Web Appendix

Web Appendix 1: Accession dates and public health spending for EU countries

Web Appendix 2: Methodological details of TB mathematical models

Web Appendix 1: Accession dates and public health spending for EU countries

		Public health spending		
Country	Accession date	Average	Min	Max
Austria	1995	52.11	37.08	66.64
Belgium	1952	-	-	-
Bulgaria	2007	13.57	5.97	27.69
Cyprus	2004	x	x	x
Czech Republic	2004	92.17	9.23	315.86
Denmark	1973	26.04	12.89	40.62
Estonia	2004	3.79	1.15	7.43
Finland	1995	6.74	4.03	12.01
France	1952	21.67	11.58	37.76
Germany	1952	13.35	10.35	22.55
Greece	1981	-	-	-
Hungary	2004	30.61	17.66	47.5
Ireland	1973	43.34	3.29	98.93
Italy	1952	10.62	6.64	13.38
Latvia	2004	4.46	4.02	14.54
Lithuania	2004	8.91	1.27	12.96
Luxembourg	1952	x	x	x
Malta	2004	x	x	x
Netherlands	1952	48.25	40.22	59.13
Poland	2004	21.51	9.95	51.38
Portugal	1986	4.44	1.71	8.61
Romania	2007	-	-	-
Slovakia	2004	-	-	-
Slovenia	2004	35.5	26.57	38.26
Spain	1986	22.42	17.12	33.19
Sweden	1995	50.14	0.17	70.12
UK	1973	2.86	0.35	7.51

Notes: Source: EuroStat.
- indicates missing data
x indicates exclude from analysis due to small population size.

Web Appendix 2: Methodological details of the mathematical models

The mathematical model used in this assessment was a dynamic, stochastic state-space mathematical model of TB pathogenesis based on extant commonly-used TB model structures [1–6]. The model is depicted in **Supplementary Figure 1**, which shows the key TB states simulated: susceptibility to TB, recent latent infection, remote latent infection, active smear-positive TB, active smear-negative or extrapulmonary TB, and recent recovery from TB. The model's parameters are further defined in **Supplementary Table 1**, which additionally provides the key data sources and parameter values used in the simulations.

Supplementary Table 1: Model parameters and data sources. All rates are in units of 1/yr.

Parameter	*Mean (95% CI)*	*Source*
b, Fertility rate per capita	0.027 (0.022-0.037), varied by country	[44]: fertility table
μ, Non-TB mortality rate per capita	0.013 (0.012-0.014), varied by country	[44]: mortality table
ψ, proportion of new active TB cases that become smear-positive	0.51 (0.20-0.65)	[9, 45, 46]
ϕ, relative infectiousness of smear-negative to smear-positive cases	0.22 (0.16-0.32)	[47]
ε, proportion smear-negative or extrapulmonary cases that are smear-negative	0.79 (0.31-1), varied by country	[9]: country tables
x, degree of susceptibility to re-infection among individuals having partial immunity from prior infection	0.5 (0.2-0.6)	[30, 48-50]
p_e, rate of rapid progression from recent infection	0.07 (0.03-0.2)	[30, 50]
p_l, rate of slow reactivation from long-term latency	0.00058 (0.00038-0.00089)	[51]
σ_e, rate of stabilization from recent infection to long-term latency per yr	0.5 (0.2-0.6)	[30, 50]
σ_r, rate of stabilization from recent treatment recovery to long-term latency	0.2 (0.1-0.5)	[30, 50]
μ_T, mortality rate from sputum positive TB	0.23 (0.20-0.40)	[30, 52]
μ_N, mortality rate from sputum-negative/ extrapulmonary TB	0.07 (0.05-0.12)	[30, 52]
ω_T, natural cure rate from sputum positive TB	0.10 (0-0.20)	[30, 52]
ω_N, natural cure rate from sputum negative/extrapulmonary TB	0.27 (0-0.54)	[30, 52]
p_r, rate of relapse	0.024 (0-0.05)	[30]
β, contact rate	10 (3-12), varied by country	calibrated to annual TB incidence, prevalence and mortality, 1990-2012, for each country [9]
θ, speed of diagnosis	1.8 (0.04-12.5), varied by country	
d, proportion of cases detected	0.82 (0.60-1), varied by country and year	data by country and year taken from country tables in [9]
κ, proportion of cases successfully treated	0.70 (0.28-1), varied by country and year	

The model can be described through a series of ordinarily differential equations, as follows.

Susceptible individuals who are not infected with tuberculosis (*S*) enter the model through birth (rate *b* applied to the overall population *P*) and leave the susceptible state through either infection (rate λ) or non-TB-related death (rate μ):

$$\frac{dS}{dt} = bP - (\lambda + \mu)S$$

Individuals with recent latent infection (*E*) enter this state from the state of susceptibility (*S*) through infection (rate λ) and from the states of remote latent infection (*L*) or recent recovery from TB (*R*) through re-infection (rate λ conditioned on the degree of susceptibility *x* to re-infection among those individuals having partial immunity from prior infection). Individuals with recent latent infection (*E*) exit this state through progression to active TB (rate p_e), regression to long-term latency (rate σ_e) or non-TB-related death (rate μ):

$$\frac{dE}{dt} = \lambda[S + x(L + R)] - (p_e + \sigma_e + \mu)E$$

Individuals with remote latent infection (*L*) enter this state through regression from recent latent infection (rate σ_e) or regression from the recently recovered group (rate σ_r from *R*), and exit this state through progression to active TB (rate p_l), reinfection (rate λ conditioned on the degree of susceptibility *x*) or non-TB-related death (rate μ):

$$\frac{dL}{dt} = \sigma_e E + \sigma_r R - (p_l + \lambda x + \mu)L$$

Individuals with active smear-positive TB (*T*) enter this state through progression from latency (rate p_e from recent latent infection *E* and rate rate p_l from remote latent infection *L*, applied to the proportion ψ that become smear-positive), relapse from recent treatment (rate p_r from *R*, applied to the proportion ψ that become smear-positive), and exit this state through case detection and treatment (rate θ describing the delay between symptoms and diagnosis, applied to the proportion of cases detected *d* and treatment success rate κ), through natural regression (rate ω_T), through TB-related death (rate μ_T), or through non-TB-related death (rate μ):

$$\frac{dT}{dt} = \psi(p_e E + p_l L + p_r R) - (\theta d\kappa + \omega_T + \mu + \mu_T)T$$

Individuals with active smear-negative or extrapulmonary TB (*N*) enter this state through progression from latency (rate p_e from recent latent infection *E* and rate rate p_l from remote latent infection *L*, applied to the proportion 1-ψ that become smear-negative or extrapulmonary), relapse from recent treatment (rate p_r from *R*, applied to the proportion 1-ψ that become smear-negative or extrapulmonary), and exit this state through case detection and treatment (rate θ describing the delay between symptoms and diagnosis, applied to the proportion of cases detected *d* and treatment success rate κ), through natural regression (rate ω_N), through TB-related death (rate μ_N), or through non-TB-related death (rate μ):

$$\frac{dN}{dt} = (1 - \psi)(p_e E + p_l L + p_r R) - (\theta d\kappa + \omega_N + \mu + \mu_N)N$$

Individuals experiencing recent recovery from TB (R) enter this state through detection and treatment (rate θ describing the delay between symptoms and diagnosis, applied to the proportion of cases detected d and treatment success rate κ), or through natural regression (rate ω_N), and exit through relapse (rate p_r), regression to latency (rate σ_r), reinfection (rate λ conditioned on the degree of susceptibility x) or non-TB-related death (rate μ):

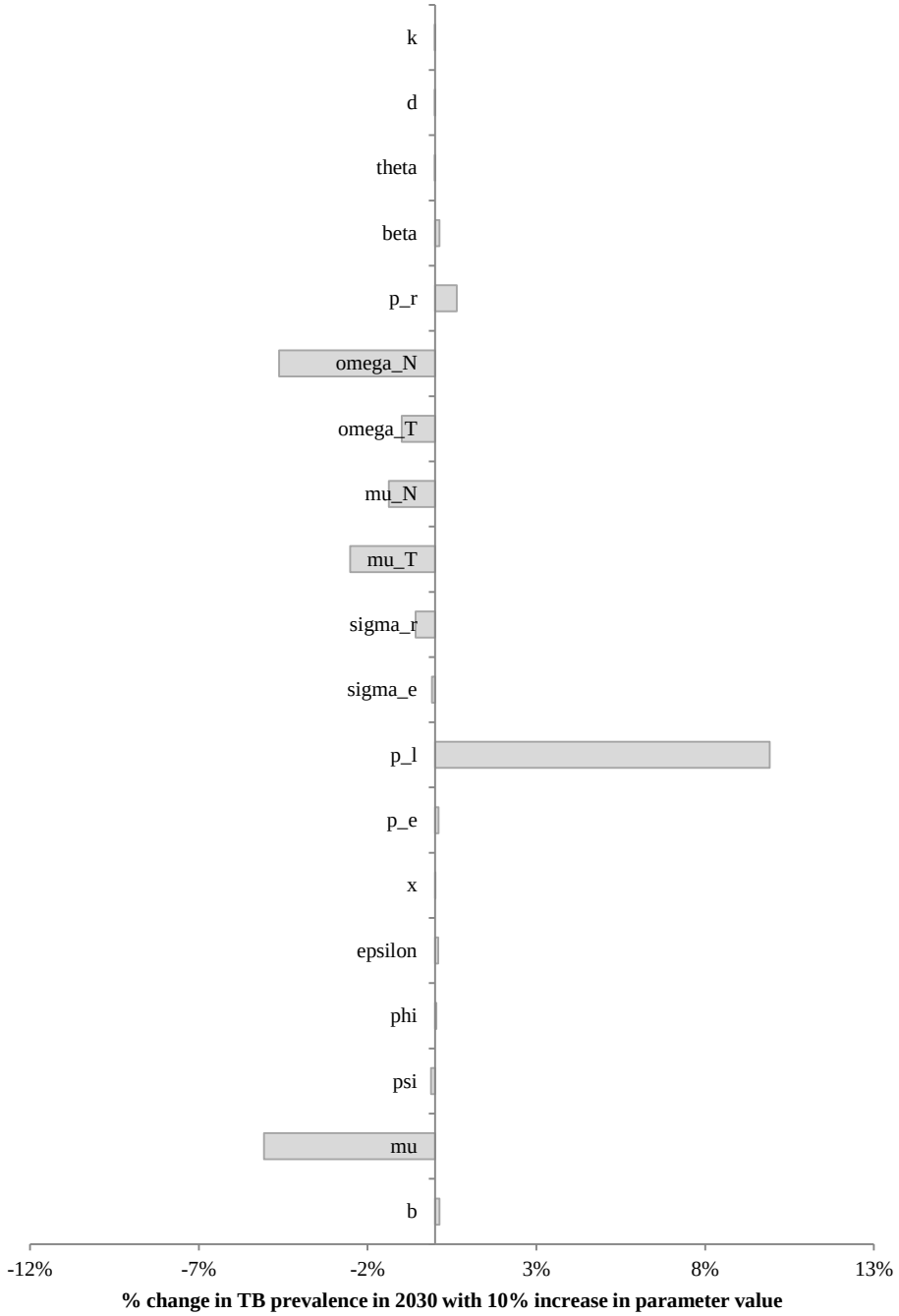
$$\frac{dR}{dt} = \theta d\kappa(T + N) + \omega_N N + \omega_T T - (p_r + \sigma_r + \lambda x + \mu)R$$

The rate of infection λ is defined by the contact rate parameter β per person (hence, proportioned over the total population P), multiplied by the proportion of active infectious TB cases, where ϕ defines the relative infectiousness of smear-negative to smear-positive cases and ε the proportion of smear-negative/extrapulmonary cases that are smear-negative:

$$\lambda = \beta(T + \phi\varepsilon N)/P$$

The mathematical model was fitted to each of the 28 studied European countries by first inserting the natural history parameters shown in Supplementary Table 1, then fitting the contact rate parameter, the starting population sizes in each cohort in year 1990, and the rate θ describing the delay between symptoms and diagnosis in each country to the longitudinal trajectory of annual TB incidence, prevalence and mortality rates per country. The model fitting was performed using the delayed rejection adaptive Metropolis algorithm in the MCMC package of MATLAB[53], and face validity was established by ensuring that all model fits (see Appendix Table 1 for fitted parameter values) were within 5% error of the observed data with no systematic evidence of over- or under-prediction as judged by the absence of over- or under-estimates for more than one consecutive year.

Supplementary Figure 1: (A) Sensitivity analyses. The tornado plot displays the percent change in modeled year 2030 TB prevalence after a 10% increase in each parameter's value. See Appendix Table 1 for parameter definitions, baseline values and sources.



Supplementary Figure 1: (B) The tornado plot displays the percent increase in the austerity-versus-counterfactual increase in modeled year 2030 TB prevalence after a 10% increase in each parameter's value. See Supplementary Table 1 for parameter definitions, baseline values and sources.