HIGH DOSES OF TREPROSTINIL COULD ENTAIL LOWER HOSPITALIZATION COSTS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION IN NINE EUROPEAN COUNTRIES

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1. INTRODUCTION AND OBJECTIVES

- Pulmonary arterial hypertension (PAH) is a progressive and severely disabling disorder characterized by luminal narrowing in the small- and medium-sized pulmonary arteries, which leads to an increase in pulmonary vascular resistance and may culminate in right ventricular failure and premature death¹.
- **Treprostinil** is a prostacyclin analogue that reduces pulmonary arterial pressure through direct vasodilation of the pulmonary and systemic arterial vascular beds and is indicated for **the treatment of PAH**².
- A recent retrospective analysis of a drug safety database showed that patients with PAH treated with **higher treprostinil doses** (either oral or parenteral) **had lower hospitalization** rates compared to lower doses²⁻⁴.
- This analysis aims to **estimate annual PAH-related hospitalization costs** in patients treated with low, medium and high treprostinil doses in **nine European countries** (Belgium, France, Germany, Italy, Poland, Portugal, Spain, the Netherlands and the United Kingdom).

• A cost model was developed to calculate hospitalization costs in patients with PAH who were treated with treprostinil at different doses:

2. METHODS

	Oral treprostinil	Subcutaneous treprostinil
Low Dose	<4.0 mg/day	<8.3 ng/kg/min
Medium Dose	4.0-9.0 mg/day	8.3-30 ng/kg/min
High Dose	>9.0 mg/day	>30 ng/kg/min

- Mean annual hospitalization costs per country were calculated using annual PAH-related hospitalization rates per dose⁵ and unit costs (local currency, 2021) from national databases or published literature⁶⁻¹⁴. When not available, heart failure-related costs were considered, as it is the final PAH consequence.
- Subgroup analyses were performed by WHO functional class (FC), gender and disease etiology.

3. RESULTS

- **PAH-related hospitalization rates** for the overall population were: 0.91 for low dose, 0.42 for medium dose, and 0.30 for high dose²⁻⁴. Specific hospitalization rates for each subgroup were also gathered: 0.53-1.55 for low dose, 0.19-0.87 for medium dose and 0.14-0.56 for high dose (**FIGURE 1-3**).
- **PAH hospitalization costs** across countries ranged from €2,859 in Portugal to €9,314 in Belgium (**TABLE 1**).
- Mean annual PAH-related hospitalization costs per patient for the overall population were €1,507 (€858-2,794), €2,110 (€1,201-3,912) and €4,571 (€2,601-8,476) for high, medium and low dose, respectively, across all analyzed countries (FIGURE 4).
- Thus, hospitalization costs for high-dose patients were approximately **3 times lower than low**dose patients and **1.4 times lower than medium-dose patients (FIGURE 4)**.
- Results were **consistent across subgroups**, leading to cost savings in both genders, all etiologies (idiopathic or familial, collagen vascular disease and others), and WHO FC II and III (FIGURE 5).
- The greatest differences in costs per patient between high and low-dose were observed in (FIGURE 5):

Males: €1,115-3,632 vs. €4,431-14,436 Idiopathic or familial PAH: €743-2,422 vs. €2,658-8,662 WHO FC III: €858-2,794 vs. €2,544-8,289

FIGURE 1. Hospitalization rates by WHO-FC and dose subgroup

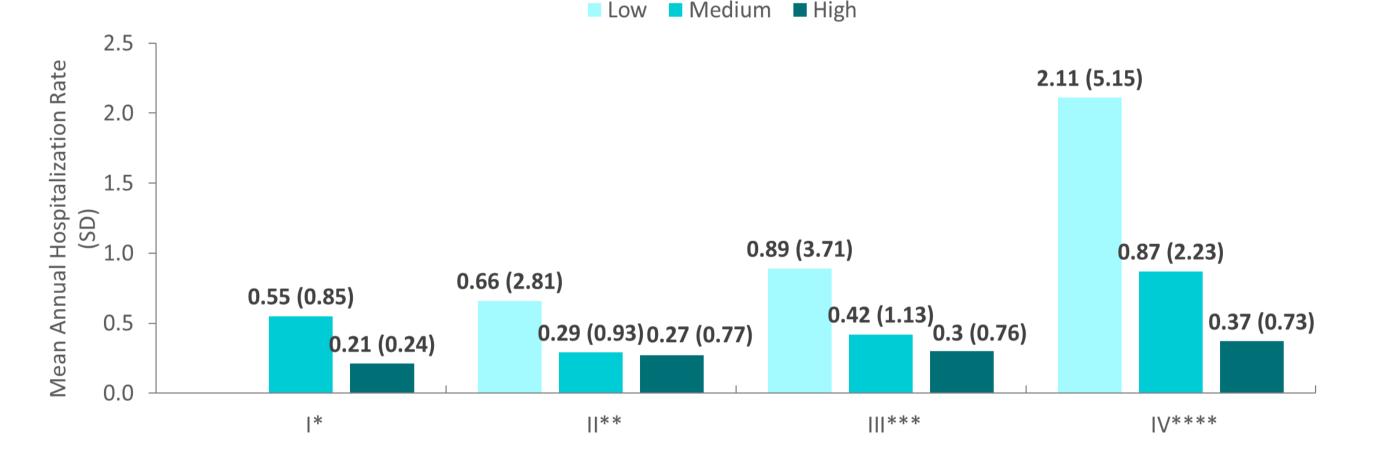
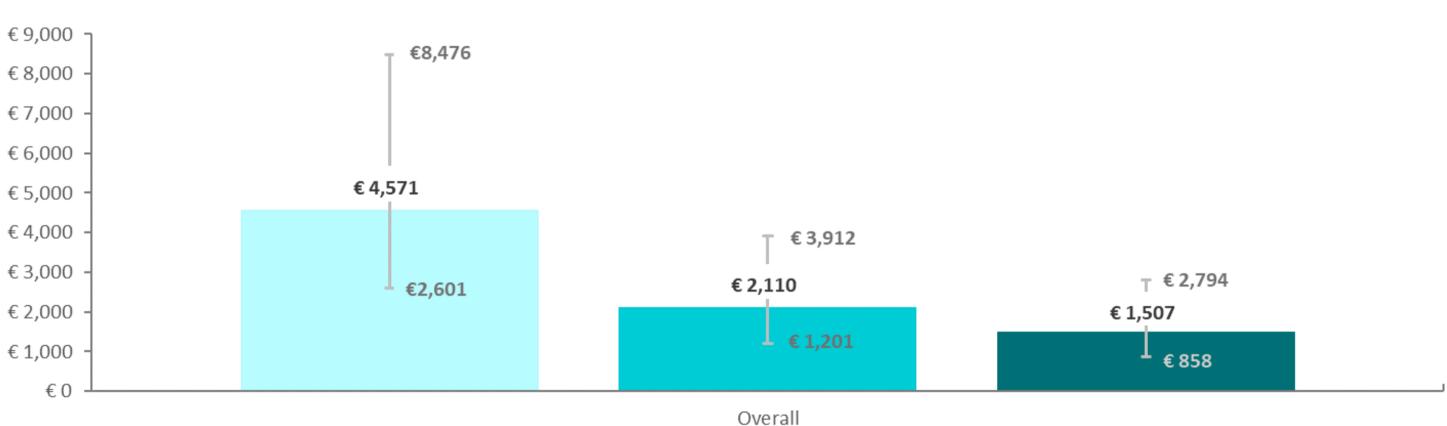
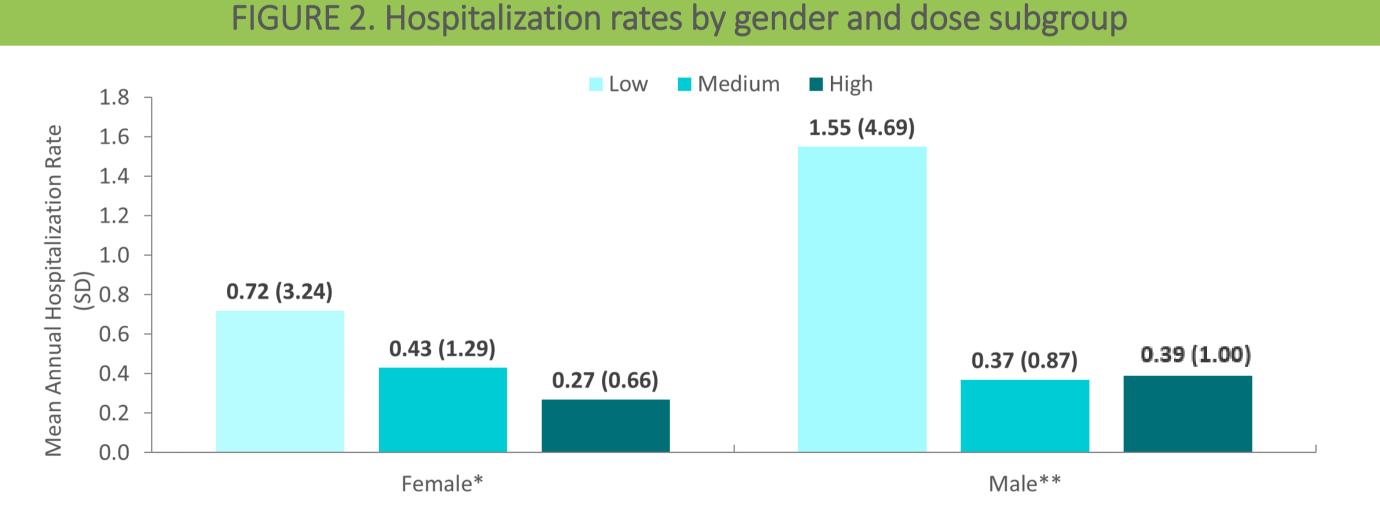


FIGURE 4. PAH-related hospitalization costs per patient



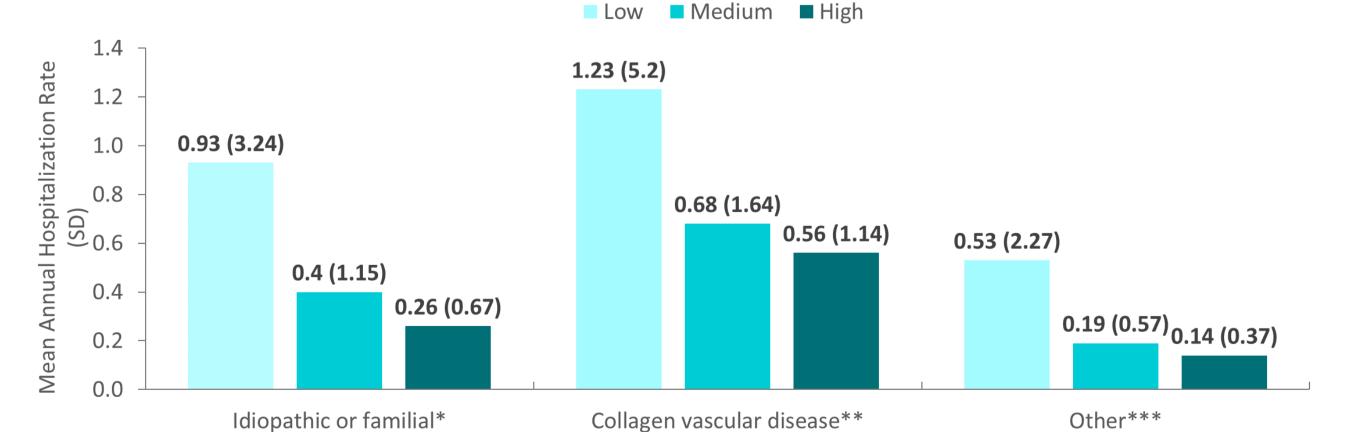
Low Medium High

*High doses (0.21) vs. medium doses (0.55); p=0.0378. **High doses (0.27) vs. low doses (0.66), p=0.0394; medium doses (0.29) vs. low doses (0.66); p=0.0052. ***High doses (0.3) vs. low doses (0.89), p= 0.0003; high doses (0.3) vs. medium doses (0.42); p=0.0006. ****Medium doses (0.87) vs. low doses (2.11); p=0.0044. FC: functional class; SD: standard deviation; WHO: World Health Organization.



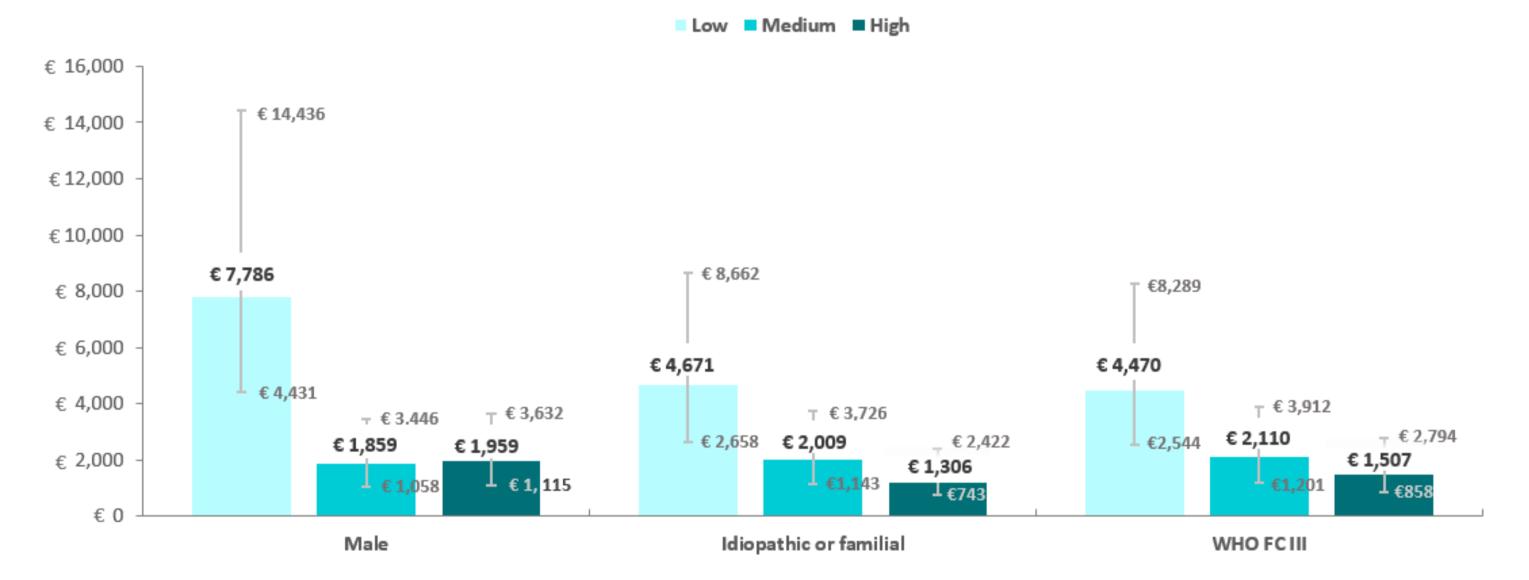
*High doses (0.27) vs low doses. (0.72), p=<0.0001; high doses (0.27) vs. medium doses (0.43); p=0.0017. **High doses (0.39) vs. low doses (1.55), p=0.0028; medium doses (0.37) vs. low doses (1.55); p=0.004. SD: standard deviation.

FIGURE 3. Hospitalization rates by etiology and dose subgroup

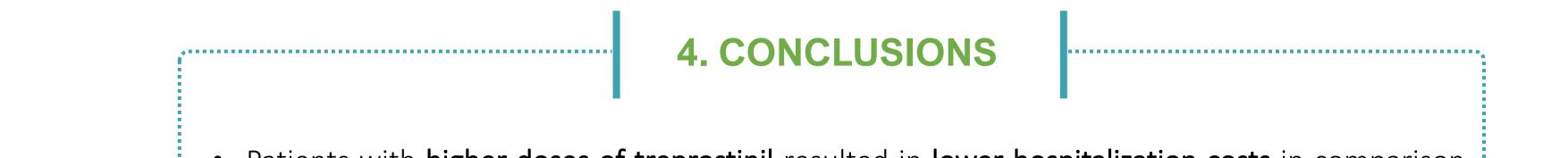


The values represented in each column correspond to the high outlier limit (upper value), average (medium value) and low outlier limit (lower value) of PAH-related hospitalization costs per patient for each dose across all countries.

FIGURE 5. PAH-related hospitalization costs per patient in specific subgroups



The values represented in each column correspond to the high outlier limit (upper value), average (medium value) and low outlier limit (lower value) of PAH-related hospitalization costs per patient for each dose across all countries. FC: functional class; WHO: World Health Organization.



*High doses (0.26) vs. low doses (0.93); p=0.0091. **High doses (0.56) vs. low doses (1.23), p=0.0003; high doses (0.56) vs. medium doses (0.68); p=0.0145. ***High doses (0.14) vs. low doses (0.53), p=0.0044; medium doses (0.19) vs. low doses (0.53); p=0.0032. SD: standard deviation.

TABLE 1. PAH hospitalization costs in each country (local currency/2021)										
Belgium ⁶	France ⁷	Germany ⁸	Italy ⁹	Netherlands ¹⁰	Poland ¹¹¹	Portugal ¹²	Spain ¹³	United Kingdom ¹⁴		
€ 9,313.79	€ 2,963.40	€ 3,520.35	€ 4,294.05	€ 4,243.96	8,426.45 zł	€ 2,858.56	€ 6,660.90	£ 2,925.33		

- Patients with **higher doses of treprostinil** resulted in **lower hospitalization costs** in comparison to those patients with low- and/or mid-dose.
- Therefore, an **appropriate drug titration might lead to potential cost savings** in different European settings.
- These results were **consistent across subgroups** in the analyzed European settings.

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