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# Management of cancer patients in COVID-19 era in solid tumors

**Stefan Rauh MD**
*Medical Oncologist*
*Centre Hospitalier Emile Mayrisch*
*Esch-sur-Alzette - Luxembourg*

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# Protecting measures and screening in cancer patients

# General consensus measures taken by ‘Cancer Core Europe’ (CCE) centers during the COVID-19 pandemic

| Category | Measure |
|---|---|
| Hospital wide | ► Hospital wide Construct a hospital-wide crisis team responsible for coordinating measures between departments. |
| | ► Encourage patients not to arrive early. Offer to text patients when you are ready to see them, so they can wait outside or in the car. |
| | ► Instruct patients not to visit the hospital if they have symptoms indicative of possible COVID-19 (unless urgent attention is required). |
| | ► Call patients the day before planned hospital admissions, to discuss the presence of any COVID-19-related symptoms. |
| | ► Screen patients at the entrance for symptoms of COVID-19 and fever. |
| | ► Quickly isolate patients with COVID-19 in specialized departments, with the intent of relocation to regional collaborating hospitals (if possible). |
| | ► Reduce preclinical research activities to a bare minimum. |
| | ► Stop patient inclusion for clinical studies or trials requiring additional actions and/or visits. |
| | ► Consider a tumor type–specific ‘exception list’ of particularly successful studies for which inclusion continues. |
| | ► Discuss each patient with a multidisciplinary team to consider alternative treatment modalities with the fewest visits or lowest capacity problems or that are the shortest in duration. |
| | ► Therapeutic adjustments (versus regular guidelines) should be discussed in a multidisciplinary team meeting. |
| | ► Conduct multidisciplinary team consultations remotely if possible or include only one representative of each discipline to limit the number of people participating in the meetings. Inform patients about a possibly increased risk associated with anticancer therapy during the COVID-19 pandemic. |
| | ► Enable telephone or video consultations for healthcare professionals who need to self-isolate. When postponing procedures or contact moments, anticipate future capacity problems. |
| | ► Do not prescribe corticosteroids as anti-emetics (if avoidable), and limit their use in patients treated with immune-checkpoint blockade, to reduce vulnerability to COVID-19. |
| | ► With each patient, discuss resuscitation status to anticipate future decisions about intensive care. |

ESMO RECOMMENDATIONS

# Cancer patient management during the COVID-19 pandemic

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

## Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus

G. Curigliano[1*], S. Banerjee[2], A. Cervantes[3,4], M. C. Garassino[5], P. Garrido[6], N. Girard[7,8], J. Haanen[9], K. Jordan[10], F. Lordick[11], J. P. Machiels[12], O. Michielin[13], S. Peters[13], J. Tabernero[14], J. Y. Douillard[15] & G. Pentheroudakis[16], on behalf of all Panel members[†]

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Curigliano G., Annals Oncol 31 (10); 1320-1335. oct 2020; Slide Sets based on the ESMO recommendations for cancer patient management during the COVID-19 pandemic.
Downloaded from ESMO website: https://www.esmo.org/guidelines/covid-19-adapted-recommendations-slide-sets. Last Access December 4th

# How manage patients flow in hospital: ESMO's guidelines: who's at risk?

**In cancer patients, categories at risk include:**

- Patients receiving chemotherapy, or who have received chemotherapy in the last 3 months
- Patients receiving extensive radiotherapy
- People who have had bone marrow or stem cell transplants in the last 6 months, or who are still taking immunosuppressive drugs
- People with some types of blood or lymphatic system cancer which damage the immune system, even if they have not needed treatment (for example, chronic leukaemia, lymphoma or myeloma)

Specific high risk for leucopenia, low Ig's, chronic immunosuppression (steroids, MoAb's)

# General consensus measures taken by ‘Cancer Core Europe’ (CCE) centers during the COVID-19 pandemic

| Category | Measure |
| --- | --- |
| Outpatient clinic | ► Do all follow up appointments by phone (except when physical examination is necessary).<br>► When possible, reduce or delay the number of radiological-response evaluations.<br>► Prioritize oral or subcutaneous treatments above infusion-based treatments to reduce time spent in the hospital.<br>► Perform blood tests outside the hospital (e.g., at a general practice or at home), when possible.<br>► Have oral medications delivered to the patient’s home, rather than being picked up at the pharmacy<br>► Consider omitting supportive treatments (e.g., no bisphosphonate infusion, except in the case of hypercalcemia)<br>► When possible, organize the administration of intravenous maintenance treatments at home<br>► When administration at home is impossible, consider temporary breaks or reductions in the frequency of intravenous maintenance treatments for less-aggressive metastatic cancers on a per-patient basis |

# How manage patients flow in hospital: ESMO's guidelines. (2) patients undergoing active treatment

- Hospitals should identify **specific pathways** in order to guarantee timing of treatment with curative intent and, when possible, also for patients with metastatic disease.
- **Outpatient visit**s for cancer patients should be **reduced to the safest and most feasible level** without jeopardising patient care.
- For patients **receiving oral treatment** for which monitoring can be done remotely**, drug supply should be provided for at least 3 courses** to **reduce access to the hospital.**
- **Blood monitoring** for those patients can be done **in local labs close to home.**
- We suggest implementation of **telemedicine** services.
- We advise to **delay all follow-up visits**.
- **More intensive surveillance** should be used during treatment **for patients with lung cancer** or who **received previous lung surgery**, and for **older patient**s or those patients with **other comorbidities**.
- Intensive measures should be undertaken to avoid nosocomial spread.
- There should be **strict and safe triaging procedures** to **assess any COVID-19 symptoms and the urgency and necessity of ho**spitalisation.
- In order to regulate access to the "Cancer Hubs", establish **"checkpoint areas" screening for early detection** of potentially infectious persons.
- Clinical staff responsible for the checkpoint area should be trained and wear PPE.
- Individuals who meet criteria for highly communicable diseases requiring isolation, such as novel COVID-19 or other emerging infections, must be placed in a private exam room as soon as possible, as per the infectious control guidance found on the WHO and CDC websites. They should be tested and transferred to COVID-19 dedicated areas.

Slide Sets based on the ESMO recommendations for cancer patient management during the COVID-19 pandemic. Downloaded from ESMO website: https://www.esmo.org/guidelines/covid-19-adapted-recommendations-slide-sets. Last Access December 4th

How much more should we do?
Is routine repeat pcr patient screening useful?

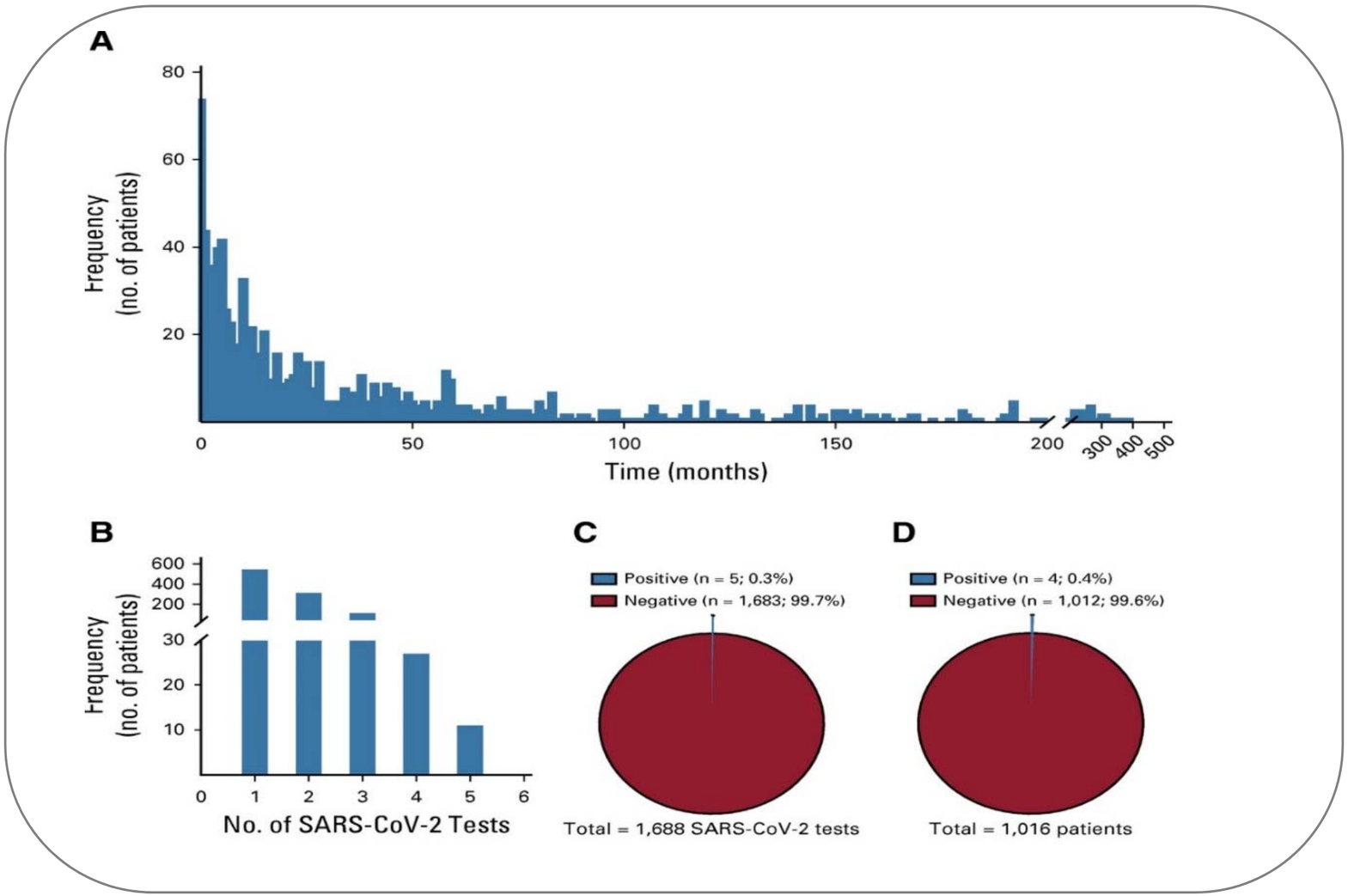
# SARS-CoV-2 Testing in Patients With Cancer Treated at a Tertiary Care Hospital During the COVID-19 Pandemic

Anna S. Berghoff, MD, PhD[1]; Margaretha Gansterer, PhD[2]; Arne C. Bathke, PhD[3]; Wolfgang Trutschnig, PhD[3]; Philipp Hungerländer, PhD[4]; Julia M. Berger[1]; Judith Kreminger[1]; Angelika M. Starzer, MD[1]; Robert Strassl, MD[5]; Ralf Schmidt, MD, PhD[5]; Harald Willschke, MD[6]; Wolfgang Lamm, MD[1]; Markus Raderer, MD[1]; Alex D. Gottlieb, PhD[7]; Norbert J. Mauser, PhD[7]; and Matthias Preusser, MD[1]

"Our data indicate that continuation of active anticancer therapy and follow-up visits in a large tertiary care hospital are feasible and safe after implementation of strict population-wide and institutional safety measures during the current COVID-19 pandemic. **Routine SARS-CoV-2 testing of patients with cancer seems advisable to detect asymptomatic virus carriers and avoid uncontrolled viral spread.**"

Berghoff A. et al, J Clin Oncol. 2020 Oct 20;38(30):3547-3554.

Characteristics of the cancer cohort. (A) Time from diagnosis of malignant disease to SARS-CoV-2 test. (B) Number of performed tests. (C) Number of SARS-CoV-2–positive test results. (D) Number of patients with SARS-CoV-2 infection




Only 0,3% of the 1016 patients were detected COVID pos by routine RT PCR

-> worth the hassle??

Berghoff A. et al, J Clin Oncol. 2020 Oct 20;38(30):3547-3554.

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# Are cancer patients at higher risk to be infected with SARS-CoV-2?

# Are cancer patients more prone to get infected by COVID 19?

## Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid

J. Rogado1 · B. Obispo1 · C. Pangua1 · G. Serrano-Montero1 · A. Martín Marino1 · M. Perez-Perez1 · A. Lopez-Alfonso1 · P. Gullón2 · M. Á. Lara1,3

Received: 28 April 2020 / Accepted: 9 May 2020


**Results** We detected 45/1069 Covid-19 diagnoses in cancer patients vs 42,450/6,662,000 in total population ($p$ < 0.00001). Mortality rate: 19/45 cancer patients vs 5586/42,450 ($p$ = 0.0001). Mortality was associated with older median age, adjusted by staging and histology (74 vs 63.5 years old, OR 1.06, $p$ = 0.03). Patients who combined hydroxychloroquine and azithromycin presented 3/18 deaths, regardless of age, staging, histology, cancer treatment and comorbidities (OR 0.02, $p$ = 0.03).

- The risk for infection is estimated based on models
- Testing/ selection bias!
- Stage and comorbidities matter!

Adapted from Rogado J., Clinical and Translational Oncol 22:2364-2368;

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# Are cancer patients at higher risk for a more severe course and poor outcome after COVID-19?

# Are cancer at higher risk to die from COVID 19?

## Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China

!!18 patients with cancer among 2007 patients within 575 hospitals
417 pat excluded due to poor records)

Logistic regression model for identifying risk factors for severe events

| Variable | OR | LL | UL | P value |
|---|---|---|---|---|
| Age | 1.048 | 1.033 | 1.064 | < 0.001 |
| Sex (Female vs. Male) | 0.613 | 0.409 | | |
| **Cancer** | **5.399** | **1.802** | | |
| Hypertension | 1.878 | 1.217 | | |
| COPD | 3.397 | 1.373 | | |
| Diabetes Mellitus | 2.206 | 1.331 | | |

A forward conditional logistic model was used. Other variables including smok
during modeling. COPD, chronic obstructive pulmonary disease

Baseline characteristics between cancer patients and non-cancer patients

| Variable | Cancer Patients | Non-cancer patients | P value |
|---|---|---|---|
| Age | 63.1±12.1 | 48.7±16.2 | **<0.001** |
| Sex (Male%) | 61.1% | 57.2% | 0.814 |
| Known smoking history | 22.2% | 6.8% | **0.032** |
| Any other comorbidity* | 22.2% | 24.2% | 1.000 |
| Abnormality in X-ray | 22.2% | 15.2% | 0.504 |
| Abnormality in CT-ray | 94.4% | 70.8% | **0.033** |
| Polypnea# | 47.1% | 23.5% | **0.039** |

*, other comorbidities include chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, coronary heart disease, cerebrovascular disease, viral hepatitis type B, malignant tumor, chronic kidney disease and immunodeficiency. #Other symptoms being compared but found no difference include fever, cough, expectoration, stuffy nose, conjunctival congestion, headache, sore throat, dyspnea, fatigue, nausea and vomiting, hemoptysis, diarrhea, muscular pain, arthralgia, shivering.

Adapted from Liang et al, Lancet Oncol. 2020 Mar;21(3):335-337

…but: …no difference, finally ?

# COVID-19 Severity and Outcomes in Patients Wi Cancer: A Matched Cohort Study

Gagandeep Brar, MD[1]; Laura C. Pinheiro, PhD, MPH[2]; Michael Shusterman, MD[1]; Brandon Swed, MD[1]; Evgeniya Reshetnyak, PhD[2]; Orysya Soroka, MS[2]; Frank Chen, BS[2]; Samuel Yamshon, MD[1]; John Vaughn, MD[1]; Peter Martin, MD[1]; Doru Paul, MD, PhD[1]; Manuel Hidalgo, MD, PhD[1]; and Manish A. Shah, MD[1]

"CONCLUSION We observed that **patients with COVID-19 and cancer had similar outcomes compared with matched patients without cancer**. This finding suggests that a diagnosis of active cancer alone and recent anticancer therapy do not predict worse COVID-19 outcomes and therefore, recommendations to limit cancer- directed therapy must be considered carefully in relation to cancer-specific outcomes and death. "

Brar G. et al, J Clin Oncol 38:3914-3924. © 2020 by American Society of Clinical Oncology

# Adjusted Association Between Cancer Status and Risk of Composite Outcome and Death for 585 Hospitalized Patients With COVID-19

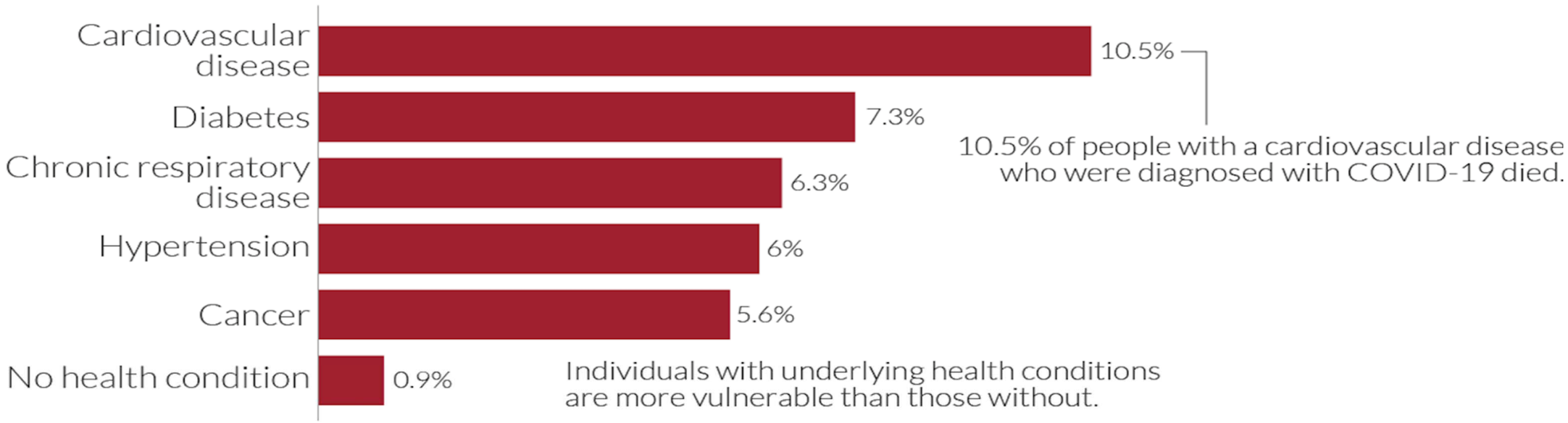
| | Composite Outcome[a] | | Death | |
|---|---|---|---|---|
| **Risk Factor** | **aHR** | **95% CI** | **aHR** | **95% CI** |
| Age | 1.19 | 1.04 to 1.36[b] | 2.04 | 1.72 to 2.42[b] |
| Cancer | 0.80 | 0.57 to 1.13 | 0.98 | 0.58 to 1.67 |
| Sex | 1.35 | 0.96 to 1.90 | 1.22 | 0.85 to 1.77 |
| Ethnicity | | | | |
| Black | 0.80 | 0.45 to 1.41 | 1.40 | 0.74 to 2.64 |
| Asian | 1.08 | 0.77 to 1.52 | 1.30 | 0.71 to 2.36 |
| Other | 1.19 | 0.86 to 1.65 | 1.36 | 0.85 to 2.19 |
| Not reported | 0.91 | 0.59 to 1.41 | 1.65 | 0.84 to 3.24 |
| Smoking history (ref = Never smoked) | | | | |
| Former smoker | 0.86 | 0.66 to 1.12 | 0.67 | 0.44 to 1.01 |
| Current smoker | 0.71 | 0.24 to 2.04 | 0.58 | 0.17 to 2.03 |
| Obesity (BMI ≥ 30 kg/m$^2$ [≥ 28 kg/m$^2$ for Asians]) | 1.85 | 1.37 to 2.50[b] | 1.35 | 0.92 to 1.97 |
| Diabetes | 0.88 | 0.63 to 1.21 | 1.17 | 0.70 to 1.95 |
| Hypertension | 0.95 | 0.65 to 1.38 | 0.97 | 0.67 to 1.41 |
| Chronic obstructive pulmonary disease | 1.33 | 0.82 to 2.16 | 1.16 | 0.80 to 1.68 |
| Coronary artery disease | 0.98 | 0.67 to 1.43 | 1.20 | 0.75 to 1.92 |
| Heart failure | 0.80 | 0.53 to 1.21 | 1.09 | 0.63 to 1.89 |

Abbreviations: aHR, adjusted hazard ratio; BMI, body mass index; COVID-19, SARS-CoV-2; ref, reference.
[a]Composite outcome = intensive care unit, intubation, or death.
[b]$P < .05$.

HR> 1 for **age** (>2!) and **co morbidities**

# Coronavirus: early-stage case fatality rates by underlying health condition in China

Case fatality rate (CFR) is calculated by dividing the total number of deaths from a disease by the number of confirmed cases.
Data is based on early-stage analysis of the COVID-19 outbreak in China in the period up to February 11, 2020.



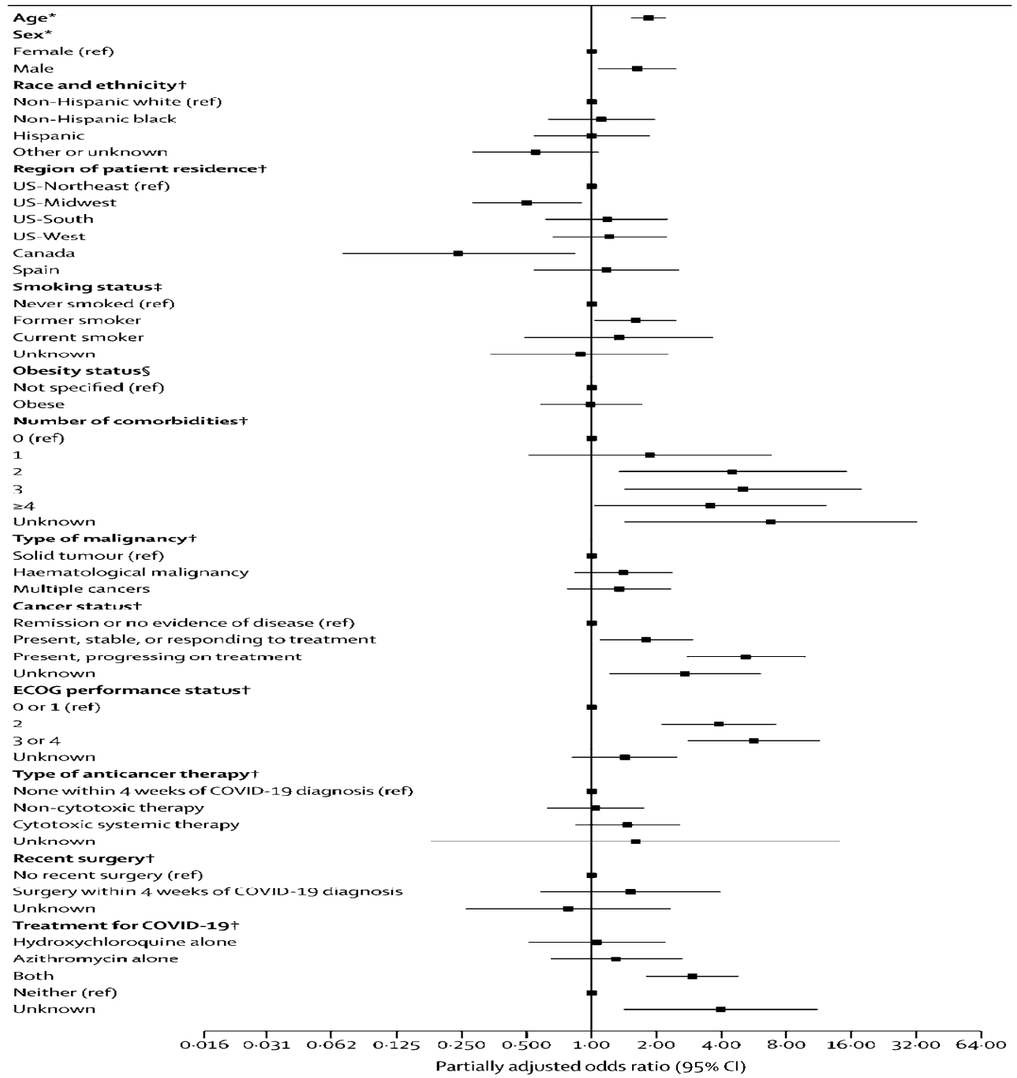

Data source: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly.





Statistics and Research. Mortality Risk of COVID-19. https://ourworldindata.org/mortality-risk-covid#case-fatality-rate-of-covid-19-by-age. Accessed Dec 12th 2020

# Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study




HR= 2 with CI > 1:
Presence of cancer

HR>>2
**Age**
**Performance status >/= 2**
Progressive disease under treatment
**2 or more co morbidities**

Kuderer N. et al, Lancet 2020; 395:1907–18

# COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study

*Lennard YW Lee*, Jean-Baptiste Cazier*, Vasileios Angelis, Roland Arnold, Vartika Bisht, Naomi A Campton, Julia Chackathayil, Vinton WT Cheng, Helen M Curley, Matthew W Fittall, Luke Freeman-Mills, Spyridon Gennatas, Anshita Goel, Simon Hartley, Daniel J Hughes, David Kerr, Alvin JX Lee, Rebecca J Lee, Sophie E McGrath, Christopher P Middleton, Nirupa Murugaesu, Thomas Newsom-Davis, Alicia FC Okines, Anna C Olsson-Brown, Claire Palles, Yi Pan, Ruth Pettengell, Thomas Powles, Emily A Protheroe, Karin Purshouse, Archana Sharma-Oates, Shivan Sivakumar, Ashley J Smith, Thomas Starkey, Chris D Turnbull, Csilla Várnai, Nadia Yousaf, The UK Coronavirus Monitoring Project Team, Rachel Kerr†, Gary Middleton†*

- In this **prospective** observational study, all patients with active cancer and presenting to our network of cancer centres were eligible for enrolment into the **UK Coronavirus Cancer Monitoring Project (UKCCMP)**

- From **March 18, to April 26, 2020**, we analysed **800 patients** with a diagnosis of cancer and symptomatic COVID-19

- 412 (52%) patients had a mild COVID-19 disease course

- 226 (28%) patients died and risk of death was significantly associated with advancing patient age (odds ratio 9·42 [95% CI 6·56–10·02]; p<0·0001), being male (1·67 [1·19–2·34]; p=0·003), and the presence of other comorbidities such as hypertension (1·95 [1·36–2·80]; p<0·001) and cardiovascular disease (2·32 [1·47–3·64]). 281 (35%) patients had received cytotoxic chemotherapy within 4 weeks before testing positive for COVID-19

Lee L. et al. Lancet 2020; 395: 1919–26

# Results

- Mortality from COVID-19 in cancer patients appears to be principally driven by **age**, gender, and **comorbidities**

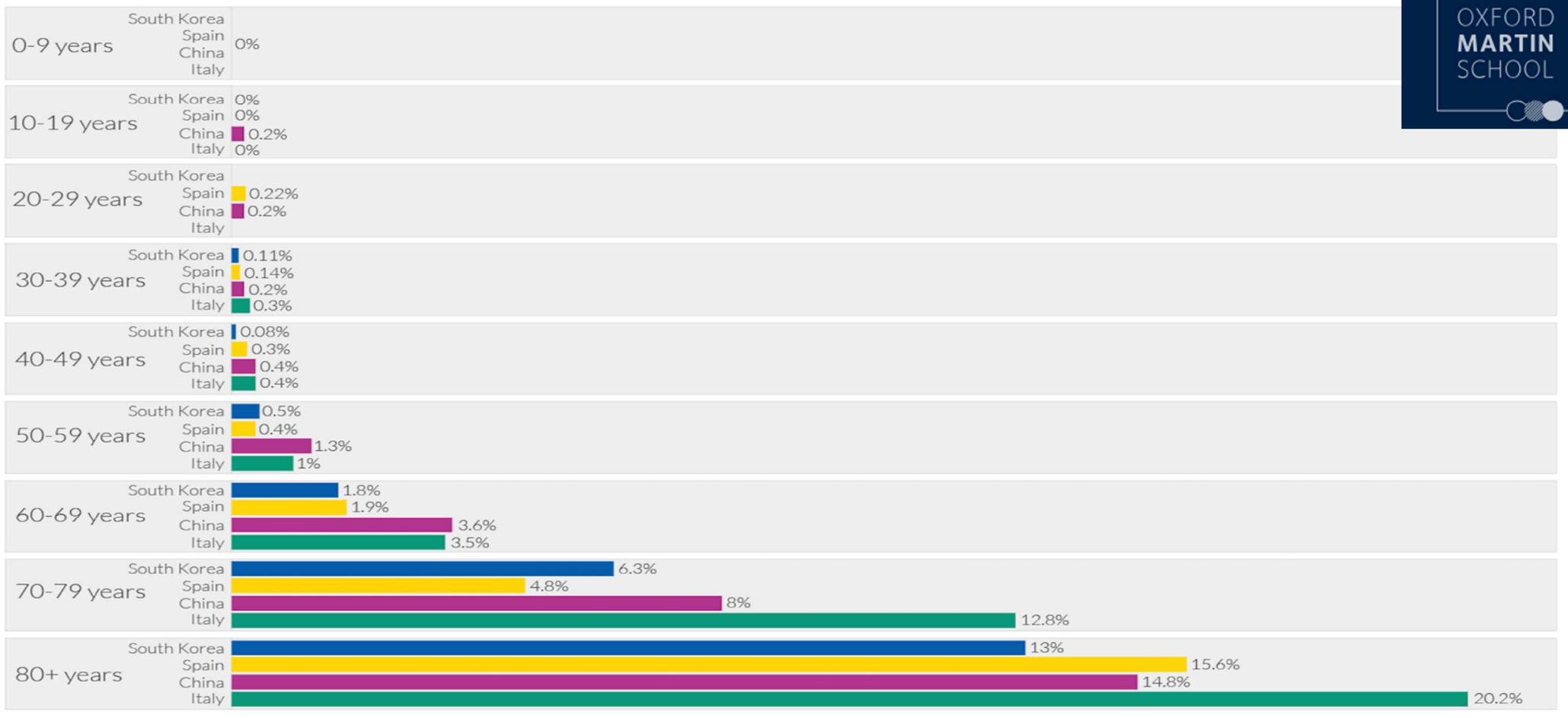
- We are not able to identify evidence that cancer patients on cytotoxic chemotherapy or other anticancer treatment are at an increased risk of mortality from COVID-19 disease compared with those not on active treatment

Lee L. et al. Lancet 2020; 395: 1919–26

# Coronavirus: case fatality rates by age

Case fatality rate (CFR) is calculated by dividing the total number of confirmed deaths due to COVID-19 by the number of *confirmed* cases.

Two of the main limitations to keep in mind when interpreting the CFR:
(1) many cases within the population are unconfirmed due to a lack of testing.
(2) some individuals who are infected will eventually die from the disease, but are still alive at time of recording.




Note: Case fatality rates are based on confirmed cases and deaths from COVID-19 as of: 17th February (China); 24th March (Spain); 24th March (South Korea); 17th March (Italy).

Data sources: Chinese Center for Disease Control and Prevention (CDC); Spanish Ministry of Health; Korea Centers for Disease Control and Prevention (KCDC).
Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA*.

OurWorldinData.org – Research and data to make progress against the world's largest problems.

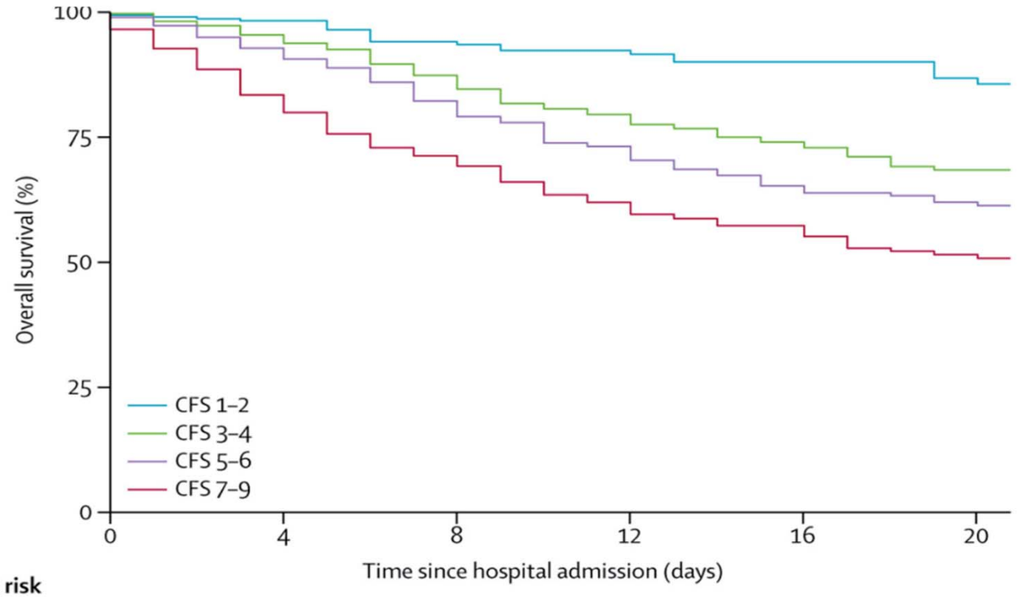


Statistics and Research. Mortality Risk of COVID-19. https://ourworldindata.org/mortality-risk-covid#case-fatality-rate-of-covid-19-by-age. Accessed Dec 12th 2020

# Survival according to frailty

## The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study

Jonathan Hewitt, Ben Carter, Arturo Vilches-Moraga, Terence J Quinn, Philip Braude, Alessia Verduri, Lyndsay Pearce, Michael Stechman, Roxanna Short, Angeline Price, Jemima T Collins, Eilidh Bruce, Alice Einarsson, Frances Rickard, Emma Mitchell, Mark Holloway, James Hesford, Fenella Barlow-Pay, Enrico Clini, Phyo K Myint, Susan J Moug, Kathryn McCarthy, on behalf of the COPE Study Collaborators*



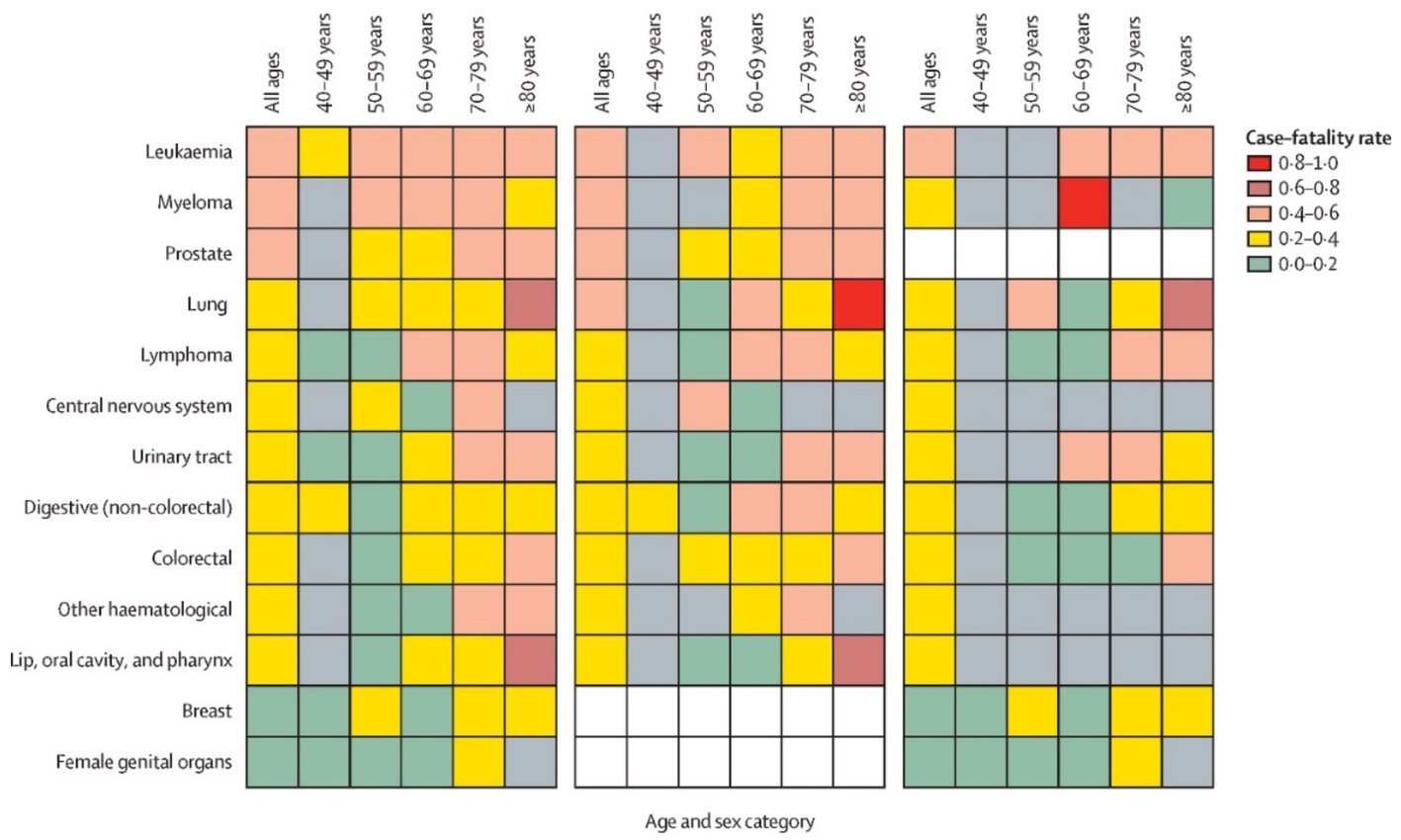

| Number at risk (number censored) | | | | | | |
|---|---|---|---|---|---|---|
| CFS 1–2 | 288 (10) | 236 (64) | 169 (115) | 126 (152) | 95 (175) | 76 (195) |
| CFS 3–4 | 472 (9) | 401 (68) | 288 (147) | 199 (200) | 136 (259) | 92 (291) |
| CFS 5–6 | 433 (3) | 381 (32) | 290 (85) | 209 (129) | 139 (184) | 90 (219) |
| CFS 7–9 | 366 (0) | 285 (32) | 210 (64) | 156 (96) | 107 (131) | 72 (154) |

CFS clinical frailty score

Hewitt J. Lancet Public Health 2020:;5 : e444-51

# COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study

*Lennard Y W Lee*, Jean-Baptiste Cazier*, Thomas Starkey*, Sarah E W Briggs, Roland Arnold, Vartika Bisht, Stephen Booth, Naomi A Campton, Vinton W T Cheng, Graham Collins, Helen M Curley, Philip Earwaker, Matthew W Fittall, Spyridon Gennatas, Anshita Goel, Simon Hartley, Daniel J Hughes, David Kerr, Alvin J X Lee, Rebecca J Lee, Siow Ming Lee, Hayley Mckenzie, Chris P Middleton, Nirupa Murugaesu, Tom Newsom-Davis, Anna C Olsson-Brown, Claire Palles, Thomas Powles, Emily A Protheroe, Karin Purshouse, Archana Sharma-Oates, Shivan Sivakumar, Ashley J Smith, Oliver Topping, Chris D Turnbull, Csilla Várnai, Adam D M Briggs, Gary Middleton†, Rachel Kerr†, on behalf of the UK Coronavirus Cancer Monitoring Project Team*




Lee LYW, et al. Lancet Oncol. 2020 Oct;21(10):1309-1316.

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# Should we adapt treatment of cancer patients during the COVID pandemic?

# Considerations to treat patients for cancer and risk of COVID-19 mortality

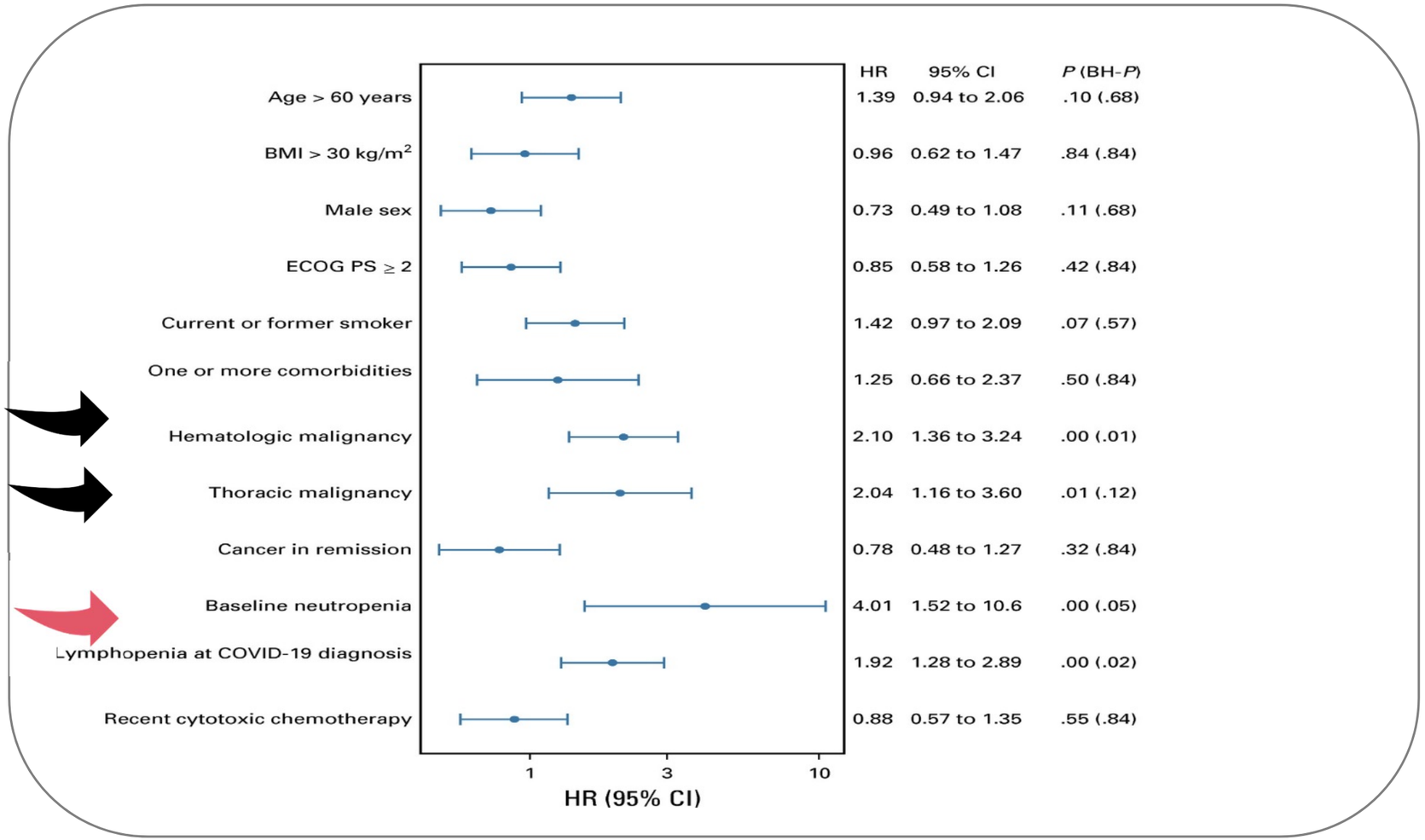
## Chemotherapy and COVID-19 Outcomes in Patients With Cancer

Justin Jee, MD, PhD[1]; Michael B. Foote, MD[1]; Melissa Lumish, MD[1]; Aaron J. Stonestrom, MD, PhD[1]; Beatriz Wills, MD[1]; Varun Narendra, MD, PhD[1]; Viswatej Avutu, MD[1]; Yonina R. Murciano-Goroff, MSc, DPhil, MD[1]; Jason E. Chan, MD, PhD[1]; Andriy Derkach, PhD[2]; John Philip, MS[3]; Rimma Belenkaya, MA, MS[3]; Marina Kerpelev, BS[4]; Molly Maloy, MS[3]; Adam Watson, PhD[3]; Chris Fong, PhD[2]; Yelena Janjigian, MD[1]; Luis A. Diaz Jr, MD[1]; Kelly L. Bolton, MD, PhD[1]; and Melissa S. Pessin, MD, PhD[5]

"Recent cytotoxic chemotherapy treatment was not associated with adverse COVID-19 outcomes. Patients with active hematologic or lung malignancies, peri–COVID-19 lymphopenia, or baseline neutropenia had worse COVID-19 outcomes. Interactions among antineoplastic therapy, cancer type, and COVID-19 are complex and warrant further investigation."

Jee J. et al, J Clin Oncol. 2020 Oct 20;38(30):3538-3546.

Multivariable Cox regression analysis of significant covariates from univariable analyses.
Multivariable analysis with suspected COVID-19–related comorbidities and significant variables from the univariable primary and secondary analyses



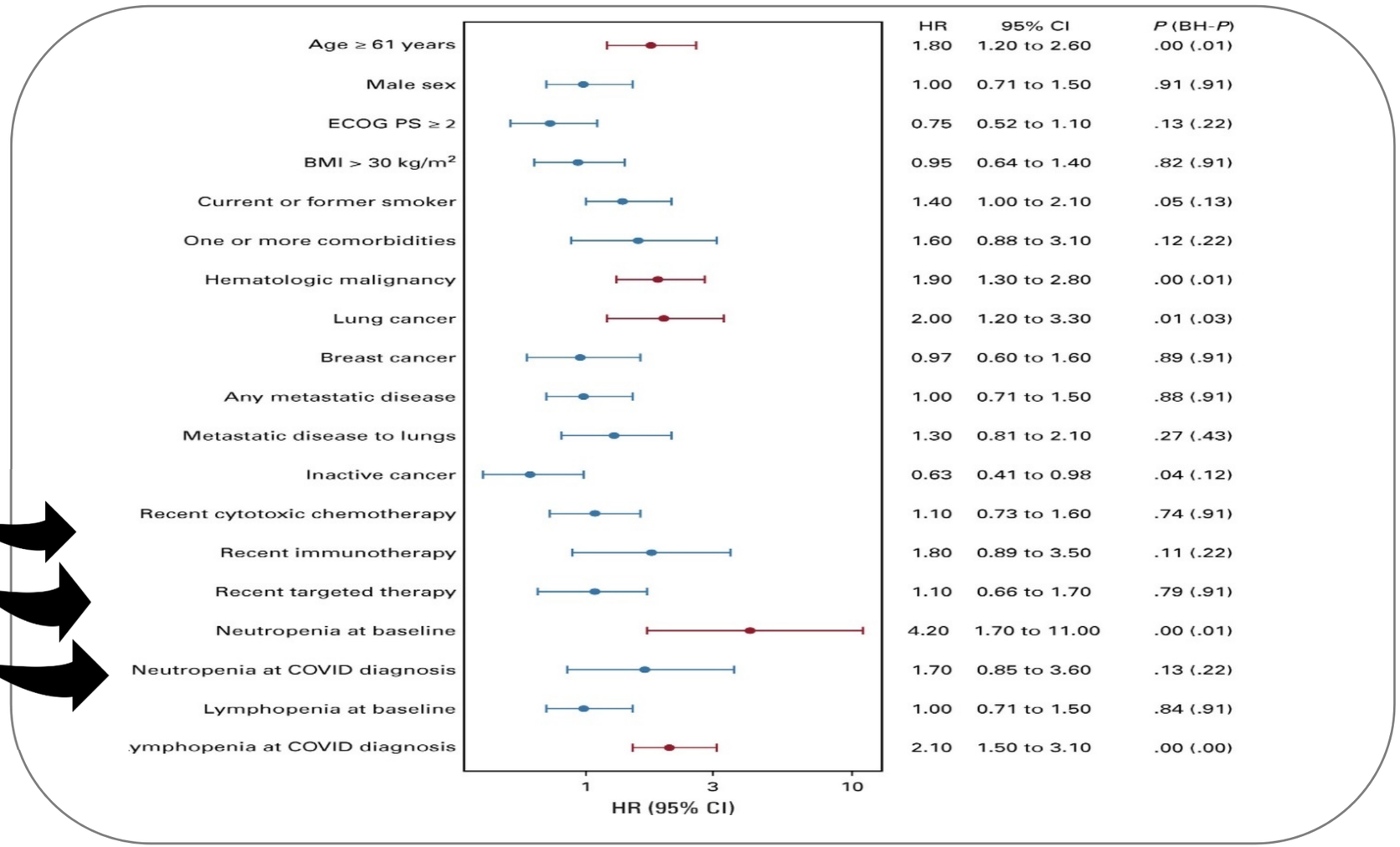

Bars represent hazard ratio (HRs) with 95% CIs. BH-P, Benjamini-Hochberg–adjusted P value; BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status

Jee J. et al. J Clin Oncol. 2020 Oct 20;38(30):3538-3546.

# Risk factors for severe COVID-19 in patients with cancer. Hazard ratios (HRs) and 95% CIs for risk factors for severe COVID-19 infection using a time-to-event analysis

- chemo
- immuno
- targeted tt

= HR 1,5-2
No signif difference




Red bars indicate that criteria were met for statistical significance with a Benjamini-Hochberg–adjusted false discovery rate P < .10 (BH-P). BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status.

Jee J. et al, J Clin Oncol. 2020 Oct 20;38(30):3538-3546.

# Should we adapt treatment of cancer during the COVID pandemic?

- GENERAL/SOLID
- Because of the expected long duration before normalisation of hospital care, treatment of the underlying disease should be continued when possible

Van Doesum, J., et al. Leukemia 34, 2536–2538 (2020).

# Should we adapt treatment of cancer during the COVID pandemic?

- GENERAL/SOLID
- Do not prescribe corticosteroids as anti-emetics (if avoidable), and limit their use in patients treated with immune-checkpoint blockade, to reduce vulnerability to COVID-19.
- Prioritize oral or subcutaneous treatments above infusion-based treatments to reduce time spent in the hospital.  Eg SCIG instead of IVIG
- Consider omitting supportive treatments (e.g., no bisphosphonate infusion, except in the case of hypercalcemia)
- When possible, organize the administration of intravenous maintenance treatments at home
- When administration at home is impossible, consider temporary breaks or reductions in the frequency of intravenous maintenance treatments for less-aggressive metastatic cancers on a per-patient basis

Van Doesum, J., et al. Leukemia 34, 2536–2538 (2020).

# Cancer treatment with ICIs in the COVID-19 context

Commentary

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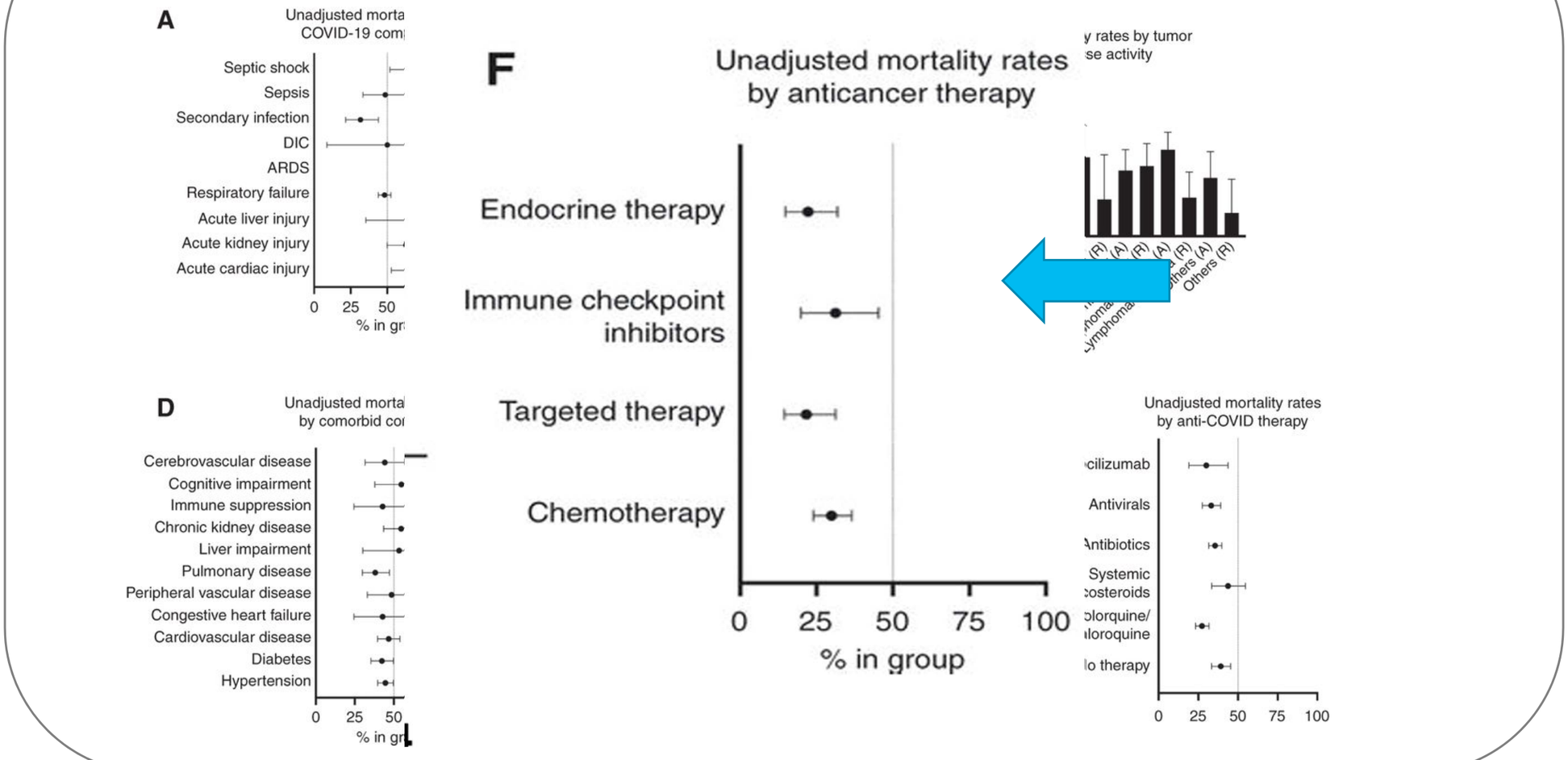
## Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors

**Melissa Bersanelli*[,1,2]**
[1]Medical Oncology Unit, University Hospital of Parma, Parma, Italy
[2]Medicine & Surgery Department, University of Parma, Parma, Italy
*Author for correspondence: Tel.: +39 0521 702 316; bersamel@libero.it

**"Since ICI can restore the immune-competence, if on one hand it can be paradoxically needed to develop the cytokine storm characterizing the acute respiratory distress syndrome (ARDS) phase, on the other hand the epidemiological features of SARS-CoV-2 infection lay for a lower probability to affect these patients compared with their chemo-treated immune-suppressed counterpart."**

Bersanelli M., et al, Immunotherapy. 2020 Apr;12(5):269-273

# ICI’s : as safe as other anti neoplastics




**The relationship between mortality from COVID-19 and clinicopathologic features of patients with cancer.**

David J. Pinato et al. Cancer Discov 2020;10:1465-1474

# Managing cancer patients during the COVID-19 pandemic: an multidisciplinary expert consensus– Use of Immunotherapy

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

**STATEMENT 11:** For the approved indication of (neo)adjuvant treatment, where there is a significant survival benefit, ICIs should not be withheld or delayed in the absence of SARS-CoV-2 infection. In patients who have tested positive for SARSCoV-2, the (neo)adjuvant ICI should be postponed until recovery.

**STATEMENT 12:** For patients with metastatic melanoma, intermediate/poor-risk mRCC, PD-L1-positive NSCLC and hepatocellular carcinoma, where there is a clear survival benefit, ICI treatment should be interrupted because of COVID-19. Restarting ICI treatment should be considered after complete resolution of COVID-19 following negative RT-PCR testing. A combination of ICI with cytotoxic ChT can be considered and discussed with patients when the cost-benefit ratio is favourable (OS gain) according to patient risk factors and preference.

**STATEMENT 13:** High-dose steroids may represent a potential risk factor for mortality in cancer patients who are infected with SARS-CoV-2. In case of the need to manage a G3e4 irAE, if possible, switch to another immunosuppressant agent.

**STATEMENT 14:** The combination of anti-CTLA4 plus anti-PD-(L)1 should be given if the patient's disease requires such ICI treatment (in case of an approved indication), in view of the lack of evidence that sequencing anti-PD-(L)1 and anti-CTLA4 agents is as effective or less toxic.

**STATEMENT 15:** For the differential diagnosis of an irAE from SARS pneumonitis, a nasopharyngeal swab should be obtained for PCR and a high-resolution thoracic CTscan should be carried out. If negative, a BAL should be considered (increased risk for pulmonary oncology team) for differential diagnosis of irAEs versus COVID-19.

Adapted from Curigliano G, et al., Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. *Ann Oncol.* 2020.

# ASCO Resource on Cancer Treatment & Supportive Care (as of September 17, 2020)

**Immune Checkpoint Inhibitors: Can/should treatment with immune checkpoint inhibitors (e.g. ipilimumab, nivolumab) be delayed or interrupted? Are any special precautions or actions needed with respect to their use?**

- There are limited data regarding the impact of immune checkpoint inhibitors (ICI) on COVID-19 infection in patients with cancer. Robliotti et al, Nat Med have reported that in a cohort of patients in a single health system in New York City, patients with cancer and COVID-19 who received an ICI had a statistically significant increase in risk of hospitalization (OR 2.84, 95% CI 1.24-6.72) based on 31 out of 423 included patients who had received an ICI.
- It may be appropriate to adjust to less frequent dosing intervals when different schedules are considered reasonable options and/or are approved in your jurisdiction for the patient's indication.
- However, there is preclinical evidence of cytokine storm and/or potentially increase inflammatory reactions and complications such as pneumonitis for some novel immunotherapy agents and T-cell therapy agents.
- These agents may cause immune-related serious adverse events and immunosuppression may not be advisable as a treatment for those events.
- The potential harms and benefits of therapy should be carefully considered for each patient. Where possible, COVID-19 testing prior to therapy with these agents is reasonable.

ASCO Resource on Cancer Treatment & Supportive Care. https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/cancer-treatment-supportive-care Accessed December 4, 2020.

# Immunotherapy: conclusions

- No clear evidence of higher toxicity / risk of cytokine storm
- Guidelines similar to other anti neoplastic treatments:
  - Consider benefit of treatment on an individual basis  for treatment
  - Interrupt treatment in case of COVID infection
  - Avoid corticoids : in case of high toxicity -> switch to other immunosuppressants
  - Differential COVID/ pulm Iao toxicity challenging , nasoph. Swab + Hr CT necessary
  - (ASCO guidelines somewhat more cautious based on the lack of good evidence,proposal of less frequent dosing intervals …)

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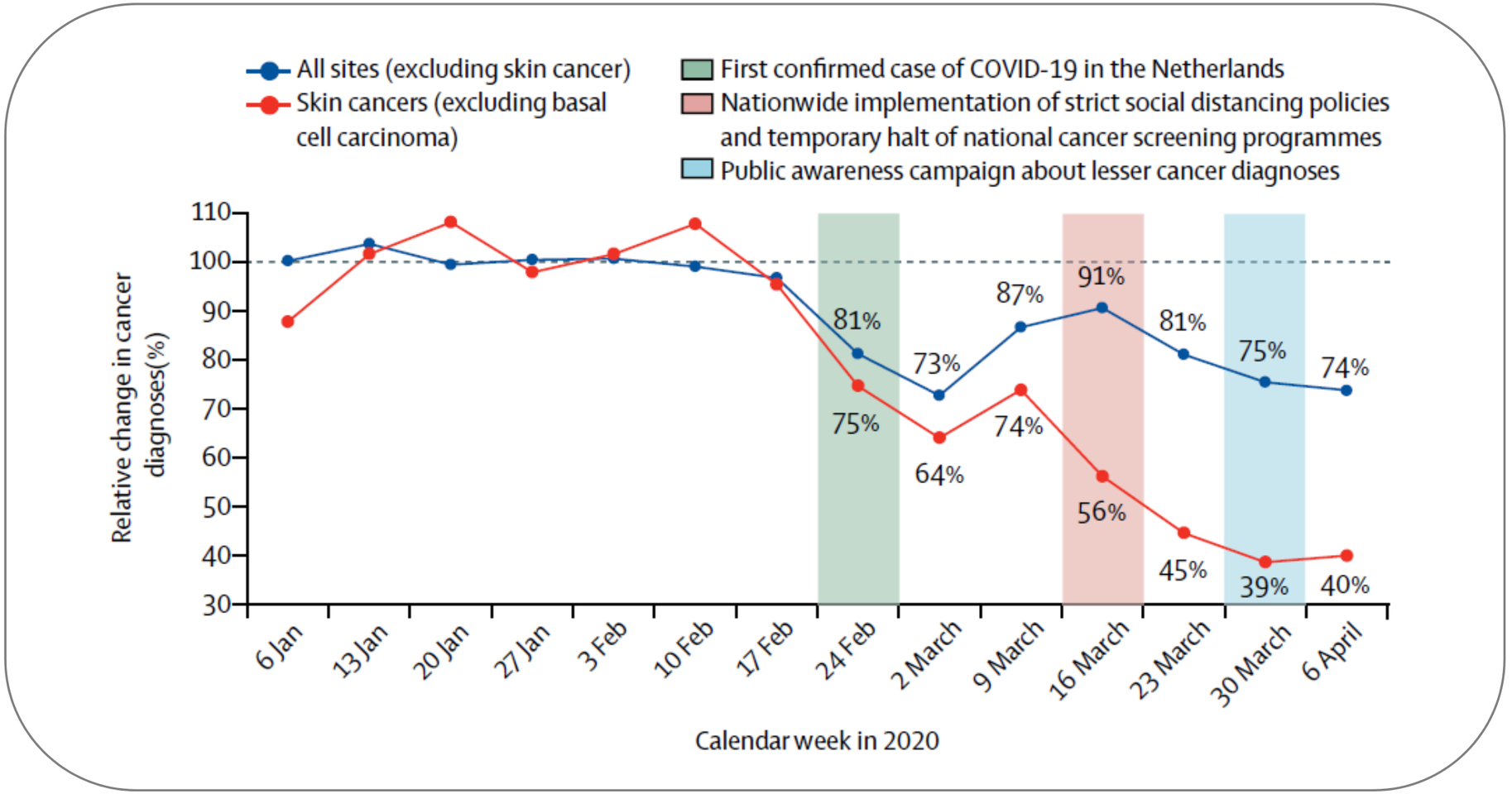
# Risks of delaying consultation, diagnosis and treatment…

# Harm of delay in cancer diagnosis  and treatment



https://www.nytimes.com/2020/11/16/world/europe/spain-coronavirus-cancer.html. Accessed December 4th 2020. https://www.bbc.com/news/uk-england-nottinghamshire-53935643?intlink_from_url=https://www.bbc.com/news/health&link. Accessed December 12th 2020

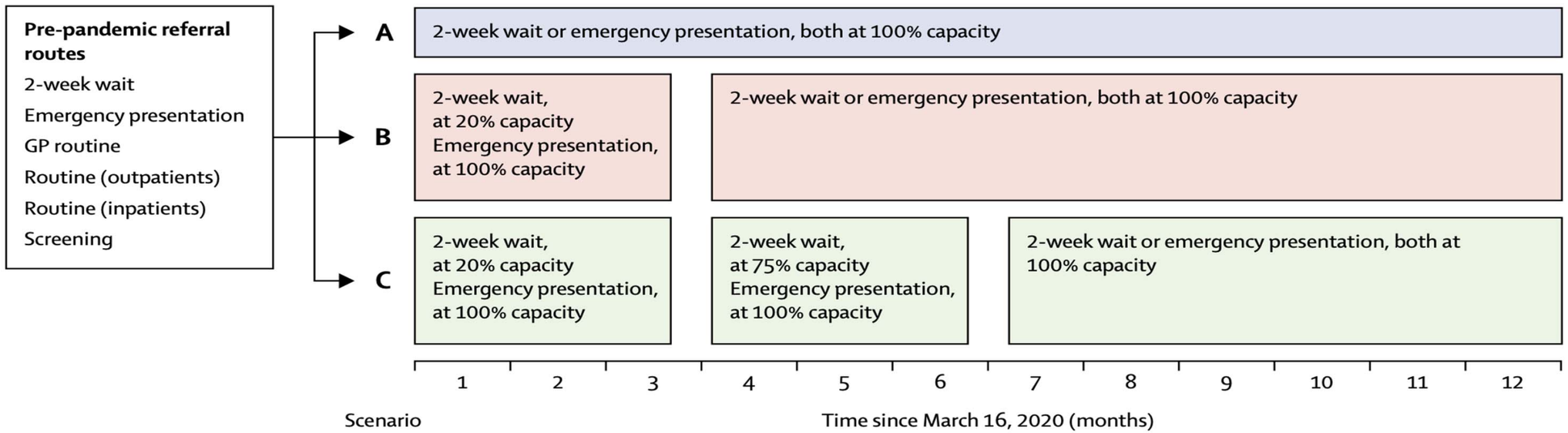
# Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands




Dinmohamed AG, et al. Lancet Oncol. 2020 Jun;21(6):750-751.

# The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study

**Conceptual framework for reallocation of pre-pandemic referral routes in three modelling scenarios (A, B, and C)**




For breast cancer, in addition to patients on routine pathways, only 25% of patients diagnosed through screening (ie, the proportion of patients with tumour stage III or IV, node-positive, or metastatic disease) were reallocated to 2-week wait or emergency presentation in the pandemic scenarios. GP=general practitioner.

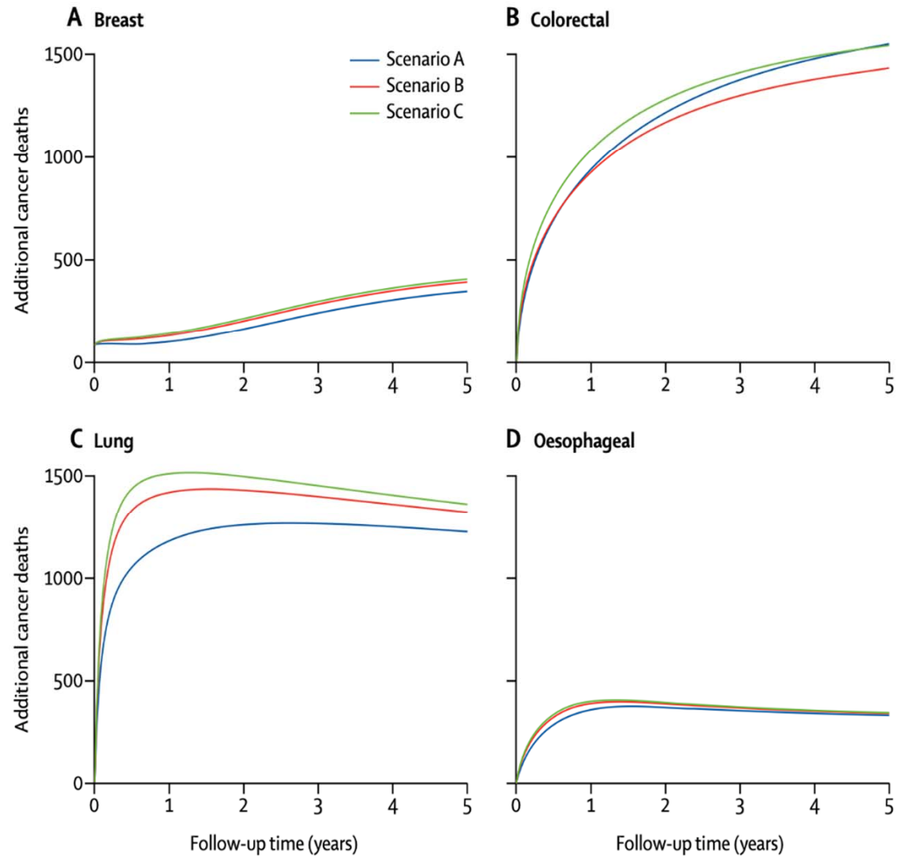
Maringe c, et al. Lancet Oncol 2020; 21: 1023–34

**Estimated years of life lost from additional deaths due to cancer, at 5 years from diagnosis, for each pandemic scenario**

| | Years of life lost (95% CI) |
|---|---|
| **Breast cancer (n=32 583)** | |
| Scenario A | 8181 (7797–8535) |
| Scenario B | 9033 (8638–9390) |
| Scenario C | 9261 (8843–9631) |
| **Colorectal cancer (n=24 975)** | |
| Scenario A | 27 735 (27 188–28 241) |
| Scenario B | 25 583 (24 792–27 744) |
| Scenario C | 27 043 (26 234–29 968) |
| **Lung cancer (n=29 305)** | |
| Scenario A | 20 537 (20 184–20 947) |
| Scenario B | 20 860 (20 250–21 277) |
| Scenario C | 20 413 (19 833–20 909) |
| **Oesophageal cancer (n=6744)** | |
| Scenario A | 5373 (5227–5530) |
| Scenario B | 5152 (5006–5301) |
| Scenario C | 5027 (4861–5213) |

Point estimates and 95% CIs were calculated from bootstrap samples of the original data.

**Estimated additional number of cancer deaths for each pandemic scenario A–C, for breast cancer (A), colorectal cancer (B), lung cancer (C), and oesophageal cancer (D)**




Maringe c, et al. Lancet Oncol 2020; 21: 1023–34

thebmj Visual Abstract

# Mortality due to cancer treatment delay

Quantification to support prioritisation and modelling

## Summary

Policies minimising system level delays to starting treatment could potentially improve survival after cancer diagnosis

## Study design

Systematic review and meta-analysis | Patients of all ages with seven major cancer types

## Data sources

34 studies on 17 cancer treatment indications
1 272 681 participants treated

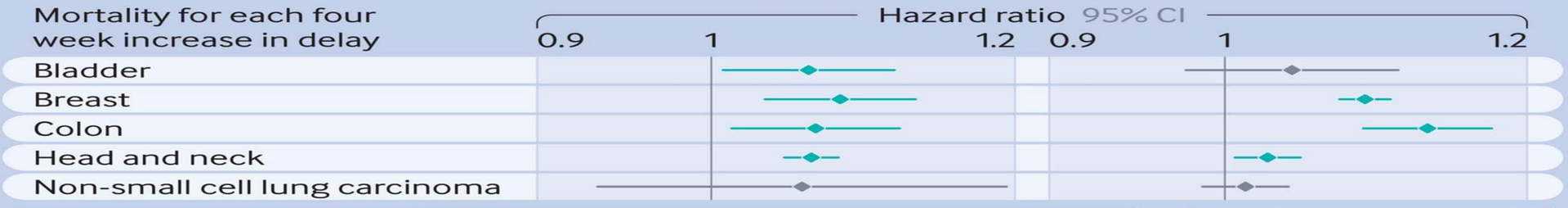
## Comparison

**Exposure and outcome**

Patient survival according to wait time for treatment including surgery, systemic treatment, or radiotherapy

## Outcomes

Mortality for each four week increase in delay




**Mortality increases as delay increases**

Breast cancer surgery delay for 1000 women (baseline 12% mortality)

**Projected additional deaths due to delay:**

4 weeks +10
8 weeks +20
12 weeks +31

**Evidence quality**

Only high validity studies accounting for major prognostic factors were included

http://bit.ly/BMJctd

* Adjuvant systemic treatment, apart from head and neck cancer, which was adjuvant radiotherapy



BMJ 2020;371:m4087

# COVID treatment of cancer patients : a simple answer (NIH/NCCN)

- “The recommendations for treating COVID-19 in patients with cancer are the same as those for the general population **(AIII)”**

COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed Dec 12th 2020

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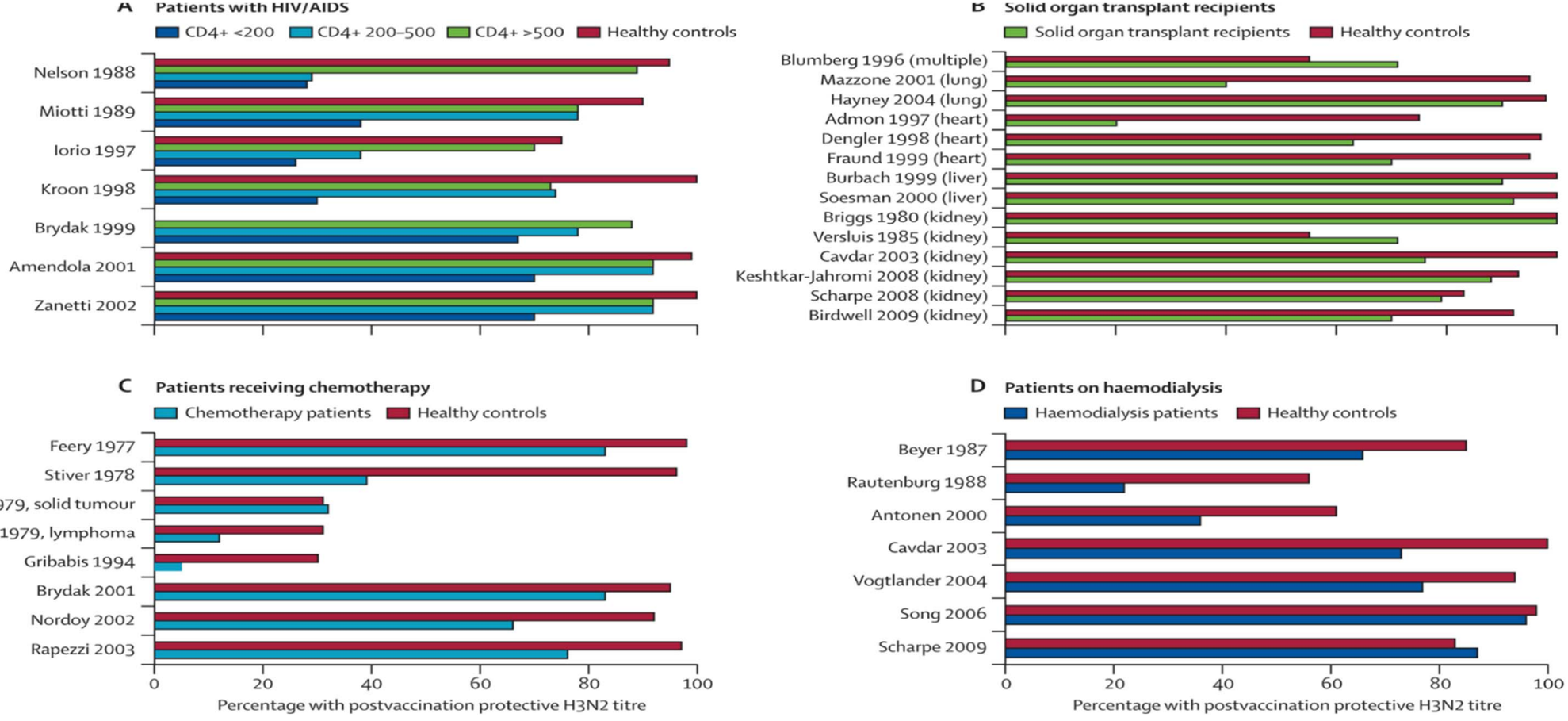
# What about vaccination of cancer patients?

# Will a COVID vaccine be effective in cancer patients? : a study on Influenza in immunocompromised patients




Post vacc H3N2 protective serum titers

Kunisak KM, et al., Lancet Infect Dis. 2009 Aug;9(8):493-504.