6B – Disease and Longevity

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2020 Living to 100 Symposium

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UNDERSTANDING MULTIMORBIDITIES

6B – Disease and Longevity

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UNDERSTANDING MULTIMORBIDITIES
What I'll cover

- What are multimorbidities
- Prevalence
- Mortality and health consequences
- Special case: cardiometabolic multimorbidities
- Effect on healthcare
- Conclusions

What are multimorbidities

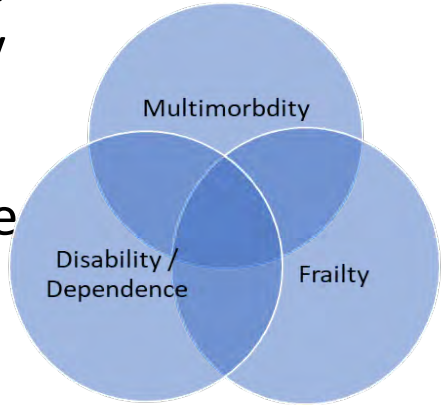
- Multimorbidities
  - Simultaneous existence of multiple (at least two) adverse health conditions
  - The total health effect can differ from a separate assessment of the individual conditions
- In contrast, comorbidities
  - Presence of co-existing or additional condition(s) with reference to an initial diagnosis or with reference to an index condition that is the subject of study
  - An example is a primary diagnosis of cardiovascular disease, with accompanying hypertension and high cholesterol risk factors

Sources

- Multiple concurrent conditions/diseases can emerge for several reasons, including:
  - random chance, especially where two diseases are common in a population
  - two diseases that are part of the same continuum
  - two diseases that share a common risk factor
  - where the presence of one disease increases the risk of a second disease
  - two diseases where one disease causes the second disease
- Thus, the conditions can be, but are not necessarily, related

Related concepts

- Frailty
  - Can consist of at least 3 of 5 elements: weakness, lack of endurance, unintentional weight loss, self-reported exhaustion, and lack of physical activity
- Disability/dependence
  - The extent a person cannot perform one or more activities, either relating to daily living or job performance if for an occupational-related purpose



Prevalence

- Problems in assessing multimorbidities
  - Inconsistent categories
  - Dearth of studies
- Factors repeatedly associated with the extent and effects of multimorbidity
  - Age, sex, and socioeconomic status

The Netherlands

Ages	At least 3 chronic conditions	At least 4 chronic conditions
45-64	16%	7%
65-74	47	30
75+	73	55

Uijen and van de Lisdonk (2008)

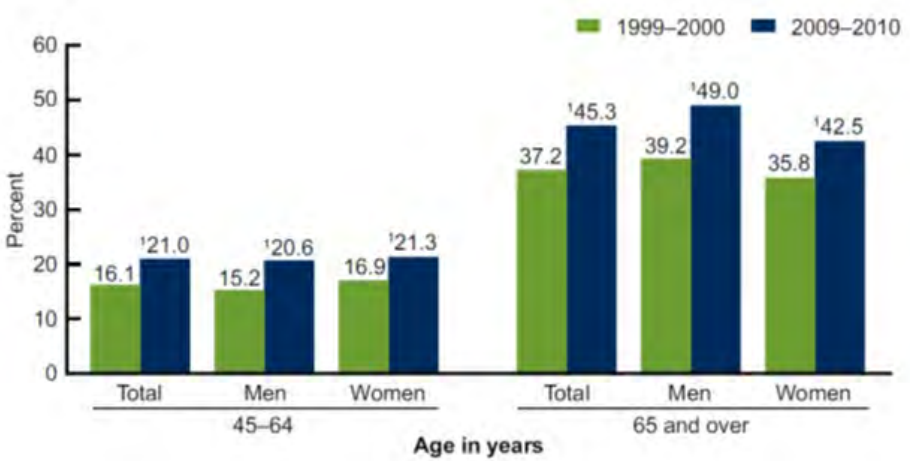
Canada

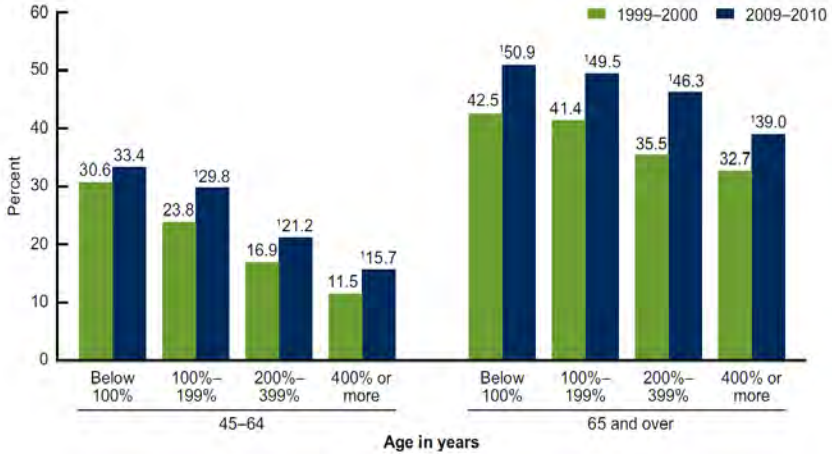
Age categories	2+ conditions		5+ conditions	
	2003	2009	2003	2009
0-17	1.4%	2.2%	0.0%	0.0%
18-44	7.4	10.6	0.05	0.1
45-54	20.4	27.4	0.5	1.0
55-64	35.3	46.6	1.8	3.5
65-74	53.6	66.4	5.1	9.2
75-89	68.3	80.9	11.0	20.9
90+	74.6	83.2	14.8	27.8

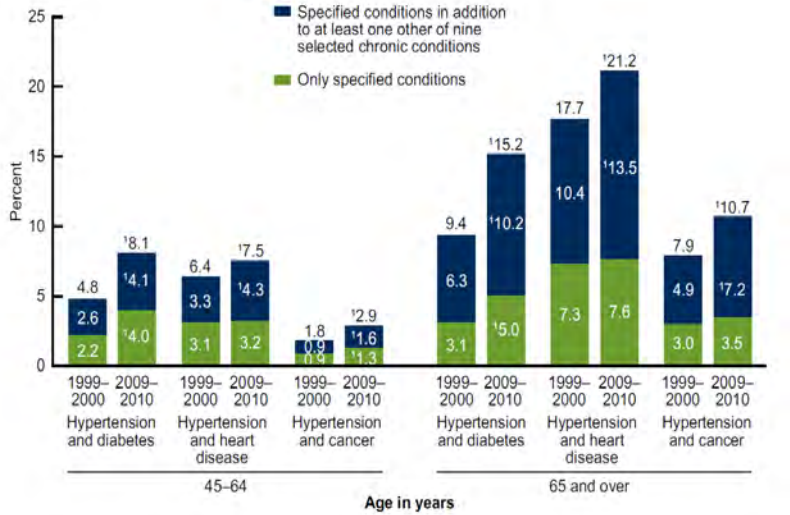
Prefayo et al. (2015)

Prevalence United States

Illustrative of age, sex, % of poverty level and conditions



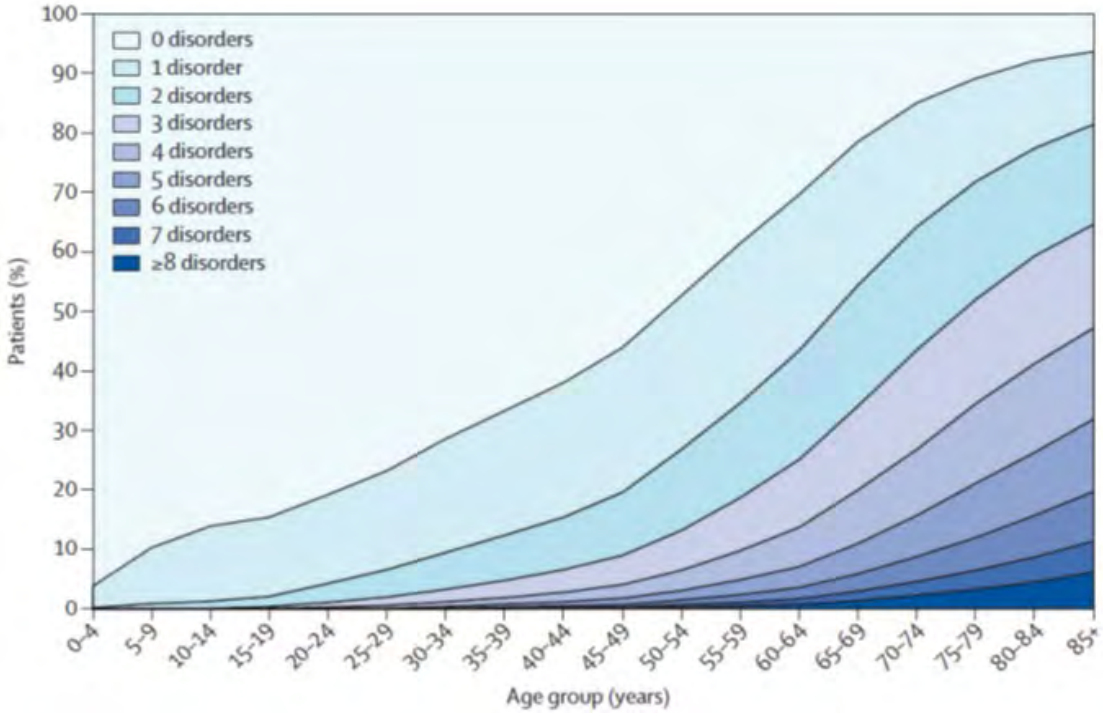




Source: CDC/NCHS. National Health Interview Survey

Prevalence
Scotland – 2007

Pattern of age and number of morbidities



Barnett et al. (2012)

Consequences

- Can affect a person's quality of life, ability to work and employability, disability, and mortality
- Especially important when the causes and consequences of multiple conditions are interrelated, with possible exacerbation of adverse health and living consequences
- Many health care systems are structurally geared around individual acute conditions, rather than multiple acute or especially single or multiple long-term chronic conditions
- Complexities and support needs of multiple adverse health conditions can contribute to poorer overall health outcomes

Consequences

- Studies have reported inconsistent results involving the relation between multimorbidities and mortality, sometimes with an increasing number of conditions found to modify the risk of expected death
- Comparisons with other or previous studies can be difficult because of limited duration of follow-up, the set of conditions, and the age range considered
- If the effect of one mortality driver is reduced or eliminated, survivors may be more susceptible to other existing or future conditions
  - Possibly due to an impaired immune system, increased susceptibility to other conditions or the cumulative adverse effects of other conditions
- Some studies have found that other factors, such as functional decline, frailty, or disability can have a greater effect than multimorbidities
- Several measurement systems have been used, ranging from the simple such as number of conditions, to types of drugs taken or severity of each condition

Frailty and multimorbidity United Kingdom

Number of chronic conditions	Pre-frail to non-frail	Frail to non-frail
0	1.00	1.00
1	1.32	2.27
2	1.72	5.12
3	2.25	10.40
4+	3.31	27.10

	Compared to non-pre-frail and non-frail			
	Pre-frail		Frail	
Ages / sex	Males	Females	Males	Females
37-45	1.36	0.87	2.70	1.42
45-55	1.51	1.28	2.41	2.38
55-65	1.40	1.37	2.52	2.20
65-73	1.45	1.50	2.42	2.53

In this study, degree of frailty and interaction between frailty and multimorbidities can be important, while gender and even age in this age range is not as significant

Source: Hanlon et al. (2018), U.K. Biobank data – between about 2008 to 2015

Multimorbidities, frailty and disability Iceland

In a study of those with an average age of 76.4, adverse health risks associated with frailty were primarily driven by increased disease burden (multimorbidities) and disability

	Mortality		Nursing home admissions	
	Age/Sex adjusted	**Further adjusted***	**Age/Sex adjusted**	**Further adjusted***
Frail only	1.13	1.01	1.24	1.40
Frail plus disability	2.80	2.00	1.14	1.20
Frail plus multimorbidities	2.10	1.47	2.10	1.47
Frail plus disability and multimorbidities	2.65	1.45	2.37	1.42

*Source: Aarts et al. (2015). *Adjusted for age, sex, educational level, smoking, alcohol, living arrangements, disability and depression symptoms*

Projection of U.K. prevalence

- Kingston et al. (2018)* estimated that, between 2015 and 2035, multimorbidity prevalence in the United Kingdom will significantly increase
  - Proportion of those with at least 4 diseases will almost double (2015:9.8%; 2035:17.0%)
  - 2/3rds of those with at least 4 diseases will suffer from a mental health condition (dementia, depression, or cognitive impairment with no dementia)
  - Multimorbidity prevalence in incoming cohorts aged 65–74 years will rise (2015:45.7%; 2035:52.8%)
- Gain in years lived with 2+ conditions is equally a result of longer survival with and increased prevalence of multimorbidity, while most gains in the life expectancy (males 3.6 years; females 2.9 years) will be spent with at least 4 diseases (males: 2.4 years, 65.9%; females: 2.5 years, 85.2%)
- Thus, a longer period of time with multimorbidity, partly due to younger cohorts with a higher prevalence of obesity, which also contributes to increased multimorbidity
- Leading disease prevalence in 2015 and projected in 2035
  - arthritis – 48.6% and 62.6%
  - hypertension – 49.0% and 55.9%
  - respiratory disease – 18.6% and 24.4%
  - cancer – 12.6% and 23.7%
  - diabetes – 14.7% and 21.6%
  - cardiovascular heart disease – 18.3% and 15.0%
  - hearing – 12.4% and 12.5%
  - dementia – 6.8% and 8.5%

* Based on U.K. Biobank data (300,000)

Cardiometabolic multimorbidities

- An especially important combination
- Usually consists of at least two of the following
  - Type 2 diabetes, coronary heart disease, and stroke
- Each combination has been associated with more than an additive mortality risk

Cardiometabolic multimorbidities Pooling of 16 U.S./European studies*

- Risk of developing cardiometabolic multimorbidity by those overweight was twice as high, 4.5 times for individuals with class I obesity, and 14.5 times higher for those with class II or III obesity combined
- Those with class II or III obesity were 2.2 times more likely to experience vascular disease only (coronary heart disease or stroke), 12.0 times for vascular disease followed by diabetes, 18.6 times for diabetes only, and 29.8 times for diabetes followed by vascular disease
  - These associations held for both males and females, white and non-white, younger and older, and were not attributable to lifestyle risk factors such as physical activity, smoking, or alcohol consumption
- Suggests that the primary focus of addressing multimorbidities should be to reduce the number or severity of cardiometabolic risk factors

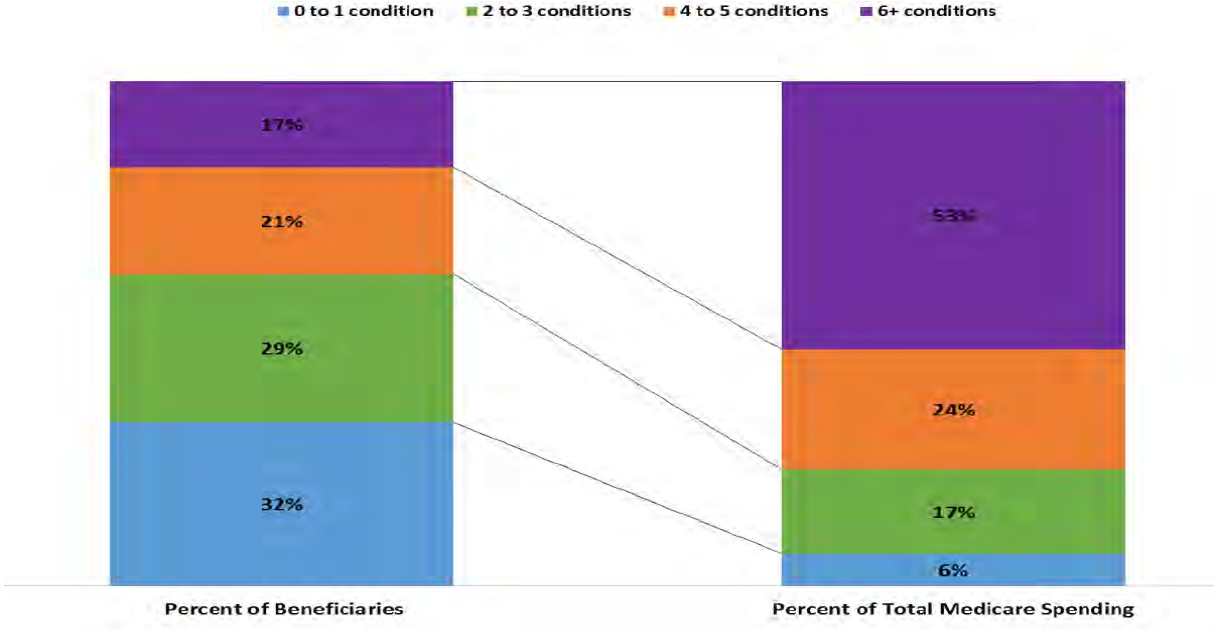
*Kivimäki et al. (2017)

Effect on health

- A focus on one stage of the health trajectory can overlook the changing role of applicable risk factors in the development, progression, and outcome of a set of cardiometabolic (or other) multimorbidities
- The existence of multimorbidities can significantly affect mortality and morbidity, sometimes more than multiplicatively
- In the United States, those in their 60s take an average of 15 prescription drugs a year to combat multimorbidities
  - It may difficult to avoid side-effect from these multimedicine regimes

Health care spending – U.S. Medicare

- 80% of Medicare funds are spent on patients with 4+ chronic conditions



Source: Medicare Conditions website: cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/Maps_Charts.html

Conclusions - 1

- Enhanced understanding, recognition and treatment of multimorbidities will be increasingly important
  - Also in the analysis of trends and as considerations in developing mortality projections
- As society achieves a degree of success regarding the mortality due to individual health conditions, other adverse conditions will tend to become more important to health, effective prevention and health care treatment
  - Especially with respect to deterioration of the immune system
  - Interrelationships among conditions is related to the dynamic mortality and morbidity processes, especially at older ages
- The epidemiology of multiple chronic conditions remains inadequately understood, since the majority of studies have assessed individual diseases or comorbid pairs in association with a single index disease
  - Further research is needed

Conclusions - 2

- Its high prevalence, especially at older ages, points to some of the problems of current medicine and organization-of-care
- Can result in uncertainty at different levels during the care process, from care planning to goal definition and therapeutic strategies
  - A major contributor to the heterogeneity of the causes and consequences of those suffering from a condition
- Information regarding multimorbidity (or the comorbidities of the condition at issue) can help actuaries identify the upcoming health risks of an individual and estimate the mortality and morbidity of a population segment

Commonly used multimorbidity metrics

- Age
- Disease counts. Based on ICD codes, between 3 to 50 conditions or diseases
- Quality and Outcomes Framework (QOF). 17 diseases
- Chronic Disease Score (CDS) / RxRisk. Based on pharmacy usage data
- Adjusted Clinical Groups (ACG) System. Uses age, sex, and diagnosis adjustments derived from medical records, insurance claims, or expected resource use for each diagnosis
- Charlson Comorbidity Index. Uses 17 to 22 weighted disease categories, reflecting age, with weights based on the observed strength of association with mortality
- Cumulative Index Illness Rating Scale (CIRS). 14 body system categories, derived by trained assessors or from medical records, using severity-weights
- Elixhauser Comorbidity index. Based on ICD diagnosis codes, using about 30 indicators
- Duke Severity of Illness Checklist (DUSOI). A severity of illness checklist for measuring the severity of an illness, using 4 parameters for each diagnosis: symptoms, complications, prognosis without treatment, and treatment potential

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HSIN-CHUNG WANG

6B, Disease and Longevity

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Chronic Diseases and Longevity risk: An Application to Type II Diabetes Insurance Products

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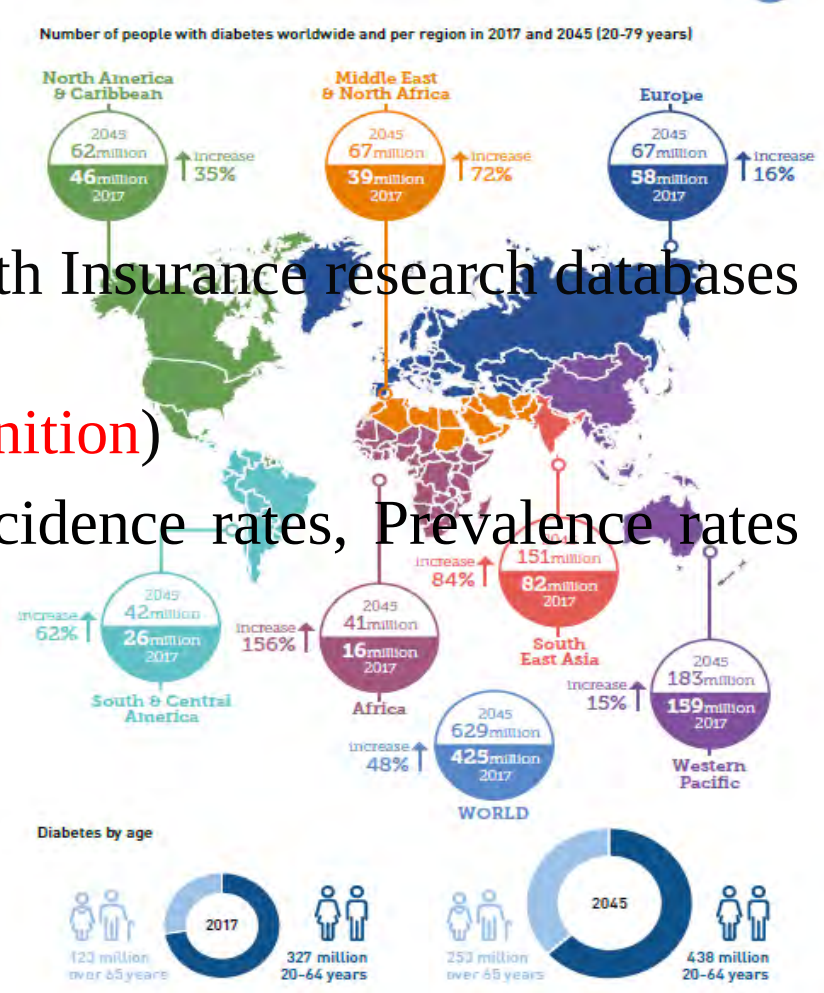
Outline

- Motivation
- Introduction to Taiwan's National Health Insurance research databases (NHIRD)
- Diagnosed with Type II Diabetes (Definition)
- Exploratory Data Analysis (EDA): Incidence rates, Prevalence rates and Mortality rates
- Modelling and Application
- Conclusion



Motivation

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- Crisis of population ageing:
  - About 89% of older adults (65+) have a least one chronic disease.
  - The proportion of elderly people with more than three chronic diseases was as high as 50%.
  - More than 56% of all healthcare costs are due to chronic diseases.
  - The top three chronic diseases in the elderly over 65 years old were: hypertension (52.3%), cataract (41.3%), and diabetes (24.2%).

(Source: 2007 and 2018 Taiwan Longitudinal Study on Aging Survey Report ,Health Promotion Administration, Ministry of Health and Welfare)

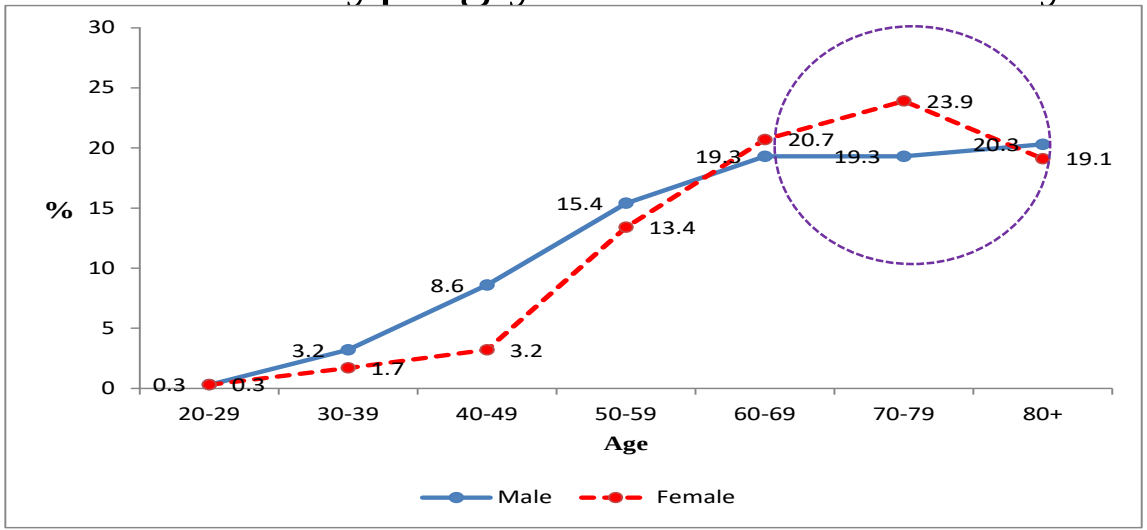
- International Diabetes Federation(IDF) Diabetes Atlas 2017:
  - More than one-third of diabetes cases are estimated to result from population growth and ageing.
- 2018 United States Renal Data System (USRDS) Annual Data Report
  - Taiwan, Japan, and U.S. had the highest reported prevalence of treated End-Stage Renal Disease(ESRD)in 2016
  - 45% of kidney dialysis patients are caused by diabetes (Taiwan)
- NCD-RisC, 2016
  - The age-standardized diabetes prevalence: Taiwan become the third highest in East Asia, second only to that in China and South Korea

National Diabetes Statistics Report, 2017

- The percentage of adults with diabetes increased with age, reaching a high of 25.2% among those aged 65 years.
- 23.8% of people with diabetes are undiagnosed.
- Diabetes was the seventh leading cause of death in the United States in 2015.
- The total direct and indirect estimated cost of diagnosed diabetes in the United States in 2012 was $245 billion.
- Average medical expenditures among people with diagnosed diabetes were about 2.3 times higher than expenditures for people without diabetes

●Prevalence of Hyperglycemia by Gender and Age in 2007

- The hyperglycemia may be regard as an early symptom of diabetes
- There is 19%-23.9% hyperglycemia for the elderly.

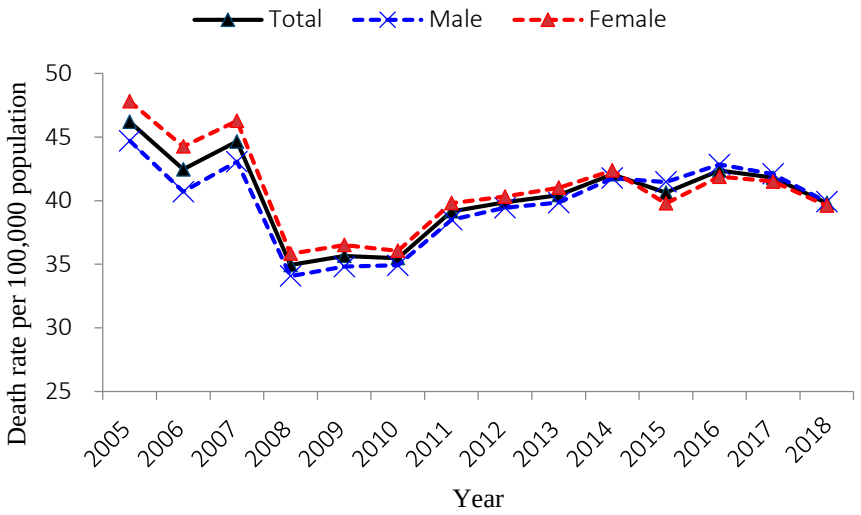


Note: Hyperglycemia is defined as blood glucose test value ≧126mg/dl after 8 or more hours on an empty stomach, or use of hypoglycemic agents.
Source: 2007 Taiwanese Survey on Hypertension, Hyperglycemia, Hyperlipidemia

- Death rate of diabetes (Source: Ministry of Health and Welfare)

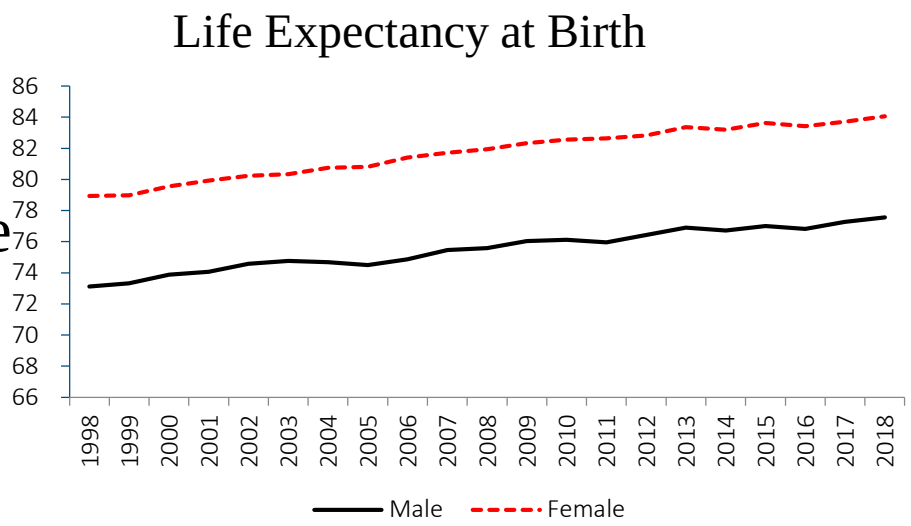
➢The position of diabetes in the male and female causes of death rankings in Taiwan has increased from 12th and 9th in 1981 to 5th places in 2018.

➢The crude death rate of diabetes per 100,000 population attain to 39.8 for men and 39.6 for women in 2018.



- In recent years, life expectancy has continued to grow in Taiwan.
  - 77.55 years –male and female- 84.05 years in 2018; about 0.25 years of growth annually.
- The annual medical expenses for the elderly (65+)are five times that of Taiwanese people aged 0-64.

We expect that the loss of life and medical expenses caused by diabetes and its complications will increase the financial burden on the community.



NHIRD

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- Taiwan launched a single-payer National Health Insurance program on March 1, 1995. As of 2018, 99.9% of Taiwan's population were enrolled.
- There are approximately 25.68 million individuals in this registry.
- Longitudinal Health Insurance Database 2005 (LHID2005) and elderly (65+) Longitudinal Health Insurance Database 2005

➢ We used inpatient and outpatient claims dataset collected during 1996–2013.

Note: Both data sets are one-million random samples of Taiwan people, one for the group of ages 0~99 and the other for ages 65~99, accounting for about 4.6% and 45.7% of Taiwan's populations in each age groups.

Note: Taiwan elderly (65+) is about 3.31 million in 2018.

- Research limitations :

- The diabetes related mortality was also higher among the elderly ➔ we should focus our goal on the group of ages 45-99
- Note that the data quality we only use the data for the period 2003-2012.
- We calculate the mortality rates of diabetes patients, according the criteria of death judgement. Due to the nature of our data, we can only estimate the mortality rates in 2006-2011.

For example: Our data were drawn in 2005, meaning that the sample were still alive in 2005. The death criteria used require two-year washout and thus we cannot estimate the mortality rates in 2012 and 2013.

Definition

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- Claims datasets from 2003 to 2012 were searched to identify any outpatient visit or inpatient admission with diabetes as one of the diagnoses (International Classification of Diseases, 9th Revision, Clinical Modification, ICD-9-CM code 250).

- Classification 1: Patients with type 2 diabetic(ICD code 250) but who were type 1 diabetic (ICD code 250.x1, 250.x3) were excluded from this study.
- Classification 2: Patients in the classification 1 and who takes refillable (continuous) prescription for chronic illnesses.

●There are different problems of diabetes prevalence and incidence researches in previous studies:

- Using interview survey.
- Observation time is too short.
- Insufficient samples.
- The different criteria for diabetes identification.
- The high proportion of diabetes patients with treatment dropout.

➔ We use two one million large samples to reduce small sample size problems and by means of conduct exploratory data analysis (EDA) to evaluate if the observation periods, the number of outpatient visits and the diabetes classification definition are appropriate reduce the problems.

Exploratory Data Analysis (EDA)

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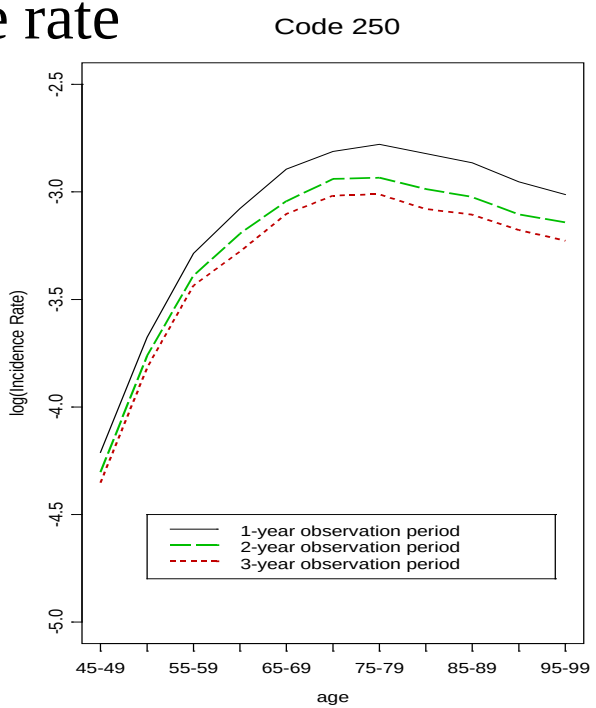
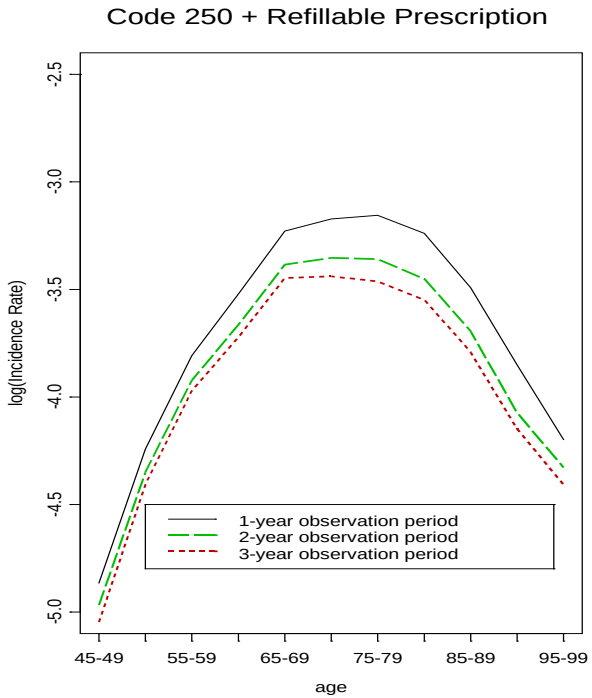
- The observation periods: one-year, two-year, or three-year diabetes-free observation period (For example: 2012 year Taiwan Female)
  - The longer the observation period➔ The lower and more stable incidence rate





- Underwriting needs: The insured only required to submit a two-year health report (Taiwan): Moral hazard and Over-estimation

We choose two years as the observation period in this study.

- We don't fully understand why some people develop type 2 diabetes and others don't. It's clear, however, that certain factors increase the risk, including: Weight, Fat distribution, Inactivity, Family history, Race, Age, Prediabetes, Gestational diabetes, Polycystic ovarian syndrome…

How to confirm the new case of Type II Diabetes.

Symptoms of hyperglycemia in diabetes may disappear due to weight loss ?

- The prescription drug is often included to decide diabetes.
  - Unfortunately, there are concerns in the data quality of prescription drug records and some people may even use diabetes prescription drugs for weight loss, according to our consultation with doctors.
  - The patients may seek for alternative treatments. (There are 46.7% of diabetes patients using complementary and alternative medicine)

➔Not using prescription drug in deciding diabetes

- Lin et al. (2005) shows that :
  - The accuracy of diabetes diagnosis in NHI claims data in Taiwan was 74.6% and The accuracy of cases with 4 outpatient visits was 96.1%
  - The number of **outpatient visits** was the factor most associated with diagnostic accuracy.

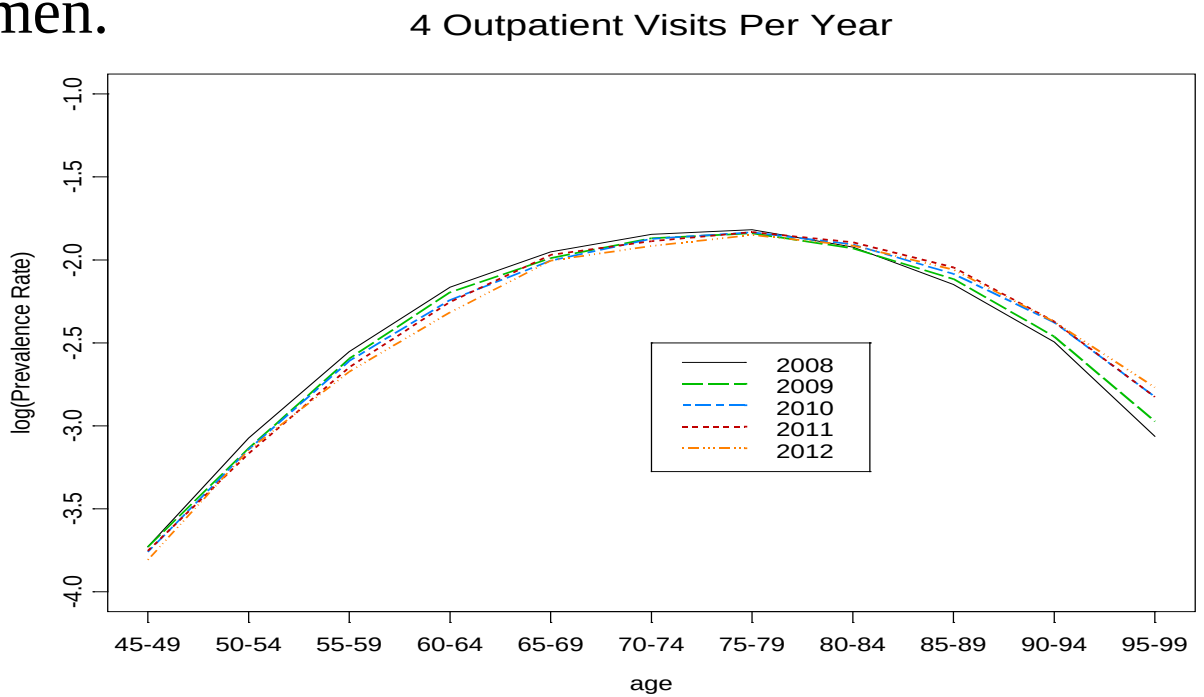
- We consider refillable (continuous) prescriptions (RP). for patients with chronic illness .
- The patients with RP are qualified to have 1-3 months of prescription drugs, which means that they only need to visit the doctors every three months.
- The RP has been enforced since 2003 and it significantly reduces the number of hospital visits.

Note:

RP: For a patient with chronic disease who needs to take same drugs continuously over 6 months and when patients' condition become stable doctor will provide RP for their long-term use.

- Prevalence rates : 4 Outpatient Visits Per Year

➢ The 5- year average prevalence of Type 2 diabetes(T2DM) increased from 2.3% (age 45-49) to 15.9% (age 75-79), and then decreased to 5.6% for women.

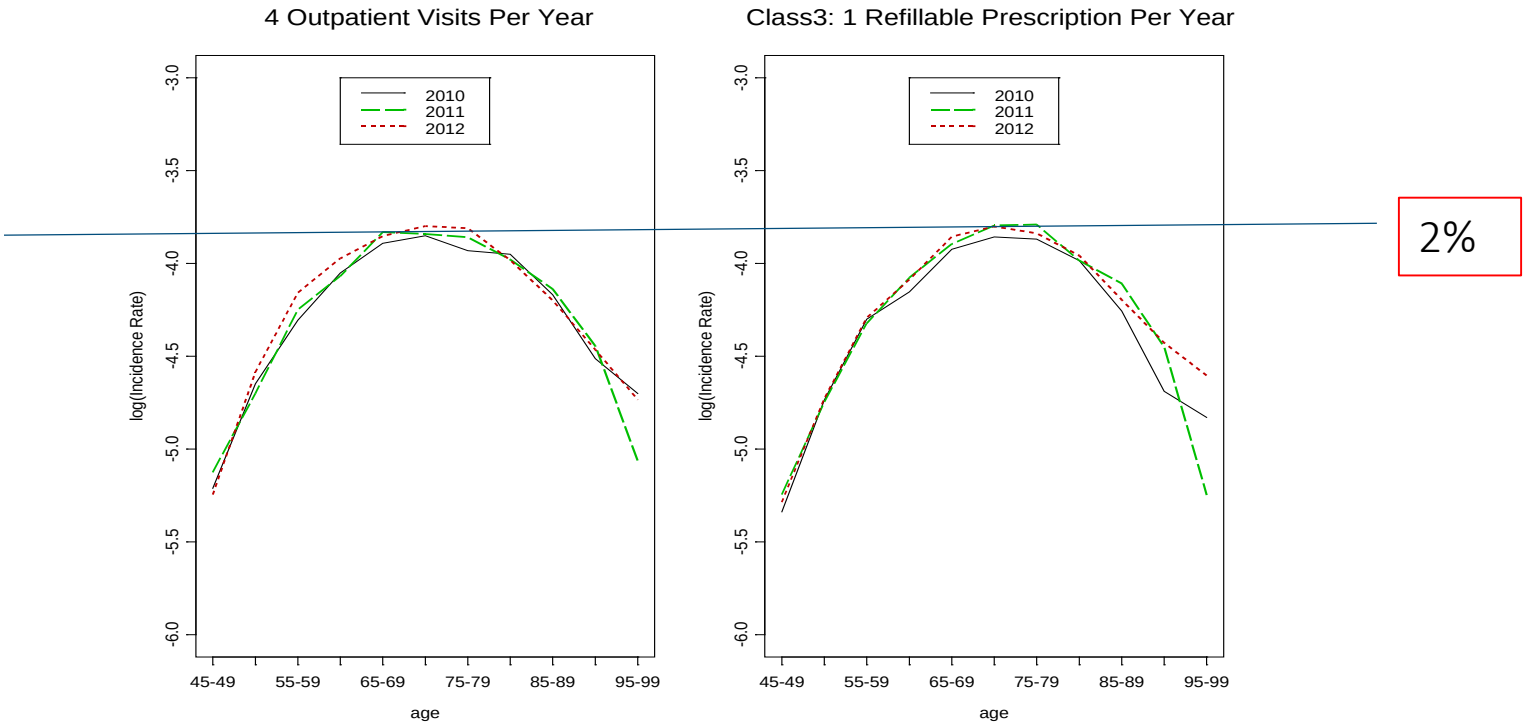


- Incidence Rates of T2DM (2010-12 Female)
  - Using the criterion of 4 outpatient visits per year are also very stable.
  - The incidence rates reach the peak 2% around age 75.
  - The incidence rates based on 4 outpatient visits per year and one RP per year are almost identical.
  - It seems that the patients with the diabetes RP are likely to have diabetes.
- Since the RP is easy to confirm➔ New judging criteria of incidence rates :

Classification 3: Patients no diabetes claim records (ICD code 250) in the previous 2 years and who first time takes RP as the new diabetics.

- Incidence Rates of T2DM (2010-12 Female)

(left: 4 Outpatient Visits per Year; 1 RP per year)

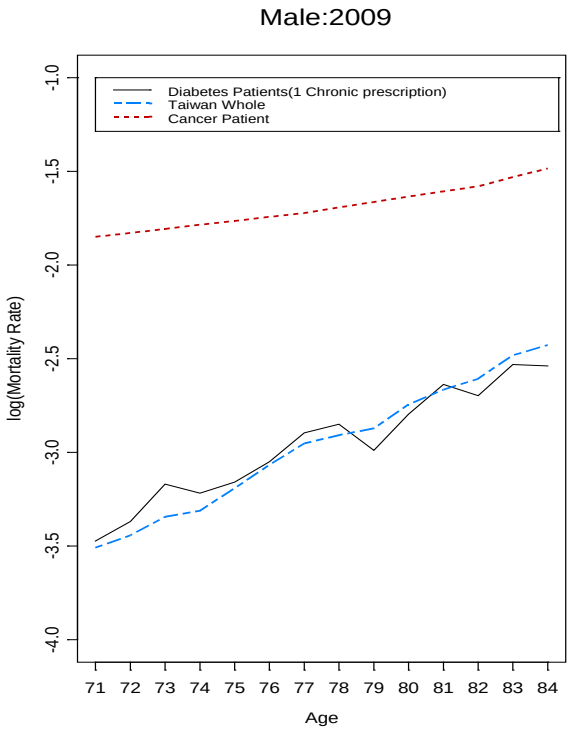


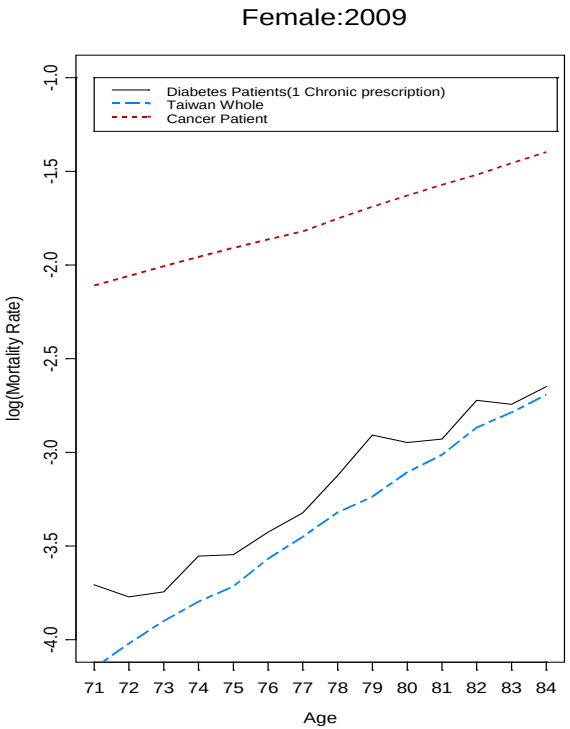
- To judge elder diabetes patients whether dead :
  - Condition 1: Withdrawal in Registry for beneficiary's dataset (ID) and no medical visits for two consecutive years.
  - Condition 2: Last outpatient records are emergency visits, and no medical visits for two consecutive years.
  - Condition 3: Last inpatient records are more than 30 days and no medical visits for two consecutive years.
  - Condition 4: No medical visits for two consecutive years for Catastrophic Illness patients.
  - Condition 5: Last medical records are death, suicide, or discharged and no medical visits for two consecutive years.

- The age-specific mortality rates of elderly diabetes patients :
  - The male mortality rates are higher.
  - The mortality rates of diabetes patients are much smaller than those of cancer patients.
  - The mortality rates of diabetes patients are similar to those of Taiwan average people, only the female mortality rates are slightly larger.
  - This result is somewhat different to those of previous studies, where older diabetes patients have higher mortality.

Our definition is connected to the willingness of constantly receiving medication and these patients may have lower mortality rates comparing with diabetes patients cannot or choosing not to take regular medication.

- The age-specific mortality rates of diabetes patients vs. Cancer patients





Model Evaluation

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- Generalised Age-Period-Cohort (GAPC) stochastic mortality models (Villegas et al., 2016) for Incidence rates and mortality rates.
  - LC model: Lee and Carter (1992)
  - RH model: Renshaw and Haberman (2006)
  - APC model: Age-Period-Cohort Model, Cairns et al. (2009)
  - CBD model: Cairns-Blake-Dowd (2006)

- The partial SMR: PSMR is one way to deal with estimating mortality rates of small populations, by adding information from other (large) population to correct possible bias.

We can combine graduation methods (PSMR) with mortality models (Wang et al., 2018 and Yue et al., 2019)

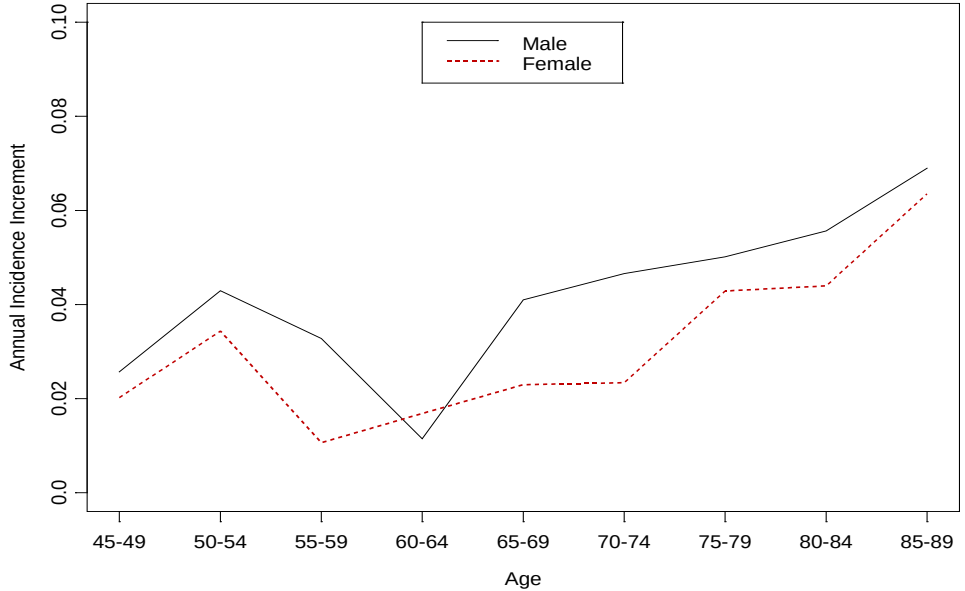
- Fitting MAPE of Incidence rates (5-age groups: 45-99)
  - The APC model has the best fitting performance in all three periods
  - If we omit the data in 2005 and 2006, the LC, APC, PSMR, and PSMR+LC models all have satisfactory fitting results.

	2005-2013		2007-2012		2008-2013		Average
	Male	Female	Male	Female	Male	Female	
LC	49.87	9.80	6.12	7.97	6.04	10.00	14.97
APC	6.40	6.71	4.49	7.03	4.07	4.89	5.60
PSMR	144.64	9.46	6.98	9.72	5.91	9.47	31.03
PSMR+LC	147.49	11.69	7.56	9.92	6.29	10.13	32.18
CBD	338.46	83.92	43.80	88.21	41.59	84.65	113.44
RH	---	78.38	68.55	68.48	37.09	74.94	65.49

- Fitting MAPE of Incidence Rates (single-age: 45-89)
  - Except the CBD model, all models have satisfactory fitting results for the single-age case.
  - Among all models, RH, LC and APC have the best performance.

	2005-2013		2007-2012		2008-2013		Average
	Male	Female	Male	Female	Male	Female	
LC	10.37	10.16	7.80	7.22	8.22	7.65	8.57
APC	10.70	9.95	7.38	7.73	7.99	7.71	8.58
PSMR	10.87	10.34	8.51	8.39	8.77	8.24	9.19
PSMR+ LC	13.21	12.46	8.95	8.66	8.95	8.62	10.14
CBD	30.24	40.40	26.34	38.43	25.87	37.23	33.08
RH	9.57	8.71	6.09	6.18	6.11	6.18	7.14

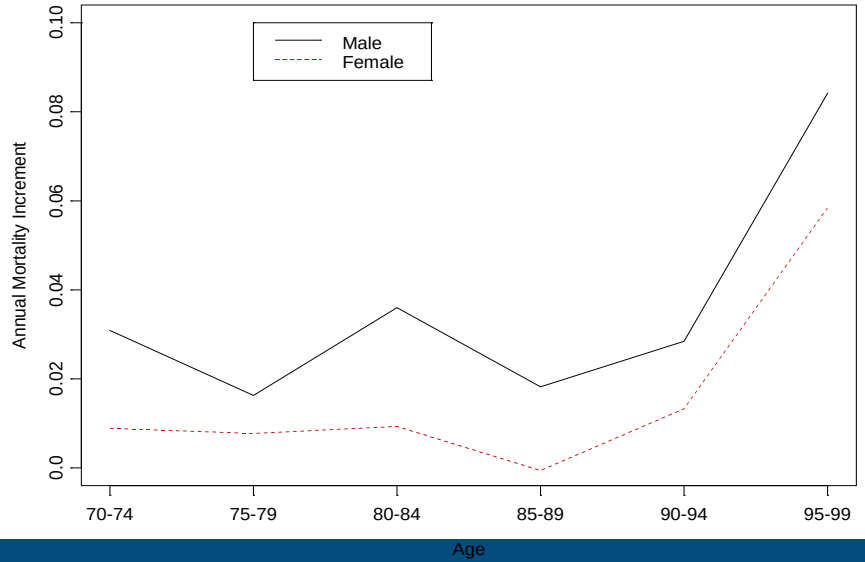
- Annual Increment of Incidence Rates (LC Model) :Years 2008-2013
  - The annual increments are smaller for younger groups
  - Increase with age, reaching to around 6% at ages 85-89.
  - The scale of annual increments is worth to pay attention.
  - Male is higher than female.



- Fitting MAPE of Mortality Rates
  - Except the RH model, all models have fairly accurate fits, with average MAPE about 5% and APC have the best performance.

	5-ages group (70-99)		Single-age (71-89)		Average
	Male	Female	Male	Female	
LC	3.76	2.74	5.48	4.75	4.18
APC	3.27	2.64	4.86	5.13	3.97
PSMR	4.60	4.41	6.37	5.75	5.28
PSMR+LC	4.94	4.41	6.42	5.75	5.38
CBD	5.56	4.41	6.59	5.95	5.63
RH	24.74	11.51	3.84	4.14	11.06

- Annual Increment of Mortality Rates (LC Model) :Years 2006-2011
  - The average annual increments are 3.6% and 1.6% for male and female, respectively.
  - If we only consider age 70-89, then the annual increments would be more stable but slightly reducing to 2.5% and 0.6% for male and female, respectively.



Application: Insurance Product Design

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Motivation

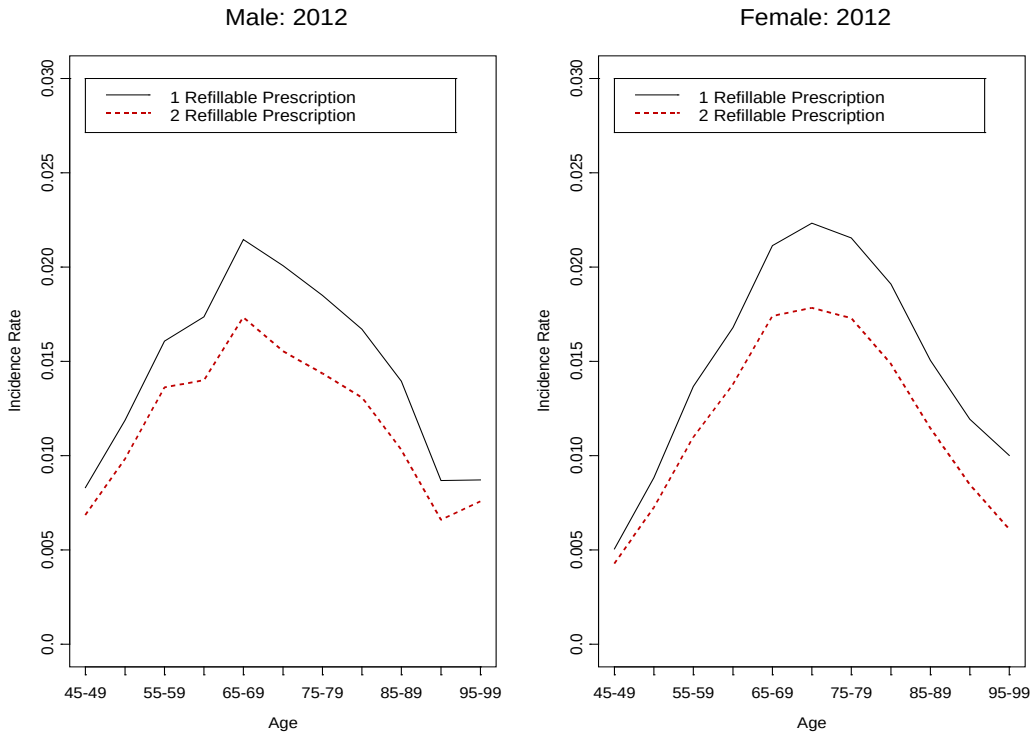
- Changes in the lifestyle of modern people (eating well and moving less)➔Increase in sub-health population
- The disease pattern changed from "acute" to "chronic" ➔Increased duration of illness and medical expenses
- Medical testing technology is changing rapidly ➔The rates of self-pay medical examination are increasing year by year
- Food crisis and food safety incidents in Taiwan ➔Conducive to health management business promotion

From: Cathay Life Insurance

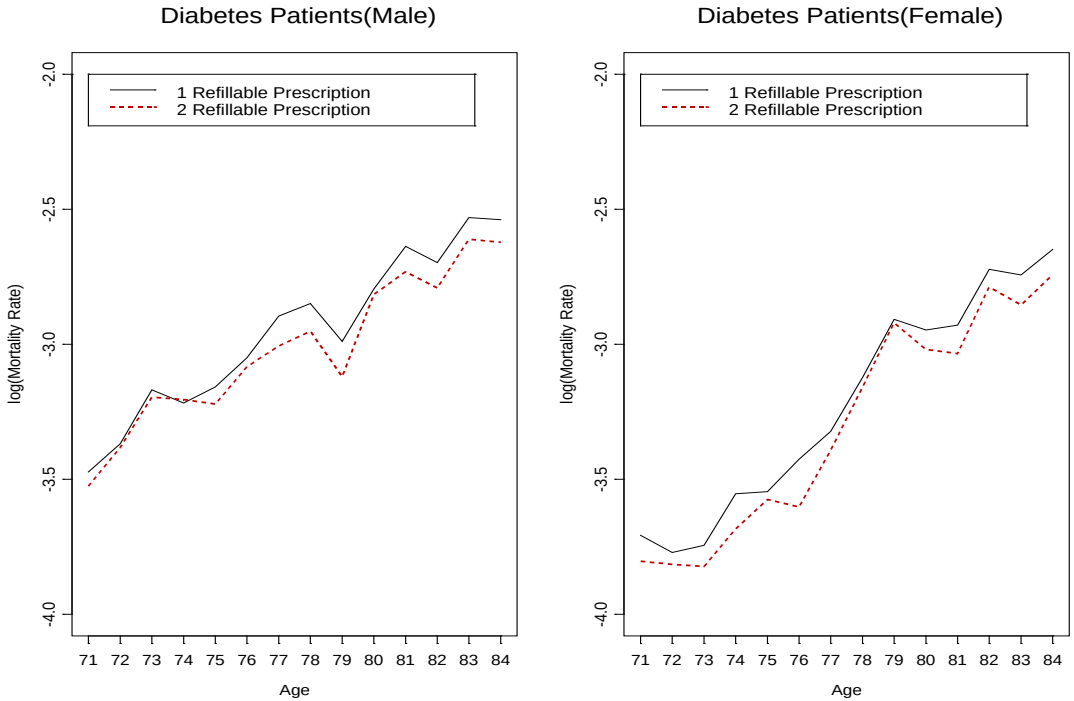
- Insurance product design were focus on the basis of:
  - For sub-health population: patient's condition is stable
  - Underwriting needs and the accuracy of diabetes diagnosis : RP is convenient than 4 outpatient visits records for policyholders to get the proof document
  - Reduce moral hazard

To design medical policies for the insured who continue receiving treatments.

- Diabetes Incidence Rates: 2RP vs. 1RP (2012)
  - The diabetes incidence rates of 2RP are about 20% less than those of 1RP



- Diabetes Mortality Rates: 2RP vs. 1RP (2009)
  - The mortality rates of diabetes patients using 2RP are about 7% less than those using 1RP



- Using the refillable (continuous) prescriptions for patients with diabetes, we can obtain stable incidence rates and mortality rates

For example:

- Use the 20%(Incidence Rates between 2RP and 1RP) or 7% gap for mortality rates

As the

1. Design medical policies with premium discount.
2. A policy with the spill-over effect : The monitor watch cost with encourage exercise to stay healthy.

3.The diabetes option: When the insured is diagnosed with diabetes, instead of receiving a benefit payment, he/she can purchase new policies using the standard price rate.

Conclusion

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- The incidence rates of is gradually increasing by year.
- The prevalence of type 2 diabetes patients declines with age after age 75, but it increased noticeably by year.
- The mortality rates of diabetes change with a stable path.
- For fitting the incidence rates and mortality rates, the APC model has the smallest MAPE errors and the LC model is also a feasible choice.
- If we consider those patients who have an at least 2 years diabetes-free observation period and at least 4 outpatient claims with the diagnosis of diabetes (or one time RP for chronic diseases) as the definition of incidence, the diabetes incidence would be the most stable.

Thank you for your attention.