Tuberculosis and COVID interactions

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GTN (Global Tuberculosis Network)

Summary

- One of the stories of the **GTN research**: implementing Global Collaborative Research without funding

- A Research Line exploring the relationship between COVID-19 and Tuberculosis
- The story of its main results

In 2020

DRAMATIC SETBACK TO PROGRESS PREDICTED IF CONTINUITY OF ESSENTIAL TB SERVICES NOT ENSURED

1.49 MILLION
DEATHS, 2018

1.85 MILLION
ESTIMATED DEATHS, 2020*

If TB detection drops by 50% over three months,
the number of TB deaths worldwide would increase by nearly 400 000.

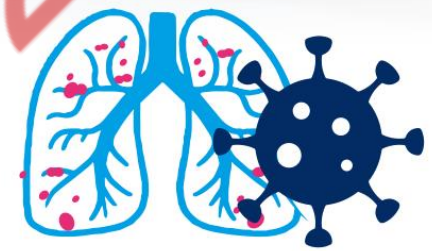
* These estimates include TB deaths among HIV-positive individuals.

END TB

World Health Organization

In 2021

THE COVID-19 PANDEMIC HAS REVERSED YEARS OF PROGRESS MADE IN THE FIGHT TO END TB



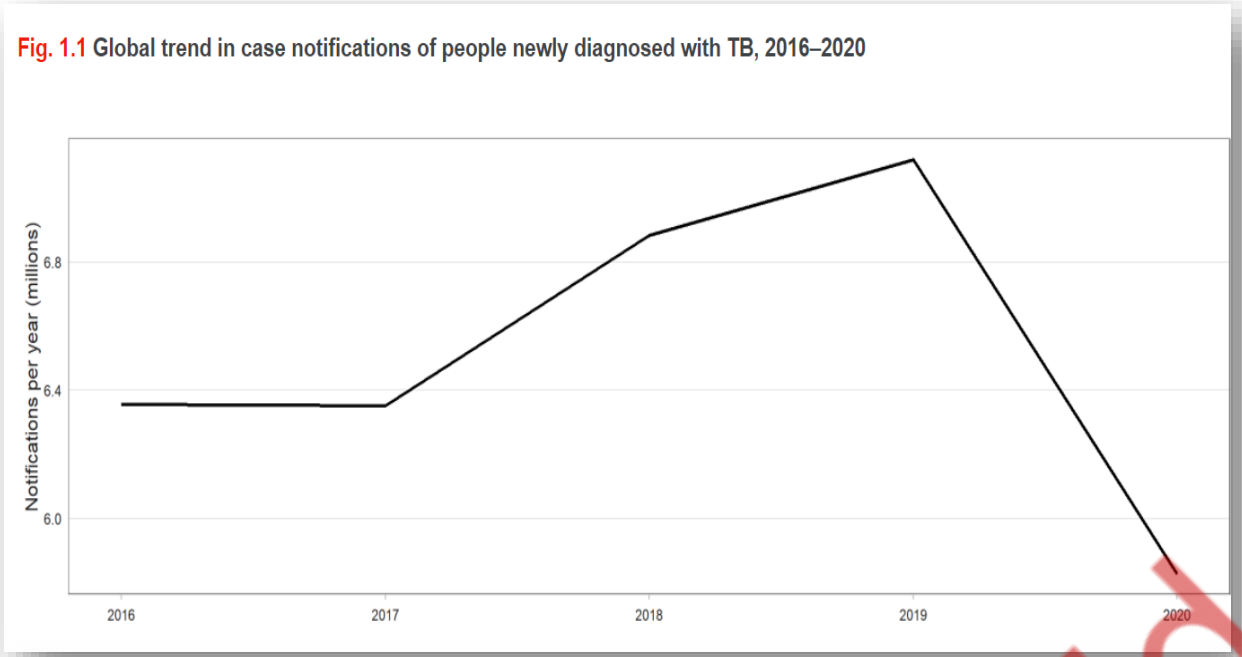
IN 2020

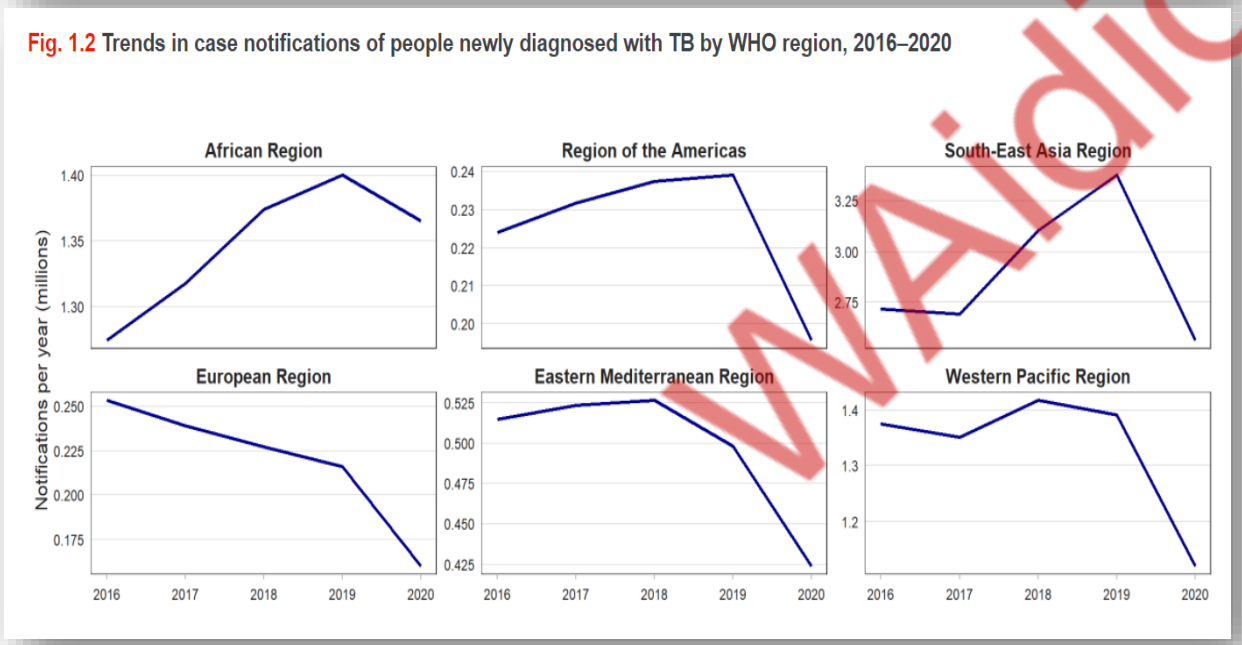
- TB DEATHS INCREASED FOR THE FIRST TIME IN OVER A DECADE
- FEWER PEOPLE WERE DIAGNOSED AND TREATED OR PROVIDED WITH TB PREVENTIVE TREATMENT
- FEWER RESOURCES FOR ESSENTIAL TB SERVICES AND TB R&D

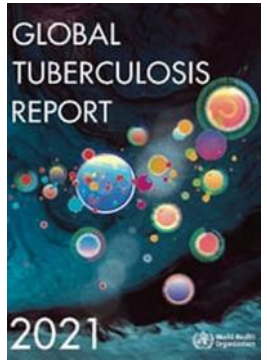
Actions to mitigate and reverse the impact of the COVID-19 pandemic on access to essential TB services are urgently needed.

END TB

World Health Organization







Global COVID-19 effect...

...and effect by region

How many infections not diagnosed and not treated evolving inot active TB?

How many infection TB and MDR-TB case who continued to transmit?

Overall, we lost 7 years of previous progress

What staff in the frontline against COVID-19: an example

Mexico City

Former MDR-TB reference center, equipped with negative pressure ventilation monitored rooms.

Transformed (permanently?) into COVID hospital.

No alternative for severe TB patients

Advantages and disadvantages of collaborative, operational research

GTbN
the Global Tb Network
fighting Tb together

Advantages	Disadvantages	Challanges
Rapid	Long time to clean data, need for queries	Quality of data
Ethical use of existing data	Need for specialised staff in charge of communication	Can be prospective or retrospective
No harm for patients	Considered of lower value than controlled clinical trials	Keeping the network together and ‘making all happy’
Rapid ethical clearance (existing ongoing global project; no need EC in ,amy countries for use retrospective non-interventional data)	Relies on network members dedication and enthusiasm	Receive the COI statements and copyright forms
Rapid publication possible		Ensuring all are cited by MEDLINE

March 2021: COVID-19 explodes

Are there global studies covering TB and COVID-19?

No

- Do we have the potentiality to make it?

Yes, via the Global Tuberculosis Network and connections with WHO

- Scientific interest?

Potentially top

Action 1: Let's talk with WHO (March-April 2020) and **make a pre-test**

Action2: Let's invite all GTN members and existing agencies/countries, etc. (April 2020)

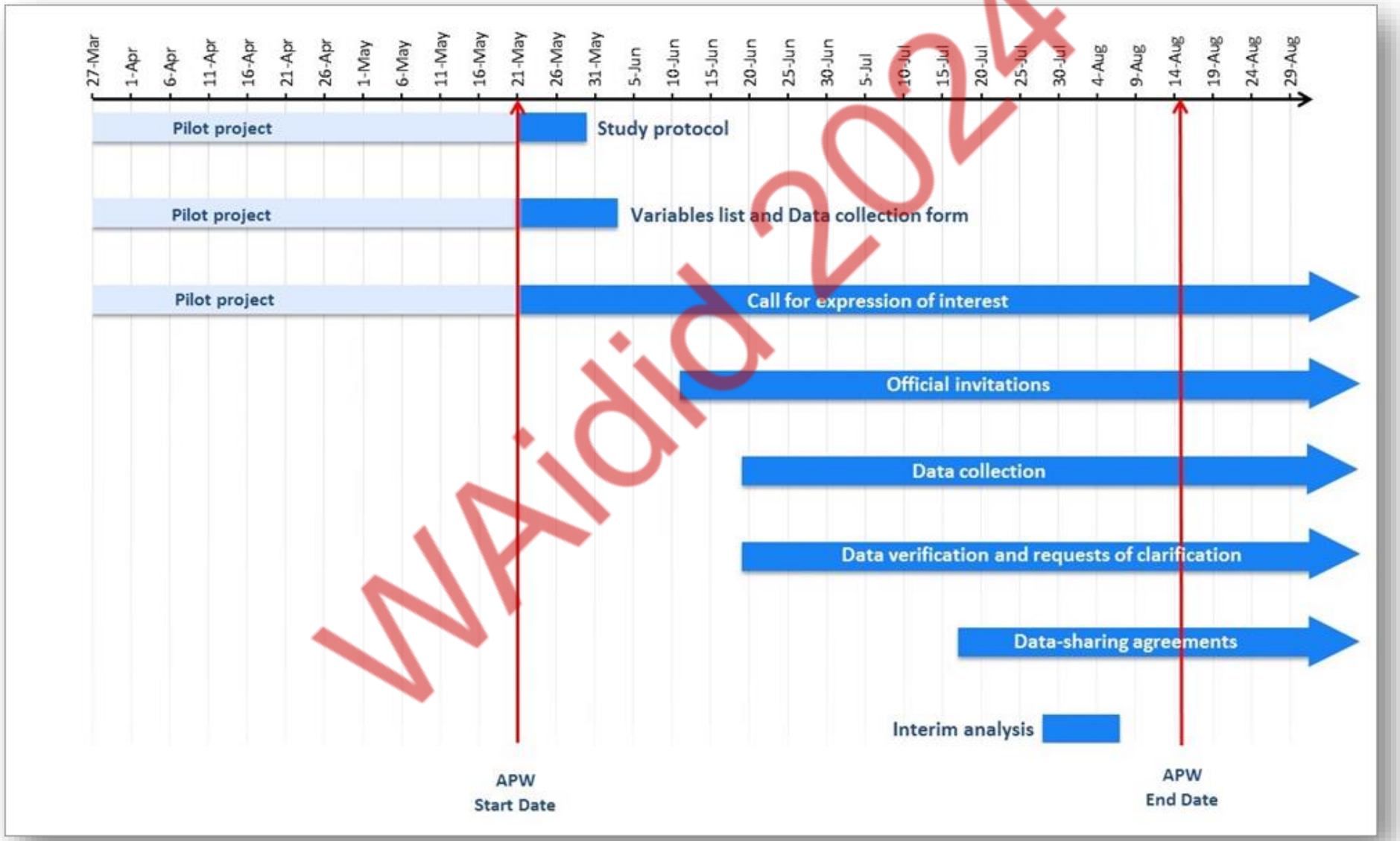
Action 3: Prepare protocol, invitation letters, data sharing agreement, etc (May 2020)

Action 4: Collect data and clean the database (June 2020), then **analyse, write and publish**

Scientific research questions

- How diagnosis occur? Before TB or COVID? Both together?
- What is the mortality rate? Higher with TB/COVID? Patients die because of TB, COVID or both?
- What are the determinants of mortality?
- Is COVID-19 boosting (as HIV) the progressione from TB infection to disease?
- What is the role of post-treatment sequelae?

Study plan (Gantt chart)



Pre-test: COVID: Study 49 cases

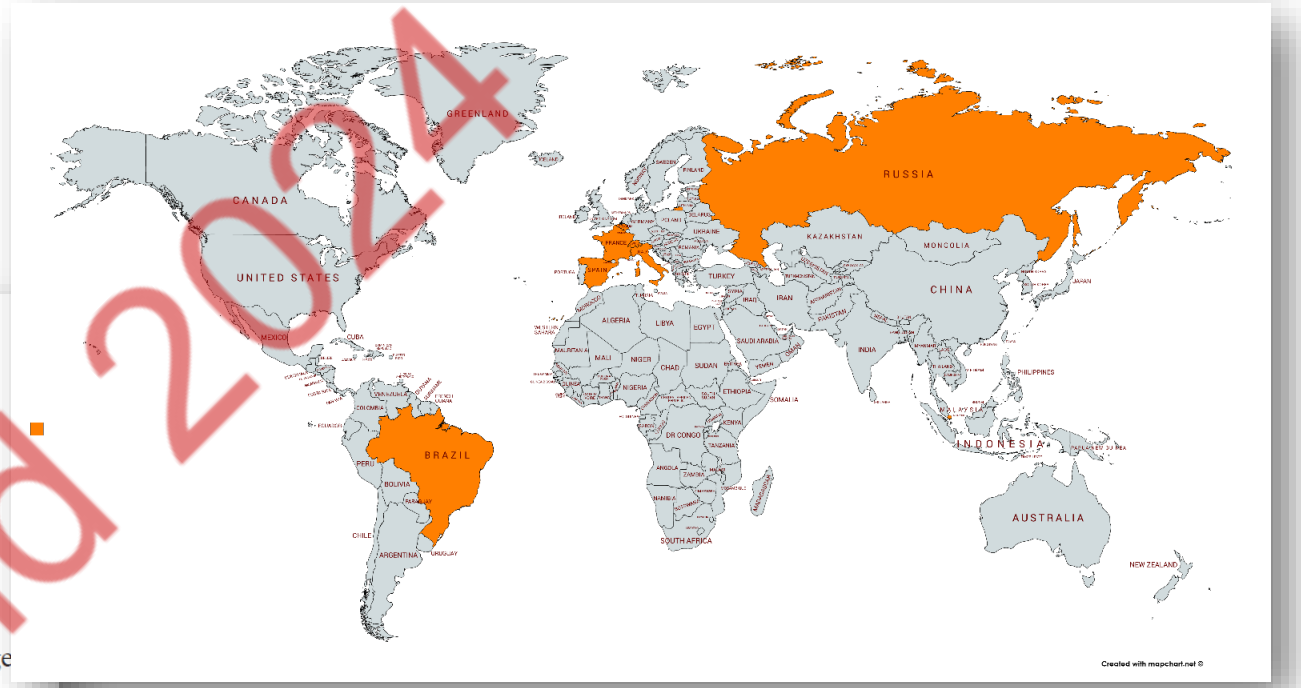
EUROPEAN RESPIRATORY *journal*
FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Research letter

Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases

Marina Tadolini, Luigi Ruffo Codecasa, José-María García-García, François-Xavier Blanc, Serge Borisov, Jan-Willem Alffenaar, Claire Andréjak, Pierre Bachez, Pierre-Alexandre Bart, Evgeny Belilovski, José Cardoso-Landivar, Rosella Centis, Lia D'Ambrosio, María-Luiza De Souza-Galvão, Angel Dominguez-Castellano, Samir Dourmane, Mathilde Fréchet Jachym, Antoine Froissart, Vania Giacomet, Delia Goletti, Soazic Grard, Gina Gualano, Armine Izadifar, Damien Le Du, Margarita Marín Royo, Jesica Mazza-Stalder, Ilaria Motta, Catherine Wei Min Ong, Fabrizio Palmieri, Frédéric Rivière, Teresa Rodrigo, Denise Rossato Silva, Adrián Sánchez-Montalvá, Matteo Saporiti, Paolo Scarpellini, Frédéric Schlemmer, Antonio Spanevello, Elena Sumarokova, Eva Tabernero, Paul Anantharajah Tambyah, Simon Tiberi, Alessandro Torre, Dina Visca, Miguel Zabaleta Murguiondo, Giovanni Sotgiu, Giovanni Battista Migliori



LETTER: rapid publication, easier

TB diagnosed first then COVID-19: 26 (53.0%)

COVID-19 first then TB: 14 (28.5%)

TB and COVID-19 in the same week: 9 (18.3%)

Active TB: 42 pts (85.7%)

TB Sequelae: 7 pts (14.3%)

1. Covid-19 can occur before, simultaneously or after the diagnosis of TB;
2. The role of COVID-19 in boosting the development of active TB is yet to be cleared
3. Role of TB sequelae in Covid-19 evolution is also unclear
4. Further studies are needed to enable analysis of interactions and determinants of outcomes in patients with both diseases.

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EUROPEAN RESPIRATORY *journal*
FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

WAS THE EDITOR HAPPY?

306 citations!! Among top Letters ever

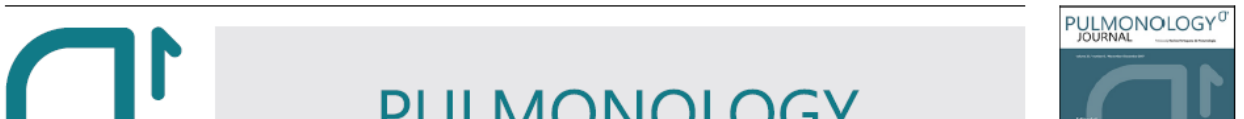
Mortality paper on 69 cases

+Model
PULMOE-1489; No. of Pages 8
ARTICLE IN PRESS

Pulmonol. 2020;xxx(xx):xxx–xxx

PULMONOLOGY

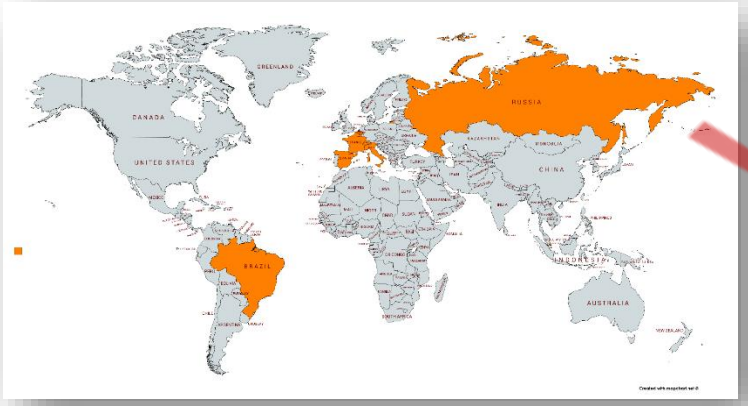
www.journalpulmonology.org



BRIEF COMMUNICATION

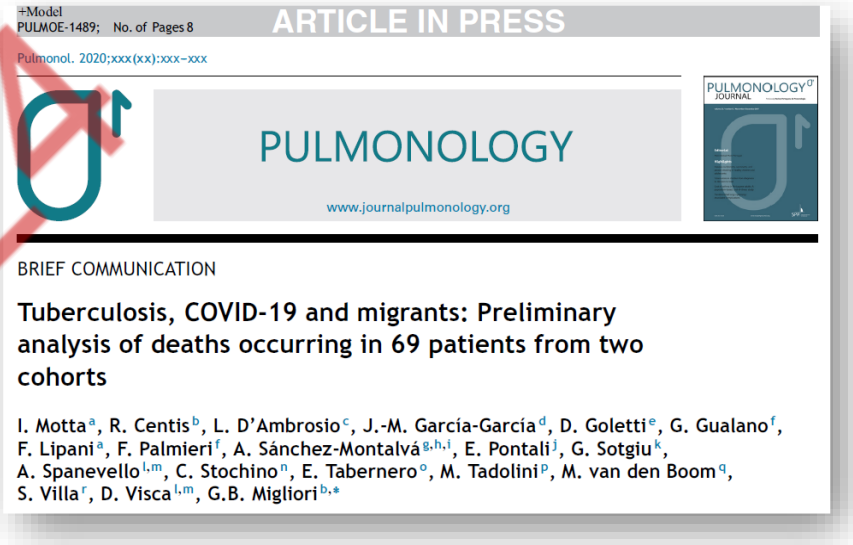
Tuberculosis, COVID-19 and migrants: Preliminary analysis of deaths occurring in 69 patients from two cohorts

I. Motta[a], R. Centis[b], L. D'Ambrosio[c], J.-M. García-García[d], D. Goletti[e], G. Gualano[f], F. Lipani[a], F. Palmieri[f], A. Sánchez-Montalvá[g,h,i], E. Pontali[j], G. Sotgiu[k], A. Spanevello[l,m], C. Stochino[n], E. Tabernero[o], M. Tadolini[p], M. van den Boom[q], S. Villa[r], D. Visca[l,m], G.B. Migliori[b,*]



- **Case fatality rate : 8/69 (11.6%)**
- 7 from cohort A (14.3%): 49 pts
- 1 from cohort B (5%): 20 pts
- **Migrants: younger, without co-morbidities, lower mortality**
- **Older patients, pre-existing co-morbidities, higher mortality**
- **Younger pts (including migrants) die less**

1. Mortality is likely to occur in elderly patients with co-morbidities
2. TB might not be a major determinant of mortality
3. Migrants had lower mortality, probably because of their younger age and lower number of co-morbidities
4. However, in settings where advances forms of TB frequently occur and are caused by drug-resistant strains of MTB, higher mortality rates can be expected in younger individuals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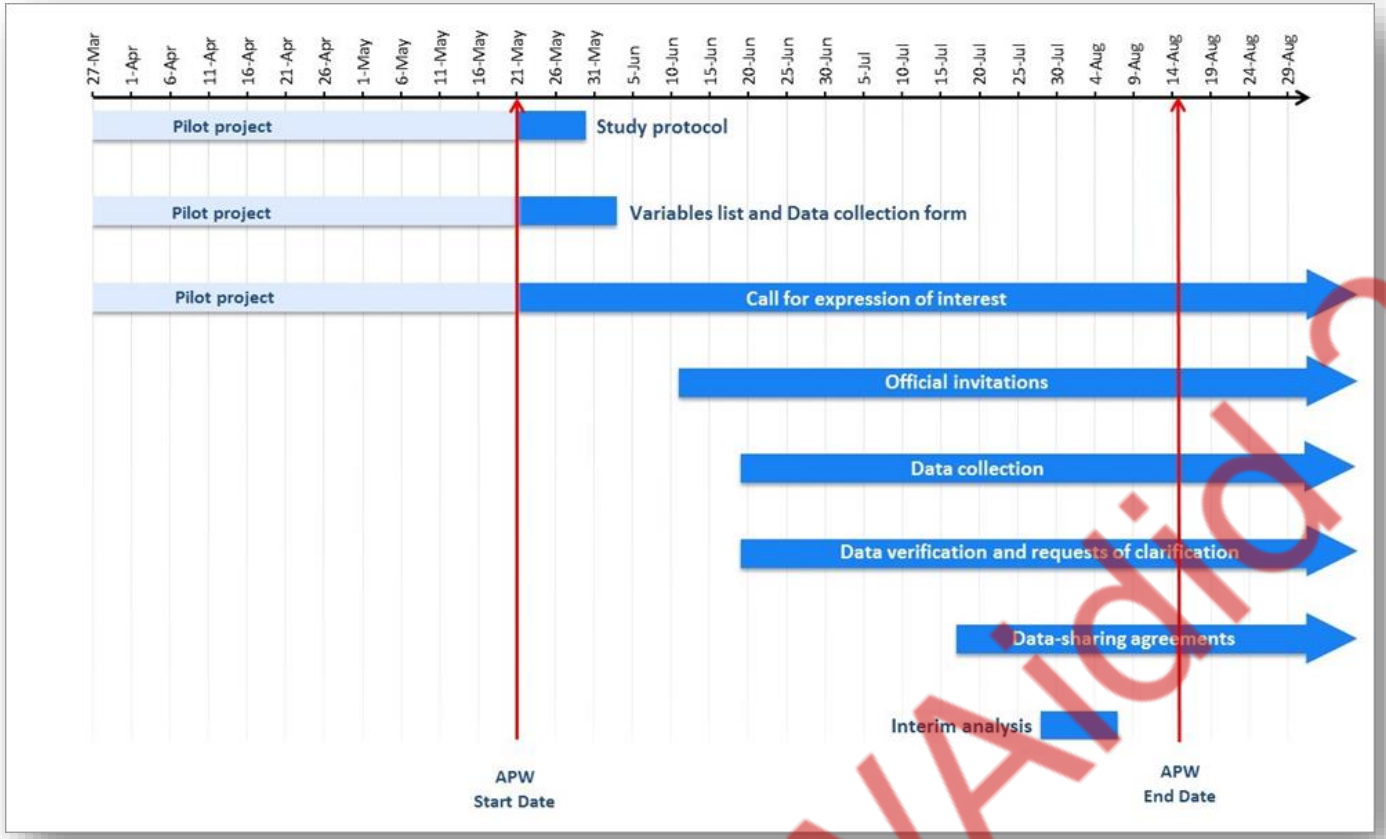
Was the Editor happy?

Yes!!

Cited 179 times

(record for the Journal)

Study plan (Gantt chart)



Study 1 aim: to describe the features of the TB/COVID-19 co-infected individuals from a prospective, anonymised, multicountry register-based cohort with special focus on the determinants of mortality and other outcomes.

Focus on early (COVID-related mortality)

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
TB/COVID-19 GLOBAL STUDY GROUP

Tuberculosis and COVID-19 co-infection: description of the global cohort

The TB/COVID-19 Global Study Group

The complete list of contributors of the TB/COVID-19 Global Study Group is provided in the Acknowledgements section

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Shareable abstract (@ERSpublications)
High mortality (11%) was observed with COVID-19/TB co-infection associated with older age, male gender and invasive ventilation. Efforts to avoid SARS-CoV-2 infection in TB patients are recommended to prevent excess morbidity and mortality. https://bit.ly/3mSylCK

Cite this article as: The TB/COVID-19 Global Study Group. Tuberculosis and COVID-19 co-infection: description of the global cohort. *Eur Respir J* 2022; 59: 2102538 [DOI: 10.1183/13993003.02538-2021].

This article has an editorial commentary: https://doi.org/10.1183/13993003.00149-2022

Received: 21 Sept 2021
Accepted: 1 Nov 2021

Abstract

Background Information on tuberculosis (TB) and coronavirus disease 2019 (COVID-19) is still limited. The aim of this study was to describe the features of the TB/COVID-19 co-infected individuals from a prospective, anonymised, multicountry register-based cohort with special focus on the determinants of mortality and other outcomes.

Methods We enrolled all patients of any age with either active TB or previous TB and COVID-19. 172 centres from 34 countries provided individual data on 767 TB-COVID-19 co-infected patients, (>50% population-based).

Results Of 767 patients, 553 (74.0%) out of 747 had TB before COVID-19 (including 234 out of 747 with previous TB), 71 (9.5%) out of 747 had COVID-19 first and 123 (16.5%) out of 747 had both diseases diagnosed within the same week (n=35 (4.6%) on the same day). 85 (11.08%) out of 767 patients died (41 (14.2%) out of 289 in Europe and 44 (9.2%) out of 478 outside Europe; p=0.03): 42 (49.4%) from COVID-19, 31 (36.5%) from COVID-19 and TB, one (1.2%) from TB and 11 from other causes. In the univariate analysis on mortality the following variables reached statistical significance: age, male gender, having more than one comorbidity, diabetes mellitus, cardiovascular disease, chronic respiratory disease, chronic renal disease, presence of key symptoms, invasive ventilation and hospitalisation due to COVID-19. The final multivariable logistic regression model included age, male gender and invasive ventilation as independent contributors to mortality.

Conclusion The data suggest that TB and COVID-19 are a "cursed duet" and need immediate attention. TB should be considered a risk factor for severe COVID disease and patients with TB should be prioritised for COVID-19 preventative efforts, including vaccination.

Introduction

Tuberculosis (TB), with its estimated 10 million cases and 1.3 million deaths annually, continues to be a global health priority [1]. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus disease 2019 (COVID-19) pandemic has required concerted public health focus and action because of its rapid global spread, clinical severity, high mortality rate with 4 million deaths, and capacity to overwhelm healthcare systems [2–5]. The impact of COVID-19 on TB services has been well described, with a reduction of the number TB cases diagnosed and managed in most countries as a combined result of reduced access, delayed diagnosis with more advanced forms and overstretched health services among other reasons [6–11]. According to the World Health Organization (WHO) report, there was a 18% decrease of TB case notifications between 2019 and 2020 (from 7.1 to 5.8 million cases) [1]. Conservative models suggest that a 20% increase in TB deaths in the next 5 years is likely as a result of the pandemic [12, 13].

The clinical and immune-pathological interaction between the two diseases and the drivers of dual COVID-19/TB disease mortality are not yet fully understood [14–17]. A first pilot study of the Global

Global TB and COVID-19 study by the Global Tuberculosis Network (GTN)- Study 1

>700 cases from 36 countries

Preliminary analysis 342 cases:

- 61 (17.8%) had TB sequelae;

-197 (57.6%) had TB diagnosed before COVID-19 (median number [IQR] of 85 (45-151,5) days

- 57 (16.7%) had concomitant TB-COVID-19 diagnoses

- 27 (7.9%) had COVID-19 diagnosed before TB with a median number [IQR] of 18 (13-33) days.

73 citations

GTN TB/COVID-19 clinical study: 1. General details

Tuberculosis		n (%)*
Males		540/767 (70.4)
Median (IQR) age, years at last birthday		44 (30-58)
TB Form	New case	618/723(85.5)
	Relapse	59/723 (8.2)
	Lost to follow-up	29/723 (4.0)
	Failure	17/723 (2.4)
Pulmonary TB		648/755 (85,8)
TB laboratory confirmed		612/732(83.6)
Solid culture		441/638 (69.3)
Liquid culture		324/638 (50.9)
Xpert MTB/RIF		410/638 (64.5)
First line LPA		105/638 (16.5)
Second line LPA		28/638 (4.4)
TB drug resistance pattern at TB diagnosis	Pan-susceptible TB	517/607 (85.2)
	Drug-resistant TB	90/607(14.8)

* Data are reported in the table as number/total number of patients for whom data are available (%).

Majority of patients are males, with Pulmonary TB, bacteriologically confirmed and drug-susceptible

2. Signs & symptoms

COVID-19 signs and symptoms	n: 538 (%)*
Abdominal pain	34 (6.3)
Arthralgia	36(6.7)
Chest pain	88 (16.3)
Diarrhoea	52 (9.7)
Dry cough	311 (57.8)
Fever	386 (71.7)
Headache	133 (24.7)
Confusion	34 (6.3)
Malaise	96 (17.8)
Myalgia	87 (12.9)
Nasal congestion	73 (13.6)
Olfactory disorders	48 (8.9)
Shortness of breath	192 (35.7)
Sore throat	96 (17.8)
Taste disorders	56 (10.4)
Tiredness	114 (21.2)
Vomiting/nausea	38 (7.1)
Other symptoms	74 (13.7)

Majority of pts report:
- Fever, dry cough, dyspnoea.
- 9-10% with typical symptoms for COVID-19

* Data are reported in the table as number/total number of patients for whom data are available (%).

3. Radiology

Radiology at COVID-19 diagnosis	n (%)*
CT scan	109/642 (17.0)
Chest X- Ray	2014/642 (33.3)
CT scan and chest X- Ray	157/642 (24.5)
Not done	162/642 (**25.2**)
Typical ground glass opacity, unilateral	40/266 (**15.1**)
Typical ground glass opacity, bilateral	126/266 (**47.4**)
Typical ground glass opacities, bilateral + atypical	6/266 (**2.2**)
Atypical opacity	56/266 (21.0)
No opacity	38/266 (14.3)

* Data are reported in the table as number/total number of patients for whom data are available (%).

Radiology at TB diagnosis	N: 633 (%)*
Unilateral pulmonary cavitary lesions	125 (**19.7**)
Bilateral pulmonary cavitary lesions	123 (**19.4**)
Unilateral pulmonary infiltrate, (no cavities)	102 (16.1)
Bilateral pulmonary infiltrates (no cavities)	115 (18.2)
Other radiological TB form	143 (22.6)
Radiology done	608/767 (**79.3**)

COVID-19: Radiology in 75% of patients
86% with typical or atypical ground glass opacities

TB: 79.3% with chest imaging done
39.1% with cavities

4. Treatment: oxygen and ventilation

Ventilation during COVID-19 treatment	n (%)*
No ventilation	513/626 (81.9)
Invasive mechanical ventilation	46/626 (**7.4**)
Non-invasive mechanical ventilation	67/626 (**10.7**)
Supplemental Oxygen	198/619 (**32.0**)

* Data are reported in the table as number/total number of patients for whom data are available (%).

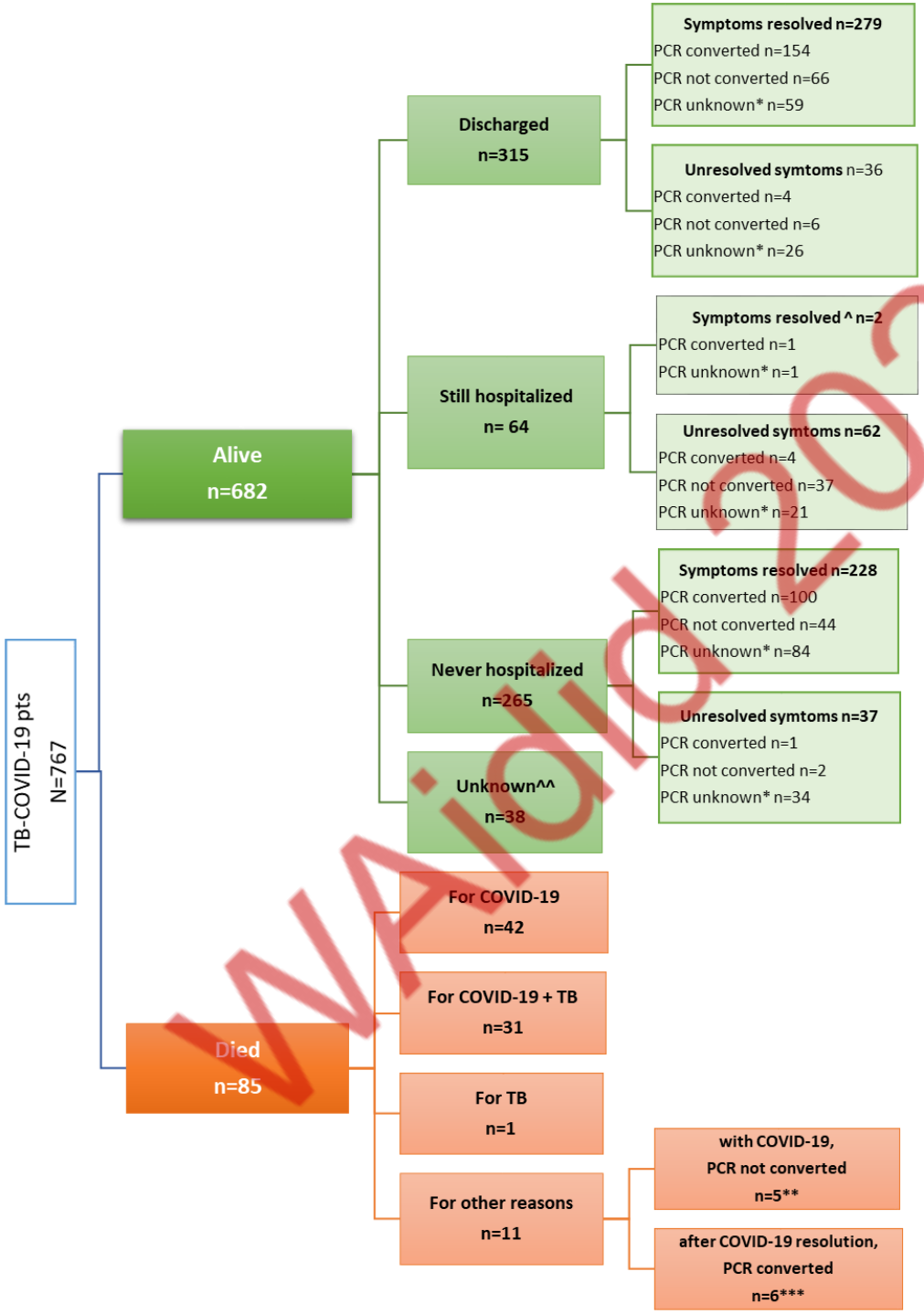
One third of patients need oxygen and >10% ventilation.

Question 2: these patients are complex to manage with important burden on health services in countries with high burden of cases.

Oxygen stock-out? Not enough ventilators? Which services/staff to take care?

5. Mortality

COVID-19 Provisional outcomes



Overall mortality
85/767: **11.1%**

Mortality excluding164 patients with unknown outcome/ unresolved COVID-19/PCR not converted-unknown
85/603: **14.1%**

Excluding other causes of death:
74/767: **9.6%**

6. Logistic regression analysis to assess the relationship between demographic, epidemiological, clinical variables and mortality

Variable (comparison)	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age, years (10 years increase)	1.82 (1.58-2.09)	<0.0001	**1.93 (1.60-2.32)**	**<0.0001**
Males (yes vs no)	2.08 (1.16-3.71)	0.014	**2.92 (1.38-6.16)**	**0.005**
≥1 comorbidity (yes vs no)	6.01 (3.21-11.27)	<0.0001	-	-
Diabetes Mellitus (yes vs no)	2.69 (1.67-4.35)	<0.0001	-	-
Cardiovascular Disease (yes vs no)	5.12 (3.19-8.22)	<0.0001	-	-
Chronic Resp. Disease (yes vs no)	3.00 (1.74-5.18)	<0.0001	-	-
HIV (yes vs no)	1.48 (0.77-2.87)	0.241	-	-
Chronic Liver Disease (yes vs no)	1.69 (0.82-3.46)	0.155	-	-
Chronic Renal Disease (yes vs no)	3.00 (1.74-5.18)	<0.0001	-	-
Invasive ventilation (yes vs no)	25.18 (12.64-50.13)	<0.0001	**28.22 (1.37-64.39)**	**<0.0001**
Active TB (yes vs no)	1.5 (1.0-2.5)	0.069	-	-
Hospitalization due to COVID-19 (yes vs no)	3.54 (1.95-6.41)	<0.0001	-	-
Duration of hospitalization (1 day increase)	0.98 (0.96-1.01)	0.072	-	-
Europe (yes vs no)	1.63 (1.04-2.57)	0.034		

Relevant research clinical & programmatic questions

1. Does COVID-19 increase progression from TBI to TB? NO
2. Are the TB / COVID-19 pts more difficult to manage (oxygen, ventilation)? YES
3. Are the preliminary results on mortality (11.6%) confirmed? YES What 'additional' risk is brough by COVID-19 on mortality? What are the determinants of mortality?
4. Will the co-infection really impact dramatically health services in high TB incidence countries? YES

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
GLOBAL TUBERCULOSIS NETWORK AND TB/COVID-19 GLOBAL STUDY GROUP

Long-term outcomes of the global tuberculosis and COVID-19 co-infection cohort

Global Tuberculosis Network and TB/COVID-19 Global Study Group

Contributors of the Global Tuberculosis Network and TB/COVID-19 Global Study Group are listed at the end of the article.

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Shareable abstract (@ERSpublications)
In 778 TB/COVID-19 co-infected patients, 77% TB treatment success and 11% TB mortality was observed, with 71% recovering from COVID-19 and 13% COVID-19-associated mortality. Mortality was higher in those diagnosed with COVID-19 before/during TB treatment. https://bit.ly/3PQSw17

Cite this article as: Global Tuberculosis Network and TB/COVID-19 Global Study Group. Long-term outcomes of the global tuberculosis and COVID-19 co-infection cohort. *Eur Respir J* 2023; 62: 2300925 [DOI: 10.1183/13993003.00925-2023].

This article has an editorial commentary: https://doi.org/10.1183/13993003.01881-2023

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Abstract

Background Longitudinal cohort data of patients with tuberculosis (TB) and coronavirus disease 2019 (COVID-19) are lacking. In our global study, we describe long-term outcomes of patients affected by TB and COVID-19.

Methods We collected data from 174 centres in 31 countries on all patients affected by COVID-19 and TB between 1 March 2020 and 30 September 2022. Patients were followed-up until cure, death or end of cohort time. All patients had TB and COVID-19; for analysis purposes, deaths were attributed to TB, COVID-19 or both. Survival analysis was performed using Cox proportional risk-regression models, and the log-rank test was used to compare survival and mortality attributed to TB, COVID-19 or both.

Results Overall, 788 patients with COVID-19 and TB (active or sequelae) were recruited from 31 countries, and 10.8% (n=85) died during the observation period. Survival was significantly lower among patients whose death was attributed to TB and COVID-19 *versus* those dying because of either TB or COVID-19 alone (p<0.001). Significant adjusted risk factors for TB mortality were higher age (hazard ratio (HR) 1.05, 95% CI 1.03–1.07), HIV infection (HR 2.29, 95% CI 1.02–5.16) and invasive ventilation (HR 4.28, 95% CI 2.34–7.83). For COVID-19 mortality, the adjusted risks were higher age (HR 1.03, 95% CI 1.02–1.04), male sex (HR 2.21, 95% CI 1.24–3.91), oxygen requirement (HR 7.93, 95% CI 3.44–18.26) and invasive ventilation (HR 2.19, 95% CI 1.36–3.53).

Conclusions In our global cohort, death was the outcome in >10% of patients with TB and COVID-19. A range of demographic and clinical predictors are associated with adverse outcomes.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has significantly affected tuberculosis (TB) services worldwide [1]. Globally, national TB programmes struggled to provide care, resulting in an unprecedented interruption of essential services. Studies have demonstrated that access to TB care has worsened during the pandemic [2–6]. The World Health Organization (WHO) reported an overall decrease in TB notifications, from 7.1 million in 2019 to 5.8 million in 2020, with a partial recovery in 2021, and an additional 100 000 TB deaths between 2019 and 2020 [1].

Since the beginning of the pandemic, TB and COVID-19 co-infected cases have been described: they can occur concomitantly, or COVID-19 can precede TB or occur in patients with TB sequelae. Both diseases primarily affect the lungs and share similar symptoms, such as fever and cough, posing diagnostic challenges and delayed diagnosis [7]. COVID-19 and TB co-infection may lead to severe acute illness [8–11]. Studies have demonstrated that concomitant TB and COVID-19 increase mortality and chronic lung sequelae [12, 13].

Despite studies suggesting synergistic amplification of mortality related to co-infection, no cohort studies have evaluated the effects of COVID-19 on long-term TB outcomes or *vice versa*, particularly since TB

TB-COVID Global Cohort Study 2

The previous study reported early mortality, mainly related to COVID-19.

This study reported long-term outcomes related to both TB and COVID 19

Global distribution of the countries/states/regions participating in the study.
Footnote: The following States/Territories are covered in the study update: Australia (New South Wales); Canada (Ontario State): China (Wenzhou and Luzhou Regions); India (New Delhi, Mumbai & Maharashtra States); Russian Federation (Arkhangelsk, Moscow and Volvograd Oblasts); Switzerland (Vaud County); USA (Virginia State)
29/34 countries participating in the first global study [10] provided treatment outcome updates and 2 countries (Nigeria and Libya) were enrolled in the study at a later stage providing data with treatment outcomes

11 citations so far

TABLE 1 Summary of anti-tuberculosis (TB) treatment outcomes in 788 patients, stratified by time of coronavirus disease 2019 (COVID-19) diagnosis after the end of TB treatment *versus* before or during TB treatment

	TB patients	COVID-19 diagnosis[#]		p-value
		After the end of TB treatment	Before or during TB treatment	
Cured	284 (36)	109 (38.7)	172 (34.7)	0.311
Treatment completed	324 (41.1)	147 (52.1)	173 (34.9)	<0.0001
Treatment successful	608 (77.2)	256 (90.8)	345 (69.7)	<0.0001[¶]
Died	85 (10.8)		83 (16.8)	
Cause of death				
TB	17/85 (20)		15/83 (18.1)	
TB+COVID-19	46/85 (54.1)		46/83 (55.4)	
TB+COVID-19+other	4/85 (4.7)		4/83 (4.87)	
COVID-19	9/85 (10.6)		9/83 (10.8)	
Other	9/85 (10.6)		9/83 (10.8)	
Failure	3 (0.4)	1 (0.4)	2 (0.4)	0.620
Lost to follow-up	92 (11.7)	25 (8.9)	65 (13.1)	0.094
Total	788	282/777	495/777	

Data are presented as n (%), n/N (%) or n, unless otherwise stated. [#]: for 11 out of 788 patients, data were unavailable on timing of COVID-19 diagnosis in relation to TB treatment; [¶]: baseline TB treatment success was significantly higher when the diagnosis of COVID-19 occurred after the end of TB treatment (90.8%), in comparison with cases where the diagnosis was made before or during TB treatment (69.7%) (p<0.0001).

788 patients with COVID-19 and TB (active or sequelae) were recruited from 31 countries, and 10.8% (n=85) died during the observation period. Survival was significantly lower among patients whose death was attributed to TB and COVID-19 versus those dying because of either TB or COVID-19 alone (p<0.001). Significant adjusted risk factors for TB mortality were higher age (hazard ratio (HR) 1.05, 95% CI 1.03–1.07), HIV infection (HR 2.29, 95% CI 1.02–5.16) and invasive ventilation (HR 4.28, 95% CI 2.34–7.83). For COVID-19 mortality, the adjusted risks were higher age (HR 1.03, 95% CI 1.02–1.04), male sex (HR 2.21, 95% CI 1.24–3.91), oxygen requirement (HR 7.93, 95% CI 3.44– 18.26) and invasive ventilation (HR 2.19, 95% CI 1.36–3.53).

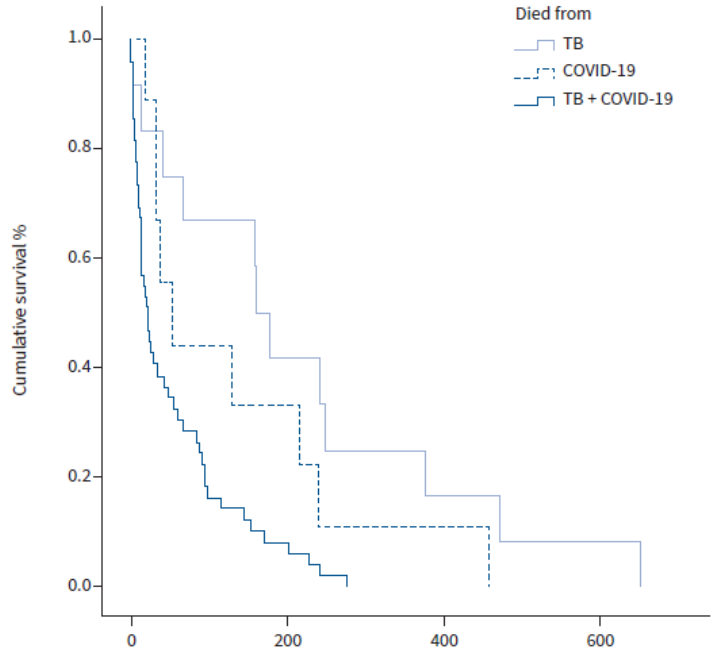


FIGURE 2 Kaplan–Meier survival curves of tuberculosis (TB) deaths, coronavirus disease 2019 (COVID-19) deaths and TB+COVID-19 deaths. Log-rank test: p=0.001.

TABLE 4 Deaths from tuberculosis (TB), coronavirus disease 2019 (COVID-19) and deaths for any reason (overall deaths) according to the geographical region

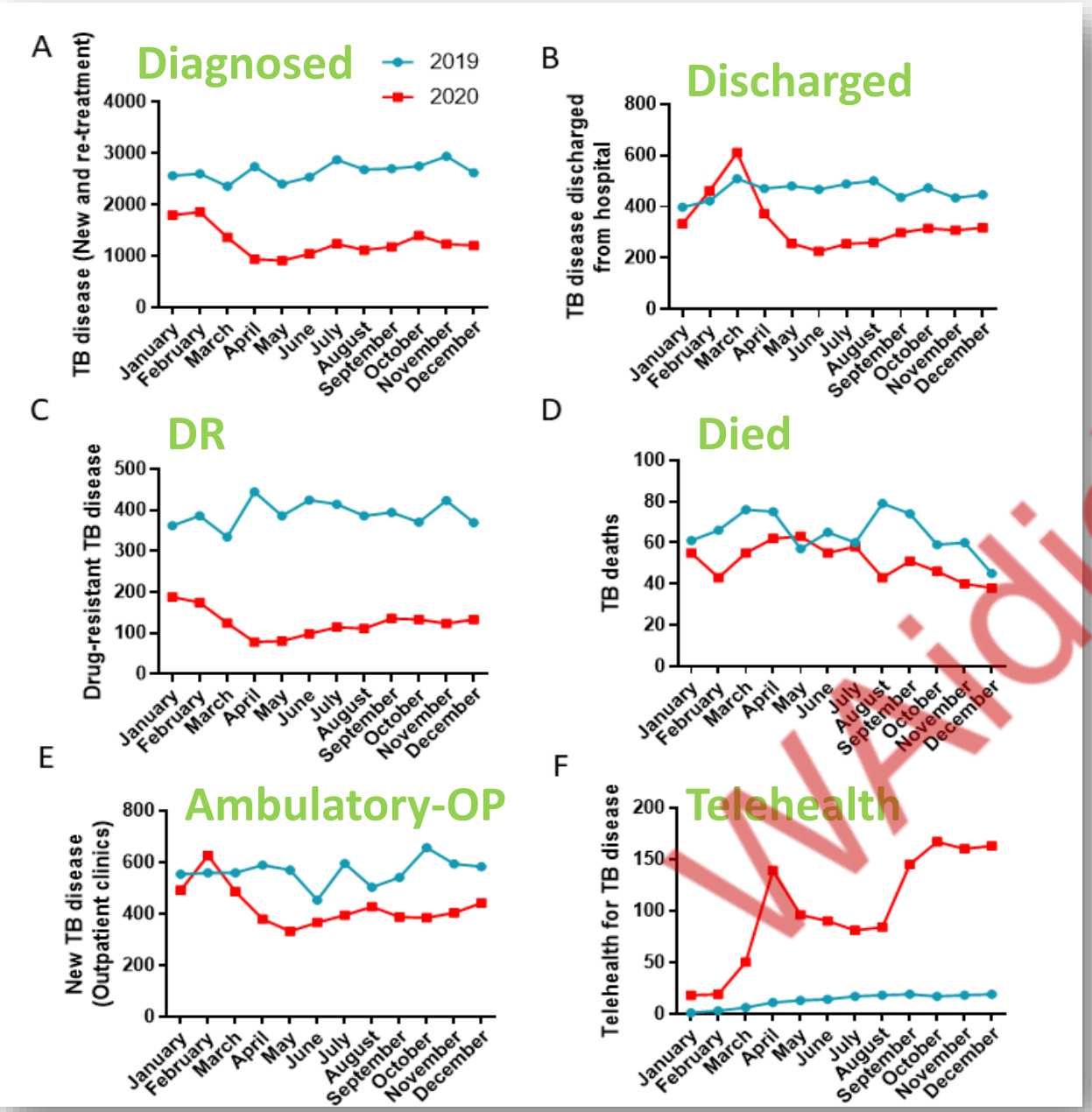
	Latin America	North America, Western Europe and the Middle East	Eastern Europe	Africa	Asia	p-value
Age years	41.7±17.7	51.7±18.8	44.6±16.1	42.5±16.1	39.8±14.4	<0.0001
Male	224 (66.1)	193 (66.8)	43 (72.9)	20 (57.1)	53 (82.8)	0.045
HIV	55 (16.6)	15 (5.2)	9 (15.3)	4 (12.1)	0	<0.0001
Drug-resistant TB	17 (5.3)	22 (9.8)	27 (45.8)	2 (8.7)	12 (26.7)	<0.0001
Hospitalised patients	127 (37.2)	226 (78.2)	59 (100)	11 (31.4)	49 (76.6)	<0.0001
Supplemental oxygen during COVID-19	67 (37.4)	95 (35.7)	9 (15.3)	5 (55.6)	11 (17.2)	<0.0001
Invasive ventilation	21 (11.7)	13 (4.8)	3 (5.2)	0	7 (10.9)	0.020
Deaths from TB	38 (11.1)	38 (11.1)	5 (8.5)	7 (20.0)	4 (6.3)	0.112
Deaths from COVID-19	43 (12.6)	45 (15.9)	4 (6.8)	2 (6.3)	8 (12.5)	0.247
Overall deaths	51 (15.0)	48 (16.6)	7 (11.9)	7 (20.0)	8 (12.5)	0.749

Data are presented as mean±SD or n (%), unless otherwise stated.

GTN Global study: 'impact on health systems'

114 citations!!!

N° telehealth examinations; TB cases (DS- and DR-TB, patients hospitalized and managed as OP) and LTBI (pts/ N ° of examinations) diagnosed in 2020 vs 2019 in >35 centers, 19 countries (6 with population-based data), 5 continents



Interim analysis TB: 2019 vs 2020

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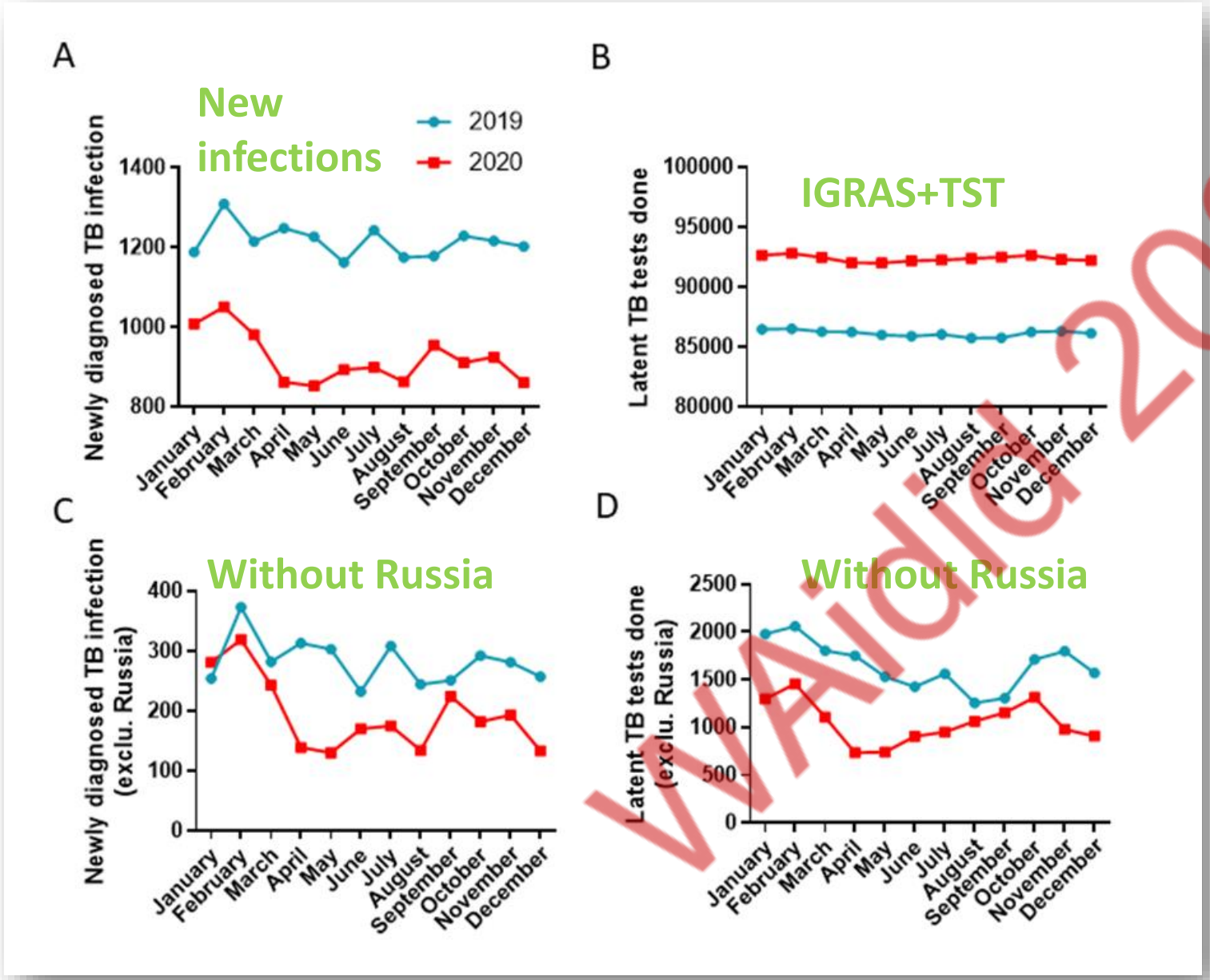

Interim analysis TBI 2019 vs 2020

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Long-term outcomes of the global tuberculosis and COVID-19 co-infection cohort

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Global Tuberculosis Network and TB/COVID-19 Global Study Group

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Singapore: COVID-19 measures increase TB detection

The exception confirming the rule

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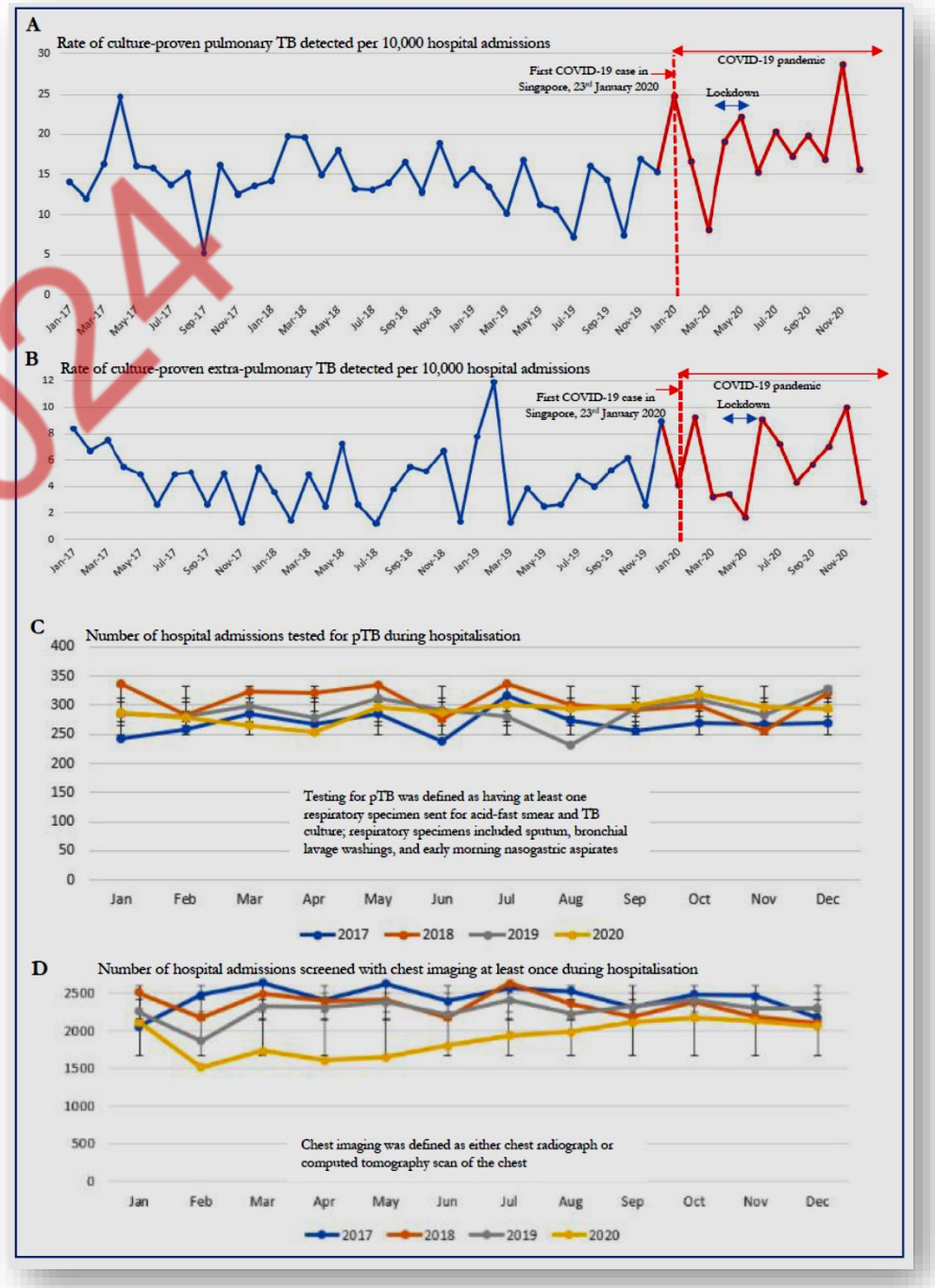

Conclusions

1. More and more information from Operational Research on TB/COVID-19 complementing routine surveillance data
2. COVID-19 can appear before, during and after TB
3. Can COVID-19 'facilitate/boost' the transition from LTBI to TB? Probably not, but studies are needed to monitor progression also in the long run.
4. Main determinats of mortality are age and co-morbidities, although HIV, TB, poverty and malnutrition may play an important role, expecially in high incidence countries
5. Infection control measures and contact tracing are crucial to limit the spread of both diseases!
6. We should be ready for the next pandemic!!

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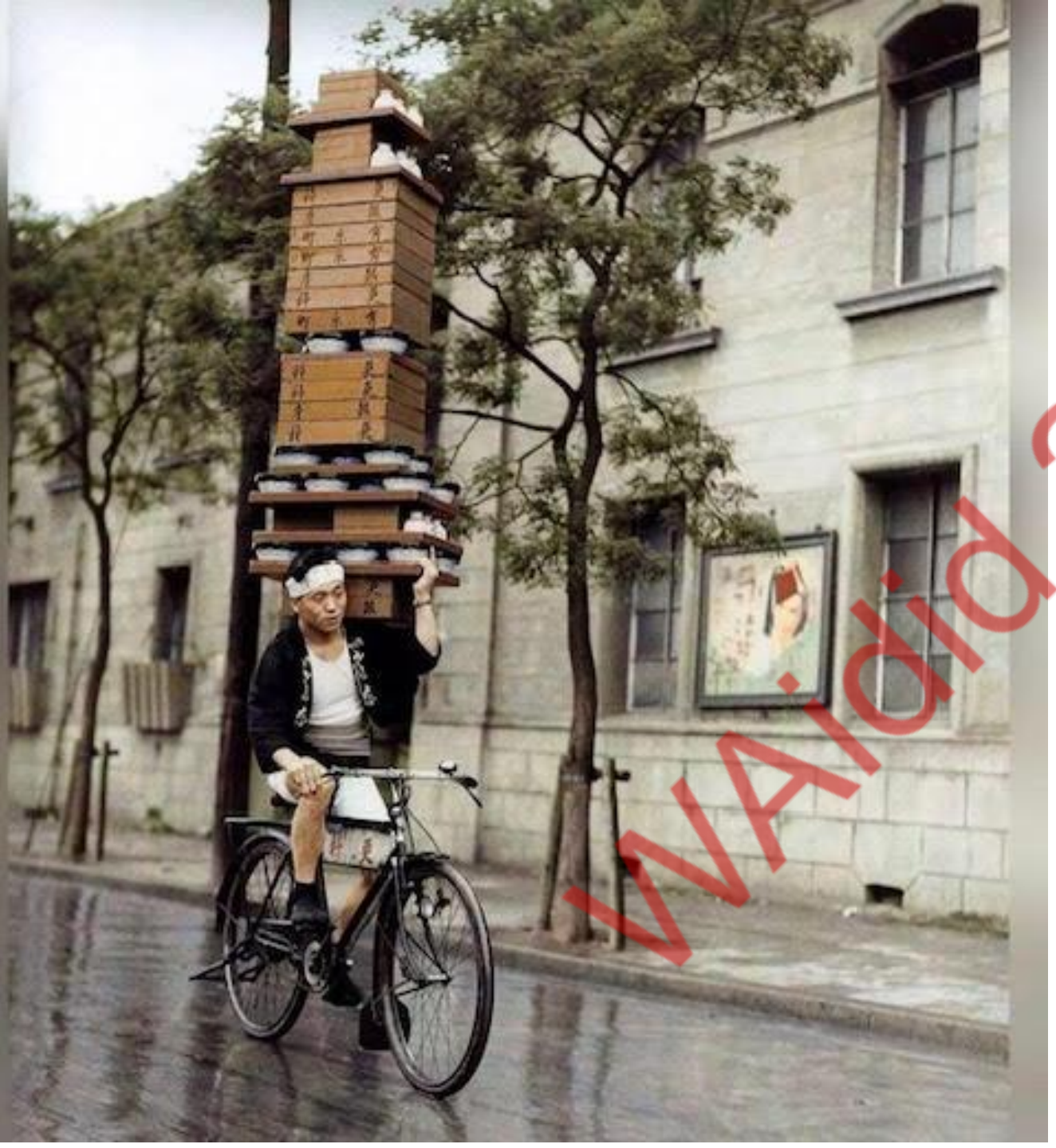
Ongoing Clinical Research Collaborations

Clinical Research Collaborations (CRCs) are ERS supported projects. They bring together multiple stakeholders, such as clinical and translational researchers, radiologists, biostatisticians, associated funding partners, and patients, to collaborate on an identified area within respiratory medicine. This multidisciplinary approach fosters a dynamic scientific community. CRCs aim to advance science and clinical research and improve respiratory health and medicine.



First we do what is necessary,
then we do what is possible

and finally,

we work to make the
impossible, possible…

Thank you!!!!

GTbN
the Global Tb Network
fighting Tb together