Developing a Multi-Country Microsimulation to Estimate the Future Impact of Guideline-Directed Medical Therapy on Potentially Avoidable Hospitalisations and Related Economic, Societal, and Environmental Outcomes: Global PAH

CODE: HSD108

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OBJECTIVE

To develop a flexible, individual-level microsimulation model that projects disease-specific potentially avoidable hospitalisations and their associated impacts, and estimate the effect of improved guideline-directed medical therapy (GDMT) uptake across five chronic conditions (asthma, chronic obstructive pulmonary disease [COPD], heart failure [HF], hypertension [HTN], and type 2 diabetes [T2D]), and eleven countries.

INTRODUCTION

- Non-communicable diseases, including asthma, COPD, HF, HTN, and T2D, drive substantial morbidity and continue to place increasing pressure on health systems worldwide [1-3].
- Despite demonstrated clinical benefits, GDMT uptake remains suboptimal, and the population-level health-system, societal and economic impacts of improving uptake are not well quantified [4-7].
- To address this evidence gap, Global PAH moves beyond conventional single-disease, single-country models to produce one scalable, individual-level framework that projects PAHs across five chronic conditions and multiple countries, as a basis to quantify how improved GDMT could affect hospital capacity, costs, productivity and emissions.
- Validation using the Netherlands as a pilot country is presented here.
- Other countries modelled are Austria, Canada, Denmark, France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States of America.

DISEASE MODEL AND KEY ASSUMPTIONS

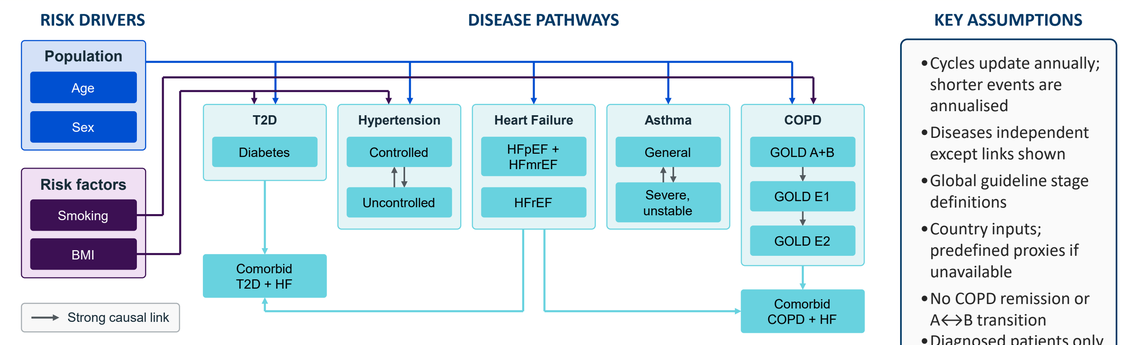


Figure 1. Disease model structure and key assumptions

METHODS

- Global PAH is a flexible individual-level microsimulation model integrating newly developed GDMT uptake modules, while retaining principles from a previously validated framework [8].
- GDMT is defined here as medication consistent with global clinical guidelines (Table 1). Current practice reflects observed prescribing assuming adherence; complete GDMT represents 100% uptake of the modelled therapy among eligible patients. Intermediate coverage scenarios can be modelled. Treatment effects were obtained from meta-analyses, clinical trials and real-world evidence selected using a study-specific quality score, incorporating study design, representativeness, confounding and data integrity with expert judgement resolving ties.
- The model simulates 50 million individuals per country. Country-specific data inform baseline age, sex, risk factors, disease status and stage, comorbidities and treatment status. Where suitable country-specific data are unavailable, proxy estimates are selected using a predefined algorithm based on epidemiological, demographic and economic similarity.
- Hospitalisations are projected from the simulated epidemiology using age-, sex- and disease-specific hospitalisation risks.
- Disease stage or severity is assigned using condition-specific clinical definitions (Table 1). Stage progression is updated annually using transition probabilities derived from published evidence.
- In T2D, only comorbidity informs treatment assignment. Disease pathways are otherwise modelled independently, except for COPD- and T2D-related HF risk, included where reported effect size was ≥2.0). Additional risk-factor pathways link obesity to hypertension and T2D, and smoking to COPD (Figure 1). Other multimorbidity interactions are not explicitly represented.
- Annual cycles match the resolution of most epidemiological, treatment and healthcare resource-use inputs. Shorter-timescale events (e.g. exacerbations) are represented as annualised probabilities.
- Dynamic risk equations link evolving demographic and clinical characteristics to disease onset and progression. Risk factors, treatments and comorbidity status update annually.
- Patient-level outcomes aggregate to country level over 2, 4 and 10 years from 2026. Outcomes include healthcare resource use (HCRU), costs, quality of life, macroeconomic impacts, caregiver burden and CO_2 emissions (based on hospitalisations, intensive care, emergency department and outpatient visits).
- Validation encompasses face validity with country experts, internal validity testing, cross- and external validity against datasets and literature varying by year across each country. The Netherlands validation is included here as a pilot study. The global Steering Committee reviewed assumptions and results throughout.
- Deterministic sensitivity analyses assess how uncertainty in key parameters and assumptions (e.g. GDMT uptake trajectories, treatment effects) affects the model outcomes. Probabilistic sensitivity analysis is not undertaken because of data and computation constraints; joint parameter uncertainty therefore remains unquantified.

Figure 2. Overview of the Global PAH Model

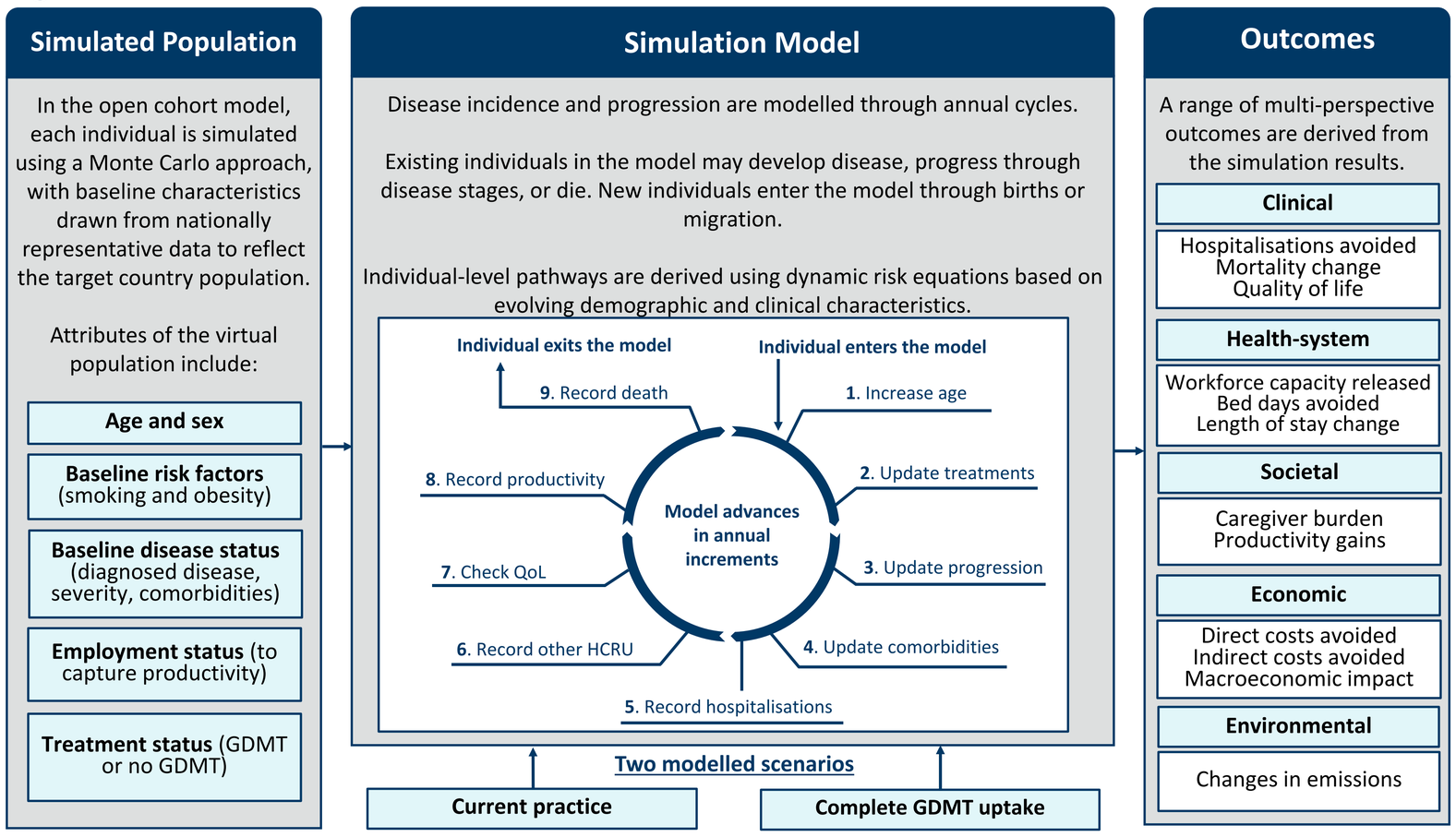
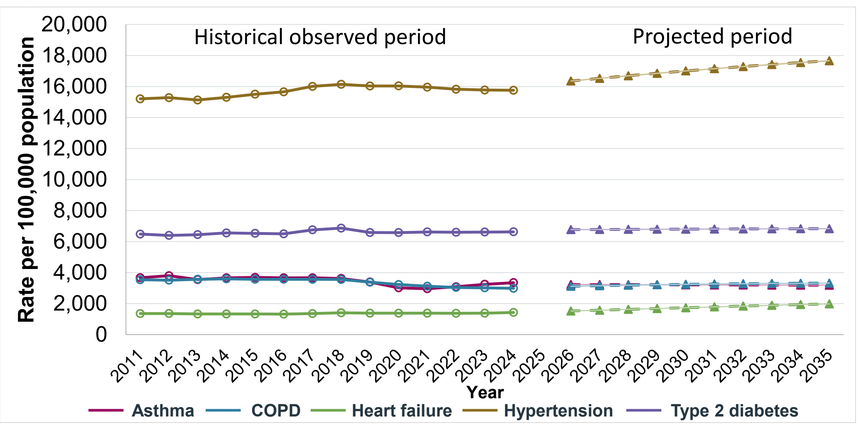
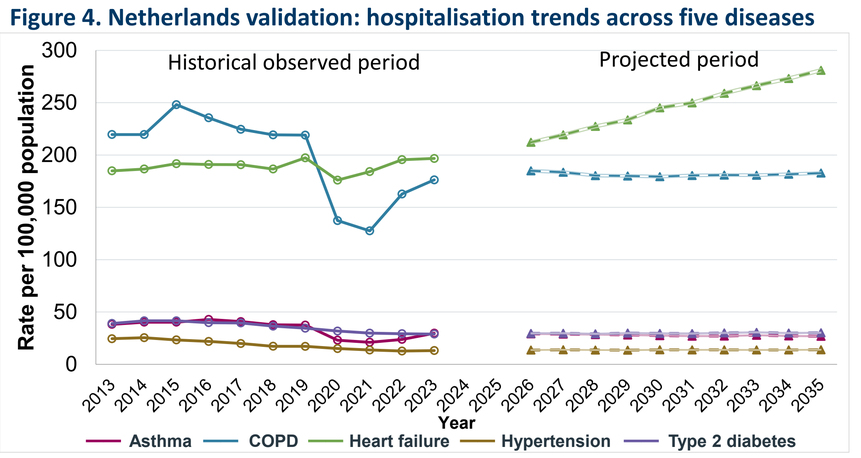


Figure 3. Netherlands validation: prevalence trends across five diseases



Historical prevalence data sourced from VZinfo [14]

Figure 4. Netherlands validation: hospitalisation trends across five diseases



Note: historical and projected hospitalisation rates are for the ≥15 population [15]; bands on modelled estimates represent Monte Carlo uncertainty intervals and do not represent parameter uncertainty.

Table 1. Guideline-directed medical therapy definitions by condition

Asthma GINA 2026 [9]	All asthma: ICS + LABA. Severe, unstable asthma: add a biologic.
COPD GOLD 2026 [10]	A: LAMA or LABA. B: LAMA + LABA. E1: LAMA + LABA or LAMA + LABA + ICS (triple). E2: triple therapy + specified biologic (dupilumab or mepolizumab).
Heart failure ACC 2024 pathway [11]	HFrEF: ARNi/ACEi/ARB, beta blocker, MRA, SGLT2i (quad therapy). HFpEF + HFmrEF: SGLT2i + other medications as required.
Hypertension AHA/ACC 2025 [12]	GDMT agnostic – goal is to achieve blood pressure control.
Type 2 diabetes ADA Standards 2026 [13]	Prediabetes: metformin if BMI ≥35 with high HbA1c and high fasting glucose. Type 2 diabetes, no comorbidities: metformin. Comorbidities: GLP-1 and/or SGLT2i. Multimorbidity: GLP-1 RA + SGLT2i.

Note: Hypertension represents improved blood-pressure control irrespective of drug regimen, whereas other conditions represent implementation of specified therapies. Combined estimates therefore include interventions defined by both treatment uptake and achieved disease control.

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RESULTS

- In the Netherlands pilot, first-year (2026) modelled prevalence and hospitalisation rates were within 10% (pre-specified threshold) of the latest observed prevalence (max. deviation 6.7%; Figure 3) and hospitalisation rates (max. deviation 8.0%; Figure 4). Remaining differences likely reflect the 2026 model start year versus 2023/24 observed data and population ageing. The latest observed years were 2024 for prevalence and 2023 for hospitalisations.
- Limitations: Where local data were unavailable, proxy-country data were selected using a predefined algorithm. The model includes diagnosed populations and primary-cause hospitalisations only, excluding downstream complications, and may therefore underestimate disease burden and GDMT impact, particularly in HTN and T2D. Partial regimens, discontinuation and reinitiation were not modelled. Computational constraints precluded probabilistic sensitivity analysis.

CONCLUSIONS

- The Global PAH framework produces country-specific projections of hospitalisations, HCRU, healthcare costs, macroeconomic impacts, quality of life, societal impacts and environmental consequences under current and improved GDMT scenarios.
- Policy implications: GDMT underuse is a modifiable driver of avoidable hospitalisations. Global PAH can quantify the hospitalisations, costs and emissions that could be avoided through improved uptake to inform budget and implementation decisions.

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