BCM Infectious Disease COVID19 Literature Review Newsletter: WEEK 23
August 31st-September 4th, 2020

Week 23 Newsletter Prepared by:

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The number of COVID-19 confirmed cases, related deaths, and total tests reported for State and County

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Last Updated</th>
<th>COVID-19 cases in Texas</th>
<th>COVID-19 cases in Harris County</th>
<th>COVID-19 related deaths in Texas</th>
<th>COVID-19 related deaths in Harris County</th>
<th>Total tests performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Texas DSHS *</td>
<td>Aug 30, 2020, 3:05 PM</td>
<td>610,354 (Estimated active cases: 110,836)</td>
<td>104,649 (Estimated active cases: 13,099)</td>
<td>12,510</td>
<td>2,188</td>
<td>4,924,712 Texas</td>
</tr>
</tbody>
</table>

*Texas DSHS daily case count now includes all cases reported publicly by local health departments around the state

* Data sources from WHO, CDC, ECDC, NHC, DXY, 1point3acres, Worldometers.info, BNO, state and national government health departments, and local media reports.

1. Data represents total viral tests performed (positive and negative) at private and public labs in Texas. N/A = not available

COVID-19 diagnoses per day in the greater Houston area

Source: County Health departments, Texas DSHS.
In the News:


2. **CDC testing asymptomatic persons with close contact to COVID+ case** Updated August 27th, 2020. [https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/contact-tracing.html#:~:text=If%20testing%20is%20not%20available%2C%20for%20those%20who%20develop%20symptoms.]
   a. Testing should be considered for all close contacts of confirmed or probably COVID-19 patients
   b. Asymptomatic contacts testing negative or those who are not tested should **self-quarantine** and be monitored for 14 days after their last exposure

Articles:

   
   **Background:**
   - Rapid and accurate diagnostics tests are needed for control of viral transmission
   - Current practices use nasopharyngeal swabs, saliva specimens may be an alternative

   **Methods:**
   - 70 inpatients confirmed positive with RT-PCR by nasopharyngeal swab at hospital admission
     - Yale-New Haven Hospital, March 23rd-June 16th, 2020
     - Every 3 days obtained a nasopharyngeal swab collected by healthcare worker and a saliva specimen collected by the patient
   - 495 asymptomatic health care workers working on COVID-19 units or with occupational exposure involved in active hospital screening protocol with RT-PCR
     - Collected self-administered nasopharyngeal swab and saliva sample every 3 days for up to 84 days or until test positive

   **Results:**
   - Inpatient Samples: More SARS-CoV-2 RNA copies were detected in the saliva specimen compared to nasopharyngeal swab (on first available test)
     - Higher percentage of saliva samples were positive up to 10 days after COVID-19 diagnosis
       - However at >11 days there is a higher percentage of nasopharyngeal samples positive and there is no statistics listed in the analysis
     - Level of SARS-CoV-2 RNA decreased after symptom onset in both saliva and nasopharyngeal swab specimens in matched samples over time
     - Greater variation in Ct values in nasopharyngeal swab than in saliva specimens
   - Healthcare Worker Samples:
13 people had positive saliva specimens, only 9 had matched nasopharyngeal samples on the same day

- 7 of the matched nasopharyngeal samples were negative on the same day but later confirmed positive (unclear how much later)
- Do not mention if there were any positive nasopharyngeal samples with negative saliva specimens

**Conclusions:**
- Self-collected saliva samples negates the need for direct interaction between healthcare workers and patients, reduces need for PPE, and has similar sensitivity as nasopharyngeal swabs
- Limitations: small, single-center study in a hospital setting may not have external validity for general population, particularly in out of hospital settings.

- Widespread SARS-CoV-2 testing is essential to safely reopening the United States, but test accuracy remains a concern
- Nasopharyngeal diagnostic test can be inaccurate in two ways:
  - False positive
    - Causes unnecessary quarantine and contact tracing
  - False negative: based on pretest probability and test sensitivity
    - Failure to isolate individuals with disease, increased transmission
- FDA currently issue EUA for diagnostic tests, performance of these tests vary among manufacturers
  - Non-EUA criteria requires a reference standard to determine true accuracy, clinical sensitivity is the proportion of positive index tests in patients who actually have the disease however it is unclear if tests under EUA are using this criteria
  - Under EUA companies demonstrate clinical test performance by establishing the new test with an authorized RT-PCR in known positive material from symptomatic specimen which leads to overestimates of test sensitivity
- A reference standard measuring sensitivity of SARS-CoV-2 tests in asymptomatic people is critical to increase confidence in test results for contact-tracing or screening purposes
- **Conclusions**
  - Diagnostic tests are helpful if they are highly sensitive and validated under realistic conditions against reference standards
  - FDA should require manufactures to provide details of tests’ clinical sensitivity/specificity
  - Determining test sensitivity in asymptomatic people should be an urgent priority
  - Negative results even on highly sensitive test can not rule out infection if the pretest probability is high


**Background:**
- Diabetes has been associated with increased COVID-19-related mortality, but the association between modifiable risk factors, including hyperglycemia and obesity, and COVID-19-related mortality among people with diabetes is unclear.
The authors assessed associations between risk factors and COVID-19-related mortality in people with type 1 and type 2 diabetes.

**Methods:**

- Population-based cohort study of people with diagnosed diabetes who were registered with a general practice in England. National population data on people with type 1 and type 2 diabetes collated by the National Diabetes Audit (NDA) were linked to mortality records collated by the Office for National Statistics from Jan 2, 2017, to May 11, 2020. The authors identified the weekly number of deaths in people with type 1 and type 2 diabetes during the first 19 weeks of 2020 and calculated the percentage change from the mean number of deaths for the corresponding weeks in 2017, 2018, and 2019.

- The associations between risk factors (including sex, age, ethnicity, socioeconomic deprivation, HbA1c, renal impairment [from estimated glomerular filtration rate (eGFR)], BMI, tobacco smoking status, and cardiovascular comorbidities) and COVID-19-related mortality between Feb 16 and May 11, 2020, were investigated by use of Cox proportional hazards models.

**Results:**

- Weekly death registrations in the first 19 weeks of 2020 exceeded the corresponding 3-year weekly averages for 2017–19 by 672 (50.9%) in people with type 1 diabetes and 16 071 (64.3%) in people with type 2 diabetes.

- Between Feb 16 and May 11, 2020, among 264 390 people with type 1 diabetes and 2 874 020 people with type 2 diabetes, 1604 people with type 1 diabetes and 36 291 people with type 2 diabetes died from all causes. Of these total deaths, 464 in people with type 1 diabetes and 10 525 in people with type 2 diabetes were defined as COVID-19 related, of which 289 (62.3%) and 5833 (55.4%), respectively, occurred in people with a history of cardiovascular disease or with renal impairment (eGFR <60 mL/min per 1.73 m2). Male sex, older age, renal impairment, non-white ethnicity, socioeconomic deprivation, and previous stroke and heart failure were associated with increased COVID-19-related mortality in both type 1 and type 2 diabetes.

- Compared with people with an HbA1c of 48–53 mmol/mol (6.5–7.0%), people with an HbA1c of 86 mmol/mol (10.0%) or higher had increased COVID-19-related mortality (hazard ratio [HR] 2.23 [95% CI 1.50–3.30, p<0.0001] in type 1 diabetes and 1.61 [1.47–1.77, p<0.0001] in type 2 diabetes). In addition, in people with type 2 diabetes, COVID-19-related mortality was significantly higher in those with an HbA1c of 59 mmol/mol (7.6%) or higher than in those with an HbA1c of 48–53 mmol/mol (6.5–7.0%) (HR 1.22, p<0.0001).

- The association between BMI and COVID-19-related mortality was U-shaped: in type 1 diabetes, compared with a BMI of 25.0–29.9 kg/m2, a BMI of less than 20.0 kg/m2 had an HR of 2.45 (95% CI 1.60–3.75, p<0.0001) and a BMI of 40.0 kg/m2 or higher had an HR of 2.33 (1.53–3.56, p<0.0001); the corresponding HRs for type 2 diabetes were 2.33 (2.11–2.56, p<0.0001) and 1.60 (1.47–1.75, p<0.0001).
Conclusion:

- Deaths in people with type 1 and type 2 diabetes rose sharply during the initial COVID-19 pandemic in England. Increased COVID-19-related mortality was associated not only with cardiovascular and renal complications of diabetes but, independently, also with glycemic control and BMI.

- Limitation: The variables included in this analysis were limited to those collated by the NDA, which do not include many non-cardiometabolic-related comorbidities such as respiratory disease, liver disease, alcohol use, or cognitive impairment, potentially leading to confounding as a result of lack of measurement. Residual confounding might also have resulted from the use of a single measurement to identify baseline characteristics. Also, it is not possible to identify whether the associations between risk factors and COVID-19-related mortality are due to increased susceptibility to infection, more severe illness following infection, or a combination of both from the published study.

Figure 1 Weekly numbers of deaths registered from week 1 to week 19 in people with type 1 (A) and type 2 (B) diabetes in England, 2017-19 and 2020