Smoking and Covid-19
A review of publications to-date

Silvano Gallus
OBJECTIVES
Background and Aims

• Several meta-analyses are available on the role of smoking on COVID-19 (Simons, 2020; Patanavanich & Glantz, 2020)

• In collaboration with WHO, we are conducting a systematic review aimed at improving our understanding of the relationship between tobacco smoking, e-cigarette or other tobacco product use and COVID-19
Main focus of the systematic review

i. The role of tobacco on SARS-CoV and MERS-CoV
ii. The risk of smokers vs. non-smokers of (prevalence and) incidence of SARS-CoV-2 infection.
iii. The risk for smokers vs. non-smokers of: i) hospitalization, ii) severity and iii) mortality (among COVID-19 patients)
iv. The role of other tobacco products (e.g., waterpipes), e-cigarettes, and exposure to SHS and SHA on COVID-19
v. The biological mechanisms involved in the development of COVID-19
PRELIMINARY RESULTS
Flow chart (15th of July)

- Traditional review (PubMed, WoS)
- Umbrella review
- Review of preprint archives (arXiv, OSF, Qeios, and bioRxiv/medRxiv)
Preliminary results: 370 publications
239 peer-reviewed (PR) and 131 pre-prints (PP)

<table>
<thead>
<tr>
<th>Topic</th>
<th>PR</th>
<th>PP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco and <strong>SARS-CoV</strong> and <strong>MERS-CoV</strong></td>
<td>13</td>
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<td>13</td>
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<tr>
<td>Incidence of <strong>SARS-CoV-2</strong></td>
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<tr>
<td>Smoking <strong>prevalence</strong> in <strong>SARS-CoV-2+</strong> (from case-series)</td>
<td>70</td>
<td>XX</td>
<td>XXX</td>
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<tr>
<td>RR of <strong>COVID-19 incidence</strong> for smokers (from cohorts)</td>
<td>8</td>
<td>24</td>
<td>32</td>
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<tr>
<td>COVID-19 severity (cohorts of patients)</td>
<td></td>
<td></td>
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<tr>
<td>RR of <strong>hospitalization</strong> for smokers among <strong>SARS-CoV-2+</strong></td>
<td>6</td>
<td>10</td>
<td>16</td>
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<tr>
<td>RR of <strong>severity</strong> for smokers among <strong>COVID-19 patients</strong></td>
<td>34</td>
<td>36</td>
<td>70</td>
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<tr>
<td>RR of <strong>mortality</strong> for smokers among <strong>COVID-19 patients</strong></td>
<td>16</td>
<td>25</td>
<td>41</td>
</tr>
<tr>
<td><strong>Other</strong> tobacco <strong>products, e-cigs, SHS and e-cig SHA</strong></td>
<td>10</td>
<td>4</td>
<td>14</td>
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<tr>
<td><strong>Biological mechanisms</strong> in smoking and <strong>COVID-19</strong></td>
<td>40</td>
<td>11</td>
<td>51</td>
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</tbody>
</table>
TOBACCO SMOKING AND COVID-19 INCIDENCE
Smoking prevalence in SARS-CoV-2+ (from case-series)

A number of studies (case series) showed the relatively low smoking prevalence among SARS-CoV-2+ or COVID-19 patients.
LIMITATIONS

- Case series (with no control group) cannot be used to support any causal conclusion
- Most studies suffered from selection biases
  - Most of the studies were not designed to address smoking and added info on smoking among the clinical characteristics of COVID patients (but smoking rarely collected in clinical setting)
  - Many studies based on selected populations with low smoking prevalence (e.g., healthcare providers)
  - Severe subjects usually excluded
- Many studies suffered from information bias
  (e.g., “smokers” vs. “current smokers”; “smokers quitting for COVID-19” excluded or erroneously considered ex-smokers)
Simons et al., 2020 - COVID-19 incidence

Current vs never smokers

Ex- vs never smokers
RR of COVID-19 incidence for smokers

We expect to find similar results. However, we are aware that high-quality publications are just a few. The evidence should rely on high-quality studies, only QUALITY MEASURE

<table>
<thead>
<tr>
<th>QUALITY MEASURE</th>
<th>N</th>
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</thead>
<tbody>
<tr>
<td>Type of publication</td>
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<tr>
<td>Peer-reviewed</td>
<td>4</td>
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<tr>
<td>Preprint</td>
<td>9</td>
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<tr>
<td>Sample size</td>
<td></td>
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<tr>
<td>≥200 cases (high)</td>
<td>8</td>
</tr>
<tr>
<td>&lt;200 cases (low)</td>
<td>5</td>
</tr>
<tr>
<td>Adjustment used</td>
<td></td>
</tr>
<tr>
<td>Adjusted estimates provided</td>
<td>5</td>
</tr>
<tr>
<td>Only crude estimates provided</td>
<td>8</td>
</tr>
<tr>
<td>Missing values on smoking</td>
<td></td>
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<tr>
<td>&lt;20% (low)</td>
<td>10</td>
</tr>
<tr>
<td>≥20% (high)</td>
<td>3</td>
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<tr>
<td>Generalizability of the population</td>
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<tr>
<td>General population</td>
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<tr>
<td>Suspected population</td>
<td>9</td>
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</table>
Selection bias for studies based on suspected populations

Assumption
Among both non-smokers and current smokers, SARS-Cov-2 positive subjects are 3/100=3%

Real OR*=1.00
* OR for current smokers vs. non smokers

Suspected population (with Covid-19 symptoms)
Among non-smokers, SARS-Cov-2 positive subjects are 3/10=30%

Apparent OR*=0.58
* OR for current smokers vs. non smokers
Among current smokers, SARS-Cov-2 positive subjects are 3/15=20%

Non-smoker
Current smoker
SARS-Cov-2 positive
Selection bias for studies based on suspected populations

Among both non-smokers and current smokers, SARS-Cov-2 positive subjects are 3/100=3%

Real OR*=1.00
* OR for current smokers vs. non smokers

Among non-smokers, SARS-Cov-2 positive subjects are 3/10=30%

Apparent OR*=0.58
* OR for current smokers vs. non smokers

Among current smokers, SARS-Cov-2 positive subjects are 3/15=20%

Cho et al., 2020

be tested and to test positive. In sex-stratified analyses, current smokers had higher adjusted Odds Ratios (OR) for being tested (male OR 1.60, 95%CI 1.32-1.95 and female OR 1.50, 1.21-.1.86). Current
TOBACCO SMOKING AND COVID-19 SEVERITY
The meta-analysis by Patanavanich and Glantz, 2020 showed that, among COVID patients, the risk of smoking progression (severity and mortality) was significantly higher (OR=1.91; 95% CI: 1.42-2.59) for ever vs. never smokers.
Simons et al., 2020 - COVID-19 severity

Current vs never smokers

Ex- vs never smokers

- Feuth: 1.48 [0.85, 3.34]
- Guan: 1.38 [1.02, 1.95]
- Rentsch: 1.3 [0.98, 1.78]
- Hadjadj: 1.21 [0.41, 3.17]
- Kuderer: 1.08 [0.8, 1.68]
- Petrilli: 1.01 [0.76, 1.3]
- Gu: 1.04 [0.42, 1.8]
- Monteiro: 1.75 [1.04, 4.08]

- Guan: 2.14 [1.4, 3.64]
- Gu: 1.84 [1.4, 2.47]
- Kuderer: 1.65 [1.34, 2.05]
- Feuth: 1.4 [0.59, 2.66]
- Petrilli: 1.3 [1.16, 1.47]
- Hadjadj: 1.26 [0.86, 1.73]
- Rentsch: 1.25 [0.89, 1.68]
- Monteiro: 1.55 [0.93, 2.68]

Pooled Effect: 1.25 [0.85, 1.93]
Pooled Effect: 1.52 [1.13, 2.07]
Simons et al., 2020 - COVID-19 mortality

Current vs never smokers

Ex- vs never smokers

Relative Risk [95% Credible Interval]
CONCLUSIONS
The prevalence studies are case-series with no control group and with major limitations: they cannot be used to support any causal conclusion.

Population-based cohort studies, more and more frequently available, are more reliable. However, the number of high quality studies are limited.

The evidence should rely exclusively on high-quality studies, particularly those not based on COVID-19 suspected population.

The excess risk for smokers vs. never smokers appears clearer.

In the absence of more data, to prevent possible complications due to COVID-19 appears to be the latest good reason to avoid smoking and to recommend smoking cessation.
Participants

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- Esteve Fernandez (Institut Català d'Oncologia - Institut d'Investigació Biomèdica de Bellvitge, Barcelona, Spain)
THANKS FOR THE ATTENTION!

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References


• Simons D, Shabab L, Brown J, Perski O. The association of smoking status with SARS-CoV-2 infection, hospitalisation and mortality from COVID-19: A living rapid evidence review with Bayesian meta-analyses (version 7). Qeios (Preprint) 2020; Available online at: https://www.qeios.com/read/UJR2AW.8