

出國報告（出國類別：會議）

主題：參與 2019 美國心臟學會(American Heart Association) 年會

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## 摘要（含關鍵字）

本團隊為國內高血壓研究的頂尖團隊，長期致力於深入了解心血管血流動力學，包括高血壓及心臟衰竭的基礎、臨床及流行病學研究。過去曾經發表許多關於行動血壓計 (Ambulatory blood pressure) 的研究。今年的研究重點之一乃是結合行動血壓計的數據資料及目前全球積極發展的新興人工智慧技術，發展使用行動血壓數據預測心血管風險的工具。初步成果發表於心臟科年度盛會：今年度的美國心臟學會 (American Heart Association) 學術年會，獲得許多的肯定。此外，為配合目前醫院發展至會醫療的業務，職也參與本次年會中智慧醫療的許多演講及研討會，了解了許多目前發展的重要方向。

關鍵字：美國心臟學會、高血壓、行動血壓

## 一、 目的

美國心臟學會 American Heart Association 是心臟學界的頂尖學術會議，每年吸引上萬名國際心臟學界的學者及臨床專家參與，本次會議代表團隊發表使用行動血壓數據預測心血管風險的工具，此研究乃是結合行動血壓計的數據資料及目前全球積極發展的新興人工智慧技術達成風險預測的目的。獲得許多迴響與肯定。

此外，為了配合醫院交辦的人工智慧發展的任務，職這次特別參與需多智慧醫療的演講及研討會，了解了目前的最新的發展趨勢，盼望能協助本院發展及建置智慧醫院。

## 二、 過程

今年的美國心臟學會(American Heart Association)在美國東岸的費城舉行，超過上萬名心血管研究領域的學者參與，分成 basic, clinical, and epidemiological research。今年還新增 digital health and precision medicine 的領域。本團隊為國內高血壓研究的頂尖團隊，長期致力於深入了解心血管血流動力學，包括高血壓及心臟衰竭的基礎、臨床及流行病學研究。過去曾經發表許多關於行動血壓計 (Ambulatory blood pressure) 的研究。今年的研究重點之一乃是結合行動血壓計的數據資料及目前全球積極發展的新興人工智慧技術，發展使用行動血壓數據預測心血管風險的工具。這次研究的摘要發表如附錄。主要研究工具乃是使用 machine learning technique，找出 24 小時血壓數據中最能夠預測心血管死亡率的風險指標，初步發現夜間血壓的預後價值最好，而且心跳最慢時的血壓數據，可能具有最好的預測價值，此與交感系統於夜間時活性降低，血管內壓力可能才是真正的 usual blood pressure 有關。

## 三、 心得

此次會議有許多重要臨床研究發表，包括 ISCHEMIA study，再次確認 Courage study 的研究發現，穩定型心絞痛的病患，使用藥物相較於使用藥物加上心導管治療，長期心血管事件的風險類似，這對於進行心導管手術的適應症，有重要的影響，使用心導管治療冠心病，最重要的適應症乃是改善症狀。此外，除了研究發表以外，職為了智慧醫院的任務，也參與了許多智慧醫療相關的研討會，其中一場演講讓我有許多學習，摘錄如下：

這個演講是由 World Economic Forum 與 AHA 共同舉辦，他提出了全球資料運用的完整架構與藍圖，強調 Data Free Flow with Trust (DFFT) 的概念，這個概念的說明如下：



Data Governance  
**Data Free Flow with Trust (DFFT)**

G20 2019 JAPAN WORLD ECONOMIC FORUM

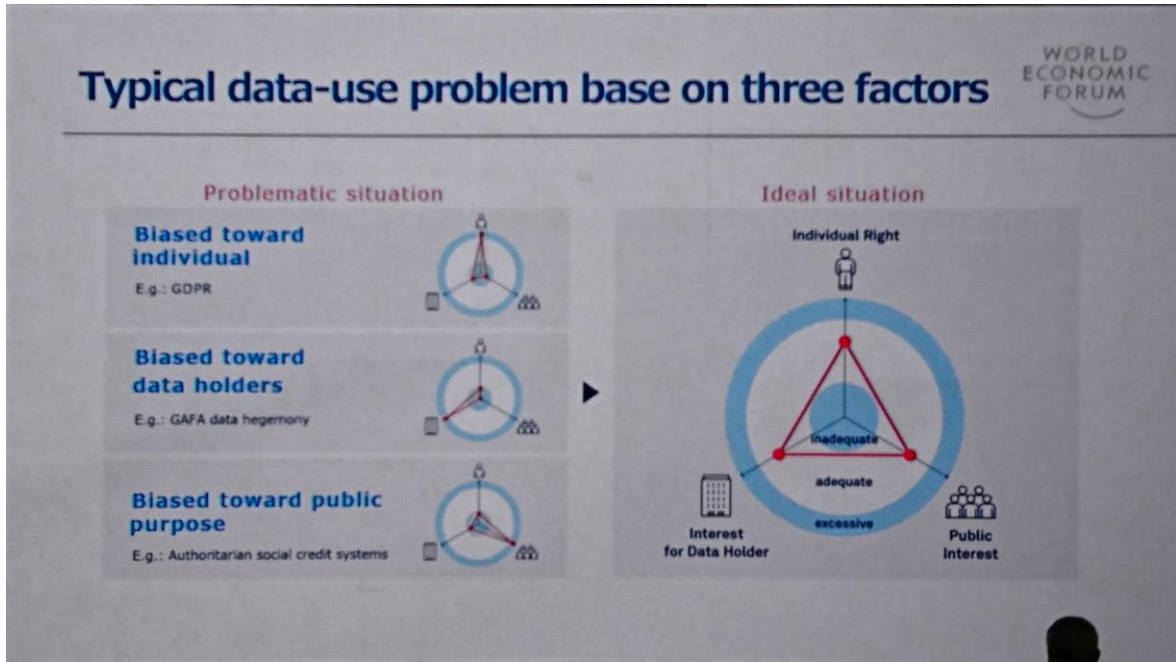
**G20 Digital Ministerial Meeting Communique**

Data Free Flow with Trust  
Reaffirming the commitments made in Hangzhou, Dusseldorf, and Salta, we share the understanding that digitalization gives us the opportunity to promote inclusive and sustainable economic growth. Digitalization also promotes social and cultural progress and development, fosters innovation, and empowers individuals and businesses, including micro, small, and medium-sized enterprises (MSMEs) to benefit from emerging technologies and data. Cross-border flow of data, information, ideas and knowledge generates higher productivity, greater innovation, and improved sustainable development. At the same time, we recognize that the free flow of data raises certain challenges. By continuing to address challenges related to privacy, data protection, intellectual property rights, and security, we can further facilitate data free flow and strengthen consumer and business trust. In order to build trust and facilitate the free flow of data, it is necessary that legal frameworks both domestic and international should be respected. Such data free flow with trust will harness the opportunities of the digital economy. We will cooperate to encourage the interoperability of different frameworks, and we affirm the role of data for development.

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簡言之，目前國際間認識到資料共享的重要性，在兼顧個人隱私、資料保護、智慧財產權、及資料安全性的前提下，不同的 Party 應該對於資料共享有基本的信任，才能極大化大家的共同利益，這個 DFFT 成為國際間資料共享的基礎。

然而，目前資料處理的原則要考慮 Individual right, data holder 以及 public purpose 這三大面向，常見的情況是 biased toward individual (台灣的現況)，或是 biased toward data holder (GAFA 指的是 Google, Amazon, Facebook, Apple 數位資訊霸權)，或是 biased toward public purpose。



真正的平衡應該是如上圖右所示。

即使是規範嚴謹的歐盟 GDPR，仍然在許多情況下我們可以使用 APPA 的精神，在未取得個人同意的情況下，讓資料共享促成公眾最大利益。

WORLD ECONOMIC FORUM

## 2. “Authorized Public Purpose Access (APPA)”

**In healthcare, there are situations in which data access without consent can provide great benefits to society (as allowed under Article 9 of the GDPR)**

Example:  
Personal medical data needed to save lives in a natural disaster

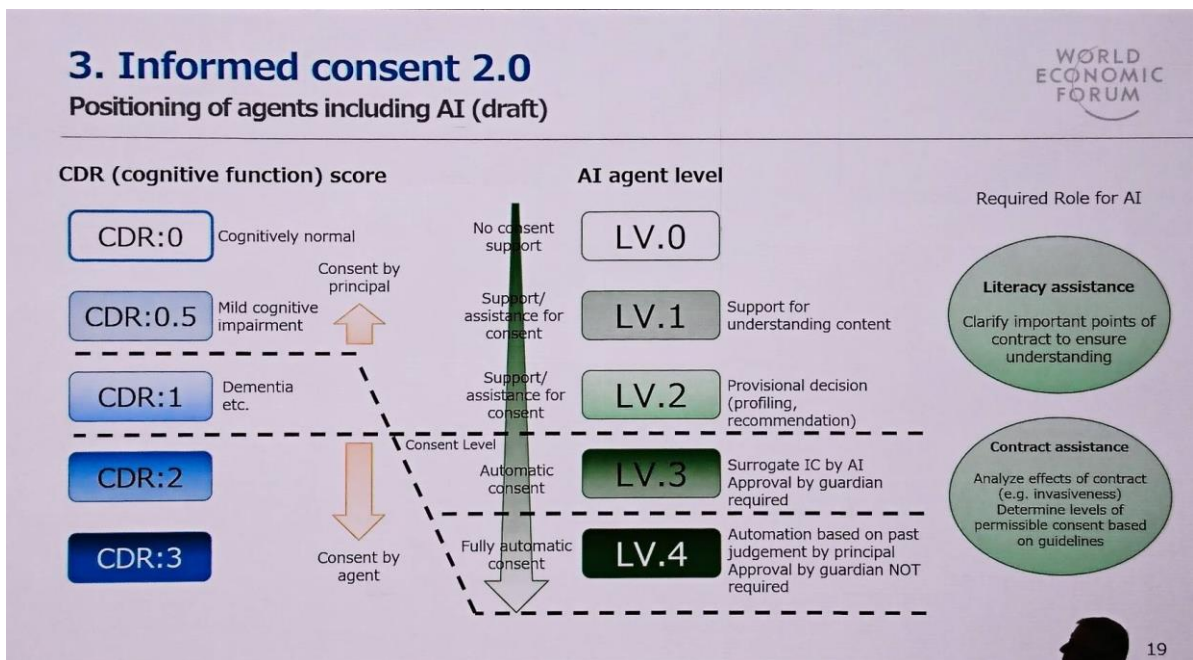
Example:  
Information on infected patients needed to prevent a disease pandemic

Example:  
Drug development for rare disease or rare fraction of cancer in precision medicine

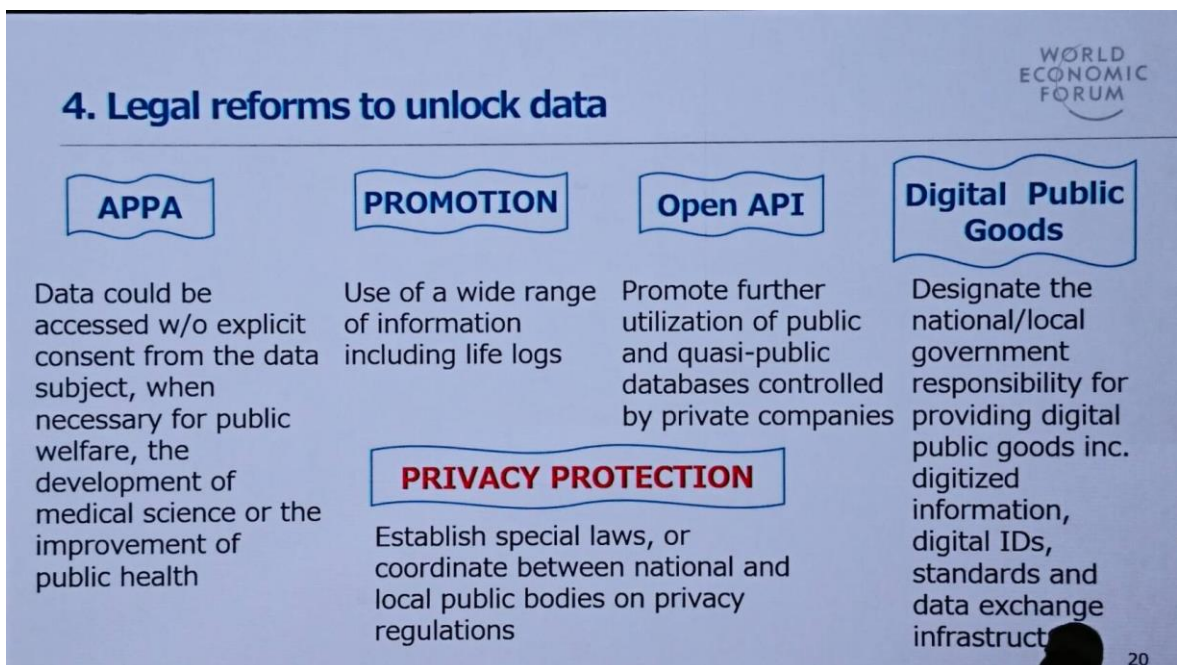
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例如，根據受試者的認知功能，可以設計出取得同意的不同方式，如此失智症的研究才有機會進行。

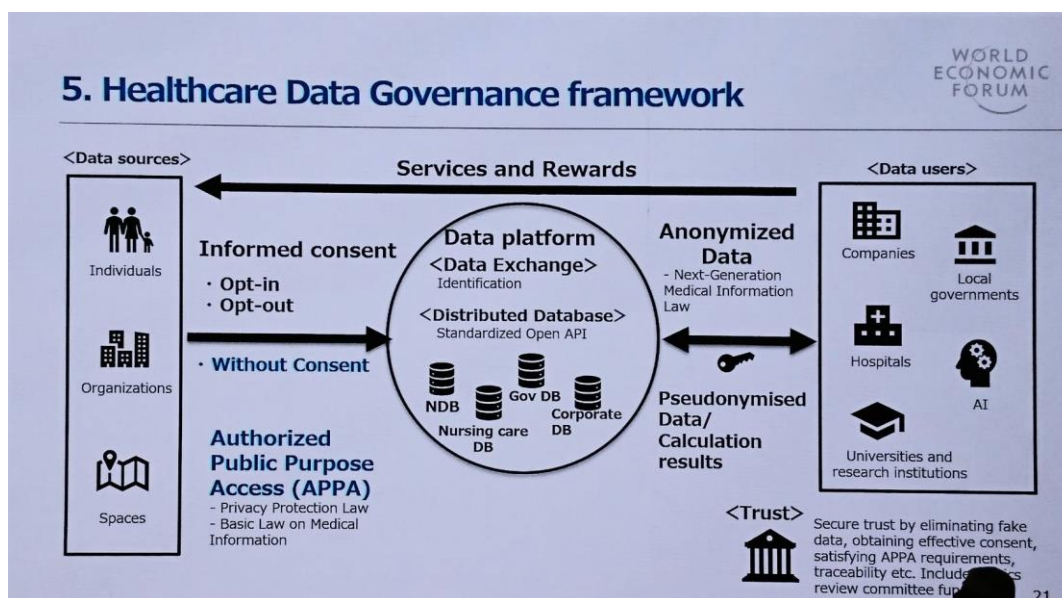


下圖是 World Economic Forum 所主張的資料共享架構，在符合法規保護隱私的前提下，達成 digital public good。



#### 四、 建議事項（包括改進作法）

在大數據的浪潮下，全世界都在往資訊共享的方向邁進，當然，保護隱私最安全的做法就是不讓資料有外流的任何風險，但是這也產生了組織孤立的風險。當全球合作研究或是照護服務成為主流的同時，我們也要正視及積極面對這個浪潮，才不會逐漸地喪失競爭力而不自知。下圖把 **healthcare data governance** 的主要架構都說明得非常清楚，去識別化的資料或是加密資料應該可以透過 **opt-in** 或是 **opt-out** 的方式讓 **data user** 使用，以達到最大的公眾利益。



此外，在準備研究報告的同時，發現台灣學術的獨特優勢：健保資料庫的優勢，本研究的預後資料乃使用健保資料庫的死亡檔串聯取得。才能夠在經費有限的情況下，仍能發表高影響係數的研究。

然而由於人權團體的不合理杯葛，目前使用資料庫充滿了許多限制。台灣沒有天然資源，缺乏廣大內需市場，要在國際間脫穎而出，需依靠高品質的人力素質，及清晰的產業發展藍圖。台灣的半導體產業領先全球，醫療產業也是眾所稱羨的高可近性，目前國家正積極發展生技醫療，如果能結合數位醫療，搭配健保資料庫的獨特優越性，台灣發展出舉世稱羨的產業鏈結將不是難事，也能改進國人健康，盼望政府能夠在兼顧隱私權保護的同時，找出極大化國家及群眾利益的政策發展方向，方是國家之福！



# Derivation and Validation of an Integrated Risk Prediction Score System Based on Comprehensive Ambulatory Blood Pressure Parameters

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## BACKGROUND & OBJECTIVE

- Elevated blood pressure (BP) and heart rate (HR) are closely associated with cardiovascular (CV) outcomes.
- The Framingham risk score is one of the established risk prediction models for predicting 10-year CV events.
- Ambulatory blood pressure monitoring (ABPM) can provide information superior to conventional office BP for confirming a diagnosis of hypertension.
- The nycterohemeral rhythm in which BP and HR gradually decline during sleep hours and soar rapidly before awakening is characterized by the variations of sympathetic activity and is hypothesized to carry important prognostic information.
- We aimed to utilize emerging automated machine learning approaches to investigate the prognostic values of the following indices in the two population cohorts:
  - The ambulatory BP during different time windows (daytime, nighttime, morning, evening and 24 hours)
  - The BP at different levels of HR for CV mortality

## RESULTS

Table 1. Descriptive statistics of basic characteristics between Kinmen and Jackson Heart Study (JHS) cohorts

	Kinmen (n=1515)	JHS (n=385)	P value
Male, n (%)	793 (52.34)	131 (34.02)	<0.001
Age, years	55.01 (13.05)	59.24 (10.80)	<0.001
Height, cm	158.97 (8.50)	165.86 (8.97)	<0.001
Weight, kilogram	63.34 (11.20)	87.07 (18.08)	<0.001
BMI, kilogram/m <sup>2</sup>	25.02 (3.77)	30.59 (8.12)	<0.001
Cholesterol, mg/dL	200.81 (38.81)	200.89 (40.18)	0.975
HDL-C, mg/dL	48.89 (12.87)	55.24 (15.08)	<0.001
LDL-C, mg/dL	124.59 (34.83)	124.71 (38.75)	0.953
Smoking, n (%)	375 (24.80)	128 (32.70)	0.003
Alcohol intake, n (%)	192 (12.70)	199 (43.90)	<0.001
Diabetes, n (%)	152 (17.60)	78 (19.70)	<0.001
<b>Office parameters</b>			
Heart rate, /min	70.63 (13.88)	67.51 (11.40)	<0.001
SBP, mmHg	142.70 (24.66)	143.06 (16.44)	0.358
DBP, mmHg	89.25 (15.17)	93.94 (11.06)	<0.001
MBP, mmHg	107.07 (18.56)	110.52 (11.08)	<0.001
PP, mmHg	53.44 (19.20)	49.72 (14.82)	<0.001
<b>ABPM parameters</b>			
Heart rate, /min	78.86 (9.44)	75.70 (10.38)	0.048
SBP, mmHg	128.90 (17.65)	127.98 (13.14)	0.448
DBP, mmHg	81.42 (11.86)	78.01 (8.84)	<0.001
MBP, mmHg	97.15 (13.14)	93.33 (9.17)	<0.001
PP, mmHg	47.17 (9.92)	51.97 (10.70)	<0.001

HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MBP, mean blood pressure; PP, pulse pressure

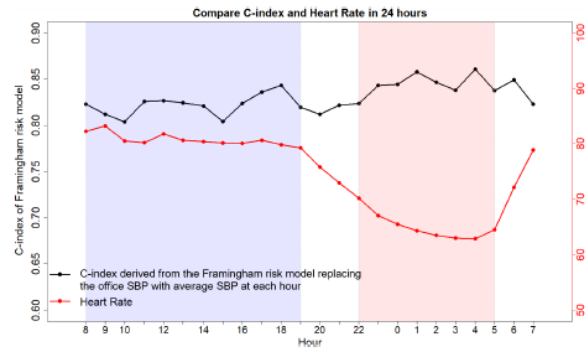


Figure 1. The line trend of average C-index for CV death risk and average HR at each hour

Table 2. The C-index of Framingham risk prediction model\* for CV death risk in different time period, HR status and ambulatory BP covariates in Kinmen cohort

	Cox model						
	Day-time			Night-time		All day	
	Average HR	Maximal HR	Minimal HR	Average HR	Maximal HR	Minimal HR	Maximal HR
SBP	0.832	0.797	0.820	0.860	0.827	0.865	0.789
SBP + DBP	0.827	0.793	0.814	0.854	0.828	0.857	0.786
MBP + PP	0.827	0.794	0.814	0.854	0.824	0.857	0.787
<b>RSF model</b>							
SBP	0.793	0.772	0.786	0.832	0.817	0.830	0.774
SBP + DBP	0.799	0.780	0.782	0.840	0.817	0.843	0.770
MBP + PP	0.799	0.782	0.790	0.824	0.822	0.848	0.774

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; PP, pulse pressure; \*Framingham risk prediction model replaced the office SBP with 24-hour ambulatory SBP, DBP, MBP and PP.

## CONCLUSIONS

- This study provides evidence that prognostic information for assessing 20-year risk of CV death is substantially improved by substituting office SBP with night-time BP at minimal heart rate in both Cox-PH and machine learning models when looking at two different cohorts.
- The transportability of the proposed cardiovascular risk function should be evaluated in future studies.

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## MATERIALS & METHODS

### METHODS

#### Cohorts

- 2020 Taiwanese subjects  
- Community-based survey (09/03/1991-06/16/1993)  
- Demographics, medical history, physical examination & biochemical laboratory data  
- 24-hour ABPM measurements  
- Causes and dates of death (until Dec 31, 2013)

#### Bootstrapping

- Training set  
- Testing set

#### Modelling

- Cox-PH & RSF Models  
- Substituting office SBP with combination of BP-related features including SBP, DBP, MBP & PP in Framingham risk formula  
- Also considering time period & heart rate

#### Performance evaluation

- Modified Framingham risk prediction model  
- Harrell's concordance index (C-index)  
- Akaike information criteria (AIC)

#### Jackson Heart Study (JHS)

- 985 African Americans  
- Community-based epidemiological data provided by BioLINCC  
- Basic biochemical and clinical information  
- 24-hour ABPM measurements  
- Health status and outcome assessment released in Mar 2019 (14 CV deaths)  
- Median follow-up of 15 years

- 1515 subjects with complete data  
- 182 CV deaths  
- Median follow-up of 19.7 years

- 1000 times

- Independent validation

- Cox-PH, Cox proportional hazards; RSF, random survival forest; MBP, mean blood pressure; PP, pulse pressure

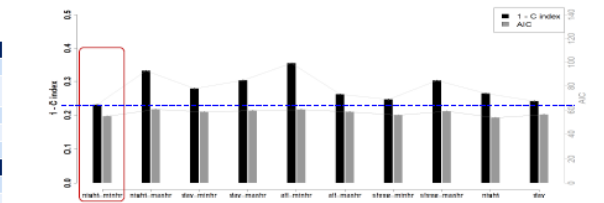


Figure 2. The C-index and AIC performance on JHS when BP covariate replaced as ambulatory mean BP and PP

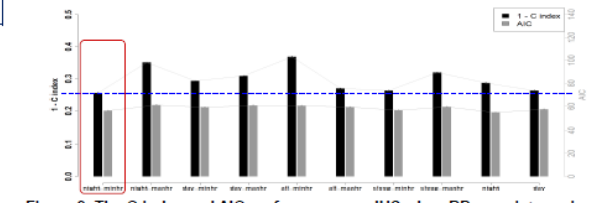


Figure 3. The C-index and AIC performance on JHS when BP covariate replaced as ambulatory SBP and DBP