[研究議題：Assessing the Relationship Between the Variability of Diagnostic Measures and the Risk of Diabetic Complications]

研究目的: 多項檢測項目變異程度對糖尿病患者各項併發症關係

目的:有助於早期預測糖尿病和相關併發症的發生

參考論文: Predictions of diabetes complications and mortality using hba1c variability: a 10‑year observational cohort study

**Data preparation:**

資料來源: 三院臨床資料庫

資料區間 : 2008-2019

目標病患:的糖尿病患者

Index Date定義: 一年內有3次門診紀錄 或 1 次住院紀錄為新患的糖尿病患者

符合條件下的首次看診日

ICD CODE: 疾病碼

糖尿病:

ICD9: 250, 251.8, 357.2, 362.01, 362.02, 366.41, 583.81

ICD10: E08, E09, E10, E11, E12

Outcome (糖尿病引起的6種相關併發症):

|  |  |  |
| --- | --- | --- |
| **糖尿病相關併發症** | **ICD CODE** | **操作定義** |
| **Eye complications**  **眼部疾病**  **EyeComp** | **ICD9: 362.01、362.02、362.55、362.11、365.44、369、361、369.60**  **ICD10: H33.0, H33.10, H33.11, H33.19, H33.2, H33.3, H33.4, H33.8, E11.31, E11.32, E11.33, E11.34, E11.351, E11.359, H35.03, H35.38, H42, H54.0, H54.1, H54.2, H54.3, H54.8, H54.4, H54.5, H54.6, H54.7** | **一年內 3次門診 或 1 次住院。** |
| **Cardiovascular disease**  **心血管疾病**  **CardioDisease** | **ICD9: 414.9、413.9、411.1、412、428、425、402**  **ICD10: I11, I20.0, I20.8, I20.9, I25.2, I25.9, I42, I43, I50.1, I50.2, I50.3, I50.4, I50.9** |
| **Cerebrovascular disease**  **腦血管疾病**  **CerebroDisease** | **ICD9: 435.9、434.91、432.9、437.1**  **ICD10: I62.9, I63.50, I63.511, I63.512, I63.519, I63.521, I63.522, I63.529, I63.531, I63.532, I63.539, I63.541, I63.542, I63.549, I63.59, I63.8, I63.9, I67.84, I67.81, I67.82, I67.89, G45.9** |
| **Peripheral vascular disease**  **周邊動脈疾病**  **PeripheralVascDisease** | **ICD9: 440.2**  **ICD10: I70.2, I70.92, I75.01, I75.02** |
| **Nephropathy**  **腎臟病**  **Nephropathy** | **ICD9: 583、585、V451**  **ICD10: E10.21, E11.21, N05.0, N05.1, N05.2, N05.3, N05.4, N05.5, N05.6, N05.7, N05.8, N05.9, N06.0, N06.1, N06.2, N06.3, N06.4, N06.5, N06.6, N06.7, N06.8, N06.9, N07.0, N07.1, N07.2, N07.3, N07.4, N07.5, N07.6, N07.7, N07.8, N07.9, N14, N15.0, N15.8, N15.9, N16, N17.1, N17.2, N18.4, N18.5, N18.6, N18.9** |
| **Diabetic neuropathy**  **神經病變**  **DiabeticNeuro** | **ICD9: 357.2、337.1、353**  **ICD10: E08.42, E09.42, E10.40, E10.42, E11.40, E11.42, E13.42, G54, G55, G99.0** |

控制疾病目的:

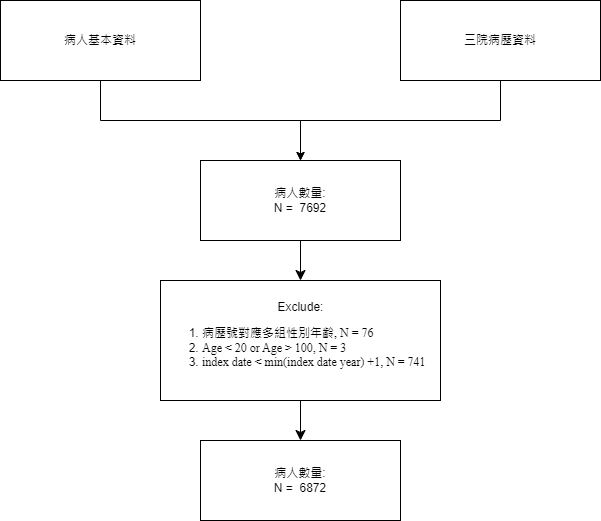
排除混雜變數的影響、提高結果的有效性、增強可比性、減少偏倚、提高統計效率

|  |  |  |
| --- | --- | --- |
| **Control diseases(糖尿病cohort study相關的11種控制疾病):** | | |
| **疾病名稱 / 簡寫** | **ICD CODE** | **操作定義** |
| **Essential hypertension**  **本態性高血壓**  **Hypertension** | **ICD9: 401**  **ICD10: I10** | **一年內3次門診 或 1 次住院** |
| **Peripheral enthesopathies and allied syndromes**  外周附著點病變及其相關聯症候群的疾病  **PeripheralEnthe** | **ICD9: 726**  **ICD10: M25.70, M25.71, M25.72, M25.73, M25.74, M25.75, M25.76, M25.77, M66.21, M66.81, M70.1, M70.2, M70.3, M70.4, M70.5, M70.6, M70.7, M75.0, M75.10, M75.11, M75.2, M75.3, M75.4, M75.5, M75.8, M75.9, M76, M77** |
| **Other ill-defined and unknown causes of morbidity and mortality**  定義不明和未知原因的發病和死亡  **UnknownCauses** | **ICD9: 799**  **ICD10: R09.0, R09.2, R41.89, R44.8, R44.9, R45.0, R45.3, R45.4, R45.87, R45.89, R46, R53.81, R64, R68.13, R68.19, R68.82, R68.89, R69** |
| **Disorders of lipoid metabolism**  脂質代謝障礙  **LipoidMetabDis** | **ICD9: 272**  **ICD10: E71.30, E75.21, E75.22, E75.24, E75.3, E75.5, E75.6, E77, E78.0, E78.1, E78.2, E78.3, E78.4, E78.5, E78.5, E78.6, E78.70, E78.79, E78.8, E78.9, E88.1, E88.2, E88.89** |
| **Acute upper respiratory infections of multiple or unspecified sites**  多部位或未明確部位的急性上呼吸道感染  **AcuteURI** | **ICD9: 465**  **ICD10: J06** |
| **Other symptoms involving abdomen and pelvis**  腹部和骨盆的其他症狀  **AbdPelvicSymptoms** | **ICD9: 724、789**  **ICD10: M43.2, M43.8X9**  **M48.00, M48.04, M48.05, M48.06, M48.07, M48.08, M51.1, M53.2X7, M53.2X8, M53.3, M53.80, M53.84, M53.85, M53.86, M53.87, M53.88, M53.9, M54.03, M54.04, M54.05, M54.06, M54.07, M54.08, M54.09, M54.14, M54.15, M54.16, M54.17, M54.3, M54.4, M54.5, M54.6, M54.89, M54.9, M62.830, M99.22, M99.23, M99.24, M99.25, M99.26, M99.27, M99.28, M99.29, M99.32, M99.33, M99.34, M99.35, M99.36, M99.37, M99.38, M99.39, M99.42, M99.43, M99.44, M99.45, M99.46, M99.47, M99.48, M99.49, M99.52, M99.53, M99.54, M99.55, M99.56, M99.57, M99.58, M99.59, M99.62, M99.63, M99.64, M99.65, M99.66, M99.67, M99.68, M99.69, M99.72, M99.73, M99.74, M99.75, M99.76, M99.77, M99.78, M99.79, R10, R16, R18.8, R19.0, R19.3, R19.8** |
| **Dermatophytosis**  真菌引起的皮膚感染  **Dermatophytosis** | **ICD9: 110**  **ICD9: B35** |
| **General symptoms**  非特定的身體症狀  **GenSymptoms** | **ICD9: 780**  **ICD10: E03.5, F51.8, G40.909, G47.0, G47.1, G47.20, G47.3, G47.5, G47.61, G47.69, G47.8, G47.9, G93.3, L74.51, L74.52, R40.0, R40.1, R40.20, R40.211, R40.212, R40.221, R40.222, R40.231, R40.232, R40.234, R40.3, R40.4, R41.0, R41.1, R41.2, R41.3, R41.82, R41.89, R41.9, R42, R44.0, R44.2, R44.3, R45.83, R45.84, R50.2, R50.81, R50.9, R52, R53.0, R53.1, R53.8, R55, R56, R61, R68.0, R68.11, R68.12, R68.81, R68.83, R68.89** |
| **Symptoms involving respiratory system and other chest symptoms**  呼吸系統和其他胸部症狀  **RespChestSymptoms** | **ICD9: 786**  **ICD10: R04.2, R04.8, R04.9, R05, R06.00, R06.01, R06.02, R06.09, R06.1, R06.2, R06.3, R06.3, R06.4, R06.6, R06.8, R06.9, R07.1, R07.2, R07.8, R07.9, R09.3, R09.89, R22.2, R91.8** |
| **Symptoms involving head and neck**  頭部和頸部的症狀  **HeadNeckSymptoms** | **ICD9: 784**  **ICD10: G44.05, G44.09, G44.1, G44.3, G44.4, G44.52, G44.53, G44.59, G44.81, G44.82, G44.83, G44.84, G44.85, G44.89, R04.0, R04.1, R06.5, R06.7, R07.0, R19.6, R22.0, R22.1, R47.0, R47.1, R47.81, R47.89, R47.9, R48.0, R48.1, R48.2, R48.8, R48.9, R49, R51, R90.0** |
| **Contact dermatitis and other eczema**  皮膚疾病  **ContactDermEczema** | **ICD9: 692**  **ICD10: L23, L24.0, L24.1, L24.2, L24.3, L24.4, L24.5, L24.6, L24.7, L24.8, L24.9, L25, L30.0, L30.2, L30.8, L30.9, L55, L56, L57.1, L57.5, L57.8, L57.9, L58, L59** |
| **Viral infection in conditions classified elsewhere and of unspecified site**  病毒引起的感染  **ViralInfection** | **ICD9: 79**  **ICD10: B34.9, E07.81, E79.0, I45.81, N39.0, O28, P09, R03, R09.0, R09.2, R19.5, R29.2, R41.81, R41.89, R44.8, R44.9, R45.0, R45.3, R45.4, R45.87, R45.89, R46, R53.81, R54, R64, R68.13, R68.19, R68.82, R68.89, R69, R70, R71, R73.01, R73.02, R73.09, R73.9, R74, R75, R76, R77, R78, R79.0, R79.1, R79.81, R79.82, R79.89, R79.9, R80.0, R80.1, R80.3, R80.8, R80.9, R81, R82, R83, R84, R85, R86, R87, R88, R89, R90.8, R91.8, R92.0, R92.1, R92.2, R92.8, R93, R94, R97, R99** |
| **Overweight, obesity and other hyperalimentation**  超重、肥胖及其他過度營養狀態  **ObesityHyperal** | **ICD9: 278**  **ICD10: E65, E66.0, E66.1, E66.2, E66.8, E66.9, E67, E68** |
| **Other and unspecified disorders of joint**  未明確指定的關節疾病  **JointDisorders** | **ICD9: 719**  **ICD10: M12.2, M12.3, M12.4, M25.0, M25.1, M25.4, M25.50, M25.51, M25.52, M25.53, M25.55, M25.56, M25.57, M25.60, M25.61, M25.62, M25.63, M25.64, M25.65, M25.66, M25.67, M25.8, M25.9, M79.643, M79.646, R26.2, R29.4, R29.898** |
| **Acute bronchitis and bronchiolitis**  呼吸道疾病  **AcuteBronchitis** | **ICD9: 466**  **ICD10: J20.8, J20.9, J21** |
| **Other disorders of soft tissues**  其他軟組織的疾病  **SoftTissueDis** | **ICD9: 729**  **ICD10: G47.62, M35.6, M54.10, M54.18, M60.8, M60.9, M70.8, M70.9, M72.9, M79, R25.2, R29.898** |
| **Nonspecific findings on examination of blood**  血液檢查時發現的一些非特定性的異常或發現  **BloodExamFindings** | **ICD9: 790**  **ICD10: B34.9, E07.81, E79.0, R70, R71, R73.01, R73.02, R73.09, R73.9, R74, R77, R78, R79.0, R79.1, R79.81, R79.82, R79.89, R79.9, R97.2** |
| **Disorders of refraction and accommodation**  屈光和調節的疾病  **RefractionDis** | **ICD9: 367**  **ICD10: H52** |
| **Disorders of conjunctiva**  眼球表面覆蓋的結膜的各種疾病  **ConjunctivaDis** | **ICD9: 372**  **ICD10: H10.0, H10.1, H10.2, H10.3, H10.4, H10.5, H10.81, H10.89, H10.9, H11** |

**三院病歷資料整理流程:**

|  |  |  |
| --- | --- | --- |
| 步驟 | 說明 | 患者數量 |
| 1 | 篩選就診紀錄的病例資料、議題相關疾病碼:  (糖尿病、相關併發症、控制疾病) 病例 |  |
| 2 | 篩選目標病患 (歸人)  操作定義: 一年內3次門診或1次住院疾病紀錄 | N = 7692 |
| 3. | 合併1. 病人基本資料、2.目標病患及相關病例資料 |  |
| 4 | Exclude:  病例資料對應多組性別年齡 (N = 76)  年齡 < 20 或 年齡 > 100 (N = 3)  index date < 2009(最早發病年後一年) (N = 741) | N = 6872 |

**流程圖:**

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**Table1. 糖尿病患者基線特徵分布**

|  |  |  |
| --- | --- | --- |
|  | | overall(N=6872) |
| AGE | | |
|  | Mean(SD) | 68.23(12.23) |
| Median(IQR) | 68.35(17.64) |
| (Min,Max) | (21.63,99.25) |
| Index\_year | | |
|  | 2009 | 309(4.5%) |
| 2010 | 294(4.28%) |
| 2011 | 653(9.5%) |
| 2012 | 889(12.94%) |
| 2013 | 568(8.27%) |
| 2014 | 456(6.64%) |
| 2015 | 1399(20.36%) |
| 2016 | 1026(14.93%) |
| 2017 | 620(9.02%) |
| 2018 | 467(6.8%) |
| 2019 | 191(2.78%) |
| SEX\_TYPE |  |  |
|  | 1 | 3823(55.63%) |
|  | 0 | 3049(44.37%) |
| AGE\_GROUP |  |  |
|  | 20-30 | 17(0.25%) |
|  | 30-40 | 71(1.03%) |
|  | 40-50 | 394(5.73%) |
|  | 50-60 | 1294(18.83%) |
|  | 60-70 | 1974(28.73%) |
|  | 70-80 | 1843(26.82%) |
|  | 80-90 | 1120(16.3%) |
|  | 90-100 | 159(2.31%) |
| Hypertension\_event |  |  |
|  | 1 | 1143(16.63%) |
|  | 0 | 5729(83.37%) |
| PeripheralEnthe\_event |  |  |
|  | 1 | 95(1.38%) |
|  | 0 | 6777(98.62%) |
| UnknownCauses\_event |  |  |
|  | 1 | 7(0.1%) |
|  | 0 | 6865(99.9%) |
| LipoidMetabDis\_event |  |  |
|  | 1 | 992(14.44%) |
|  | 0 | 5880(85.56%) |
| AcuteURI\_event |  |  |
|  | 1 | 33(0.48%) |
|  | 0 | 6839(99.52%) |
| AbdPelvicSymptoms\_event |  |  |
|  | 1 | 135(1.96%) |
|  | 0 | 6737(98.04%) |
| Dermatophytosis\_event |  |  |
|  | 1 | 102(1.48%) |
|  | 0 | 6770(98.52%) |
| GenSymptoms\_event |  |  |
|  | 1 | 654(9.52%) |
|  | 0 | 6218(90.48%) |
| RespChestSymptoms\_event |  |  |
|  | 1 | 196(2.85%) |
|  | 0 | 6676(97.15%) |
| HeadNeckSymptoms\_event |  |  |
|  | 1 | 96(1.4%) |
|  | 0 | 6776(98.6%) |
| ContactDermEczema\_event |  |  |
|  | 1 | 103(1.5%) |
|  | 0 | 6769(98.5%) |
| ViralInfection\_event |  |  |
|  | 1 | 200(2.91%) |
|  | 0 | 6672(97.09%) |
| ObesityHyperal\_event |  |  |
|  | 1 | 13(0.19%) |
|  | 0 | 6859(99.81%) |
| JointDisorders\_event |  |  |
|  | 1 | 17(0.25%) |
|  | 0 | 6855(99.75%) |
| AcuteBronchitis\_event |  |  |
|  | 1 | 35(0.51%) |
|  | 0 | 6837(99.49%) |
| SoftTissueDis\_event |  |  |
|  | 1 | 191(2.78%) |
|  | 0 | 6681(97.22%) |
| BloodExamFindings\_event |  |  |
|  | 1 | 82(1.19%) |
|  | 0 | 6790(98.81%) |
| RefractionDis\_event |  |  |
|  | 1 | 9(0.13%) |
|  | 0 | 6863(99.87%) |
| ConjunctivaDis\_event |  |  |
|  | 1 | 142(2.07%) |
|  | 0 | 6730(97.93%) |

**討論:**

**資料問題: 從Index\_year可以看到三院的臨床資料糖尿病患者大多發生在2015和2016 , 是否之前做的分析也有發現相同的情況?**

資料數從文獻中有看到隨年分增加

Reference:

Nguyen, P.-A., Hsu, M.-H., Chang, T.-H., Yang, H.-C., Huang, C.-W., Liao, C.-T., Lu, C. Y., & Hsu, J. C. (2024). Taipei Medical University Clinical Research Database: A Collaborative Hospital Ehr Database aligned with International Common Data Standards. *BMJ Health &amp; Care Informatics*, *31*(1). https://doi.org/10.1136/bmjhci-2023-100890

**lab定義: 檢驗結果報告**

lab 處理方式: lab result 皆只有 test item id, 需要找對應的test name

1. 資料來源: 萬芳與其他兩院儲存方式不同
2. 萬芳: exper\_sign\_w
   1. 檢驗項目ID: GROUP\_CODE (健保碼)
   2. 處理方式: 從萬芳的檢驗資訊查詢系統找檢驗項目的健保碼
3. 雙和、北醫: labresult\_s(t)
   1. 檢驗項目ID: R\_ITEM
   2. 處理方式: 從exp\_item\_s(t) 找出對應 R\_ITEM\_NAME
4. 資料整理流程:
   1. 先將兩院與萬芳lab資料做合併
   2. 保留ID、 檢驗日、檢驗項目、檢驗值並rename col
   3. 找尋所需的檢驗項目, ex: HbA1c, Albumin
   4. 將單位分開儲存同時排除無法辨識的資料, ex: <, >, NA

篩選要分析的糖尿病患者：在定義好的Index\_date後的一年內，定期進行檢測的患者

目的：避免在計算變異程度時受時間影響

篩選方法：

從Index\_date開始，觀察該日期前後45天內是否有檢測紀錄，有的話記為1，沒有則記為0。接著每隔90天進行一次相同的觀察，直到觀察到第360天，確認患者整年是否有進行定期檢測。最終，所有觀察期間內都有檢測紀錄的患者作為分析的對象。

**Table2.糖尿病目標病患各季度HbA1c中位數及檢驗頻率**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | overall(N=1133) |  |  | overall(N=1133) |
| median\_value\_0 |  |  | total |  |  |
|  | Mean(sd) | 8.07(1.97) |  | Mean(sd) | 5.84(0.94) |
|  | Median(IQR) | 7.5(2.45) |  | Median(IQR) | 6(1) |
|  | (Min,Max) | (4.75,17.9) |  | (Min,Max) | (1,3) |
| median\_value\_1 |  |  |  |  |  |
|  | Mean(sd) | 7.29(1.36) |  |  |  |
|  | Median(IQR) | 7(1.5) |  |  |  |
|  | (Min,Max) | (3.5,14) |  |  |  |
| median\_value\_2 |  |  |  |  |  |
|  | Mean(sd) | 7.24(1.32) |  |  |  |
|  | Median(IQR) | 6.9(1.4) |  |  |  |
|  | (Min,Max) | (4.2,14.2) |  |  |  |
| median\_value\_3 |  |  |  |  |  |
|  | Mean(sd) | 7.22(1.28) |  |  |  |
|  | Median(IQR) | 6.9(1.4) |  |  |  |
|  | (Min,Max) | (4,13.4) |  |  |  |
| median\_value\_4 |  |  |  |  |  |
|  | Mean(sd) | 7.24(1.37) |  |  |  |
|  | Median(IQR) | 6.9(1.3) |  |  |  |
|  | (Min,Max) | (4.1,15.5) |  |  |  |
| n\_0 |  |  |  |  |  |
|  | Mean(sd) | 1.35(0.55) |  |  |  |
|  | Median(IQR) | 1(1) |  |  |  |
|  | (Min,Max) | (1,4) |  |  |  |
| n\_1 |  |  |  |  |  |
|  | Mean(sd) | 1.19(0.42) |  |  |  |
|  | Median(IQR) | 1(0) |  |  |  |
|  | (Min,Max) | (1,4) |  |  |  |
| n\_2 |  |  |  |  |  |
|  | Mean(sd) | 1.13(0.36) |  |  |  |
|  | Median(IQR) | 1(0) |  |  |  |
|  | (Min,Max) | (1,3) |  |  |  |
| n\_3 |  |  |  |  |  |
|  | Mean(sd) | 1.1(0.3) |  |  |  |
|  | Median(IQR) | 1(0) |  |  |  |
|  | (Min,Max) | (1,3) |  |  |  |
| n\_4 |  |  |  |  |  |
|  | Mean(sd) | 1.08(0.28) |  |  |  |
|  | Median(IQR) | 1(0) |  |  |  |
|  | (Min,Max) | (1,3) |  |  |  |

**Table3糖尿病整體病患各季Albumin的檢驗值中位數、次數**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | overall(n=174) |  |  | overall(n=174) |
| median\_value\_0 |  |  | total |  |  |
|  | Mean(sd) | 3.75(0.55) |  | Mean(sd) | 11.4(5.32) |
|  | Median(IQR) | 3.85(0.74) |  | Median(IQR) | 12(8) |
|  | (Min,Max) | (2.3,4.8) |  | (Min,Max) | (5,40) |
| median\_value\_1 |  |  |  |  |  |
|  | Mean(sd) | 3.85(0.48) |  |  |  |
|  | Median(IQR) | 3.9(0.6) |  |  |  |
|  | (Min,Max) | (2.5,4.8) |  |  |  |
| median\_value\_2 |  |  |  |  |  |
|  | Mean(sd) | 3.88(0.5) |  |  |  |
|  | Median(IQR) | 3.9(0.6) |  |  |  |
|  | (Min,Max) | (2,4.9) |  |  |  |
| median\_value\_3 |  |  |  |  |  |
|  | Mean(sd) | 3.84(0.52) |  |  |  |
|  | Median(IQR) | 3.9(0.6) |  |  |  |
|  | (Min,Max) | (2.1,4.9) |  |  |  |
| median\_value\_4 |  |  |  |  |  |
|  | Mean(sd) | 3.85(0.5) |  |  |  |
|  | Median(IQR) | 3.9(0.65) |  |  |  |
|  | (Min,Max) | (2.15,4.8) |  |  |  |
| n\_0 |  |  |  |  |  |
|  | Mean(sd) | 2.26(1.47) |  |  |  |
|  | Median(IQR) | 2(2) |  |  |  |
|  | (Min,Max) | (1,11) |  |  |  |
| n\_1 |  |  |  |  |  |
|  | Mean(sd) | 2.27(1.25) |  |  |  |
|  | Median(IQR) | 2(2) |  |  |  |
|  | (Min,Max) | (1,9) |  |  |  |
| n\_2 |  |  |  |  |  |
|  | Mean(sd) | 2.24(1.25) |  |  |  |
|  | Median(IQR) | 2(2) |  |  |  |
|  | (Min,Max) | (1,11) |  |  |  |
| n\_3 |  |  |  |  |  |
|  | Mean(sd) | 2.33(1.48) |  |  |  |
|  | Median(IQR) | 2(2) |  |  |  |
|  | (Min,Max) | (1,12) |  |  |  |
| n\_4 |  |  |  |  |  |
|  | Mean(sd) | 2.29(1.5) |  |  |  |
|  | Median(IQR) | 2(2) |  |  |  |
|  | (Min,Max) | (1,13) |  |  |  |

**糖尿病患者相關併發症的整理流程:**

Exclude：

index date 前有發生併發症

index date 後一年內發生併發症

**Table4: 糖尿病患者各併發症情況:**

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome\_test | # of event | sum of follow up | IR% |
| EyeComp\_HbA1c | 71 | 2206525 | 1.174 |
| CardioDisease\_HbA1c | 260 | 1481514 | 6.406 |
| CerebroDisease\_HbA1c | 142 | 2145730 | 2.415 |
| PeripheralVascDisease\_HbA1c | 10 | 2522218 | 0.145 |
| Nephropathy\_HbA1c | 131 | 2174790 | 2.199 |
| DiabeticNeuro\_HbA1c | 76 | 2220496 | 1.249 |
| EyeComp\_ALBUMIN | 9 | 271929 | 1.208 |
| CardioDisease\_ALBUMIN | 36 | 147782 | 8.891 |
| CerebroDisease\_ALBUMIN | 22 | 285877 | 2.809 |
| PeripheralVascDisease\_ALBUMIN | 4 | 338207 | 0.432 |
| Nephropathy\_ALBUMIN | 16 | 57896 | 10.087 |
| DiabeticNeuro\_ALBUMIN | 8 | 313118 | 0.933 |

**分析結果 :**

1. 模型: cox model
2. 解釋變數:
   1. 固定變數: SEX\_TYPE, Index year, AGE\_GROUP, baseline mean, control disease 發生與否
   2. 放入不同檢驗項目的變異程度指標: SD, CV, RMS
3. 反應變數: 病患追蹤日期、是否有發生併發症
4. 模型指標: HR (Hazard ratios), 95% CI, P-value
5. P-value: \*: p < 0.05, \*\*: p < 0.01, \*\*\*: p < 0.001

Table5: Cox model 分析結果

Outcome: Eye complications、Test item: HbA1c (N = 1052)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 1.149 | 1.035,1.277 | \*\* |
| Model2: Baseline + SD | Baseline | 1.234 | 0.997,1.528 | . |
|  | SD | 0.793 | 0.432,1.455 |  |
| Model3: Baseline + CV | Baseline | 1.276 | 1.077,1.511 | \*\* |
|  | CV | 0.037 | 0,2.803 |  |
| Model4: Baseline + RMS | Baseline | 0.879 | 0.734,1.053 |  |
|  | RMS | 1.768 | 1.343,2.326 | \*\*\* |

Table6: Cox model 分析結果

Outcome: Eye complications、Test item: ALBUMIN (N = 151)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.228 | 0.05,1.037 | . |
| Model2: Baseline + SD | Baseline | 0.394 | 0.075,2.065 |  |
|  | SD | 187.034 | 0.045,769457.059 |  |
| Model3: Baseline + CV | Baseline | 0.626 | 0.095,4.11 |  |
|  | CV | 6.66E+10 | 0,3.67299051294872e+25 |  |
| Model4: Baseline + RMS | Baseline | 0.796 | 0.062,10.171 |  |
|  | RMS | 0.139 | 0.006,3.294 |  |

Table7: Cox model 分析結果

Outcome: Cardiovascular disease、Test item: HbA1c (N = 791)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.966 | 0.904,1.033 |  |
| Model2: Baseline + SD | Baseline | 0.973 | 0.874,1.084 |  |
|  | SD | 0.975 | 0.713,1.331 |  |
| Model3: Baseline + CV | Baseline | 0.972 | 0.885,1.067 |  |
|  | CV | 0.825 | 0.087,7.859 |  |
| Model4: Baseline + RMS | Baseline | 0.935 | 0.841,1.04 |  |
|  | RMS | 1.069 | 0.906,1.26 |  |

Table8: Cox model 分析結果

Outcome: Cardiovascular disease、Test item: ALBUMIN (N = 93)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.573 | 0.242,1.353 |  |
| Model2: Baseline + SD | Baseline | 0.37 | 0.127,1.082 | . |
|  | SD | 0.033 | 0,2.66 |  |
| Model3: Baseline + CV | Baseline | 0.286 | 0.086,0.954 | \* |
|  | CV | 0 | 0,4.17 | . |
| Model4: Baseline + RMS | Baseline | 0.256 | 0.06,1.087 | . |
|  | RMS | 4.189 | 0.528,33.235 |  |

Table9: Cox model 分析結果

Outcome: Cerebrovascular disease、Test item: HbA1c (N = 965)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.994 | 0.914,1.08 |  |
| Model2: Baseline + SD | Baseline | 1.09 | 0.947,1.256 |  |
|  | SD | 0.708 | 0.461,1.087 |  |
| Model3: Baseline + CV | Baseline | 1.057 | 0.94,1.19 |  |
|  | CV | 0.106 | 0.005,2.27 |  |
| Model4: Baseline + RMS | Baseline | 0.92 | 0.803,1.054 |  |
|  | RMS | 1.168 | 0.949,1.437 |  |

Table10: Cox model 分析結果

Outcome: Cerebrovascular disease、Test item: ALBUMIN (N = 150)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.208 | 0.084,0.515 | \*\*\* |
| Model2: Baseline + SD | Baseline | 0.155 | 0.049,0.491 | \*\* |
|  | SD | 0.092 | 0,20.66 |  |
| Model3: Baseline + CV | Baseline | 0.114 | 0.026,0.494 | \*\* |
|  | CV | 0 | 0,8474.83 |  |
| Model4: Baseline + RMS | Baseline | 0.079 | 0.015,0.408 | \*\* |
|  | RMS | 4.449 | 0.529,37.409 |  |

Table11: Cox model 分析結果

Outcome: Peripheral vascular disease、Test item: HbA1c (N = 1129)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.844 | 0.576,1.239 |  |
| Model2: Baseline + SD | Baseline | 0.709 | 0.5,1.004 | . |
|  | SD | 1.978 | 0.826,4.735 |  |
| Model3: Baseline + CV | Baseline | 0.738 | 0.516,1.054 | . |
|  | CV | 109.683 | 0.113,106797.343 |  |
| Model4: Baseline + RMS | Baseline | 0.808 | 0.549,1.188 |  |
|  | RMS | 1.1 | 0.612,1.977 |  |

Table12: Cox model 分析結果

Outcome: Peripheral vascular disease、Test item: ALBUMIN (N = 173)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 2.811 | 0.122,64.751 |  |
| Model2: Baseline + SD | Baseline | 2.359 | 0.103,54.224 |  |
|  | SD | 11.58 | 0.003,46631.821 |  |
| Model3: Baseline + CV | Baseline | 2.714 | 0.129,57.164 |  |
|  | CV | 2697.67 | 0,111656906414237000 |  |
| Model4: Baseline + RMS | Baseline | 0.706 | 0.009,57.332 |  |
|  | RMS | 13.928 | 0.035,5554.871 |  |

Table13: Cox model 分析結果

Outcome: Nephropathy、Test item: HbA1c (N = 1033)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 1.09 | 1.003,1.185 | \* |
| Model2: Baseline + SD | Baseline | 1.187 | 1.011,1.393 | \* |
|  | SD | 0.752 | 0.472,1.197 |  |
| Model3: Baseline + CV | Baseline | 1.21 | 1.063,1.379 | \*\* |
|  | CV | 0.033 | 0.001,0.967 | \* |
| Model4: Baseline + RMS | Baseline | 0.938 | 0.819,1.073 |  |
|  | RMS | 1.381 | 1.119,1.704 | \*\* |

Table14: Cox model 分析結果

Outcome: Nephropathy、Test item: ALBUMIN (N = 43)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 56.347 | 19.89,159.627 | \*\*\* |
| Model2: Baseline + SD | Baseline | 50.498 | 17.855,142.821 | \*\*\* |
|  | SD | 0.602 | 0.002,163.39 |  |
| Model3: Baseline + CV | Baseline | 63.139 | 22.317,178.629 | \*\*\* |
|  | CV | 5.726 | 0,949422374.438 |  |
| Model4: Baseline + RMS | Baseline | 14456.14 | 4683.458,44620.855 | \*\*\* |
|  | RMS | 0.006 | 0.001,0.021 | \*\*\* |

Table15: Cox model 分析結果

Outcome: Diabetic neuropathy、Test item: HbA1c (N = 1035)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.943 | 0.835,1.065 |  |
| Model2: Baseline + SD | Baseline | 1.014 | 0.824,1.249 |  |
|  | SD | 0.766 | 0.411,1.429 |  |
| Model3: Baseline + CV | Baseline | 1.025 | 0.86,1.222 |  |
|  | CV | 0.053 | 0.001,5.128 |  |
| Model4: Baseline + RMS | Baseline | 0.767 | 0.629,0.936 | \*\* |
|  | RMS | 1.516 | 1.138,2.022 | \*\* |

Table16: Cox model 分析結果

Outcome: Diabetic neuropathy、Test item: ALBUMIN (N = 161)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Models | Variables | HR | 95%CI | P-value |
| Model1: Baseline | Baseline | 0.343 | 0.076,1.548 |  |
| Model2: Baseline + SD | Baseline | 0.096 | 0.016,0.576 | \* |
|  | SD | 0 | 0,0.457 | \* |
| Model3: Baseline + CV | Baseline | 0.102 | 0.017,0.614 | \* |
|  | CV | 0 | 0,3.377 | . |
| Model4: Baseline + RMS | Baseline | 0.58 | 0.127,2.638 |  |
|  | RMS | 0.439 | 0.072,2.683 |  |

**結論:**

1. 預期結果: 變異程度大, 理論上風險上升HR > 1且顯著, 才可以說考慮這個生理數值是有意義的。
2. 模型結果顯示HbA1c的的變異程度對於Eye complications、 Nephropathy、 Diabetic neuropathy等併發症為重要因子, 符合其他文獻結果, 代表這份資料是具準確性。
3. 資料不顯著的原因: 樣本數過小、發病率太低、baseline 每季只算一個mean資訊丟失部分資訊
4. 後續可以做的研究方向:
   1. 探索加入其他可能的變異性指標，如HVS
   2. Outlier 討論
   3. 目前已驗證的數據準確性，進行與中風相關的分析

**Appendix:**

找尋相關文獻討論到常見的檢驗項目、併發症與糖尿病之間的關係

檢驗項目: HbA1c、ALBUMIN、Uric、HDL、LDL

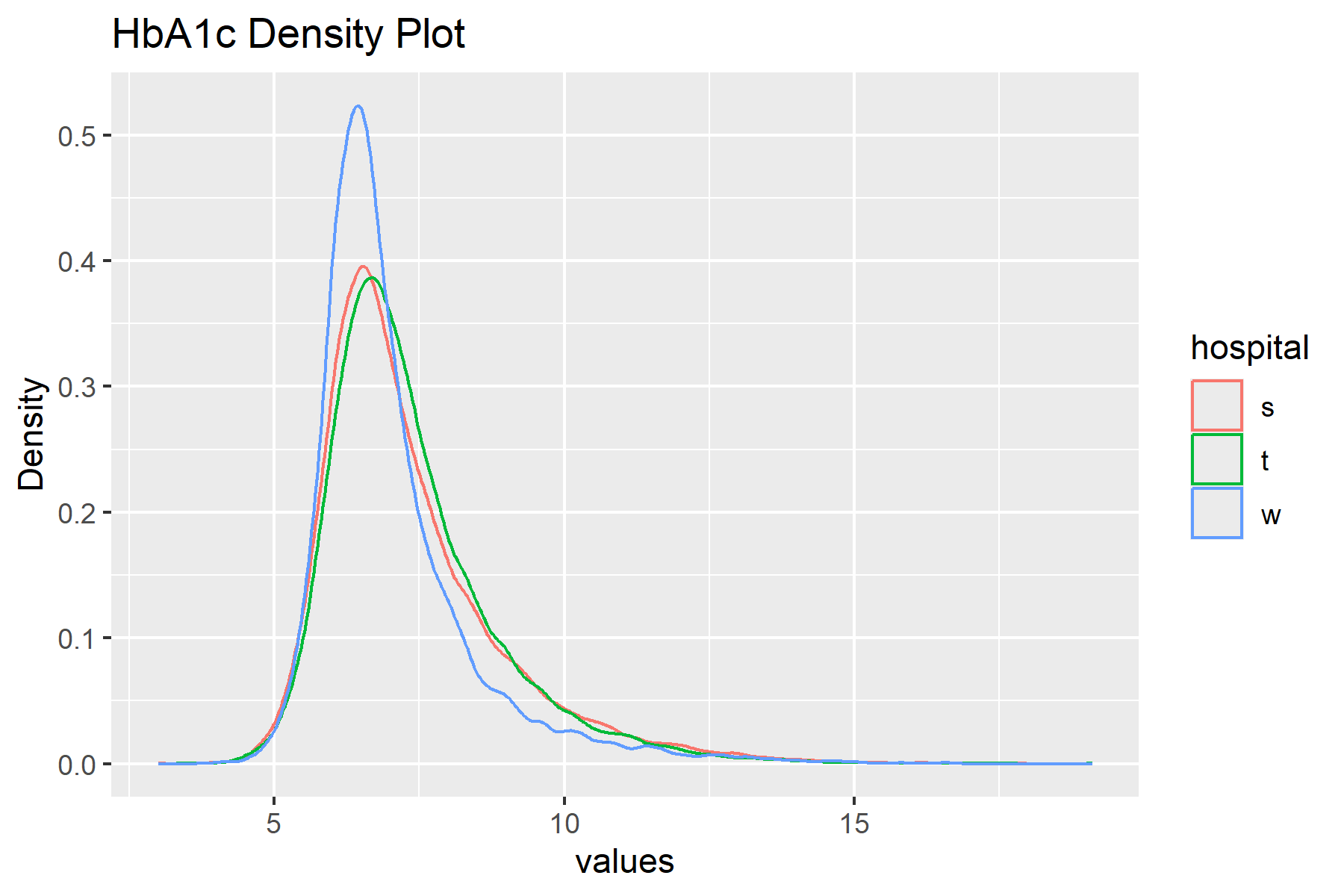
結論: 5 種併發症、4種模型組合、6 種檢驗項目 = 120模型結

模型顯示，對於各併發症的檢驗項目中，以下檢驗項目的變異程度為顯著因子:

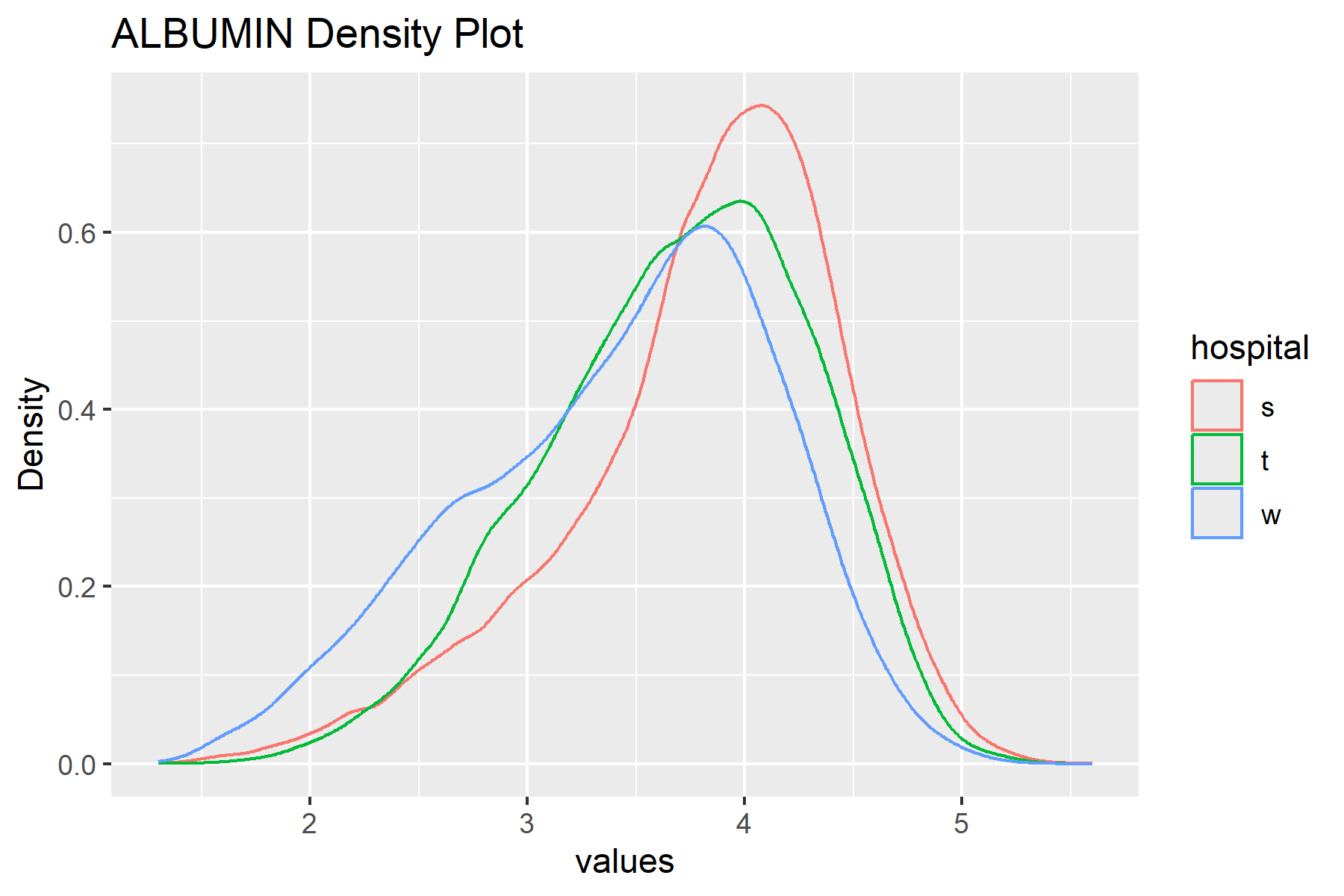
1. HbA1c: EyeComp、Nephropathy、DiabeticNeuro
2. ALBUMIN: 無
3. Uric: Nephropathy
4. HDL: CerebroDisease
5. LDL: 無

**Outlier 的討論: 檢驗項目在各醫院的density plot**

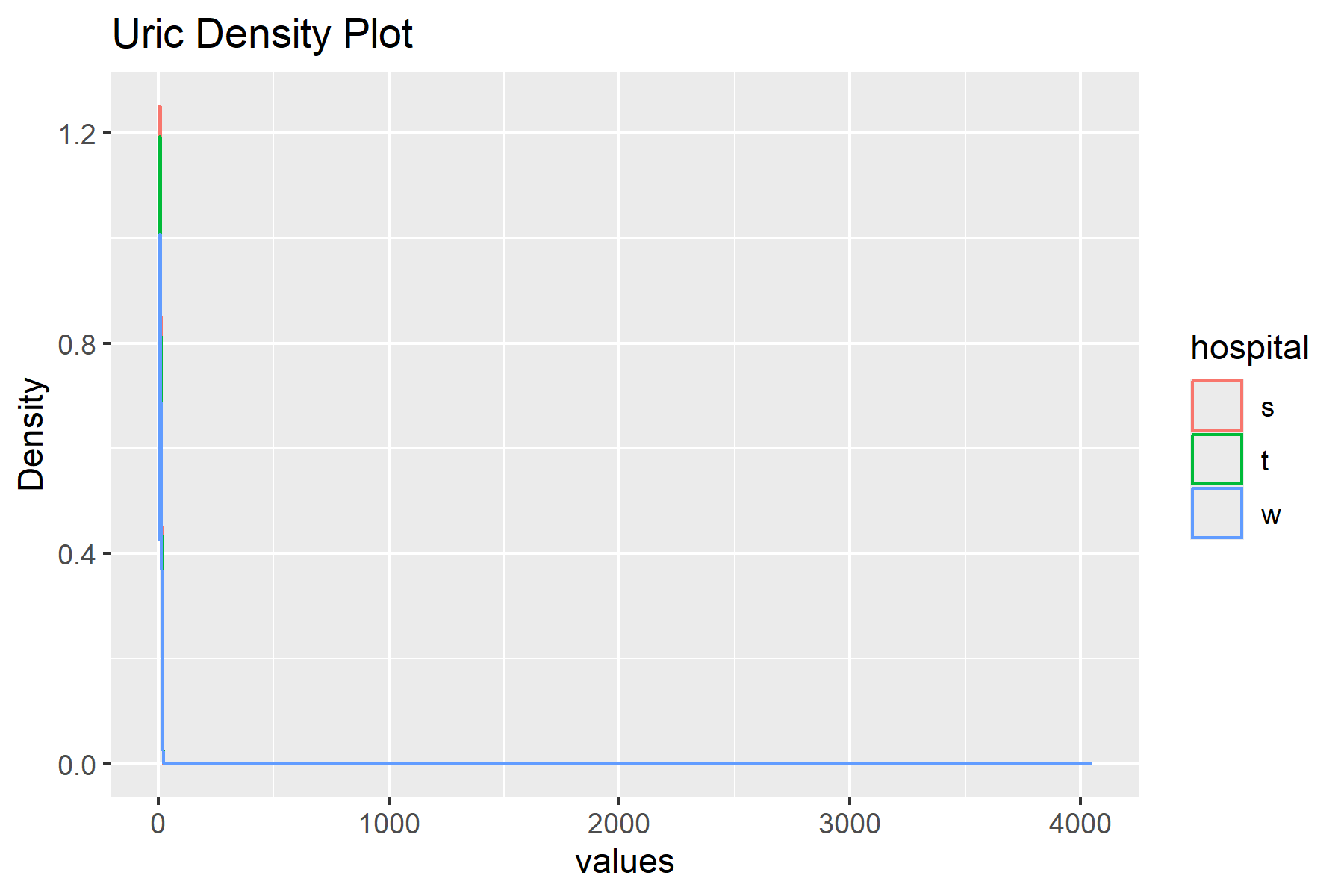
HbA1c Test ID: "014701", "F09006B"



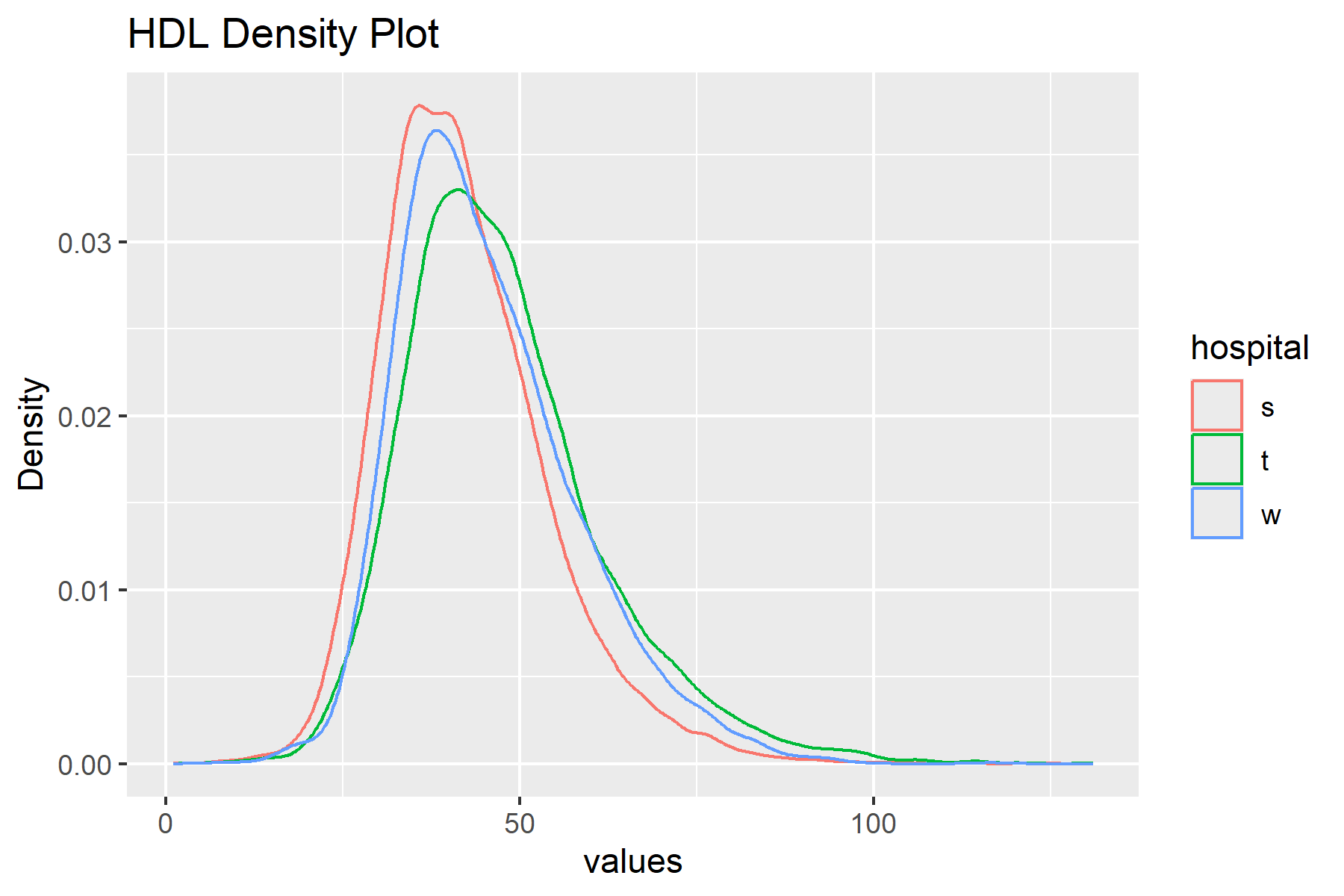
ALBUMIN Test ID: "010301", "11D101", "F09038C"



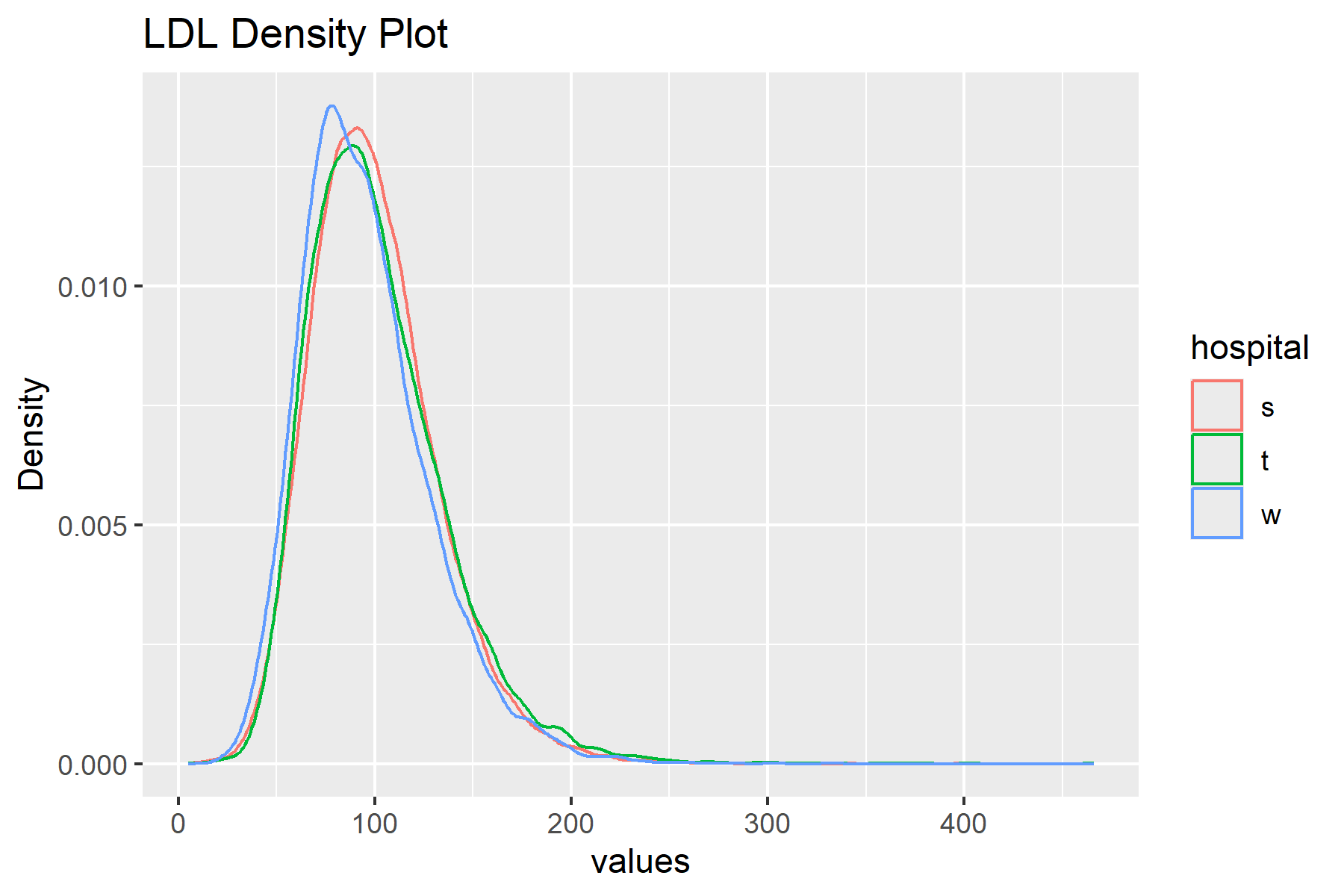
Uric Test ID: "011001"



HDL Test ID: "F09043A", "011301"



LDL Test ID: "F09044A", "011401"



**討論:**

1. 可以明顯看出Uric acid 檢驗項目在萬芳的檢驗項目裡單位是不一致的
2. 過大或過小的數值是否要剔除, ex: LDL 有 > 400數值

**中風相關主題:**

**自變量**（獨立變量）：生理數值檢測項目的變異性

* 血壓變異性（如日間和夜間的血壓波動）
* 血糖變異性（如血糖的日間波動）
* 血脂變異性（如LDL和HDL的波動）

**因變量**（依賴變量）：中風併發症

 **運動功能障礙**: Motor Function Impairment

 **語言障礙**: Speech Impairment

 **認知障礙**: Cognitive Impairment

 **情緒和心理問題**: Emotional and Psychological Problems

 **吞嚥困難**: Dysphagia

 **褥瘡**: Pressure Ulcers

**控制變量**：年齡、性別、控制疾病、生活方式因素（如吸煙、飲酒）、中風類型和嚴重程度等。

Control Variables:

 **高脂血症**（Hyperlipidemia）

 **冠心病**（Coronary Artery Disease）

 **慢性腎病**（Chronic Kidney Disease）

 **慢性阻塞性肺病**（Chronic Obstructive Pulmonary Disease, COPD）

 **心房顫動**（Atrial Fibrillation）

 **周邊動脈疾病**（Peripheral Artery Disease）

 **肥胖**（Obesity）

 **代謝綜合徵**（Metabolic Syndrome）

 **睡眠呼吸暫停綜合徵**（Sleep Apnea Syndrome）

 **甲狀腺疾病**（Thyroid Disorders）

 **腦外傷史**（History of Traumatic Brain Injury）

 **抑鬱症**（Depression）

 **焦慮症**（Anxiety Disorders）

 **酒精使用障礙**（Alcohol Use Disorder）

 **藥物濫用**（Substance Abuse）

 **缺乏運動**（Physical Inactivity）

 **不良飲食習慣**（Unhealthy Dietary Habits）

 **家族中風史**（Family History of Stroke）

 高血壓

 糖尿病