing for these countries is 153), including six which have no data for any SEF (denoted R in the following list): Andorra, Brunei Darussalam, Central African Republic, DR Congo (R), Cook Islands, Czech Republic (and Czechoslovakia), Dominican Republic, Ivory Coast (R), Marshall Islands, Monaco, Nauru, Niue, occupied Palestinian territory (R), Republic of Moldova (R), Russia (and former USSR), Saint Kitts and Nevis, San Marino, Slovakia, Timor Leste (R), Tuvalu, Yemen. These countries are from a range of WHO regions and we thus do not expect noticeable bias to be introduced into the system.

1.1.7 Imputation of vaccine coverage

The same imputation process is used to impute vaccine coverage data. Missing data is much less prevalent in vaccine coverage data with only 14% missing across all vaccines: BCG has the highest missing data fraction at 26.6% followed by MCV (13.1%), POL3 (11.1%), DTP3 (10.9%), and DTP1 (10.4%). When imputing vaccine coverage data, we use LA rather than L2, since vaccine coverage tends to be more variable than socio-economic factors and less accurately predicted by the most recent trend. Almost all vaccine coverage data contains at least two coverage values in a time-series: there are no time-series imputed by mean-replacement, and 99.9% of values are imputed using the LA method.

1.2 Gaussian Processes

1.2.1 Gaussian Process Regression

Gaussian processes are fit to countries’ vaccine coverage time-series to model time-varying trends in vaccine uptake. For each country, we transform vaccine coverage using the logistic transform, $y'(t_i) = -\log(100/y(t_i)-1)$ (where $y(t_i)$ is a country’s raw vaccine coverage level at time t_i), before we perform Gaussian process regression (GPR) to obtain a predictive distribution over coverage in future years and obtain the vaccine performance index as described in the main text and below.

For each country, we model vaccine coverage as $y'(t_i) = f(t_i) + \epsilon_i$, where $y'(t_i)$ is observed (transformed) vaccine coverage, $f(t_i)$ is a Gaussian process prior, $f(t) \sim \mathcal{GP}(m(t), k(t, t'))$ (where $m(t)$ is the mean function and $k(t, t')$ is the covariance function, and $\epsilon \sim \mathcal{N}(0, \sigma_n^2)$ is understood as the measurement error). Vaccine coverage data forms our test data set and is specified by $\mathcal{D} = \{(t_i, y'(t_i)) | i = 1, \dots, N\}$, where i indexes the year and N is the index corresponding to the most recent time point used in the regression. (The latest WHO vaccine coverage estimates are used in our GPR analysis to more accurately forecast vaccine coverage values into 2015.²)

²The most recent estimates can be found here: http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tswu

Since coverage is broadly increasing over the past few decades in most countries, we choose the mean function $m(t) = \beta_0 + \beta_1 t$. We use a squared exponential kernel $k(t, t') = \sigma_f^2 \exp(-\frac{|t-t'|^2}{2l^2})$, where l is a characteristic time-scale over which the coverage values covary.

We optimise over our parameter set $\theta = \{l, \sigma_n^2, \sigma_f^2, \beta_0, \beta_1\}$ by maximising the posterior marginal likelihood with respect to our parameters

$$p(\theta|\mathbf{y}, \mathbf{t}) \propto p(\mathbf{y}|\mathbf{t}, \theta)p(\theta) \quad (4)$$

$$= \int p(\mathbf{y}|\mathbf{t}, \mathbf{f})p(\mathbf{f}|\theta)d\mathbf{f} \times p(\beta_0)p(\beta_1)p(\sigma_n^2)p(\sigma_f^2)p(l), \quad (5)$$

where $\mathbf{y}'|\mathbf{t}, \mathbf{f} \sim \mathcal{N}(\mathbf{0}, \sigma_n^2)$ and $\mathbf{f}|\theta \sim \mathcal{N}(\mathbf{m}(\mathbf{t}), K(\mathbf{t}, \mathbf{t}'))$ (\mathbf{y}' and \mathbf{t} represent time-ordered vectors of y'_i and t_i (respectively), and \mathbf{f} is the Gaussian process prior) and where we specify the priors $p(\beta_0) = \mathcal{N}(3, 4)$, $p(\beta_1) = \mathcal{N}(0, 1)$, $p(\sigma_n^2) = \mathcal{N}(0, 2)$, $p(\sigma_f^2) = \mathcal{N}(0, 2)$, and $p(l) = \mathcal{N}(0, 2)$. These choice of priors are motivated by the scales involved: we might expect the time-scale, l over which data points interact to be a few years; the prior for the intercept of the linear trend (in raw space) is centred at 95% (which is $-\log(100/95 - 1) \approx 3$ in transformed space); the gradient prior is centred at 0 to account for growing and declining coverage rates.

The parameter estimates are then inserted into the predictive distribution [47],

$$y'_*|t_*, \mathbf{t}, \mathbf{y}' \sim \mathcal{N}(K(t_*, \mathbf{t})K(\mathbf{t}, \mathbf{t})^{-1}\mathbf{f}, k(t_*, t_*) - K(t_*, t)K(\mathbf{t}, \mathbf{t})^{-1}K(\mathbf{t}, t_*) + \sigma_n^2\mathbb{I}), \quad (6)$$

where $K_{i,j} = k(t_i, t_j)$, and t_* is the year in which we would like to make a prediction. The vaccine performance index is then defined by,

$$PI(t_N) = P(y_* > \nu) - P(y_* < y(t_N) - d), \quad (7)$$

where ν is a threshold value, d is the size of a drop, t_N is the most recent point in the training data, $P(y_* > \nu) = \int_{-\infty}^{-\log(100/\nu-1)} p(y'_*|t_*, \mathbf{t}, \mathbf{y}')dy'_*$ and $P(y_* < y(t_N) - d) = \int_{-\log((100/(y(t_N)-d)-1))}^{\infty} p(y'_*|t_*, \mathbf{t}, \mathbf{y}'(t_N))dy'_*$. Gaussian process regression is implemented using GPML Matlab code version 3.5 [48].

1.2.2 Selecting number of time-series points for GPR

In order to establish the number of previous coverage data points n_{train} to use in GPR, we consider forecasting coverage using varying numbers of previous coverage points, and select the value of n_{train} which minimises the RMSE prediction error. We do this for values of n_{train} ranging from five to 20. The results are also compared to those obtained using a simple linear regression fit to the same data. (We apply the inverse logistic transform before computing the RMSE error.) The results are presented in Figure S10A below, from which we see that GPR outperforms linear regression (LR), and that $n_{\text{train}} = 20$ has the lowest RMSE error from all the number of training points we consider (this is unsurprising for a non-parametric method of this kind). We display the observed versus predicted values for all forecasted values when $n_{\text{train}} = 20$ in Figure S10B.

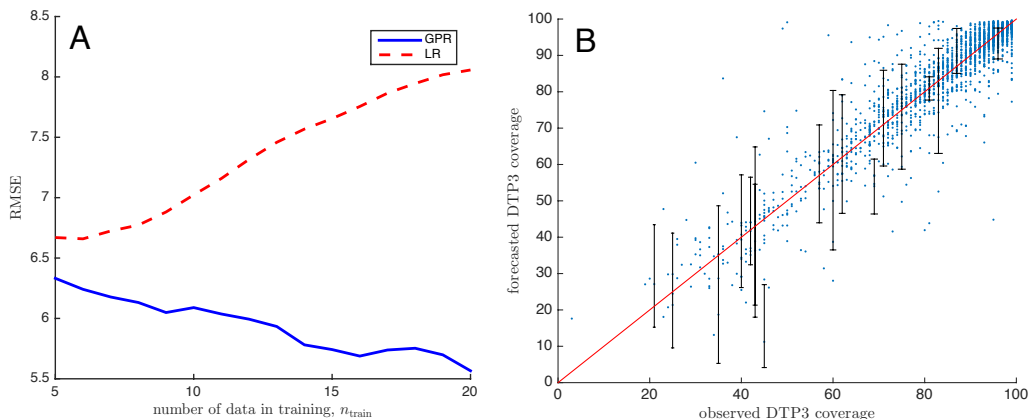


Figure S6: **Optimising the number of data points in the Gaussian process regression** A: Gaussian Processes with increasing values of training points results in a lower RMSE prediction error: the lowest error obtained from all previous training lengths we consider is when $n_{\text{train}} = 20$. B: Scatter plot of all observed versus predicted values obtained from Gaussian process forecasts on all training sets of length $n_{\text{train}} = 20$, for which the RMSE is 5.6 (error bars for 95% prediction intervals are shown in black.)

1.3 Alternative forms of the Vaccine Performance Index

A strength of the index structure that we propose in the main text is its flexibility. We have chosen a weighting of terms congruent with our picture of desirable vaccination characteristics; readers and policymakers focussed on different aspects of vaccine coverage can re-weight these terms to, for example, focus more strongly on avoiding sudden drops in coverage. To illustrate this re-weighting potential, here we consider the alternative indices obtained when setting $d = 5$ and $d = 0$ (with $\nu = 95$ and $\tau = 1$, as before) in Equation (2) in the manuscript for DTP3 coverage. In addition, we also consider only the second term of Equation (2), setting $d = 0$, to investigate the probability of a forecasted drop to coverage.

These indices are compared in Figure S7. Each alternative index is plotted against the original VPI suggested in the manuscript (Equation (2) with parameters $d = 2$, $\tau = 1$, and $\nu = 95$) using data from 1993-2012 to forecast (and thus obtain a VPI value) for coverage in 2013. In Figure S7 A and B we display the two alternatives to the VPI in 2013 with $d = 5$ (A) and $d = 0$ (B), referring to the former as $P(> 95) - P(\text{drop} > 5)$ and the latter as $P(> 95) - P(\text{drop})$. Each country's data point is coloured by the WHO region and we label the two countries in each region which see the biggest shift between original VPI – denoted ‘VPI’ in Figure S7 – and the alternative. (We plot DTP3 coverage time-series of these twelve countries for the first two alternatives in Figure S8). In Figure S7A, we see that using an increased value of a drop serves to increase the VPI values of all countries, with notable increases for countries with lower VPI values, resulting in a tighter grouping of these countries. In Figure S7B, however, we observe the opposite effect: rather than an increased similarity of VPI values for many countries, we see that countries with VPI values around +1 now have a range of values under the alternate scheme. Although this may seem beneficial – that there are now a range of values for a group of countries with similarly

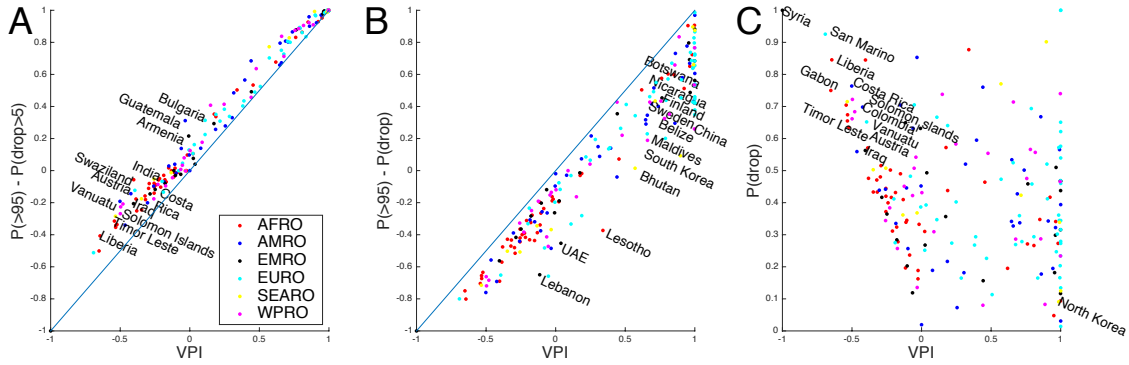


Figure S7: **Possible alternatives for the Vaccine Performance Index reveal sensitivity to drop parameter values** VPI values are sensitive to values of the drop parameter d in Equation (2). (A) Increasing the value of the drop parameter to $d = 5$ results in higher index values for all countries compared to the original VPI (VPI). (B) Allowing $d = 0$ in Equation (2) – resulting in a term representing the probability of a drop of any size – has the effect of decreasing the index values for all countries, including large increases for many countries with with an original VPI value of $\sim +1$. This is an undesirable effect since these countries have stable coverage rates. (C) The probability of a drop $P(\text{drop})$ against our original VPI.

high VPI values – this alternative formulation causes harsh punishment of countries with high (e.g. with coverage greater than 95%) but steady (e.g. with high probability of obtaining a value at least as big as the previous year) coverage, since under the Gaussian Process model, countries with stable coverage will have a roughly 50% chance of any drop. This is readily evidenced for Finland and Sweden, two countries with exemplary DTP3 coverage rates (Figure S8B). This drop in value is – in the case of Sweden and Finland – due to stable coverage levels which result in a symmetric Gaussian probability density over the forecasted point, resulting in a roughly 50% change of drop (despite a low variance). This is motivation for the choice of drop parameter $d = 2$, which does not unfairly punish countries with optimal time-series properties, nor bunches together countries with different time-series properties, as is the case if we increase the value of d above 2.

In Figure S7C, we display the original VPI against the probability of a drop between 2012 and 2013 under our Gaussian Process fit. Interestingly, we find that most of the correlation structure is broken, since countries are now no longer rewarded for having high coverage (as they were under the previous schemes), and countries are simply identified by the probability of a drop in coverage. We see clearly that there are a number of European countries which have a large probability of a drop, suggesting either high but volatile coverage, or high but decreasing coverage (or, as previously mentioned, stable coverage rates with an equal chance of increase and decrease).

In Figure S8, we display those countries which have the biggest difference between alternate and original VPI. In comparing the original index with the alternative when $d = 5$, we see that the biggest movers are countries with high recent variability in DTP3 coverage, and thus have a large probability of a drop in DTP3 coverage from the most recent training point (2012) to 2013 (Figure S8A). This set of countries may be interpreted as the most

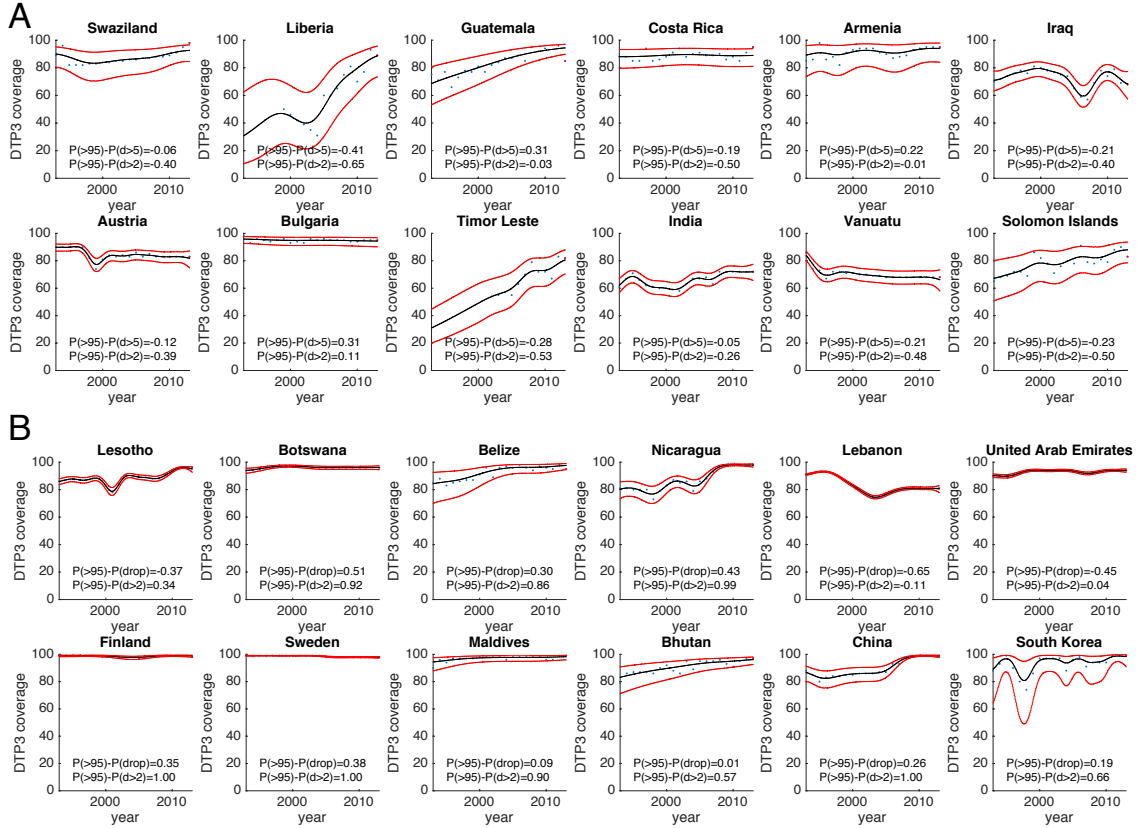


Figure S8: **Time-series of countries with the biggest difference between alternative and VPI values** A) Those countries with the biggest difference (two from each WHO region) for our first alternative (with $d = 5$) and B) for our second alternative (with $d = 0$).

volatile that are also most in danger of not reaching the $\nu = 95\%$ threshold. In Figure S8B, we display the biggest movers for the second alternative VPI when $d = 0$, we see that most countries would be unfairly punished by this alternative form of VPI, since a time-series with zero gradient would result in a predictive distribution symmetric about the most recent coverage point. This, in turn, results in a roughly even chance of a drop in coverage. Our original form of the VPI with $d = 2$ mitigates this.

1.4 Selection of SEFs for Figure 3A

To restrict the number of socio-economic factors we consider in our comparative analysis between socio-economic factors across time and between WHO regions, we choose the top-ten correlating SEFs in each region and for each time-period over which our Spearman statistic is calculated. To include only the strongest signals, we restrict our choice of factors to those with a mean-averaged p -value of less than 0.01 for at least one region. During this process, many identical factors appear in the agglomerated list more than once; further, these lists contain factors which are almost identical to each other, for example, income per person (GDP per capita inflation-adjusted) (2) and GDP per capita USD inflation adjusted (26), and in which case we only include one of the two. Moreover, for utility of

comparison, we include some factors which have a natural counterpart, and are thus useful for comparison; for instance, water access: urban (%) (337) is added for contrast with the other water and sanitation variables.

In total for DTP3 we remove factors which are replicated for GDP and GNI (26, 34, 444, 445, 456), primary education (74), child death and maternal mortality (277, 370, 441, 495, 508), cell phones (326), and population age distributions (108-111, 113, 122, 128) which can be summarised by median age (382). We *include* the following factors as they provide useful comparison to included factors with high correlation and significance: primary completion male (86), improved sanitation access overall (332) and rural (334), and improved water access urban (337).

We do not go through the same process as described above for each of the other vaccines (whose correlations are displayed in Supplementary Figures S7 and S8). However, we list here correlates within the agglomerated top-ten list which differ from DTP3. **BCG**: Dollar billionaires per million (20), Total health spending per person (260), Blood pressure women (290), All forms TB death per 100000 (303), Children and elderly per 100 adults (381), human development index (HDI) (389); **DTP1 no differences**; **MCV** Mean years in school (women to men) (96), energy use per person (98), CO2 intensity of economic output (140), total health spending (% of GDP) (253), Out of pocket share of total health spending (256), HDI (389); **POL3** All forms of TB deaths per 100000 (303), 15-24 employment rate (male) (412).

1.5 Multiple Hypothesis Testing

A total of 5,890 (190 SEFs \times 31 time points) individual correlations are performed and so a multiple hypothesis testing approach needs to be applied to control for the simultaneous correlations. A procedure such as Bonferroni correction will apply a large correction to p-values since each p-value is multiplied by the number of tests. This correction will be unnecessarily harsh since we know that data from successive years is correlated: we are thus overstating the number of independent hypotheses by using conventional Bonferroni correction.

To address this concern, we consider a meta p-value approach for combining dependent p-values which we adapt from Delongchamp *et. al.* [50] and which accounts for the correlation structure amongst p-values which is present when considering averages of correlations of variables dependent throughout time. The meta p-value – described below – may be interpreted as an overall significance level for a set of p-values from correlated observations.

Under the null hypothesis, the p-value for a test statistic is a $U(0, 1)$ random variable, and thus it can be transformed to a standard normal random variable using the inverse cumulative normal distribution function $z_i = \Phi^{-1}(1-p_i)$. When there exists a correlation structure between p-values, then we assume that $\mathbf{z} \sim N(\mathbf{0}, R)$ under the null hypothesis, where R is the correlation matrix between the z-transformed p-values. We can then obtain an overall significance level for the set of p-values by forming the test statistic $T = \sum_{i=1}^m z_i / \sqrt{\mathbb{I}^T R \mathbb{I}}$, where $\mathbb{I} = (1, 1, \dots, 1)^T$. R is unknown and rather than estimate R from the specific type

of data as suggested in [50], we instead estimate R by bootstrapping a number of p-values from the raw data and then estimate the covariance of the z-transformed values. The overall p-value is then obtained from $P = 1 - \Phi(T)$ and multiplied by 190 to Bonferroni correct for the number of socio-economic factors. These meta p-values are displayed Figure 3 in the main text.

2 Supplementary Figures and Tables

2.1 Supplementary Table 2

All socio-economic factors in the reduced Gapminder dataset X are displayed overleaf. Those factors which are displayed in Figure 3A in the main text are highlighted grey.

SEF	$N_C (\geq 3)$	$N_C (0)$	av. data	ALL	AFR	AMR	EMR	EUR	SEAR	WPR
0-Children-per-woman-(total-fertility)	168	28	26.5	14.4	8.5	11.8	4.7	18.5	9.1	29.6
1-CO2-emissions-(tonnes-per-person)	175	21	25.3	18.5	10.9	10.7	4.5	31.8	19.6	25.1
2-Income-per-person-(GDP-capita-PPP-inflation-adjusted)	181	14	28.0	9.8	6.5	2.9	6.0	18.9	9.1	8.7
3-Child-mortality-(0-5-year-olds-dying-per-1000-born)	182	14	28.4	8.5	6.5	4.4	5.0	15.1	9.1	6.2
4-Life-expectancy-(years)	168	28	26.6	14.3	8.5	11.8	4.5	18.2	9.1	29.6
18-Aid-received-per-person-(current-USD)	142	54	20.3	34.4	5.6	16.1	10.7	80.5	18.2	29.7
19-Aid-received-(p-of-GNI)	140	56	18.7	39.7	10.6	19.3	28.4	81.2	28.7	45.4
20-Dollar-billionaires-per-million-people	183	13	3.7	88.0	87.9	87.5	87.7	88.5	88.3	87.6
21-Average-age-of-dollar-billionaires-(years)	183	13	3.7	88.0	87.9	87.5	87.7	88.5	88.3	87.6
22-Total-number-of-dollar-billionaires	183	13	3.7	88.0	87.9	87.5	87.7	88.5	88.3	87.6
26-GDP-capita-(USD-inflation-adjusted)	172	23	25.0	19.3	9.0	10.8	25.5	23.4	31.7	29.3
29-GDP-capita-growth-over-next-10-years	151	39	10.4	66.3	59.4	62.0	68.2	74.8	62.5	66.8
30-GDP-capita-growth-(p-per-year)	178	18	25.6	17.6	11.5	4.3	26.5	23.2	23.5	23.8
33-GNI-capita-(Atlas-method-current-USD)	175	21	23.6	23.9	11.5	12.0	29.3	32.3	33.1	35.2
34-GNI-per-capita-(PPP-current-international-D)	167	29	23.5	24.3	12.2	15.2	28.6	30.9	32.0	37.0
43-Inflation-(annual-p)	176	20	25.0	19.4	9.2	10.1	22.1	26.2	25.2	30.6
45-Investments-(p-of-GDP)	174	22	23.6	23.9	19.0	5.5	28.3	28.9	24.6	41.7
47-Foreign-direct-investment-net-inflows-(p-of-GDP)	174	22	23.9	22.9	14.3	4.8	20.8	37.4	35.5	27.4
56-Agriculture-(p-of-GDP)	163	32	22.3	27.9	15.4	22.1	29.9	35.7	24.9	41.0
57-Industry-(p-of-GDP)	169	27	22.9	26.0	16.7	16.9	37.1	31.4	23.2	34.9
58-Services-(p-of-GDP)	168	28	22.8	26.5	16.7	16.5	36.8	33.3	23.2	35.2
59-Exports-(p-of-GDP)	169	26	24.0	22.6	11.0	10.8	24.8	31.3	19.9	39.4
60-Imports-(p-of-GDP)	170	25	24.2	22.1	15.2	5.6	28.2	31.1	18.8	32.7
62-Arms-imports-(USD-inflation-adjusted)	155	26	15.5	50.0	60.2	52.5	24.5	48.8	34.6	58.3
64-High-technology-exports-(p-of-manufactured-exports)	151	38	12.8	58.6	64.4	45.3	61.6	54.0	65.4	69.2
65-Merchandise-trade-(p-of-GDP)	173	23	24.6	20.7	10.9	4.2	19.9	36.2	27.6	24.6
67-Trade-balance-(p-of-GDP)	170	25	24.2	22.0	15.2	5.6	28.2	30.8	18.8	32.7
71-Military-expenditure-(p-of-GDP)	150	43	15.1	51.3	45.2	53.6	41.5	49.5	55.4	68.7
74-Ratio-of-girls-to-boys-in-primary-and-secondary-education-(p)	169	23	16.8	45.7	44.9	44.7	35.3	41.2	56.3	61.8
82-Children-out-of-school-primary	156	31	13.3	57.2	52.9	52.8	50.1	55.8	74.8	71.3
83-Children-out-of-school-primary-female	150	33	11.0	64.6	57.4	61.9	58.7	63.5	78.9	82.0
84-Children-out-of-school-primary-male	150	33	11.0	64.6	57.4	61.9	58.7	63.5	78.9	82.0
85-Primary-completion-rate-total-(p-of-relevant-age-group)	158	30	14.2	54.3	41.8	48.7	47.5	58.3	71.0	73.5
86-Primary-school-completion-(p-of-boys)	154	33	12.7	59.0	44.2	56.7	50.4	63.9	78.0	76.6
87-Primary-school-completion-(p-of-girls)	154	33	12.7	59.0	44.2	56.7	50.4	63.9	78.0	76.6
91-Mean-years-in-school-(women-25-years-and-older)	163	33	24.9	19.5	9.4	20.3	12.0	24.3	29.6	28.3
92-Mean-years-in-school-(men-25-years-and-older)	163	33	24.9	19.5	9.4	20.3	12.0	24.3	29.6	28.3
93-Mean-years-in-school-(women-25-to-34-years)	163	33	24.9	19.5	9.4	20.3	12.0	24.3	29.6	28.3
94-Mean-years-in-school-(men-25-to-34-years)	163	33	24.9	19.5	9.4	20.3	12.0	24.3	29.6	28.3
95-Mean-years-in-school-(women-of-reproductive-age-15-to-44)	163	33	24.9	19.5	9.4	20.3	12.0	24.3	29.6	28.3
96-Mean-years-in-school-(women-p-men-25-to-34-years)	163	33	24.9	19.5	9.4	20.3	12.0	24.3	29.6	28.3
98-Energy-use-per-person	153	42	19.2	37.9	55.5	26.1	14.8	29.0	33.4	61.2
101-Pump-price-for-gasoline-(USD-per-liter)	149	41	4.6	85.3	81.1	85.1	83.9	86.3	86.2	91.4
128-Flood—deaths-annual-number	155	41	22.9	26.0	22.4	17.5	27.7	30.3	15.0	37.6
129-Storm—deaths-annual-number	143	53	21.2	31.7	44.3	14.7	44.7	33.7	15.0	23.8
136-Flood—affected-annual-number	155	41	22.9	26.0	22.4	17.5	27.7	30.3	15.0	37.6
137-Storm—affected-annual-number	143	53	21.2	31.7	44.3	14.7	44.7	33.7	15.0	23.8
140-CO2-intensity-of-economic-output-(kg-CO2-per-2005-PPP-D-of-GDP)	169	27	22.3	28.0	21.4	13.1	31.2	38.2	28.2	35.0
142-Sulfur-emissions-per-person-(kg)	153	43	16.4	47.1	45.2	46.2	35.3	45.8	44.6	64.9
143-Yearly-CO2-emissions-(1000-tonnes)	171	25	24.7	20.3	13.0	13.6	8.9	33.0	19.6	25.1
144-Total-sulfur-emission-(kilotonnes)	153	43	16.4	47.1	45.2	46.2	35.3	45.8	44.6	64.9
149-Forest-coverage-(p)	173	23	2.6	91.5	90.9	90.6	91.6	92.4	91.2	91.4
155-Agricultural-land-(p-of-land-area)	178	18	25.4	18.2	11.2	6.1	9.4	34.0	12.0	22.9
158-Renewable-water-(cu-meters-per-person)	161	35	4.7	84.8	82.7	83.5	81.8	86.8	82.4	89.2
159-Internal-renewable-water-(cu-meters-per-person)	160	36	4.7	84.8	82.7	83.5	82.7	86.6	82.4	89.2
167-Infant-mortality-(rate-per-1000-births)	183	13	24.3	21.7	22.3	16.7	13.3	29.3	20.8	18.6
253-Total-health-spending-(p-of-GDP)	144	52	11.7	62.3	59.6	59.3	63.6	63.4	67.2	65.7
254-Government-share-of-total-health-spending-(p)	178	18	14.4	53.7	51.4	53.2	50.9	55.0	57.8	56.0
255-Private-share-of-total-health-spending-(p)	178	18	14.4	53.7	51.4	53.2	50.9	55.0	57.8	56.0

missing data (%)

SEF	$N_C (\geq 3)$	$N_C (0)$	av. data	ALL	AFR	AMR	EMR	EUR	SEAR	WPR
256-Out-of-pocket-share-of-total-health-spending-(p)	140	56	11.3	63.6	52.5	92.4	50.9	63.4	57.8	60.0
257-Government-health-spending-of-total-gov.-spending-(p)	178	18	14.4	53.7	51.4	53.2	50.9	55.0	57.8	56.0
258-Total-health-spending-per-person-(international-D)	178	18	14.4	53.7	51.4	53.2	50.9	55.0	57.8	56.0
259-Government-health-spending-per-person-(international-D)	176	20	14.2	54.2	51.4	53.2	50.9	55.0	67.2	56.0
260-Total-health-spending-per-person-(USD)	178	18	14.4	53.7	51.4	53.2	50.9	55.0	57.8	56.0
261-Government-health-spending-per-person-(USD)	174	20	11.5	62.9	76.3	69.4	64.5	41.1	69.2	71.8
262-Medical-Doctors-(per-1000-people)	138	52	15.0	51.6	41.2	45.6	62.8	51.3	44.0	71.8
264-Adults-with-HIV-(p-age-15-49)	146	24	5.7	81.6	87.9	76.0	85.0	75.8	82.4	86.7
273-Births-attended-by-skilled-health-staff-(p-of-total)	166	24	2.6	91.6	90.8	91.4	90.3	92.0	92.1	93.4
275-Maternal-mortality-ratio-(per-100000-live-births)	158	30	2.5	92.0	91.1	91.9	90.3	92.2	92.1	94.9
279-Suicide-(per-100000-people)	179	15	8.9	71.2	89.4	63.0	87.0	48.1	89.1	77.1
281-Sugar-per-person-(g-per-day)	159	37	19.1	38.3	27.1	21.7	46.8	48.9	34.0	52.2
282-Food-supply-(kilocalories-per-person-and-day)	160	34	21.6	30.3	18.3	12.3	40.2	40.8	26.1	46.5
287-Body-Mass-Index-(BMI)-men-Kg-m2	178	18	26.3	15.0	12.4	9.2	10.7	21.8	15.0	16.8
288-Body-Mass-Index-(BMI)-women-Kg-m2	178	18	26.3	15.0	12.4	9.2	10.7	21.8	15.0	16.8
289-Blood-pressure-(SBP)-men-mmHg	178	18	26.3	15.0	12.4	9.2	10.7	21.8	15.0	16.8
290-Blood-pressure-(SBP)-women-mmHg	178	18	26.3	15.0	12.4	9.2	10.7	21.8	15.0	16.8
291-Cholesterol-(fat)-in-blood-men-mmol-L	178	18	26.3	15.0	12.4	9.2	10.7	21.8	15.0	16.8
292-Cholesterol-(fat)-in-blood-women-mmol-L	178	18	26.3	15.0	12.4	9.2	10.7	21.8	15.0	16.8
293-Infectious-TB-new-cases-per-100000-estimated	182	14	16.7	46.1	44.4	43.6	47.2	48.3	47.2	46.2
294-Infectious-TB-new-cases-per-100000-reported	182	14	12.7	59.0	60.1	55.4	59.2	60.9	57.2	58.1
297-Infectious-TB-detection-rate-(p)	177	19	12.4	59.9	60.8	57.3	59.2	62.2	57.2	58.3
298-Infectious-TB-detection-rate-(p)-DOTS-only	168	23	8.8	71.8	70.1	71.3	67.3	77.8	63.9	69.7
299-Infectious-TB-treatment-(DOTS)-completed-(p)	165	27	8.2	73.6	70.7	73.2	68.9	80.6	64.5	72.2
300-TB-programme-(DOTS)-population-coverage-(p)	182	14	10.8	65.3	66.4	64.0	64.7	65.8	63.3	65.0
301-All-forms-of-TB-new-cases-per-100000-estimated	182	13	16.7	46.1	44.4	43.6	47.2	48.2	47.2	46.2
302-All-forms-of-TB-existing-cases-per-100000-estimated	182	14	16.7	46.1	44.4	43.6	47.2	48.3	47.2	46.2
303-All-forms-of-TB-deaths-per-100000-estimated	182	14	16.7	46.1	44.4	43.6	47.2	48.3	47.2	46.2
304-All-forms-of-TB-new-cases-per-100000-reported	182	14	24.5	21.1	22.4	14.6	22.6	22.6	23.2	20.2
309-All-forms-of-TB-detection-rate-(p)	177	19	11.1	64.1	65.0	63.5	63.0	65.6	60.7	62.7
310-All-forms-of-TB-detection-rate-(p)-DOTS-only	168	23	8.8	71.5	70.1	70.7	67.3	77.8	63.9	68.6
311-TB-with-HIV+-new-cases-per-100000-estimated	182	14	15.5	50.1	45.6	47.1	55.1	52.5	47.2	54.1
312-TB-with-HIV+-existing-cases-per-100000-estimated	182	14	15.7	49.4	45.6	47.1	51.5	51.3	47.2	54.1
313-TB-with-HIV+-deaths-per-100000-estimated	150	46	13.7	55.9	48.1	53.9	59.2	57.2	47.2	69.9
324-Broadband-subscribers-(per-100-people)	178	18	9.4	69.6	70.6	66.6	69.1	70.1	67.7	71.7
326-Cell-phones-(per-100-people)	176	20	27.1	12.6	4.8	10.1	3.2	17.0	18.2	25.6
327-Fixed-line-and-mobile-phones-subscribers-(per-100-people)	176	20	22.6	27.1	21.6	19.5	22.1	33.3	24.0	38.6
329-Internet-users-(per-100-people)	176	20	15.5	50.1	48.9	47.4	47.2	48.5	53.4	59.6
331-Personal-computers-(per-100-people)	167	24	10.2	67.0	69.9	64.9	64.5	66.4	65.4	68.5
332-Improved-sanitation-overall-access-(p)	170	26	17.3	44.2	39.2	40.8	40.8	47.4	46.9	52.4
333-Improved-sanitation-urban-access-(p)	173	23	18.0	42.0	37.9	40.2	33.0	44.6	46.9	51.3
334-Improved-sanitation-rural-access-(p)	169	27	17.1	44.7	38.8	40.8	40.8	48.6	46.9	54.1
335-Roads-paved-(p-of-total-roads)	156	26	9.8	68.3	71.7	65.7	63.3	66.8	69.2	72.8
336-Improved-water-source-overall-access-(p)	174	22	17.9	42.3	38.5	42.3	39.3	44.8	46.6	44.2
337-Improved-water-source-urban-access-(p)	177	19	18.6	40.0	37.2	39.1	34.2	42.3	44.6	44.2
338-Improved-water-source-rural-access-(p)	171	25	16.8	45.8	41.1	44.8	41.9	48.4	49.0	51.6
339-Population-aged-0-4-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
340-Population-aged-5-9-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
341-Population-aged-10-14-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
342-Population-aged-15-19-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
343-Population-aged-20-29-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
344-Population-aged-30-39-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
345-Population-aged-40-49-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
346-Population-aged-50-59-years-both-sexes-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
347-Population-aged-60-69-years-(total-number)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
348-Population-aged-70-79-years-(total-number)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
349-Population-aged-80-89-years-(total-number)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1

SEF	N _C (≥3)	N _C (0)	av. data	missing data (%)						
				ALL	AFR	AMR	EMR	EUR	SEAR	WPR
350-Population-aged-20-39-years-(total-number)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
351-Population-aged-40-59-years-(total-number)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
352-Population-aged-60+years-(total-number)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
353-Population-aged-0-4-years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
354-Population-aged-5-9-years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
355-Population-aged-10-14-years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
356-Population-aged-15-19-years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
357-Population-aged-20-39-years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
358-Population-aged-40-59-years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
359-Population-aged-60+years-female-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
360-Population-aged-0-4-years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
361-Population-aged-5-9-years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
362-Population-aged-10-14-years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
363-Population-aged-15-19-years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
364-Population-aged-20-39-years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
365-Population-aged-40-59-years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
366-Population-aged-60+years-male-(p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
367-Population-growth-(annual-p)	176	20	27.8	10.3	4.3	8.8	0.6	12.7	18.2	22.3
368-Crude-birth-rate-(births-per-1000-population)	168	28	5.1	83.4	82.3	82.9	81.5	84.2	82.4	86.4
369-Crude-death-rate-(deaths-per-1000-population)	168	28	5.1	83.4	82.3	82.9	81.5	84.2	82.4	86.4
370-Teen-fertility-rate-(births-per-1000-women-ages-15-19)	180	15	17.1	44.8	54.8	43.1	49.4	30.7	54.3	50.5
372-Sex-ratio-(all-age-groups)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
373-Sex-ratio-(0-14-years)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
374-Sex-ratio-(15-24-years)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
375-Sex-ratio-(15-49-years)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
376-Sex-ratio-(above-50-years)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
379-Urban-population-(p-of-total)	176	20	27.8	10.2	4.3	8.8	0.0	12.7	18.2	22.2
380-Urban-population-growth-(annual-p)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
381-Children-and-elderly-(per-100-adults)	168	28	6.0	80.6	79.3	80.1	78.4	81.5	79.5	84.1
382-Median-age-(years)	178	18	28.2	9.2	4.3	8.8	0.0	12.7	18.2	14.8
383-Population-density-(per-square-km)	180	15	9.5	69.5	88.9	57.6	86.4	46.9	85.3	76.5
386-Murder-(per-100000-people)	154	42	24.0	22.5	12.2	29.4	6.0	23.8	18.2	44.4
388-Democracy-score-(use-as-color)	163	33	6.0	80.7	78.7	78.7	78.2	81.9	81.8	85.7
389-HDI-(Human-Development-Index)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
408-Aged-15-24-employment-rate-(p)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
409-Aged-15+employment-rate-(p)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
410-Females-aged-15-24-employment-rate-(p)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
411-Females-aged-15+employment-rate-(p)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
412-Males-aged-15-24-employment-rate-(p)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
413-Males-aged-15+employment-rate-(p)	157	39	13.6	56.1	51.0	56.5	50.1	57.1	50.1	69.5
414-Aged-15-64-labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
415-Aged-25-54-labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
416-Aged-15+labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
417-Aged-65+labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
418-Females-aged-15-64-labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
419-Females-aged-25-54-labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
420-Females-aged-15+labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
421-Females-aged-65+labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
422-Males-aged-15-64-labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
423-Males-aged-25-54-labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
424-Males-aged-15+labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
425-Males-aged-65+labour-force-participation-rate-(p)	164	32	23.4	24.4	17.4	23.0	13.8	29.4	17.9	39.8
441-Under-five-mortality-from-CME-(per-1000-born)	182	14	28.3	8.6	6.5	4.4	5.0	15.1	12.0	6.2
442-Under-five-mortality-from-IHME-(per-1000-born)	159	37	25.1	18.9	8.5	14.7	9.1	21.8	18.2	44.4
443-Old-version-of-Income-per-person-(version-3)	174	21	23.1	25.4	16.3	23.0	27.6	32.7	17.9	30.9
444-Old-version-of-Income-per-person-(version-8)	180	15	26.9	13.2	9.5	6.2	9.2	21.6	12.3	14.8
445-Alternative-GDP-capita-(PPP)-inflation-adjusted-from-PWT	160	32	18.6	40.0	30.4	35.3	43.3	49.0	36.1	42.9
446-Subsistence-incomes-per-person	181	14	27.1	12.7	9.5	6.2	9.2	21.6	12.0	11.2

SEF	missing data (%)										
	$N_C (\geq 3)$	$N_C (0)$	av. data	ALL	AFR	AMR	EMR	EUR	SEAR	WPR	
454-Economic-growth-over-the-past-10-years	151	39	17.3	44.1	31.2	35.4	47.5	60.1	36.7	45.3	
456-Income-per-person-with-projections	181	14	28.0	9.8	6.5	2.9	6.0	18.9	9.1	8.7	
457-Life-expectancy-at-birth-with-projections	168	28	26.6	14.3	8.5	11.8	4.5	18.2	9.1	29.6	
458-Children-per-woman-(total-fertility)-with-projections	168	28	26.5	14.4	8.5	11.8	4.7	18.5	9.1	29.6	
462-Population-growth-(annual-p)-with-projections	182	14	5.6	82.0	81.9	81.2	81.5	83.1	82.4	81.4	
465-Traffic-deaths-(per-100000-people)	161	10	9.2	70.2	89.4	61.5	87.5	45.3	90.0	76.2	
495-Maternal-mortality-ratio-WHO	166	30	4.2	86.3	84.9	86.2	83.9	86.8	86.8	89.8	
497-Armed-forces-personnel-total	161	35	16.1	48.1	41.9	46.2	38.1	50.3	46.9	65.0	
498-Armed-forces-personnel-(p-of-labor-force)	157	39	15.8	49.0	42.9	47.6	38.6	51.7	46.9	65.0	
505-Exports-unit-value-(index:2000=100)	148	48	20.4	34.1	20.6	10.4	20.8	68.5	25.2	31.9	
507-Net-barter-terms-of-trade-(2000=-100)	150	46	17.3	44.2	21.6	29.9	52.5	65.7	41.1	52.4	
509-Dead-kids-per-woman	168	28	26.6	14.3	8.5	11.8	4.5	18.2	9.1	29.6	
511-Alternative-GDP-per-capita-PPP-WB	169	27	24.5	21.1	12.7	7.0	25.8	29.2	32.0	28.4	
512-Alternative-GDP-per-capita-PPP-PWT-7.1	173	23	26.0	16.1	7.2	2.9	10.9	30.6	27.3	18.5	

2.2 Supplementary Table 3: Vaccine Performance Index values

AFR	2001	2005	2009	2013		2001	2005	2009	2013
					Peru	0.99	0.11	0.29	-0.06
Algeria	-0.01	-0.09	-0.38	0.46	Saint Kitts and Nevis	0.85	0.75	0.94	0.65
Angola	-0.15	-0.19	-0.73	-0.22	Saint Lucia	-0.09	-0.03	0.01	0.40
Benin	-0.19	-0.34	-0.19	-0.30	Saint Vincent and the Grenadines	0.77	0.99	0.99	0.86
Botswana	1.00	0.94	0.96	0.92	Trinidad and Tobago	0.00	0.27	-0.07	-0.11
Burkina Faso	-0.15	-0.62	-0.31	-0.11	United States	-0.37	0.72	0.91	0.91
Burundi	-0.32	-0.34	0.28	0.76	Uruguay	0.06	0.16	0.15	0.66
Cameroon	-0.21	-0.18	-0.17	-0.03	Venezuela	-0.73	-0.89	-0.15	-0.47
Cape Verde	-0.03	0.06	0.98	0.19	EMR				
Central African Republic	-0.20	-0.36	-0.54	-0.22		2001	2005	2009	2013
Chad	-0.30	-0.19	-0.21	-0.38	Afghanistan	-0.29	-0.52	-0.22	-0.10
Comoros	-0.45	-0.39	-0.63	-0.53	Armenia	-0.38	0.15	-0.16	-0.01
Congo	-0.26	-0.11	-0.46	-0.53	Bahrain	0.94	0.94	0.92	1.00
Cote d'Ivoire	-0.22	-0.16	-0.06	-0.39	Djibouti	-0.14	-0.56	-0.34	-0.29
Democratic Republic of the Congo	-0.44	-0.58	-0.19	-0.21	Egypt	0.93	0.87	0.88	0.17
Equatorial Guinea	-0.84	-0.42	-0.54	-0.52	Iran (Islamic Republic of)	1.00	0.98	0.94	0.97
Eritrea	-0.31	0.81	0.58	0.62	Iraq	-0.30	-0.47	-0.05	-0.40
Ethiopia	-0.45	-0.28	-0.45	-0.32	Jordan	0.71	0.70	0.70	0.76
Gabon	-0.17	-0.24	-0.19	-0.65	Kuwait	0.95	0.82	0.97	0.96
Gambia	-0.21	-0.26	0.42	0.96	Lebanon	-0.62	-0.21	-0.03	-0.12
Ghana	-0.01	-0.06	-0.05	0.02	Libyan Arab Jamahiriya	0.64	0.97	1.00	1.00
Guinea	-0.32	-0.21	-0.22	-0.26	Morocco	0.84	0.69	0.88	1.00
Guinea-Bissau	-0.39	-0.38	-0.43	-0.32	Oman	0.99	0.99	1.00	1.00
Kenya	-0.15	-0.21	-0.43	-0.54	Pakistan	-0.21	-0.16	-0.02	-0.07
Lesotho	-0.56	-0.47	-0.02	0.34	Qatar	-0.78	0.51	0.72	0.44
Liberia	NaN	-0.97	-0.45	-0.65	Saudi Arabia	0.70	0.77	0.90	1.00
Madagascar	-0.14	-0.00	-0.73	-0.24	Somalia	-0.14	-0.08	-0.09	-0.25
Malawi	-0.32	-0.23	-0.11	0.18	Sudan	-0.04	-0.12	-0.14	0.03
Mali	-0.40	-0.24	-0.23	-0.18	Syrian Arab Republic	-0.15	-0.21	-0.48	-1.00
Mauritania	-0.47	-0.50	-0.31	-0.35	Tunisia	1.00	0.89	0.98	0.96
Mauritius	-0.26	0.11	0.95	0.98	UAE	0.36	0.33	-0.09	0.04
Mozambique	-0.17	-0.01	-0.07	-0.09	Yemen	-0.26	-0.39	-0.38	-0.18
Namibia	-0.46	-0.28	-0.14	-0.11	EUR				
Niger	-0.12	-0.07	-0.22	-0.03		2001	2005	2009	2013
Nigeria	-0.26	-0.36	-0.56	-0.12	Albania	0.70	0.75	0.90	0.99
Rwanda	-0.25	-0.22	0.48	0.85	Andorra	-0.23	0.97	0.95	0.98
Sao Tome and Principe	-0.37	0.20	0.85	0.81	Austria	-0.00	-0.47	-0.44	-0.40
Senegal	-0.23	-0.58	-0.13	-0.02	Azerbaijan	-0.07	-0.05	-0.04	-0.08
Seychelles	0.82	0.99	0.99	1.00	Belarus	1.00	0.32	0.63	0.57
Sierra Leone	NaN	-0.51	-0.44	-0.13	Belgium	-0.36	0.03	0.99	1.00
South Africa	-0.21	-0.20	-0.43	-0.29	Bosnia and Herzegovina	-0.26	-0.19	0.26	0.03
Suriname	-0.26	-0.38	-0.39	-0.26	Bulgaria	0.08	0.07	-0.07	0.11
Swaziland	-0.30	-0.30	-0.52	-0.40	Croatia	-0.00	0.99	1.00	0.99
Togo	-0.24	-0.26	-0.27	-0.26	Cyprus	0.85	0.99	1.00	1.00
Uganda	-0.01	-0.06	-0.06	-0.19	Czech Republic	0.99	0.99	0.99	1.00
United Republic of Tanzania	-0.17	0.55	-0.20	-0.15	Czechoslovakia	NaN	NaN	NaN	NaN
Zambia	-0.21	-0.20	-0.76	-0.17	Denmark	0.14	0.73	0.16	0.25
Zimbabwe	-0.28	-0.44	-0.29	0.95	Estonia	0.12	0.39	0.74	-0.05
AMR	2001	2005	2009	2013	Finland	0.99	0.93	0.99	1.00
Antigua and Barbuda	0.95	0.89	0.93	0.96	France	0.88	0.89	1.00	1.00
Argentina	-0.07	-0.07	0.11	0.18	Georgia	-0.27	-0.26	0.25	0.22
Bahamas	0.09	0.27	0.21	0.74	Germany	-0.05	0.43	0.78	0.81
Barbados	0.20	-0.27	-0.03	-0.18	Greece	-0.33	0.41	1.00	1.00
Belize	-0.20	0.23	0.78	0.86	Hungary	1.00	1.00	1.00	1.00
Bolivia	-0.25	-0.23	-0.11	0.30	Iceland	0.99	1.00	0.59	0.02
Brazil	0.99	0.29	0.99	0.94	Ireland	-0.11	-0.04	0.01	0.83
Canada	-0.15	-0.12	0.22	0.65	Israel	0.92	0.93	0.87	0.38
Chile	-0.43	0.21	0.29	0.08	Italy	0.10	0.35	0.72	0.79
Colombia	-0.47	-0.15	-0.14	-0.42	Kazakhstan	0.34	0.39	0.68	0.91
Costa Rica	-0.28	-0.32	-0.32	-0.50	Kyrgyzstan	0.90	0.99	0.18	0.72
Cuba	0.65	0.35	-0.23	-0.15	Latvia	0.25	0.86	0.88	0.11
Dominica	0.89	0.98	0.66	0.69	Lithuania	0.51	0.36	0.98	0.51
Dominican Republic	-0.27	-0.36	-0.09	-0.10	Luxembourg	1.00	1.00	1.00	1.00
Ecuador	-0.19	-0.05	0.99	1.00	Malta	0.25	0.51	-0.62	1.00
El Salvador	0.78	0.09	0.76	-0.00	Monaco	1.00	1.00	1.00	1.00
Grenada	0.24	0.58	0.54	0.71	Montenegro	NaN	NaN	NaN	0.47
Guatemala	-0.36	-0.20	-0.67	-0.03	Netherlands	1.00	1.00	1.00	1.00
Guyana	-0.05	-0.11	0.12	0.44	Norway	-0.15	0.19	0.08	0.19
Haiti	-0.19	-0.23	-0.09	-0.00	occupied Palestinian territory	NaN	NaN	NaN	NaN
Honduras	0.73	0.20	0.55	0.26	Poland	1.00	1.00	1.00	1.00
Jamaica	0.27	0.98	0.28	0.32	Portugal	0.95	0.99	0.85	0.90
Mexico	0.92	1.00	0.97	1.00	Republic of Moldova	-0.24	0.95	0.07	-0.01
Nicaragua	-0.16	-0.19	0.99	0.99	Romania	0.89	0.97	0.74	-0.20
Panama	0.58	0.85	-0.18	-0.30	Russia	0.66	1.00	1.00	0.97
Paraguay	-0.22	-0.32	-0.34	-0.26	San Marino	0.89	0.35	0.09	-0.69
					Serbia	0.59	-0.27	0.43	0.28

					WPR	2001	2005	2009	2013
Slovakia	1.00	1.00	1.00	1.00	Australia	0.04	-0.12	-0.17	-0.07
Slovenia	-0.23	-0.29	0.80	0.66	Brunei Darussalam	0.54	0.01	0.81	0.09
Spain	0.11	0.96	0.90	0.98	Cambodia	-0.11	-0.09	-0.38	0.68
Sweden	1.00	1.00	1.00	1.00	China	-0.28	-0.36	0.97	1.00
Switzerland	-0.01	-0.03	0.42	0.99	Cook Islands	0.23	0.26	0.91	0.48
Tajikistan	-0.24	-0.09	-0.11	0.39	Fiji	0.12	0.30	0.99	1.00
Macedonia	0.59	0.56	0.54	0.68	Japan	-0.31	0.19	0.65	0.86
Turkey	-0.42	-0.50	0.20	0.79	Kiribati	-0.12	-0.17	-0.41	-0.04
Turkmenistan	0.36	0.21	0.68	0.70	Lao People's Democratic Republic	-0.37	-0.33	-0.29	-0.23
Ukraine	1.00	0.98	0.44	-0.19	Malaysia	0.99	0.35	0.93	0.78
Former USSR	NaN	NaN	NaN	NaN	Marshall Islands	-0.37	-0.64	-0.30	-0.26
United Kingdom	-0.01	-0.01	-0.01	1.00	Micronesia, Federated States of	-0.62	-0.23	-0.62	-0.17
Uzbekistan	0.73	0.86	0.72	1.00	Mongolia	0.04	1.00	0.46	1.00
SEAR	2001	2005	2009	2013	Nauru	-0.35	-0.44	0.48	0.44
Bangladesh	-0.28	0.96	0.45	0.71	New Zealand	-0.27	-0.08	-0.11	-0.05
Bhutan	0.29	0.14	0.18	0.57	Niue	0.97	0.93	0.62	0.76
Korea, Democratic People's Republic of	-0.26	-0.45	-0.12	0.99	Palau	0.13	0.56	0.64	-0.12
India	-0.34	-0.15	-0.64	-0.26	Papua New Guinea	-0.20	-0.20	-0.11	-0.50
Indonesia	-0.33	-0.25	-0.03	-0.03	Philippines	-0.38	-0.06	-0.16	-0.03
Maldives	0.77	0.69	0.96	0.90	Korea, Republic of	0.20	0.20	0.33	0.66
Burma	-0.20	-0.21	-0.36	-0.35	Samoa	0.92	-0.10	-0.26	0.00
Nepal	-0.01	-0.16	-0.05	-0.13	Singapore	0.94	0.73	0.86	0.82
Sri Lanka	1.00	1.00	0.97	0.99	Solomon Islands	-0.16	-0.20	-0.16	-0.50
Thailand	1.00	1.00	1.00	1.00	Tonga	0.62	0.32	0.89	0.89
Timor Leste	NaN	NaN	-0.02	-0.53	Tuvalu	0.18	0.21	0.30	0.25
					Vanuatu	-0.20	-0.32	-0.38	-0.48
					Vietnam	0.37	0.74	0.40	0.15

2.3 Supplementary Figures: Correlates of BCG, DTP1, MCV, POL3

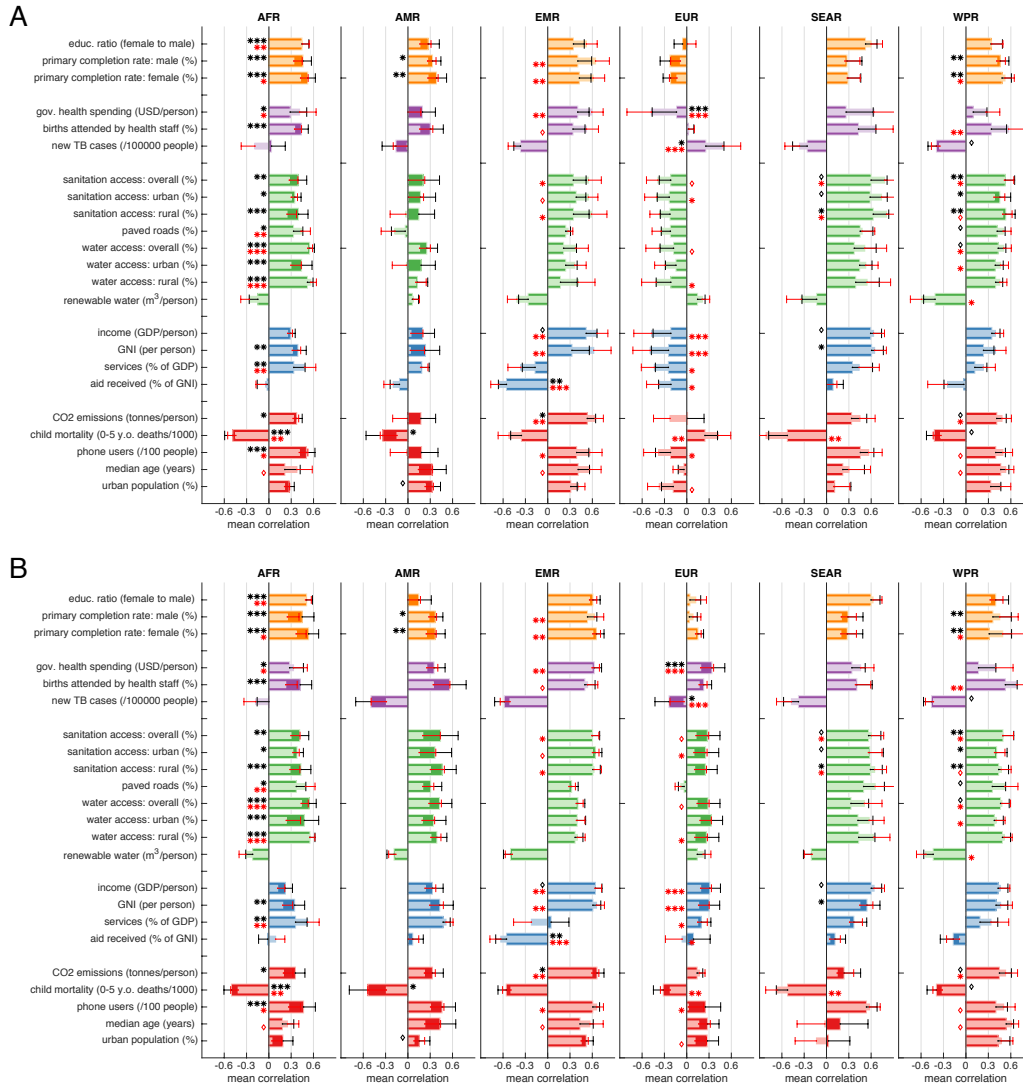


Figure S9: **Historic and recent best-performing correlates with BCG and DTP1 coverage**
 Time-averaged Spearman's rank correlation values between socio-economic factors and BCG (A)
 and DTP coverage (B).

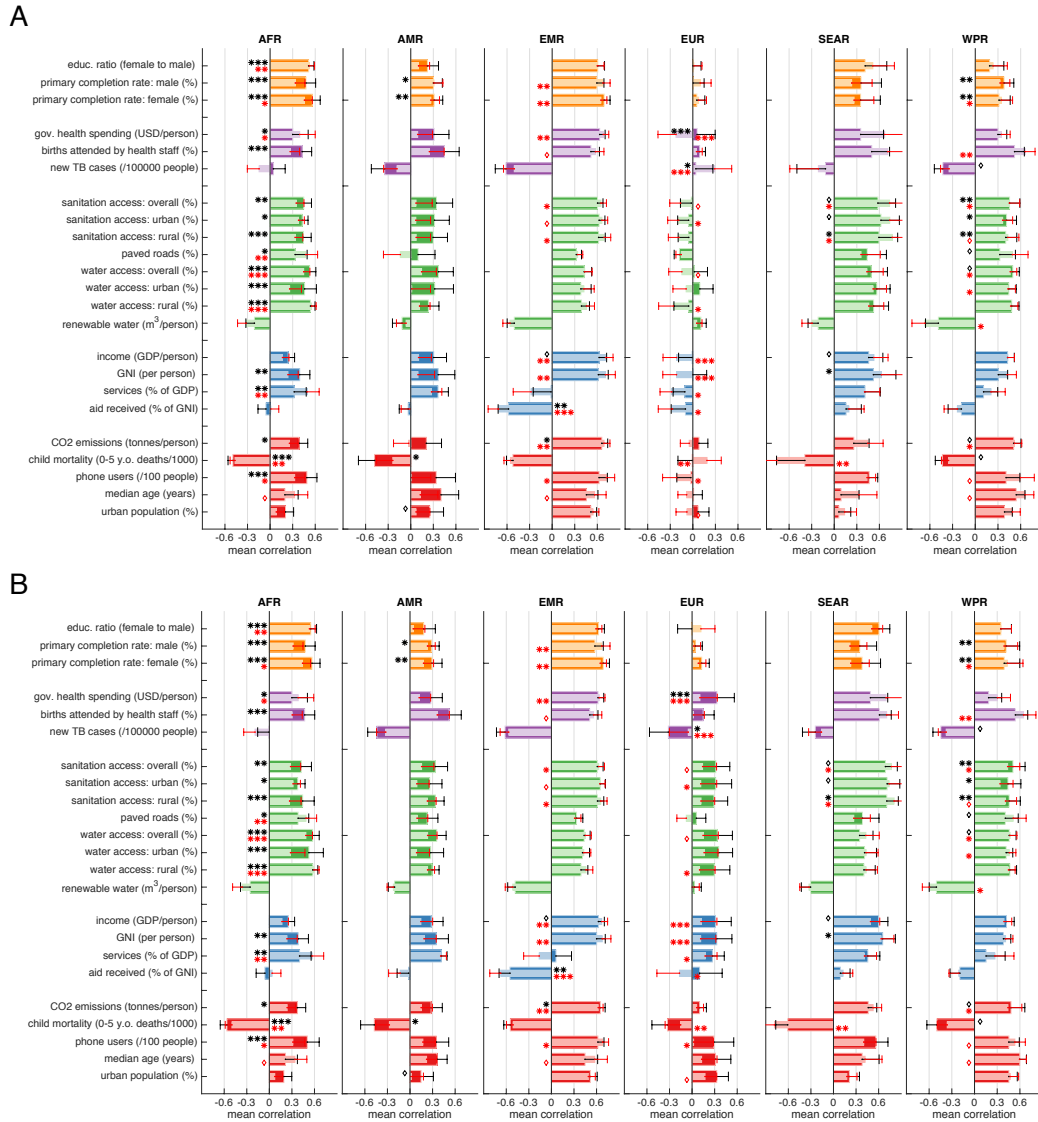


Figure S10: **Historic and recent best-performing correlates with MCV and POL3 coverage** Time-averaged Spearman's rank correlation values between socio-economic factors and MCV (A) and POL3 coverage (B).

References

- [43] A. R. T. Donders, *et. al.* *Review: A gentle introduction to imputation of missing values.* Journal of Clinical Epidemiology, 59:1087-1091, 2006.
- [44] C. K. Enders, *et. al.* *Applied Missing Data Analysis.* The Guildford Press, 6-8: 2010.
- [45] E. Acuña and C. Rodriguez. *Classification, Clustering, and Data Mining Applications.* Springer, 642: 2004.
- [46] P. Jonsson and C. Wohlin. *An Evaluation of k-Nearest Neighbour Imputation Using Likert Data.* Proceedings of the 10th IEEE International Software Metrics Symposium. IEE Computer Society, Los Alamitos, USA: 108-118.
- [47] C. E. Rasmussen and C. K. I. Williams. *Gaussian processes for machine learning.* MIT Press, 2006.
- [48] C. E. Rasmussen and H. Nickisch. *The GPML Toolbox version 3.5.* <http://www.gaussianprocess.org/gpml/code/matlab/doc/>.
- [49] Y. Ge, S. Dudoit, T. P. Speed. *Resampling-based Multiple Testing for Microarray Data Analysis.* Test 12.1: 1-77, (2003).
- [50] R. DeLongchamp, L. Taewon, V. Cruz. *A method for computing the overall statistical significance of a treatment effect among a group of genes.* BMC bioinformatics 7.Suppl 2: S11 (2006).