

EPIDEMIOLOGY OF PROLIFERATIVE DIABETIC RETINOPATHY (PDR):
EVIDENCE FROM A LITERATURE REVIEW

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BACKGROUND

- Proliferative diabetic retinopathy (PDR) is the most advanced stage of diabetic retinopathy (DR) which is characterised by the presence of neovascularization on the retinal surface. These new fragile blood vessels are prone to fluid leakage leading to scar-tissue build-up manifesting into retinal detachment and blindness.^[1,2]
- Without medical intervention, PDR can result into severe vision loss and even blindness, imposing substantial vision related burden to patients.^[3,4]

OBJECTIVE

- This study aims to gather evidence related to the epidemiology of PDR among diabetic patients.

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 incidence and/or prevalence of PDR were included.

Selection of studies

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

Table 1. Literature review methodology

Parameters	Inclusion Criteria
Databases	- MEDLINE® and Embase® via Embase.com - MEDLINE® In-process and Cochrane via OvidSP®
Population	Patients with PDR
Interventions	Not applicable
Comparator	Not applicable
Outcomes	Epidemiological burden of PDR among patients with DM or general population - Prevalence - Cumulative incidence - Annualized incidence - Risk factors
Study design	- Systematic literature reviews - Real-world studies and observational studies (prospective, retrospective, or cross-sectional) - Any other relevant study design capturing outcomes of interest
Language	English
Publication date	Database inception to January 2019
DM: Diabetes mellitus; PDR: proliferative diabetic retinopathy	

RESULTS

Prevalence

- Literature findings suggest that prevalence rates of DR among the general population (with or without diabetes) ranged from 1.2%^[5] to 6%^[6] which could be attributed to different DM prevalence rates and socio-demographic characteristics among study subjects.^[7] However, among diabetic patients, DR prevalence rates ranged from 1.2%^[5] to 48%^{[8],[7]}
- The age-standardized prevalence rate for any DR (2010 world diabetes population, aged 20-79 years) was 34.6%. However, for PDR specifically, the estimated rate was 7.24% equating to 17.2 million patients world-wide.^[9]
- A meta-analysis estimated the pooled prevalence of PDR among Asian patients with T2DM at 6%. Further sub-group analyses showed higher prevalence among Indians (17%) followed by Malaysians (5%), South Koreans (3%), Chinese (3%) and others (2%).^[10]

- Identified studies showed varied prevalence rates among patients with DM [(0.1% (UK) to 12.2% (Spain)], patients with type-1 DM [1.0% (Spain) to 38.0% (Norway)], and patients with type-2 DM [0.4% (China and New Zealand) to 7.2% (Global)] (**Figure 1**).

- Studies reporting gender-wise prevalence estimates (**Table 2**), showed numerically higher PDR prevalence among males compared to females.^[16]
- As expected, age-group wise prevalence estimates (**Table 3**) showed higher PDR prevalence with increasing age.

Table 2. Country-wise prevalence rate of PDR, segregated by gender

Country (follow-up period)	Population	Gender	Prevalence rate, % (95% CI), p value
Worldwide (2010) ^[9]	Diabetic patients	Male	7.53 (7.39 to 7.66)
		Female	6.98 (6.86 to 7.10)
China (2014) ^[11]	Diabetic	Male	0.56 (0.01 to 3.11), p=0.720
		Female	0.33 (0.01 to 1.85)
Germany (2007 to 2012) ^[14]	T2DM patients	Male	0.6* (0.01 to 3.18)
		Female	0* (NR)
USA - Chinese Americans (2010 to 2013) ^[16]	T2DM patients	Male	3.6 (1.8 to 6.3), p=0.049
		Female	1.4 (0.5 to 3.2)
USA - American Indians and Alaska natives (2011 to 2016) ^[17]	Diabetic patients	Male	2.5 (NR)
		Female	2.2 (NR)

*Weighted prevalence; *among newly diagnosed type-2 diabetes mellitus patients
NR: not reported; PDR: proliferative diabetic retinopathy; T1DM: type-1 diabetes mellitus; T2DM: type-2 diabetes mellitus; USA: United States of America

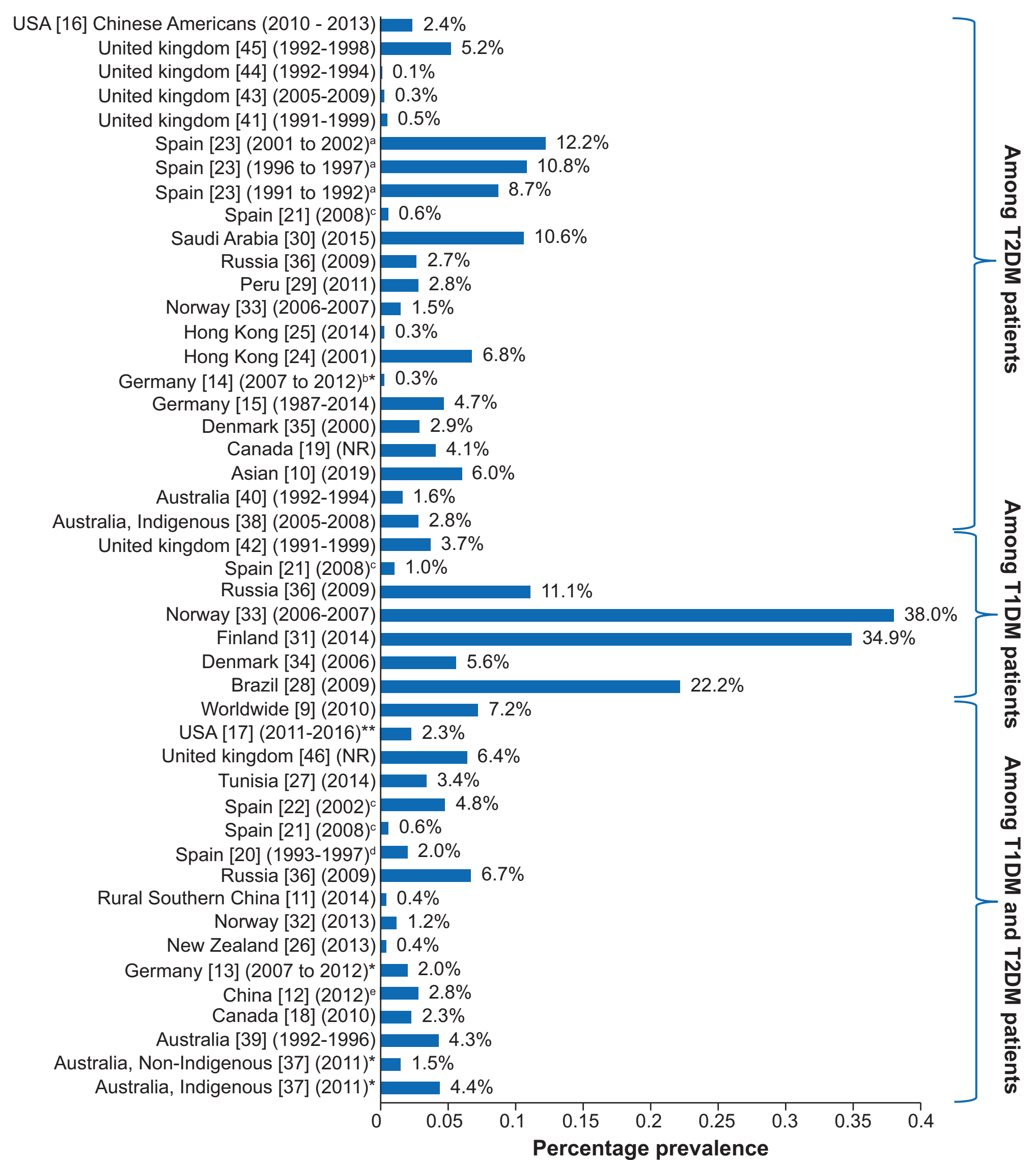


Figure 1. Country-wise prevalence of PDR (%), segregated by diabetes sub-type
*Weighted prevalence rate; **prevalence rate among American Indians and Alaska natives; *medical record review; *among newly diagnosed type-2 diabetes mellitus patients; *fundus photography; *clinical funduscopy; *based upon meta-analysis of Chinese studies
NR: not reported; PDR: proliferative diabetic retinopathy; T1DM: type-1 diabetes mellitus; T2DM: type-2 diabetes mellitus; USA: United States of America

Table 3. Country-wise prevalence rate of PDR, segregated by age-groups

Country (follow-up period)	Population	Age-group	Prevalence rate, % (95% CI), p value
USA - American Indians and Alaska natives (2011 to 2016) ^[17]	Diabetic patients	<50 years	2.2 (NR), p<0.0001
		50-59 years	2.3 (NR)
		60-69 years	2.5 (NR)
		≥70 years	2.3 (NR)
China (2014) ^[11]	Diabetic patients	50-59 years	0.73 (0.02 to 4.03), p=0.582
		60-69 years	0.56 (0.01 to 3.07)
		≥70 years	0 (0 to 2.27)
Germany (2007 to 2012) ^[14]	T2DM patients	<65 years	0.5* (0.01 to 3.05)
		>65 years	0* (NR)
Germany (1987 to 2014) ^[15]	T2DM patients	<5 years	1.1 (NR)
		5-9 years	1.0 (NR)
		10-14 years	2.1 (NR)
		15-19 years	5.6 (NR)
		20-24 years	8.9 (NR)
		25-30 years	11.5 (NR)
		≥30 years	13.0 (NR)
USA - Chinese Americans (2010 to 2013) ^[16]	T2DM patients	50-59 years	1.8 (0.5 to 4.5)
		60-69 years	2.9 (1.3 to 5.7)
		70-79 years	1.9 (0.2 to 6.7)
		≥80 years	3.2 (0.4 to 11.2)

*Weighted prevalence; *among newly diagnosed type-2 diabetes mellitus patients
NR: not reported; PDR: proliferative diabetic retinopathy; T1DM: type-1 diabetes mellitus; T2DM: type-2 diabetes mellitus; USA: United States of America

Incidence

- The annualized incidence rates for PDR among diabetics ranged from 0.07% (Mauritius) to 0.54% (China), while it ranged from 0.03% (Singaporean Indians) to 1.10% (USA) among T2 diabetics (**Figure 2**).
- Furthermore, a Hong Kong based study estimated the 4-year incidence of progression to PDR at 9.9%.^[24]

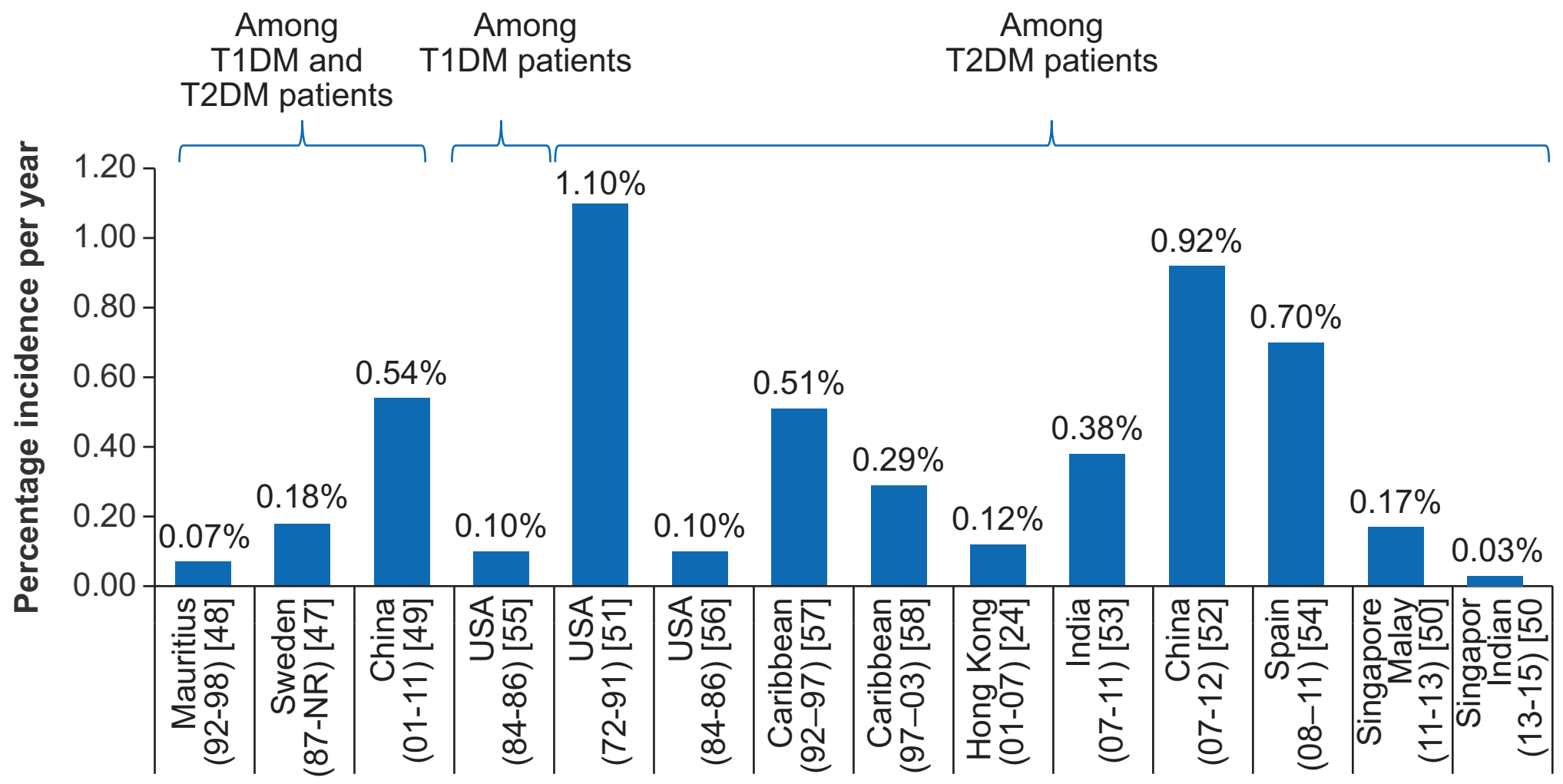


Figure 2. Annualized incidence of PDR among diabetic patients
PDR: proliferative diabetic retinopathy; T1DM: type-1 diabetes mellitus; T2DM: type-2 diabetes mellitus; USA: United States of America

Risk factors

- Duration of diabetes and its sub-type predisposes patients to the development of retinopathy (**Table 4**). The likelihood of getting PDR is exponentially higher for diabetics with ≥20 years of T1DM compared to <10 years with T2DM [Relative risk (RR): 15.33 (95% CI: 11.29 to 20.8) vs. 9.79 (95% CI: 7.14 to 13.43), respectively].^[9]

- Among Chinese Americans with T2DM, the prevalence of PDR was almost 10-fold higher among patients with ≥15 years of diabetes compared to patients newly diagnosed (10.2% vs. 1.0%, respectively).^[16]

- In addition, many of the risk factors involved in the development of DR have also been found to be associated with DR progression. The risk factors associated with disease progression are pregnancy (increases risk of DR progression by 2.3 times, p<0.005), intra-capsular/extra-capsular cataract extraction surgery, and poor glycaemic control during pre-operative phased of cataract surgery.^[59-61]

Table 4. Adjusted relative risk (RR) of PDR among diabetics stratified by diabetes duration and type			
DR type	Population	DM duration (years)	Adjusted relative risk* (95% CI)
Worldwide* ^[9]	T1DM	<10 years	0.90 (0.44 to 1.86)
		10 to <20 years	6.72 (4.70 to 9.61)
		>20 years	15.33 (11.29 to 20.80)
	T2DM	<10 years	1.0 (ref)
		10 to <20 years	4.32 (3.16 to 5.91)
		>20 years	9.79 (7.14 to 13.43)
USA ^[16]	T2DM	newly diagnosed	1.0 (NR)
		≥15 years	10.2 (NR)

*Adjusted for age, race, hypertension, HbA1c and study
DM: diabetes mellitus; NR: not reported; PDR: proliferative diabetic retinopathy; ref: reference for relative risk; T1DM: type-1 diabetes mellitus; T2DM: type-2 diabetes mellitus; USA: United States of America

CONCLUSIONS

- There is a substantial public health burden associated with PDR, as it constitutes a major part of severe vision-threatening DR.
- Poor glycaemic control and its associated risk factors play an important role in the progression of DR to PDR.
- Further research is required to elucidate the epidemiological burden of PDR (specifically in T1DM) and its associated risk factors.

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