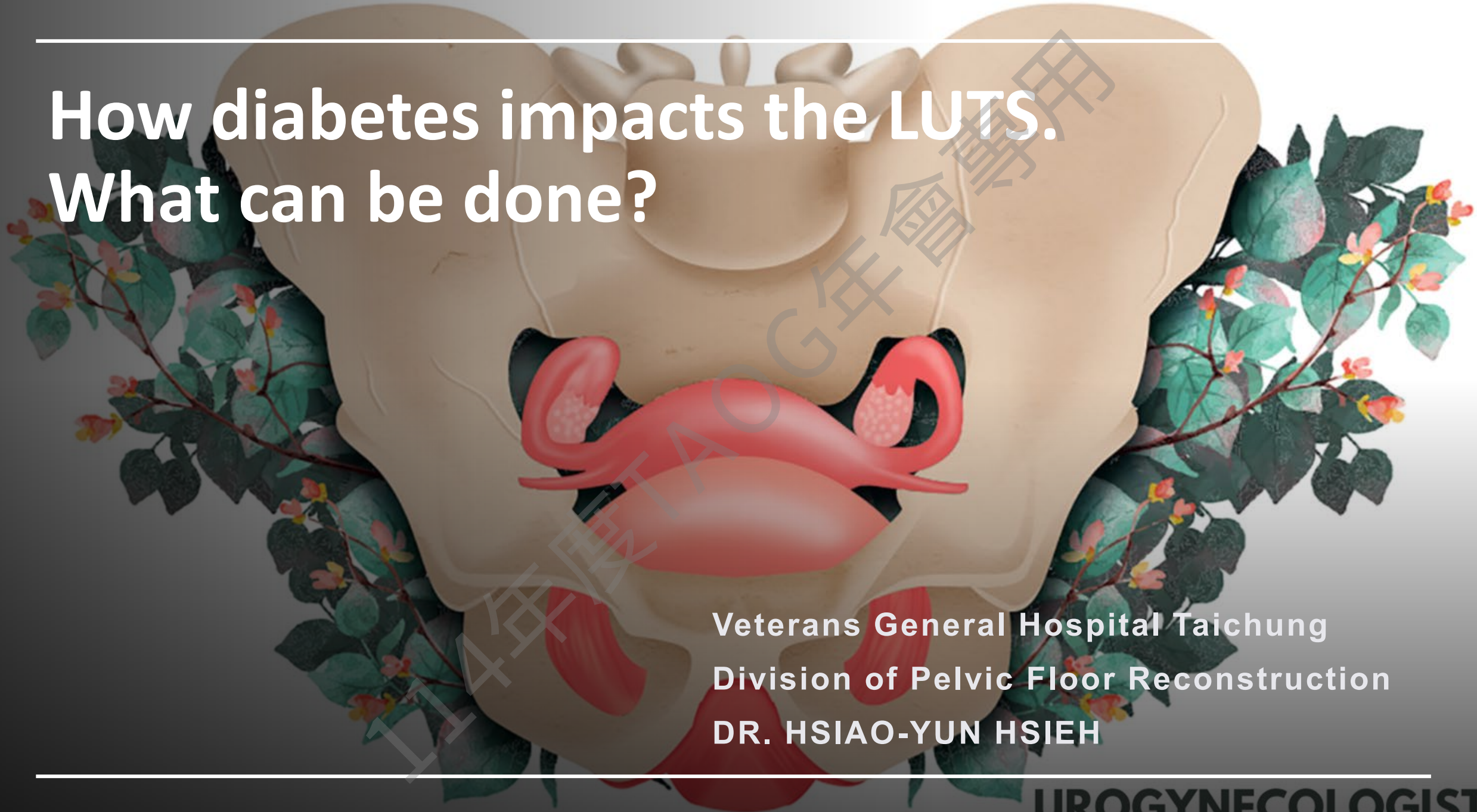
How diabetes impacts the LUTS. What can be done?



Veterans General Hospital Taichung
Division of Pelvic Floor Reconstruction
DR. HSIAO-YUN HSIEH

UROGYNECOLOGIST

謝筱芸醫師

現任

臺中榮民總醫院 婦產部骨盆機能重建科主治醫師
茂盛醫院婦女泌尿主治醫師
國立中興大學講師
台灣福爾摩沙婦女泌尿醫學會 副秘書長
更年期醫學會 副秘書長

學經歷

國立陽明大學醫學系
高雄長庚婦產部住院醫師、總醫師
中華民國婦產專科醫師

喝多
Always thirsty

尿多
Frequent urination

吃多
Always hungry

Outline

Diabetes global effect

Diabetic Bladder Dysfunction

1. Prevalence
2. Presenting symptoms
3. UDS

Clinical Practice and Care

Diabetes– Global Impact

Diabetes is a huge and growing problem, and the costs to society are high and escalating.

1 in 10

Adults (20-79 years) has diabetes
537 million people

11.5%

Of global health expenditure spent on diabetes (USD 966 billion)

1 in 2

Adults is undiagnosed
240 million people

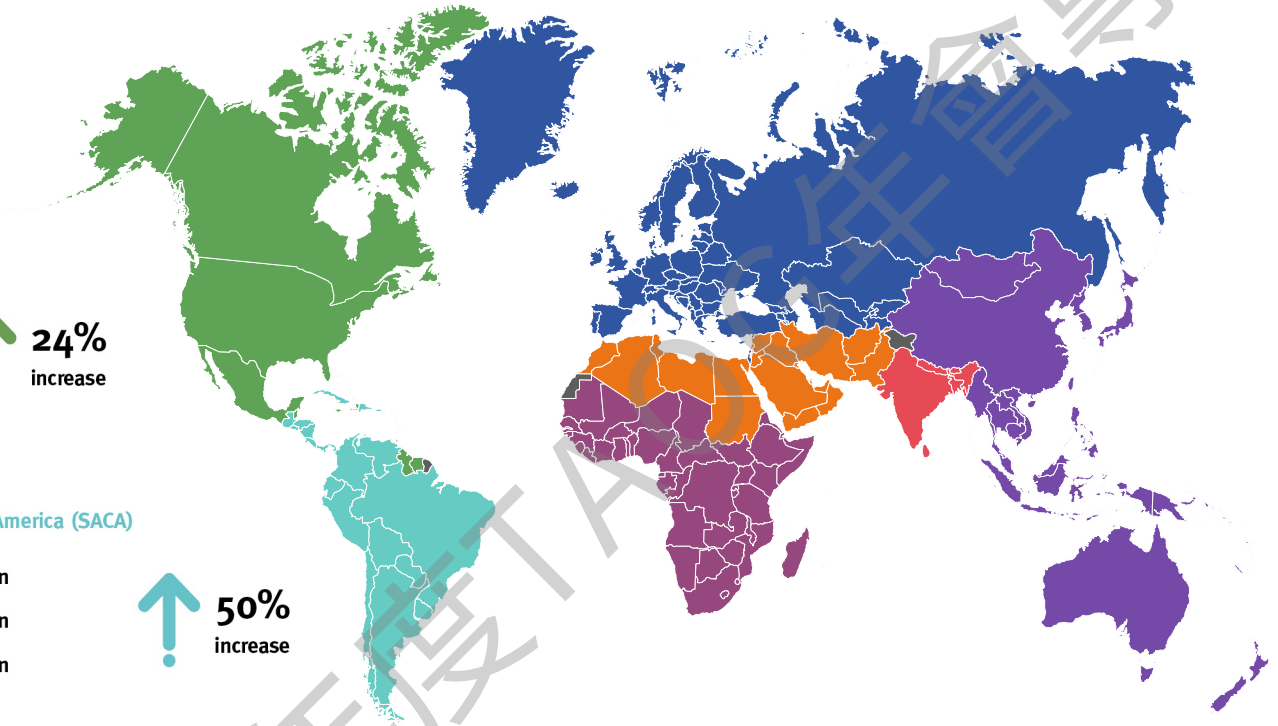
3 in 4

People with diabetes live in low and middle-income countries

Federation, I.D., IDF Diabetes atlas, 10th ed. 2021, International Diabetes Federation: Brussels, Belgium

Number of people with diabetes

Aged 20–79 years globally and by IDF region



North America & Caribbean (NAC)

2045	63 million
2030	57 million
2021	51 million

24% increase

South & Central America (SACA)

2045	49 million
2030	40 million
2021	32 million

50% increase

Africa (AFR)

2045	55 million
2030	33 million
2021	24 million

129% increase

Middle East & North Africa (MENA)

2045	136 million
2030	95 million
2021	73 million

87% increase

Europe (EUR)

2045	69 million
2030	67 million
2021	61 million

13% increase

South-East Asia (SEA)

2045	152 million
2030	113 million
2021	90 million

68% increase

Western Pacific (WP)

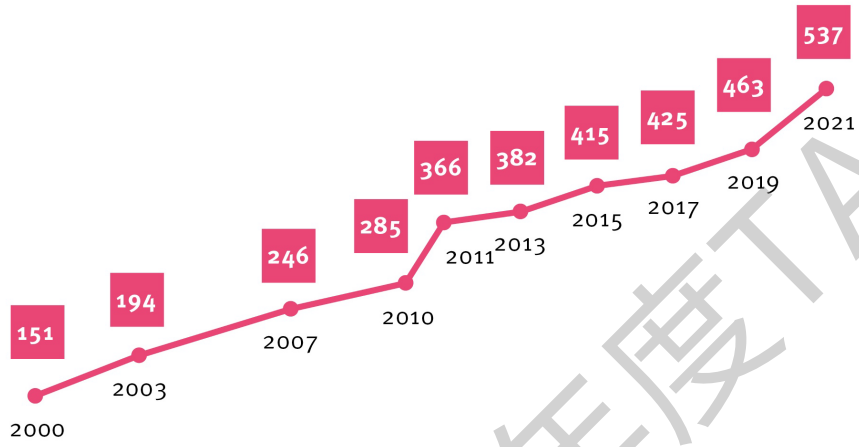
2045	260 million
2030	238 million
2021	206 million

27% increase

Estimates and projections

Global number of adults (20–79 years) in millions

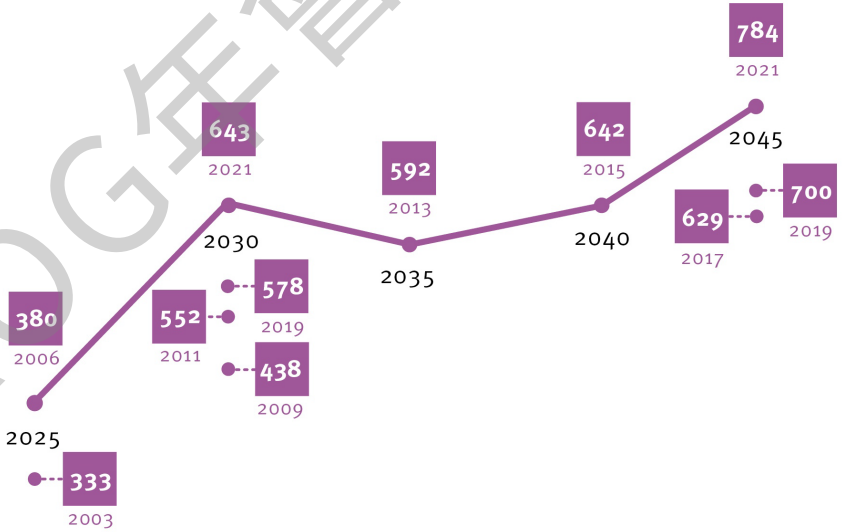
Estimates of the global prevalence of diabetes in the 20–79 year age group (millions)



Key

151 Number of people with diabetes in millions

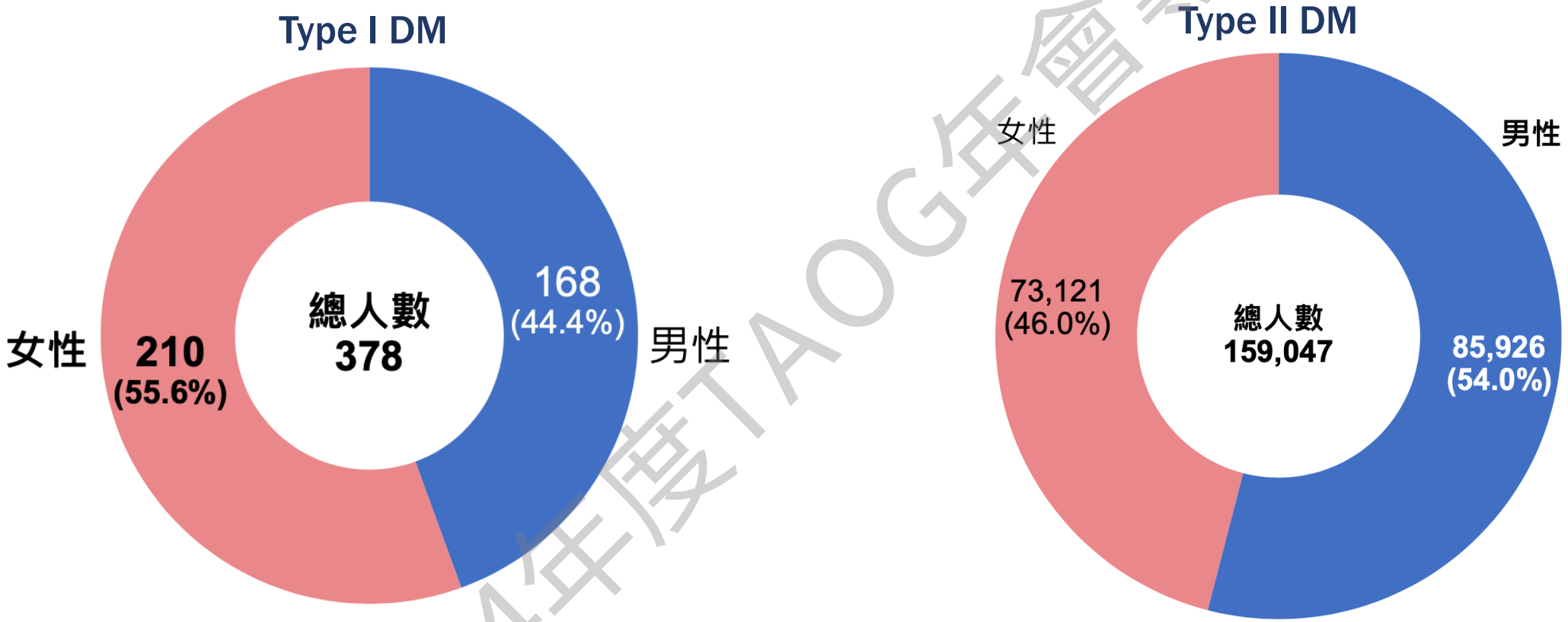
Projections of the global prevalence of diabetes in the 20–79 year age group (millions)



Key

333 2003 Projection in millions, Year projection made

臺灣每年新發生糖尿病人數16 萬人
大多數為Type II DM

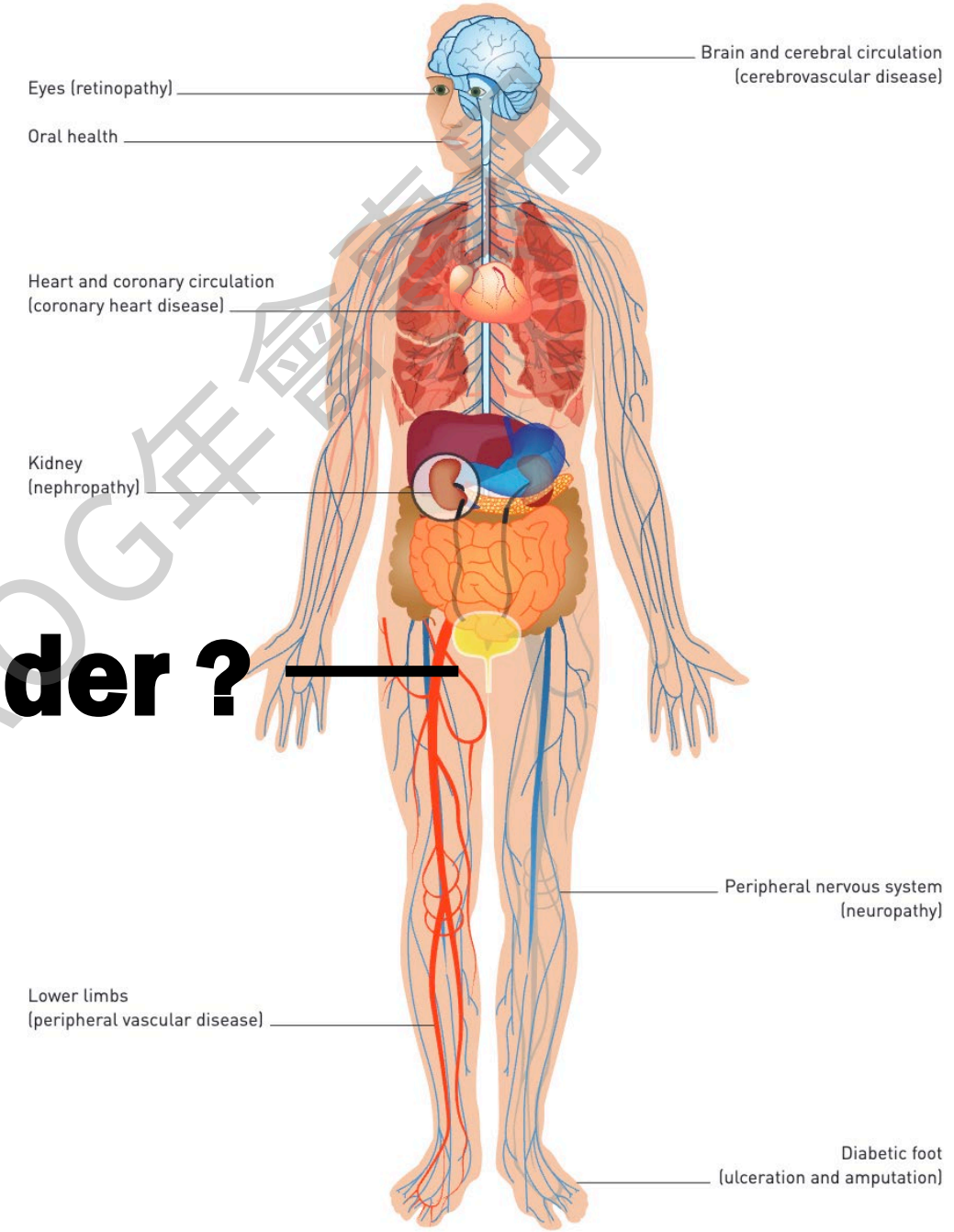


第 1 型糖尿病以女性居多
第 2 型糖尿病以男性為多

Diabetes Complications

- Diabetes is a leading cause of CV disease, blindness, kidney failure, and lower-limb amputation.
- Maintaining blood glucose level, blood pressure and cholesterol close to normal can help delay or prevent diabetes complications.
- People with diabetes need regular monitoring for complications.

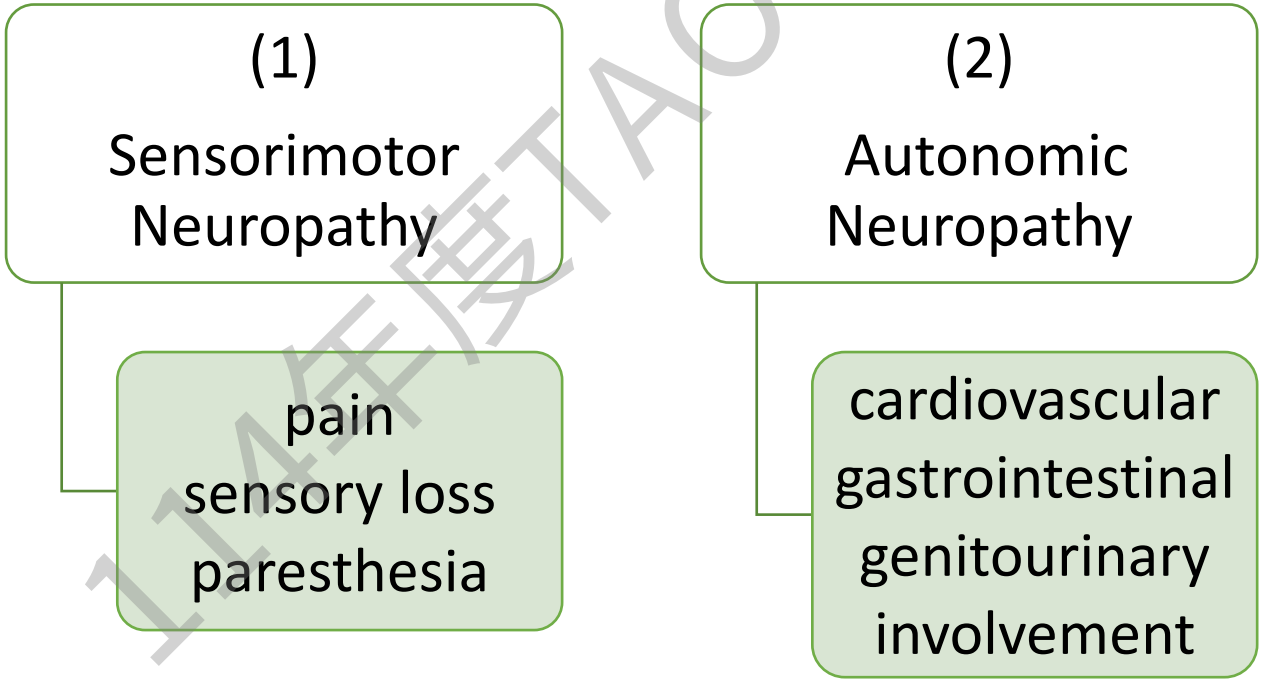
How about bladder ?



Federation, I.D., IDF Diabetes atlas, 6th edn. 2013, International Diabetes Federation: Brussels, Belgium

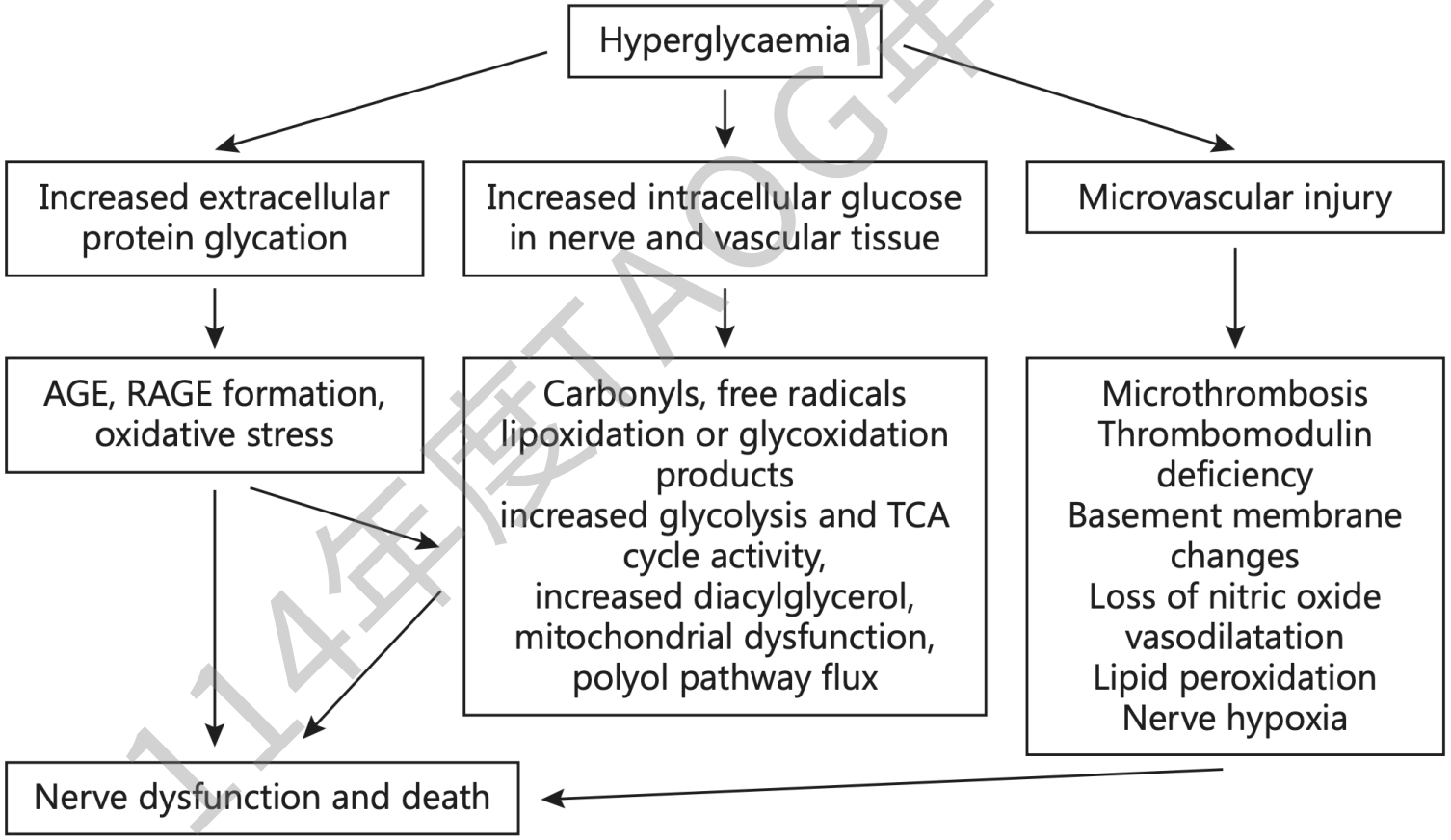
Diabetes Neuropathy

- Common complication of diabetes, affecting 30-50% of patients
- Major risk factors: Hyperglycemia, age, smoking, hypertension, obesity, alcohol
- Two main types:



Diabetes Neuropathy - Pathophysiology

氧化壓力（**Oxidative Stress**）



Deli G, Bosnyak E, Neuroendocrinology. 2013

Diabetes Neuropathy - Pathophysiology

離子通道的變化

- 鈉離子電流異常（Persistent Sodium Currents）
  - Na^+通道表現過度增加（over-expression），導致神經容易異常放電。
  - Na^+/K^+ Pump活性下降，Na^+累積，使神經細胞更興奮，產生異常的疼痛訊號。
- 鉀離子通道的變化（Potassium Channels）
  - 鉀離子通道（Voltage-Gated Potassium Channels）有助於神經細胞恢復靜息狀態，防止過度放電。
  - 在糖尿病神經病變中，這些通道發生變化，增加神經的興奮

Diabetes Neuropathy

(1)
Sensorimotor Neuropathy

- Pain
- Sensory loss
- Paresthesia

(2)
Autonomic Neuropathy

- Cardiovascular
- Gastrointestinal
- Genitourinary

Diabetic Bladder Dysfunction (DBD)

Diabetic Bladder Dysfunction (DBD)

- first described by WR Jordan et al. in 1935

PARALYSIS OF THE BLADDER IN DIABETIC PATIENTS

WILLIAM R. JORDAN, M.D.

CASE 4,023.—A woman, 60 years old, with diabetes of three years' duration and moderate arteriosclerosis, complained of pain in the right leg on walking. Paresthesia disturbed her at night. Examination revealed a distended bladder (residual urine, 2,580 cc.). The pelvic and neurologic examinations gave negative results. The Wassermann reactions of the blood and spinal fluid were normal. Dr. James B. Ayer found no evidence of a nondiabetic lesion in the spinal cord. Cystoscopy revealed general redness of the bladder mucosa, with an abnormal amount of trabeculation.

CASE 6,360.—A woman, 55 years old, with diabetes of seven years' duration and mild arteriosclerosis, was found to have a distended bladder (residual urine, 900 cc.). She had no other neurologic symptoms. Examination revealed absence of the ankle jerks but no other neurologic signs. The Wassermann reaction of the blood was negative. There was no history of the use of alcohol. Cystoscopic examination revealed moderate chronic inflammation of the bladder. No cause other than neurologic disturbance was found.

CASE 8,404.—A woman, 42 years old, with diabetes of four and eight-tenths years' duration and slight arteriosclerosis, had diarrhea for six months and finally hematuria. Examination revealed no neurologic signs except sluggish knee jerks and absence of the ankle jerks. The bladder was distended (residual urine, from 360 to 900 cc.), and considerable gas was present. From rough tests the gas was thought to be air which presumably entered the bladder during catheterization. There was no history of the use of alcohol. No cause for the diarrhea was found except achlorhydria and a weak anal sphincter. The Wassermann reaction of the blood was negative, as was the spinal fluid except for the slightest possible trace of globulin. Cystoscopic examination revealed marked chronic cystitis with a number of hemorrhagic spots in the wall of the bladder. No tumor or diverticulum was present. The appearance was consistent with a neurologic cause. Roentgenograms of the urinary tract showed no abnormality other than air in the bladder.

Gastric analysis revealed an absence of free hydrochloric acid. Two years previously the red blood cells numbered 3,350,000, and liver therapy was recommended. At the time of our examination she was not anemic, but the possibility of pernicious anemia was considered. She died four months later of pneumonia.

CASE 9,025.—A woman, 50 years old, with mild diabetes of eleven and eight-tenths years' duration, a blood pressure of 200 systolic and 120 diastolic and moderate arteriosclerosis, entered the hospital because of urinary retention and uremia. At first the retention was thought to be due solely to a urethral stricture, but correction of this defect, while causing some amelioration of the symptoms, did not abolish the retention, which seemed to be due to paralysis of the wall of the bladder. There were no neuritic symptoms. Examination revealed normal pupils.

Jordan wr, crabtree hh. Paralysis of the bladder in diabetic patients. Arch intern med (chic). 1935;55(1):17–25

Diabetic Bladder Dysfunction (DBD)

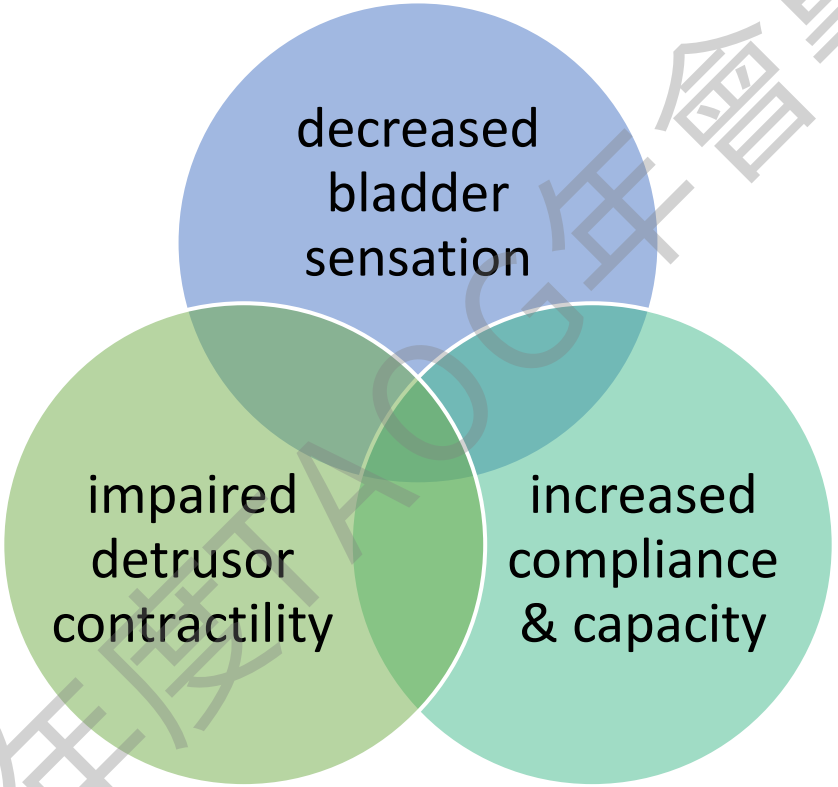
Key Characteristics

- DBD occurs due to involvement of **autonomic** and **sensory** nerve fibers.
- The proposed natural history begins with impaired bladder sensation, ultimately progressing to impaired contractility and urinary retention.
- This can happen asymptomatically, becoming the dysfunction evident when a UTI occurs secondary to the increase in residual urine volume.

Quiroz-Aldave J, Durand-Vásquez M, Gamarra-Osorio E, et al. Diabetic neuropathy: Past, present, and future. Caspian J Intern Med. 2023

Diabetic Bladder Dysfunction (DBD)

Key Characteristics- Traditional Triad



Wittig L, et al. Diabetic bladder dysfunction: a review. Urology. 2019

Diabetic Bladder Dysfunction (DBD)

Key Characteristics

Storage Problems

Overactive bladder with urgency incontinence.

Voiding Problems

Impaired bladder emptying and urinary retention.

Overflow Incontinence

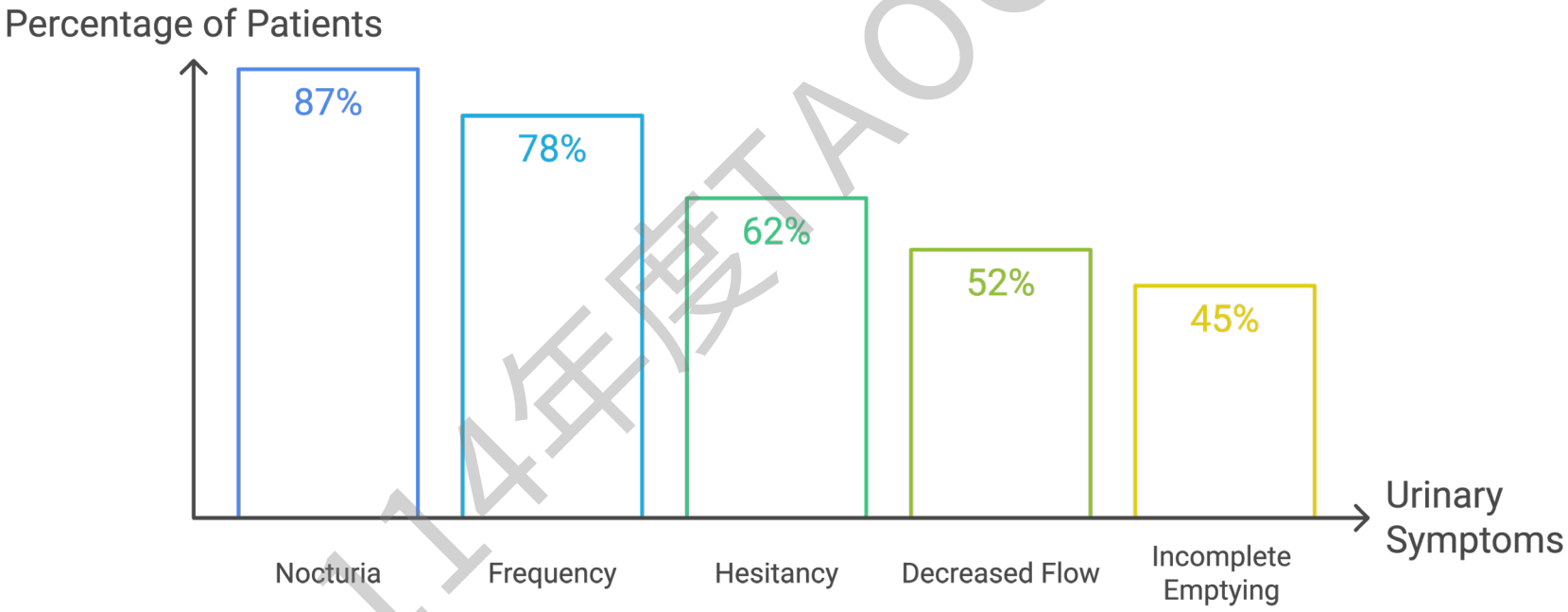
Condition where the bladder overfills and leaks.

Wittig L, et al. Diabetic bladder dysfunction: a review. Urology. 2019

Diabetic Bladder Dysfunction (DBD)

Prevalence of LUTS in Diabetes:

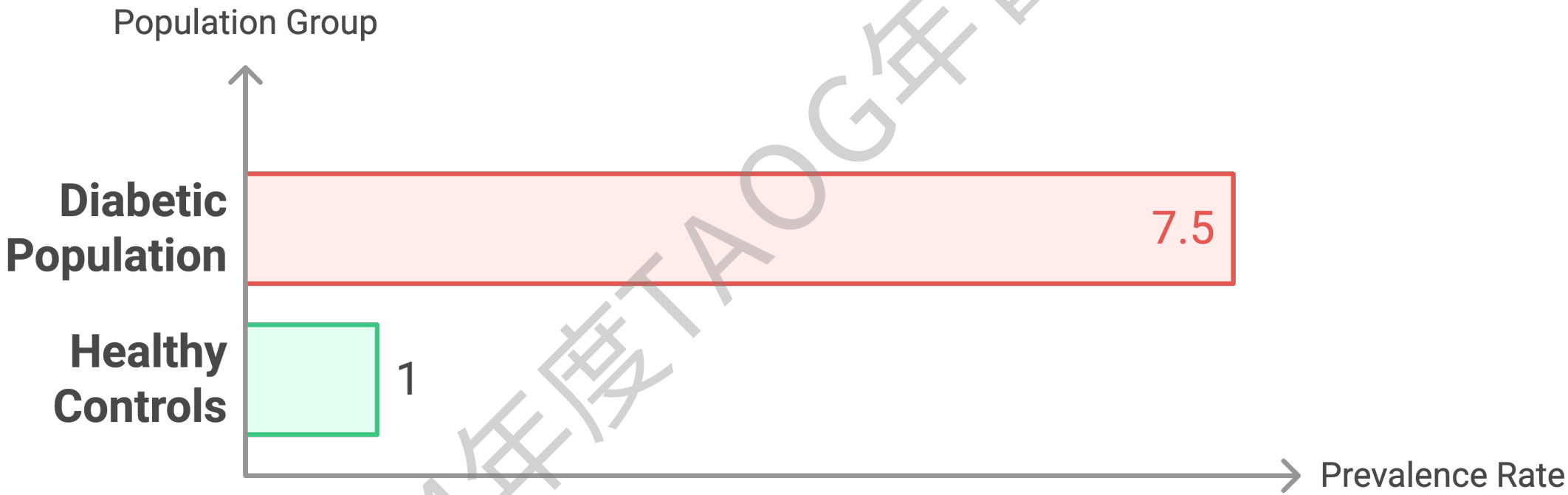
- Type I: 43% - 87% , Type II : 25%
- Commons symptoms:



Kaplan SA, Te AE, Blaivas JG. J Urol. 1995

Diabetic Bladder Dysfunction (DBD)

OAB risk

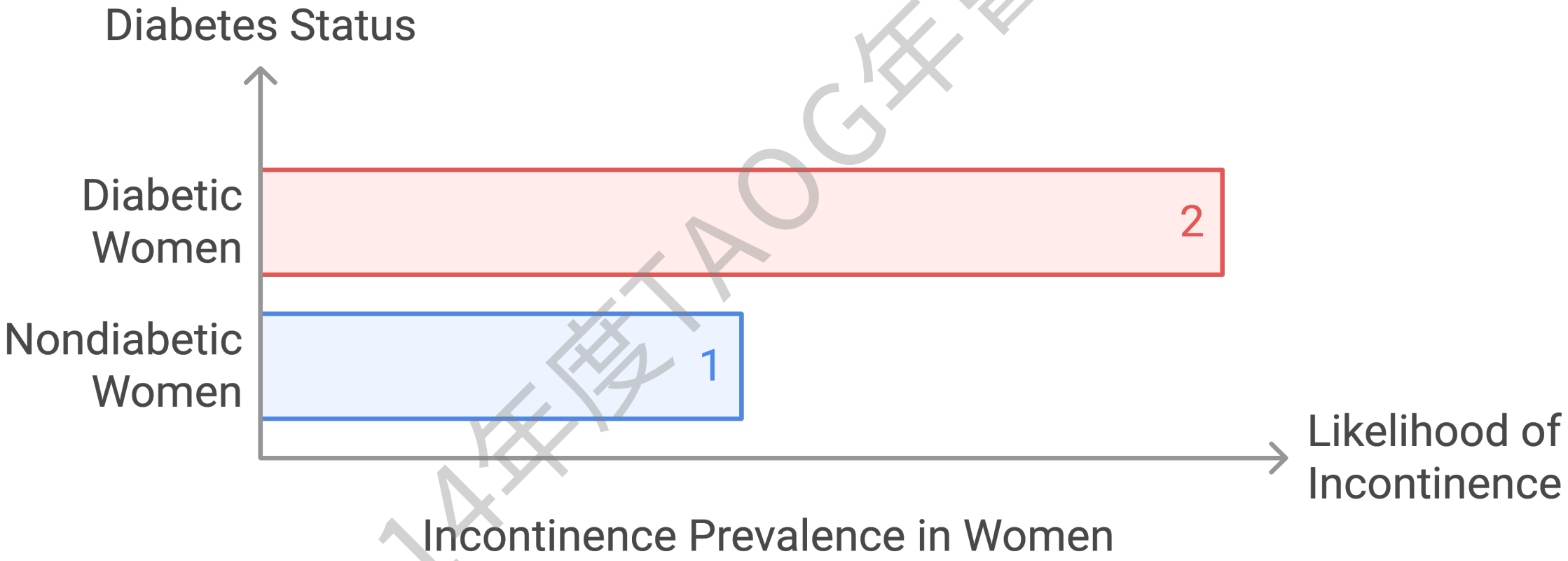


Prevalence of OAB in Diabetic vs. Healthy Individuals

Palleschi G. World J Urol 2013.

Diabetic Bladder Dysfunction (DBD)

Urinary Incontinence



Wang R, Female Pelvic Med Reconstr Surg. 2015.

Diabetic Bladder Dysfunction (DBD)

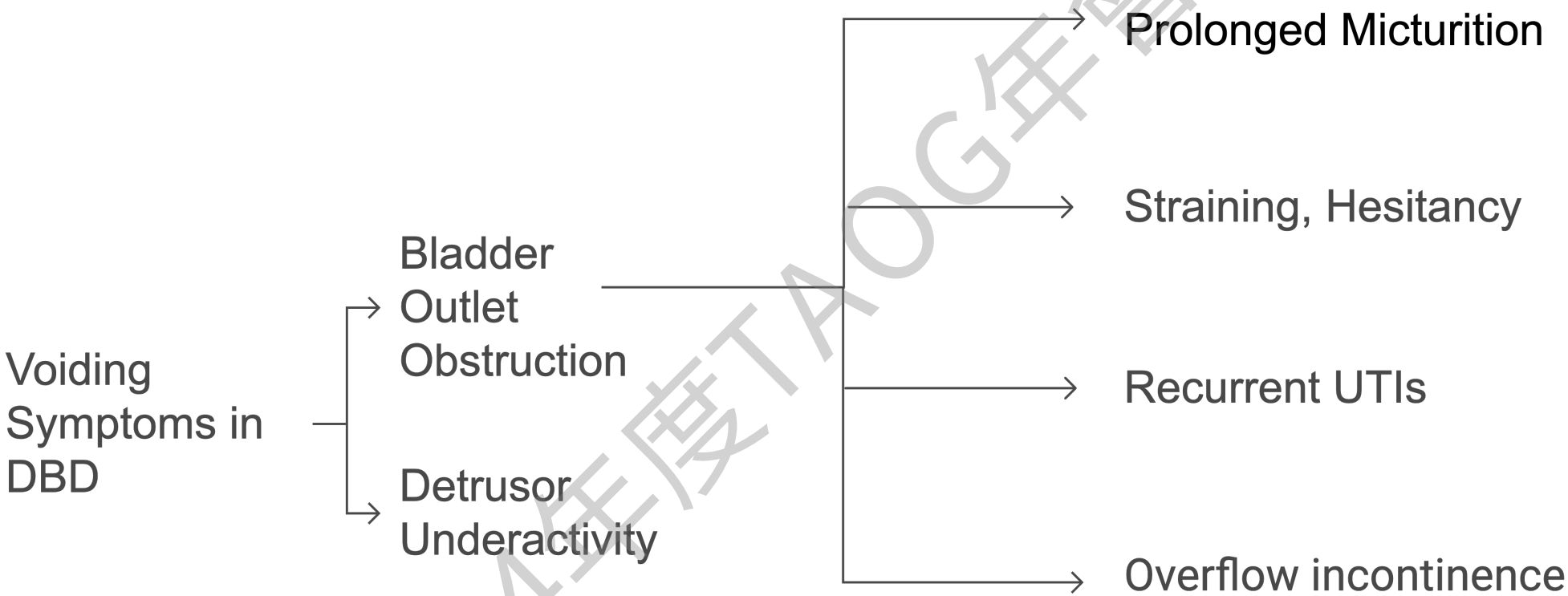
OAB and UI

- OAB symptoms can be severe and impact patients' QOL greatly.
- **OAB symptoms and UI were the most bothersome symptoms of DBD.**
- OAB symptoms are often what drives a diabetic patient to seek medical attention.

Xu D, Health Qual Life Outcomes.2018

Diabetic Bladder Dysfunction (DBD)

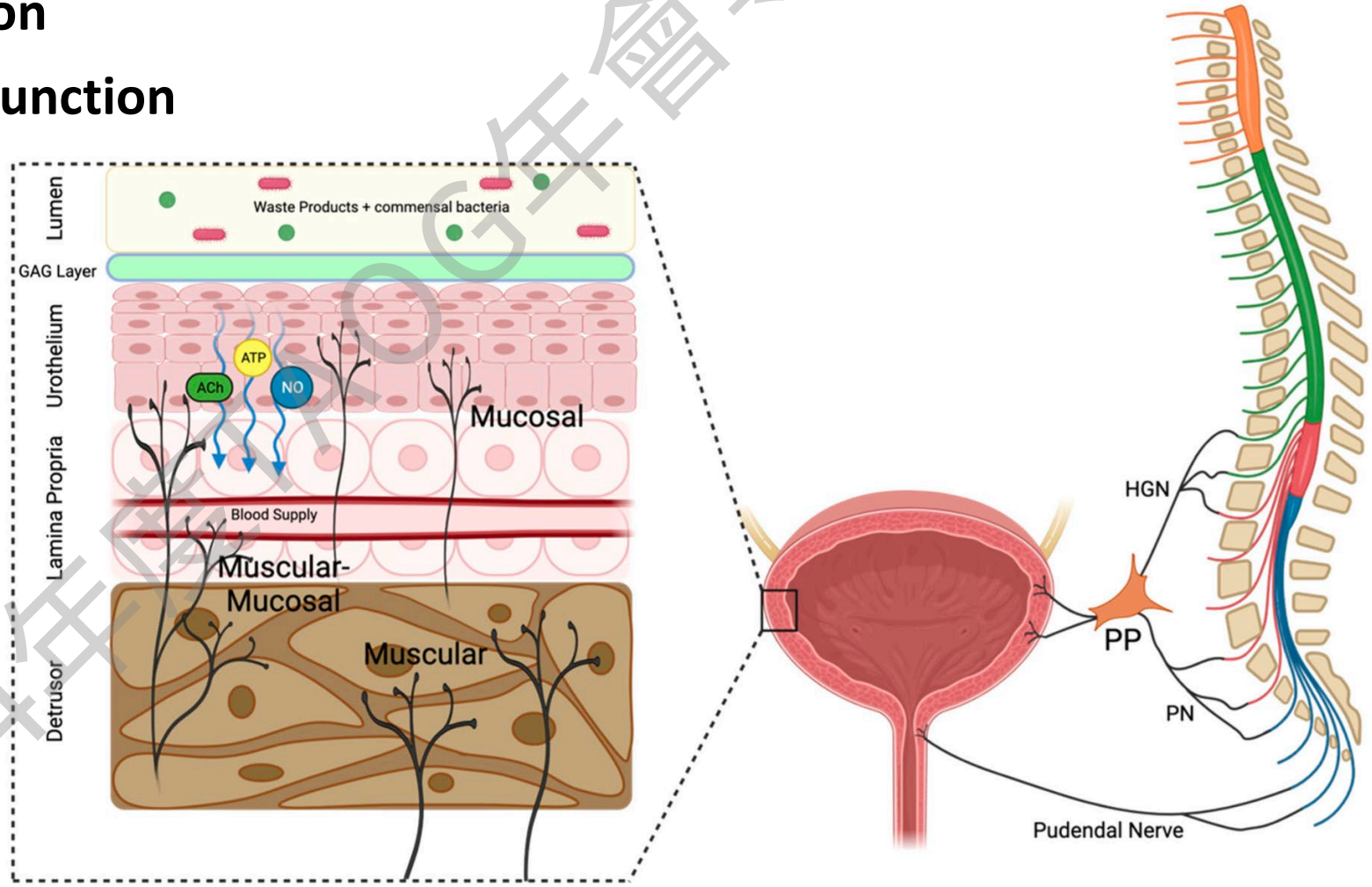
Voiding symptoms



Wittig L, et al. Diabetic bladder dysfunction: a review. Urology. 2019

Main Hypotheses Driving DBD

1. Urothelial Dysfunction
2. Smooth Muscle Dysfunction
3. Neuropathy



Urodynamic Findings

DBD presents diverse urodynamic findings due to its broad spectrum of symptoms and contributing comorbidities (e.g., age, obesity, BPH).

Progressive nature:

1. Initial **storage** changes due to impaired bladder sensation.
2. Development of **voiding dysfunction** from chronic detrusor overdistention.
3. Eventual **decompensation**, leading to reduced bladder contractility.

Urodynamic Findings

Key UDS Findings

- Delayed first sensation of filling
- low detrusor pressure at end-filling
- Detrusor areflexia
- Increased PVR and detrusor decompensation
- Urethral dysfunction and loss of detrusor-sphincter coordination
- Increased bladder outlet resistance or obstruction
- Urinary incontinence

Urodynamic Findings

TABLE 2 Urodynamic parameters for diabetic versus nondiabetic women adjusting for BMI and age.

Variable (standard error)	Diabetic	Nondiabetic	*p* Value
Capacity (mL)	348.5 (15.2)	353.5 (8.37)	0.78
Compliance (mL/cm H_2O)	16.7 (12.7)	36.2 (6.94)	0.18
Bladder voided efficiency	78.3 (2.36)	80.0 (1.36)	0.54
Bladder contractility index	96.8 (4.32)	87.6 (2.38)	0.07
Detrusor overactivity[a]	73 (45.2%)	161 (33.5%)	***0.01***
Pdet (cmH_2O)	26.9 (1.62)	23.9 (0.90)	0.17
Voided volume (mL)	320.7 (25.4)	293.0 (14.5)	0.35
Qmax (mL/s)	13.6 (0.82)	12.6 (0.45)	0.29
PVR (mL)	83.4 (11.4)	80.3 (6.54)	0.82

An analysis of urodynamic parameters in diabetic and nondiabetic women

Ramzy T. Burns MD[1] | Peter J. Arnold MD[1] | Leo Song MD[1] | Kevin L. Moss ASCS[2] | Charles R. Powell MD[1]

652 female patients
152 (23.3%) had diabetes,
average diagnosis of 82mo

diabetic showing higher rates of DO (p = 0.01), particularly associated with increasing BMI (p = 0.03).

Who Should Undergo UDS in Diabetic Patients?

- **Bladder dysfunction**

AUA recommends **PVR + UDS** for individualized treatment

- **Peripheral neuropathy**

High prevalence of bladder dysfunction; UDS aids in early detection.

- **Asymptomatic**

Survey underlying DBD; early UDS may guide management.

- **Diabetic nephropathy**

Proteinuria is linked to high PVR; urinalysis can help identify at-risk patients.

UDS is crucial for early diagnosis, treatment planning, and complication prevention.

Risk Factors for LUTS in Diabetes

Longer disease duration (>10 years)

Hgb A1c >7.5%.

Differences Between DM1 and DM2

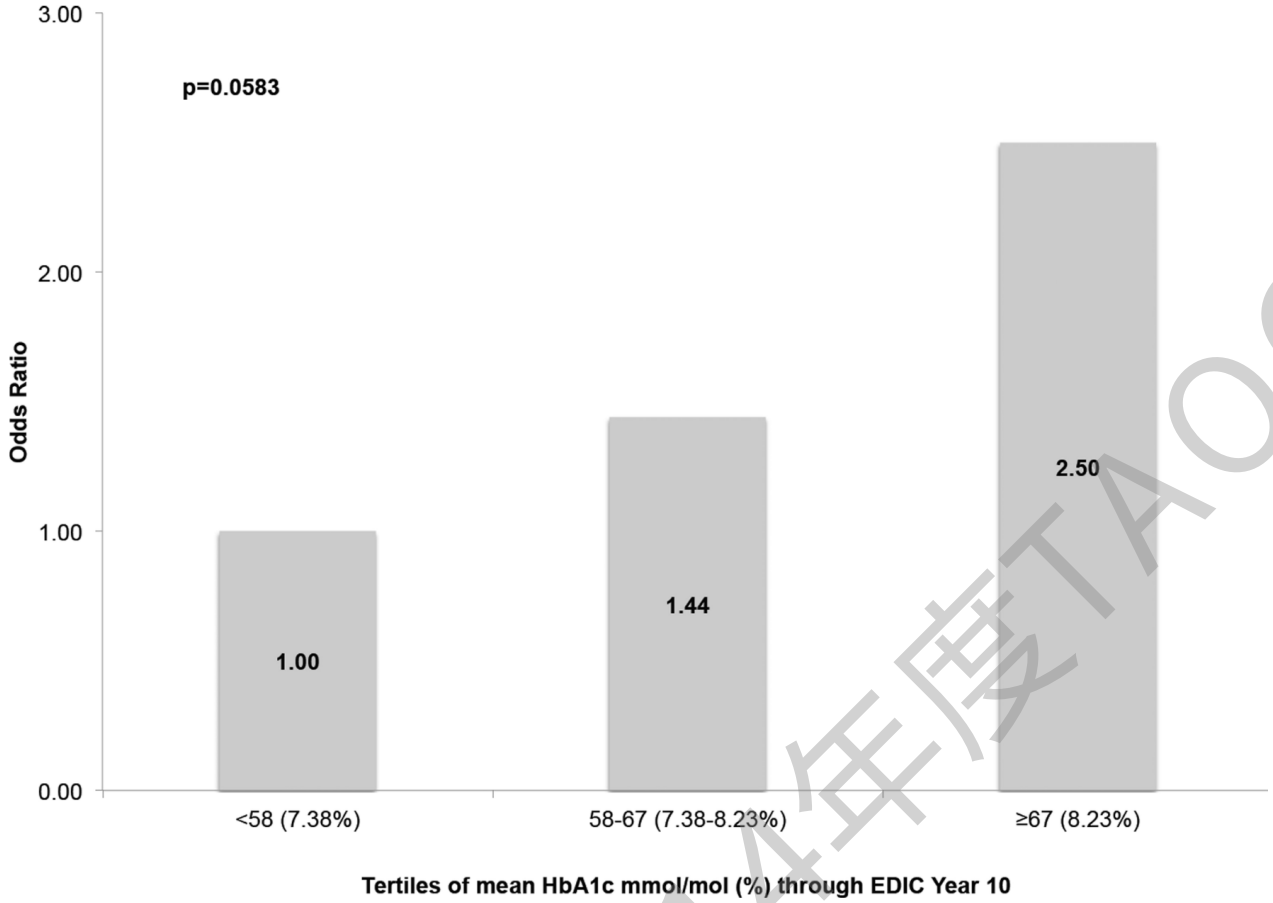
DM1 and Incontinence:

- The EDIC study revealed a 1.41 increase in odds ratio for incontinence for every 1% increase in HbA1c (95% CI 1.07–1.89).
- Associated with impaired sensation and contractility.

DM2 and Incontinence:

- Higher prevalence of incontinence
- Nurse's Health Study (NHS) showed a 20% increased prevalence of urinary incontinence in women with DM2 (OR 1.2, 95% CI 1–1.3).

DM1 and Incontinence



- Epidemiology of Diabetes Interventions and Complications (EDIC) is a longitudinal prospective observational trial
- All subjects were women with DM1 who completed a urology-specific questionnaire after 10 years of involvement and after 17 years.
- 41% increased odds of incident weekly UI associated with per % increase in HbA1c level in women with DM1.

Lifford KL. J Am Geriatr Soc. 2005

DM2 and Incontinence

- **Nurse's Health Study:**
- longitudinal prospective observational studies
- 71,650 nurses , ages 37–79 , from 1976 to 2000.
- completed a mailed questionnaire.

Risk of Weekly Urinary Incontinence by Type 2 Diabetic Status

Incontinence	No Diabetes Mellitus			Diabetes Mellitus	
				RR	
	n	RR	n	Adjusted*	Multivariate†
Prevalent in 1996					
Any‡	13,242	1.0 (reference)	1,044	1.24 (1.14–1.35)	1.28 (1.18–1.39)
Severe§	9,191	1.0 (reference)	821	1.37 (1.25–1.50)	1.42 (1.29–1.56)
Very severe‖	1,378	1.0 (reference)	177	1.75 (1.47–2.08)	1.78 (1.49–2.12)
Incident from 1996 to 2000					
Any‡	2,784	1.0 (reference)	173	1.21 (1.02–1.43)	1.21 (1.02–1.43)
Severe§	1,675	1.0 (reference)	128	1.42 (1.17–1.72)	1.40 (1.15–1.71)
Very severe‖	176	1.0 (reference)	23	1.98 (1.26–3.12)	1.97 (1.24–3.12)

患有糖尿病的女性尿失禁的風險
顯著高於未患糖尿病的女性20%

DM2 and Incontinence

Relative Risk of Developing UI by Duration of DM

		Type 2 Diabetes Mellitus by Duration (Years)						
	No Diabetes Mellitus	<5		5–10		>10		
Incontinence	n	n	Multivariate RR* (95% CI)	n	Multivariate RR* (95% CI)	n	Multivariate RR* (95% CI)	*P*-value†
Prevalent								
Any	13,242	285	1.13 (0.97–1.32)	337	1.36 (1.17–1.57)	422	1.34 (1.18–1.53)	.03
Severe‡	9,191	220	1.24 (1.05–1.47)	274	1.54 (1.32–1.80)	327	1.46 (1.27–1.68)	.04
Very severe§	1,378	37	1.23 (0.86–1.74)	64	2.01 (1.51–2.68)	76	2.04 (1.58–2.63)	<.001
Incident								
Any	2,784	43	0.86 (0.62–1.19)	56	1.29 (0.97–1.72)	74	1.47 (1.15–1.89)	.001
Severe‡	1,675	28	0.86 (0.57–1.28)	44	1.60 (1.16–2.21)	56	1.75 (1.32–2.33)	<.001
Very severe§	176	2	0.51 (0.13–2.10)	10	2.78 (1.42–5.41)	11	2.62 (1.39–4.96)	<.001

尿失禁的風險隨著 DM 的持續時間而增加

Lifford KL. J Am Geriatr Soc. 2005

DM2 and Incontinence

Absolute Effect of DM on Incident Urinary Incontinence

Age	Incontinence		
	Weekly (Any Quantity)	Severe*	Very Severe†
	Risk Difference per 100,000 Participants‡		
≤60	1,239	1,388	359
61–70	1,550	1,860	456
>70	2,085	2,640	844
Attributable risk, %	17.4	28.6	49.2

透過預防糖尿病
可以避免 17% 的任何程度的失禁
50% 的嚴重失禁

Lifford KL. J Am Geriatr Soc. 2005

Clinical Evaluation for DBD

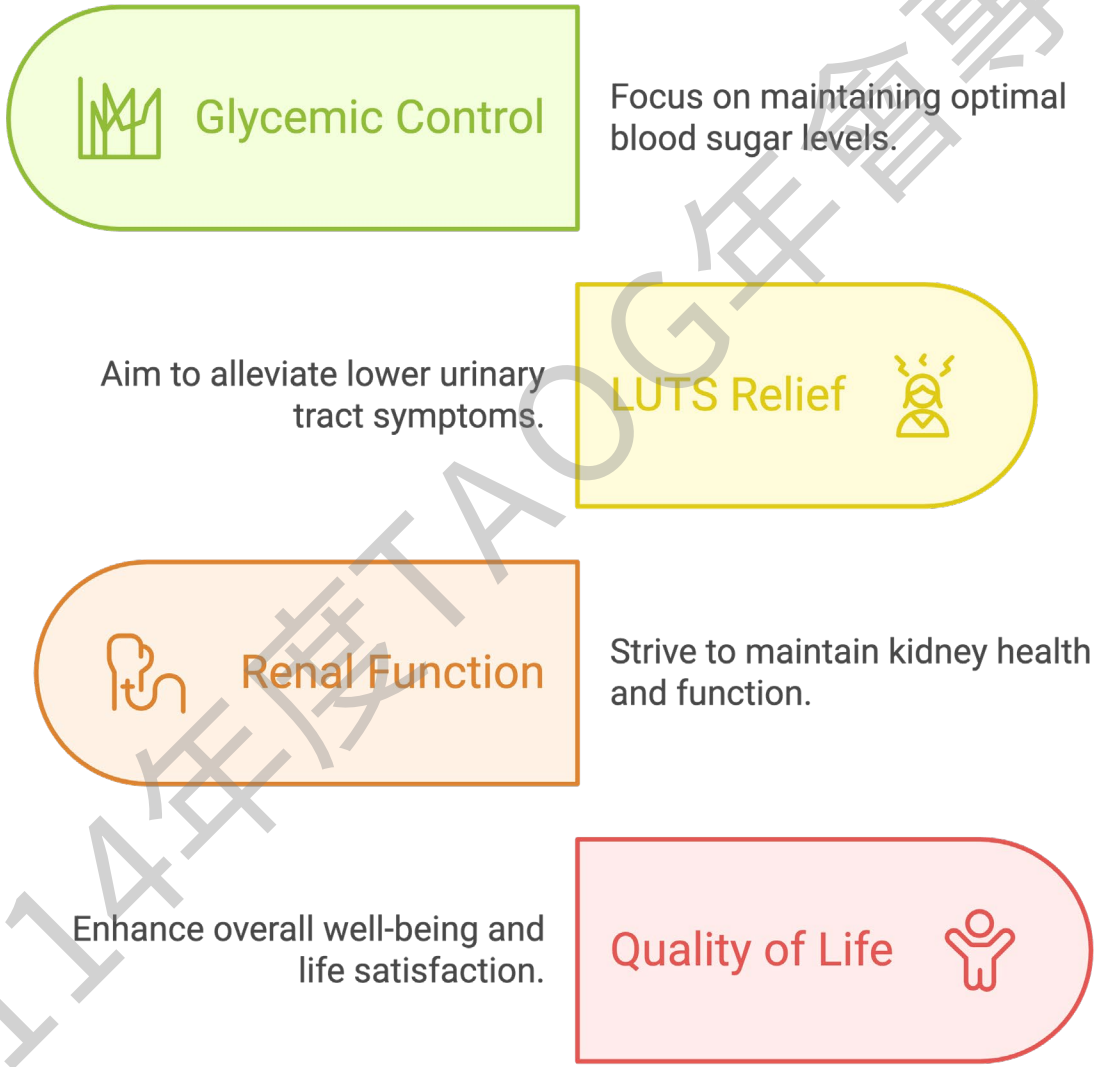
- **Digital Rectal Examination** (in males):
  - Evaluates prostate size and sphincter tone
- **Gynecological Examination** (in females):
  - Assesses for **pelvic organ prolapse (POP)**, which can contribute to voiding dysfunction.

Clinical Evaluation for DBD

Differential diagnosis:

- BPH or prostate cancer
- UTIs
- Pelvic muscle weakness
- neurological conditions
  - spinal cord injury
  - cerebrovascular events

Management Goals for DBD



Lifestyle & Behavioral Therapy

1.Optimize Glycemic Control

- Keep HbA1c levels <7.5% to slow down LUTS progression

2.Lifestyle Modifications

- 5-10% weight loss reduces incontinence episodes by 60%
- Manage fluid intake

3. Bladder Training & Crede's maneuver

4. Pelvic Floor Exercises

5. Monitor Symptoms with Voiding Diaries

Pharmacological Therapy

For OAB:

- Anticholinergics
- β3 Agonist

Pharmacological Therapy

For Voiding Dysfunction & Retention:

- No highly effective pharmacological agents exist for detrusor underactivity.
- Parasympathomimetic drugs (bethanechol):
  - Historically used to stimulate muscarinic receptors
  - Limited efficacy in improving bladder contractility
  - severe side effects: flushing, salivation, GI distress, cardiac arrest
- Rarely recommended due to poor risk-benefit profile

Surgical Treatment

For OAB Symptoms:

- Botulinum Toxin Injections
- PTNS (Percutaneous Tibial Nerve Stimulation):

  Over 90% success rate in non-diabetic OAB, but limited data in diabetic patients
- Sacral Neuromodulation (SNM)

For SUI: Midurethral Sling

For Severe Voiding Dysfunction (High PVR):

- Clean Intermittent Catheterization (CIC) → managing underactive bladder

Take Home Message

1. Global Impact of Diabetes:

- Diabetes is a growing problem with high societal costs.
- 1 in 10 adults has diabetes.

2. Diabetic Bladder Dysfunction (DBD):

- Involves autonomic and sensory nerve fibers.
- Key characteristics: decreased bladder sensation, increased compliance and capacity, impaired detrusor contractility.

Take Home Message

3. Lifestyle and Behavioral Therapy:

- Optimize glycemic control, weight loss, fluid intake management, bladder training, and pelvic floor exercises.

4. Pharmacological Therapy:

- For OAB: Anticholinergics and β3 agonists.
- For voiding dysfunction : Parasympathomimetic drugs had limited benefits.

Take Home Message

5. Surgical Treatment:

- Botulinum toxin injections
- PTNS, sacral neuromodulation
- midurethral sling
- clean intermittent catheterization

6. Key Takeaways:

- DBD affects a significant percentage of diabetic patients.
- Early intervention and personalized treatment are essential for optimal management

THANK YOU FOR YOUR TIME

HSIAOYUN HSIEH

urogyn.drhsieh@gmail.com