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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Historical approach to modelling impact of MPP licensing in light of the new methodology presented in this paper

This section describes an approach developed by Juneja et al., which has been used previously by the Medicines Patent Pool (MPP) to assess the impact of its licences, and explains how and why the model presented in this paper differs from it.[1]

The Juneja et al. model offered a straight-forward method for estimating what would have been the costs of procuring equivalent volumes of MPP-licensed products in the absence of those licences. The approach multiplied the number of pills sold for licensed treatments over a given period of time by the price difference between originator and MPP-licensed generic products in countries that would have otherwise likely not been able to access generic products. The model provided a simple, consistent way of estimating impact across a range of different products and diseases, providing insights on how much it would have cost countries to achieve similar health impact without MPP intervention (i.e. the size of investments needed to reach the same health impact).

The historical MPP approach to impact modelling had a number of limitations. [1]

- First, licensing was assumed to have no impact on uptake of medicines, regardless of its contribution to decreasing prices. Without the licences, countries were assumed to procure the same volumes of products, but at higher prices. Thereby, the licences were portrayed as not having any health impact.
- Second, the model assumed that without those licences, countries that were buying originator products would have continued to pay the same tiered prices until patent expiry (i.e. without projected prices decreasing over time, although with adjustments made on factual prices).
- Third, the licences were assumed to only have an impact in countries that would have otherwise not been able to procure generics. In other words, the licences were assumed to only change the number of countries that could benefit from access to more affordable treatments without influencing the market dynamics in other ways. For example, the model did not take into account that licences could also expand the number of manufacturers that could enter a given market (thereby having an effect on country-level competition), or accelerate generic market entry (thereby anticipating the start of impact and/or making the period of impact longer).

Using this approach in 2017, Juneja et al. had estimated cost savings from MPP licences for HIV medicines between 2010-2028 at USD 2·3 billion saved, equivalent to 24 million patient-years of first-line HIV treatment as of 2016 costs. *

The methodology presented in this paper revisits previous MPP impact assessment methodology assumptions, exploring the contribution of licensing to affordability, scale-up rates and uptake volumes, as well as the consequences in terms of health impact and cost savings, more broadly. The revised methodology differs from the previous MPP impact assessment methodology in that:

- Uptake is no longer constant between factual and counterfactual scenarios (i.e. access to quality-assured, affordable MPP-licensed medicines facilitates country decisions to roll out and scale up optimal recommended treatment options, leading to public health impact).
- Assumptions are made on not only generic price evolution, but also on evolution of originator tiered prices in the counterfactual scenario. †
- Market dynamics, uptake, and both economic and health impacts are modelled across all countries individually, taking into consideration the effect of licences on accelerating and increasing generic competition in individual countries.‡ In addition, interactions between multiple licences are taken into account and modelling is fully based on data and data-informed assumptions.
- Health impact is now estimated. Both direct and indirect health impacts of enabling more people to access recommended treatments are considered. Direct effects are when licences enable people to switch to better treatments (which would have not been affordable otherwise), resulting in lower morbidity and mortality. Indirect effects result from expanded treatment coverage (i.e. larger treatment numbers). Both direct and indirect effects of licensing are made possible by access to more affordable medicines.

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* Although this figure is close to the cost savings estimated by the revised model for DTG alone in the equivalent years (USD 3.0 billion), the steps used to calculate these numbers were markedly different. The former value by Juneja et al. was derived by applying more generous assumptions to a smaller number of countries, and recording no savings at all in countries within the counterfactual scenario bilateral licence area. Crucially, the revised model makes rules-based predictions of counterfactual treatment uptake choices, which tend to reduce the degree of cost savings predicted (since countries can also chose an alternative, cheaper regimen). If we were to model cost savings today applying the same assumption of constant uptake as in Juneja et al., the estimated impact would be of USD 19·2 billion to be saved by 2028. That figure corresponds to what the international community would have to spend to achieve the same level of health impact to be achieved with the licence.

† Originator tiered prices used in the model are based on reported values for available years, and extrapolated assuming a 5% annual price decay until patent expiry for future years. Past patent expiry, originator tiered prices are not used anymore as the model assumes that generic competition would take over (see Table S-1 for sources of data used to estimate originator tiered prices).

‡ However, the absence of reliable epidemiological and treatment uptake data for a few countries prevents these countries to be modelled. This is often the case for high-incomes countries (which are also generally not covered by MPP licences), as well as a number of lower-burden low- and middle-income countries (LMICs; e.g., Iraq, North Korea, or Turkmenistan), for which data on the number of PLHIV on ART is not available from UNAIDS. These countries generally also see little uptake of MPP-licensed products.

Detailed methodology

This section provides additional details on the methodology used to estimate the impact of licensing DTG and DAC. It sets out an overview of how the chain of effects (shown in Figure 1 in the main paper) linking licensing to health outcomes and cost savings has been formalised in an Excel-based model, and provides further details on four sequential steps: (1) licensing, (2) generic competition and pricing, (3) uptake, and (4) outcomes.

Overview

The methodology attempts to define realistic counterfactual scenarios for what *would have happened* without MPP licensing, including: most-likely country-level decision-making regarding uptake of WHO-recommended products; existence or not of other access strategies, including other (bilateral, non-MPP) licences and/or tiered pricing strategies; disease burden, market, and pricing evolution during patent and licence lifespans; and impact on uptake, cost savings, morbidity, and mortality of switching to quality-assured and affordable optimal WHO-recommended treatments. The model quantifies the impact of licensing interventions by estimating retrospective and future impact and ranges for a set of health and economic outcomes.

The model uses year-by-year, often country-specific, inputs from existing literature from academic research and international organisations (see Table S-1). In particular, the MPP contractual situation with licensees provides a unique data set of sales volumes and prices of licensed products that is updated on a quarterly basis.[§] This data has informed previous impact assessment calculations and is also used in the new model to inform the factual scenario, while available forecasts from credible sources are used to estimate uptake in the future. The model also offers the possibility to evaluate sensitivities to specific variables and thereby extract confidence intervals (ranges), and it is adaptable to other medicines and disease areas.

Table S-1. Selected sources of data informing the model.

Data type	Sources
Patents and licences information	[2]
World Bank country income classification	[3]
Clinical guidance (including WHO, regional and national guidelines)	[4,5,6,7,8,9,10,11,12]
Epidemiological and treatment coverage data	[13,14]
Treatment and market share forecasts	[14,15]
Quarterly sales and prices of MPP-licensed products [§]	[16]
Other drug pricing information	[17,18,19,20,21,22,23]

Step 1 – Licensing

Licences negotiated by MPP generally expand the number of countries that could benefit from the procurement of generics, increase the number of generics that can supply, and/or accelerate the introduction of a given product. The model defines licence coverage at the product-country-year level through a simple discrete indicator as either: not covered or covered by the MPP licence. Product availability in the absence of the licence is defined similarly at the product-country-year level as either: not available, available from originator only, available as generic through another (e.g., bilateral) licence, or available through generics from the absence of a blocking patent (e.g., because the patent has expired).

Product availability in the counterfactual scenario is the first major assumption in the model as there is inherent uncertainty with regards to what would have happened in the absence of a given licence (i.e. what would a patent holder decide to do if not licensing a product to MPP). A counterfactual scenario in which a product would have been available from the originator only in a given country gives rise to a larger impact of the licence under study in that specific country, whereas a counterfactual scenario in which a product would have been available from multiple generics sources (either bilaterally licensed or in the absence of patents) gives rise to a smaller or no impact in that country. This assumption, which is largely based on patent holders' stated access policies, also includes considerations about the speed of access from bilateral (non-MPP) licences relative to licensing through MPP, as well as other considerations related to which

[§] In the case of DTG, in addition to the MPP-ViiV Healthcare licence with 17 licensees, there is also a bilateral licence between ViiV Healthcare and Aurobindo, with identical coverage. The analysis contained in this paper relies on data from all factual DTG licensees. Importantly, what is referred to as counterfactual bilateral licensing is a hypothetical situation that is different from the existing (factual) ViiV Healthcare-Aurobindo bilateral licence.

patents are considered to be blocking generic product supply and market entry, and the evolution of the patent landscape over time. The assumption of earlier in-country uptake with MPP (which can be enabled or not) reflects faster timelines for in-licensing; more proactive management of sub-licences to support and accelerate development and market entry (e.g., by guidance and support to manufacturers with regards to product development and regulatory affairs, coordination on priority formulations, and business insights to stimulate competition among licensees); and work with civil society, governments, procurement, and other public health agencies to stimulate demand and accelerate in-country uptake of the products.

Step 2 – Generic competition and pricing

Translating licensing into impact requires making assumptions about how licensing affects generic competition and how competition affects price. In addition to data showing how generic competition reduces prices more than tiered pricing and other strategies, there is also empirical evidence that being covered by an MPP licence increases the proportion of a market served by generics and that a greater number of generics serving a specific country-product market decreases prices. [24,25,26,27] The model brings these observations together by estimating a price for every product-country-year with and without MPP based on factual price information and estimations of future price evolution, in light of the number of generics that would be expected to serve each market for that product.

Price information used in the model is obtained quarterly from MPP licensees for all licensed products, and from several recognized sources for non MPP-licensed products.[16,17,18,19,20,21,22,23,§] The difference between the estimated average country-level number of generics with and without MPP is translated into a price mark-up based on estimates from the literature that is added to the generic price with MPP to give a counterfactual price (without MPP).[26,**] This mark-up approach compares the impact of generic competition in different scenarios by translating actual and projected factual scenario prices into counterfactual scenario prices (see Table S-2). It is important to note that the country-level number of generics with MPP is different from the total number of MPP licensees and that the model generally takes a conservative approach to this assumption. For example, while MPP (as of June 2020) had 17 licensees for DTG, including 15 licensees developing TLD and 11 companies with quality assurance for the product, the country-level number of competing generics considered by the model was 4 (see Table S-9 further below). This is because not all licensees have developed the product, not all have registered the product in a given country, and not all are willing/ready to supply a given country at any given time.

Table S-2. Price erosion as a function of the number of generic manufacturers in a given market.[26] This empiric information is used to estimate the counterfactual generic price mark-up (i.e. the price increment added to the factual generic price in recognition of potential stronger generic competition with MPP). This is calculated by dividing the value corresponding to the number of generics in the counterfactual scenario by the equivalent value for the factual scenario. For example, the counterfactual price mark-up corresponds to 15% in the case of counterfactual and factual scenarios with 3 (green) and 4 (blue) generics, respectively (i.e. 0·60 / 0·52 = 1·15).

Number of generics in a given market	**0**	**1**	**2**	**3**	**4**	**5**	**6**
Generic to originator price ratio	100%	87%	77%	60%	52%	46%	38%

While licences cover individual medicines, treatment is often delivered as a regimen (e.g., typically three drugs for HIV treatment and two for HCV treatment). The model therefore combines the prices of each component of a regimen into a regimen price.

A licence's impact on price is assumed to end once full generic competition triggered by patent expiry without the licence would have brought product prices down to the same level as with the licence. However, health and economic impact continue after this point because uptake with and without a licence converges more slowly than prices, while health outcomes can take place over multiple years after treatment (this is notably the case for HCV, in view of disease progression to either cirrhosis and/or hepatocellular carcinoma and death – see Tables S-6 and S-8).[28]

Step 3 – Uptake

Predicting the effect of price on uptake requires slightly different approaches tailored to specific disease areas. The model is deterministic and uses a weighted scoring system (algorithm) of regimen prices and recommendations from clinical guidelines, to predict country-level procurement decisions (i.e. which regimens are "preferred" by each country in every year and for every subgroup of the treatment population).

** This is an important assumption because results rely heavily on the price advantages assumed from moving between levels of generic competition. An alternative source of generic-to-brand price ratios was published by the US FDA (although not peer-reviewed) in 2019 (here). Using values from the US FDA report would imply greater generic price reductions, and therefore larger impact from MPP licensing. By using the values published by Dave et al., the model therefore takes a conservative approach to estimate the impact of MPP licences on induced price reductions.

Relative weights assigned to prices and guidelines can be changed, and an optimal value can be defined by sensitivity testing, inspecting both global and country-specific uptake and impact outputs. Putting too much weight on clinical guidelines implies that countries' procurement decisions will always follow clinical guidelines regardless of prices for alternative regimens. Such a setting removes a licence's ability to influence uptake and have health impact, but allows for generating very large cost savings. This has been MPP's historic approach to impact modelling (as described above under "Historical approach to modelling impact of MPP licensing in light of the new methodology presented in this paper"). Conversely, putting too much weight on prices implies that countries always choose the cheapest regimen applicable for a treatment subgroup, increasing the potential for the licence to influence uptake decisions (because of lower prices). With this setting, a licence may lead to some cost savings but mostly has a very large health impact, as it assumes countries will switch to a more effective treatment when price is low enough. As a compromise, the model assumes that, within the context of sufficient supplies of quality-assured medicines being available, both criteria (price and clinical guidelines) affect country decisions on which medicines to procure and assigns the same relative weights to the two factors (50% each for results presented in this paper) to arrive at what is considered to be a realistic expectation of country decisions, as per inspection of country uptake profiles.

Figure S-1 demonstrates the process through which sensitivities were used to "calibrate" the weight placed on prices relative to guidelines in countries' drug uptake decisions – in this case, for DTG. A 0% weight implies that countries's uptake decisions are completely unaffected by price, so licensing will only result in cost savings. A 100% weight on price implies that countries will always wish to adopt the cheapest available regimen, so licensing may trigger large changes in uptake and resulting health impact. The authors consider both extremes to be unrealistic. The results presented in this paper are instead based on an equal 50:50 split – giving country-level uptake dynamics that the authors believe to be plausible. Other weights could have been chosen anywhere in the range of 40-90%. Choosing a different weight within this range would affect the composition of predicted impact between economic and health impact, rather than the overall scale of impact.

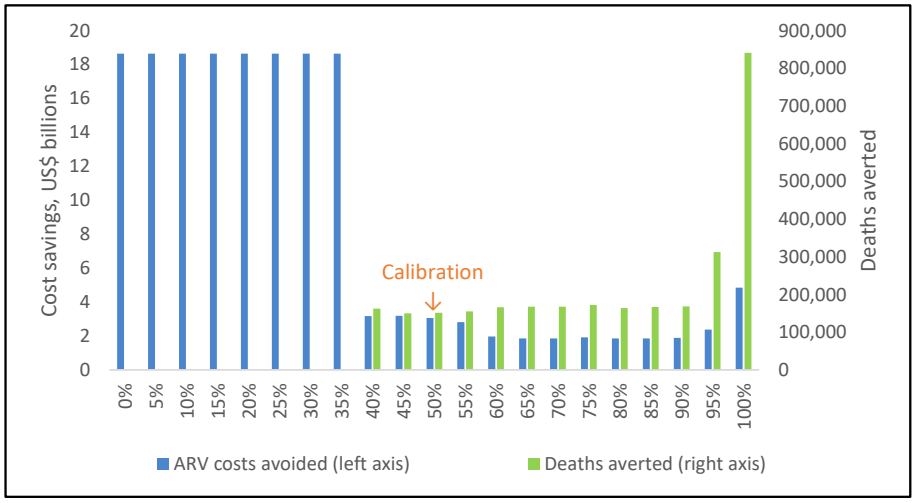

Figure S-1. Calibration of price / guideline weights for country-level drug uptake decision making. Cost savings (left axis) and deaths averted (right axis) from MPP licence for DTG (central scenario), by % weight placed on price relative to guidelines in country uptake decisions.

The model splits the potential treatment population into subgroups. For HIV, the model distinguishes between first- and second-line antiretroviral therapy (ART), as per WHO recommendations, with no distinction between people being initiated on treatment, or switched from an alternative treatment option (see Tables S-3 and S-4), while for HCV the model splits the potential treatment population by virus genotypes 1-6 (see Table S-5) and disease stages (non-cirrhotic, cirrhotic – compensated and decompensated, or with hepatocellular carcinoma – see Table S-6).[28,29] These splits allow the model to predict intermediate levels of scale-up, such as adopting DTG for second-line treatments only, or adopting DAC for a specific genotype or disease stage only.

Table S-3. Adult HIV treatment population numbers and split between WHO-recommended lines of treatment. This information is taken from UNAIDS and used in WHO/MPP/CHAI annual forecasts of antiretroviral (ARV) market shares (2020 edition) for the period until 2024 (in blue), with subsequent values (for 2025 onwards, in yellow) being either annually incremented (this is the case for the number of adult living with HIV on ART) or equal to the last data point available (this is the case for the split between first and second lines of treatment). [13,15]

	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
Number of adults living with HIV on ART (millions)	19·11	19·59	21·72	25·14	26·72	28·15	29·54	30·85	32·05	33·05	33·85	34·55	35·15	35·65	36·05	36·35
Proportion on first line	0·940	0·937	0·936	0·935	0·933	0·932	0·930	0·929	0·929	0·929	0·929	0·929	0·929	0·929	0·929	0·929
Proportion on second line	0·060	0·063	0·064	0·065	0·067	0·068	0·070	0·071	0·071	0·071	0·071	0·071	0·071	0·071	0·071	0·071

Table S-4. Main regimens used in first-line adult HIV treatment. This information is taken from WHO/MPP/CHAI annual forecasts of ARV market shares (2020 edition) for the period until 2024 (in blue), with subsequent values (for 2025 onwards, in yellow) being equal to the last data point available.[15]

	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
DTG-based	0%	8%	23%	53%	81%	89%	92%	93%	93%	93%	93%	93%	93%	93%	93%	93%
EFV-based	81%	79%	69%	45%	18%	11%	8%	7%	7%	7%	7%	7%	7%	7%	7%	7%
NVP-based	19%	13%	8%	2%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%

Table S-5. Distribution of HCV cases by genotype (approximate weighted average of country-level distributions).[28]

Disease stage	Distribution
Genotype 1	44.1%
Genotype 2	10.8%
Genotype 3	26.2%
Genotype 4	10.9%
Genotype 5	0.6%
Genotype 6	2.9%
Mixed or others	4.5%

Table S-6. Disease stage distribution at HCV diagnosis.[28]

Disease stage	Distribution
Non-cirrhosis	85%
Compensated cirrhosis	12%
Decompensated cirrhosis	3%
Hepatocellular carcinoma	0%

Treatment numbers can be considered as an exogenous or endogenous variable. For HIV the model assumes that the number of people living with HIV on ART is exogenous to the model, so that the licence contribution only affects ARV regimen market shares rather than the number of people receiving treatment (which is considered identical in both factual and counterfactual scenarios). This is in recognition of the existence of well-established, large, often donor-funded national HIV treatment programmes and a wide range of possible HIV medicines that can be used (though not all with equally-optimal outcomes). For HCV, while the model assumes that the number of diagnosed HCV cases is exogenous, whether those cases are treated or not is affected by the price of the regimen selected for each subgroup. The response of treatment uptake to price is characterised by a price elasticity parameter such that a given increase in counterfactual prices causes a pre-defined drop in treatment uptake, as has been used by others previously (see table S-7).[30] The model also

imposes a "catch-up" mechanism whereby accumulated diagnosed cases (i.e. the pool of diagnosed people that have not yet been treated) may be treated once drug prices become sufficiently low – with options over how the stock of untreated cases changes year-on-year in response to previous treatment uptake; this is characterized by an annual attrition rate as defined in Table S-10 further below. Such dynamics are adopted because most countries still do not routinely treat known HCV cases, and people in many countries still have to pay for their treatment out-of-pocket. Also, HCV treatment (which is a cure) reduces the number of known cases – unlike HIV treatment which is continuous and does not reduce the population of diagnosed cases (with people living with HIV having to remain on treatment year after year). HCV treatment catch-up of accumulated cases in the counterfactual scenario is set to spread over three years once price parity with the factual scenario is achieved. This is meant to account for health system constraints (especially because catch-up efforts take place in addition to the estimated numbers of treatments projected for that year).

Table S-7. Elasticity of counterfactual scenario HCV treatment uptake with respect to price. The approach and value used for low-income countries, whereby a 1% increase in counterfactual prices causes a 0.2% drop in treatment uptake, have been used by Woode et al.[30] For middle- and high-income countries, it was deemed relevant to reduce the price elasticity value, as those countries might be less sensitive to price differences.

Country categories	Elasticity of demand following a 1% price increase
Low-income countries	-0·20%
Lower-middle-income countries	-0·15%
Upper-middle-income countries	-0·10%
High-income countries	-0·05%

Adjustments for locally-produced DAC products are made in the HCV model. The model does not consider DAC usage in countries relying on local suppliers only or those without Polaris Observatory estimates.[14] For Pakistan, estimated DAC use is considered to reflect the actual use of all DAC (irrespective of whether it was produced by an MPP licensee or not). Actual sales from MPP licensees are therefore used to determine the market share of MPP-supported DAC as part of the whole DAC market in Pakistan. The estimated market share was around 9% in both 2018 and 2019; it was assumed that the market share calculated for the last year with existing data would be indicative of the market share going forward. Conversely, local production in Egypt where patents on DAC were rejected is not modelled due to the use of locally produced DAC only (no MPP licensed products) for Egypt's elimination programme (i.e. MPP supported DAC has not been sold in Egypt and is also not expected to be sold in the future).

Factual and counterfactual uptake profiles are modelled for all countries worldwide. The profiles will look different in each country where those countries have reported actual sales, but otherwise fall into three categories depending on whether the country is predicted to access generic products: irrespective of MPP licensing prior to patent expiry; with MPP only; or not at all. Figure S-2 demonstrates the rough shape of these uptake profiles for a notional country in the HIV model. Clearly, the greatest health impact would occur when the difference between factual and counterfactual uptake is greatest. Cost savings can occur with or without changes in uptake.

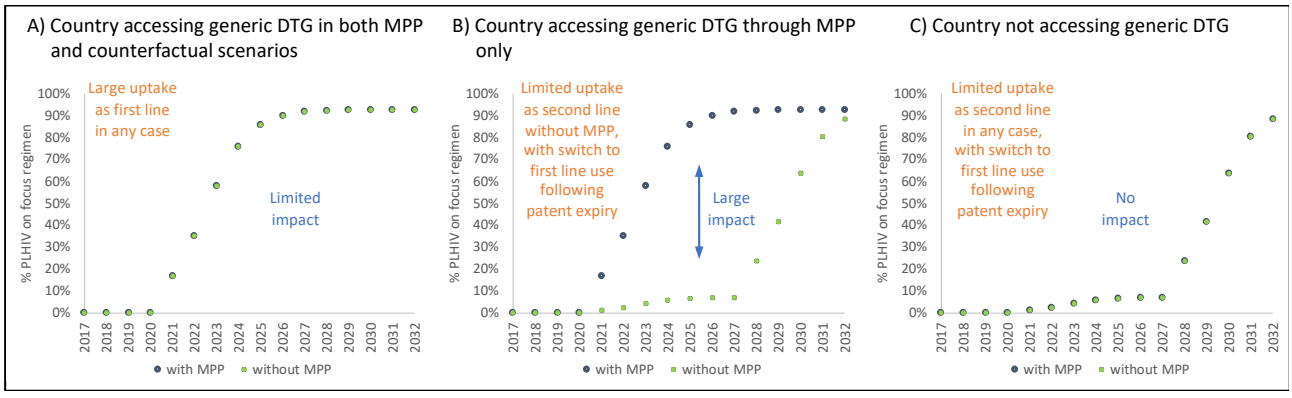

Figure S-2. DTG uptake curves with and without MPP for different country categories. Some countries are able to access generic DTG in both factual and counterfactual scenarios (A, leading to large uptake as first line treatment in any case), while some countries are only able to access generic DTG through the MPP licence (B, leading to limited uptake, as second line treatment only, without MPP, until patent expiry), or not at all (C, leading to limited uptake, as second line treatment only, in any case, until patent expiry).

The speed of regimen switching from one year to the next can be adjusted in consideration of specific disease realities. For HIV, the model assumes that people living with HIV on ART can only change regimens gradually, for clinical reasons, and are unlikely to move back to a previous suboptimal regimen after having made the switch to a better option (i.e. the

switch to DTG-based regimens is a one-way process). In the model, when a country changes its preferred HIV treatment, the population of people living with HIV on ART in the relevant subgroup will transition over several years – following a trajectory described by a logistic function that is roughly s-shaped (see Box S-1). For HCV, the model contains no barriers to changing regimen from one year to the next, since it is considered that subsequent treatments are for different people and continuity of treatment, which lasts 8-24 weeks, is therefore irrelevant.

Box S-1. Logistic function describing country-level HIV product uptake.

The HIV model assumes that the speed with which a preferred regimen can replace existing regimens is described by a logistic function (or sigmoid curve) characterised by the following parameters:

$$f(x) = \frac{L}{1 + e^{-k(x - x_0)}}$$

where:

- L is the curve's maximum value – i.e. the proportion of people living with HIV on ART for which the regimen is preferred (e.g., L could jump from 0 to 7% when it becomes the preferred second-line regimen, then jump to 93% when it becomes the preferred first-line regimen, as based on trends in Table S-3)
- e is the natural logarithm base (also known as Euler's number)
- k is the logistic growth rate or steepness of the curve (set to 1 in the model)
- x is the number of years since uptake has started
- x_0 is the value of the sigmoid's midpoint (set to 2·5 in the model) – i.e. the number of years it would take for half of the people living with HIV on ART for a given treatment line to switch regimens when the country preference for that treatment line changes.

Setting parameters to values described above creates a universal uptake curve which takes approximately five years (twice the value of the sigmoid's midpoint) from start to reaching >90% of its maximum value (see Figure S-3 for an example uptake curve). This five year span not only approximately corresponds to the projected time for effective scale up in the factual scenario, but also approximately corresponds to the time taken for uptake in the counterfactual scenario to catch up with the factual scenario (e.g., following patent expiry, hence the five year period after patent expiry being reported in this study, and during which impact in the HIV model is fading, but still sizeable).

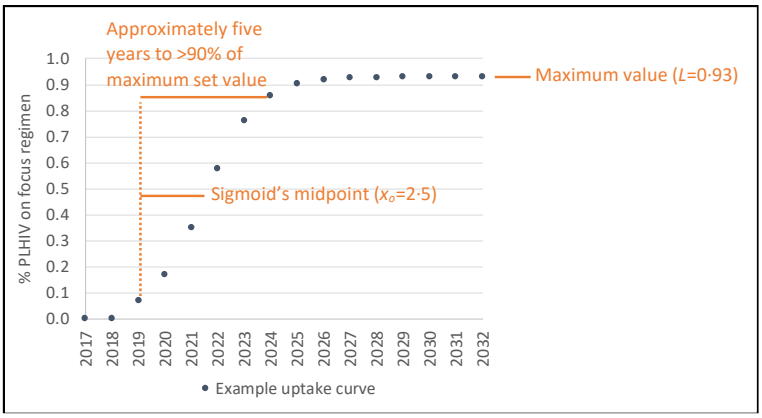

Figure S-3. Example uptake curve, as used in the HIV model. The starting point for this example is in 2019 and parameters detailed in Box S-1 are set as follows: L=0·93 (for uptake as first-line HIV treatment), k=1, and x_0=2·5 (for a midpoint after 2·5 years). It takes approximately five years to reach >90% of the set maximum value of 0·93. PLHIV: people living with HIV.

The parameters of the logistic function can be modified to reflect better information on how transition is actually occurring in countries wishing to scale-up DTG usage. The authors selected parameters which imply that a country wishing to transition to a new first-line ARV regimen could transition half of all first-line users within two and a half years (midpoint = 2.5), with an average gradient which implies that scale-up is mostly achieved after five years (steepness coefficient = 1). The authors believe that these values are realistic, but acknowledge that a range of alternative values could have been used. Figure S-4 demonstrates how different parameters would affect the scale and composition of estimated impact from MPP's DTG licence under "central" scenario assumptions.

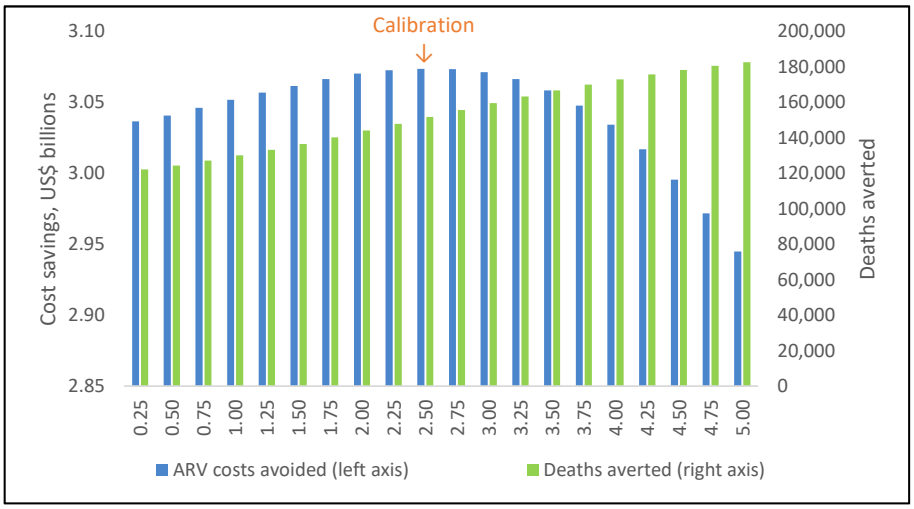

Figure S-4. Cost savings and deaths averted from the MPP licence for DTG (central scenario), by varying the value of "midpoint" parameter determining the speed of DTG uptake. A low midpoint value implies that countries can scale-up a new ARV regimen quickly, and a high value implies a slow scale-up. The main interaction with estimated impact is through the speed with which DTG would have been introduced as a second-line regimen in the counterfactual scenario. Up to a point, a slower transition increases both cost savings and health impact. Beyond this, cost savings would decline. The authors chose a midpoint of 2.5 years based on their understanding of the speed of transition for DTG so far, and from previous transitions to other regimens.

Total modelled uptake with the licence under study is adjusted to agree with actual sales data available from MPP licensees for previous years and external market share forecasts for future years.[††,‡‡,§§] Uptake without the licence is scaled by the same factor in order to preserve the relative levels between modelled uptake with and without the licence. For HIV, future uptake with the licence is scaled with regards to WHO/MPP/CHAI annual forecasts of ARV market shares (2020 edition), which were first published by Gupta et al. in 2016, and are now updated annually.[15] For HCV, future uptake with the licence is aligned with treatment forecasts made by the CDA Foundation's Polaris Observatory.[14] Modelled uptake trajectories are finally transformed into numbers of people treated in each country-year through matching with epidemiological information (UNAIDS data on the number of people living with HIV on ART and Polaris Observatory data on diagnosis and treatment numbers for people living with HCV).[13,14]

Step 4 – Outcomes

The model applies evidence-informed assumptions to translate uptake into outcomes – including health outcomes (mortality, morbidity and adverse effects linked to disease progression) and economic outcomes (drugs costs and health system costs associated to untreated disease progression). Impact is derived from the comparison of factual and counterfactual outcomes (i.e. the difference between scenarios).

Calculating health outcomes is highly disease- and medicine-specific. For HIV, the model calculates outcomes associated with switching from one regimen to another. It uses parameters from the available literature that estimate differences in clinical outcomes for people living with HIV on ART that depend on the regimens used (in particular, the estimated benefits of using TDF/3TC/DTG, also known as TLD, over TDF/3TC/EFV, also known as TLE, in the DTG model are based on a modelling study by Phillips et al. that has informed WHO guidance development, see Table S-9).[31]

The HCV model estimates outcomes associated with treating patients who would otherwise not have been treated, or not until later (once prices would have dropped, for example from generic entry upon patent expiry). It creates a cascade of disease stages for HCV patients and which progresses at a fixed rate (using annual transition numbers between disease stages) unless successfully treated.[28] In this cascade, non-cirrhotic HCV cases develop into compensated cirrhosis, followed by decompensated cirrhosis (and sometimes directly to hepatocellular carcinoma), decompensated cirrhosis

†† Actual sales are adjusted to account for some level of supply chain and treatment delivery wastage: 1% for HIV products and 5% for HCV products, reflecting mechanisms in place for each disease area, i.e. in recognition of the existence of large, well-established HIV procurement and treatment programmes, compared to the more limited infrastructure supporting HCV treatment rollout.

‡‡ The model reallocates some of the DTG sales going to redistribution centres (e.g., those from some pooled procurement mechanisms for which destination country information is not available) to a set of destination countries, currently defined as all countries in Sub-Saharan Africa, which is thought to be the most likely final destination. Some DTG sales with inherent uncertainty are not counted, while no reallocation is done for DAC sales going to redistribution centres, in view of the uncertainty on the final destination for those sales. See Table S-11 and S-18 for details on country-level sales, including reallocation.

§§ The model adjusts DAC 30 mg sales to 5% of their reported quantities, assuming that DAC 30 mg is mostly used as a booster for over-dosing DAC 60 mg to 90 mg daily in cases of drug-drug interactions with moderate CYP3A inducers (such as efavirenz, EFV, used for HIV treatment), and less as a standalone dose with strong CYP3A inhibitors (see US FDA label for daclatasvir here). Overall, cumulative sales of DAC 30 mg have represented approximately 4% of the DAC sales, so any impact of missassigning DAC 30 mg sales may be limited.

potentially leads to hepatocellular carcinoma, and both lead to HCV-related death (see Table S-8). The model assumes that the likelihood of cirrhosis cases (compensated and decompensated) to be treated is twice as high compared to non-cirrhosis cases (which is adjusted downwards accordingly). The model also assumes that the proportion of cirrhosis cases among diagnosed cases decreases over time, by 2% annually (based on expert discussion), to account for the fact that more cirrhosis cases are treated and that, over time, newly-diagnosed cases have a higher likelihood to be non-cirrhotic.

Table S-8. Annual transition rates from HCV disease progression. Estimates from a cost-effectiveness study of HCV treatment in India are used as a proxy in light of MPP-licensed DAC sales having been dominated by supply to this country so far (see Table S-18).[28]

Disease transition event	Annual rate
Non-cirrhosis to compensated cirrhosis	1·4%
Compensated cirrhosis to decompensated cirrhosis	3·5%
Compensated cirrhosis to hepatocellular carcinoma	2·4%
Decompensated cirrhosis to hepatocellular carcinoma	6·8%
Decompensated cirrhosis to death	21·6%
Hepatocellular carcinoma to death	41·1%
Other causes of death (non related to HCV disease progression)	0·7%

The HCV model does not imply any clinical superiority of one WHO-recommended regimen over another (although it does consider the effect on costs of varying recommended treatment durations as a function of HCV genotype, HCV disease stage, and treatment regimen used). Indeed, alternative regimens are considered highly similar with regards to their sustained virologic response (SVR) rates, which are set to 95% for all WHO-recommended regimens in the HCV model, as has been done in other modelling exercises.[32] While the model assumes similar SVR rates of 95% for all regimens, it does so for recommended regimens on a per genotype basis only (i.e. it assumes that recommended treatments and durations indicated for a certain genotype are equally effective). Although SVR rates do differ slightly across recommended drug regimens and genotypes, these are also dependent on disease stage and other factors such as treatment history, for which detailed mapping at the country level is challenging. This is outlined in detail in Annex 8 of WHO 2018 HCV treatment guidelines where GRADE evidence profiles are presented.[6] The specific case of NS5A polymorphism and its effects on SVR rates following treatment with first generation NS5A inhibitors such as DAC is another aspect not considered as the modelling approach attempts to balance complexity with feasibility.[33] Indeed, instead of affecting effective SVR rates, licensing of DAC indirectly improves health outcomes by triggering faster and/or more extensive treatment uptake (i.e. treating more people earlier) and associated clinical benefits as a result of freeing up financial resources through reduction of treatment expenses (by allowing use of cheaper medicines of similar efficacy).

The model follows similar steps to estimate cost savings. These are usually positive because countries are able to access regimens containing licensed medicines at lower prices due to enhanced competition in the market. In some cases, however, cost savings can include negative components – for example, when licences lead to countries increasing uptake of a more expensive (but more effective) regimen or a much larger treatment scale-up (i.e. treating more people) than without the licence. In these cases, negative components of cost savings are associated with improved health outcomes; this is the case in the HCV model where advantageous prices trigger additional uptake.

Cost savings are generally calculated at the country level as follows below, where the comparator price corresponds to the weighted average of drugs which the focus regimen is expected to replace.

$$\begin{aligned} \textit{Cost savings} = {} & (\textit{focus regimen price}_{\textit{without MPP}} * \textit{focus regimen uptake}_{\textit{without MPP}}) \\ & - (\textit{focus regimen price}_{\textit{with MPP}} * \textit{focus regimen uptake}_{\textit{with MPP}}) \\ & + (\textit{comparator price} * (\textit{comparator price uptake}_{\textit{with MPP}} - \textit{comparator price uptake}_{\textit{without MPP}})) \end{aligned}$$

For HCV, the model also calculates cost savings that emerge from avoiding more serious health issues from HCV infection. These are health system costs related to caring for cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma. The calculation is based on annual cost estimates to health systems for each of the disease stages considered; this information is then combined with the difference in the stock of each of the disease stages between the factual and counterfactual scenarios. Here too, estimates from a cost-effectiveness study of HCV treatment in India are used as a proxy for this in light of MPP-licensed DAC sales having been dominated by supply to this country so far (see Table S-18).[34]

Licence-specific assumptions

This section describes the assumptions used to characterise the effect of MPP licensing under "low", "central", and "high" scenarios for DTG and DAC.

Licence-specific assumptions for DTG

Public-health and economic impact of the MPP licence for DTG are predicated on the following key assumptions:

- A counterfactual scenario in which the patent holder would have bilaterally licensed DTG to a smaller number of generic manufacturers, leading to weaker generic competition and higher prices.
- A geographical scope expansion in the MPP licence from 68 countries (namely, all least-developed countries, all low-income countries, all countries in sub-Saharan Africa, and India) in the counterfactual scenario, to over 95 countries now being able to procure generic versions of the product.[35,36,***,†††,‡‡‡]
- Alternatives to MPP-licensed generic DTG-based regimens considered as counterfactual treatment options include the use of generic EFV-based first-line regimens, originator and bilaterally-licensed generic DTG-based first- and second-line regimens, and lopinavir/ritonavir (LPV/r) based second-line regimens, among other options. Other, more expensive ART regimens, used only in some high-income countries, but not recommended by WHO, are not considered.
- Cost savings from the MPP licence for DTG are obtained from comparing the costs of MPP-licensed DTG-based products for adults across all lines of treatment (as per WHO recommendations) with a weighted average cost of the regimens that would have been used in the counterfactual scenario (i.e. in absence of MPP).[§§§]
- Health impact considers the scale of uptake of DTG and its benefits over alternative treatments (i.e. EFV as first-line alternative) – these are taken from Phillips et al. and include more sustained viral suppression and lower rates of mortality, morbidity and mother-to-child transmission of HIV, as obtained from "TLD for all" vs "TLE for all" treatment policies (which both include small proportions of patients on other second-line drugs, thereby allowing a consistent approach between how health impact and cost savings are calculated).[31]

Low, central, and high scenarios for health and economic impact are obtained by considering a set of ranges for key health and generic competition parameters, namely: the approach to counterfactual generic prices (based on the difference in numbers of generic manufacturers in each market, if any), AIDS-related death rates, disability-adjusted life-years, viral load suppression, and mother-to-child transmission with DTG- vs EFV-based ART – see Table S-9.

*** Inclusion of India from 2018 onwards, despite not being part of the patent holder's stated policy, is based on the high burden of disease in this country and the fact that most of the leading ARV manufacturers are based in India, where a Certificate of Pharmaceutical Product would have been needed to be issued by the Indian regulator (the Central Drugs Standard Control Organization) to enable export and delivery to other licensed countries.

††† Beyond direct licence coverage, sales outside the licensed territory are permitted where there is no granted patent in force, or where sales of a generic version do not infringe on an existing patent, such as in cases in which a compulsory licence has been issued. As a result, sublicensees are able to sell generic DTG to at least an additional 32 countries – this is discussed here.

‡‡‡ This study, which considered MPP-licensed DTG sales data until June 2020 and inclusion of Algeria to the MPP licence for DTG (announced in October 2020 – here), did not consider the additional impact from the separate MPP-ViiV Healthcare licence for DTG specifically agreed for four upper-middle-income countries (Azerbaijan, Belarus, Kazakhstan and Malaysia) in November 2020 (here). The study also did not model the impact of adapted paediatric DTG formulations (e.g., the DTG 10 mg scored dispersible tablets entering the market in 2021).

§§§ Cost savings originating from increased uptake of DTG take into consideration the displacement of a portion of second-line drug costs due to better long-term efficacy of DTG relative to EFV, as predicted by Phillips et al.[31] The model uses a weighted average by which 94% of DTG scale-up displaces first-line regimens (such as EFV-based), and 6% replaces more expensive second-line regimens (such as LPV/r-based).These cost savings accrue in all countries effectively covered by the MPP licence – with limited price reductions for countries that would still have had access to generic DTG in the counterfactual scenario, and larger price reductions for countries that would otherwise have accessed originator products only.

Table S-9. Low, central, and high modelling scenario parameters for MPP licence for DTG.

		Scenario		
Parameter		**Low**	**Central**	**High**
Generic competition	Additional competition and price advantage in countries also covered by counterfactual scenario licences	No	Yes, 1 additional generic manufacturer with MPP (4 vs 3): 15% price mark-up without MPP	Yes, 2 additional generic manufacturers with MPP (4 vs 2): 48% price mark-up without MPP
Health benefits, comparing outcomes from TLD vs TLE [31]	Δ AIDS-related deaths per hundred person-years	-0·24	-0·98	-2·02
	Δ disability-adjusted life-years (DALYs) per person-year on ART [****]	-0·02	-0·07	-0·14
	Δ % people on ART with viral load < 1000 copies per ml (mean over 20 years)	2	9	18
	Δ % mother-to-child transmissions among women living with HIV	-0·3	-1·4	-2·9

Licence-specific assumptions for DAC

The overall methodology for impact assessment of the MPP licence for DAC is based on the same principles as for modelling impact of the licence for DTG, with a few elements being different. Contrary to HIV, where overall treatment scale-up is not affected by entry of MPP-licensed products, higher prices in the HCV counterfactual scenario not only impact regimen choice (e.g., sofosbuvir/DAC [SOF/DAC] and SOF/DAC/ribavirin [SOF/DAC/RBV] vs SOF/ledipasvir [SOF/LED], SOF/velpatasvir [SOF/VEL], SOF/RBV, SOF/LED/RBV, and/or glecaprevir/pibrentasvir [G/P]) but can also lead to overall changes in country/individual decisions to address HCV at all (i.e. the availability of affordable DAC products may convince some countries or individuals to consider treating HCV). Note that the decision to treat HCV infection often relies on individual people living with HCV given the high level of out-of-pocket expenditures in HCV, where no large international donor programme is in place. Better access to HCV treatments may lead to substantial public health impact (from lower incidence of compensated and decompensated cirrhosis, hepatocellular carcinoma, and overall liver-related mortality) and cost savings (from not having to address health complications from progression of HCV infections at a later stage).

Public-health and economic impact of the MPP licence for DAC are predicated on the following key assumptions:

- A counterfactual scenario in which the patent holder would have bilaterally licensed DAC to a smaller number of generic manufacturers that would have taken longer for in-country uptake.
- A geographical scope expansion in the MPP licence from 90 countries in the counterfactual scenario, to over 112 countries now being able to procure generic versions of the product.[37,38,††††]
- Alternatives to MPP-licensed generic DAC-based regimens considered as counterfactuals include the use of more expensive originator and bilaterally-licensed generic SOF/DAC, SOF/LED, SOF/VEL, SOF/RBV, SOF/DAC/RBV, SOF/LED/RBV and G/P (as either fixed dose combinations or individual components).[39]
- Cost savings from the MPP licence for DAC are obtained from comparing the costs of MPP-licensed DAC-based products with those of other selected treatments in the counterfactual scenario. Additional expenses from scaling up treatment are subtracted from these savings (thereby ensuring that benefits are not counted twice).
- Health impact is obtained by earlier treatment of existing diagnosed HCV cases, as well as expanded treatment programmes (larger treatment numbers) enabled from access to more affordable recommended treatment options.

Low, central, and high scenarios for health and economic impact are obtained by considering a set of ranges for key health parameters and generic competition input variables, namely: the approach to counterfactual generic prices (based on the difference in numbers of generic manufacturers in each market, if any, as well as any further delay applied to counterfactual generic price trajectories); immediate or delayed in-country generic market entry in the counterfactual scenario; and annual attrition rates for patients untreated in the counterfactual scenario but treated in the factual scenario (see Table S-10).

[****] The study by Phillips et al. reported a central estimate of 0·98 deaths averted per 100 patient-years (with a 90% confidence interval from -0·24 to -2·02), averaging over a twenty-year assessment period.[31]

[††††] The MPP licence for DAC enables manufacturers that do not rely on BMS technology to sell outside the 112 countries if no granted patent is being infringed. As a result, sublicensees are able to sell generic DAC to at least an additional 38 countries (therefore reaching 150 countries in total, as of February 2021).

Table S-10. Low, central, and high modelling scenario parameters for MPP licence for DAC.

		Scenario		
Parameter		**Low**	**Central**	**High**
Generic competition	In-country generic entry one year earlier with MPP	No	Yes	Yes
	Approach to counterfactual generic prices	Mark-up based on number of generics	Mark-up based on number of generics	Mark-up based on number of generics (with forecasted price trajectory delayed by one year)
	Price advantage in bilateral territory	Yes, 1 additional generic manufacturer with MPP (2 vs 1): 13% price mark-up without MPP	Yes, 2 additional generic manufacturers with MPP (3 vs 1): 45% price mark-up without MPP	Yes, 3 additional generic manufacturers with MPP (4 vs 1): 67% price mark-up without MPP
Treatment uptake	Annual attrition rate before treatment catch-up in the counterfactual scenario	5%	10%	20%

Modelling of the impact of public-health licensing in the HCV space is more sensitive to assumptions due to difficult-to-predict country decisions to treat HCV cases or not (and the variability of treatment uptake from one year to the next), the absence of large international funders and procurement agencies focused on HCV, the differentiated use by countries of different clinical guidelines[‡‡‡‡], and the scarcity of epidemiological data. However, given that most MPP-licensed DAC sales have occurred in a limited number of countries so far (with sales in India, Kazakhstan, Myanmar, Pakistan, Rwanda, Uzbekistan and Vietnam representing 95% of MPP-licensed DAC sales so far), it was possible to sense-check modelling results in key countries to ensure that assumptions reflected the reality.

Uptake, health, and economic impact estimates

This section presents impact estimates for MPP's licences for DTG and DAC under "low", "central", and "high" scenarios. Figures are supplemented with tables reporting estimated impact by year.

Impact of the MPP licence for DTG

Figure 2 in the main paper presents three key metrics of impact arising from the DTG licence: uptake of MPP-licensed generic DTG products in LMICs, as well as deaths averted, and cost savings for low, central, and high scenarios. The underlying data for these graphs is shown in Tables S-12, S-13, and S-14, and Figure S-5, while Table S-15 shows the breakdown of costs saved from DTG displacing either first- or second-line HIV treatment in the counterfactual scenario, and Tables S-16 and S-17 respectively show deaths averted and costs saved across different country income categories. Figure S-6 shows the results disaggregated by World Bank geographic regions for low, central, and high scenarios. As of June 2020, quality-assured generic DTG-based products had been supplied to 106 countries, the breakout of which is presented in Table S-11.[§§§§]

[‡‡‡‡] The HCV model relies on WHO guidelines only (as done in the HIV model) for low-income countries, but also considers EASL guidance for middle-income countries (with equal weight to WHO guidance).[9,10,11] One exception is India (which accounts for 76% of sales, 84% of economic impact, and 87% of health impact), where national guidelines only are considered (i.e. not WHO's nor EASL's).

[§§§§] The 106 countries supplied with quality-assured generic DTG-based products as of June 2020 were: Afghanistan, Albania, Anguilla, Antigua and Barbuda, Argentina, Armenia, Azerbaijan (for paediatric use only), Bahamas, Barbados, Benin, Bermuda, Bolivia, Botswana, British Virgin Island, Burkina Faso, Burundi, Cabo Verde, Cambodia, Cameroon, Central African Republic, Chad, Chile, Comoros, Congo, Costa Rica, Côte d'Ivoire, CubaDemocratic Republic of the Congo, Dominica, Dominican Republic, Ecuador, Egypt, El Salvador, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Fiji, Gabon, Gambia, Georgia, Ghana, Grenada, Guatemala, Guinea, Guinea-Bissau, Guyana, Haiti, Honduras, India, Indonesia, Iran, Jamaica, Kenya, Kosovo, Kyrgyzstan, Lao, Lebanon, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Moldova, Mongolia, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, Oman, Pakistan, Panama, Papua New Guinea, Paraguay, Peru, Rwanda, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Senegal, Sierra Leone, South Africa, South Sudan, Sudan, Suriname, Syria, Tajikistan, Tanzania, Thailand, Timor-Leste, Togo, Turk and Caicos, Uganda, Ukraine, Uzbekistan, Venezuela, Viet Nam, Yemen, Zambia, and Zimbabwe.

Table S-11. Total country-level MPP-licensed DTG product actual sales as of June 2020. Data is shown as patient-years treated for 106 countries supplied with quality-assured generic DTG-based products as of June 2020.[§§§§]

Country	Total MPP-licensed DTG product sales, as of June 2020 (patient-years treated)
Afghanistan	144
Albania	98
Anguilla	6
Antigua and Barbuda	66
Argentina	22,457
Armenia	2,466
Azerbaijan (for paediatric use only)	732
Bahamas	642
Barbados	21
Benin	11,646
Bermuda	7
Bolivia	11,201
Botswana	480,558
British Virgin Islands	2
Burkina Faso	47,317
Burundi	42,238
Cambodia	41,320
Cameroon	125,063
Cape Verde	2,676
Central African Republic	18,423
Chad	5,442
Chile	2,759
Comoros	10
Congo	115,083
Congo, Dem. Rep.	296,476
Costa Rica	1,598
Cote d'Ivoire	79,332
Cuba	9,214
Dominica	6
Dominican Republic	17,369
Ecuador	1,443
Egypt	395
El Salvador	5,807
Equatorial Guinea	5,587
Eritrea	2,897
Swaziland	336,454
Ethiopia	681,667
Fiji	28
Gabon	12,799
Gambia	4,470
Georgia	1,793
Ghana	97,226
Grenada	33
Guatemala	11,458
Guinea	13,009
Guinea-Bissau	20,357
Guyana	2,972
Haiti	125,605
Honduras	862
India	166,899
Indonesia	12,329
Iran	8,455
Jamaica	1,875
Kenya	1,587,377
Kosovo	2
Kyrgyzstan	6,572
Laos	11,480
Lebanon	47
Lesotho	316,716
Liberia	15,853
Madagascar	2,089
Malawi	1,860,737
Mali	31,757
Mauritania	2,028
Mauritius	2,671
Moldova	9,255
Mongolia	205
Morocco	99
Mozambique	1,109,296
Myanmar	39,602
Namibia	126,530
Nepal	4,578
Nicaragua	445
Niger	6,335
Nigeria	707,689
Oman	14
Pakistan	9,646
Panama	7,538
Papua New Guinea	32,553
Paraguay	1,097
Peru	2,398
Rwanda	129,953
Saint Lucia	13
Saint Kitts and Nevis	6
Saint Vincent and the Grenadines	178
Senegal	6,605
Sierra Leone	18,445
South Africa	1,728,553
South Sudan	49,637
Sudan	36
Suriname	1,906
Syria	80
Tajikistan	2,737
Tanzania	1,442,000
Thailand	1,760
Timor-Leste	276
Togo	22,174
Turks & Caicos	10
Uganda	1,307,131
Ukraine	134,898
Uzbekistan	6,459
Venezuela	80,075
Vietnam	18,746
Yemen	2,083
Zambia	322,851
Zimbabwe	670,651
Redistribution centres (total) [‡‡]	2,186,055
• Reallocated	• 1,587,515
• Not reallocated	• 589,540
Total	**16,876,720**

Table S-12. - DTG uptake with and without MPP (central scenario). Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled. Figure S-5 shows annual and cumulative additional patient-years treated with DTG through the MPP licence (central scenario).

Year	**Uptake with MPP** (patient-years treated annually)	**Uptake without MPP** (patient-years treated annually)	**Difference** (additional patient-years treated annually with MPP)
2017	93,250	73,818	19,433
2018	2,816,628	2,730,282	86,346
2019	6,885,815	6,747,336	138,480
2020	10,426,761	10,084,453	342,308
2021	18,953,801	17,779,799	1,174,002
2022	21,779,956	20,238,903	1,541,053
2023	23,558,673	21,849,360	1,709,314
2024	24,935,169	23,197,199	1,737,970
2025	25,905,189	24,159,323	1,745,866
2026	26,713,539	24,943,585	1,769,954
2027	27,360,219	25,560,134	1,800,085
2028	27,926,064	26,463,087	1,462,977
2029	28,411,074	27,320,690	1,090,384
2030	28,815,249	28,204,950	610,299
2031	29,138,589	28,908,198	230,391
2032	29,381,094	29,346,225	34,869
Cumulative (2017-2032)	333,101,070	317,607,340	15,493,730

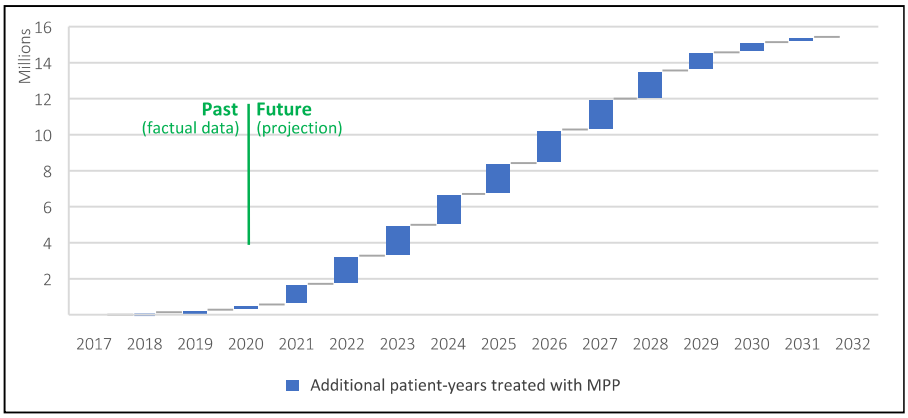

Figure S-5. Additional patient-years treated with DTG through the MPP licence (central scenario). The annual and cumulative differences in patients-years treated with DTG between the factual and counterfactual scenarios are displayed. The underlying data for this graph is shown in Table S-12 above, while Figure S-6 shows those results disaggregated by World Bank geographic regions for low, central, and high scenarios.

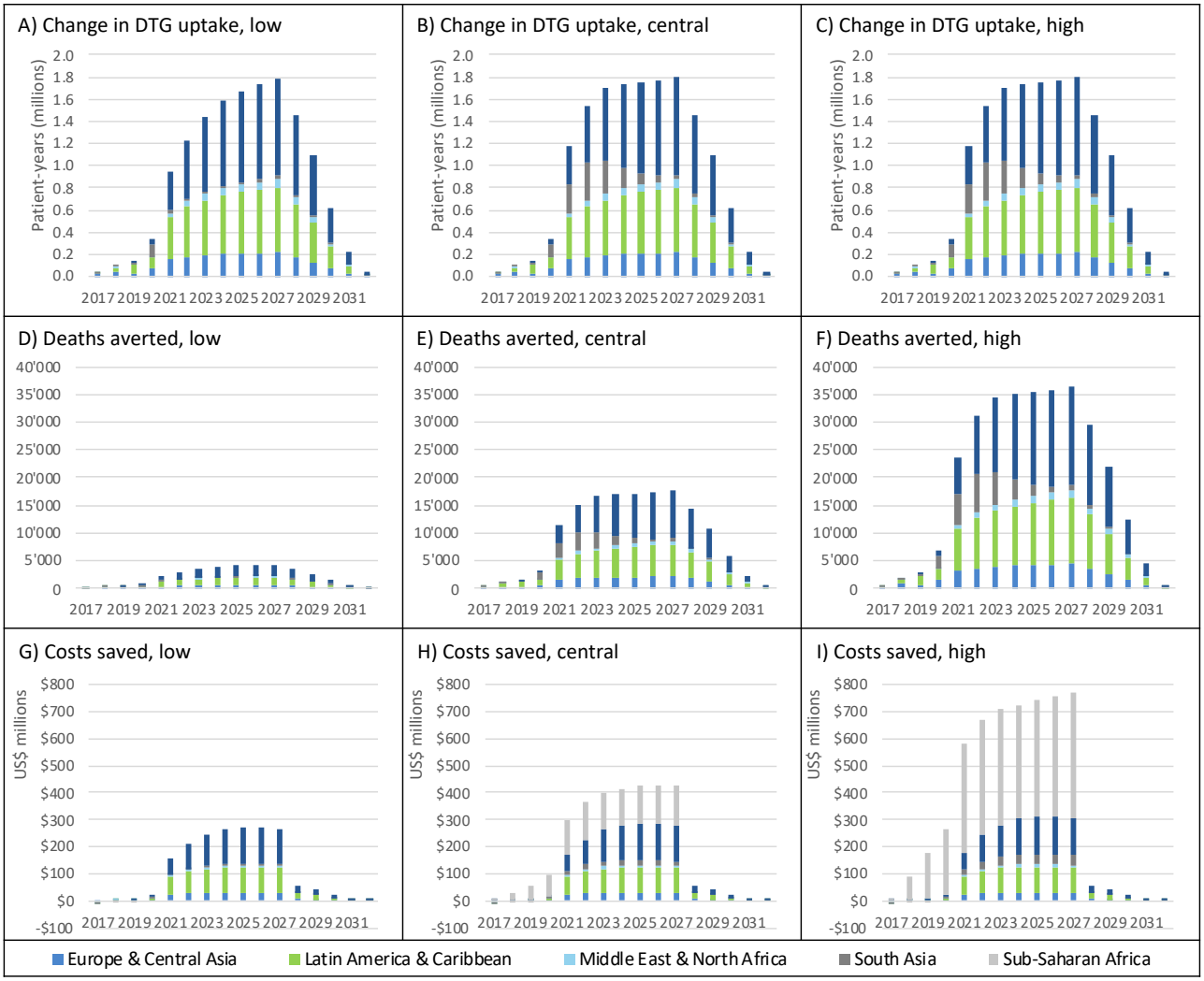

Figure S-6. Annual uptake (A, B, C), deaths averted (D, E, F), and costs saved (G, H, I) through the MPP licence for DTG disaggregated by World Bank geographic regions for low, central, and high scenarios.

Table S-13. Cumulative deaths averted from MPP licence for DTG: low, central, and high scenarios. Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative deaths averted		
	Low scenario	Central scenario	High scenario
2017	47	190	393
2018	254	1,037	2,137
2019	586	2,394	4,934
2020	1,408	5,748	11,849
2021	3,684	17,254	35,563
2022	6,616	32,356	66,693
2023	10,062	49,107	101,221
2024	13,862	66,139	136,328
2025	17,886	83,249	171,594
2026	22,067	100,594	207,347
2027	26,361	118,235	243,709
2028	29,863	132,572	273,261
2029	32,476	143,258	295,287
2030	33,939	149,239	307,615
2031	34,492	151,497	312,269
2032	34,575	151,839	312,973

Table S-14. Cumulative costs saved from MPP licence for DTG: low, central, and high scenarios. Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative costs saved (USD)		
	Low scenario	Central scenario	High scenario
2017	-545,036	121,887	1,539,098
2018	1,126,421	29,594,745	90,089,933
2019	4,157,472	87,478,998	264,537,240
2020	20,796,760	183,685,748	529,824,848
2021	176,966,282	479,953,157	1,108,067,612
2022	386,337,359	844,061,527	1,775,859,905
2023	629,672,458	1,243,207,838	2,484,263,898
2024	893,864,424	1,658,517,138	3,208,318,330
2025	1,162,978,638	2,081,526,330	3,952,763,059
2026	1,431,921,730	2,507,688,181	4,710,744,744
2027	1,698,336,435	2,934,520,693	5,477,577,871
2028	1,757,138,861	2,993,482,212	5,536,539,391
2029	1,801,417,117	3,037,820,480	5,580,877,658
2030	1,826,419,749	3,062,845,584	5,605,902,762
2031	1,835,859,177	3,072,293,326	5,615,350,505
2032	1,837,287,557	3,073,724,783	5,616,781,961

Table S-15. Cumulative costs saved from MPP licence for DTG: low, central, and high scenarios, split between impact from DTG displacement of first- and second-line HIV treatment. Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative costs saved (USD)					
	Low scenario		Central scenario		High scenario	
	First-line treatment displacement	Second-line treatment displacement	First-line treatment displacement	Second-line treatment displacement	First-line treatment displacement	Second-line treatment displacement
2017	-924,968	379,932	-258,045	379,932	1,159,166	379,932
2018	-991,498	2,117,919	27,476,826	2,117,919	87,972,014	2,117,919
2019	-1,002,442	5,159,914	82,319,084	5,159,914	259,377,326	5,159,914
2020	8,410,201	12,386,558	171,299,189	12,386,558	517,438,289	12,386,558
2021	142,299,521	34,666,761	439,982,305	39,970,852	1,068,096,760	39,970,852
2022	320,278,253	66,059,106	764,503,673	79,557,854	1,696,302,051	79,557,854
2023	526,415,757	103,256,701	1,119,354,688	123,853,150	2,360,410,748	123,853,150
2024	749,748,068	144,116,356	1,489,824,973	168,692,165	3,039,626,166	168,692,165
2025	975,699,896	187,278,741	1,867,888,582	213,637,748	3,739,125,311	213,637,748
2026	1,199,876,041	232,045,689	2,248,563,500	259,124,681	4,451,620,063	259,124,681
2027	1,420,307,454	278,028,981	2,629,134,726	305,385,967	5,172,191,905	305,385,967
2028	1,441,616,814	315,522,047	2,650,498,456	342,983,757	5,193,555,634	342,983,757
2029	1,457,911,814	343,505,302	2,666,814,387	371,006,093	5,209,871,566	371,006,093
2030	1,467,244,545	359,175,204	2,676,155,103	386,690,481	5,219,212,281	386,690,481
2031	1,470,768,406	365,090,770	2,679,681,919	392,611,408	5,222,739,097	392,611,408
2032	1,471,302,650	365,984,907	2,680,217,256	393,507,527	5,223,274,434	393,507,527

Table S-16. Cumulative deaths averted from MPP licence for DTG across country categories (central scenario). Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative deaths averted – Central scenario			
	Low-income countries	Lower-middle-income countries	Upper-middle-income countries	High-income countries
2017	0	189	2	0
2018	0	671	363	2
2019	0	1,284	990	120
2020	0	3,768	1,787	194
2021	2	9,748	6,753	750
2022	5	17,308	13,626	1,417
2023	7	24,991	21,935	2,174
2024	10	31,931	31,201	2,997
2025	13	38,325	41,046	3,865
2026	16	44,525	51,287	4,766
2027	18	50,714	61,812	5,691
2028	20	55,712	70,396	6,445
2029	21	59,425	76,804	7,008
2030	21	61,498	80,397	7,322
2031	21	62,271	81,765	7,440
2032	21	62,363	82,000	7,454

Table S-17. Cumulative costs saved from MPP licence for DTG across country categories (central scenario). Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative costs saved (USD) – Central scenario			
	Low-income countries	Lower-middle-income countries	Upper-middle-income countries	High-income countries
2017	13,745	-485,493	593,753	-119
2018	10,622,906	10,443,850	8,520,714	7,275
2019	48,366,036	20,102,891	18,550,038	460,032
2020	88,237,507	57,668,452	37,003,375	776,415
2021	125,347,276	173,063,088	170,430,698	11,112,095
2022	164,051,203	311,345,424	344,812,990	23,851,911
2023	202,748,414	458,081,013	544,345,775	38,032,636
2024	240,870,305	606,352,298	758,116,564	53,177,971
2025	280,279,203	755,735,284	976,993,692	68,518,152
2026	320,834,048	905,881,170	1,197,159,156	83,813,807
2027	362,338,523	1,056,532,394	1,416,705,489	98,944,287
2028	362,346,045	1,076,568,140	1,452,452,083	102,115,945
2029	362,350,293	1,091,611,198	1,479,358,257	104,500,732
2030	362,351,878	1,100,091,717	1,494,557,992	105,843,997
2031	362,352,065	1,103,252,625	1,500,343,356	106,345,281
2032	362,352,065	1,103,633,042	1,501,334,592	106,405,084

Impact of the MPP licence for DAC

Figure 3 in the main paper presents three key metrics of impact arising from the DAC licence: uptake of MPP-licensed generic DAC products in LMICs, as well as deaths averted, and cost savings for low, central, and high scenarios. The underlying data for these graphs is shown in Tables S-19, S-20, and S-21, and Figure S-7. Figure S-8 shows those results disaggregated by World Bank geographic regions for low, central, and high scenarios. As of June 2020, quality-assured generic DAC-based products had been supplied to 30 countries, the breakout of which is presented in Table S-18.[*****]

Table S-18. Total country-level MPP-licensed DAC product actual sales as of June 2020. Data is shown as 12-week treatment courses for 30 countries supplied with quality-assured generic DAC-based products as of June 2020.[*****]

Country	Total MPP-licensed DAC product sales, as of June 2020 (12-week treatment courses)
Armenia	781
Azerbaijan	1,564
Bangladesh	494
Bolivia	40
Cambodia	2,953
Cameroon	83
Congo	67
Ethiopia	24
India	753,786
Indonesia	5,545
Kazakhstan	30,266
Kyrgyzstan	822
Laos	100
Malaysia	6,253
Mauritius	2
Mongolia	196
Myanmar	16,433
Nepal	557
Nigeria	1,400
Pakistan	70,431
Rwanda	43,525
South Africa	27
Sri Lanka	37
Timor-Leste	30
Turkmenistan	750
Uganda	81
Ukraine	20,150
Uzbekistan	12,633
Vietnam	10,207
Zimbabwe	16
Redistribution centres (total) ‡‡	18,044
• Reallocated	• 0
• Not reallocated	• 18,044
Total	**997,297**

Table S-19. Annual DAC uptake with and without MPP (central scenario). Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled. Figure S-7 shows annual and cumulative additional patient-years treated with DAC through the MPP licence (central scenario).

Year	Uptake with MPP (patients treated annually)	Uptake without MPP (patients treated annually)	Difference (additional patients treated annually with MPP)
2015	0	0	0
2016	191,225	23,708	167,516
2017	214,734	141,403	73,331
2018	147,979	104,850	43,129
2019	183,534	128,986	54,548
2020	206,048	140,729	65,319
2021	240,340	197,884	42,456
2022	257,406	263,856	-6,450
2023	254,372	260,174	-5,802
2024	258,229	264,031	-5,802
2025	260,353	260,353	0
2026	262,469	262,469	0
Cumulative (2015-2026)	2,476,689	2,048,445	428,244

[*****] The 30 countries supplied with quality-assured generic DAC-based products as of June 2020 were: Armenia, Azerbaijan, Bangladesh, Bolivia, Cambodia, Cameroon, Congo, Ethiopia, India, Indonesia, Kazakhstan, Kyrgyzstan, Lao, Malaysia, Mauritius, Mongolia, Myanmar, Nepal, Nigeria, Pakistan, Rwanda, South Africa, Sri Lanka, Timor-Leste, Turkmenistan, Uganda, Ukraine, Uzbekistan, Viet Nam, and Zimbabwe.

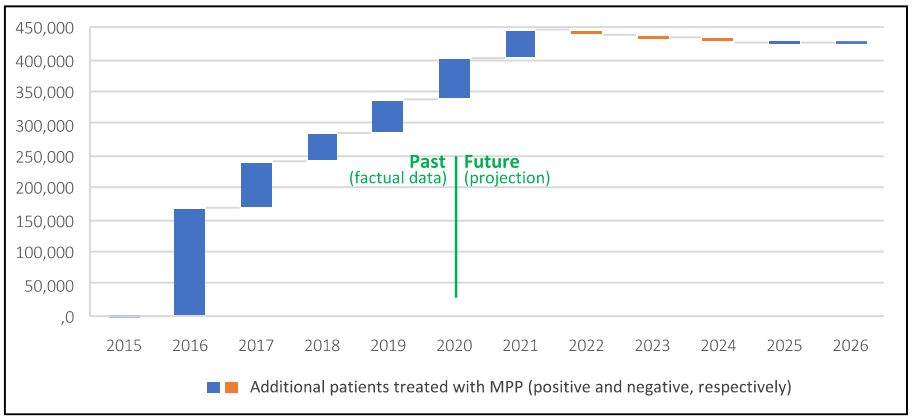

Figure S-7. Additional patients treated with DAC through the MPP licence (central scenario). The annual and cumulative differences in patients treated with DAC between the factual and counterfactual scenarios are displayed. There is some limited additional predicted DAC uptake in patients treated in the counterfactual scenario (compared to the factual scenario) for the years 2022-2024 due to the imposed treatment catch-up mechanism by which countries may increase treatment of accumulated diagnosed cases (i.e. the pool of diagnosed people that have not yet been treated) once drug prices become sufficiently low. The underlying data for this graph is shown in Table S-19 above, while Figure S-8 shows those results disaggregated by World Bank geographic regions for low, central, and high scenarios.

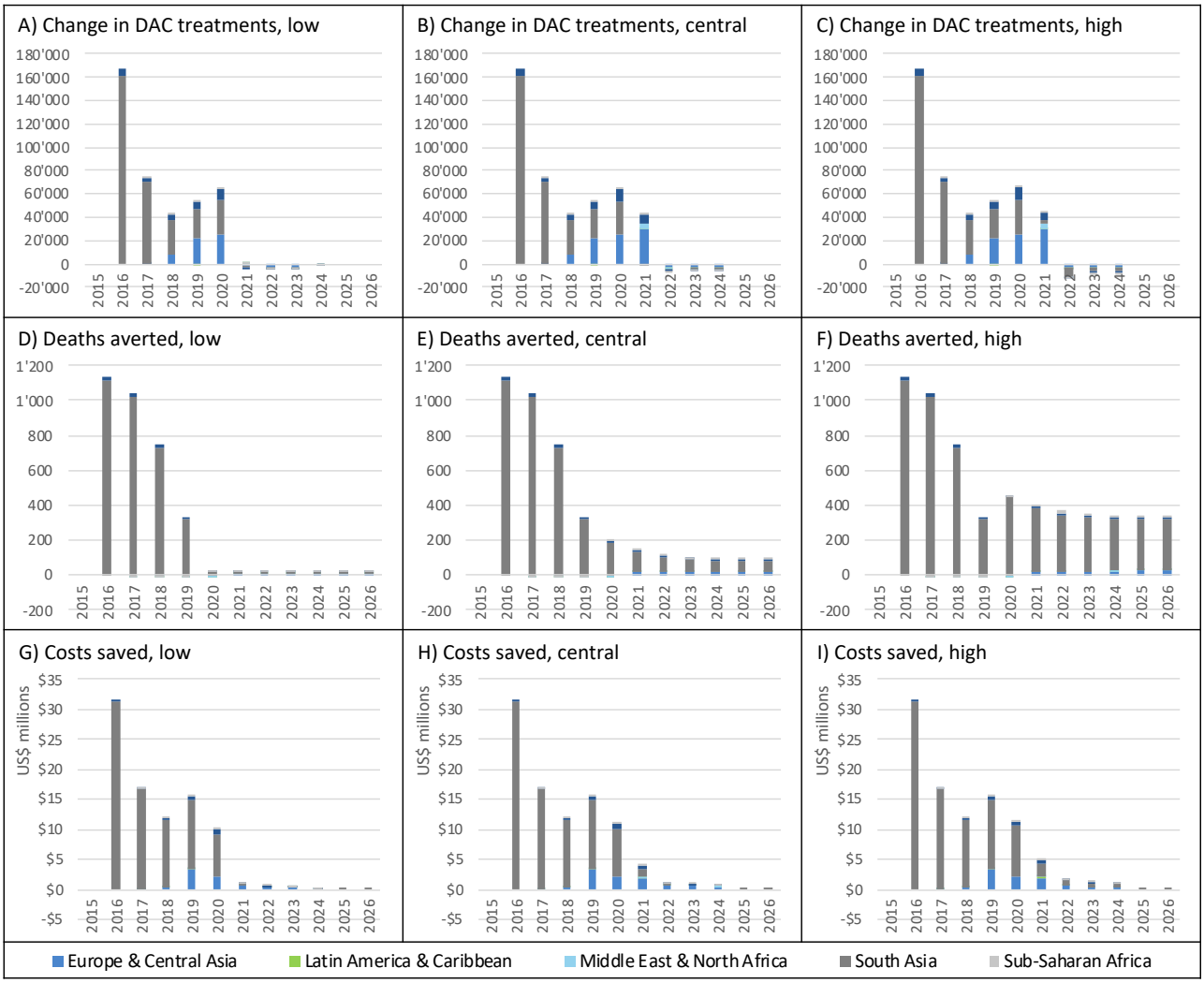

Figure S-8. Annual uptake (A, B, C), deaths averted (D, E, F), and costs saved (G, H, I) through the MPP licence for DAC disaggregated by World Bank geographic regions for low, central, and high scenarios.

Table S-20. Cumulative deaths averted from MPP licence for DAC: low, central, and high scenarios. Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative deaths averted		
	Low scenario	Central scenario	High scenario
2015	0	0	0
2016	13	1,139	1,139
2017	42	2,173	2,228
2018	79	2,915	3,141
2019	106	3,240	3,716
2020	123	3,431	4,169
2021	140	3,584	4,578
2022	157	3,702	4,949
2023	173	3,802	5,301
2024	190	3,891	5,642
2025	207	3,980	5,982
2026	225	4,070	6,323

Table S-21. Cumulative costs saved from MPP licence for DAC: low, central, and high scenarios. Numbers until 2019 (in blue) are based on actual sales data, which were available until Q2-2020. Missing data points for 2020 (i.e. Q3-2020 and Q4-2020, in green) are based on a rolling average over the preceding four quarters (i.e. from Q3-2019 until Q2-2020), while subsequent data points (for 2021 onwards, in yellow) are modelled.

Year	Cumulative costs saved (USD)		
	Low scenario	Central scenario	High scenario
2015	0	0	0
2016	2,464,145	53,688,707	53,688,707
2017	5,473,125	67,190,611	68,308,698
2018	7,686,701	76,083,580	79,282,634
2019	18,639,630	89,961,032	101,130,041
2020	29,020,052	101,353,109	113,271,613
2021	29,857,621	106,233,268	119,147,253
2022	30,108,832	106,739,444	120,077,859
2023	30,346,024	107,172,025	120,694,119
2024	30,370,104	107,582,977	121,279,565
2025	30,373,650	107,588,138	121,281,828
2026	30,376,850	107,592,551	121,283,548

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