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Supplementary materials to the "The HCV investment case in Morocco: transforming political commitment to action"

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Appendix S1. The disease model

For this investment case analysis, we relied on the Center for Disease Analysis (CDA) HCV disease progression model, which has been peer-reviewed and used in more than 100 countries to support the design of national strategies and inform policy decisions [1].

CDA has been working with the Moroccan Ministry of Health since 2016. The Ministry of Health first used the approximations of treatment targets from the CDA model in developing Morocco's national strategic plan. In collaboration with CDA, the original model inputs were refined and the model was adapted to meet the needs of the investment case analysis. The Ministry of Health was informed of this collaboration with CDA.

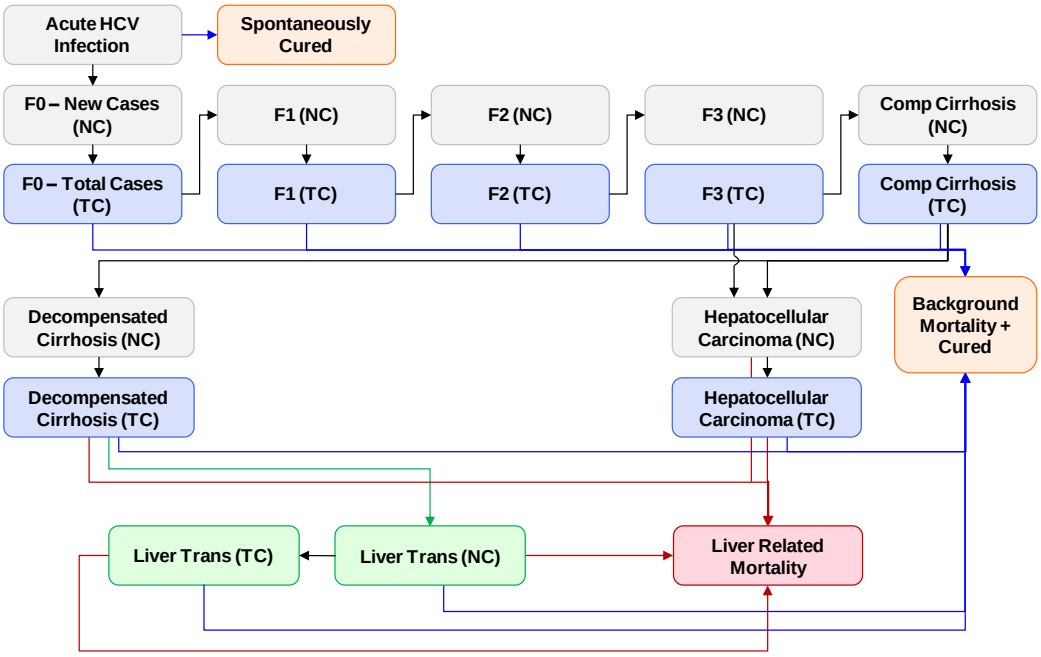
The full details of the CDA model are documented in "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9." Below the pages from the original supplementary materials are cited for key model details.

The Markov model

For more information on the Markov model, see pages 8-9 of the supplementary materials from "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9" for full specifications of the Markov model.

Figure S1 below is copied from p. 9 of the supplementary materials for reference.

Figure S1. The flow of the HCV disease progression model



Source: "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9."

Model equations

See pages 9-10 for the model equations in the supplementary materials of "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9."

Calculating incidence

For information on how historical incidence was estimated, see page 13 in the supplementary materials of "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9."

Future incidence was an input to this model [2]. It was assumed new infections would remain constant in the baseline scenario at about 5,500 new cases per year. See page 13 in the supplementary materials from "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9." For scale-up scenarios, incidence declined as a function of specific events tied to input years. Previous work has demonstrated incidence declines as a result of treatment as prevention [2]. The model assumed incidence declines as the number of untreated chronic infections declines. In the rapid scenario, incidence dropped by 90% (to about 500 cases) by 2026 while the Gradual scenario achieved the same 90% reduction in 2029.

Progression rates

For the progression rates used in the model, see pages 10-12 in the supplementary materials from "The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2016; published online Dec 15. http://dx.doi.org/10.1016/ S2468-1253(16)30181-9."

Parameters

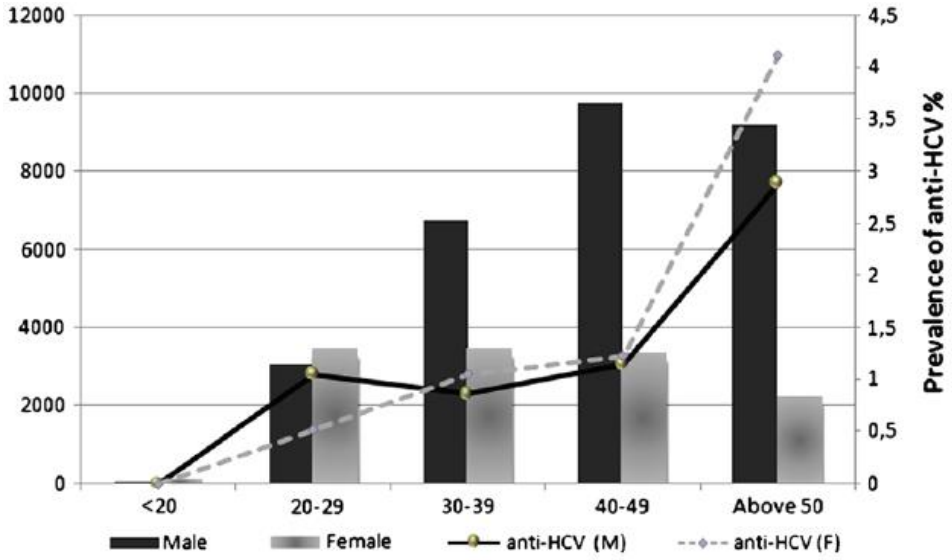
The main model parameters of interest included: viremic HCV prevalence, genotype distribution, and baseline annual number of diagnosed and treated patients. These parameters were originally collected by CDA during visits to Morocco in 2016 [3]. These parameters were reviewed at the beginning of the investment case project by CDA and all authors and then again validated with the Ministry of Health.

These key parameter inputs are listed below in **Table S1**.

Table S1. Key model parameters

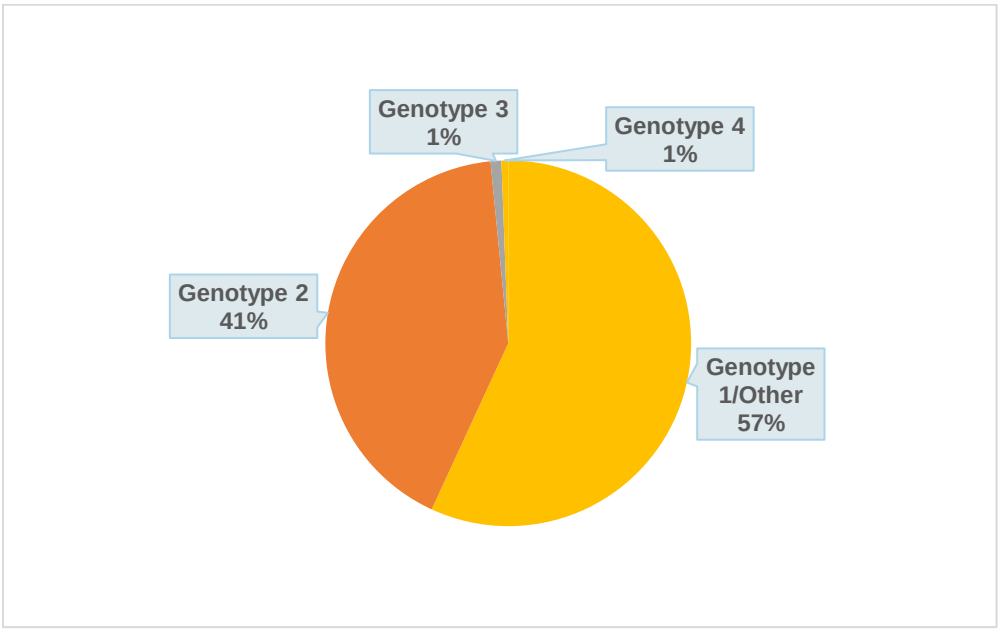
Parameters	Estimation
Anti-HCV prevalence	1.2% (2015) 413, 000 anti-HVC positive individuals (2015)
Viremic prevalence	0.9% (2015) 309 000 RNA positive individuals (2015)
New infections annually	5,600 (2016)
Age and sex distribution	See **Figure S2**. [4]
Genotype distribution	See **Figure S3**. [5]

Figure S2. Anti-HCV age and sex distribution in Morocco



Source: Baha W, Foullous A, Dersi N, They-they TP, El alaoui K, Nourichafi N, et al. Prevalence and risk factors of hepatitis B and C virus infections among the general population and blood donors in Morocco. BMC Public Health. 2013; 13(50): https://doi.org/10.1186/1471-2458-13-50.

Figure S3. HCV genotype distribution in Morocco



Source: Bennani, A, Baha W, Dersi N, Ennaji MM, Lazaar F, El Malki A, et al. Hepatitis B & C epidemiology in Morocco. BMC Proceedings. 2011; 5(Suppl 1), P20. http://doi.org/10.1186/1753-6561-5-S1-P20

Appendix S2

Status quo

During the 2016 visit to Casablanca by CDA, a three-day conference was hosted titled the "Strategic and Technical Consultation on Viral Hepatitis in the Eastern Mediterranean Region" in Casablanca. At this conference, Ministry of Health representatives presented data that suggested as of 2016, 1,500 patients were being treated with DAAs annually and 3,090 were being diagnosed annually. In total, experts stated that 30,940 individuals had been diagnosed to date [3].

For the baseline scenario, which represented the counterfactual to a scaled up government response, we assumed that a constant 1,500 patients would continue to be treated annually and 3,090 would be diagnosed annually.

Treatment scale-up scenarios

The two treatment scenarios were designed to capture the spectrum of the policy options Morocco could pursue for its national hepatitis program. The scenarios were developed in an iterative process with modeling analysts at the Center for Disease Analysis and the local stakeholders in Morocco.

The annual treatment targets were adapted from previous elimination scenarios modeled for Morocco.

The rapid scenario for elimination by 2030 was designed by first taking into account our understanding of the five-year national strategic plan targets for 2018-2022. Over the iterative process, the rapid scenario shifted away from an exact representation of the national strategy and instead was molded to be a representation of an aggressive approach to scale-up in the early years that then tails off in intensity prior to 2030.

The gradual scenario for elimination by 2030 was developed conceptually as an alternative to the rapid scenario with less ambitious targets in the early years but then increases intensity in the last years before 2030. The goal when designing this scenario was to put as few individuals on treatment as possible in the first five years of the program but still reach elimination by 2030. This delay was intended to relieve both financial and operational pressure on the Moroccan health system in the early years. Below **Table S2** shows the number of patients treated each year under these three scenarios.

Table S2. Number of patients treated annually under the three scenarios

	Status quo	Rapid scenario	Gradual scenario
2018	1,500	8,000	2,000
2019	1,500	14,750	2,750
2020	1,500	21,630	3,500
2021	1,500	28,020	5,000
2022	1,500	34,410	6,500
2023	1,500	28,933	10,250
2024	1,500	23,455	14,000
2025	1,500	17,978	18,140
2026	1,500	12,500	22,280
2027	1,500	12,500	26,420
2028	1,500	12,500	30,560
2029	1,500	12,500	34,700
2030	1,500	12,500	34,700

2031	1,500	12,500	34,700
2032	1,500	12,500	34,700
2033	1,500	12,500	5,365
2034	1,500	12,500	751
2035	1,500	12,500	483
2036	1,500	1,761	457
2037	1,500	547	453
2038	1,500	469	451
2039	1,500	462	450
2040	1,500	462	447

Patient allocation

In each scenario, all patients, regardless of disease state, had the same probability of filling a treatment spot.

Appendix S3. Costing

In all scenarios, three costing categories were included as part of this analysis: 1) DAA program costs 2) Costs of managing advanced liver disease and 3) Monetary valuation of DALYs. The original CDA disease Markov model is coupled with a costing module that included the first two costing components of DAA program costs and costs of managing advanced liver disease. The computation for monetization of the DALYs was conducted separately by the authors. Therefore, the net monetary benefit assessed included the net financial costs (those that would appear in the financial accounts) and also the monetary value of the health benefits (which would not be reflected in these accounts).

1) Program costs

The following tables key assumptions for the costing.

Table S3. Assumptions for diagnosis and treatment protocols and unit costs.

		Number of units per individual				Unit	Price, MAD (USD)
Screening	**Anti-HVC**	1				Per test	50 (5)
Diagnosis	**Viral load (confirmatory test)**	4				Per test	360 (37)
	Genotyping	1				Per test	520 (54)
	Fibroscan	1				Per test	420 (43)
Treatment	**DAAs**		**G 1/4/5/6**	**G2**	**G3**	Per treatment	13,500 (1,398)
		Non-cirrhotic	1	1	2		
		Cirrhotic	2	1	2		

Total costs in the model were calculated by multiplying the unit costs by quantities according to the formula in **Table S4**. All quantities were outputs from the CDA model. Costs are shown in MAD and USD, using an exchange rate of MAD 9.66 = USD 1.

Table S4. Total cost calculation approach for screening and treatment inputs

Cost components of the program	Price, MAD (USD)$_t$	Quantity$_t$	Total cost
Screening (Anti-HCV test)	50 (5)	Total number screened	
Diagnostics (Viral load testing, genotyping, and fibroscan)	1,300 (135)	Number newly diagnosed	
Treatment			
G1/G4/G5/G6 non-cirrhotic	13,500 (1,398)	Number treated $_t$ X % genotype X % cirrhotic	**= Price X quantity**
G1/G4/G5/G6 cirrhotic	27,000 (2,795)	Nombre de traités $_t$ X % genotype X (1-% cirrhotic)	
G2 all	13,500 (1,398)	Number treated $_t$ X % genotype	
G3 all	27,000 (2,795)	Number treated$_t$ X % genotype	

In addition, for each scenario program costs due to screening and treatment were supplemented by the costs of other supporting activities required to launch and sustain a comprehensive program. These supporting activity costs were extracted from Morocco's five-year national strategy (see **Table S5** below) and then extrapolated through 2040 based on the authors' judgement. These costs were not originally accounted for within the costing module part of the CDA model, but the model was adapted to include an additional module for the supporting activity costs. These supporting costs were assumed to be fixed and held constant across scenarios.

Table S5. Supporting activity costs in Morocco's five-year national strategy

	2019	2020	2021	2022	2023	Total, MAD millions (USD millions)
Sensibilization	0.61 (0.06)	0.38 (0.04)	0.38 (0.04)	0.38 (0.04)	0.38 (0.04)	2.14 (0.22)
Prevention	0.64 (0.07)	0.39 (0.04)	0.39 (0.04)	0.39 (0.04)	0.39 (0.04)	2.19 (0.23)
Screening support	0.48 (0.05)	0.34 (0.04)	0.34 (0.04)	0.34 (0.04)	0.34 (0.04)	1.82 (0.19)
Strategic information	4.27 (0.44)	0.42 (0.04)	0.43 (0.04)	0.38 (0.04)	0.68 (0.07)	6.18 (0.64)
Laboratory strengthening	10.36 (1.07)	10.32 (1.07)	0.32 (0.03)	0.32 (0.03)	0.30 (0.03)	21.62 (2.24)
Total (MAD millions)	**16.37 (1.69)**	**11.84 (1.23)**	**1.86 (0.19)**	**1.80 (0.19)**	**2.08 (0.22)**	**33.95 (3.51)**

2) Costs of managing advanced liver disease

The costs of managing (or treating) advanced liver disease were not considered a part of the DAA program but rather represent the costs of treating hepatitis complications in the absence of DAAs. These are costs the health system would absorb related to HCV in the absence of DAA treatment. These advanced disease management costs were calculated to estimate the cost offset, or cost savings, to the DAA program costs described above in (1). The greater degree to which HCV patients are treated with DAAs, the more the burden of advanced liver disease is diminished in future years, and the greater the savings in advanced liver disease costs to the Moroccan health system are observed.

Assumptions about the annual costs of treating the sequelae were collected by CDA during a panel of experts in 2016 [3]. See **Table S6** for these unit costs. The frequency of the sequelae were a CDA model output and derived from the disease transition probabilities. It was assumed 100% of advanced liver disease cases would receive treatment or care.

Table S6. Annual costs of managing advanced liver disease

	Average annual cost per person diagnosed	
Disease state	**Public cost, MAD (USD)**	**Private cost, MAD (USD)**
Annual costs of monitoring (F0-F3)	800 (83)	1,700 (176)
Compensated cirrhosis	1,700 (176)	3,400 (352)
Decompensated cirrhosis	5,700 (590)	8,200 (849)
HCC	23,700 (2,453)	28,350 (2,935)
Liver transplant	470,000 (48,654)	-
Monitoring post-liver transplant	42,000 (4,348)	-

3) Monetization of DALYs

Calculating DALYs

To translate the health benefits into a common unit, DALYs were calculated based on the epidemiological output or annual prevalence of cases of liver disease and mortality. Disability weights were applied to cases diagnosed for F0-F3 and for all prevalent cases in F4 and other advanced disease stages. The disability weights used in the calculation are found in **Table S7**.

Table S7. Disability Weights

Disease state	Segment	Disability weight	Source
F0	Diagnostic	0.075	[6]
F1	Diagnostic	0.075	[6]
F2	Diagnostic	0.075	[6]
F3	Diagnostic	0.075	[6]
F4	Prevalent	0.033	[6]
Decomp Cirrhosis	Prevalent	0.809	[7]
HCC	Prevalent	0.809	[7]
Liver transplant	Prevalent	0.330	Assumed the same disability weight as F4

These values were inputs from the CDA model.

Monetization

Once the DALYs were calculated, the authors monetized the DALYs assuming 1 DALY = 1 X GDP. GDP per capita was assumed to be USD 3,196 or 31,000 Moroccan Dirhams [8]. It is important to note that this valuation assumes that Moroccans are willing to pay for health programs that produce profits up to an amount of 31,000 Dirhams per DALY averted. Monetization of DALYs was only used in the return on investment or "break-even analysis" due to the sensitivity of this interpretation.

Appendix S4. Cost-effectiveness analysis

Incremental cost-effectiveness ratios were calculated. Total costs accounted for the sum of program costs and costs of treating advanced liver disease from 2018-2040. Incremental health benefits were measured in DALYs for 2018-2050. Benefits were calculated until 2050 (and costs only until 2040) in order to capture the life years gained in people treated during the later years of the program. Some might be concerned that some costs were omitted in years where benefits were counted. The authors decided these costs would be negligible given this is so far in the future when the number of cases treated per year would have declined significantly, and the effects of cost discounting would result in these minimal costs being reduced even further in net present value terms.

Incremental cost-effectiveness analysis was used so that the incremental costs represent the additional costs compared to the next scenario. Costs were discounted at 3% for this analysis. Health benefits were not discounted.

$$\text{ICER} = \frac{\text{Incremental total costs 2018-2040}}{\text{Incremental health benefits 2018-2050}}$$

Appendix S5.. Budget impact analyses

The complete list of analyses conducted and the sources of information are listed in **Table S8.**

Table S8. List of budget impact analyses

	Analysis	*Sources*
Assessment of health financing context	• Assessment of macroeconomic • context and growth prospects • What health expenditure is relative to GDP and per capita health expenditure • Public health expenditure / general government expenditure	• [9-13]
Impact of HCV program costs on health spending	• Annual program cost as% of total health expenditure • Share of the annual cost of the MOH program as a% of the MOH budget	• [9, 14] • Investment case modeling results
Impact of DAA costs on drug budget	• HCV drug costs under MOH as% of national health program budget in MoH budget	• [14] • Investment case modeling results

Supplementary References

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