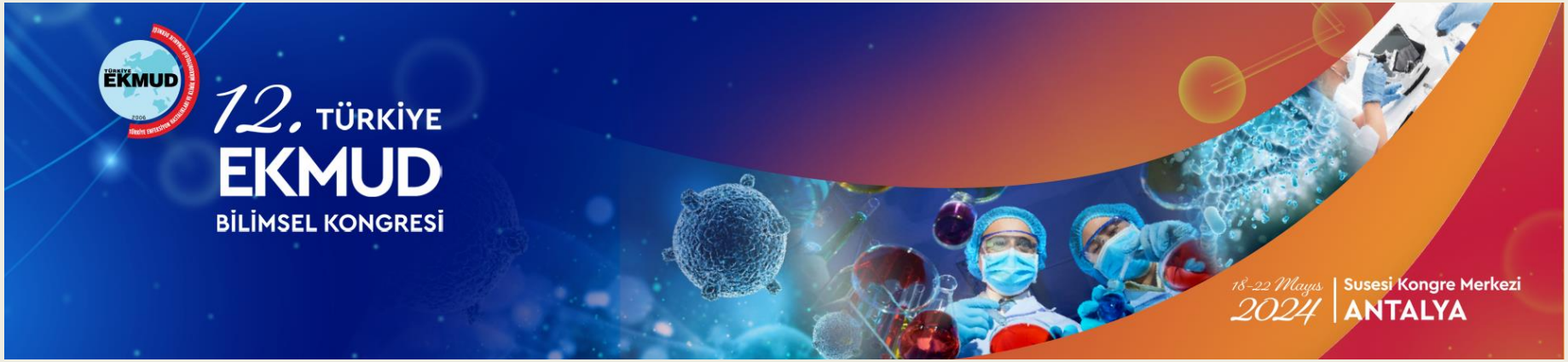
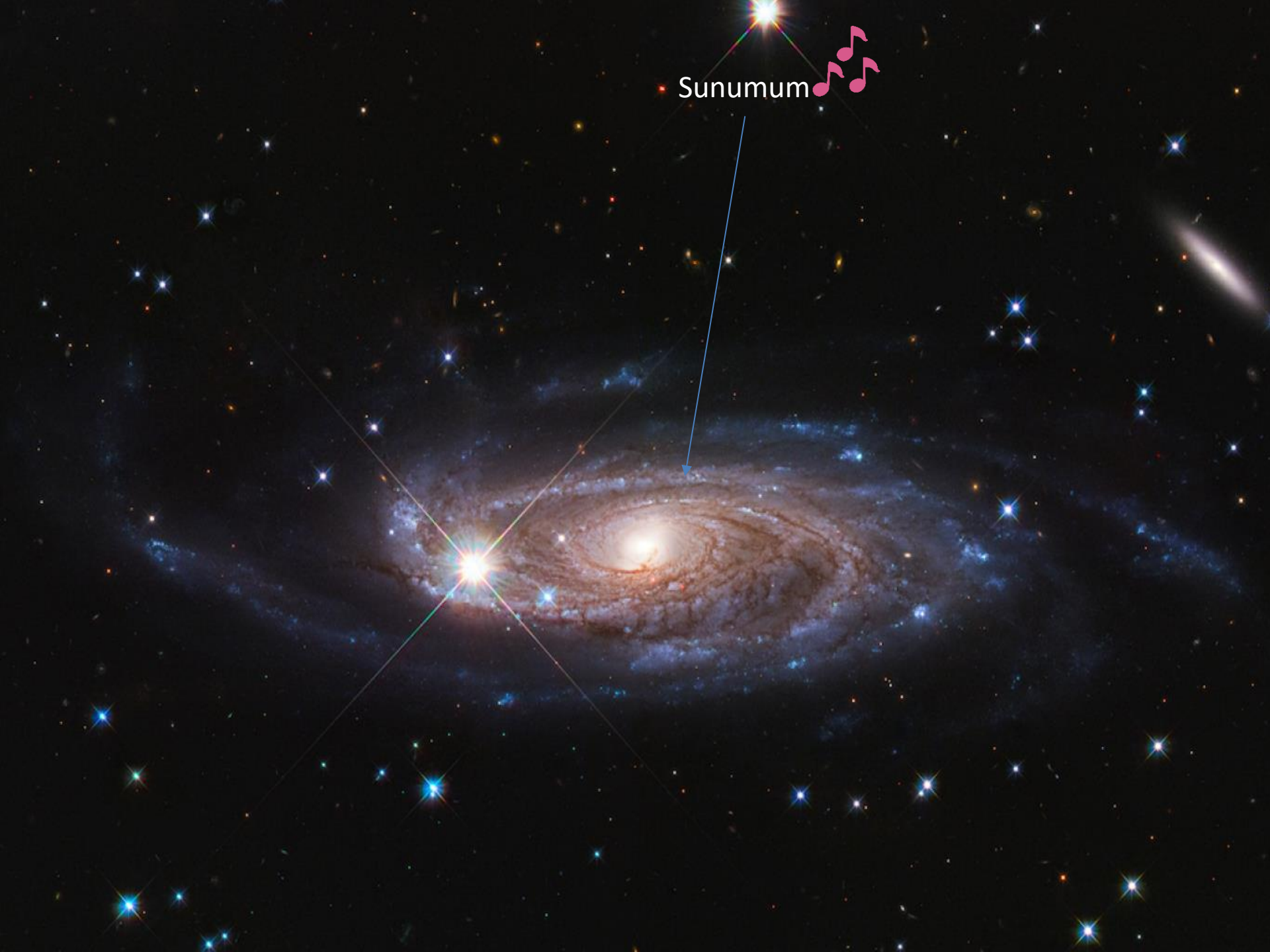


"Büyük Taklitçi" - Tüberkülozu Unutma

Akciğer Dışı Tüberküloz

Dr. Cemal BULUT
Gülhane Tıp Fakültesi,
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği


Sunumum

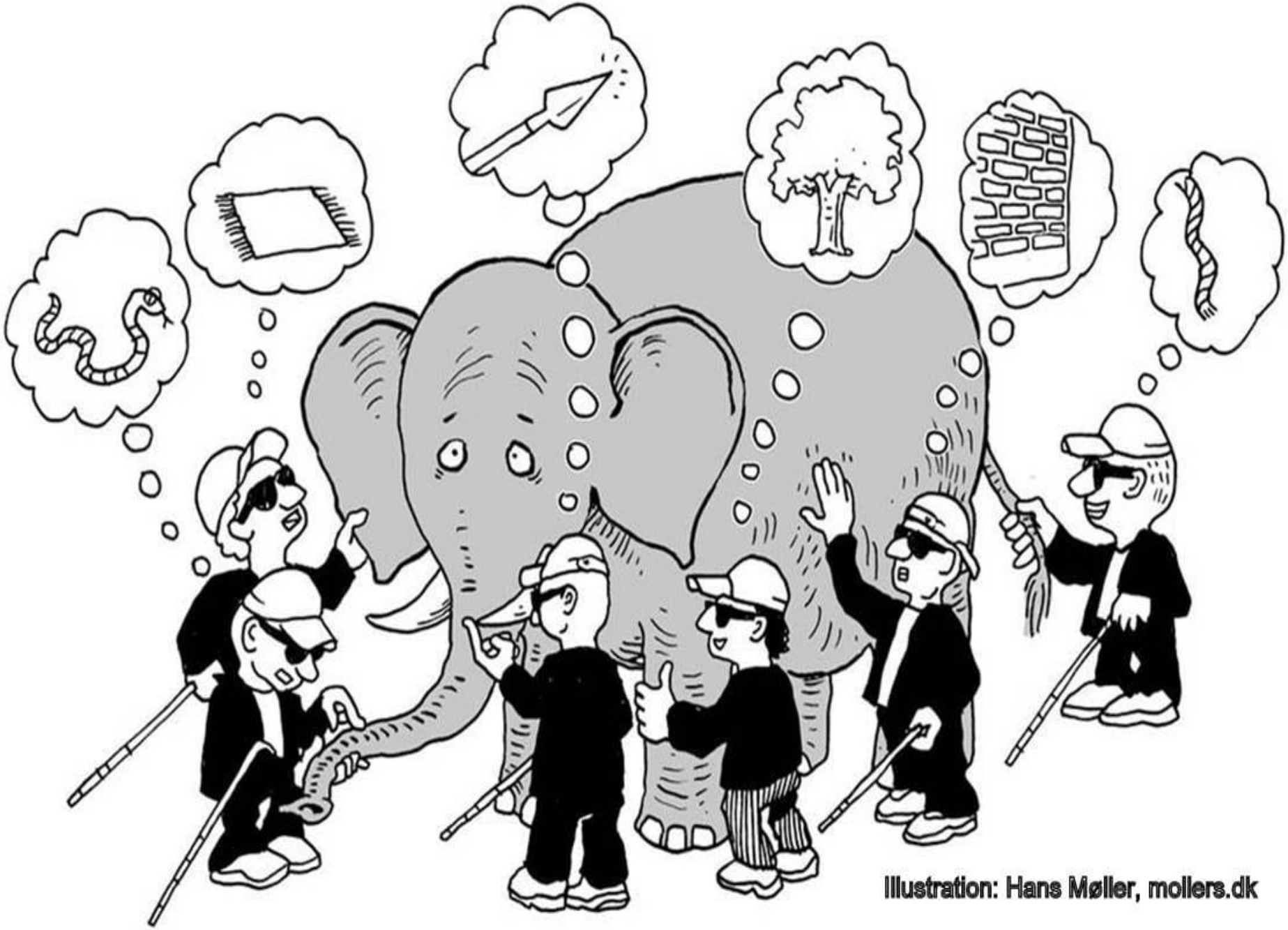
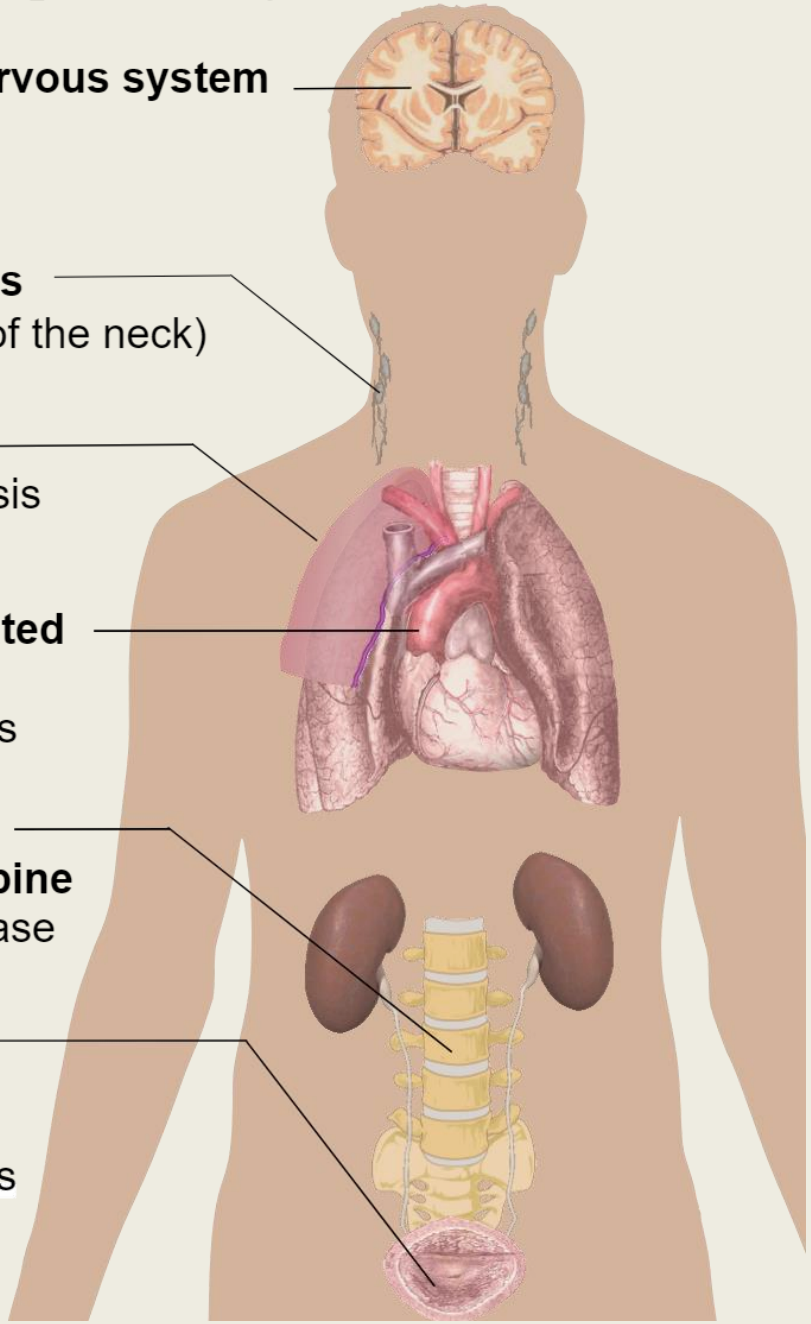


Illustration: Hans Møller, mollers.dk

Main sites of

Extrapulmonary tuberculosis



Central nervous system
- Meningitis

Lymphatics
- Scrofula (of the neck)

Pleura
- Tuberculosis pleurisy

Disseminated
- Miliary tuberculosis

Bones and joints of spine
- Pott's disease

Genito-urinary
- Urogenital tuberculosis

- Plevral Tüberküloz
- Gastrointestinal ve Peritoneal Tüberküloz
- Hepatobilier ve Splenik Tüberküloz
- Lenfatik Tüberküloz
- Tüberküloz Artrit ve Osteomyelit
- Tüberküloz Spondylodiskit
- Tüberküloz Menenjit
- Tüberküloz Ensefalit
- Spinal Tüberküloz
- Ürogenital Tüberküloz
- Kardiyovasküler Tüberküloz
- Kutanöz Tüberküloz
- OkülerTüberküloz

Perikardial tutulum
Endokardit,
Myokardit,
Valvülar veya koroner tutulum
Arterit,
Anevrizma

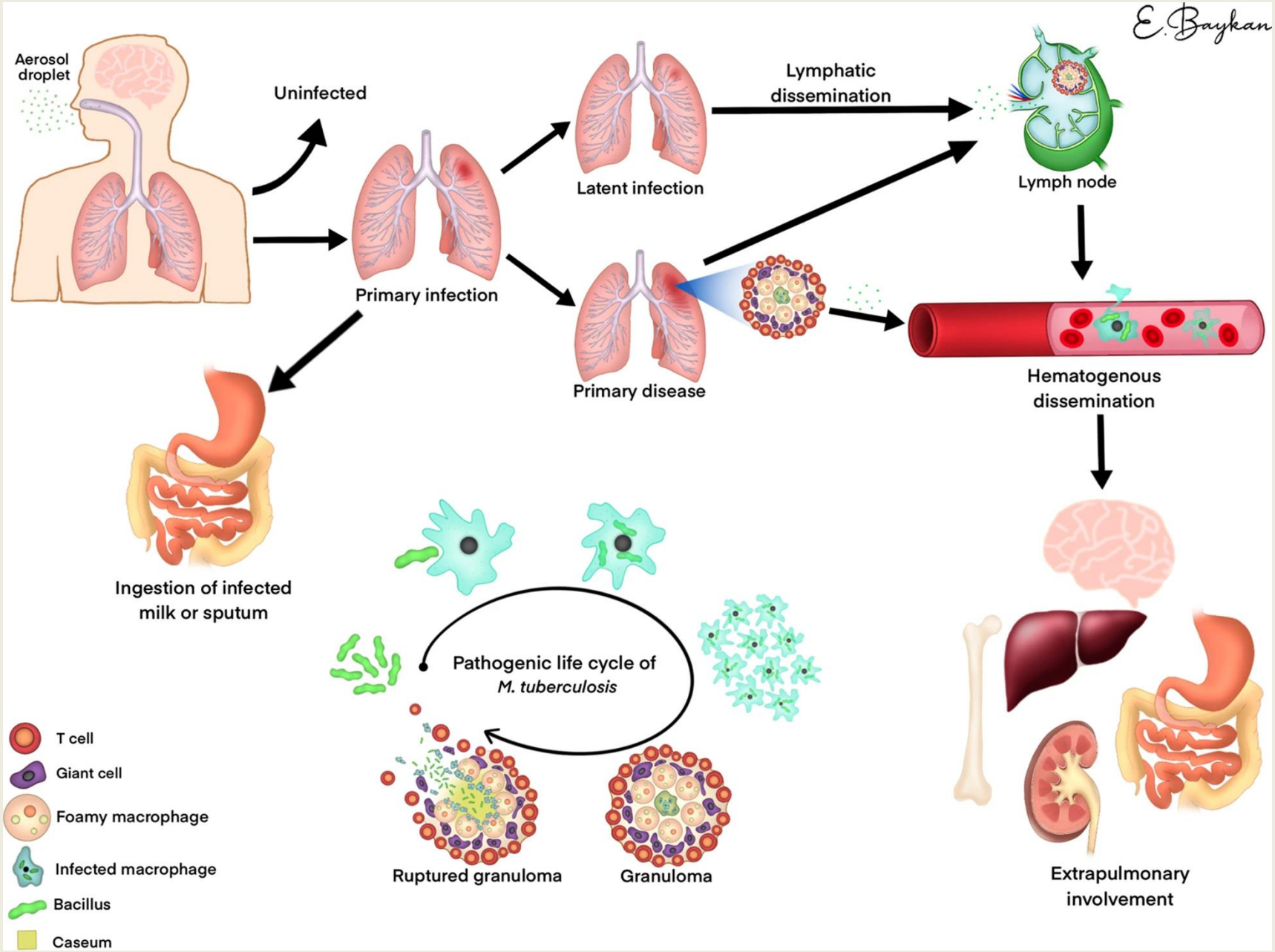
Tablo 3. İntraoküler tüberkülozun klinik sunumları

Tutulum	Özellikleri
1. Ön üveit	Granülomatöz, nongranülomatöz, iris nodülleri, siliyer cisim tüberkülü
2. İntermediyer üveit	Pars plana ve periferik üveada organize eksudalar ile birlikte granülomatöz, nongranülomatöz
3. Arka üveit ve panüveit	Koroidal tüberkülomu, koroidde tüberküller, subretinal abse, serpi jinöz benzeri koroidit
4. Retinit ve retinal vaskülit*	
5. Nöroretinit ve optik nöropati	
6. Endoftalmi ve panoftalmi	

*: Eales hastalığı bazı yazarlar tarafından TBC enfeksiyonu/aşırı duyarlılık yanıtı olarak kabul edilmektedir

Tablo 1. Deri tüberkülozlarının sınıflandırılması

DERİ TÜBERKÜLOZLARI			
KLASİFİKASYON		SENSİTİZASYON	İNFEKSİYON
PRİMER	Tüberküloz primer kompleks	Duyarlanmamış	Ekzojen
	Milyer deri tüberkülozu	Duyarlanmamış	Hematojen
SEKONDER	Reinfeksiyon		
	Lupus vulgaris	Duyarlı	Endojen
	Tüberkülozis kutis verrükoza	Duyarlı	Ekzojen
	Reaktivasyon		
	Skrofuloderma	Duyarlı	Direk yayılım
	Tüberkülozis kutis orifisyalis	Duyarlı	Otoinokülasyon
	Metastatik tüberküloz abseleri	Duyarlı	Hematojen



Baykan, A.H., Sayiner, H.S., Aydin, E. *et al.* Extrapulmonary tuberculosıs: an old but resurgent problem. *Insights Imaging* **13**, 39 (2022). https://doi.org/10.1186/s13244-022-01172-0

If the infection occurs outside of the lungs, symptoms are related to the site of the disease: For example, TB in the vertebral column can cause back pain; TB in the lymph nodes can cause enlargement of the lymph nodes in the neck, armpit or groin; TB in the kidney can cause blood in the urine or have the same symptoms as a regular urinary tract infection.

outside the lungs

Extrapulmonary **tuberculosis** can present with **a variety of symptoms** that may mimic symptoms of other diseases

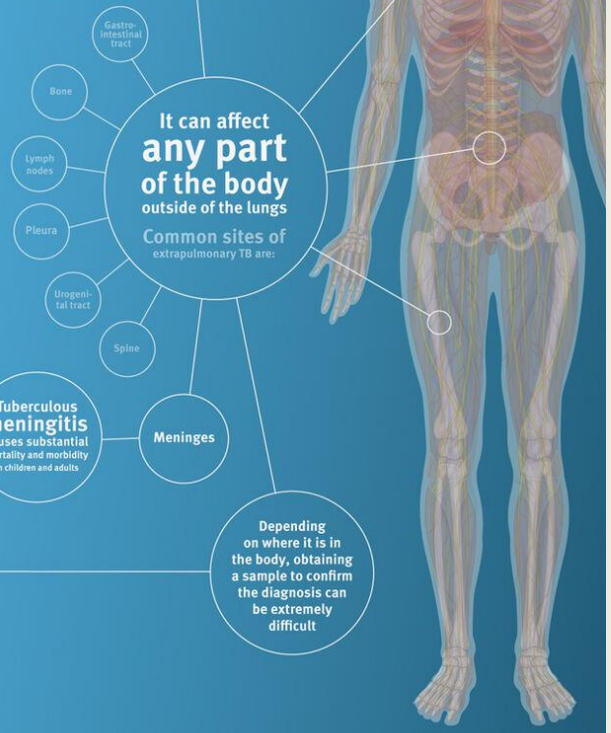
Inhaled bacteria travel via the circulatory and lymphatic systems to other parts of the body. When the infection occurs somewhere other than the lungs, the disease is called:

Extrapulmonary tuberculosis

Children are at least twice as likely to be reported with extrapulmonary TB as adults

Patients with extrapulmonary tuberculosis are usually not infectious

Easy to miss: Symptoms are unspecific and clinicians may not consider it in their differential **diagnosis**



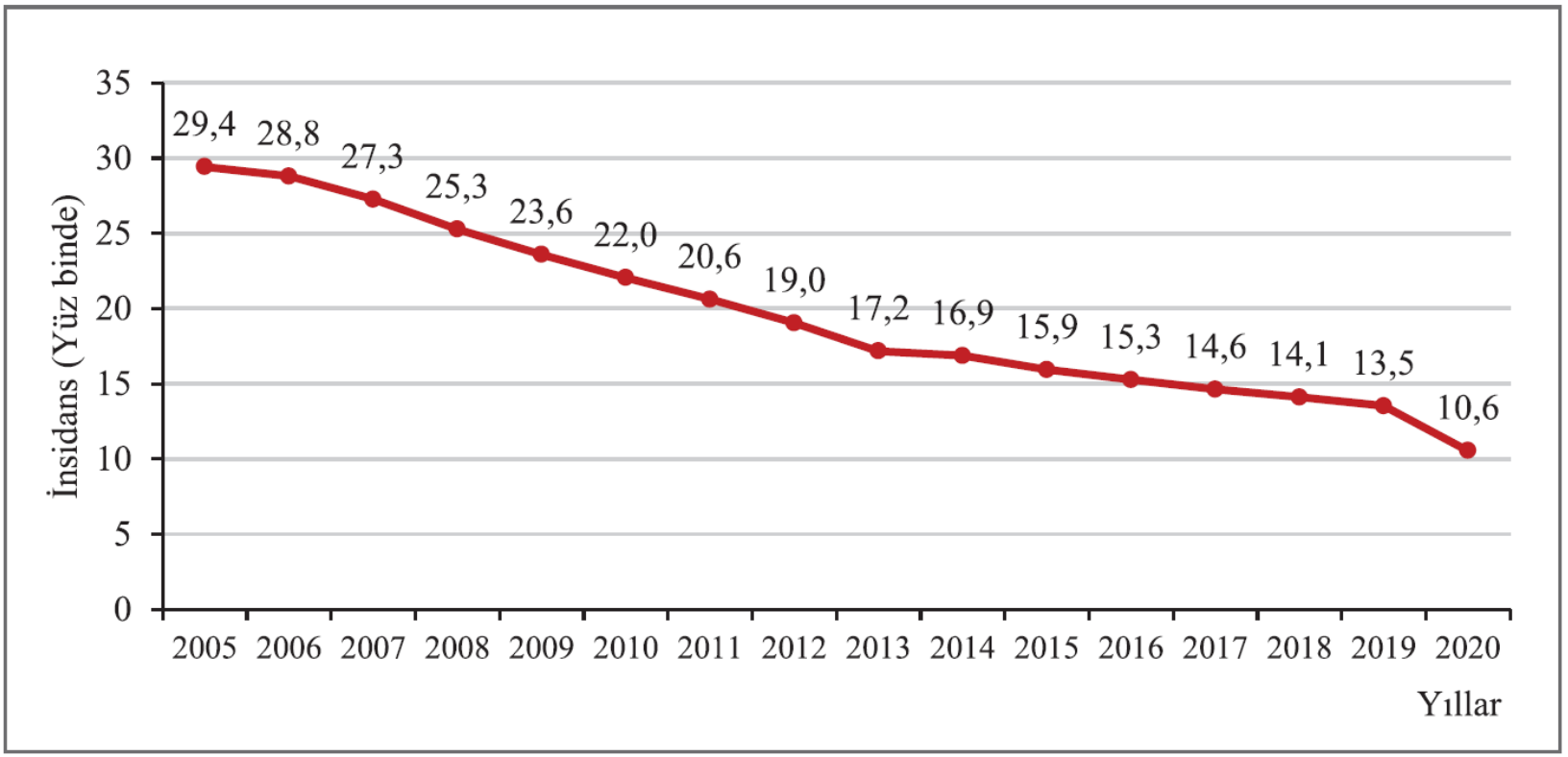
ecdc

Data from the ECDC/WHO Europe Tuberculosis Surveillance and Monitoring in Europe 2013. Stockholm, 2013

1 in every 5 tuberculosis patients has extrapulmonary tuberculosis

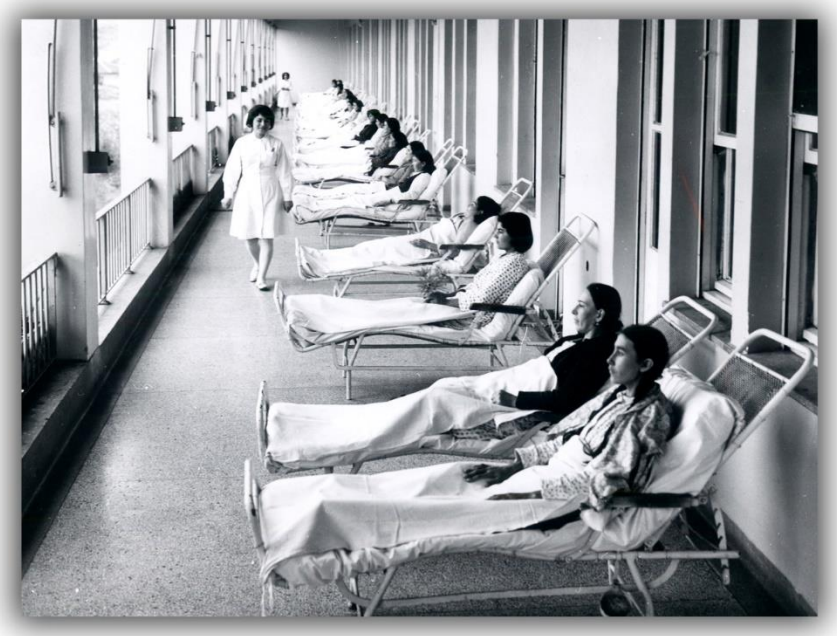
YILLARA GÖRE TOPLAM TB OLGU SAYISI, TOPLAM OLGU HIZI VE İNSİDANS HIZI, 2005-2018

Yıllar	Nüfus*	Toplam olgu sayısı	Toplam olgu hızı** (100.000'de)	İnsidans*** (100.000'de)
2005	68.860.540	20.535	29,8	**29,4**
2006	69.729.970	20.526	29,4	**28,8**
2007	70.586.256	19.694	27,9	**27,3**
2008	71.517.100	18.452	25,8	**25,3**
2009	72.561.312	17.402	24,0	**23,6**
2010	73.722.988	16.551	22,5	**22,0**
2011	74.724.269	15.679	21,0	**20,6**
2012	75.627.384	14.691	19,4	**19,0**
2013	76.667.864	13.409	17,5	**17,2**
2014	77.695.904	13.378	17,2	**16,9**
2015	78.741.053	12.772	16,2	**15,9**
2016	79.814.871	12.417	15,6	**15,3**
2017	80.810.525	12.046	14,9	**14,6**
2018	82.003.882	11.786	14,4	**14,1**



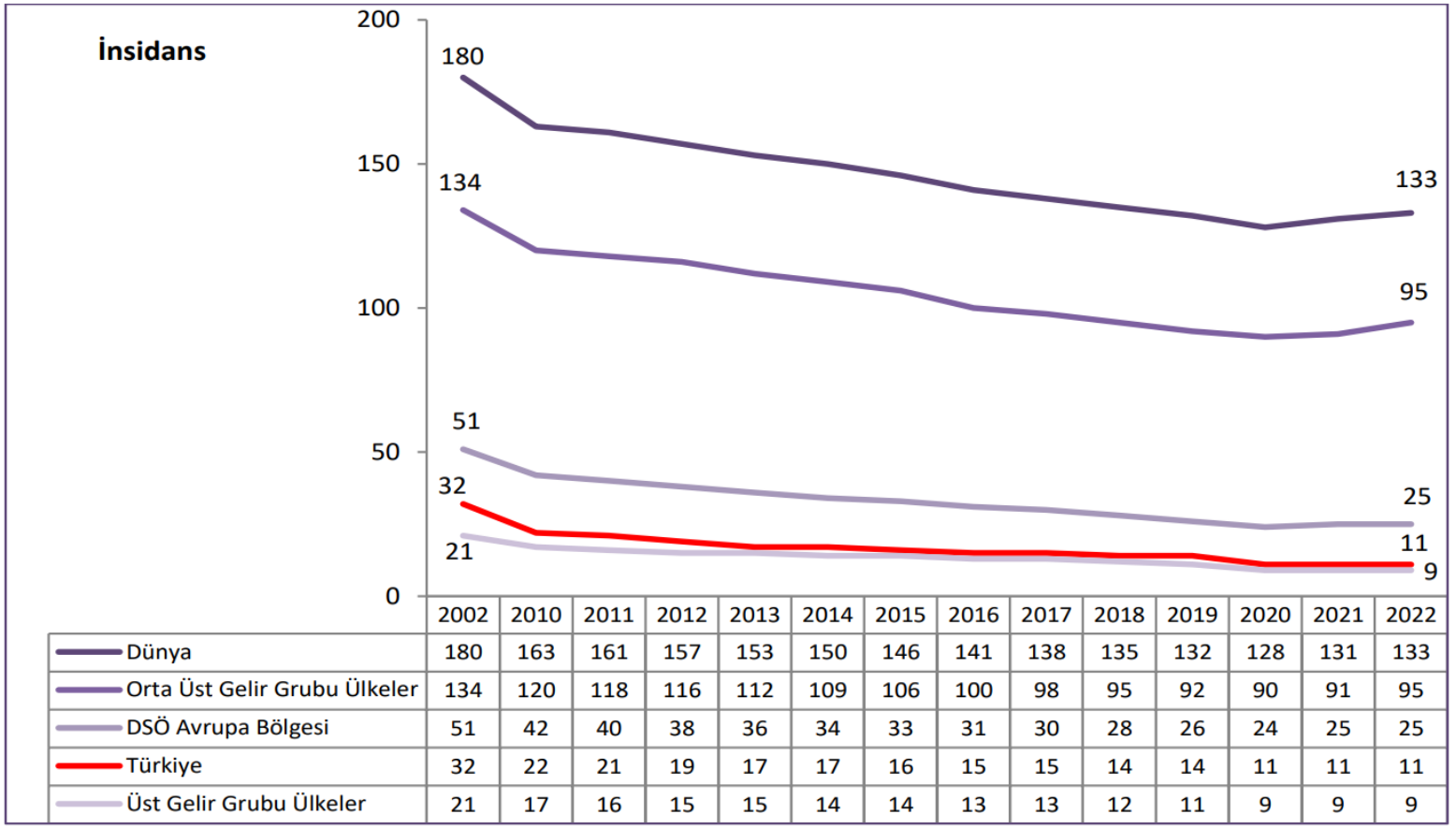
Şekil 15. Yıllara Göre TB İnsidansı, 2005-2020


BCG
VEREM AŞISI
İSTASYONU
T.C.
SAĞLIK ve SOSYAL YARDIM BAKANLIĞI
B.C.G. KAMPANYASI
35 NUMARALI
GEZİCİ RÖNTGEN VEREM TARAMA
EKİP BAŞKANLIĞI




T.C.
İZMİR HEREKEN
SİZBEYLİ İLKOKULU
T.C.
SAĞLIK ve SOSYAL YARDIM BAKANLIĞI
B.C.G. KAMPANYASI
4 NOLU GEZİCİ RÖNTGEN VEREM TARAMA

Şekil 3.4. Yıllara Göre Tüberküloz İnsidansının Uluslararası Karşılaştırması, (100.000 Nüfusta)



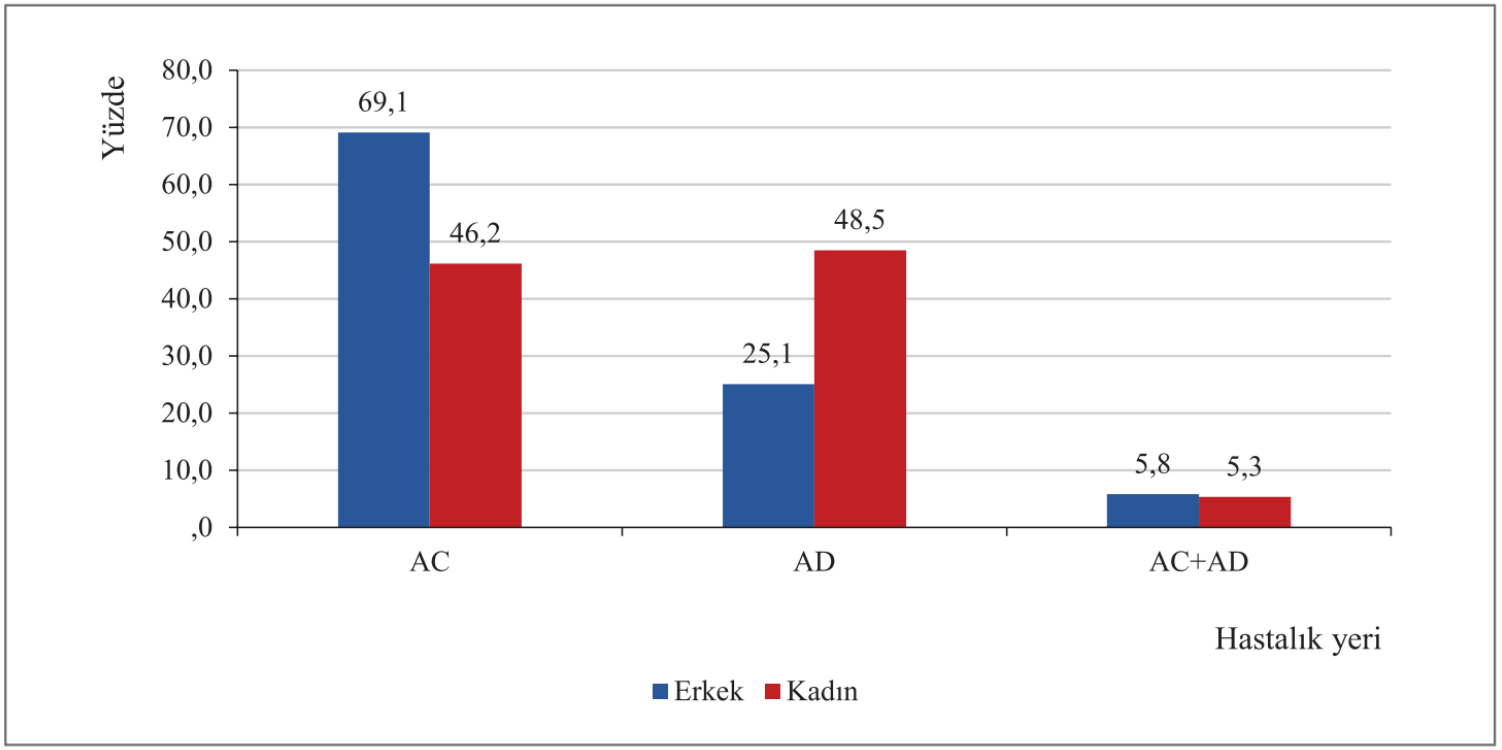
	2002	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Dünya	180	163	161	157	153	150	146	141	138	135	132	128	131	133
Orta Üst Gelir Grubu Ülkeler	134	120	118	116	112	109	106	100	98	95	92	90	91	95
DSÖ Avrupa Bölgesi	51	42	40	38	36	34	33	31	30	28	26	24	25	25
Türkiye	32	22	21	19	17	17	16	15	15	14	14	11	11	11
Üst Gelir Grubu Ülkeler	21	17	16	15	15	14	14	13	13	12	11	9	9	9

Kaynak: Halk Sağlığı Genel Müdürlüğü, DSÖ Global Health Observatory Veri Tabanı

Not: Türkiye verisi; 2002-2004 yılları DSÖ Tüberküloz (TB) Veri Tabanından, diğer yıllar Halk Sağlığı Genel Müdürlüğü - Tüberküloz Veri Tabanından elde edildi.

Tablo 25. Toplam TB Olgularında Cinsiyete Göre Hastalığın Tutulum Yeri, 2019

Cinsiyet	Hastalığın Yeri						Toplam	
	AC		AD		AC+AD			
	Sayı	%*	Sayı	%*	Sayı	%*	Sayı	%**
Erkek	4.610	69,1	1.674	25,1	387	5,8	6.671	58,5
Kadın	2.184	46,2	2.294	48,5	252	5,3	4.730	41,5
Toplam	6.794	59,6	3.968	34,8	639	5,6	11.401	100,0

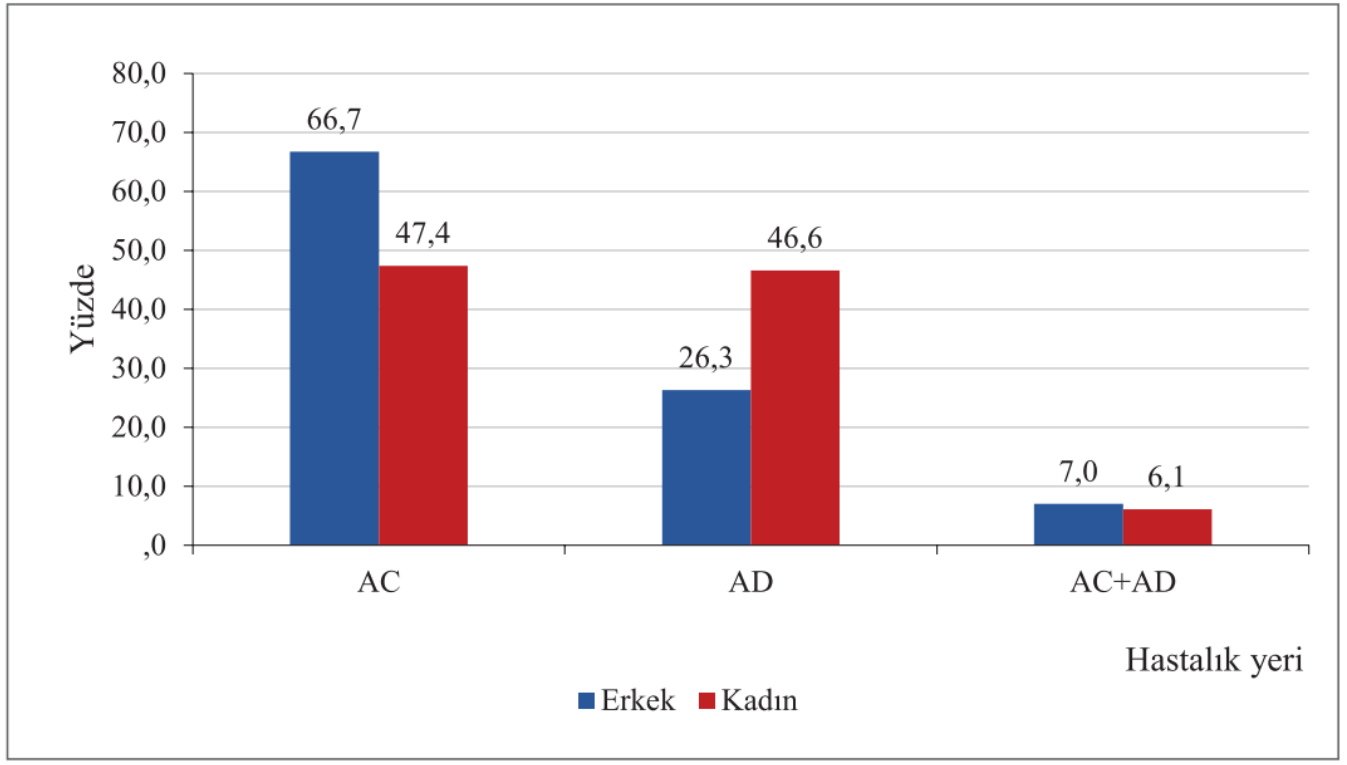


Şekil 24. Toplam TB Olgularında Cinsiyete Göre Hastalığın Tutulum Yeri, 2019

Tablo 26. Toplam TB Olgularında Cinsiyete Göre Hastalığın Tutulum Yeri, 2020

Cinsiyet	Hastalığın Yeri						Toplam	
	AC		AD		AC+AD			
	Sayı	%*	Sayı	%*	Sayı	%*	Sayı	%**
Erkek	3.407	66,7	1.345	26,3	356	7,0	5.108	57,2
Kadın	1.808	47,4	1.778	46,6	231	6,1	3.817	42,8
Toplam	5.215	58,4	3.123	35,0	587	6,6	8.925	100,0

** Satır yüzdesi ** Sütun yüzdesi*



Şekil 25. Toplam TB Olgularında Cinsiyete Göre Hastalığın Tutulum Yeri, 2020

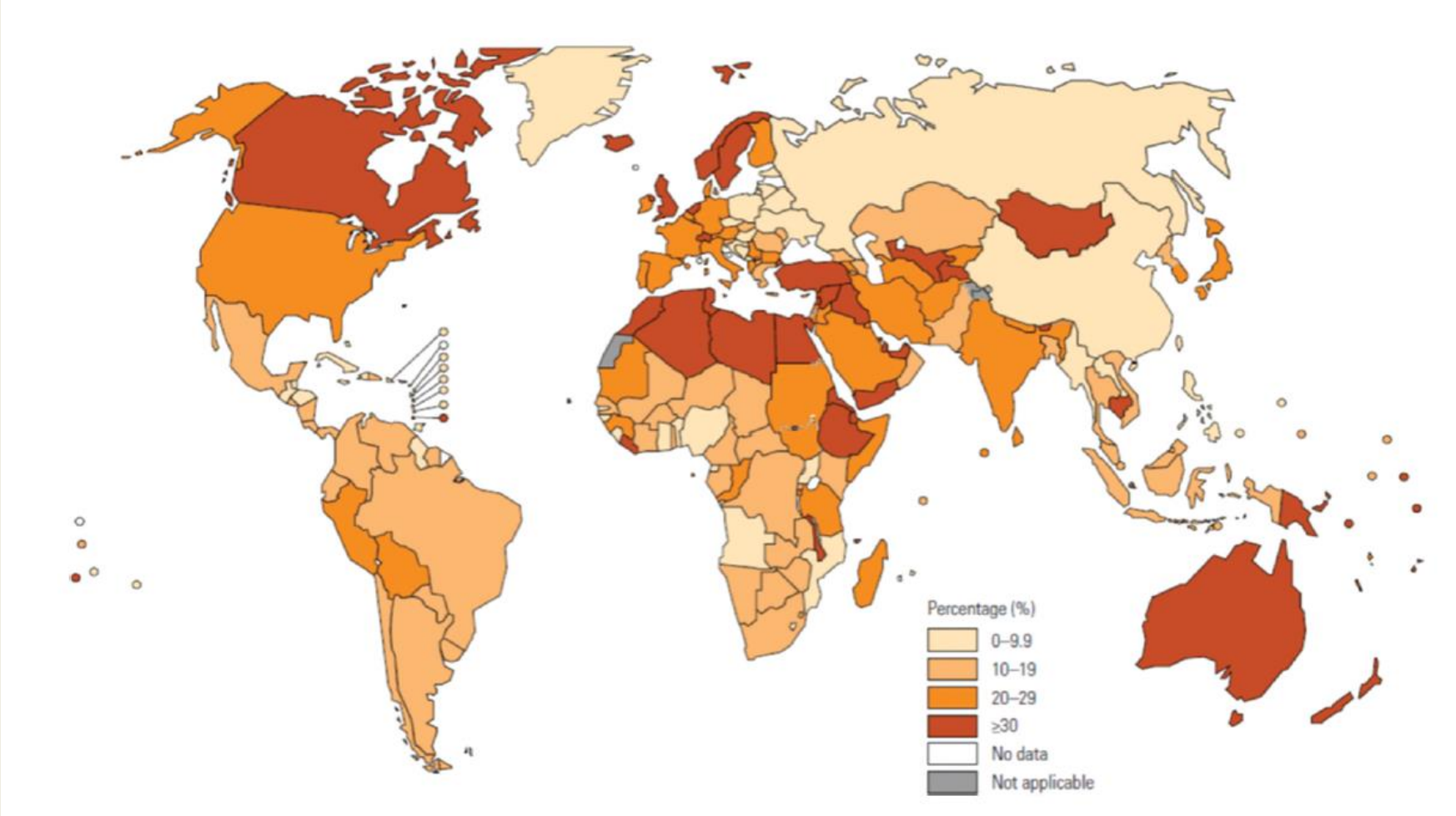


Figure Percentage of extrapulmonary cases among new and relapse TB cases, 2019. (Reproduced with permission from WHO Report 2020

Tablo 31. Yıllara Göre Akciğer ve Akciğer Dışı Yeni TB Olgularının Dağılımı, 2005-2020

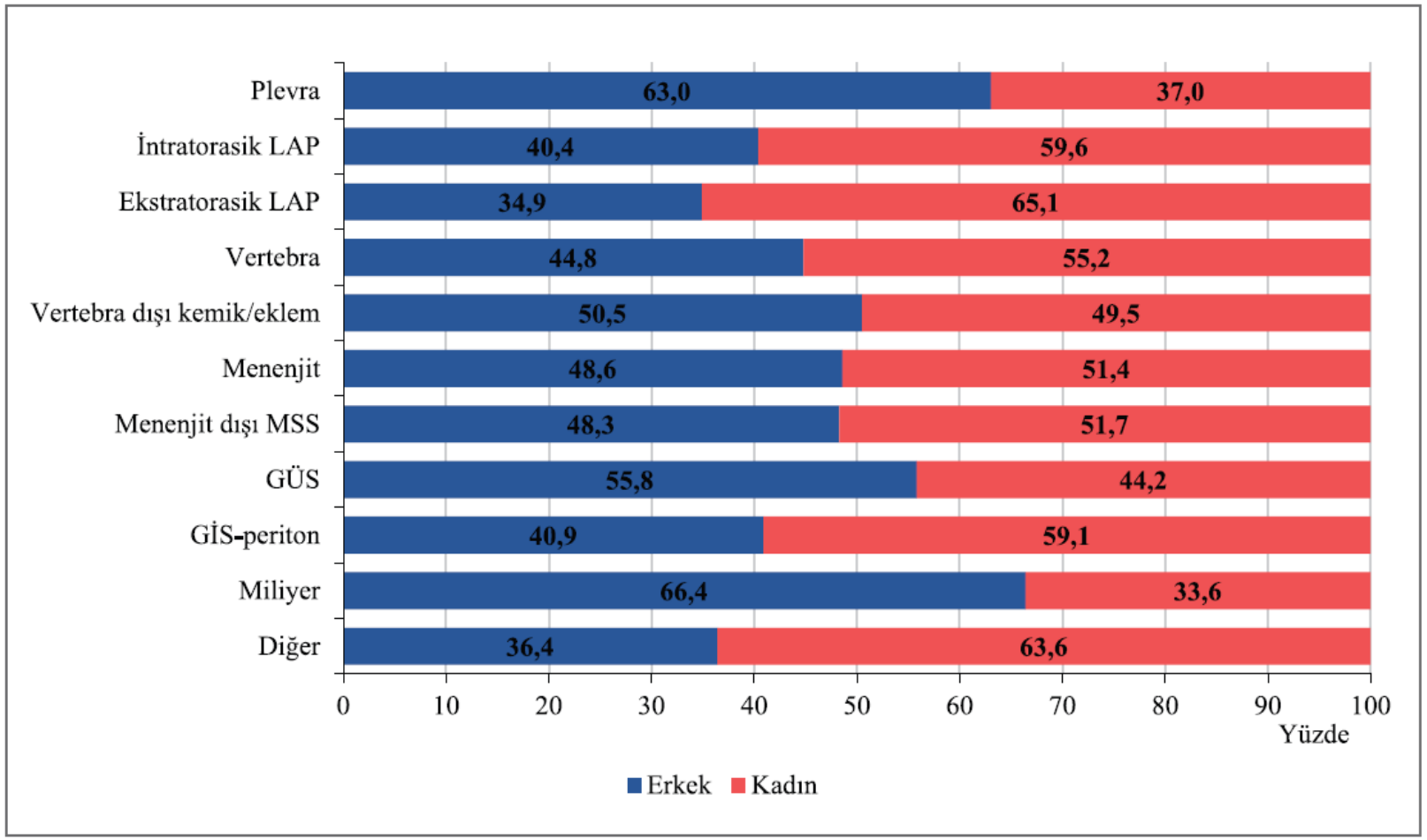
Yıl	AC*		AD		Yeni Olgu Sayısı
	Sayı	%	Sayı	%	
2005	13.394	71,4	5.359	28,6	18.753
2006	12.935	69,8	5.609	30,2	18.544
2007	11.996	67,5	5.785	32,5	17.781
2008	11.318	67,5	5.442	32,5	16.760
2009	10.296	64,6	5.647	35,4	15.943
2010	9.566	63,0	5.617	37,0	15.183
2011	8.852	61,4	5.565	38,6	14.417
2012	8.414	62,2	5.121	37,8	13.535
2013	7.791	63,1	4.561	36,9	12.352
2014	7.696	62,8	4.557	37,2	12.253
2015	7.427	62,9	4.376	37,1	11.803
2016	7.463	65,2	3.979	34,8	11.442
2017	7.198	64,8	3.903	35,2	11.101
2018	7.069	64,6	3.879	35,4	10.948
2019	6.857	64,3	3.812	35,7	10.669
2020	5.346	64,0	3.012	36,0	8.358

** AC olguları + "AC+AD" olgular*

Tablo 35. Akciğer Dışı Tüberküloz Olgularında Tutulan Organların Dağılımı, 2020

Tutulan Organ	Hastalığın Yeri				Toplam	
	AD		AC+AD			
	Sayı	%	Sayı	%	Sayı	%
Ekstratorasik LAP	1.114	35,7	95	16,2	1.209	32,6
Plevra	652	20,9	176	30,0	828	22,3
İntratorasik LAP	289	9,3	60	10,2	349	9,4
GİS ve periton	233	7,5	31	5,3	264	7,1
Vertebra	179	5,7	22	3,7	201	5,4
GÜS	158	5,1	14	2,4	172	4,6
Miliyer*	-	-	122	20,8	122	3,3
Menenjit	112	3,6	30	5,1	142	3,8
Vertebra dışı kemik/eklem	94	3,0	9	1,5	103	2,8
Menenjit dışı MSS	21	0,7	8	1,4	29	0,8
Diğer	271	8,7	20	3,4	291	7,8
Toplam	3.123	100,0	587	100,0	3.710	100,0

Tablo 37. Akciğer Dışı (AD ve AC+AD) TB Olgularında Cinsiyete Göre Tutulan Organların Dağılımı,



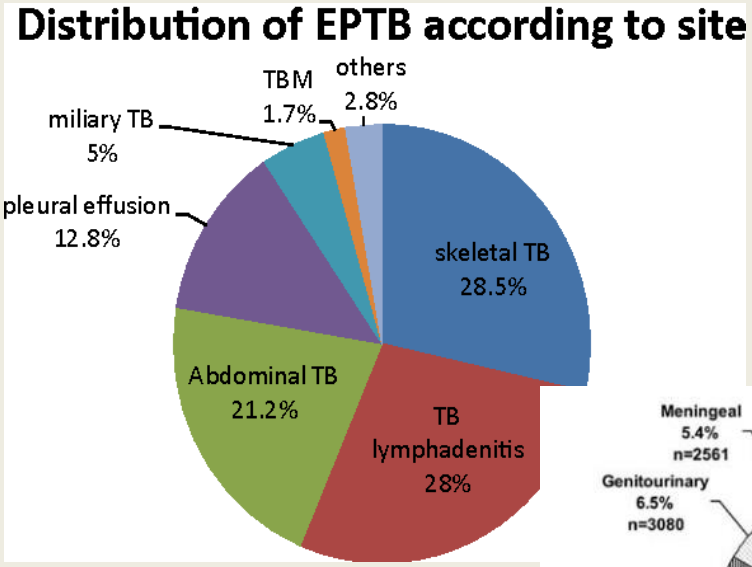
Şekil 29. Akciğer Dışı TB Olgularının Tutulan Organ ve Cinsiyete Göre Dağılımı, 2020

Tablo 40. Akciğer Dışı TB Olgularında Tutulan Organların Yaş Gruplarına Göre Dağılımı, 2020

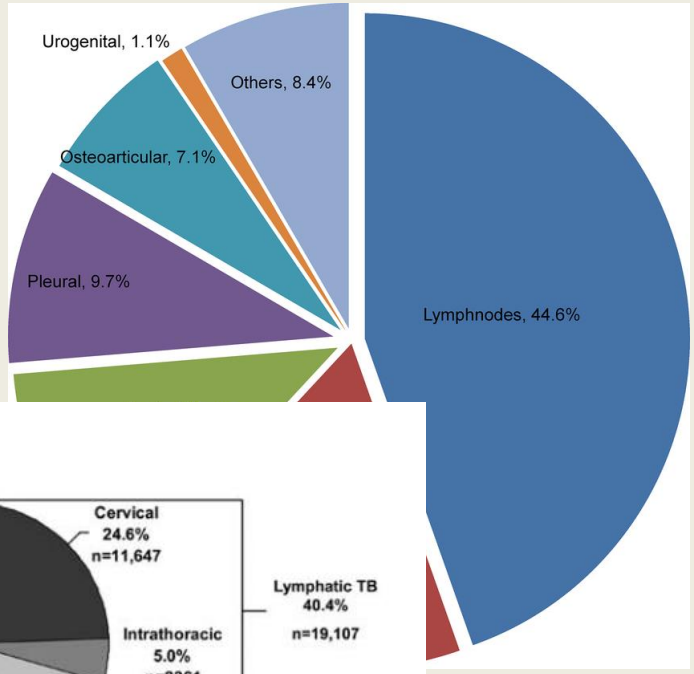
Tutulan Organ	Yaş Grubu																Toplam*	
	0-4		5-14		15-24		25-34		35-44		45-54		55-64		65 ve +			
	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%
Plevra	9	8,3	12	8,8	220	34,8	207	31,5	110	20,8	68	15,1	80	15,0	122	18,4	828	22,3
İntratorasik LAP	3	2,8	4	2,9	34	5,4	36	5,5	42	8,0	64	14,2	91	17,0	75	11,3	349	9,4
Ekstratorasik LAP	55	50,5	75	55,1	217	34,3	194	29,5	178	33,7	142	31,6	162	30,3	186	28,1	1.209	32,6
Vertebra	1	0,9	4	2,9	16	2,5	21	3,2	24	4,5	27	6,0	43	8,1	65	9,8	201	5,4
Vertebra dışı kemik/eklem	11	10,1	5	3,7	14	2,2	14	2,1	7	1,3	10	2,2	16	3,0	26	3,9	103	2,8
Menenjit	13	11,9	7	5,1	26	4,1	27	4,1	20	3,8	12	2,7	17	3,2	20	3,0	142	3,8
Menenjit dışı MSS	2	1,8	5	3,7	4	0,6	4	0,6	4	0,8	3	0,7	1	0,2	6	0,9	29	,8
GÜS	-	-	1	0,7	5	0,8	25	3,8	26	4,9	29	6,4	35	6,6	51	7,7	172	4,6
GİS, periton	2	1,8	12	8,8	55	8,7	47	7,1	43	8,1	30	6,7	42	7,9	33	5,0	264	7,1
Miliyer	2	1,8	5	3,7	21	3,3	13	2,0	11	2,1	20	4,4	9	1,7	41	6,2	122	3,3
Diğer	11	10,1	6	4,4	20	3,2	70	10,6	63	11,9	45	10,0	38	7,1	38	5,7	291	7,8
Toplam	109	100,0	136	100,0	632	100,0	658	100,0	528	100,0	450	100,0	534	100,0	663	100,0	3.710	100,0

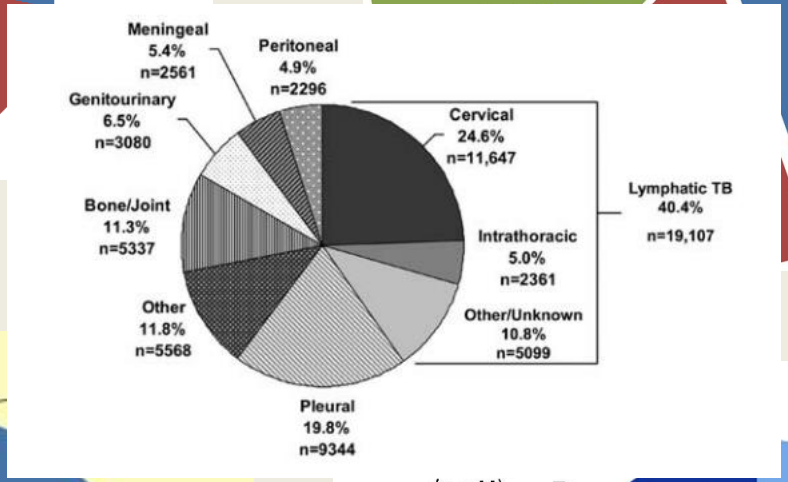
**Sadece AD tutulum olan 3.123 olgu ile AC+AD organ tutulumu olan 587 olgu alınmıştır.*

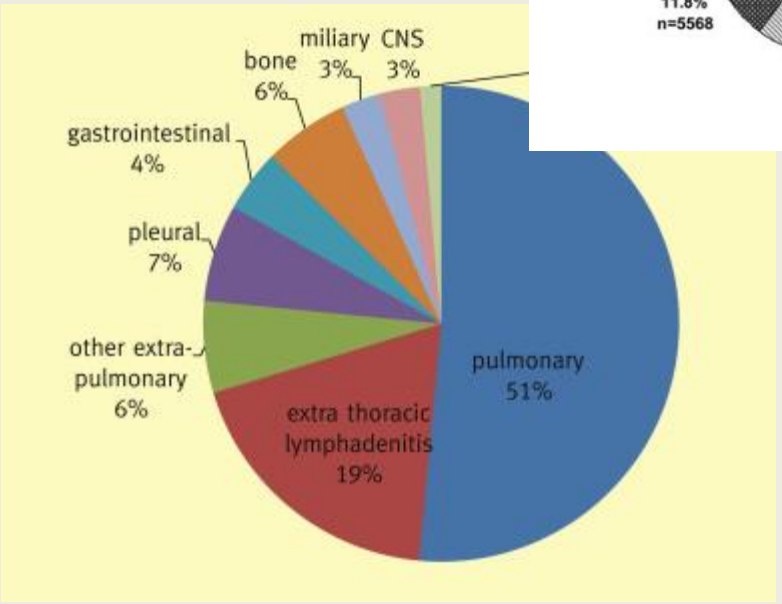
Nijerya

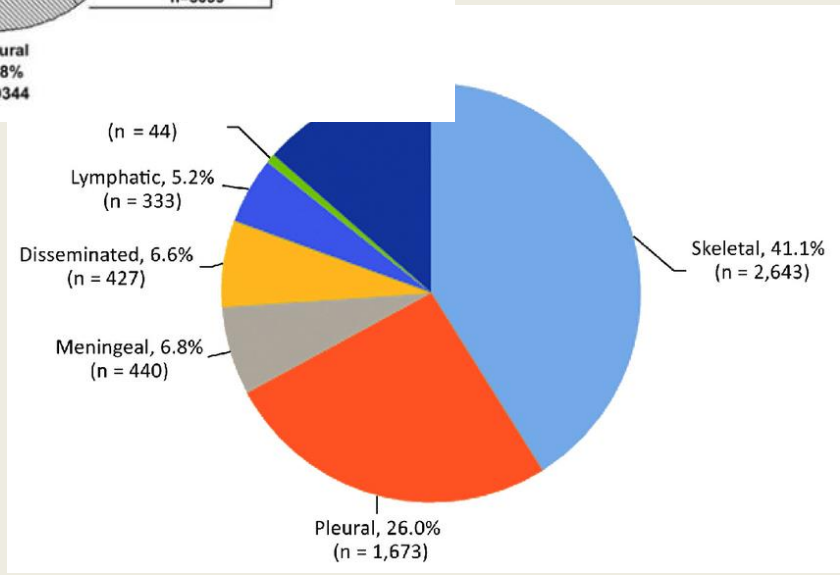


Suudi Arabistan

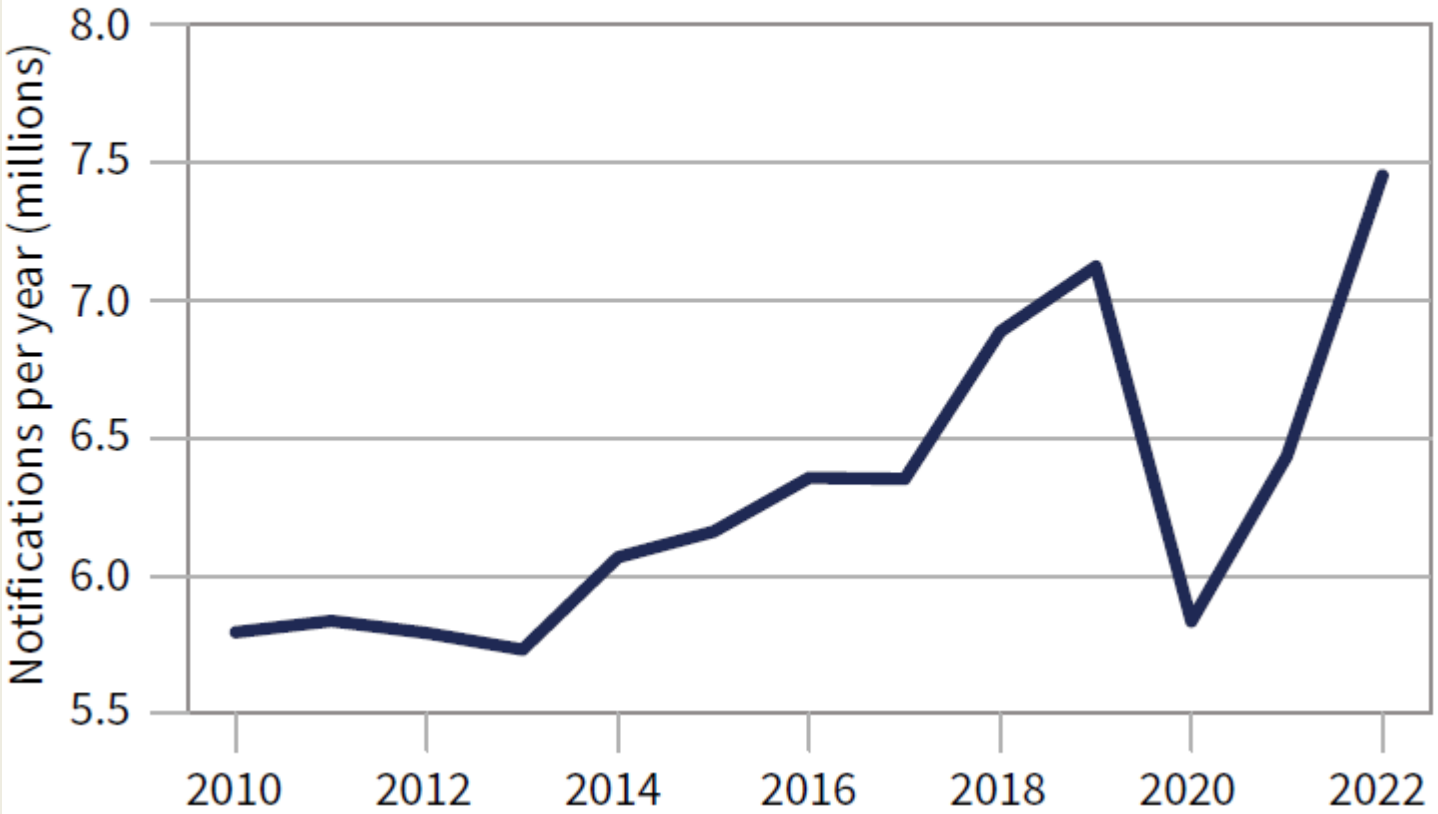




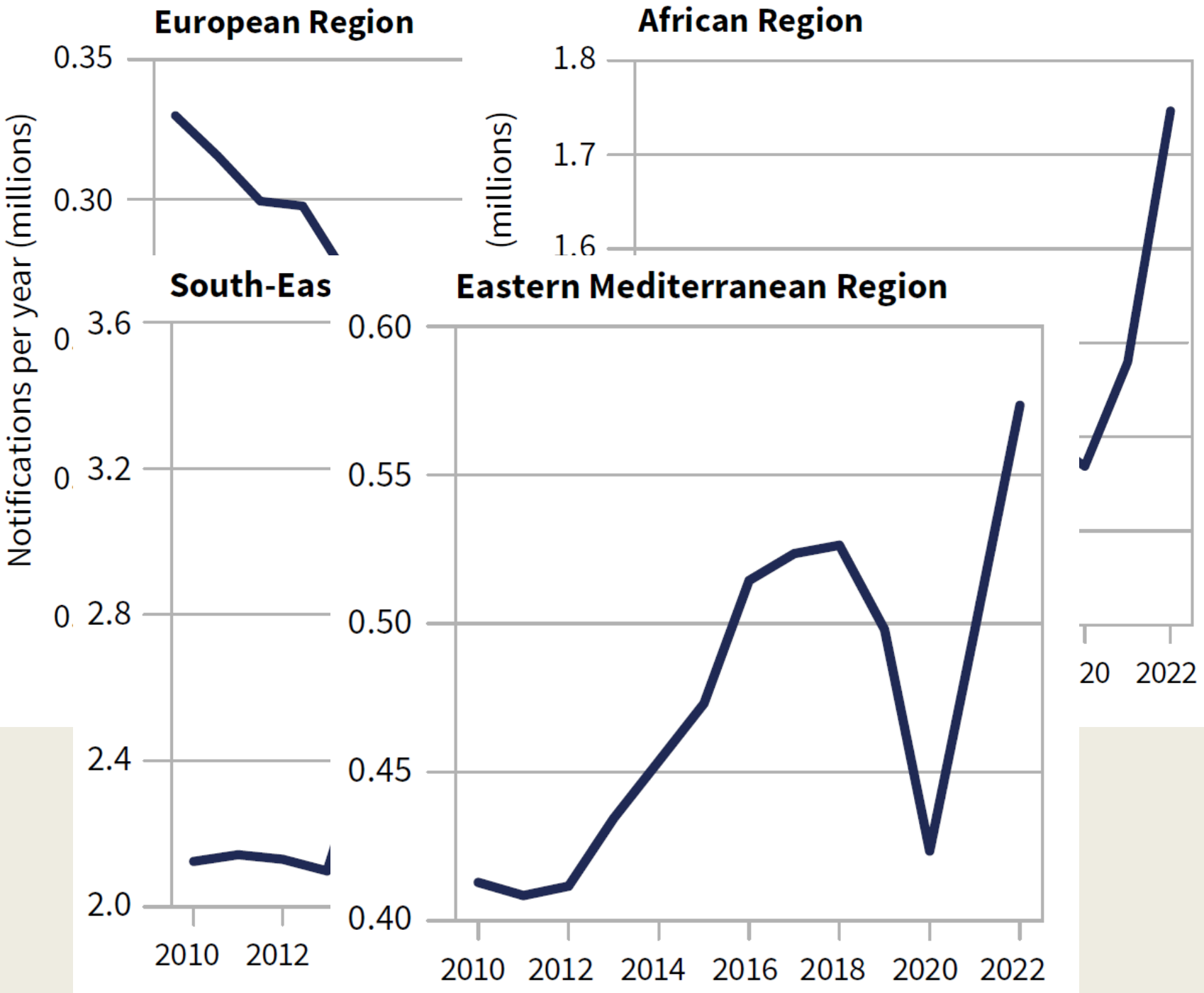




Global trend in case notifications of people newly diagnosed with TB, 2010–2022

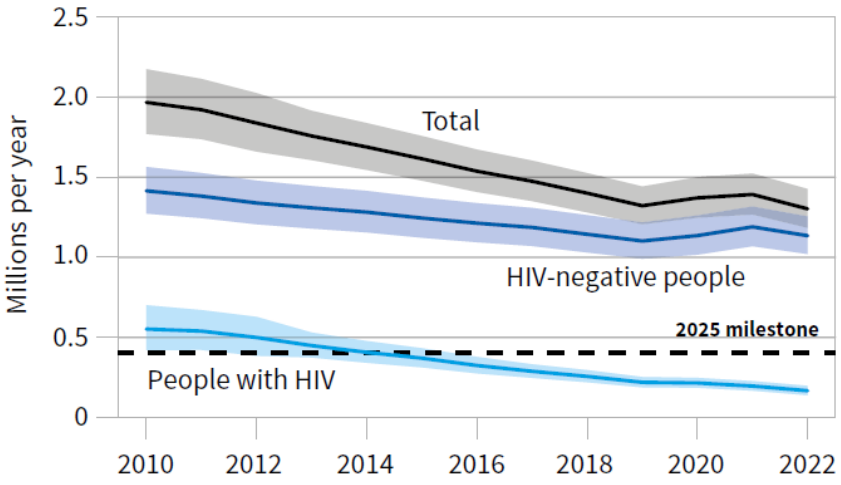


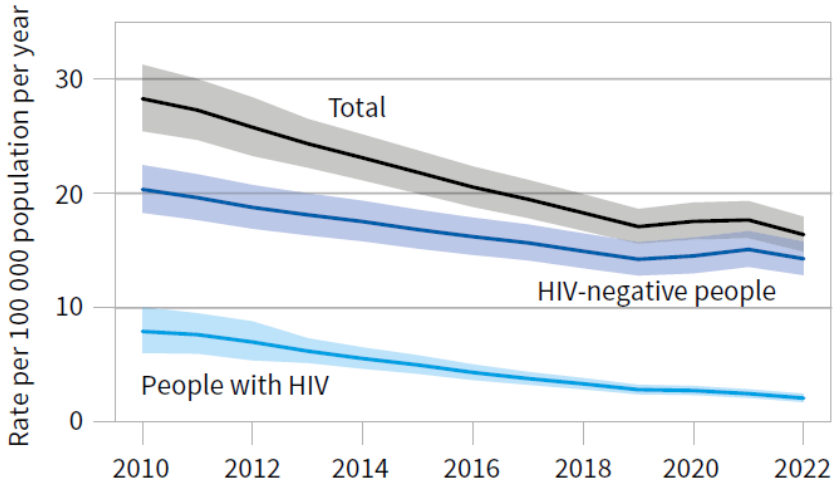
Global tuberculosis report, WHO 2023


European Region
African Region
South-Eas
Eastern Mediterranean Region
Notifications per year (millions)
(millions)
0.35
0.30
1.8
1.7
1.6
3.6
3.2
2.8
2.4
2.0
0.60
0.55
0.50
0.45
0.40
2010
2012
2014
2016
2018
2020
2022

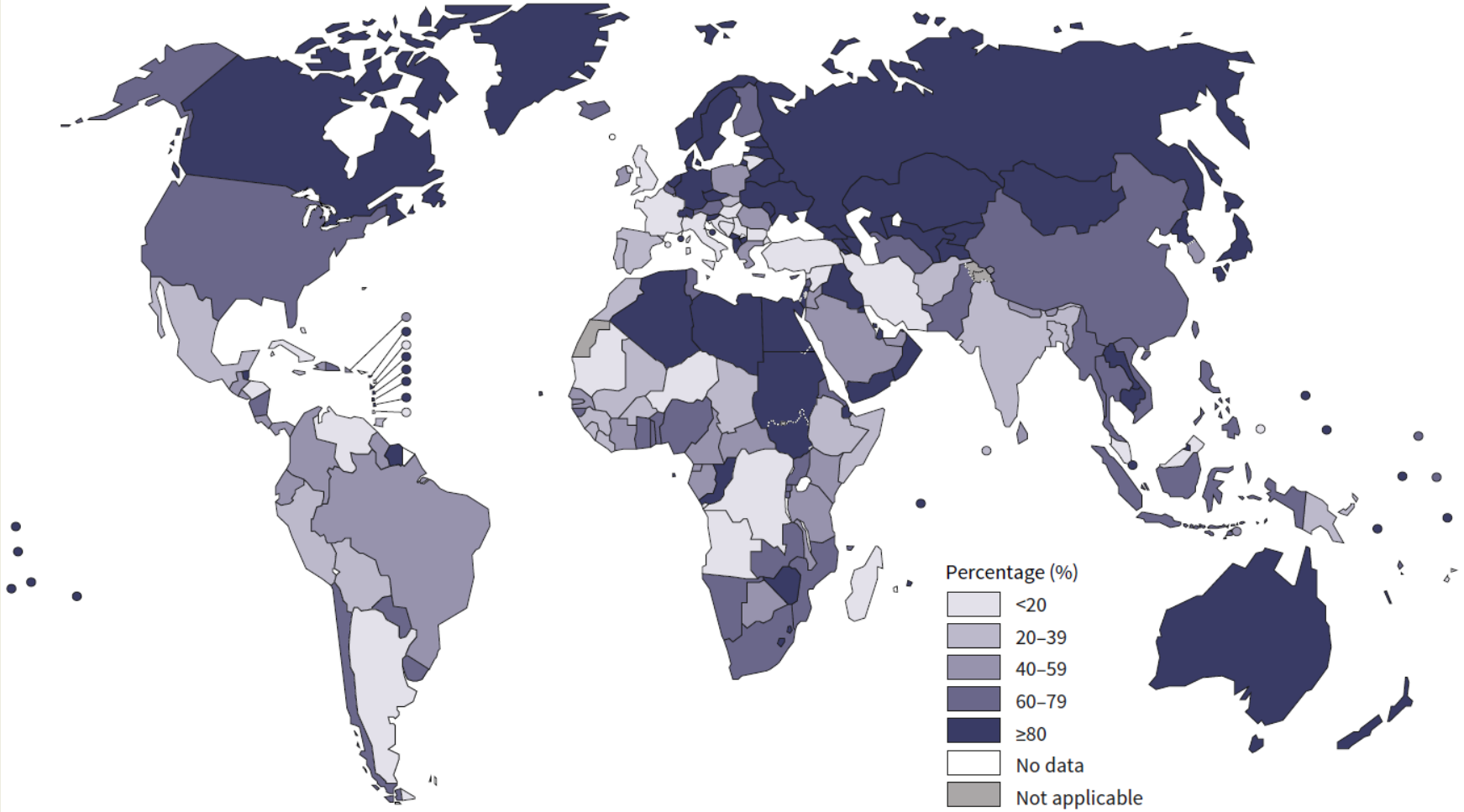
Global trends in the estimated number of deaths caused by TB (left) and the TB mortality rate (right),[a] 2010–2022

The horizontal dashed line shows the 2025 milestone of the End TB strategy, which is a 75% reduction in the total number of TB deaths between 2015 and 2025. Shaded areas represent 95% uncertainty intervals.





Percentage of people newly diagnosed with TB who were initially tested with a WHO-recommended rapid diagnostic test (WRD), by country, 2022



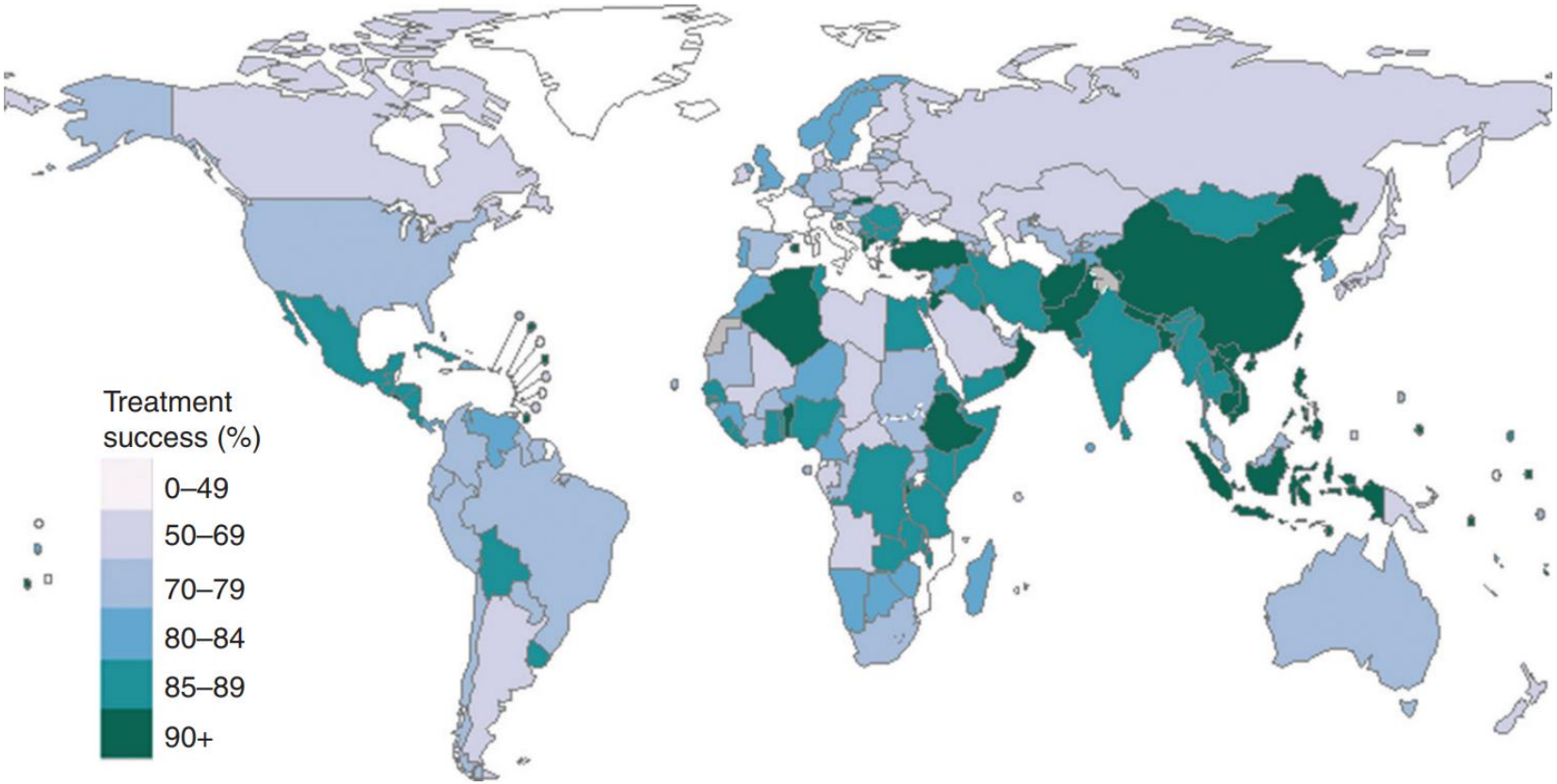


Figure 4. Treatment success rate, 2011 cohort of newly diagnosed TB cases (all forms). Countries shown in white did not report data to WHO for the 2011 cohort.

Global epidemiology of tuberculosis. Cold Spring Harb Perspect Med. 2014 Oct 30;5(2):a017798. doi: 10.1101/cshperspect.a017798. PMID: 25359550; PMCID: PMC4315920.

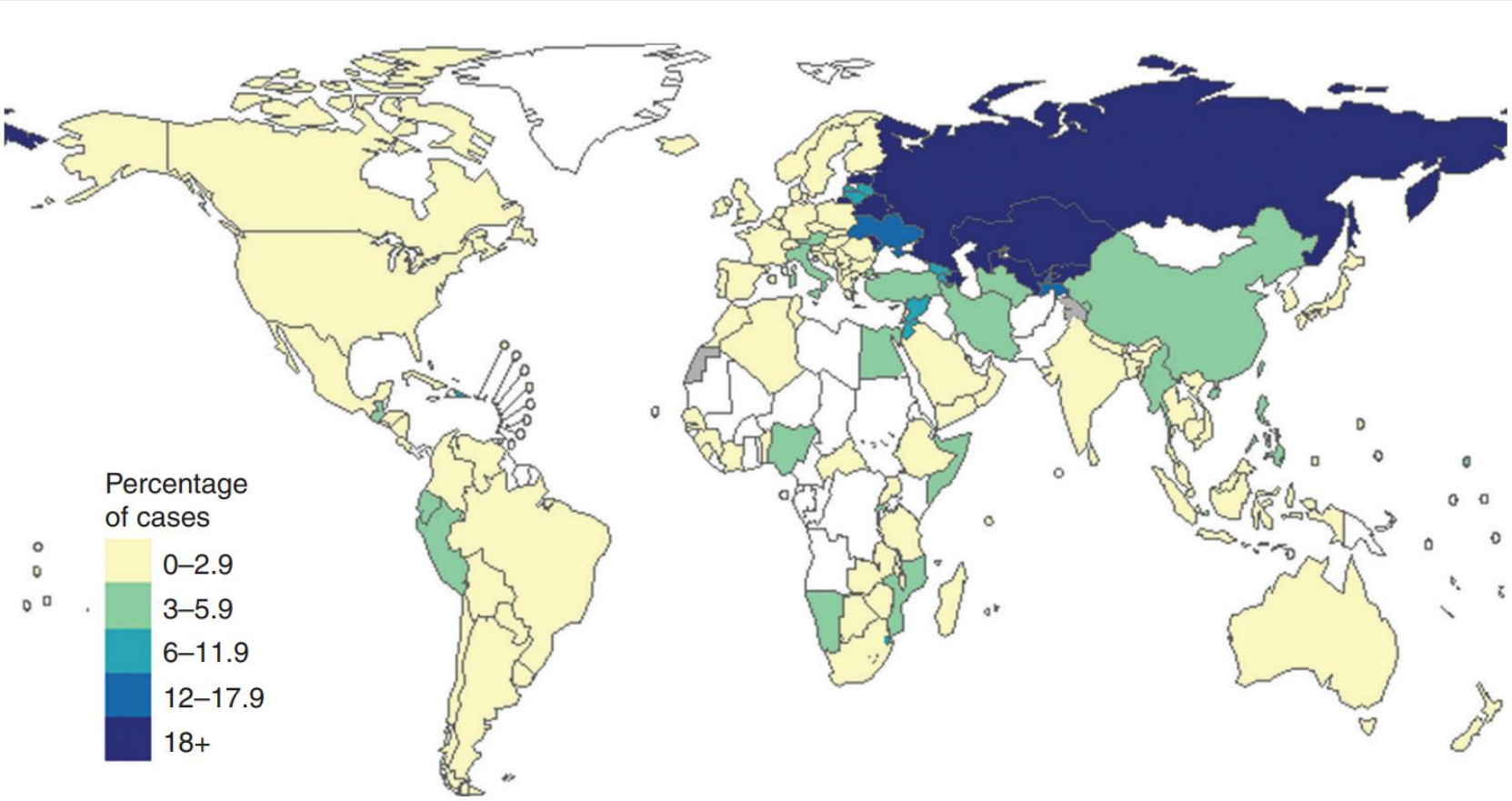


Figure 5. Percentage of new TB cases with MDR-TB, based on the most recent year for which data have been reported, which varies between countries. Countries and territories shown in white have reported no data. In Brazil, Spain, Central African Republic, Russia, Turkmenistan, India, Malaysia, and Indonesia, drug resistance surveillance data was only subnational.

Global epidemiology of tuberculosis. Cold Spring Harb Perspect Med. 2014 Oct 30;5(2):a017798. doi: 10.1101/cshperspect.a017798. PMID: 25359550; PMCID: PMC4315920.

TUBE
AND

IN 2017, 10 MILLION P
ILL WITH TB AND 1.6 MI
FROM T

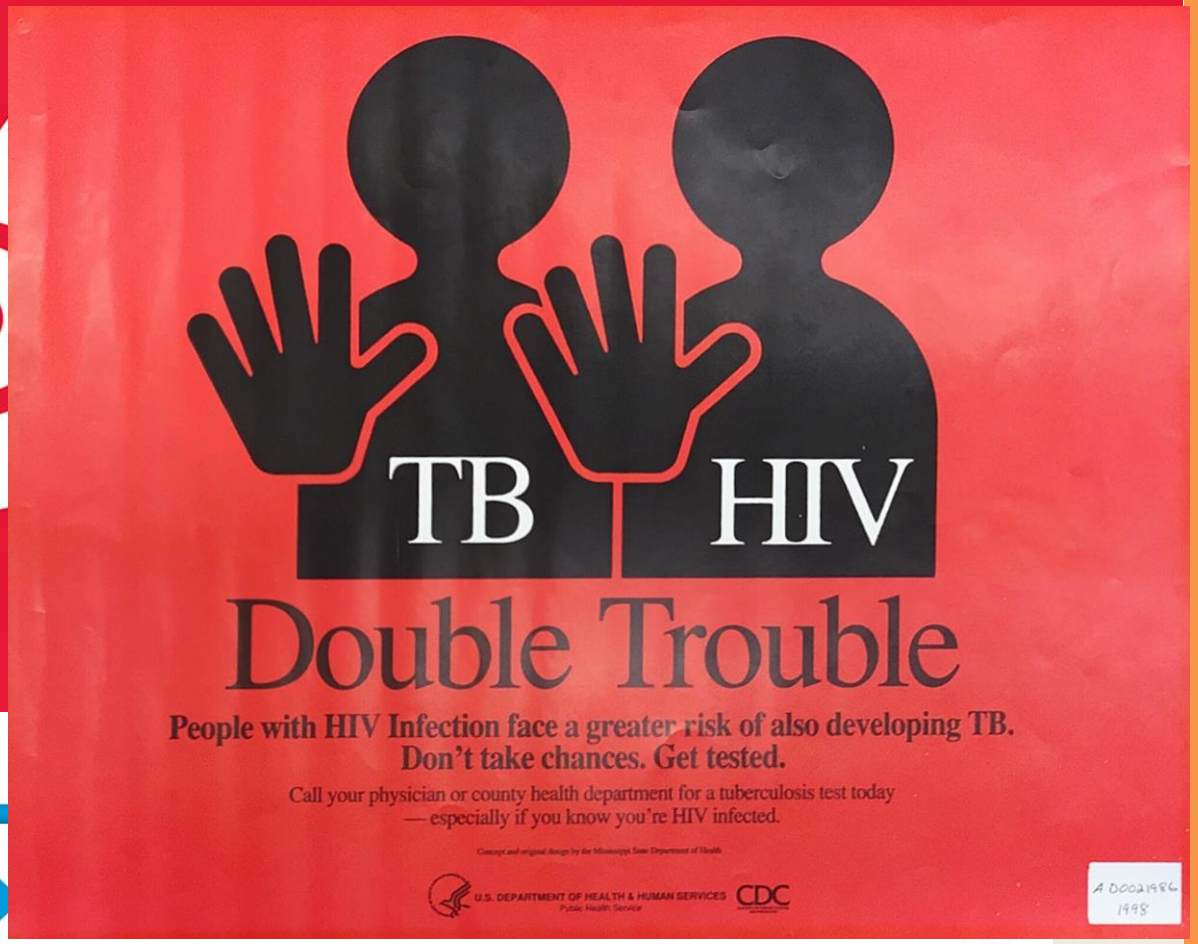
TB IS T
AMON

UNAIDS IS
WORKING WITH PAR
TO REDUCE TB-ASSO
DEATHS AMONG PEO
LIVING WITH HIV
BY 75% BY 2

TB IS CURABLE:
45 MILLION
LIVES HAVE
BEEN SAVED
SINCE 2000

TUBERCULOSIS IS THE LEADING
KILLER OF PEOPLE WITH HIV

2015



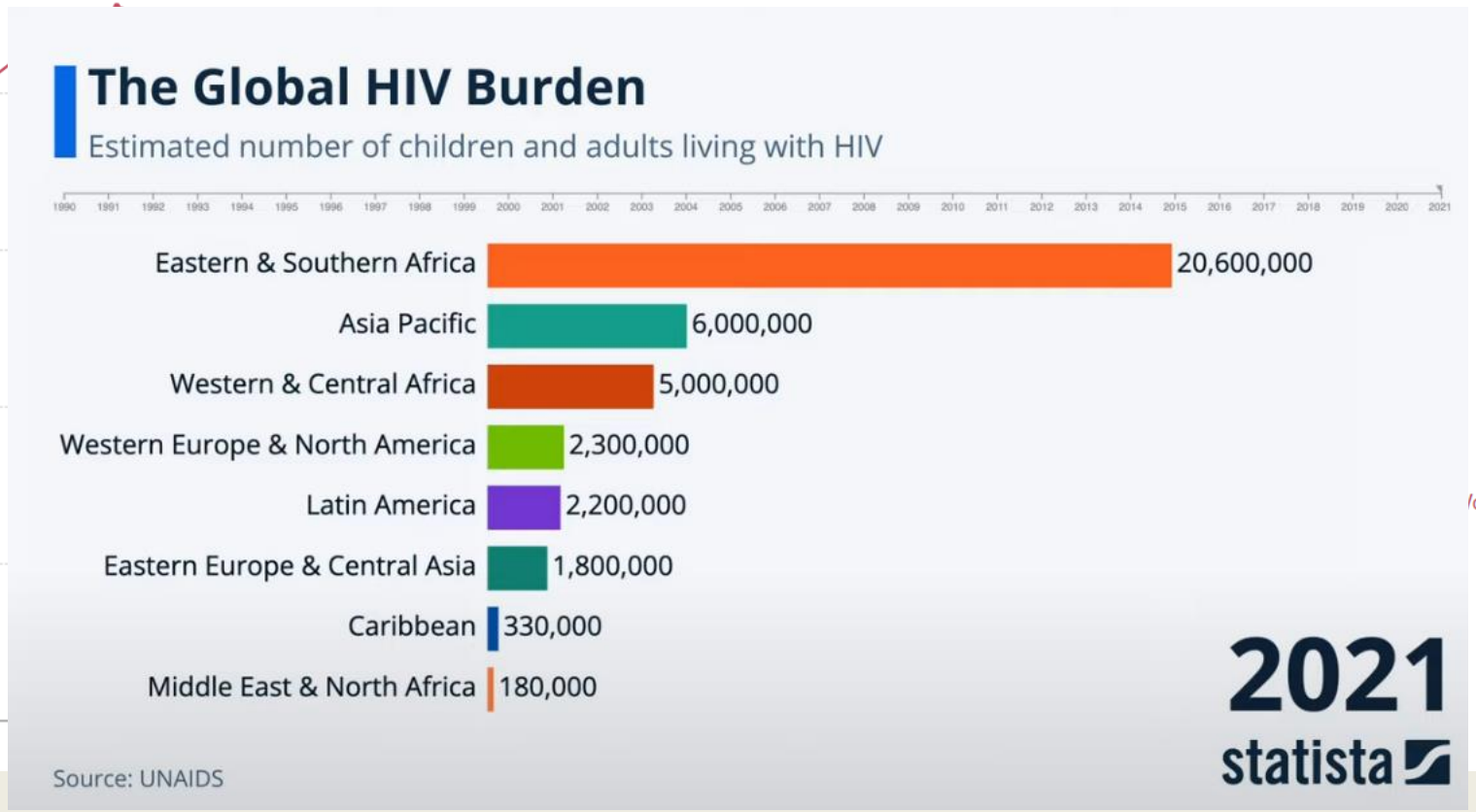
Annual incidence rate of HIV, 1990 to 2022

The number of new HIV infections among the uninfected population aged 15-49, expressed per 1,000 uninfected people in the year before.

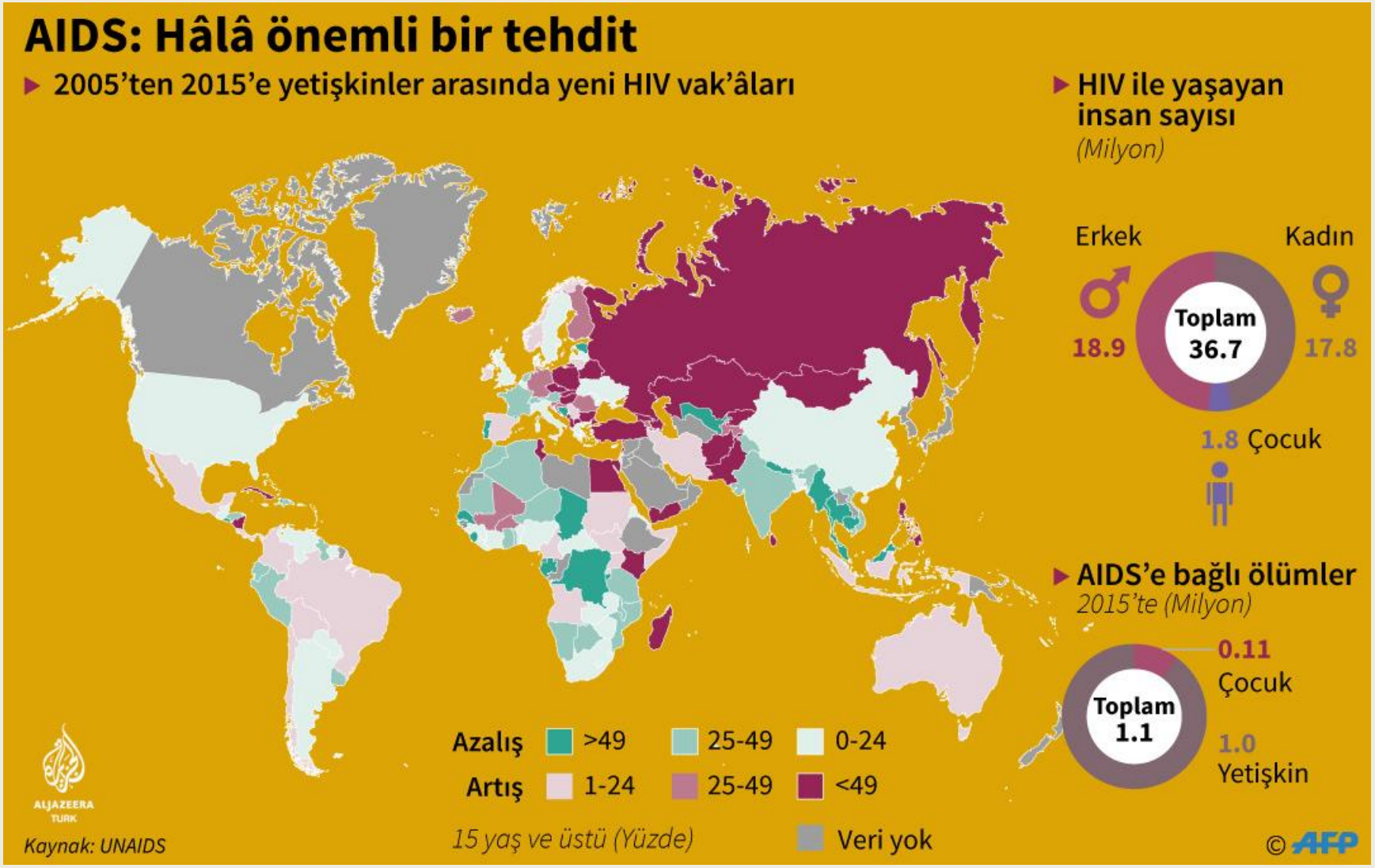
Our World in Data

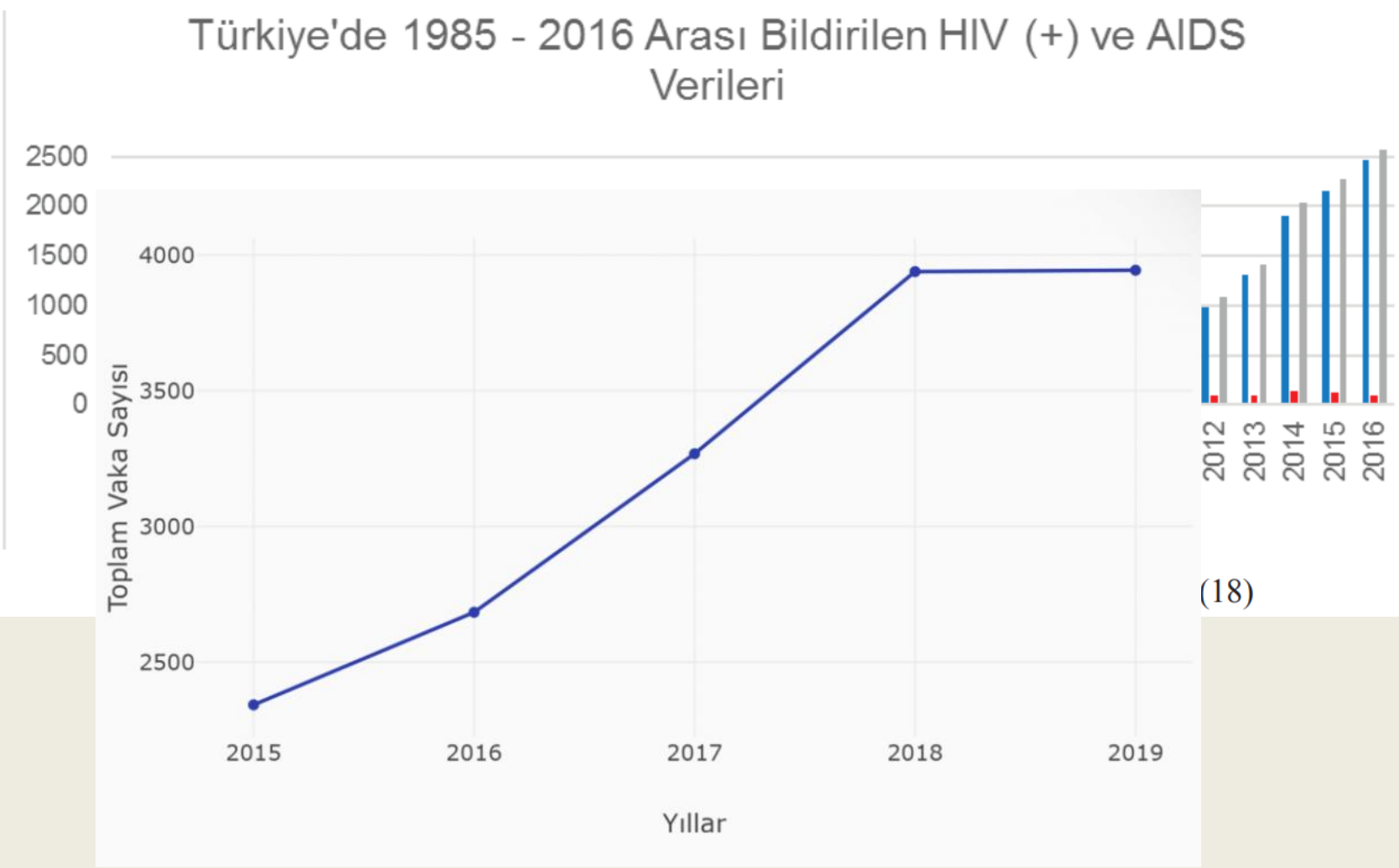
Table | Map | Chart

Settings



0.8
0.6
0.4
0.2
0
1990


AIDS: Hâlâ önemli bir tehdit
2005'ten 2015'e yetişkinler arasında yeni HIV vak'âları
HIV ile yaşayan insan sayısı
(Milyon)
Erkek
Kadın
18.9
Toplam 36.7
17.8
1.8 Çocuk
AIDS'e bağlı ölümler
2015'te (Milyon)
0.11 Çocuk
Toplam 1.1
1.0 Yetişkin
Azalış >49 25-49 0-24
Artış 1-24 25-49 <49
Veri yok
15 yaş ve üstü (Yüzde)
ALJAZEERA TURK
Kaynak: UNAIDS
© AFP


Türkiye'de 1985 - 2016 Arası Bildirilen HIV (+) ve AIDS Verileri
2500
2000
1500
1000
500
0
2012
2013
2014
2015
2016
4000
3500
3000
2500
Toplam Vaka Sayısı
2015
2016
2017
2018
2019
Yıllar

(18)

HIV / AIDS İSTATİSTİKLERİ

HIV / AIDS TOPLAM VAKA VE ÖLÜM SAYILARININ SON 5 YIL DAĞILIMI

YILLAR	HIV	AIDS	TOPLAM	ÖLÜM
2019	4159	139	4298	40
2020	3128	75	3203	47
2021	4182	103	4285	52
2022	5591	119	5710	67
2023	1677	51	1728	17

JOURNAL ARTICLE

Site of Extrapulmonary Tuberculosis is Associated with HIV Infection

Ira L. Leeds, Matthew J. Magee, Ekaterina V. Kurbatova, Carlos del Rio, Henry M. Blumberg, Michael K. Leonard, Colleen S. Kraft

Incidence and predictors of extrapulmonary tuberculosis among people living with *Human Immunodeficiency Virus* in Addis Ababa, Ethiopia: A retrospective cohort study

Ayinalem Alemu, Aman Yesuf, Ewenat Gebrehanna, Betselot Zerihun, Melak Getu, Teshager Worku, Zebenay Workneh Bitew

Published: May 6, 2020 • https://doi.org/10.1371/journal.pone.0232426

Infection. 2017 Feb; 45(1): 11–21. PMID: 27830524

Published online 2016 Nov 9. doi: 10.1007/s15010-016-0960-5

Association of HIV infection with extrapulmonary tuberculosis: a systematic review

Rupak Shivakoti,[#1] Da

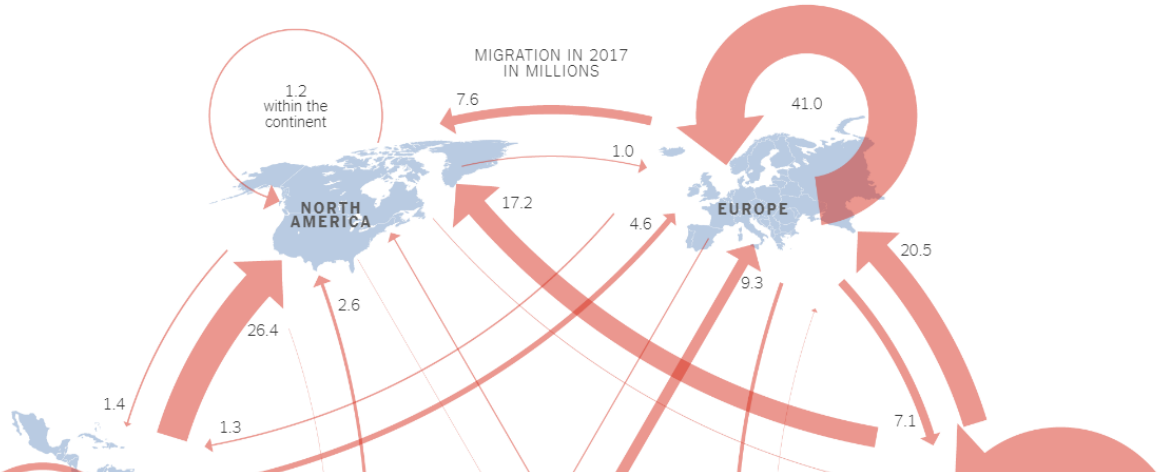
Mortality among extrapulmonary tuberculosis patients in the HIV endemic setting: lessons from a tertiary level hospital in Mbeya, Tanzania

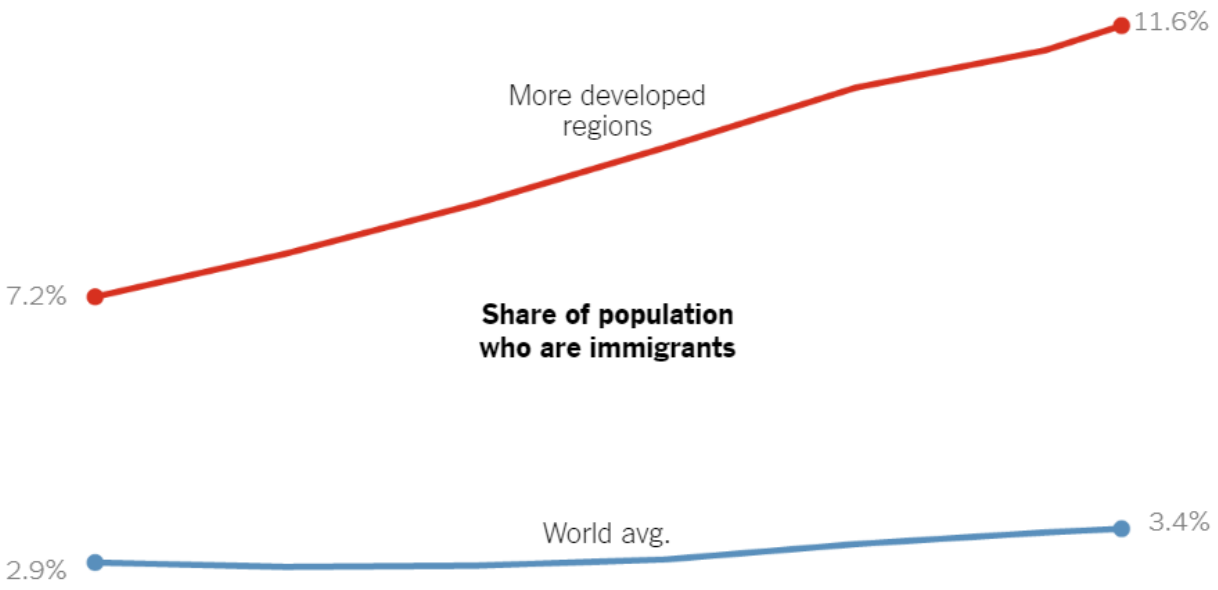
Erlend Grønningen [1 2], Marywinnie Nanyaro [3], Bjørn Blomberg [4 5], Shoaib Hassan [4], Esther Ngadaya [3], Tehmina Mustafa [6 7]

J Int AIDS Soc.

Diagnosis tuberculo low- and study

Yıllara göre Türkiye'ye gelen göç sayısı.





Largest diaspora populations in 2017 in millions

1.	India	16.6	6.	Syria	6.9	11.	Afghanistan	4.8	16.	Palestine	3.8	21.	United States	3.0	26.	South Korea	2.5
2.	Mexico	13.0	7.	Pakistan	6.0	12.	Poland	4.7	17.	Romania	3.6	22.	Morocco	2.9	27.	Portugal	2.3
3.	Russia	10.6	8.	Ukraine	5.9	13.	Indonesia	4.2	18.	Turkey	3.4	23.	Myanmar	2.9	28.	France	2.2
4.	China	10.0	9.	Philippines	5.7	14.	Germany	4.2	19.	Egypt	3.4	24.	Colombia	2.7	29.	Uzbekistan	2.0
5.	Bangladesh	7.5	10.	Britain	4.9	15.	Kazakhstan	4.1	20.	Italy	3.0	25.	Vietnam	2.7	30.	Somalia	2.0

İstanbul’da yasal olarak yaşayan yabancıların sayısı belli oldu

06-03-2024

PAYLAŞ

FAVORI LISTEME EKLE

TÜRKIYE

İstanbul'daki İstiklal Caddesi'nden kare

Haber Merkezi _ Türkiye İçişleri Bakanı Ali Yerlikaya, İstanbul’da yasal kalış hakkı bulanan toplam yabancı sayısı 1 milyon 92 bin 697 olarak açıkladı.

Bakanın verdiği bilgiye gör geçici korumadaki Suriyeli sayısı 350 bin 532.

Son paylaşılanlar

Table 1. Immunostimulators.

FAMILY	DRUG	PHARMACOLOGICAL EFFECT
Bacterial and fungal products	Bacillus Calmette-Guérin	Activation of macrophages (APC), NK cells, and B lymphocytes
	(BCG) Muramyl dipeptide (MDP) L-MTP-PE	Activation of macrophages (APC and phagocytosis) Activation of macrophages (APC and phagocytosis)
	Lipopolysaccharides (LPS)	Activation of macrophages and B lymphocytes
	Propionibacterium species	APC, phagocytosis, Activation of Tc and B lymphocytes
	Glucan	Phagocytosis
Thymic factors	Thymosins	Maturation of thymocytes into T lymphocytes
Synthetic drugs	Levamisole Isoprinosine	Maturation and activation of T lymphocytes, phagocytosis, and chemotaxis

Na
Immun

Table 2. Immunosuppressants.

FAMILY	DRUG	PHARMACOLOGICAL EFFECT
Drugs that bind to immunophilins	Cyclosporine A, Tacrolimus and Sirolimus	Inhibition gene transcription of cytokines (e.g., IL-2) in T lymphocytes (blocking their proliferation), Inhibition of cytokines of T lymphocytes
Glucocorticoids	Prednisone and dexamethasone	Inhibition of transcription of cytokines into T lymphocytes and macrophages
Cytostatics	Azathioprine, Cyclophosphamide, Mophetil mycophenolate and Leflunomide	Inhibition of cell proliferation, Inhibition of proliferation of T and B lymphocytes, Inhibition of cell proliferation
Antilymphocyte antibodies	Polyclonal antibodies Anti-thymocytes	Triggering effector phase of specific immunity against lymphocytes
Monoclonal antibodies	Muromonab (OKT3) Anti-cytokines and anti-receptors	Destruction of CD3+ cells (T lymphocytes),Neutralization or destruction of molecules of the immune system
Hyposensitization	Allergens	Reversal of response from type IgE to IgC (from Th2 to Th1), Reduction in reactivity to allergen

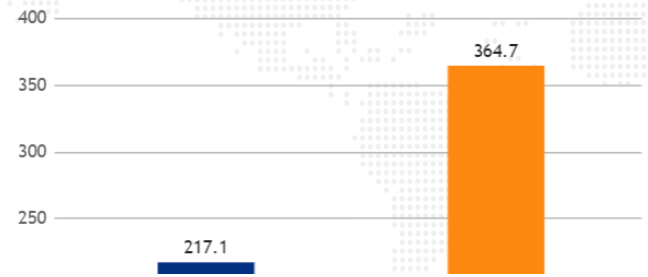
Mohamed SIAet a
Immunopharmacc
Bascones, Antonic
10.4317/medoral.19087.


PRECEDENCE RESEARCH
IMMUNOMODULATORS MARKET SIZE 2022 TO 2032 (USD BILLION)
1000
900
800
700
600
500
400
300
200
100
0
$ 238.5
$ 273.80
$ 314.59
$ 361.78
$ 416.41
$ 479.71
$ 553.10
$ 638.28
$ 737.21
$ 852.22
$ 986.02
2022
2023
2024
2025
2026
2027
2028
2029
2030
2031
2032
Source: www.precedenceresearch.com

Global Immunomodulators Market – Industry Trends and Forecast to 2030

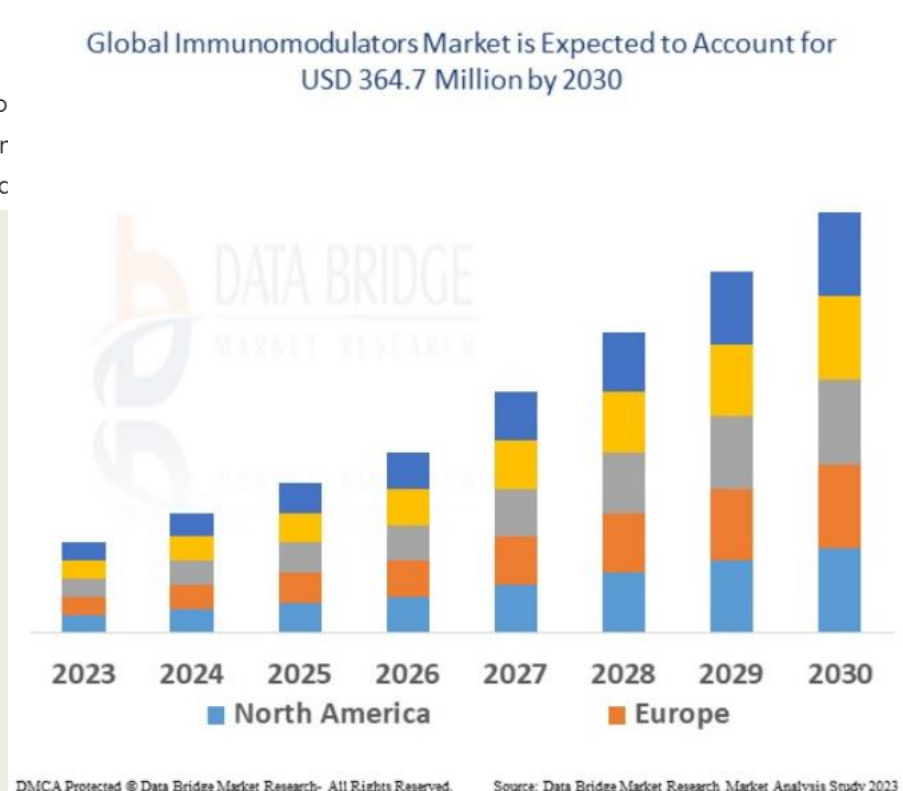
Market Size in USD Billion

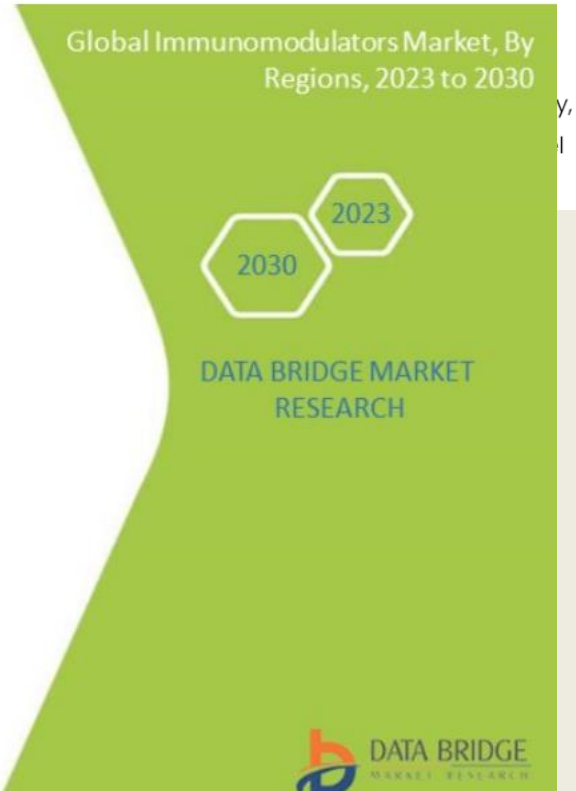
CAGR : 6.70%



Forecast Period	2022–2030
Market Size (Base Year)	USD 217.10 Billion
Market Size (Forecast Year)	USD 364.70 Billion
CAGR	6.70 %

Glo y, Human
Imr l (Hospital
Pha





Zumla *et al. BMC Medicine* (2016) 14:89
DOI 10.1186/s12916-016-0635-1

BMC Medicine

World TB Day

Table 1 List of immunomodulatory agents for the treatment of multidrug-resistant tuberculosis

Immunomodulatory agent	Host target	Currently licensed indication(s)	Biological activity
Small molecules			
Metformin	AMPK activator	Diabetes	Augments mitochondrial reactiv mediated intracellular MDR *M. tb* of lung bacterial burden and path via increased mitochondrial turno cell responses, possibly by increas involvement in memory cells. Sho tumour CD8 T cell memory gene TNF receptor associated factors kr FAO restoration
Zileuton	5-lipoxygenase inhibitor	Asthma	Inhibits 5-lipoxygenase and subs leukotrienes; promotes reduced and pathology in mice by increa and augmenting IL-1β-mediated control
Ibuprofen	COX inhibitor	Pain and fever relief	Inhibits COX2 and suppresses pr thromboxane production; inhibit lung pathology and *M. tb* load i susceptible TB mouse model
Aspirin (acetylsalicylic acid)	COX inhibitor	Pain and fever relief	Inhibits COX1 to suppress prosta thromboxane production to dam overt inflammation; aids tissue re *M. tb* burden
Valproic acid	Histone deacetylase inhibitor	Epilepsy and bipolar disorder	Inhibits HDAC I, II and IV to bloc deacetylation and enhance gene activates latent HIV reservoirs an efficacy as well as increased CD8 induce autophagy and apoptosis
Carbamazepine	GABA receptor agonist and sodium channel stabiliser	Epilepsy and neuropathic pain	Induces autophagy via inositol d macrophages, potentiating killin *M. tb*; reduces lung pathology a immune responses in a mouse m
Vorinostat	Histone deacetylase inhibitor	Cutaneous T cell lymphoma	Inhibits HDAC I, II and IV to bloc deacetylation and enhance gene induces reactivation of latent HI improves CD8 T cell responses efficacy – presently in clinical tr individuals; can induce autopha shown to dampen neuroinflam model of West Nile virus infecti an experimental antiviral drug c
Phenylbutyrate	Histone deacetylase inhibitor, chemical chaperone	Urea cycle disorders	Inhibits HDAC I to block histone enhance gene transcription; ind activating expression of antimic macrophages to kill intracellular with vitamin D3; shown to be ve short-course therapy (with vitam study involving patients with pul
Cyclophosphamide	DNA alkylating agent	Lymphomas and pre-transplant preconditioning	Forms lethal phosphoramide m activation specifically in low prc dehydrogenase (largely Tregs); potentiate renal cell carcinoma candidate; Treg depletion may beneficial immune responses in s
Etoposide	Topoisomerase inhibitor	Various cancer types	Inhibits DNA topoisomerase I a cell proliferation; depletion of pat T cells in influenza-induced he lymphohistiocytosis shown to
Imatinib mesylate	Tyrosine kinase inhibitor	Leukaemias and gastrointestinal stromal tumours	Inhibits mutant BCR-ABL tyrosin reduces colony forming unit lo lungs of *M. tb*-infected mice; in
Niraparib	PARP inhibitor	Ovarian and breast cancers	Inhibits PARP1/2 to cause double strand DNA breaks in cells, abrogating proliferation; niraparib has been shown to restore mitochondrial respiration in human muscle fibres, likely by improving FAO, thus promoting maintenance of anti-TB memory CD8 T cells
Prednisone	Glucocorticoid receptor agonist	Immunosuppressant used in cancer and inflammatory diseases	Activated downstream signalling of the GC receptor; has pleiotropic outcomes, including anti-inflammatory effects; use in community-acquired pneumonia showed improved survival among patients; results in TB patients inconclusive and requires further validation
Nutraceuticals			
Resveratrol	Sirtuin agonist	Over-the-counter antioxidant	Increases cellular mitochondrial turnover, thus increased respiratory capacity; may promote maintenance of anti-TB memory CD8 T cells via FAO increase; alternatively, may also induce apoptosis of activated T cells during severe inflammation
Vitamin D3	Innate immune response activator	Dietary supplement	Kills intracellular *M. tb*; activates innate immune responses in macrophages, thus improving ensuing T cell responses in combination with phenylbutyrate; also augments IL-32 and IL-15-mediated immune responses in clinical TB
Biologicals			
Interleukin 15	Involved in CD8 memory T cells maintenance	In clinical trials for various cancers	Signals via IL-15Rβ and the common chain to activate STAT3 and STAT5; increases mitochondrial mass and fatty acid oxidation in memory CD8 T cells to prolong survival and maintenance; augments IFN-γ and vitamin D3-mediated immune responses in human TB
Nivolumab/ pembrolizumab (anti-PD-1)	Immune checkpoint inhibitor	Melanoma; in clinical trials for various other cancers	Inhibits PD-1 expressed on T cells, and abrogates interaction with PD-L1 on tumour cells and myeloid cells to reverse T cell exhaustion increases tumour-specific CD8 T cell activity and tumour regression in metastatic melanoma patients; highly expressed on Tregs isolated from peripheral blood of MDR-TB patients; in vitro blockade of PD-1 on T cells from TB patients potentiated *M. tb* antigen-dependent IFN-γ secretion; anti-TB treatment success is commensurate with lower PD-1 expression in patients

Table 1 List of immunomodulatory agents for the treatment of multidrug-resistant tuberculosis *(Continued)*

			in MDR-TB patients infected with HIV may aid in management of ART-induced TB-IRIS	
Bevacizumab (anti-VEGF)	Angiogenesis inhibitor	Various cancer types (mostly solid tumours)	Inhibits binding of VEGF-A to its receptor to block signalling and subsequent formation of new blood vessels; bevacizumab inhibited neovascularisation and improved lung pathology in a rabbit model of TB; may also facilitate drug penetration into granulomas and increased oxygenation, with implications for enhancing anti-TB drug efficacy	[79, 144]
Cellular therapy				
Bone marrow-derived mesenchymal stromal cells	Reduction of inflammation and improved tissue regeneration	In clinical trials for various inflammatory indications	Successful phase 1 safety study of mesenchymal stromal cell reinfusion into patients with MDR/ extensively drug resistant-TB in Belarus; showed improved lung radiographic findings, pulmonary function (57 % cure); promoted fine-tuning of T cell responses to specific *M. tb* antigens in recipients; trial is currently being repeated in Durban, South Africa	[112, 114, 145]
Antigen-specific T cells	Targeted killing of *M. tb*-infected host cells	Cancer and viral infections	Currently used in cancer immunotherapy; successfully used in treating post-transplantation opportunistic viral infections, i.e. cytomegalovirus, Epstein–Barr virus	[111–113, 115, 116, 118, 146]

ART **antiretroviral therapy,** ***IRIS*** **immune reconstitution inflammatory syndrome,** ***FAO*** **fatty acid oxidation,** ***HDAC*****, Histone deacetylase inhibitors,** ***MDR*** **multidrug resistant;** ***M. tb Mycobacterium tuberculosis, TB*** **tuberculosis**

Table 2. Patient Characteristics and Type of Tuberculosis in Patients Who Developed Tuberculosis on Infliximab Therapy

Patient no.	Baseline demographic and clinical characteristics							Screening for TB before biologics				Characteristics of TB		
	Age (yr)	Sex	Disease type	Disease location (CD)	Disease behavior (CD)	Past history of TB	ATT before diagnosis of CD	Mantoux	Chest X-ray	IGRA	CECT chest	Site	Duration of IFX at which TB developed (wk)	No. of doses of IFX at which TB developed
1	37	M	CD	L3	B1	No	No	Yes	Yes	No	Yes	PTB	24	5
2	24	F	UC (E2)	-	-	Yes	No	Yes	Yes	Yes	Yes	EPTB	94	14
3	64	M	CD	L3	B2	No	No	Yes	Yes	No	No	Disseminated	14	4
4	28	F	CD	L2	B1	Yes	No	Yes	Yes	No	Yes	Disseminated	6	3
5	15	M	CD	L4	B1	No	No	Yes	Yes	No	Yes	Disseminated	92	13
6	18	M	CD	L1	B2	No	Yes	Yes	Yes	Yes	Yes	Disseminated	14	4
7	25	F	CD	L2	B1	No	No	Yes	Yes	Yes	Yes	EPTB	14	4
8	55	M	CD	L3+L4	B2	No	Yes	Yes	Yes	Yes	Yes	Disseminated	62	10

L1, terminal ileal; L2, colonic; L3, ileocolonic; L4, upper gastrointestinal; B1, inflammatory; B2, stricturing; B3, penetrating.
TB, tuberculosis; ATT, anti-tubercular therapy; IGRA, interferon gamma release assay; CECT, contrast-enhanced CT; IFX, infliximab; M, male; PTB, pulmonary tuberculosis; F, female; EPTB, extra-pulmonary tuberculosis.

Agarwal A,et al. High risk of tuberculosis during infliximab therapy despite tuberculosis screening in inflammatory bowel disease patients in India. Intest Res. 2018 Oct;16(4):588-598.

Risk of Tuberculosis in Patients With Inflammatory Bowel Disease on Infliximab or Adalimumab Is Dependent on the Local Disease Burden of Tuberculosis: A Systematic Review and Meta-Analysis

Saurabh Kedia, MD, DM[1], Venigalla Pratap Mouli, MD, DM[1], Nagesh Kamat, PhD[1], Jeeva Sankar, MD, DM[2], Ashwin Ananthakrishnan, MD, MPH[3], Govind Makharia, MD, DM[1] and Vineet Ahuja, MD, DM[1]

OBJECTIVES: **Infliximab (IFX) or adalimumab (ADA) use in patients with inflammatory bowel disease (IBD) leads to increased risk of tuberculosis (TB). This meta-analysis evaluated the factors which determine this risk, with special focus on local TB incidence.**

METHODS: **All studies until January 31, 2019, which reported the development of TB in patients with IBD on IFX/ADA, were included after searching PubMed and Embase. Data regarding disease type, number of patients on IFX/ADA, number of patients who developed TB, mean age at IFX/ADA initiation, median duration of development of TB, and latent TB (LTB) were extracted. The details on local TB incidence were obtained from the World Health Organization database, and the studies were stratified into low (<10/100,000), intermediate (10–40/100,000), and high TB burden countries (>40/100,000). Random effect meta-analysis was performed to calculate the overall pooled prevalence and prevalence based on local TB burden.**

RESULTS: **Of 130,114 patients (128 studies), 373 developed TB (pooled prevalence: 0.08% [95% confidence interval {CI}: 0.05%–0.10%]). The risk increased with increasing TB burden, pooled prevalence being 0.02% (95% CI: 0.02%–0.03%), 0.21% (95% CI: −0.02% to 0.43%), and 1.59% (95% CI: 1.19%–2.00%) for low, intermediate, and high TB burden countries, respectively. Seventy-three percent of patients who developed TB had no evidence of LTB on screening, the proportion being independent of TB burden. There was no effect of disease or treatment type, study type, gender, age at IFX/ADA initiation, and follow-up duration on TB prevalence.**

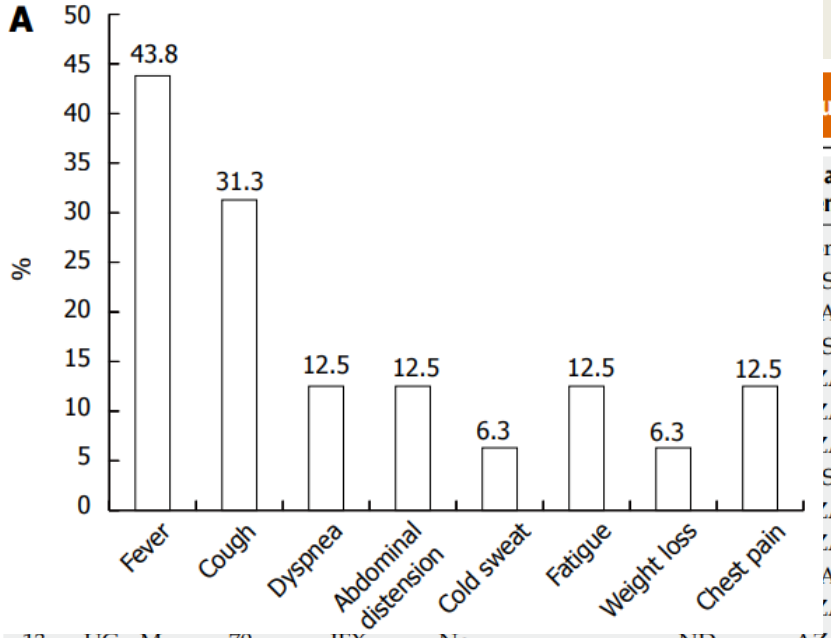
DISCUSSION: **TB risk in patients with IBD on IFX/ADA depends on the local TB burden and is independent of disease/treatment type.**

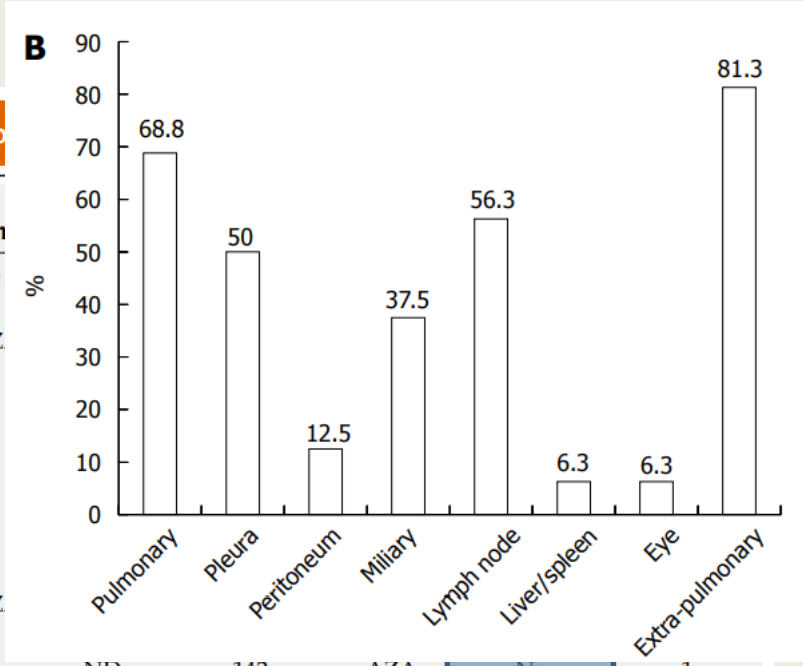
Kedia S. et al. Risk of Tuberculosis in Patients With Inflammatory Bowel Disease on Infliximab or Adalimumab Is Dependent on the Local Disease Burden of Tuberculosis: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2020 Mar;115(3):340-349.

World Journal of Gastroenterology

Significant risk and associated factors of active tuberculosis infection in Korean patients with inflammatory bowel disease using anti-TNF agents

Table 1 Baseline characteristics of patients treated with anti-TNF agent





13	UC	M	70	IFX	No	-	ND	AZA	ND	142	AZA	No	1
14	UC	M	21	IFX	No	-	ND	CS +AZA	ND	52	AZA	Yes	3
15	UC	M	56	IFX	No	-	ND	AZA	ND	47	AZA	Yes	2
16	UC	F	25	IFX	No	+	-	AZA	ND	12	AZA	Yes	2

Original Article

Negative Screening Does Not Rule Out the Risk of Tuberculosis in Patients with Inflammatory Bowel Disease Undergoing Anti-TNF Treatment: A Descriptive Study on the GETAID Cohort

Table 1. Characteristics of patients with inflammatory bowel disease at the time of tuberculosis diagnosis.

Characteristics	*n* [%]
Age	
-range	
-median [years]	
Sex	
-Men	
-Women	
Type of IBD	
-Crohn's disease	
-Ulcerative colitis	
Remission	
-Harvey Bradshaw <4	
-Mayo score[a] <2	
CD location	
-L1	
-L2	
-L3	
-L4	
CD behavior	
-B1	
-B2	
-B3	
-P[b]	
UC location	
-E1	
-E2	
-E3	
Ongoing treatment	
-corticosteroids	
-immunosuppressors	
-azathioprine	
-methotrexate	
-anti-TNF	
-infliximab	
-adalimumab	10 [23%]
-triple immunosuppression	4 [9%]
TB location	
-pulmonary tuberculosis	
-extra-pulmonary	4 [9%]
-pulmonary and extra-pulmonary	19 [43%]
-disseminated	21 [48%]
-extra-pulmonary location:	19 [43%]
-pleural	11
-lymph nodes	23
-peritoneum	6
-pericardium	4
-spleen	3
-liver	1
-joints	1
-bones	1
-ETN	2
-ileo-colic	1
-kidney	1
-jugular-carotid	1
-ophtalmologic	1

Journal of Crohn's and Colitis, 2016, 1179–1185

Biologics for the Management of Inflammatory Bowel Disease: A Review in Tuberculosis-Endemic Countries

Table 2. Summary Data on TB Reactivation with the Use of Anti-TNF Therapies in IBD and Other Rheumatological Conditions

Publication	Brief description of methodology	Country	Key findings
Meta-analyses			
Bonovas *et al*. (2016)[20]	Meta-analysis of 49 RCTs, focused on risk of infections with biologics	NA	Odds of TB numerically higher with biologics vs placebo (OR, 2.04; 95% CI, 0.71–5.89). 9 Cases (0.36%) of TB infection with biologics vs 1 (0.07%) with placebo.
Ford *et al*. (2013)[21]	Meta-analysis of 22 RCTs, focused on risk of opportunistic infections with anti-TNF in IBD	NA	Risk of TB numerically higher with anti-TNF vs placebo (RR, 2.52; 95% CI, 0.62–10.21). 8 Cases (0.2%) of TB infection with anti-TNF vs zero with placebo. All except 1 case occurred in trials that screened patients for exposure prior to entry.
Review			
Cantini *et al*. (2014)[40]	RCTs, PMS, national registries; focused on risk of TB with anti-TNF	NA	Increased risk of TB with any of the 3 anti-TNF drugs. A 3–4 times higher risk with infliximab & adalimumab vs etanercept.
Observational studies from Asian countries (in reverse chronological order)			
Tan *et al*. (2017)[41]	Review of RA patients treated with anti-TNF agents (77%) and other drugs; 2003–2014; n=301	Malaysia	3.7% of the patients developed TB.
Hong *et al*. (2017)[42]	Insurance database analysis; 2011-2013; n=38,830 IBD patients	South Korea	Incidence of TB: 5-ASA (1.44 per 1,000 PY), corticosteroids (2.09), immunomodulators (2.85), anti-TNF (5.54). Incidence of TB significantly higher in those using anti-TNF vs not using anti-TNF (SIR, 6.53; 95% CI, 5.99–7.09).
Puri *et al*. (2017)[43]	Retrospective data analysis; n=79 UC patients treated with infliximab	India	Despite TB screening, 7 (8.8%) patients developed TB. 3 Patients (42%) developed disseminated disease, 4 (57%) developed pulmonary disease.
Jung *et al*. (2015)[39]	Database analysis; 2005–2009; 8,421 patients; 10,021 PY exposure (patients prescribed anti-TNFs)	South Korea	Compared to etanercept (reference), IRR for TB: infliximab (IRR, 6.8; 95% CI, 3.74–12.37), adalimumab (IRR, 3.45; 95% CI, 1.82–6.55). Compared to ankylosing spondylitis (reference), IRR for TB: IBD (IRR, 5.97; 95% CI, 3.34–10.66), RA (IRR, 1.02; 95% CI, 0.57–1.83), and psoriatic arthritis (IRR, 1.00; 95% CI, 0.14–7.30).
Byun *et al*. (2015)[44]	Retrospective cohort study; 2001–2013; n=525 IBD patients	South Korea	Incidence of TB: overall (1.84 per 1,000 PY), anti-TNF-α (4.89 per 1,000 PY), non-anti-TNF-α (0.45 per 1,000 PY). Crude incidence of TB significantly higher in patients receiving TNF-α blockers compared to TNF-α-blocker-naïve patients (3.1% vs 0.3%, p=0.011). LTBI diagnosed in 17 (10.6%) patients; none experienced reactivation of TB.
Cohen *et al*. (2018)[65]	PMS data Review of worldwide tofacitinib PMS data in RA	NA	During a 3-year reporting period covering 34,223 PY, 4,352 SAEs were reported, of which there were 6 TB SAEs.

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REVIEW

Preventive therapy for tuberculosis in rheumatological patients undergoing therapy with biological drugs

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ABSTRACT

Introduction: Latent tuberculosis infection (LTBI) accounts for almost a quarter of the world population, and, in 5–10% of the subjects with impaired immune-response against *M. tuberculosis* growth, it may progress to active tuberculosis (TB). In this review, we focus on the need to propose a screening for LTBI including preventive therapy offer in rheumatic patients undergoing therapy with biological drugs.

Areas covered: We report on evidence that biologics are associated with an increased risk of active TB reactivation. This effect seems to be mainly limited to treatment with anti-tumor necrosis factor (TNF) agents, while non-anti-TNF-targeted biologics are not likely associated to any increased risk. We introduce the concept that the patients' coexisting host-related risk factors, such as comorbidities, are crucial to identify those at higher risk to reactivate TB. We report that preventive TB therapy is well tolerated in patients treated with biological drugs.

Expert commentary: Availability of non-anti-TNF targeted biologics, that are not associated with an increased risk of TB reactivation, offers a great opportunity to tailor a therapeutic intervention at low/absent TB risk. After proper LTBI screening investigations, preventive TB therapy has been demonstrated to be effective and well-tolerated to reduce the risk of TB reactivation in rheumatic patients requiring biological drugs.

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KEYWORDS
Tuberculosis; therapy; preventive therapy; latent tuberculosis infection; TST; IGRA; rheumatological diseases; rheumatoid arthritis

Risk of tuberculosis reactivation associated with traditional disease modifying anti-rheumatic drugs and non-anti-tumor necrosis factor biologics in patients with rheumatic disorders and suggestion for clinical practice

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ABSTRACT

Introduction: Two classes of biologics, anti-tumor necrosis factor (TNF) and non-anti-TNF targeted, are currently available for the treatment of rheumatic diseases.

Areas covered: Discussion on the need for LTBI diagnosis in rheumatic patients treated csDMARDs and non-anti-TNFs through a review of the literature. The literature, updated to 15 April 2019, on tuberculosis (TB) reactivation risk in patients exposed to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and non-anti-TNF biologics was reviewed.

Expert opinion: An increased risk of TB reactivation in patients receiving csDMARDs (except sulphasalazine) resulted, while a review of clinical trials, and Periodic Safety Update Reports from pharmaceutical Companies evidenced a very low or absent risk for non-anti-TNF biologics. Hence, a contradiction emerges considering that latent TB infection (LTBI) screening is recommended for non-anti-TNF candidates but not for csDMARDs. Concerning the low TB incidence countries, several actions could be undertaken, including to screen all patients independently on the treatment, to omit the procedure in non-anti-TNF candidates, or to perform the LTBI investigations only in high-risk patients. According to WHO guidelines, LTBI screening in low TB risk countries seems unnecessary, except in high TB risk subjects.

ARTICLE HISTORY

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LTBI; non-anti-TNF biologics; tuberculosis; csDMARDs

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Isoniazid Prophylaxis for Latent Tuberculosis Infections in Liver Transplant Recipients in a Tuberculosis-Endemic Area

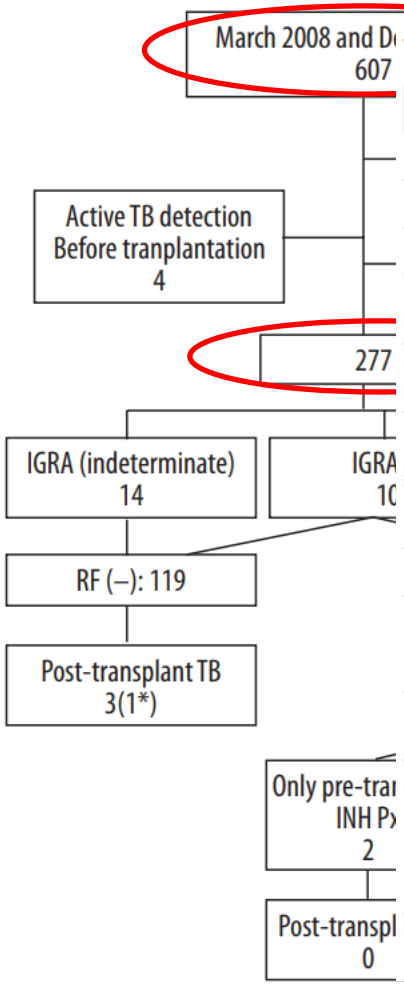

Table 3. Case review of post-liver transplant recipients with active tuberculosis infections.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7*
Age (y)/Sex	55/M	58/F	59/M	71/M	56/M	51/M	50/M
TST	Negative	Positive	Positive	Unknown	Negative	Negative	Negative
IGRA	Positive	Positive	Positive	Positive	Negative	Negative	Negative
Chest XR	Not suspicious TB lesion	Not suspicious TB lesion	Not suspicious TB lesion	Suspicious TB lesion (+)	Not suspicious TB lesion	Not suspicious TB lesion	Not suspicious TB lesion
Chest CT	Not suspicious TB lesion	Not checked	Not suspicious TB lesion	Suspicious TB lesion (+)	Not checked	Not checked	Not suspicious TB lesion
Past history	No	Yes, completely treated	Yes, completely treated	No	No	No	No
INH Px	Not administered	Not administered	Not administered	Not administered	Not administered	Not administered	Not administered
CNI	TAC	TAC	TAC	CsA	TAC	TAC	TAC
Interval between LT and TB detection	5 months	5 months	5 months	2 months	8 months	3 months	1.5 months
Site of TB	Lung	lung, intra-abdominal	Lung	pleural	lung	lung	Graft liver, lung
Anti-TB medication	Surgical treatment was performed; patient refused medication	INH, LVX, PZA, ETB	INH, ETB, PZA, rifabutin	HERZ + rifabutin	LVX + EMB + CS	HER + levofloxacin	ETB + CS + AMK + LVX
Adverse effect of anti-TB drug	None	Blurred vision d/t ETB	Hepatotoxicity	Cytopaenia d/t INH, rifabutin	None	Arthritis	Hepatotoxicity

Screening for Latent Tuberculosis Infection in Solid Organ Transplant Recipients to Predict Active Disease: A Systematic Review and Meta-Analysis of Diagnostic Studies

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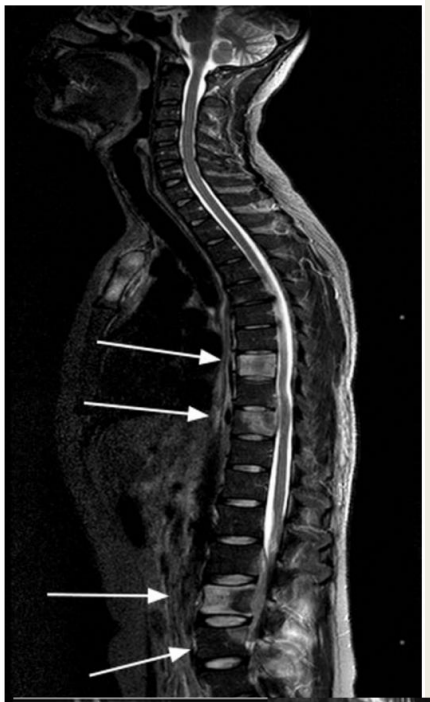
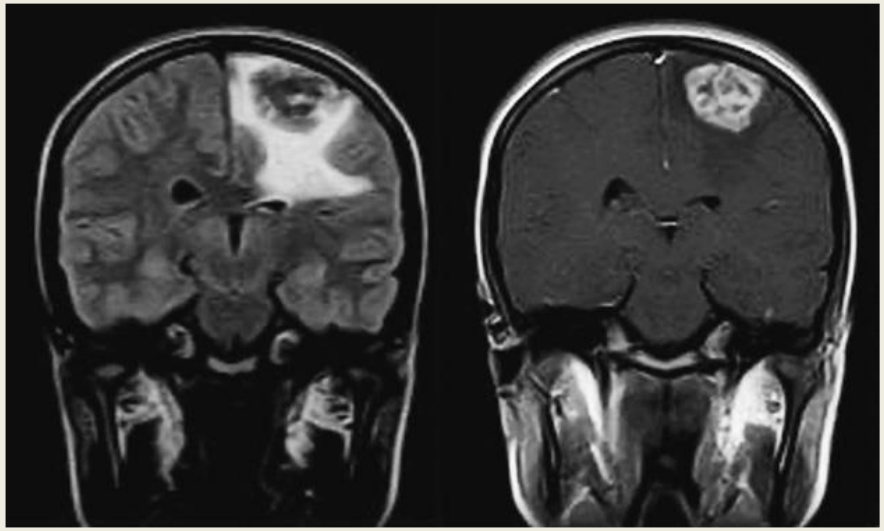
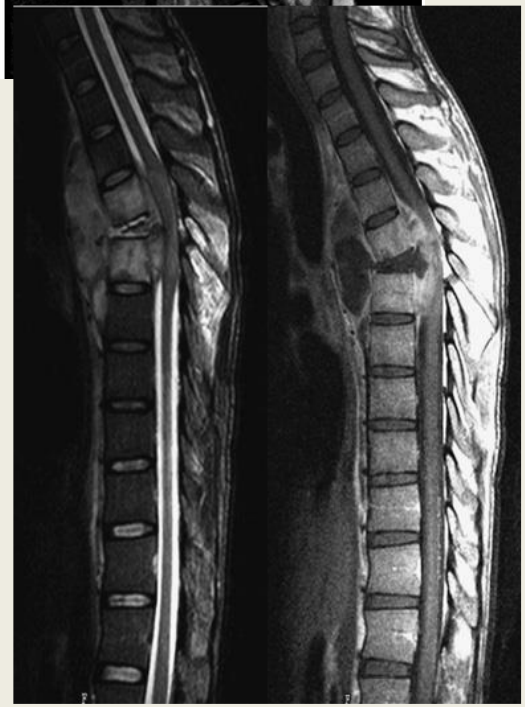
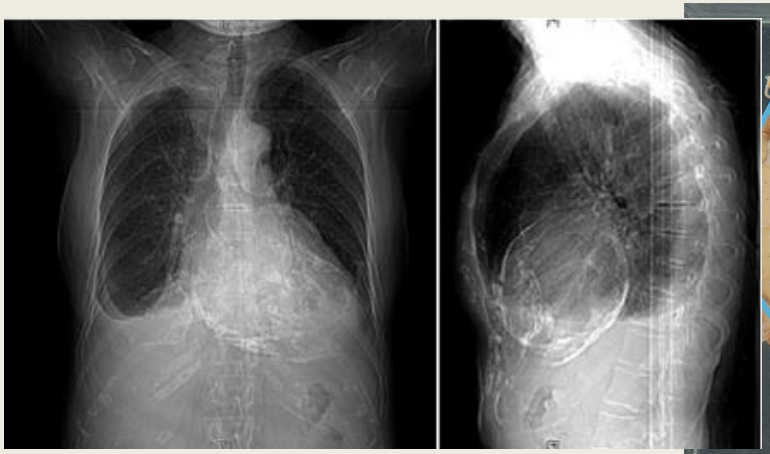
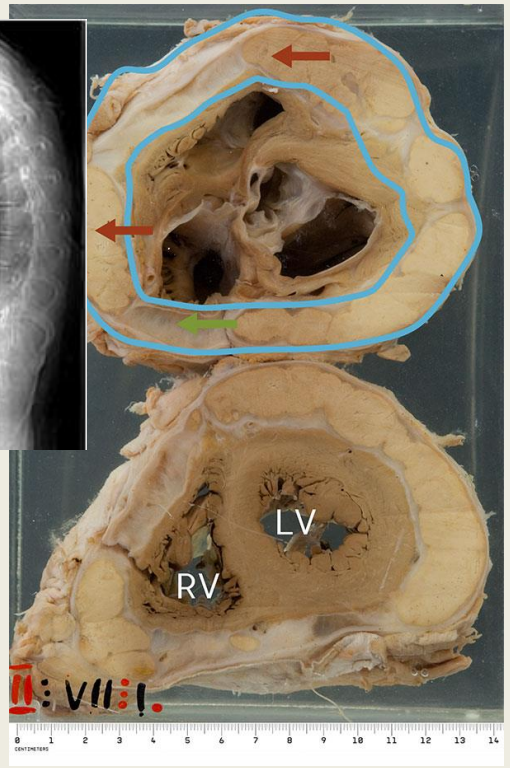
First Author, Year of Publication	Country or Region	TB Burden[a]	Design	LTBI Test	Participants	N	Universal Prophylaxis[b]	N (%) Received Prophylaxis[c]	Follow Up (Month)	N Active TB
Comparative Studies										
Kim, 2013 [19]	South Korea	Low	Prospective	TST vs QFT-GIT	Kidney transplant recipients	109	No	NS	Mean 24.6 (SD 14.4)	1
Ahmadinejad, 2013 [20]	Iran	Low	Prospective	TST vs QFT-GIT	Solid organ transplant candidates	164	No	100% (26/26)	Mean 18 (range 1–36)	0
					Solid organ transplant recipients	40		100% (4/4)		
Kim, 2013 [21]	South Korea	Low	Prospective	TST vs QFT-GIT	Kidney transplant recipients	126	No	0% (0/56)	Median 12.9 (0.4–22.0) after transplantation	0
Sester, 2014 [22]	Europe	Low	Prospective	TST vs QFT-GIT vs T-SPOT.TB	Solid organ transplant recipients	197	No	NS	Median 21.6 (IQR, 24–36)	0
Sherkat, 2014 [23]	Iran	Low	Prospective	TST vs T-SPOT.TB	Kidney transplant candidates	44	No	100% (10/10)	12 (all patients)	1
Muñoz, 2015 [24]	Spain	Low	Prospective	TST vs QFT-GIT	Liver transplant recipients	50	No	0% (0/26)	Median 47.5 (range 35–53.9) after transplantation	1
Torre-Cisneros, 2015 [10]	Spain	Low	Prospective (RCT)	TST vs IGRA	Liver transplant recipients	64	Yes	100% (64/64)	Median 9.3 (range 1.7–18.0)	0
Kim, 2015 [25]	South Korea	Low	Prospective	TST vs T-SPOT.TB	Kidney transplant recipients	312	No	100% (40/40)	Median 14.5 (IQR, 9.9–19.6)	6
Edathodu, 2017 [26]	Saudi Arabia	Low	Prospective	TST vs QFT-GIT	Kidney transplant candidates	278	No	100% (53/53)	Median 25, mean 27 (range 2–58)	0
					Kidney transplant recipients	173				
Ishikawa, 2017 [9]	Japan	Low	Prospective	QFT-GIT vs T-SPOT.TB	Kidney transplant recipients	92	No	NS	Median 33.1 (IQR, 31.5–35.1) after IGRA testing	0
Fitzpatrick, 2010 [27]	USA	Low	Retrospective	TST vs QFT-GIT	Solid organ transplant candidates	83	No	100% (14/14)	Median 11.6 (range 2.2–25.5)	0
Goto, 2010 [28]	Japan	Low	Retrospective	TST vs QFT-GIT	Kidney transplant recipients	100	No	NS	24 for QFT-GIT positive	2
Jafri, 2011 [29]	USA	Low	Retrospective	TST vs QFT	Liver transplant recipients	420	No	60% (15/25)	Mean 34 for recipients with latent tuberculosis	0
Jeong, 2014 [30]	South Korea	Low	Retrospective	TST vs QFT-GIT	Kidney transplant recipients	129	No	NS	Median 8.4 (IQR, 6.8; range 1.1–29.7)	2
Sidhu, 2014 [31]	Canada	Low	Retrospective	TST vs QFT-GIT	Solid organ transplant candidates	461	No	95% (189/200)	Mean 58.8, median 61.2 (a minimum of 12)	0
					Solid organ transplant recipients	123				
Liu, 2014 [11]	China	High	Retrospective	TST vs IGRA	Liver or kidney transplant recipients	1914	No	0% (0/12)	Median 74.4 (IQR, 31.2–141.6) after transplantation	17 (tested, overall there were 45 active TB cases)
Jambaldorj, 2017 [32]	South Korea	Low	Retrospective	TST vs QFT-GIT	Kidney transplant recipients	446	No	0% (0/18)	Median 30.2	3
Moon, 2017 [33]	South Korea	Low	Retrospective	TST vs QFT-GIT	Liver transplant recipients	277	No	50% (19/38)	Median 32.5 (range 1.5–74.2)	7
Noncomparative Studies										
Ravi Shankar, 2005 [12]	India	High	Prospective	TST	Kidney transplant candidates	108	No	0% (0/46)	Transplant recipients: Mean 23.34 (range 20–30)	4
					Kidney transplant recipients	79				
Bravo, 2005 [34]	Spain	Low	Prospective	TST	Lung transplant recipients	187	Yes	82% (50/61) of those with positive TST; 51% (95/187) of the entire cohort	Mean 18.9 (1.7–78.3)	3
Torre-Cisneros, 2009 [2]	Spain	Low	Prospective	TST	Solid organ transplant recipients	4388	No	43% (147/338)	Median 12 (range 0–24)	6







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- Tb kontrol programlarında yer almaması
- Göçmenler
- HIV pandemisi
- İmmünmodülatör ilaçlar
- Akılcı olmayan ab kullanımı

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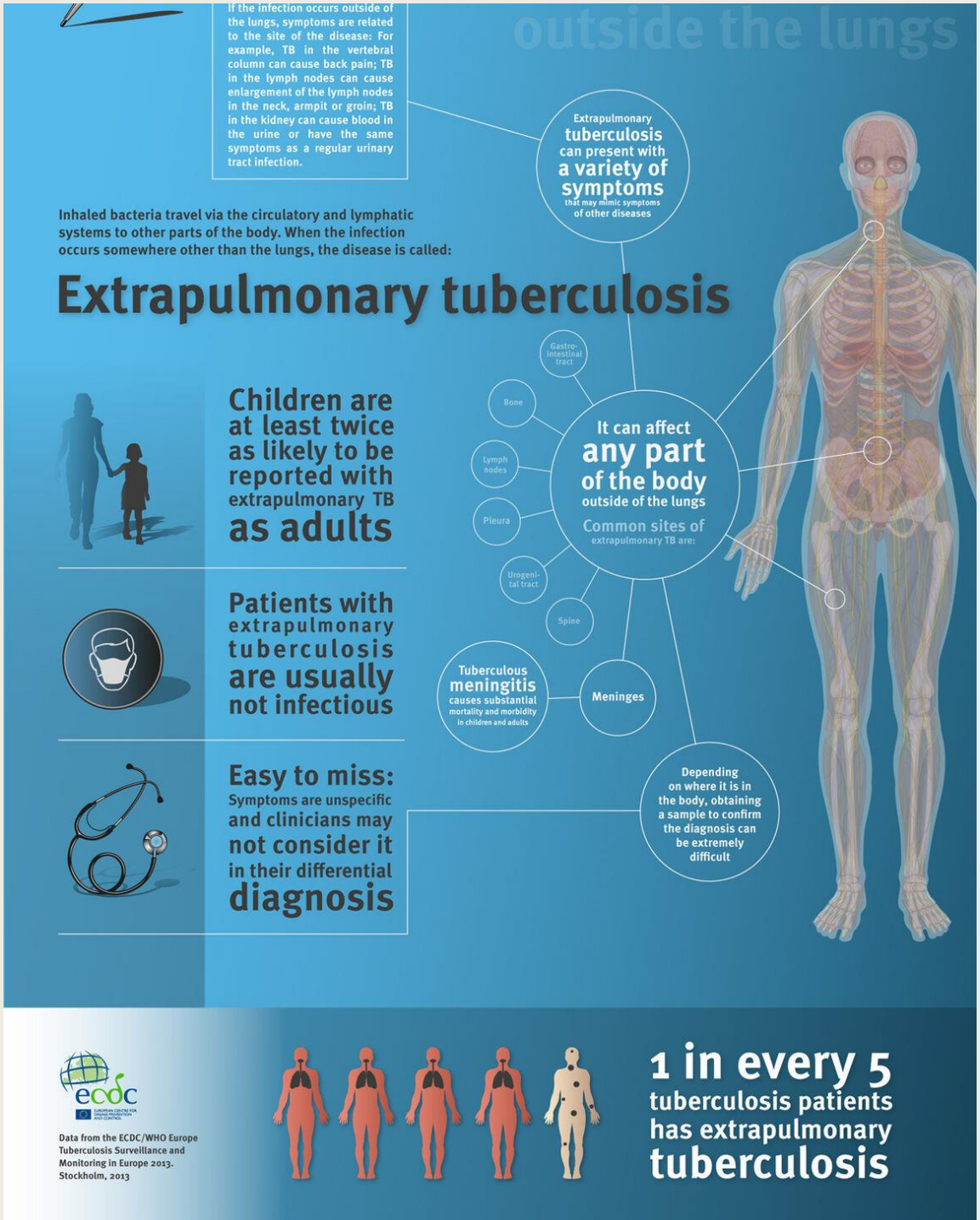
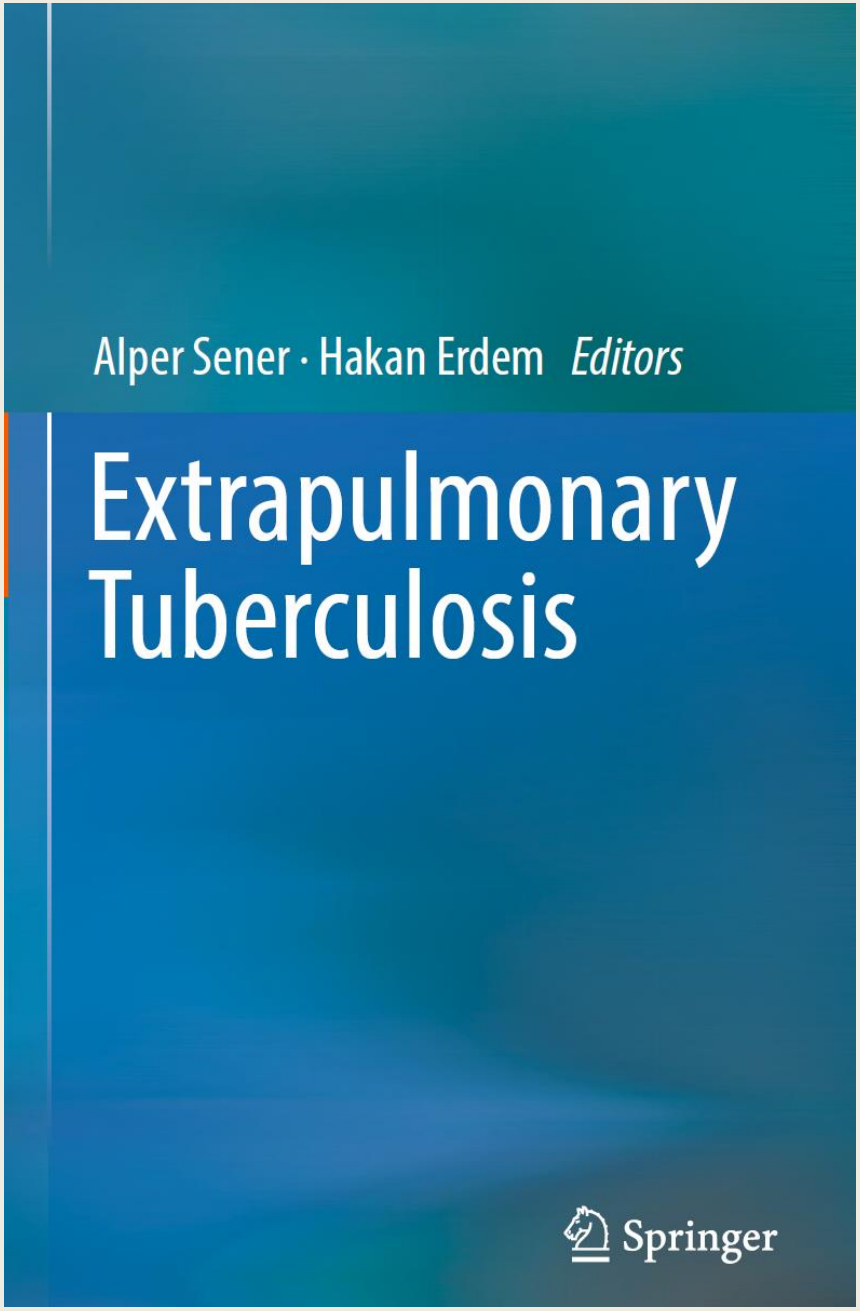


“Nal sesleri duyduğunuzda atları düşünün zebraları değil”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