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HIV
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Geneva
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rifampicin
symptoms
use
following
confirmed
evaluation
Group
approach
young
NTP
range
important

Outcome of a modelling study to evaluate the impact of COVID-19 on child TB notifications

Annual Meeting of the Child and Adolescent TB Working Group

Tuesday 29 November 2022

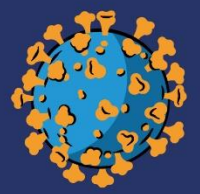
James Seddon

Reader in Global Child Health, Imperial College London

Consultant in Paediatric Infectious Diseases, St. Mary's Hospital

Associate Professor, Stellenbosch University

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

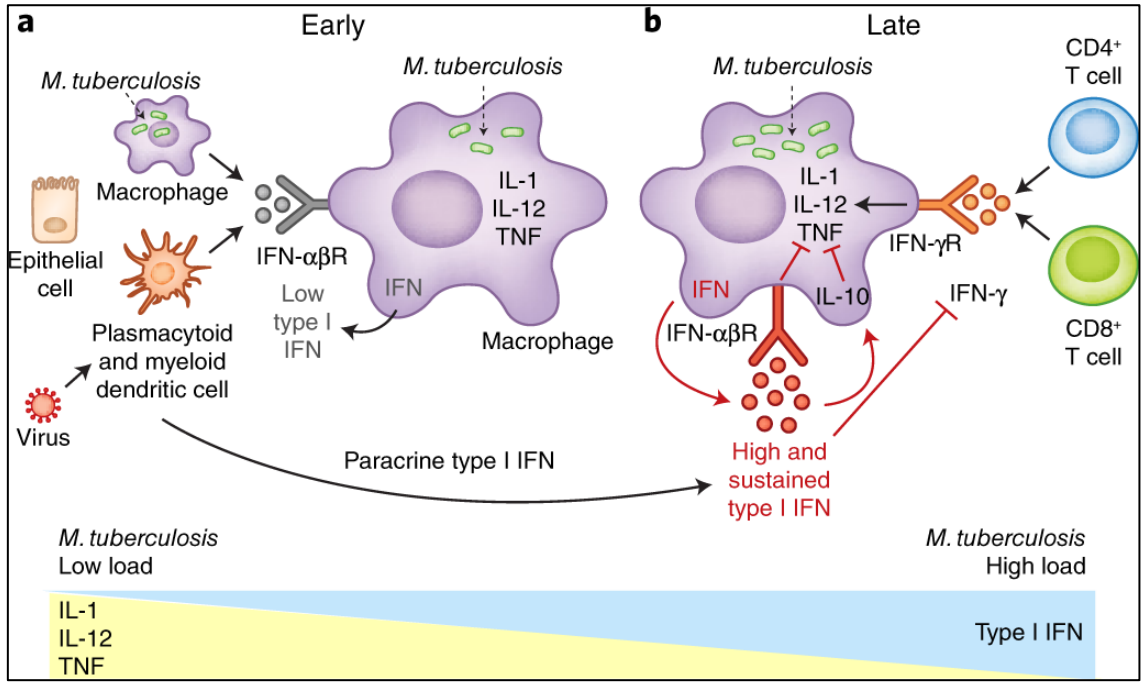
Actions to mitigate and reverse the impact of the COVID-19 pandemic on access to essential TB services are urgently needed

INVEST TO END TB SAVE LIVES

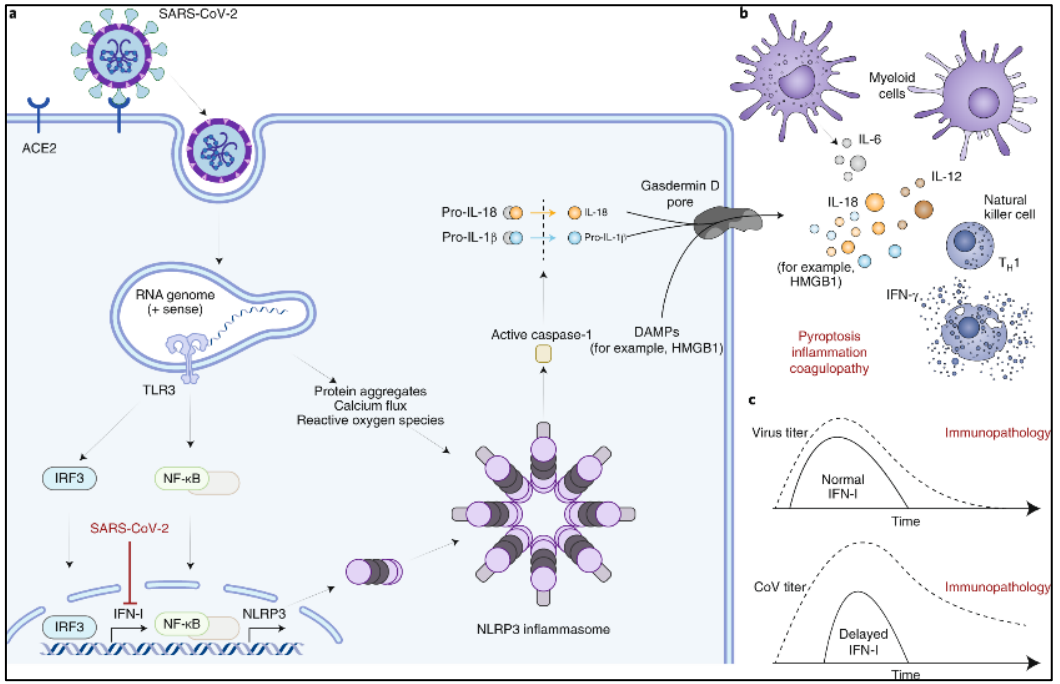
END TB

World Health Organization

Overlap in immune responses Mtb & SARS-CoV-2



Singhania et al. Nat Immunol 2018; 19: 1159–1168



Brodin. Nat Med 2021; 27: 28–33

- CD4+ T cell responses, Innate regulation, Type I interferons

Coinfection of tuberculosis and COVID-19 limits the ability to in vitro respond to SARS-CoV-2

Linda Petrone[a], Elisa Petruccioli[a], Valentina Vanini[a], Gilda Cuzzi[a], Gina Gualano[b], Pietro Vittozzi[b], Emanuele Nicastri[c], Gaetano Maffongelli[c], Alba Grifoni[d], Alessandro Sette[d], Giuseppe Ippolito[e], Giovanni Battista Migliori[f], Fabrizio Palmieri[b] Delia Goletti[a,*]

Petrone et al. Int J Infect Dis. 2021; 113: S82-S87

Relationship of SARS-CoV-2–specific CD4 response to COVID-19 severity and impact of HIV-1 and tuberculosis coinfection

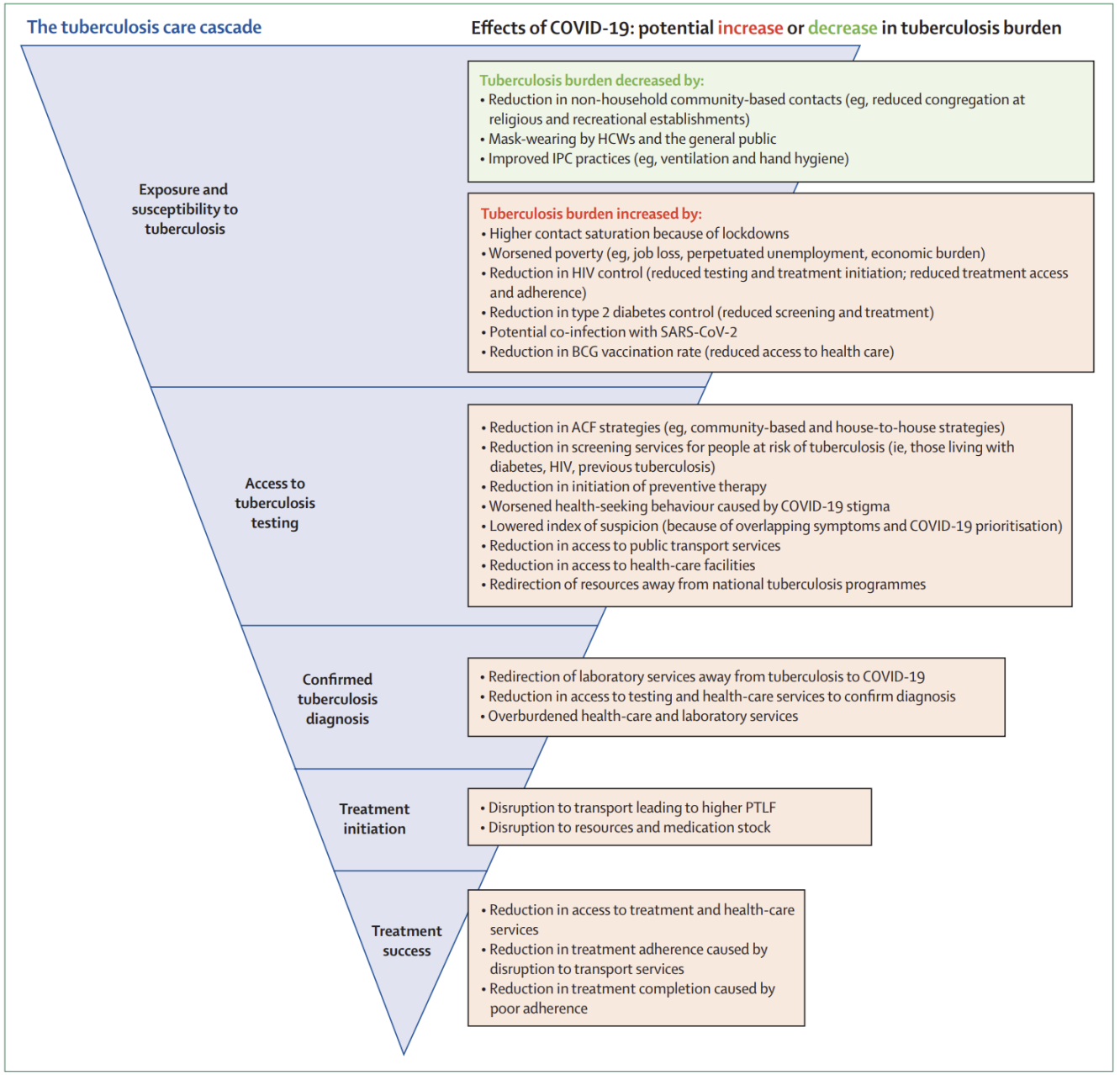
Catherine Riou,[1,2] Elsa du Bruyn,[1,3] Cari Stek,[1,3,4] Remy Daroowala,[1,3,4] Rene T. Goliath,[1] Fatima Abrahams,[1] Qonita Said-Hartley,[5] Brian W. Allwood,[6] Nei-Yuan Hsiao,[2,7] Katalin A. Wilkinson,[1,3,8] Cecilia S. Lindestam Arlehamn,[9] Alessandro Sette,[9,10] Sean Wasserman,[1,3] Robert J. Wilkinson,[1,3,4,8] and on behalf of the HIATUS consortium[11]

Riou et al. J Clin Invest. 2021; 131: e149125

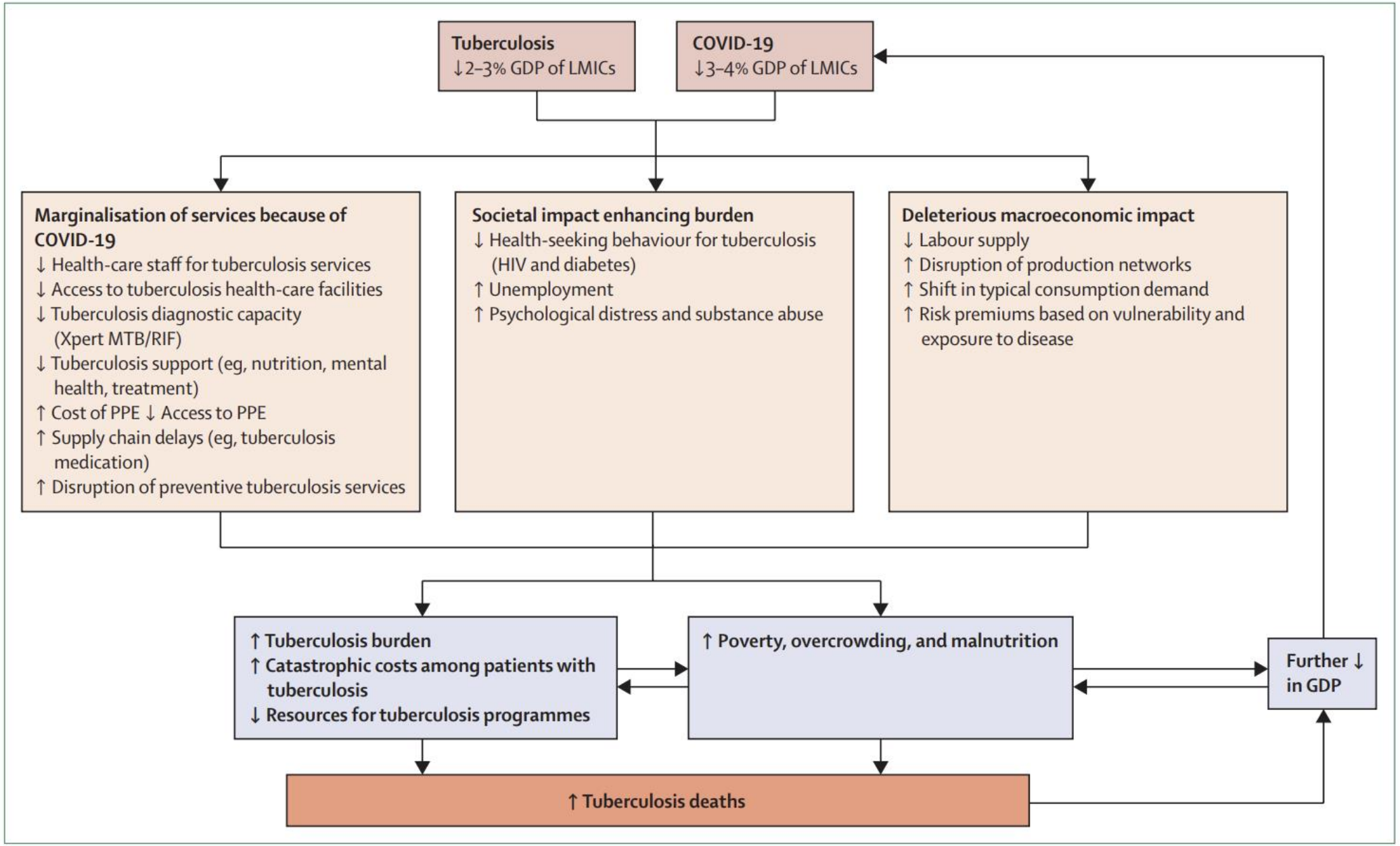
- …. T cells in SARS-CoV-2- *Mtb* co-infection showed poor polyfunctional potential, reduced proliferation capacity, and enhanced HLA-DR expression
- HIV/TB co-infection – sub-optimal T and B cell responses
- COVID-19 patients – reduced frequency of *Mtb* specific CD4+ T cells – implications for TB disease progression

The intersecting pandemics of tuberculosis and COVID-19: population-level and patient-level impact, clinical presentation, and corrective interventions

Keertan Dheda, Tahlia Perumal*, Harry Moultrie, Rubeshan Perumal, Aliasgar Esmail, Alex J Scott, Zarir Udwadia, Kwok Chiu Chang, Jonathan Peter, Anil Pooran, Arne von Delft, Dalene von Delft, Neil Martinson, Marian Loveday, Salome Charalambous, Elizabeth Kachingwe, Waasila Jassat, Cheryl Cohen, Stefano Tempia, Kevin Fennelly, Madhukar Pai*



Dheda et al. Lancet Resp Med 2022; 10: 603-22



Dheda et al. Lancet Resp Med 2022; 10: 603-22

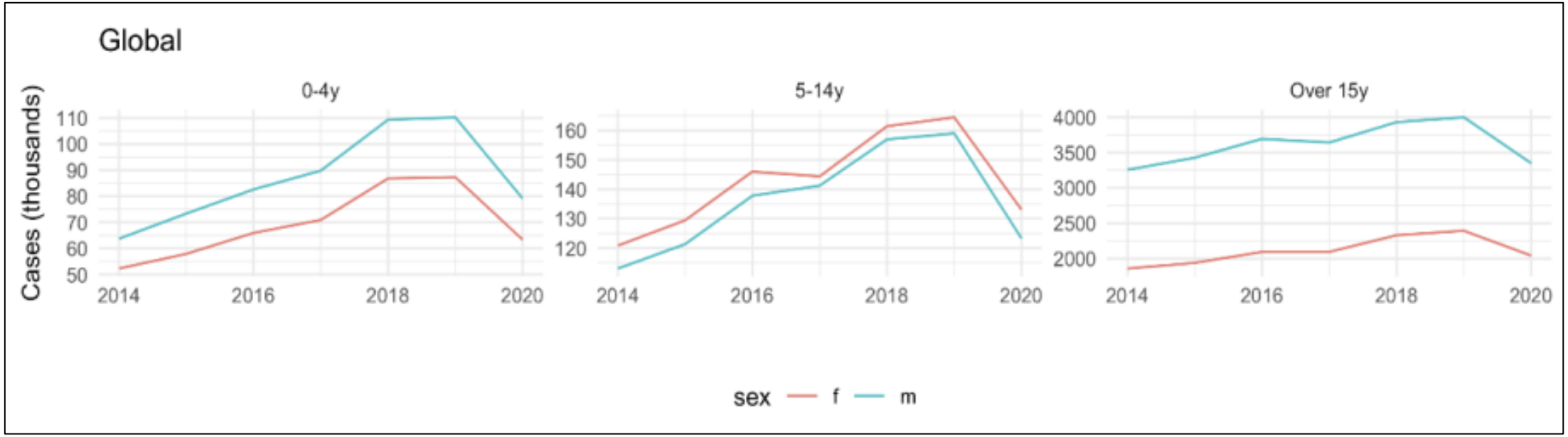
Paediatric specific impacts

- Biological impact of SARS-CoV-2 on *Mtb* pathogenesis may be even more pronounced in children given different immune response to adults
- Delayed adult PTB presentations lead to prolonged household exposure – particularly an issue in young children
- Staff from TB clinics re-deployed
- Equipment (GeneXpert platforms) re-deployed for COVID-19
- Staff frequently off (with COVID-19 or following COVID-19 exposure)
- Government responses – restricted access to child TB services (social and travel restrictions, financial implications of loss of work)
- Many children with TB not evaluated properly or misdiagnosed with COVID-19
- Caregiver anxiety about accessing health care facilities – concern re exposure to COVID-19
- Economic impact of COVID-19 – poverty

What has been the impact of COVID-19 on child TB?

Data sources

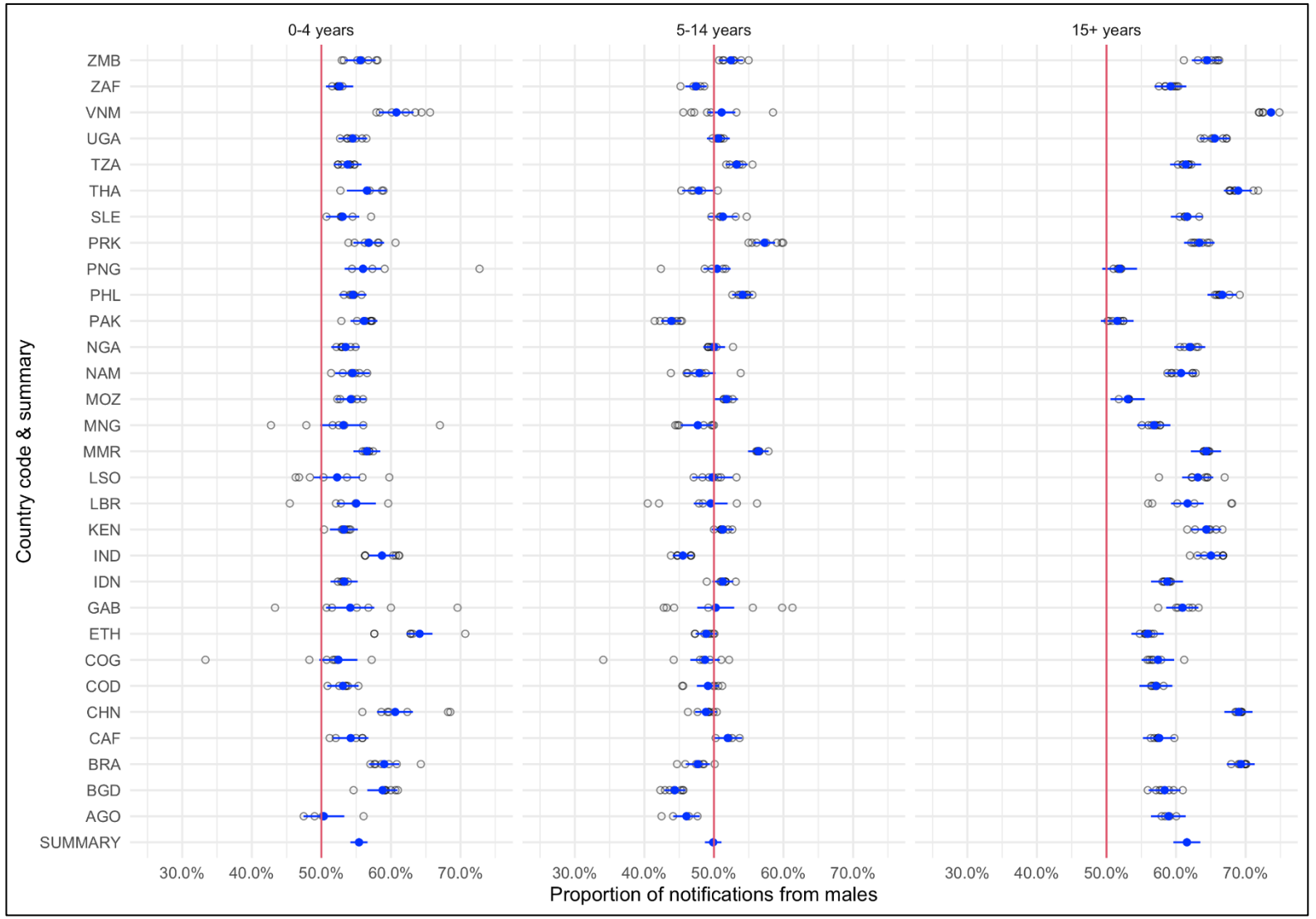
- Annual case notification data reported to WHO by 215 countries were used
- New and relapse case notification counts were extracted by country, sex, and age group from 2014 to 2020
- Three age groups were used: 0–4 years, 5–14 years, and 15 years or older
- Data from all 215 reporting countries were used to estimate annual WHO regional and global notification counts



Global trends in notifications

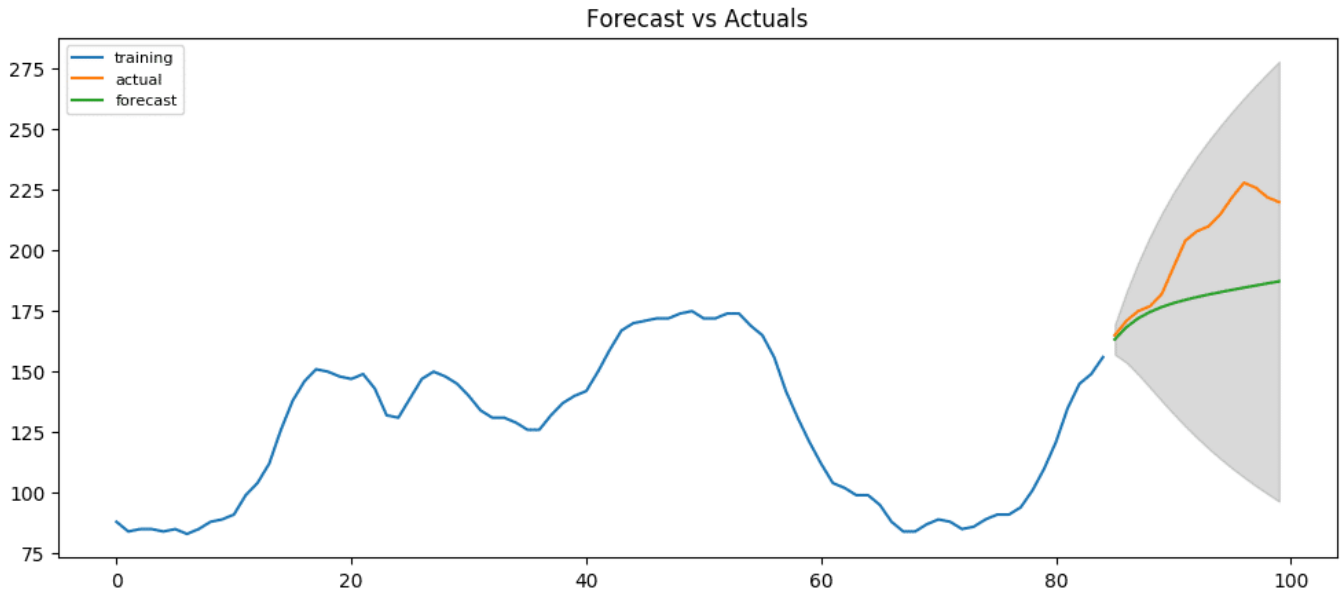
	Age 0–4 years				Age 5–14 years				Age ≥15 years			
	Male	Female	Difference	M:F ratio	Male	Female	Difference	M:F ratio	Male	Female	Difference	M:F ratio
2014	63 706	52 273	11 433	1·219	113 040	120 846	−7806	0·935	3 255 905	1 859 085	1 396 820	1·751
2015	73 319	57 900	15 419	1·266	121 347	129 457	−8110	0·937	3 426 488	1 939 862	1 486 626	1·766
2016	82 590	65 916	16 674	1·253	137 812	146 025	−8213	0·944	3 693 715	2 094 826	1 598 889	1·763
2017	89 789	70 895	18 894	1·267	141 237	144 385	−3148	0·978	3 641 494	2 094 775	1 546 719	1·738
2018	109 305	86 792	22 513	1·259	156 977	161 444	−4467	0·972	3 930 278	2 330 710	1 599 568	1·686
2019	110 224	87 302	22 922	1·263	158 996	164 479	−5483	0·967	3 998 138	2 393 191	1 604 947	1·671
2020	79 151	63 374	15 777	1·249	123 317	133 081	−9764	0·927	3 349 079	2 042 674	1 306 405	1·640

Gender differences



Time series modelling

- Autoregressive integrated moving average (ARIMA) time-series modelling was used to predict 2020 case notifications on the basis of data from 2014 to 2019
- We used data from 2014 to 2018, stratified by sex, age group, and location, to develop 216 independent time series for training
- We fitted ARIMA models to these training time series, and the best ten were taken forward for assessment of predictive accuracy
- The predictive accuracy of these models was evaluated by comparing the total absolute difference between their predicted 2019 values and the observed 2019 values



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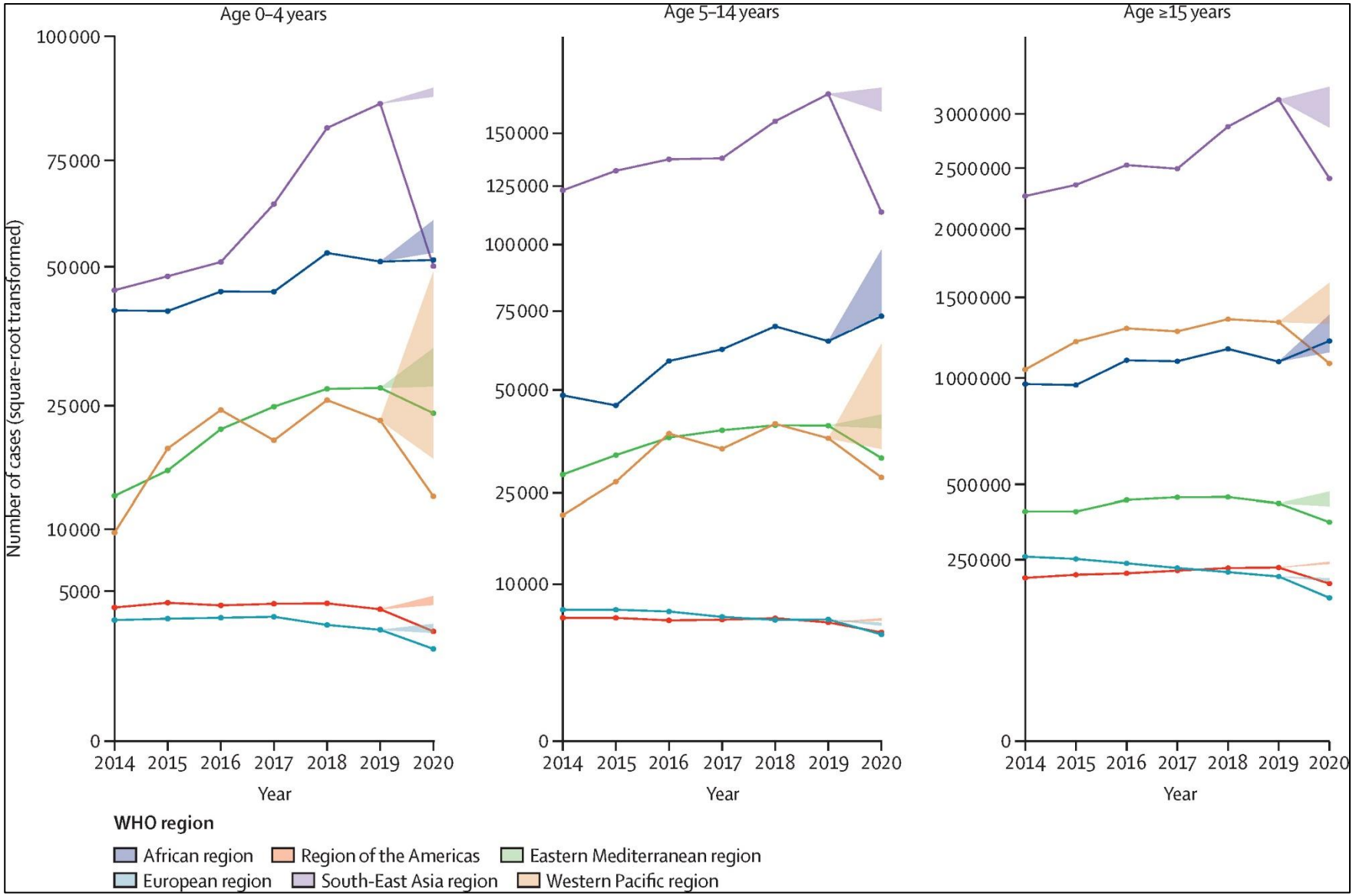
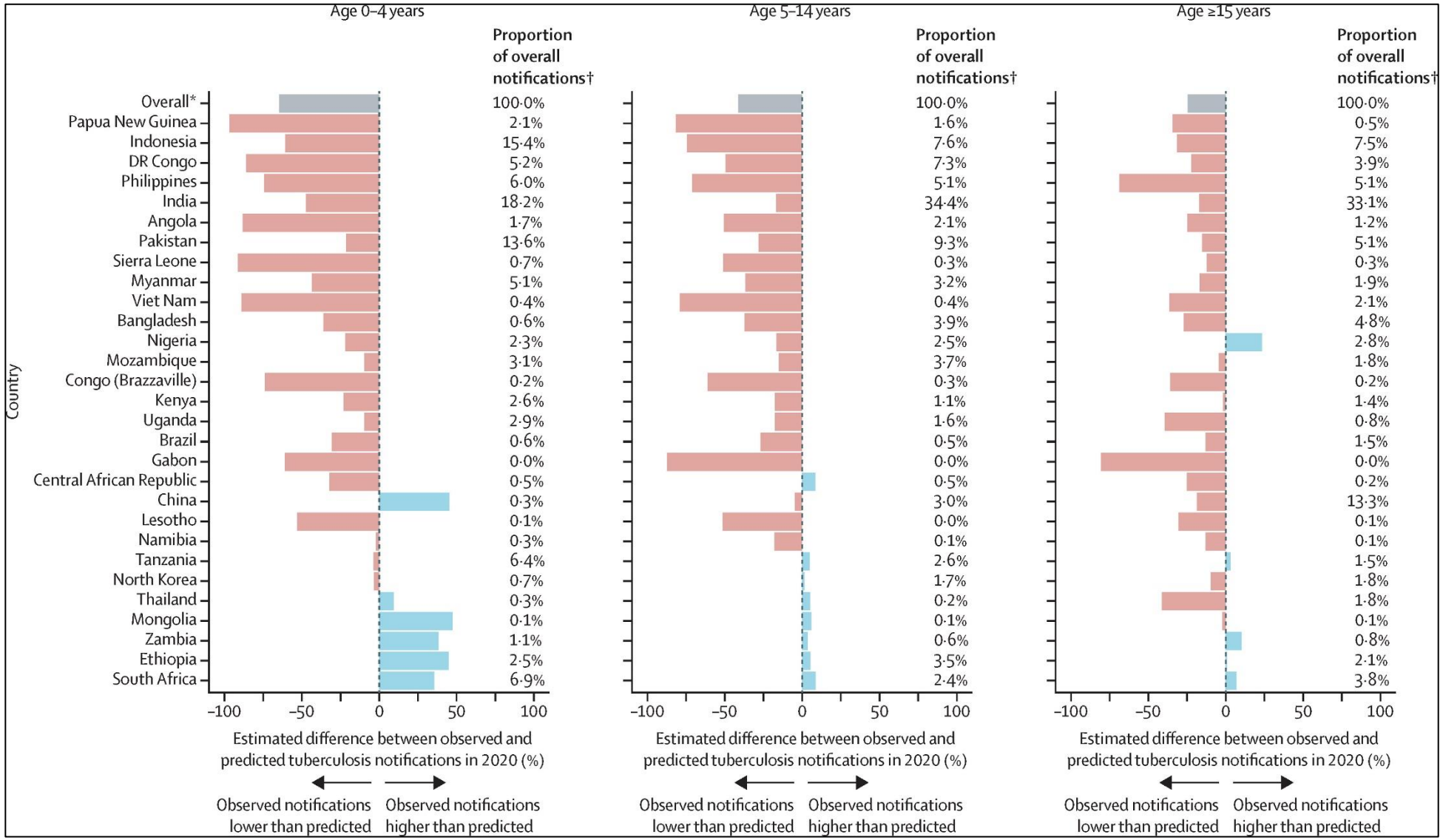


Differences between predicted and observed notifications for 30 HBCs



Global impact of COVID-19 on childhood tuberculosis: an analysis of notification data

Lasith Ranasinghe, Jay Achar*, Matthias Gröschel, Elizabeth Whittaker, Peter J Dodd, James A Seddon*

	Observed notifications	Predicted notifications	Difference, observed vs predicted	
			n	%
Age 0–4 years				
Male	79 151	122 371 (110 665 to 134 076)	−43 220 (−31 514 to −54 925)	−35·3% (−28·5 to −41)
Female	63 374	98 423 (87 101 to 109 744)	−35 049 (−23 727 to −46 370)	−35·6% (−27·2 to −42·3)
All	142 525	220 794 (204 509 to 237 078)	−78 269 (−61 984 to −94 553)	−35·4% (−30·3 to −39·9)
Age 5–14 years				
Male	123 317	178 403 (163 963 to 192 842)	−55 086 (−40 646 to −69 525)	−30·9% (−24·8 to −36·1)
Female	133 081	176 175 (162 548 to 189 801)	−43 094 (−29 467 to −56 720)	−24·5% (−18·1 to −29·9)
All	256 398	354 578 (334 724 to 374 431)	−98 180 (−78 326 to −118 033)	−27·7% (−23·4 to −31·5)
Age ≥15 years				
Male	3 349 079	4 119 747 (3 906 774 to 4 332 719)	−770 668 (−557 695 to −983 640)	−18·7% (−14·3 to −22·7)
Female	2 042 674	2 519 800 (2 363 013 to 2 676 586)	−477 126 (−320 339 to −633 912)	−18·9% (−13·6 to −23·7)
All	5 391 753	6 639 547 (6 375 086 to 6 904 007)	−1 247 794 (−983 333 to −1 512 254)	−18·8% (−15·4 to −21·9)

Data are n, n (95% PI), or % (95% PI). PI=prediction interval.

Table 2: **Global time-series predictions for 2020 generated using data from 2014–19 compared with observed notifications for 2020, by sex and age**

Ranasinghe et al. Lancet Global Health. 2022; 10; E1774-E1781

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Ranasinghe et al. Lancet Global Health. 2022; 10; E1774-E1781

nature human behaviour

RESOURCE

https://doi.org/10.1038/s41562-021-01079-8

Check for updates

A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker)

Thomas Hale[1]✉, Noam Angrist[1], Rafael Goldszmidt[2], Beatriz Kira[1], Anna Petherick[1], Toby Phillips[1], Samuel Webster[3], Emily Cameron-Blake[1], Laura Hallas[1], Saptarshi Majumdar[1] and Helen Tatlow[1]

Table 1 | OxCGRT Indicators

ID	Name	Type	Targeted/ general?
Containment and closure			
C1	School closing	Ordinal	Geographic
C2	Workplace closing	Ordinal	Geographic
C3	Cancel public events	Ordinal	Geographic
C4	Restrictions on gathering size	Ordinal	Geographic
C5	Close public transport	Ordinal	Geographic
C6	Stay-at-home requirements	Ordinal	Geographic
C7	Restrictions on internal movement	Ordinal	Geographic
C8	Restrictions on international travel	Ordinal	No
Economic response			
E1	Income support	Ordinal	Sectoral
E2	Debt/contract relief for households	Ordinal	No
E3	Fiscal measures	Numerical	No
E4	Giving international support	Numerical	No
Health systems			
H1	Public information campaign	Ordinal	Geographic
H2	Testing policy	Ordinal	No
H3	Contact tracing	Ordinal	No
H4	Emergency investment in health care	Numerical	No
H5	Investment in COVID-19 vaccines	Numerical	No
H6	Facial coverings	Ordinal	Geographic
H7	Vaccination policy	Ordinal	Funding
Miscellaneous			
M1	Other responses	Text	No

For detailed descriptions and coding information, see the project website: https://www.bsg.ox.ac.uk/covidtracker.

Table 2 | OxCGRT index composition and values

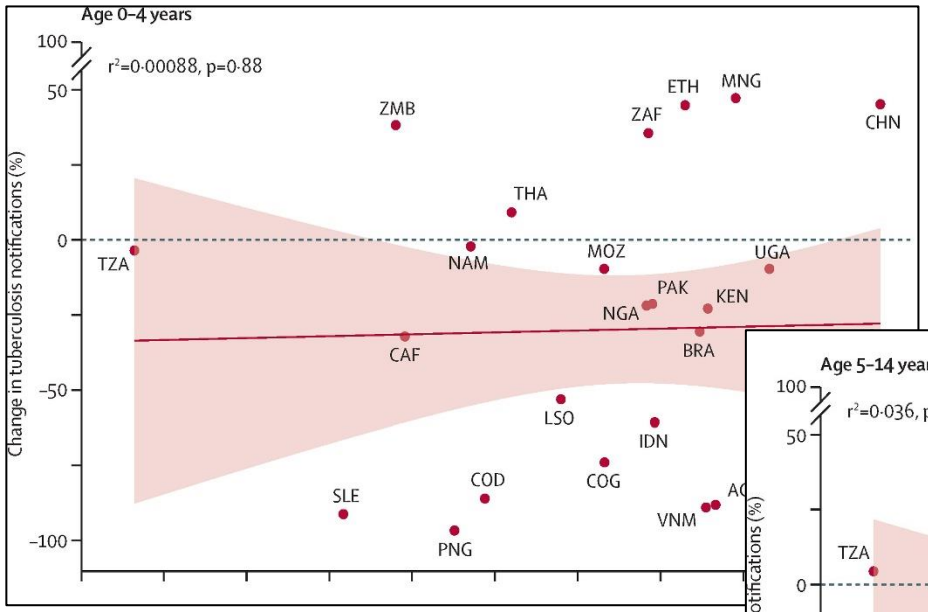
	GRI	CHI	Stringency index	ESI	Legacy stringency index	Maximum value (N_j)	Flag (F_j)
k	13	11	9	2	7		
C1	x	x	x		x	3 (0, 1, 2, 3)	Yes=1
C2	x	x	x		x	3 (0, 1, 2, 3)	Yes=1
C3	x	x	x		x	2 (0, 1, 2)	Yes=1
C4	x	x	x			4 (0, 1, 2, 3, 4)	Yes=1
C5	x	x	x		x	2 (0, 1, 2)	Yes=1
C6	x	x	x			3 (0, 1, 2, 3)	Yes=1
C7	x	x	x		x	2 (0, 1, 2)	Yes=1
C8	x	x	x		x	4 (0, 1, 2, 3, 4)	No=0
E1	x			x		2 (0, 1, 2)	Yes=1
E2	x			x		2 (0, 1, 2)	No=0
E3							
E4							
H1	x	x	x		x	2 (0, 1, 2)	Yes=1
H2	x	x				3 (0, 1, 2, 3)	No=0
H3	x	x				2 (0, 1, 2)	No=0
H4							
H5							
H6	x	x				4 (0, 1, 2, 3, 4)	Yes=1
H7	x	x				5 (0, 1, 2, 3, 4, 5)	Yes=1
M1							

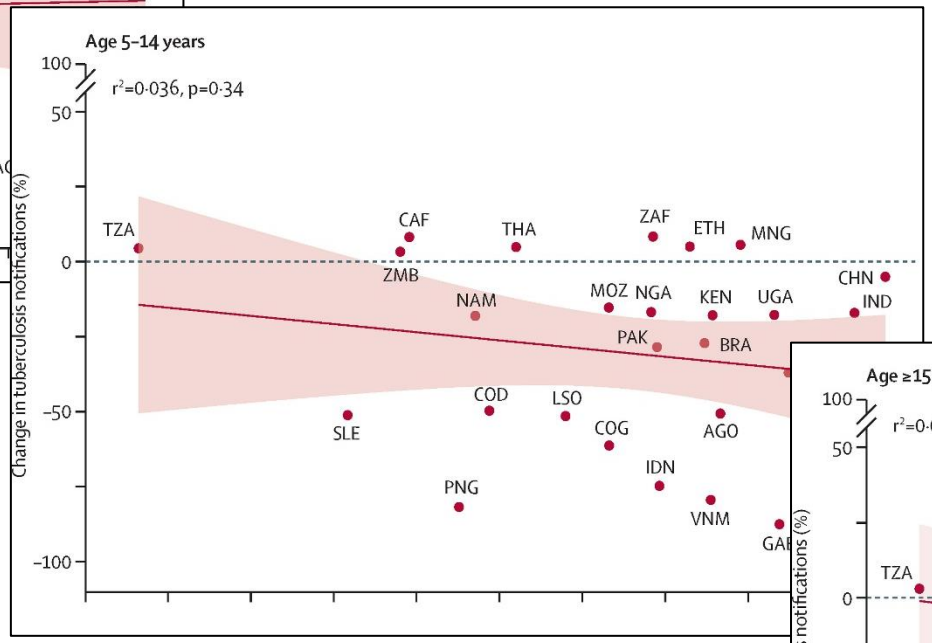
k is the number of component indicators in an index (see Methods); x indicates that an indicator contributes to that index.

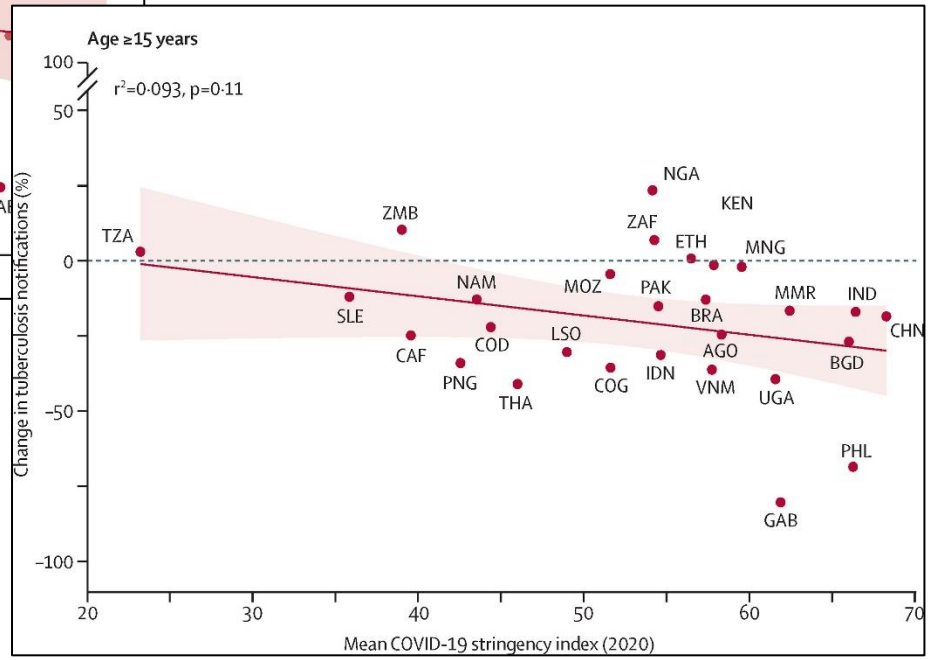
Stringency Index

We used linear regression to examine whether there was a correlation between estimated percentage reductions in tuberculosis notifications in 2020 and magnitude of government-imposed restrictions on mixing to mitigate COVID-19, quantified as the mean of a COVID-19 stringency index for 2020 for the 30 high-burden countries

Relationship between stringency index and difference between predicted and observed notifications







Summary

- COVID-19 and TB share many similarities
- Gender differences are seen in all ages that require further examination and targeted approaches
- The pandemic has had a negative impact on TB notifications globally, worst in children
- A concerted effort to address this is required

Questions?