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## BACKGROUND

- Diabetic Retinopathy (DR) is a major microvascular complication of both Type-1 and Type-2 diabetes and is considered as the leading cause of visual impairment in working-aged adults worldwide.<sup>(1,2)</sup>
- There are two primary types of DR: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). PDR is the more advanced form of the disease, if left untreated, PDR can cause severe vision loss and even blindness.<sup>(3)</sup>
- It is projected that the DR patient population will grow to 191 million by 2030, including 56.3 million patient suffering from vision-threatening diabetic retinopathy; thus posing a significant impact on the world's health systems.<sup>(2)</sup>

## OBJECTIVE

- This study aims to identify and collate evidence related to the economic burden of DR among diabetics.

## METHODS

- A comprehensive targeted literature search was performed for studies published in English from database inception to January 2019 in EMBASE®, MEDLINE®, MEDLINE® In-Process, and Cochrane library.
- Studies reporting data on the economic burden in adult DR patients were included.

### Selection of studies

- Abstracts of all identified studies were screened for relevance followed by full-text evaluation for inclusion based on predefined criteria presented in Table 1.

Table 1. Literature review methodology

Parameters	Inclusion Criteria
Databases	<ul style="list-style-type: none"> <li>MEDLINE® and Embase® via Embase.com</li> <li>MEDLINE® In-process and Cochrane via OvidSP®</li> </ul>
Population	Adult patients with DR
Interventions	Not applicable
Comparator	Not applicable
Outcomes	<ul style="list-style-type: none"> <li>Economic burden of PDR among diabetics or general population</li> <li>Direct cost</li> <li>Indirect cost</li> <li>Healthcare resource utilisation/consumption</li> </ul>
Study design	<ul style="list-style-type: none"> <li>Systematic literature reviews</li> <li>Real-world prospective, retrospective, or cross-sectional observational studies</li> <li>Any other relevant study design capturing outcomes of interest</li> </ul>
Language	English
Publication date	Database inception to January 2019

PDR: proliferative diabetic retinopathy

## RESULTS

- In total, the current review identified 21 studies reporting healthcare resources consumed and costs (direct/indirect) associated with patients with DR and its subtypes.
- Literature findings suggest that the mean total cost (2002, Euro) of DR in Germany was €1,433 from a societal perspective and €911 from the insurance/healthcare payer (GKV) perspective.<sup>(4)</sup>
- Mean healthcare consumption and associated direct cost is substantially higher among patients with severe NPDR/PDR compared to patients without DR or with mild/moderate NPDR.<sup>(5,6)</sup>
- In the US, the mean annual total (direct and indirect) cost associated with employees having DR or PDR was statistically significantly greater than that of employees without DR or PDR, respectively (DR vs. non-DR: \$18,218 vs. \$11,898, p<0.0001; PDR vs. non-PDR: \$30,135 vs. \$13,445, p<0.0001; 2005 USD).<sup>(7)</sup>

### Direct costs

- The total annual healthcare cost (direct medical cost) incurred by patients with DR was \$493 million (2004 USD) in the US<sup>(8)</sup> and €9.9 million (2008 Euro; additional cost compared to patients without DR) in Sweden.<sup>(9)</sup>
- Furthermore, total direct medical costs associated with DR were lower among patients aged ≥65 years (\$195 million) compared to those aged 40 to 64 years (\$298 million), partly attributable to lower outpatient cost of care (major constituting factor).<sup>(8)</sup>
- In Italy, the 10-year mean cost for DR patients was €17,361 and hospital admissions contributed 36%-45% to this cost followed by drugs (30%-34%) and outpatient care (25%-30%).<sup>(10)</sup>
- Costs associated with DR tend to increase with disease severity<sup>(4,11)</sup> such that costs incurred by patients with severe DR are roughly 10 fold higher compared to patients with mild NPDR.<sup>(4)</sup>
- In Sweden, the mean additional healthcare cost incurred by diabetic patients with PDR [€257 (95%CI, €155 to 359)] was almost three fold compared to patients with any DR [€72 (95%CI, €53 to €91)], respectively (Figure 1).<sup>(9)</sup>

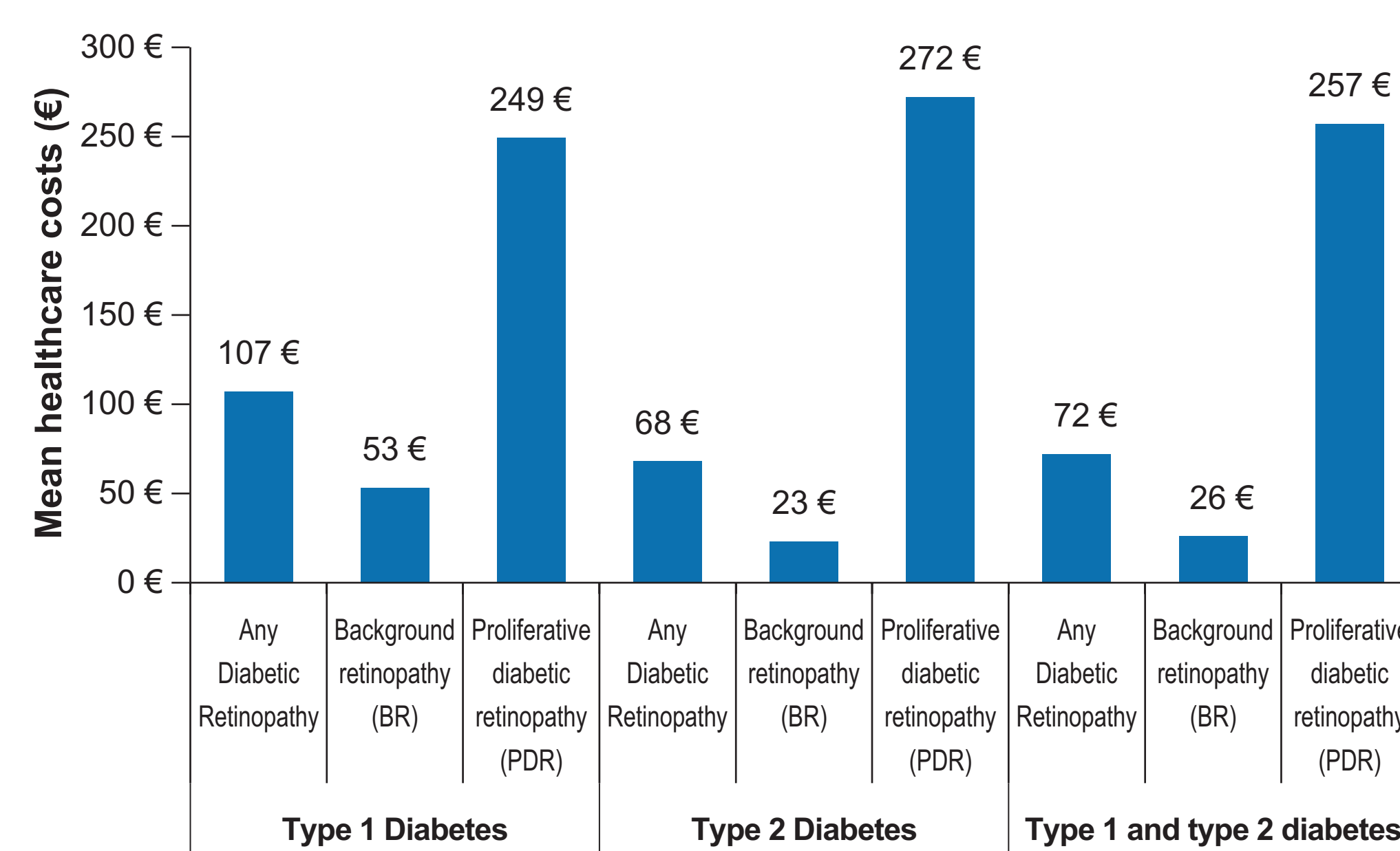


Figure 1. Mean additional healthcare costs associated with DR and its subtypes, per year (Sweden, 2008)<sup>(9)</sup>

- In the US, patients with PDR (\$13,806/case) incurs statistically significantly higher (>35% higher; p<0.0001) Medicare payments (for inpatient/outpatient care) compared to patients with NPDR (\$10,163/case) or those without any DR (\$9,981/case). Similarly, the mean total Medicare payments for ophthalmic care were statistically significantly higher for PDR and NPDR compared to patients without DR (p<0.0001).<sup>(12)</sup>
- In Taiwan, from 2000-2004, the mean medical cost increased by US \$1760 for normal people developing NPDR or PDR (2000: \$1566; 2004: \$3326), and by US \$3482 for patients progressing from NPDR to PDR (2000: \$2723; 2004: \$6204).<sup>(13)</sup>
- In Spain, the mean direct cost of diagnosis and yearly treatment were higher in PDR group compared to any other DR group (mild, moderate and severe DR) (Table 2).<sup>(14)</sup>

Table 2. Mean annual direct costs associated with DR (Spain)<sup>(14)</sup>

Mean annual costs	Treatment cost	Follow-up cost
Any DR	€ 184.67	€ 288.15
STDR	€ 2191.00	€ 441.37
DMO	€ 777.09*	€ 509.42*
	€ 7153.62**	€ 473.56**
Mild DR	€ 139.27	€ 145.00
Moderate DR	€ 5319.01	€ 448.76
Severe DR	€ 7970.93	€ 475.13
PDR	€ 12,177.74	€ 995.78

\*Treatment or follow up of DMO patients treated with laser, \*\*treatment of DMO patients treated with anti-VEGF; DMO: diabetic macular oedema; DR: diabetic retinopathy; PDR: proliferative diabetic retinopathy; STDR: sight threatening diabetic retinopathy

- Using a societal perspective in Germany when comparing direct medical costs between any DR and PDR, medical devices (24% vs. 37%) accounted for a major proportion followed by hospitalisation (10% vs. 16%) and ophthalmologist fee (9% vs. 14%); the associated direct cost is detailed in Figure 2.<sup>(4)</sup>

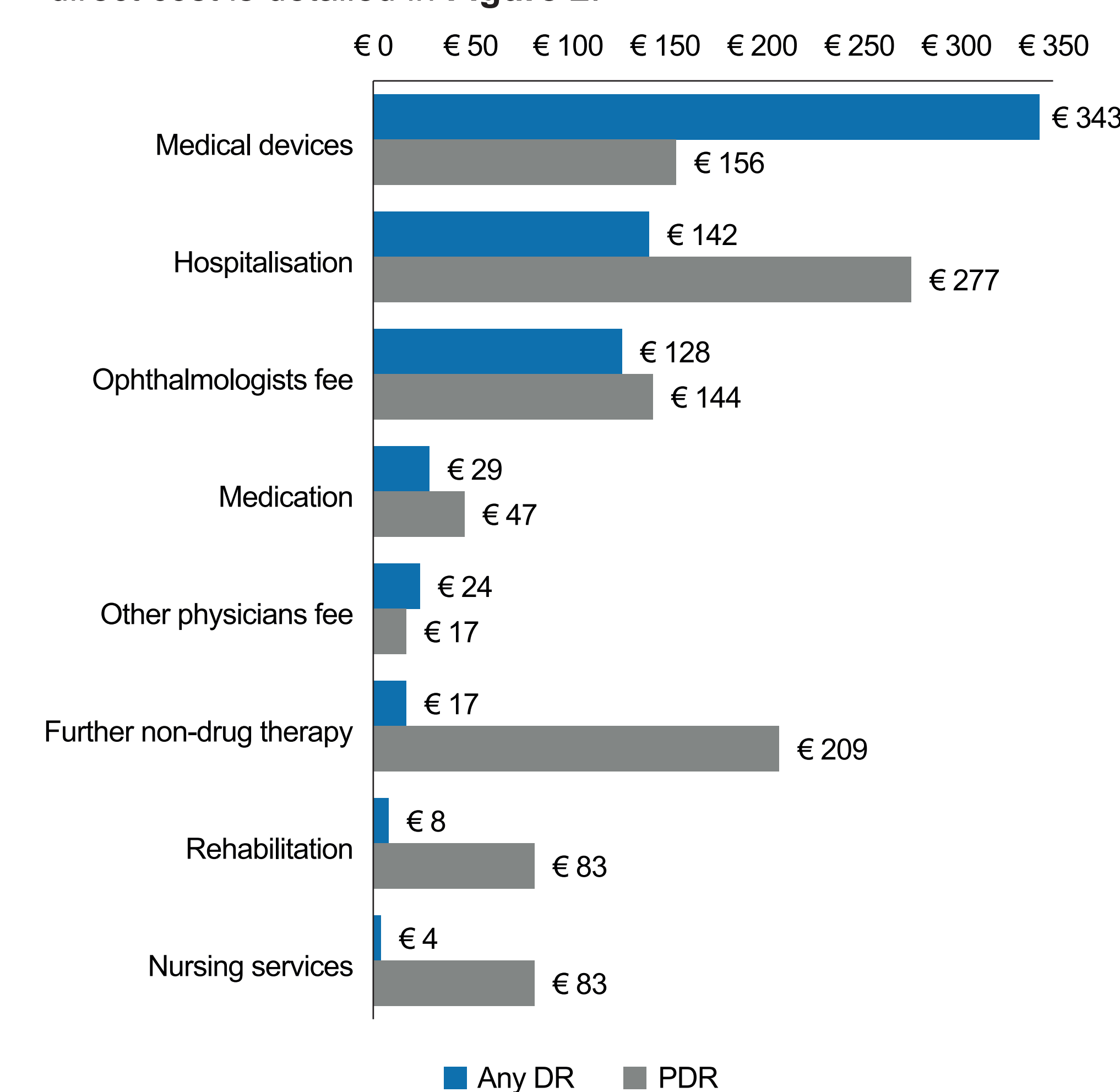


Figure 2. Mean direct costs associated with DR and PDR from societal perspective, per year (Germany, 2002)<sup>(4)</sup>

DR: diabetic retinopathy; PDR: proliferative diabetic retinopathy

### Indirect costs

- From an employers perspective, indirect costs incurred by patients with DR were substantially higher than that of controls (non-DR) (\$3548 vs. \$2374, p<0.0001). Furthermore, mean annual indirect costs were higher for patients with PDR compared to non-PDR patients.<sup>(7)</sup>
- Patients who underwent DR related treatments incurred greater indirect costs compared to those who hadn't (photocoagulation: \$5493 vs. \$3288, p<0.0001; vitrectomy: \$6942 vs. \$3475, p<0.0001; 2005 USD).<sup>(7)</sup>
- Indirect costs associated with DR increased substantially with the increase in disease severity (Figure 3).<sup>(4)</sup>

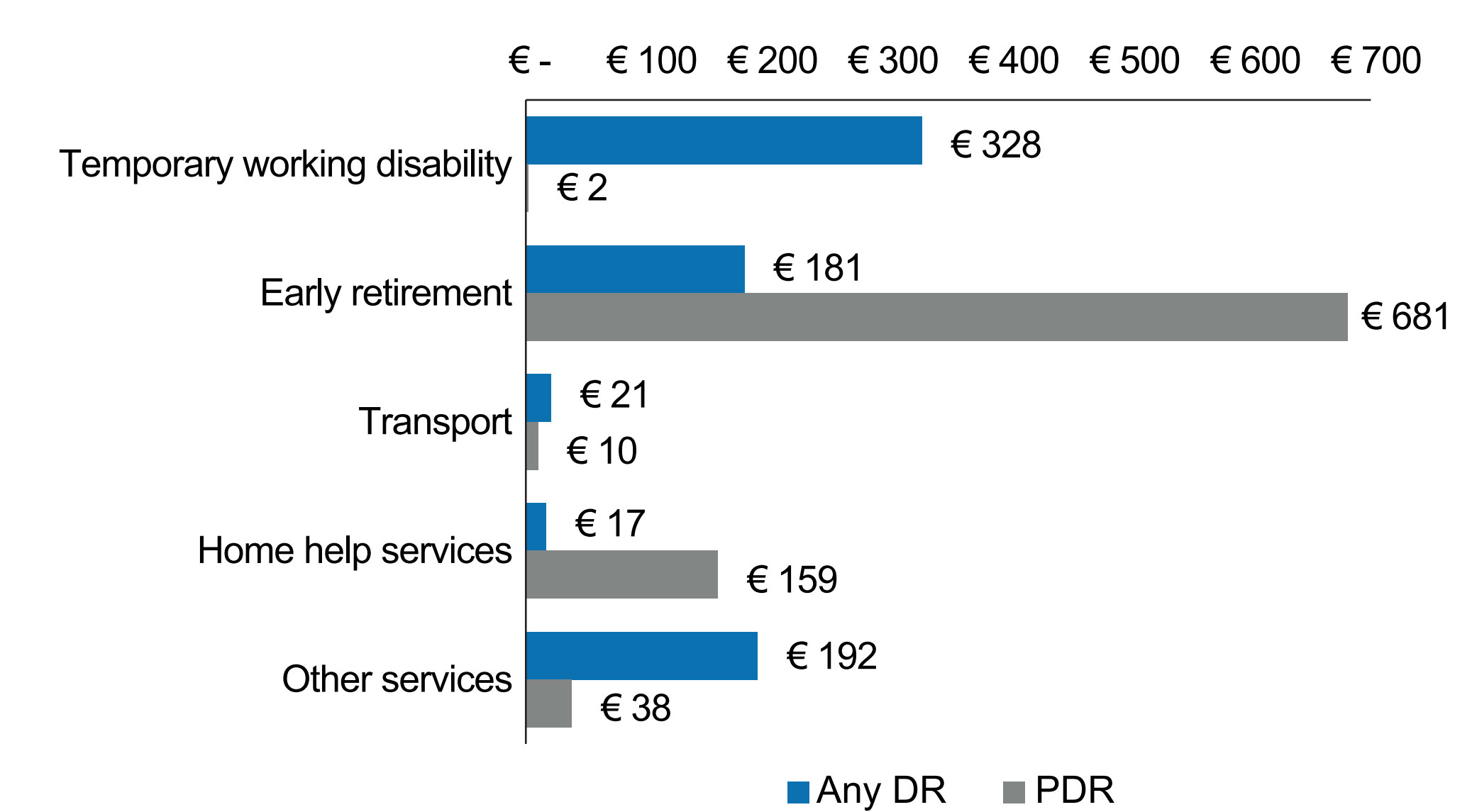


Figure 3. Mean annual indirect costs associated with DR and PDR from a societal perspective (Germany, 2002)<sup>(4)</sup>

DR: diabetic retinopathy; PDR: proliferative diabetic retinopathy

### Healthcare resource utilisation

- In the US, diabetic patients with DR consume more healthcare resources compared to patients without DR (diabetic education/nutrition specialist visits: 55.9% vs. 30.4%, p=0.13; dilated eye examination visit: 93.8% vs. 62.2%, p=0.01 for severe NPDR/PDR and no DR, respectively).<sup>(6)</sup>
- On average, patients with DR visited the ophthalmologist five times, GP twice, and internist/diabetologist once per year with a statistically significant (p=0.0001) trend of increasing resource consumption with increase in disease severity (Figure 4).<sup>(4)</sup>

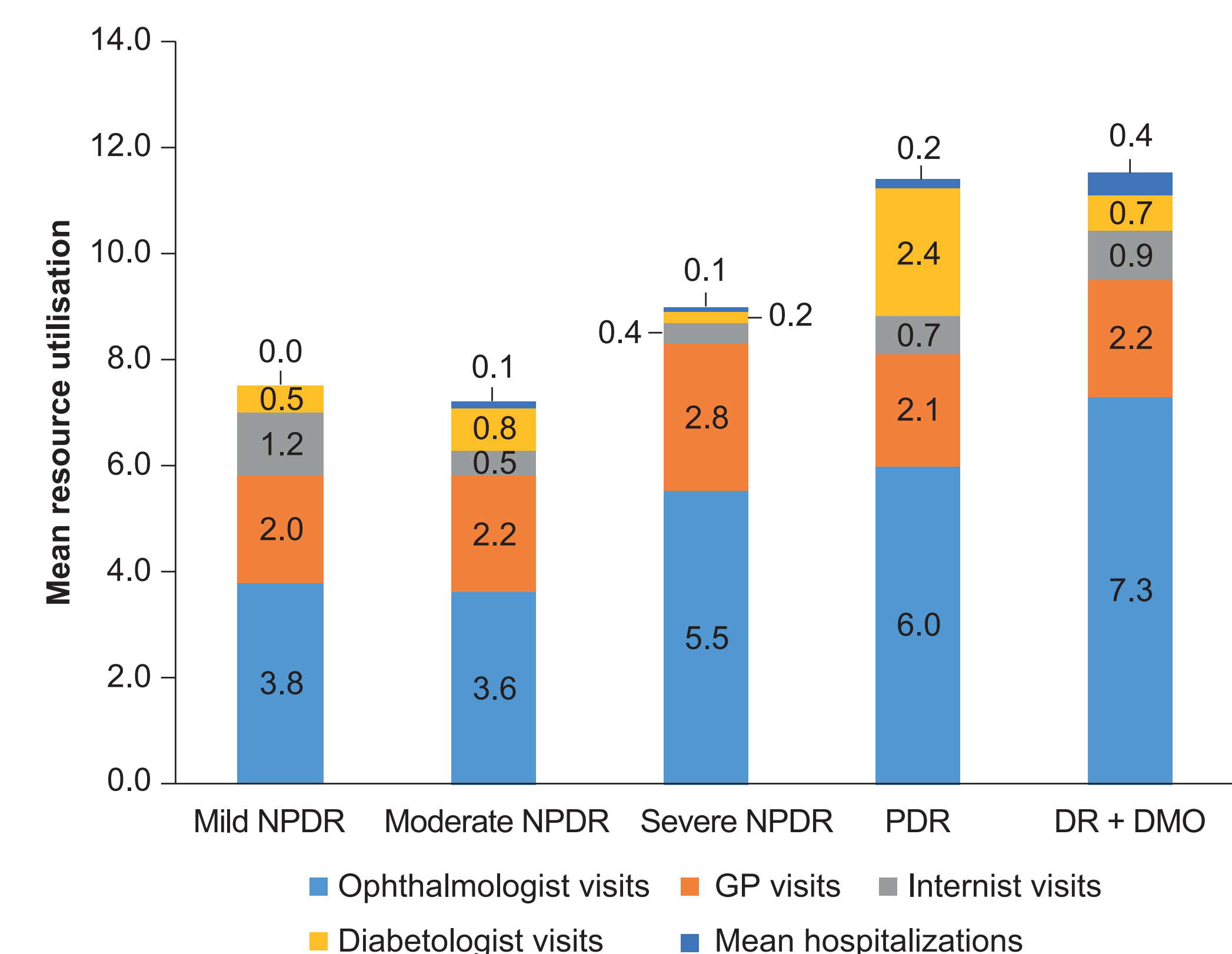


Figure 4. Annual resource consumption because of retinopathy (Germany, 2002)<sup>(4)</sup>

GP: general physician; DMO: diabetic macular oedema; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy

## CONCLUSIONS

- DR imposes a substantial economic burden over and above the cost (direct and indirect) of diabetes to the health care system, employers and payers.
- As total costs associated with DR increase with increasing disease severity, preventing the progression of DR from mild to severe stages is crucial to limit the associated economic burden.

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