The risks of interstitial cystitis/bladder pain syndrome (IC/BPS) among patients with systemic lupus erythematosus

Jen-Yu Wen[1], Chung-Han Ho[2], Shih-Feng Weng[2], Ming-Ping Wu [1,3]

Division of Urogynecology and Pelvic Floor Reconstruction, **Department of Obstetrics and Gynecology, Chi Mei Foundation, Hospital, Tainan, Taiwan** [1]

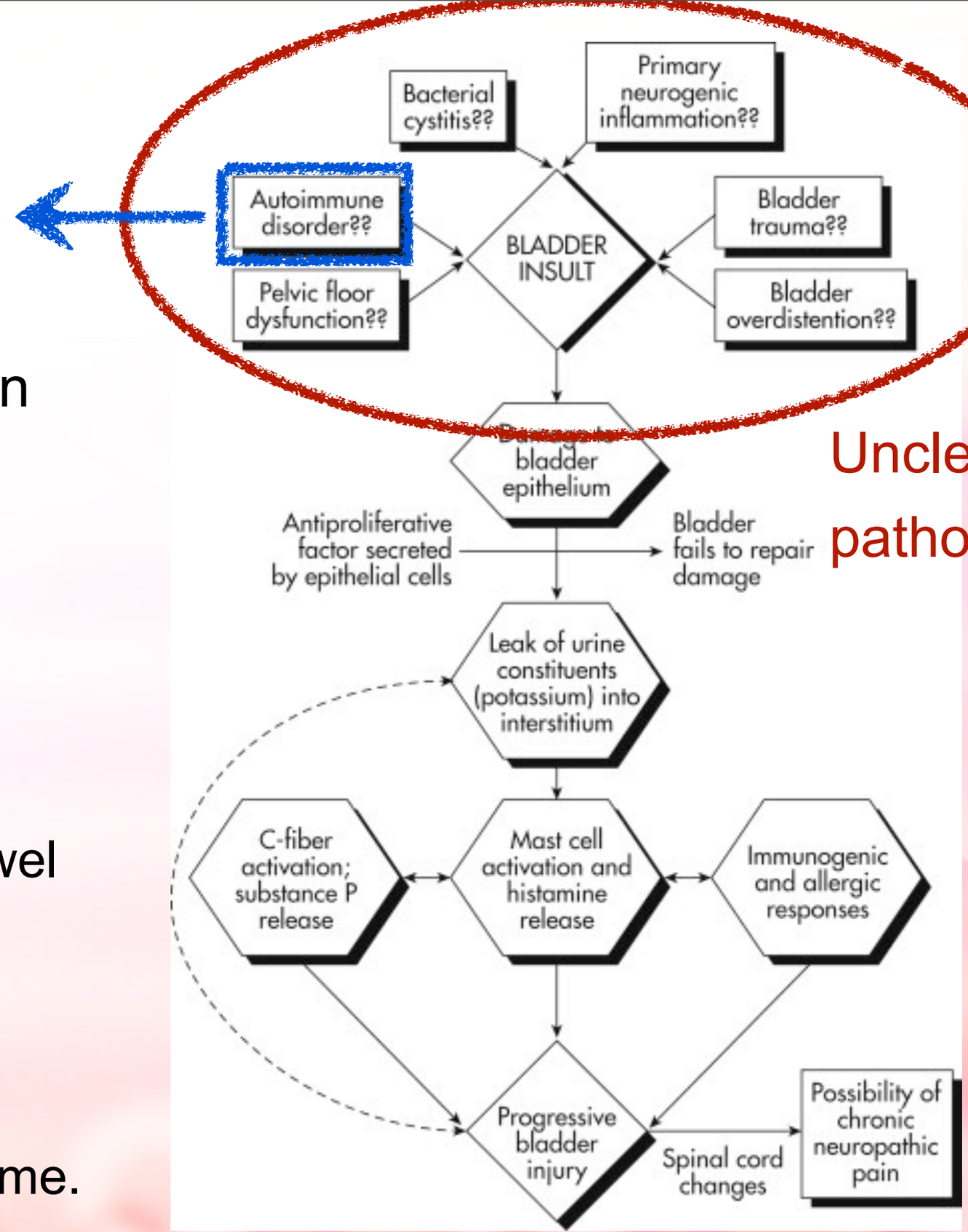
Department of Medical Research, Chi Mei Medical Center, Tainan, Taiwan [2]

Department of Obstetrics and Gynecology, College of Medicine, Taipei Medical University, Taipei, Taiwan [3]

溫仁育[1] 何宗翰[2] 翁世峰[2] 吳銘斌[1, 3]

奇美財團法人附設醫學中心婦產部[1] 奇美醫學中心醫學研究部[2] 台北醫學大學醫學院婦產部[3]

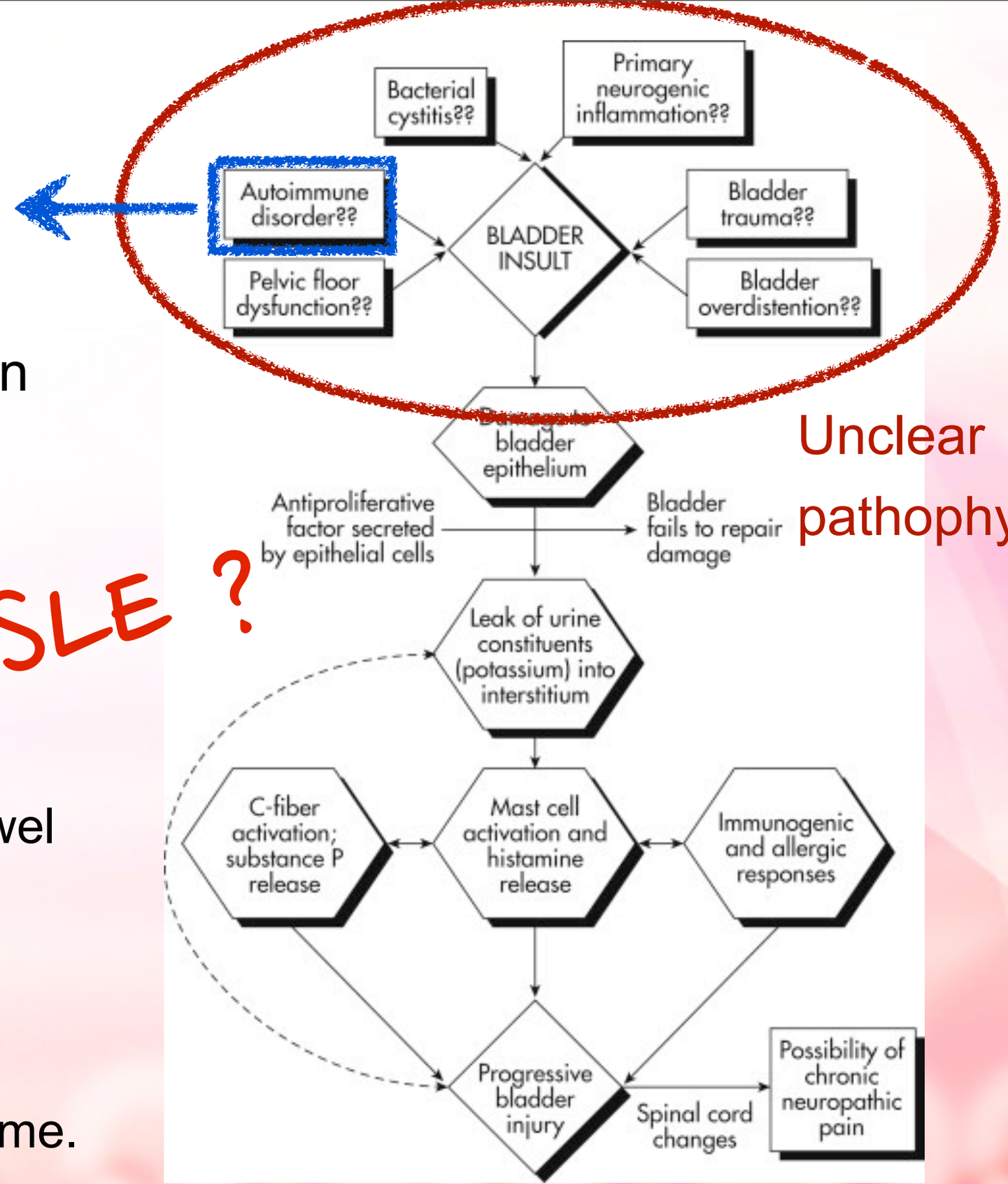
- Autoimmune character
  - clinical association with autoimmune diseases
    - Allergies
    - irritable bowel syndrome
    - fibromyalgia
    - inflammatory bowel disease (Crohn's disease and ulcerative colitis)
    - RA
    - Sjögren's syndrome.



Unclear pathophysiology

Hypothesis for etiologic cascade of painful bladder syndrome/interstitial cystitis.
(From Wein AJ: Painful bladder syndrome/interstitial cystitis and related disorders. In Wein AJ et al (eds): *Campbell-Walsh urology* , 11th ed, Philadelphia, 2007, Elsevier.)

- Autoimmune character
  - clinical association with autoimmune diseases
    - Allergies
    - irritable bowel syndrome
    - fibromyalgia
    - inflammatory bowel disease (Crohn's disease and ulcerative colitis)
    - RA
    - Sjögren's syndrome.



SLE ?

Unclear pathophysiology

Hypothesis for etiologic cascade of painful bladder syndrome/interstitial cystitis.
(From Wein AJ: Painful bladder syndrome/interstitial cystitis and related disorders. In Wein AJ et al (eds): *Campbell-Walsh urology* , 11th ed, Philadelphia, 2007, Elsevier.)

Aim

- To investigate the incidence of IC/BPS among patients with SLE in Taiwan

- Case-control retrospective cohort study
- National Health Insurance Research Database (NHIRD) as data source

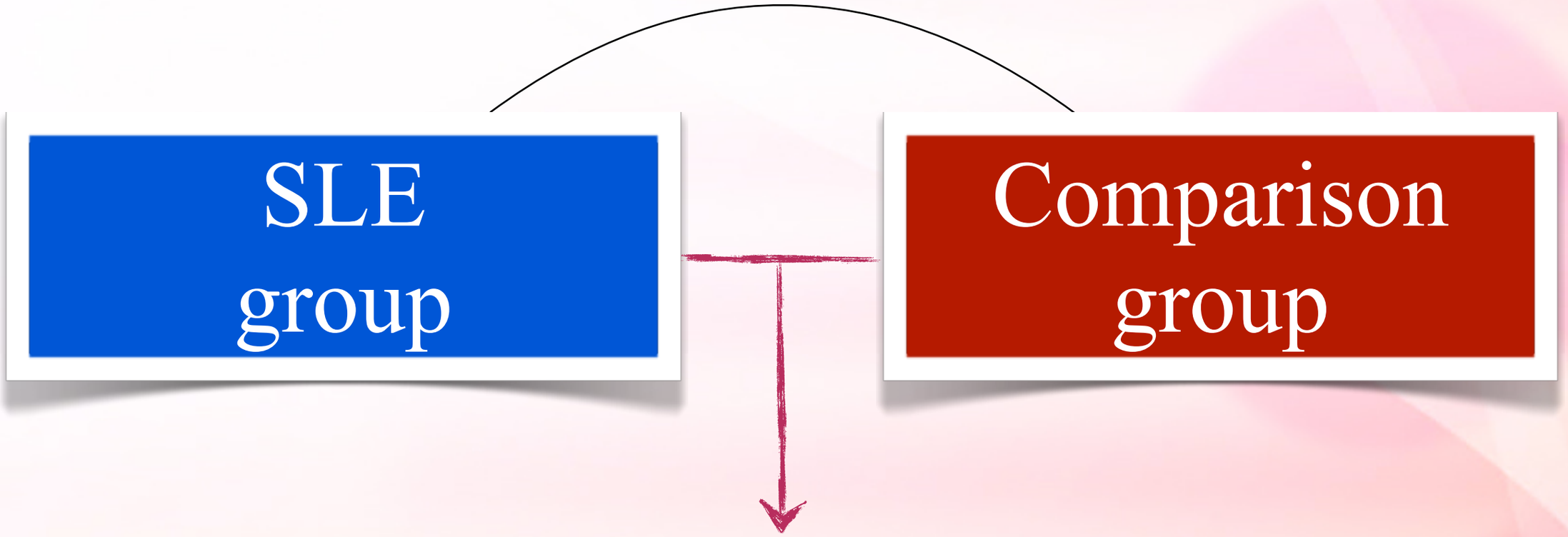
SLE group

- Women ≥ 18 year-old
- 2001 ~2008
- First Diagnosis of SLE (ICD-9-CM code 710.0)
- possessed IC card for severe illness approved by NHI

Comparison group

- Randomly selected from the NHIRD at the year of 2000
- matching with gender and age (±30 days)
- SLE: non-SLE=1:8

- Case-control retrospective cohort study
- National Health Insurance Research Database (NHIRD) as data source

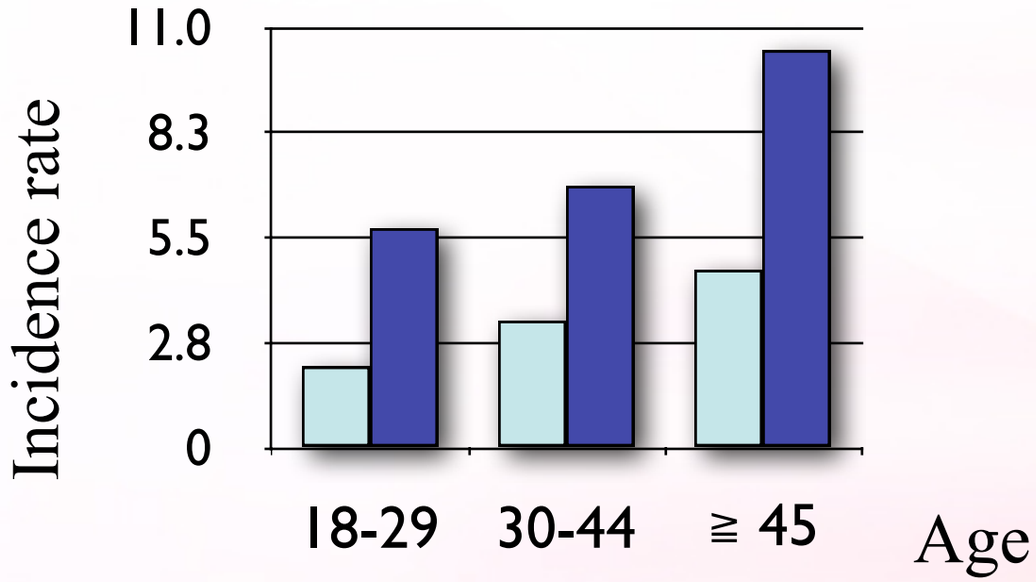


Endpoint : being diagnosed as BPS/IC with the ICD-9 CM code 591.1

Follow-up until the **end of 2011**

Result

Significantly higher incidence rate of BPS/IC in the SLE group



PY= person-year
IR= incidence Rate: per 10000 person-years
IRR= incidence rate ratio

	SLE				Non-SLE					
	N	IC	PY	IR	N	IC	PY	IR	IRR (95% CI)	P value
All	**7240**	**36**	**48414.80**	**7.44**	**57920**	**136**	**413858.95**	**3.29**	**2.26(1.57-3.27)**	**<0.0001**
Age										
18-29	2520	10	17427.41	5.74	20171	31	145919.83	2.12	2.70(1.32-5.51)	0.0063
30-44	2583	12	17521.46	6.85	20672	49	147633.75	3.32	2.06(1.10-3.88)	0.0245
≧ 45	2137	14	13465.94	10.40	17077	56	120305.36	4.65	2.23(1.24-4.01)	0.0072

Table 2. Risk of IC for SLE Patients and comparison group by age stratification

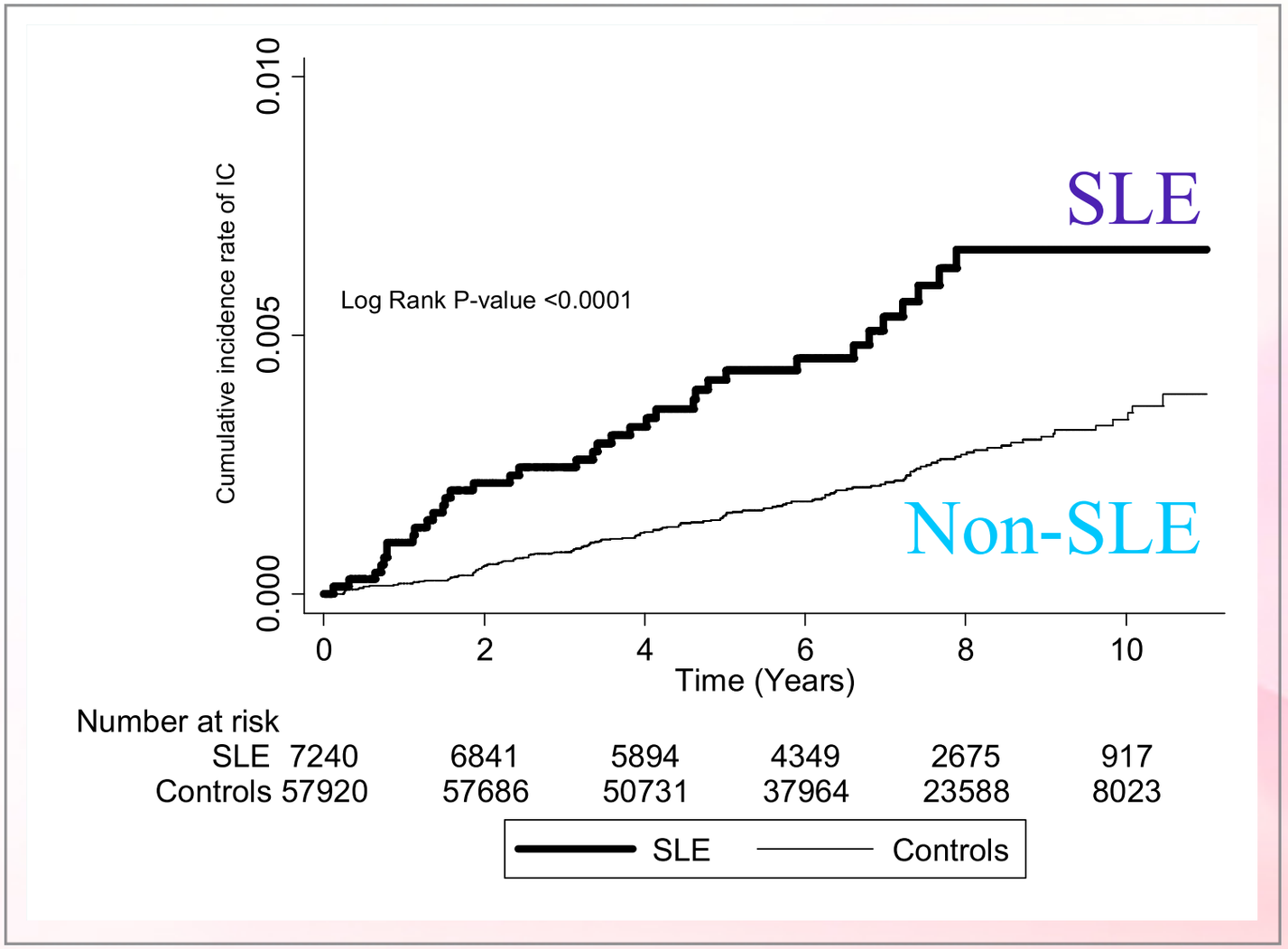
Table 3. Crude and Adjusted hazard ratios of Cox proportional hazard regressions and 95% confidence interval for the development of IC/BPS during the follow-up period for study cohort.

Cohort	Crude HR (95% CI)	Adjusted HR (95% CI)
SLE	**2.268*(1.571-3.275)**	**2.452*(1.676-3.587)**
Age (years)		
18-29	1.000	1.000
30-44	1.474(0.992-2.190)	1.479(0.995-2.197)
≧45	**2.086*(1.419-3.068)**	**2.071*(1.370-3.132)**
DM	1.649(0.811-3.353)	1.218(0.563-2.633)
HTN	1.582(0.958-2.610)	1.053(0.599-1.853)
Renal	1.242(0.461-3.347)	0.628(0.224-1.765)
Hyperlipidemia	1.627(0.720-3.673)	1.082(0.451-2.5933

*p-value <0.05
adjusted by age, Comorbidities, geographic region, and income.

SLE group showed significantly increased incidence of BPS/IC **after adjustment.**

Figure 1. Cumulative incidence rate of BPS in subjects with and without SLE



Kaplan-Meier survival curves show that the SLE group was more likely to develop BPS/IC than the control group with significant more cumulative IRR ($p<0.0001$).

Summary

- The first population-based retrospective cohort study investigating the incidence of BPS among patient with SLE.

- Female with SLE was associated with increased risk of developing BPS/IC (aHR 2.45 in SLE, 95% CI= 1..67~3.58)

Thank you

Table 3. Crude and Adjusted hazard ratios of Cox proportional hazard regressions and 95% confidence interval for the development of IC during the follow-up period for study cohort.

Cohort	Crude HR (95% CI)	Adjusted HR (95% CI)
Age (years)		
18-29	1.000	1.000
30-44	1.474(0.992-2.190)	1.479(0.995-2.197)
≧45	**2.086*(1.419-3.068)**	**2.071*(1.370-3.132)**

*p-value <0.05
adjusted by comorbidities(DM,HTN,Renal disease, Hyderlipedemia), geographic region, and income.

Age≥45 were significantly associated with increased incidence of BPS/IC, either before or after adjustment.

BPS/IC and SLE

- Previous studies
  - –Case reports
  - –Alagiri et al, 1997
    - A questionnaire-based study showed that IC patients, when compared with the general population, were 30– 50 times more likely to have systemic lupus erythematosus.

Urology. 1997 May;49(5A Suppl):52-7

  - –Keller et al, 2012.
    - The study included 9269 subjects with BPS/IC and 46 345 randomly selected comparison subjects.
      - –to calculate the odds ratio of 32 medical comorbidities
      - –higher odds of SLE in IC group (OR: 2.57)

BJU Int. 2012 Dec;110(11 Pt C):E903-9.

Thank you for your listening

Jen-Yu Wen[1], Chung-Han Ho[2], Shih-Feng Weng[2], Ming-Ping Wu [1,3]

Division of Urogynecology and Pelvic Floor Reconstruction, Department of Obstetrics and Gynecology, Chi Mei Foundation, Hospital, Tainan, Taiwan [1]

Department of Medical Research, Chi Mei Medical Center, Tainan, Taiwan [2]

Department of Obstetrics and Gynecology, College of Medicine, Taipei Medical University, Taipei, Taiwan [3]

- Substantial evidence pointing to the autoimmune character of BPS/IC.
  - Immune competent cells such as lymphocytes, plasma cells, and mast cells have been shown to accumulate in the detrusor muscle and lamina propria of individuals with BPS/IC.
  - A number of studies have shown that autoantibodies are present in patients with BPS/IC.
  - Various antinuclear antibodies (ANA) have been demonstrated in 36% of patients.
  - Antibodies have also been found that recognize urinary epithelial cells in the urine and serum of IC patients.
- But, there is no evidence to date indicating whether autoimmune reactivity has either a primary or secondary role in the pathophysiology of BPS/IC, and there is therefore no confirmation for BPS/IC as an autoimmune disease.

BPS/IC and other autoimmune diseases

- Higher prevalence of several generalized autoimmune diseases among pt with BPS/IC
  - –Systemic lupus erythematosus
  - –RA
  - –Sjo¨gren’s syndrome
  - –inflammatory bowel disease (Crohn's disease and ulcerative colitis)

Strength

- A national-based population cohort study
- First study conducted investigating the incidence and risk of BPS/IC among patient with SLE.

Limitations

- Both the SLE and IC/BPS diagnoses relied on administrative claims data reported by physicians and hospitals.
  - These data may be less accurate than diagnoses made according to standardized criteria.
- Some patient information were not available through the administrative dataset.
  - tobacco use
  - family history
  - alcohol and betel quid consumption
  - dietary habits
  - body mass index

Limitations

- Some patient information were not available through the administrative dataset.
  - –tobacco use
  - –family history
  - –alcohol and betel quid consumption
  - –dietary habits
  - –body mass index

Limitations

- Surveillance bias.
  - –As SLE patients have more outpatient visits than healthy controls, it is possible that they were more likely to be diagnosed with BPS/IC purely on account of their increased exposure to the medical community.

- adjusted comorbidities 太少？
- 沒有考慮其他autoimmune diseases 加入變數校正

- Roberts et al, Incidence of physician-diagnosed interstitial cystitis in Olmsted County: a community-based study.
  "Median (range) age at initial diagnosis was 44.5 (27-76) years in women"

BJU Int. 2003 Feb;91(3):181-5.

- Jones et al. reported a higher prevalence in those aged ≥ 50 years than in the total population

Jones CA, Harris MA, Nyberg L. Prevalence of interstitial cystitis in the United States. *J Urol* 1994; **151**: 423A