Nouvelles formes de tuberculoses avec atteinte rénale:

New aspects of tuberculosis involving the kidneys

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Characterization of *Mycobacterium tuberculosis* Complex DNAs from Egyptian Mummies by Spoligotyping

Albert R. Zink,[1] Christophe Sola,[2] Udo Reischl,[3] Waltraud Grabner,[1] Nalin Rastogi,[2] Hans Wolf,[3] and Andreas G. Nerlich[1]*

JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2003, p. 359–367

TABLE 1. Detailed information on the tombs analyzed

Tomb complex[a]	Period of construction[c]	Period of use (approx)	No. of individuals identified[d]	No. of individuals subjected to molecular investigation
TT 196	Middle Kingdom	2050–1650BC	211	37
DAN 95.1	Middle Kingdom	2050–500BC	92	10
DAN 93.11	New Kingdom	1550–500BC	70	10
TT 84	New Kingdom	1550–500BC	20	2
TT 85	New Kingdom	1550–500BC	147	6
TT 95	New Kingdom	1450–500BC	73	10
TT 453[b]	New Kingdom	1450–500BC	33	4
TT 183	New Kingdom	1250–500BC	92	6

1. **Middle Kingdom tomb (used exclusively between ca. 2050 and 1650 BC) suggest that these samples bear an *M. africanum*-type specific signature.**

2. **The samples from later periods provided patterns typical for *M. tuberculosis*.**

3. **In addition, our results do not support the theory that *M. tuberculosis* originated from the *M. bovis* type but, rather, suggest that human *M. tuberculosis* may have originated from a precursor complex probably related to *M. africanum*.**

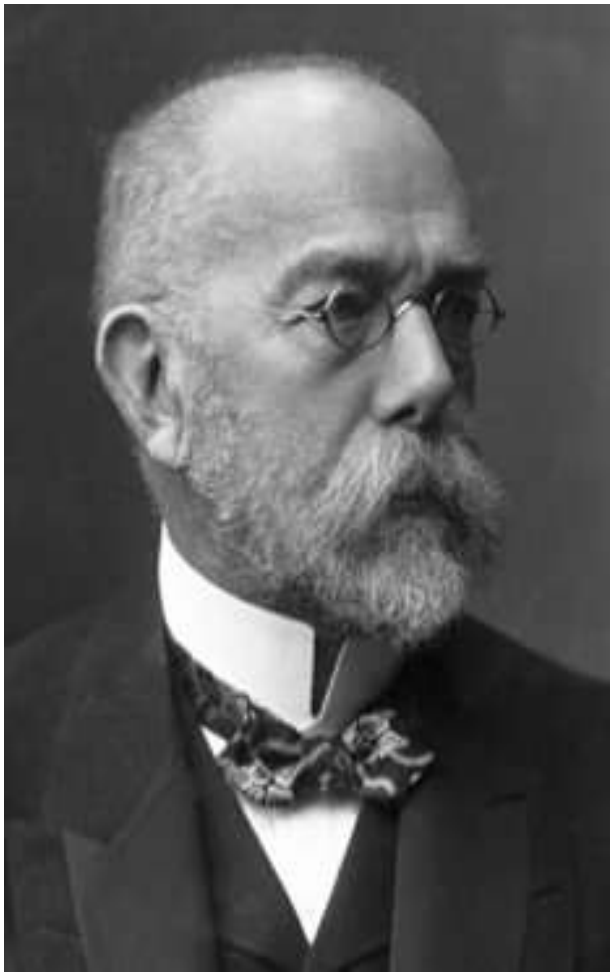
On March 24, 1882, Robert Koch announced to the Berlin Physiological Society that he had discovered the cause of tuberculosis.

Koch R. Die Atiologic der Tuberkulose. Berliner Klinische Wochenschrift 1882; 15:221-30.

In 1890, he announced the discovery of tuberculin, a substance derived from tubercle bacilli, which he thought was capable of arresting bacterial development in-vitro and in animals.

In 1905, when Koch was awarded the Nobel Prize in medicine, he devoted his acceptance speech to promoting greater understanding of tuberculosis and its causative agent.

Koch died in 1910, leaving the scientific community and the world in general with a valuable inheritance of knowledge and understanding resulting from his seminal work on anthrax, cholera, trypanosomiasis, and especially tuberculosis.



Robert Koch
1843-1910

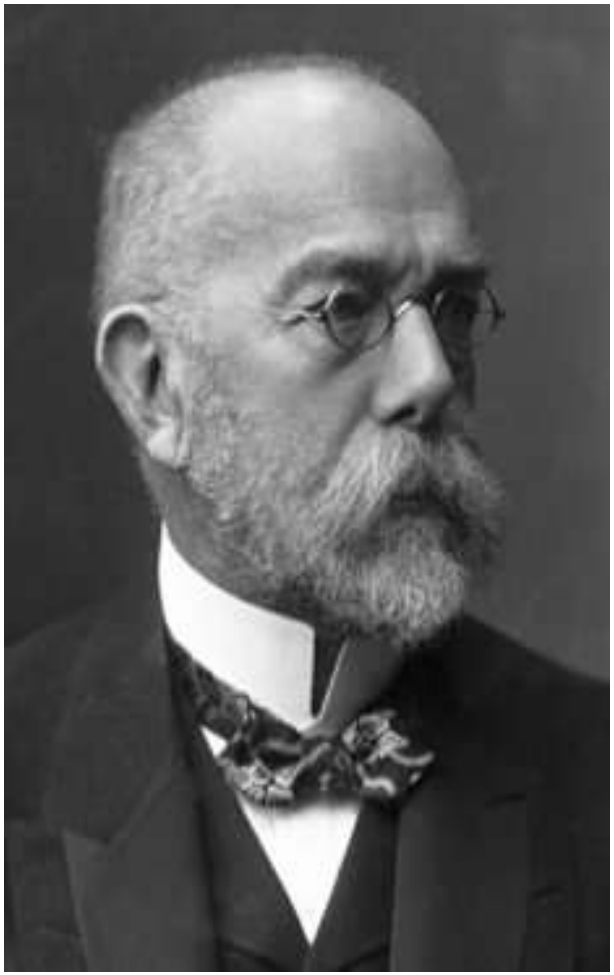
Further developments alongside and post Great Man's Contributions in Tuberculosis

Diagnosis of tuberculosis was aided by discovery of the:

1. **Acid-fast nature of the bacillus by Ehrlich in 1882,**
2. **Discovery of X rays by Roentgen in 1895**
3. **Development of the tuberculin skin test by Von Pirquet and Mantoux in 1907-1908,**
4. **Preparation of purified protein derivative (PPD) of tuberculin by Seibert in 1931.**

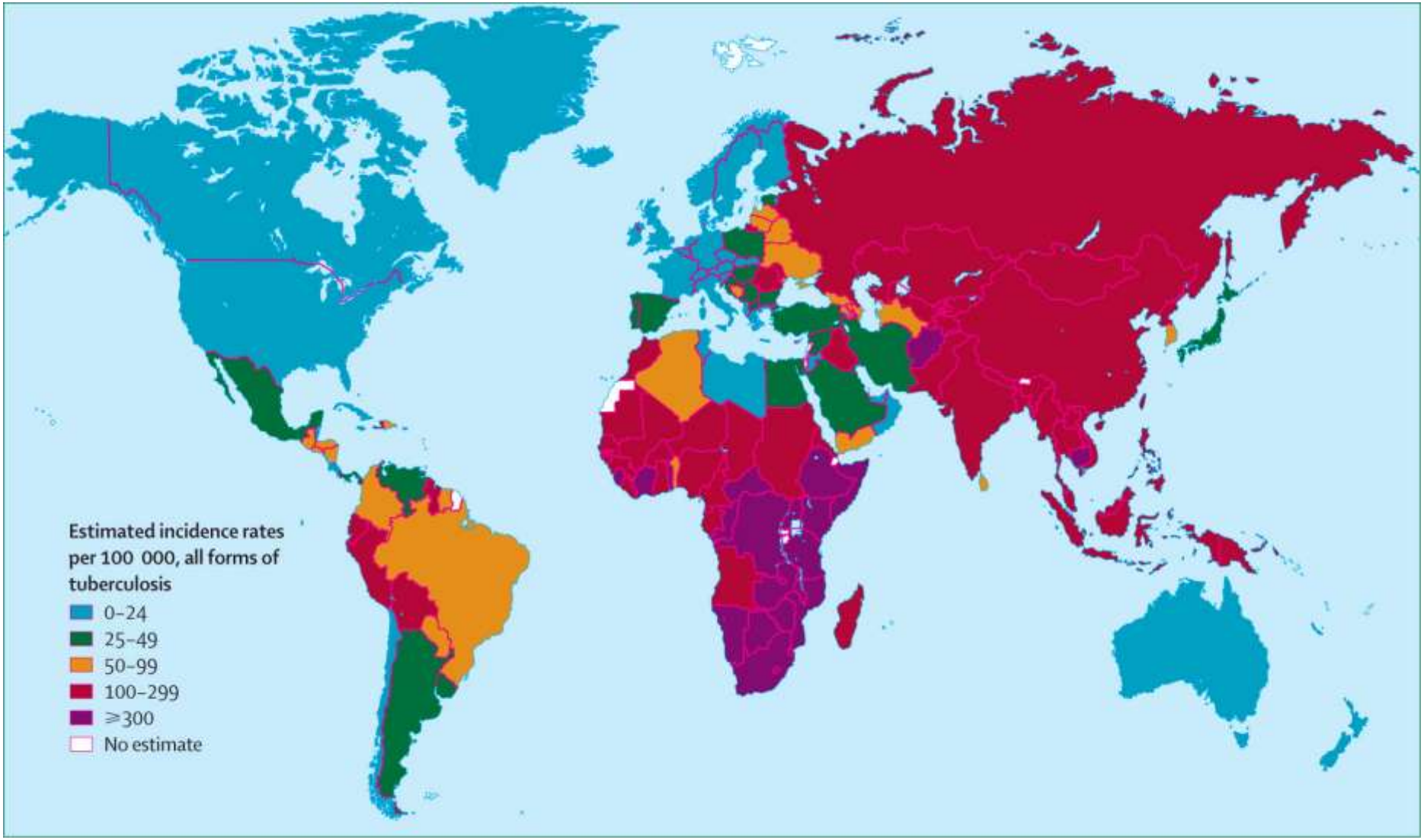
Prevention and treatment of tuberculosis

1. **In 1921, Calmette and Guerin (BCG) developed an attenuated strain of Mycobacterium bovis as a vaccine.**
2. **subclinical tuberculous infection (tuberculous infection without disease) with isoniazid.**
3. **Specific chemotherapy (streptomycin in 1947, para-aminosalicylic acid in 1949, isoniazid in 1952, and in 1965 rifampin.**

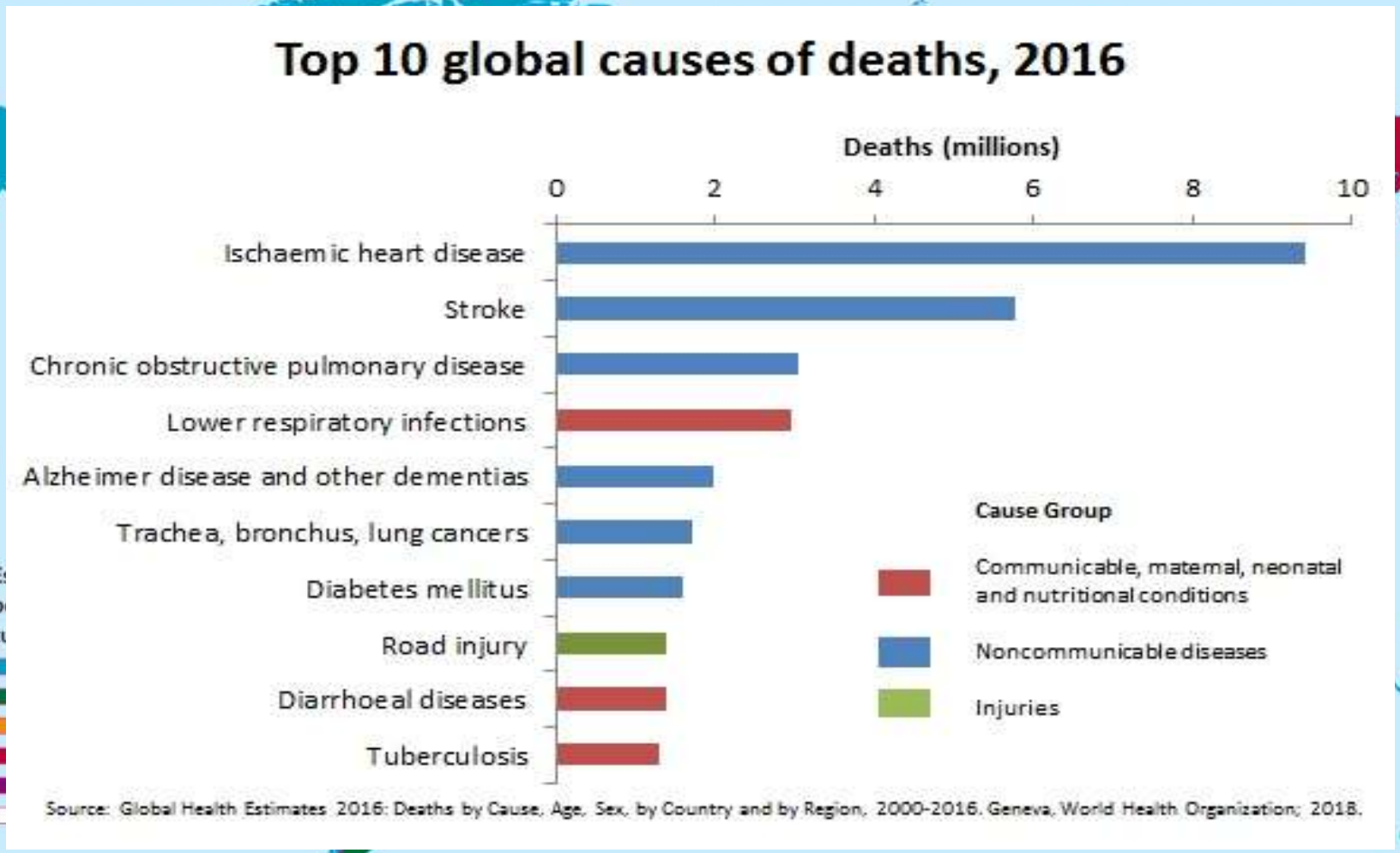


Robert Koch

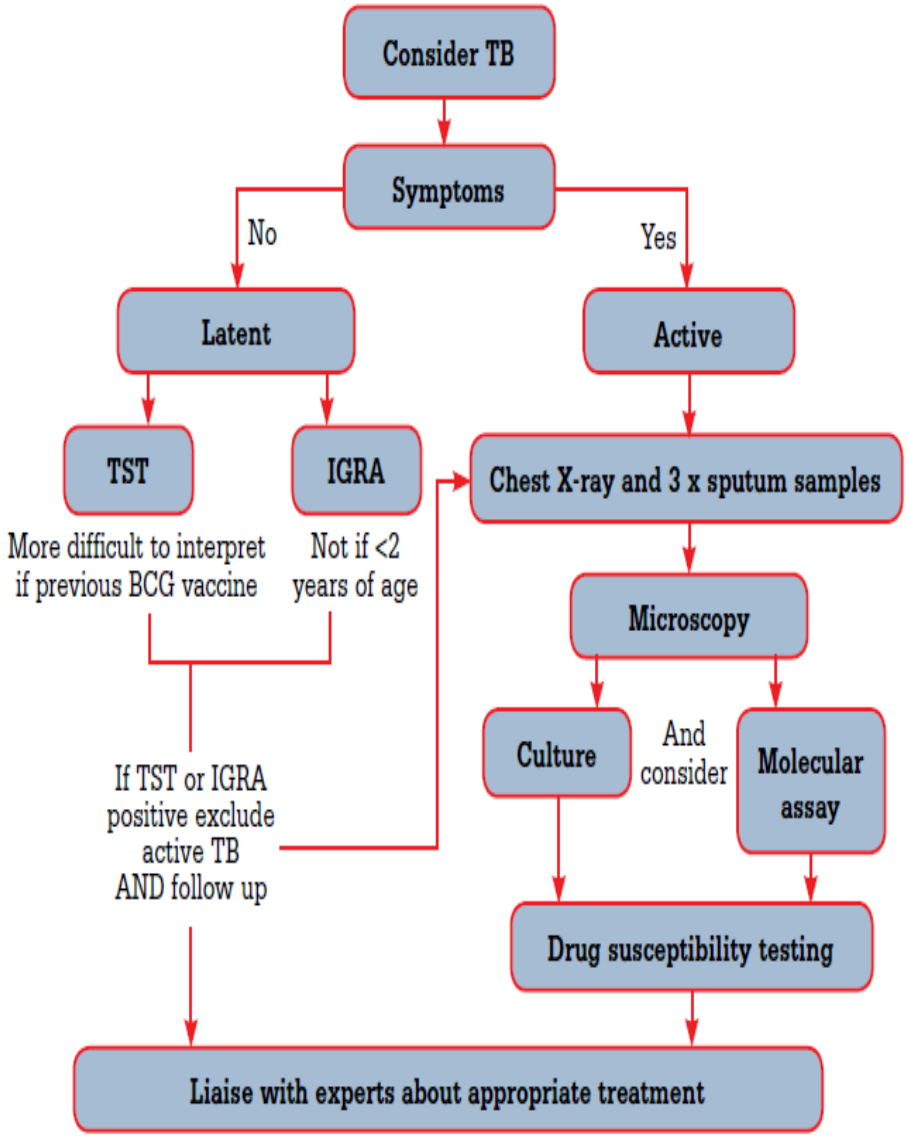
Tuberculosis remains the leading cause of death from CHRONIC infectious disease among adults worldwide, with more than 10 million people becoming newly sick and 1.4 million dying annually



Tuberculosis remains the leading cause of death from an infectious disease among adults worldwide, with more than 10 million people becoming newly sick and 1.4 million dying annually



Diagnosis of Tuberculosis



Molecular technologies for definitive species identification

MALDI-TOF MS

DNA sequencing.

Nucleic acid amplification

allows detection of *Mycobacterium tuberculosis* complex without relying on culture growth.

Gene Xpert MTB/RIF60 and Hain MTBDR plus assays with high sensitivity and specificity enabling rapid diagnosis of rifampicin resistance

Urinary lipoarabinomannan (tuberculosis bacilli antigen) point of care lateral flow assay is a relatively novel addition of a low-cost diagnostic test shown to be useful in people with HIV with a CD4 cell count of less than 200 cells per µL, especially in those who are sputum scarce or smear negative

Drug Resistant Tuberculosis

1. **Drug-resistant TB is caused by TB bacteria that are resistant to at least one first-line anti-TB drug.**

2. **Multidrug-resistant TB (MDR TB) is resistant to more than one anti-TB drug and at least isoniazid (INH) and rifampin (RIF). 0.5 million cases per year**

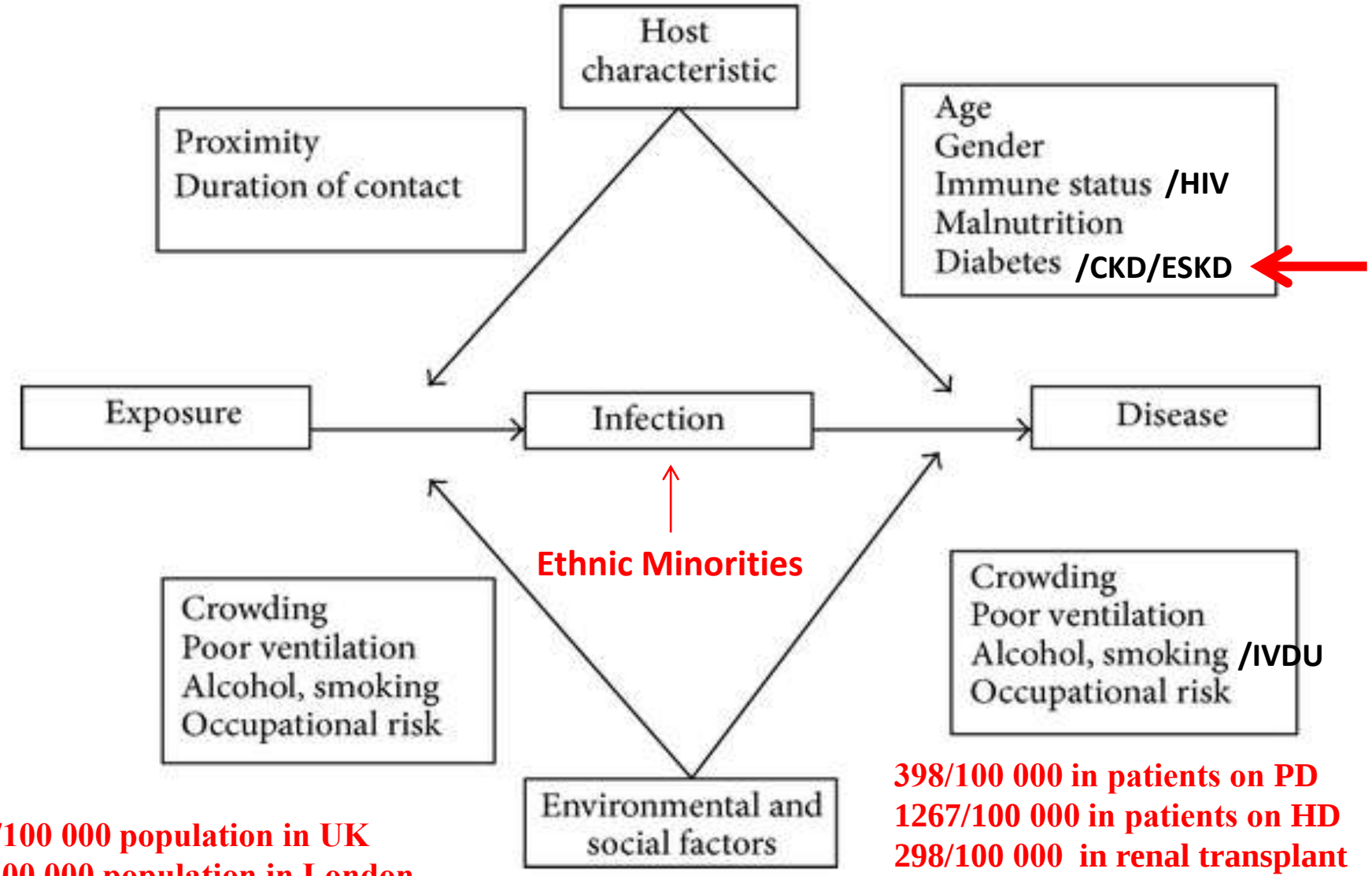
3. **Extensively drug-resistant TB (XDR TB) is a rare type of MDR TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin). 50,000 cases Per year**

4. **Treating and curing drug-resistant TB is complicated. Inappropriate management can have life-threatening results. Drug-resistant TB should be managed by or in close consultation with an expert in the disease**

	Drugs	Comments
Group A	Levofloxacin or moxifloxacin; bedaquiline; linezolid	Include all three medicines (unless they cannot be used)
Group B	Clofazimine; cycloserine or terizidone	Add both medicines (unless they cannot be used)
Group C	Ethambutol; delamanid; pyrazinamde; imipenem-cilastatin or meropenem (both must be given with clavulanic acid); amikacin or streptomycin; ethionamide or prothionamide; para-aminosalicylic acid	Add to complete a four-drug to five-drug regimen and when medicines from groups A and B cannot be used

Table 2: 2018 WHO grouping of medications for second-line drug-resistant tuberculosis[130]

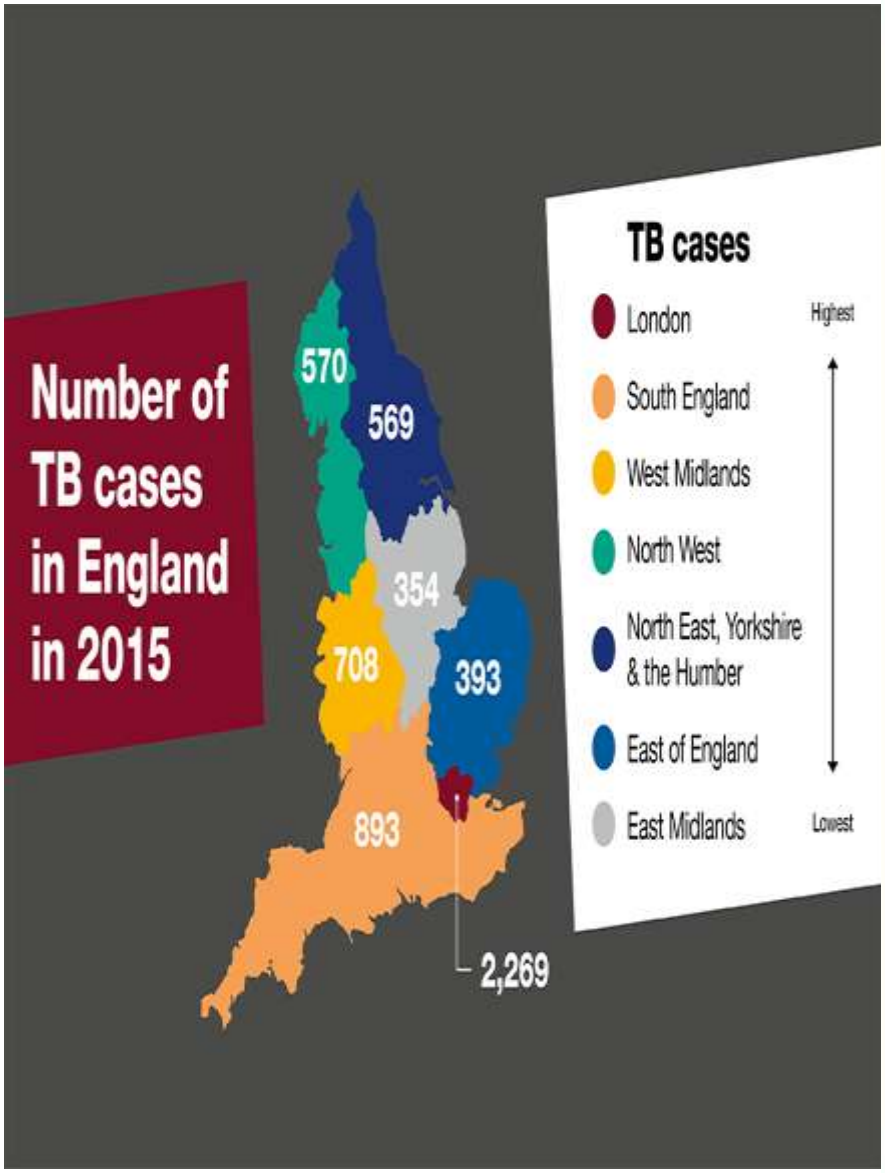
Risk Factors for contracting or reactivation of Tuberculosis

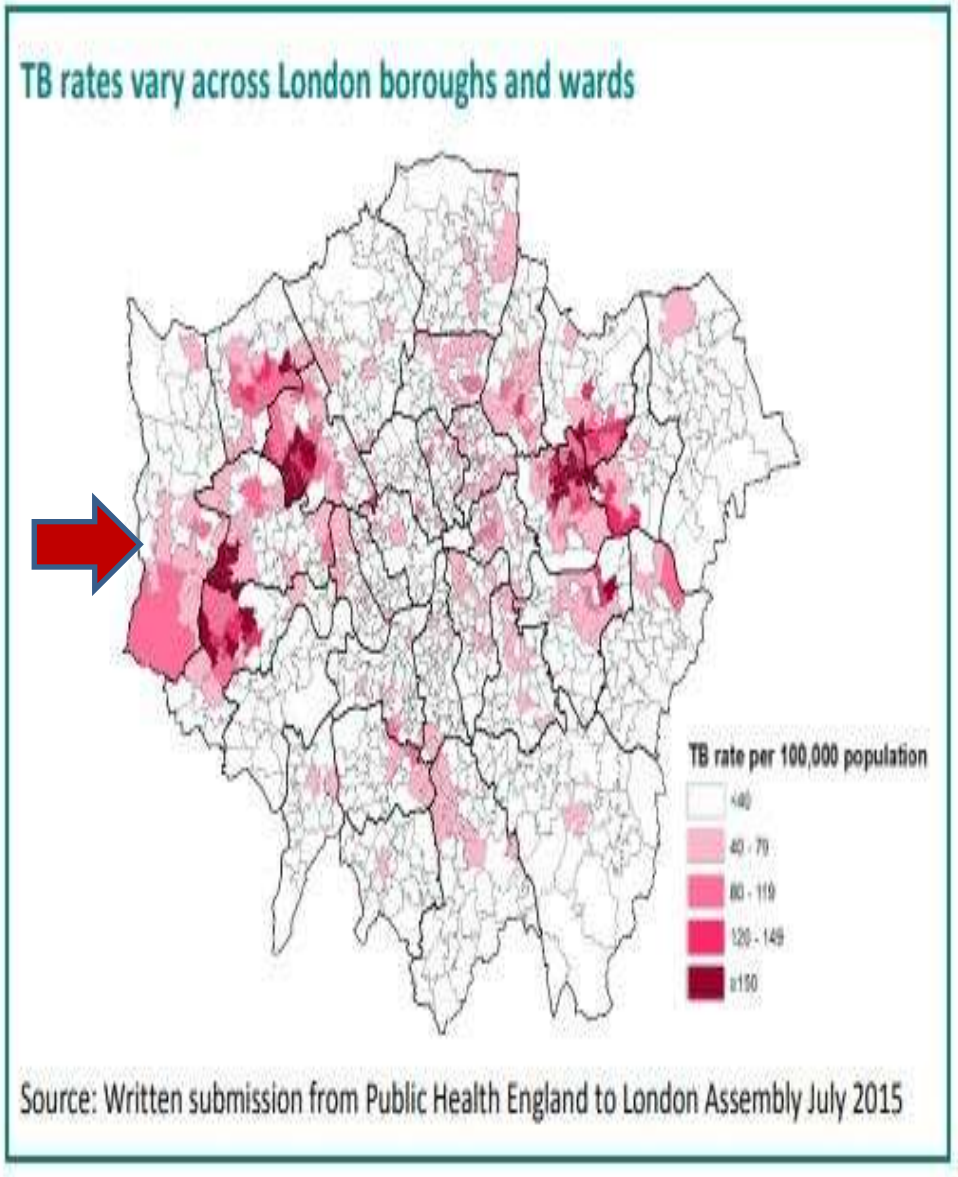


14.9/100 000 population in UK
43/100 000 population in London

398/100 000 in patients on PD
1267/100 000 in patients on HD
298/100 000 in renal transplant recipients.

Incidence of Tuberculosis in UK

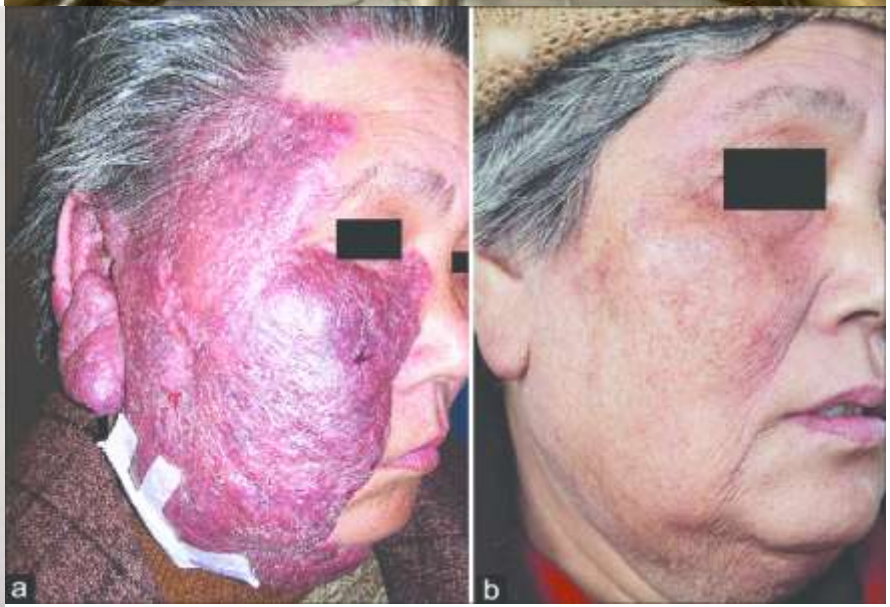




NIELS FINSEN

- ***FATHER OF PHOTOTHERAPY:***

- Won Nobel Prize in Physiology & Medicine in 1903 "In recognition of his contribution to the treatment of diseases, especially Lupus Vulgaris, with concentrated light radiation, whereby he has opened a new avenue for medical science"
- Dr. Finsen's contribution to medicine is unparallel. He treated 300 patients with Lupus Vulgaris and demonstrated, 100% success rates. Today, we have nothing in our arsenal of medications that can produce such results.



Royal London Hospital

Brick Lane

1990

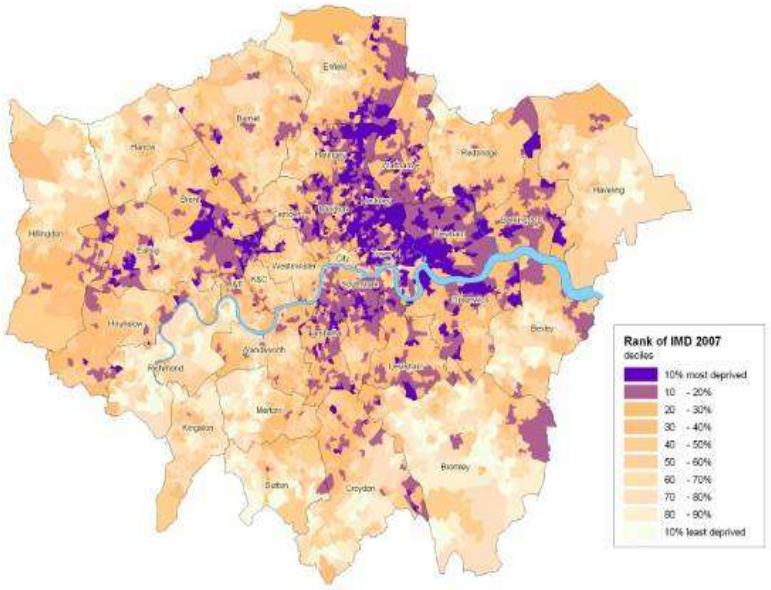
1994-1995

Denver-Colorado, USA to “Bangla Town”-East London, UK

Our population

3.5 million population
African Ancestry: 20%
South Asians 40%

Index of multiple deprivation



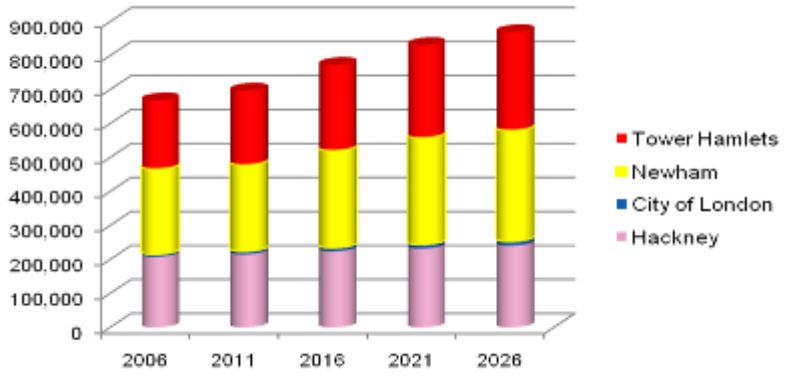
Concentrated deprivation - Hackney second, Tower Hamlets third and Newham sixth most deprived boroughs in the UK

Over half the population is from an minority ethnic background - 38% in City and Hackney, 60% in Newham

A young population - 32% <20yrs; largest group (circa 35%) is 20 -39 yr olds

Significant number of children living in families dependant upon benefits 45.7% in Tower Hamlets (8.4% Richmond)

Rapid population growth - 773,000 residents 2010/11 – more than 869,000 by 2021



Population Growth 2006 – 2026 *(source GLA)*

Wider Determinants of Health

Deprivation
Fourth Highest IMD score in country (80% live in 20% most deprived areas in the country)

Income
67% under 15 live in low income households (highest in the country)

Employment
11% unemployed compared to 7% in London (2007/8)

Education
23% of working age population with no qualifications compared to 12% in London (2008)

Housing
59% council housing, 15% housing association and 33% private rented accommodation classified 'non decent'

Crime
6700 cases of violent crime in 2007/8 – 37% higher than London rate
46% perceive high level of ASB compared to 27% across London

Lifestyle Risk Factors

Smoking
27% smoke compared to 21% nationally (40% in Bangladeshi males), highest death rate attributable to smoking in London)

Alcohol
50% have not had an alcoholic drink in the past year but 40% of white population classified as problem drinkers compared to 20% nationally

Healthy Eating
90% eat less than 5 a day compared to 70% nationally

Physical Activity
18% participate in sport/active recreation compared to 21% nationally. Lowest levels in Bangladeshi females

People who adopt four healthy behaviours would expect to live on average fourteen years longer than those who adopt none (based on EPIC-Norfolk)

4 in 10 of the Tower Hamlets population adopt only one healthy behaviour (mainly alcohol abstinence)


BRICK LANE E.I.
ব্রিক লেন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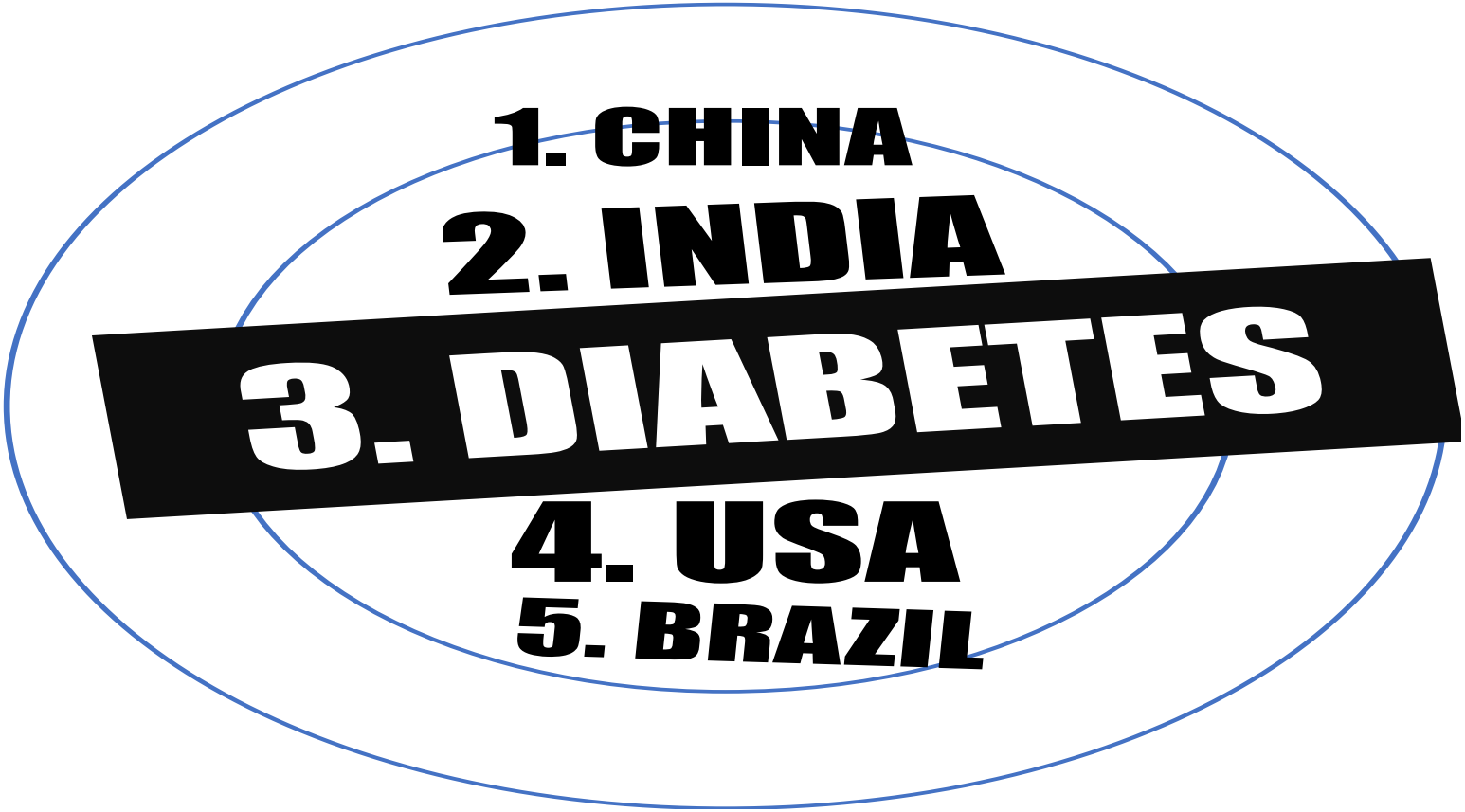
Masala Potato Roll
£5.00
Tikka
£5.00

WORLD'S MOST POPULATED COUNTRIES



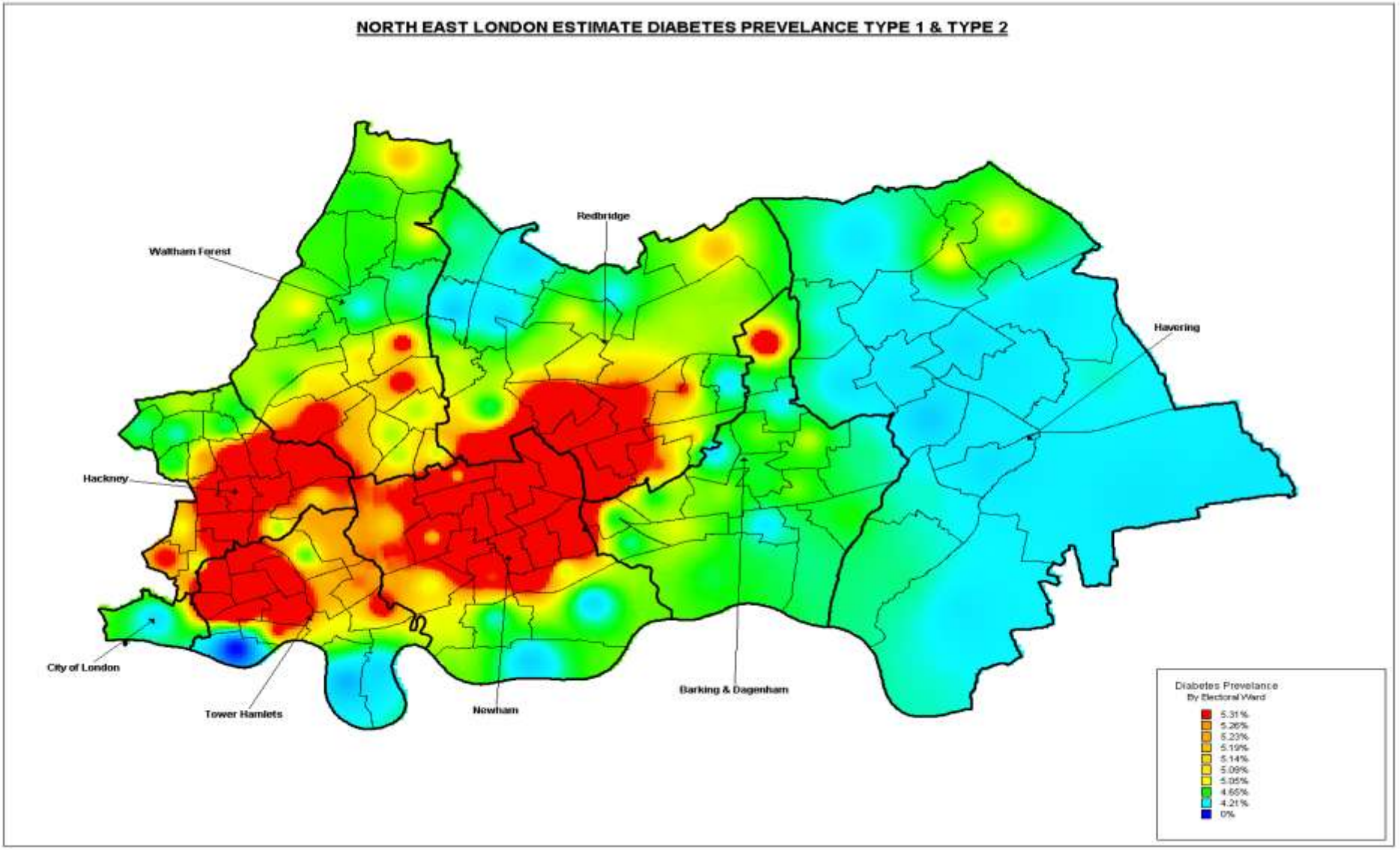
The global economic burden of diabetes in adults aged 20–79 years: a cost-of-illness study

Christian Bommer, Esther Heesemann, Vera Sagalova, Jennifer Manne-Goehler, Rifat Atun, Till Bärnighausen, Sebastian Vollmer

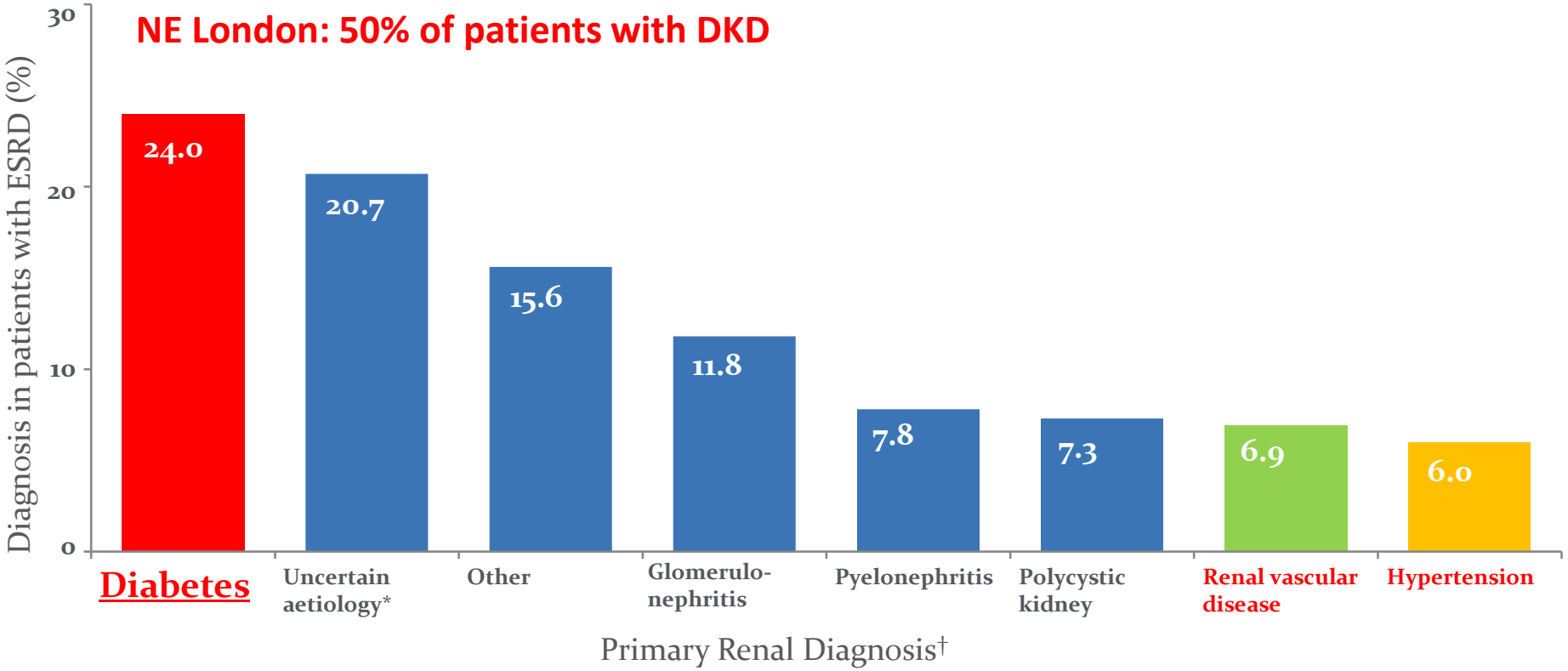
Lancet Diabetes Endocrinol 2017; 5: 423–30

Global cost of diabetes for 2015 was US$1·31 trillion (95% CI 1·28–1·36) or 1·8% (95% CI 1·8–1·9) of global gross domestic product (GDP).

Diabetes in NE London



The most common cause of renal failure in most Western Countries



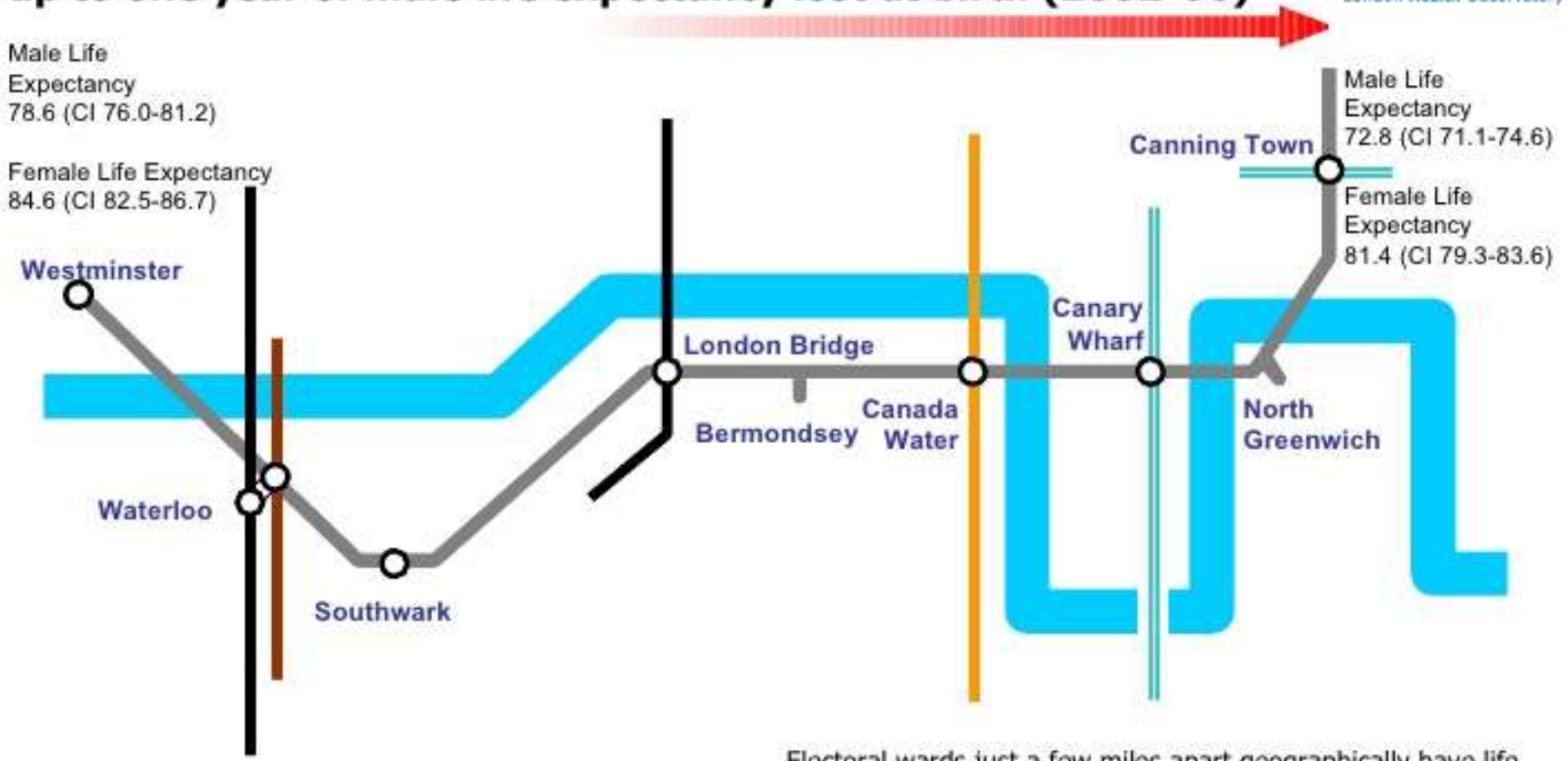
*Includes presumed glomerulonephritis not biopsy proven.
† Figures shown are calculated excluding data not available. Data for primary renal diagnosis (PRD) missing in 10.8% of patients. In centres with >25% missing PRD data, percentages in the other diagnostic categories not calculated. Centres with very high rates of uncertain diagnosis also excluded.

Adapted from: The Renal Association. UK Renal Registry. Twelfth Annual Report 2009.

The Jubilee Line of Health Inequality

Travelling east from Westminster, each tube stop represents up to one year of male life expectancy lost at birth (2002-06)

London Health Observatory



London Underground **Jubilee Line**

Electoral wards just a few miles apart geographically have life expectancy spans varying by years. For instance, there are eight stops between Westminster and Canning Town on the Jubilee Line – so as one travels east, each stop, on average, marks up a year of shortened lifespan. [1]

[1] Source: Analysis by London Health Observatory using Office for National Statistics data revised for 2002-06. Diagram produced by Department of Health

Quarterly Journal of Medicine, New Series 74, No. 273, pp. 105–109, January 1990

Bovine Genitourinary Tuberculosis Revisited

MUHAMMAD YAQOOB, HENRY JOHN GOLDSMITH, and RASHEED AHMAD

From the Regional Renal Unit, Sefton General Hospital/Royal Liverpool Hospital, Liverpool

Pasteurization obligatory 1945

Heating Milk till 71 degree centigrade for 15 seconds

Named after French scientist Louis Pasteur

Still Raw Milk is sold in many parts of world

Presentation, diagnosis, and treatment outcome of tuberculous-mediated tubulointerstitial nephritis

Ananda Chapagain[1], Hamish Dobbie[1], Michael Sheaff[2] and Muhammad M. Yaqoob[1]

Kidney International (2011) **79,** 671–677;

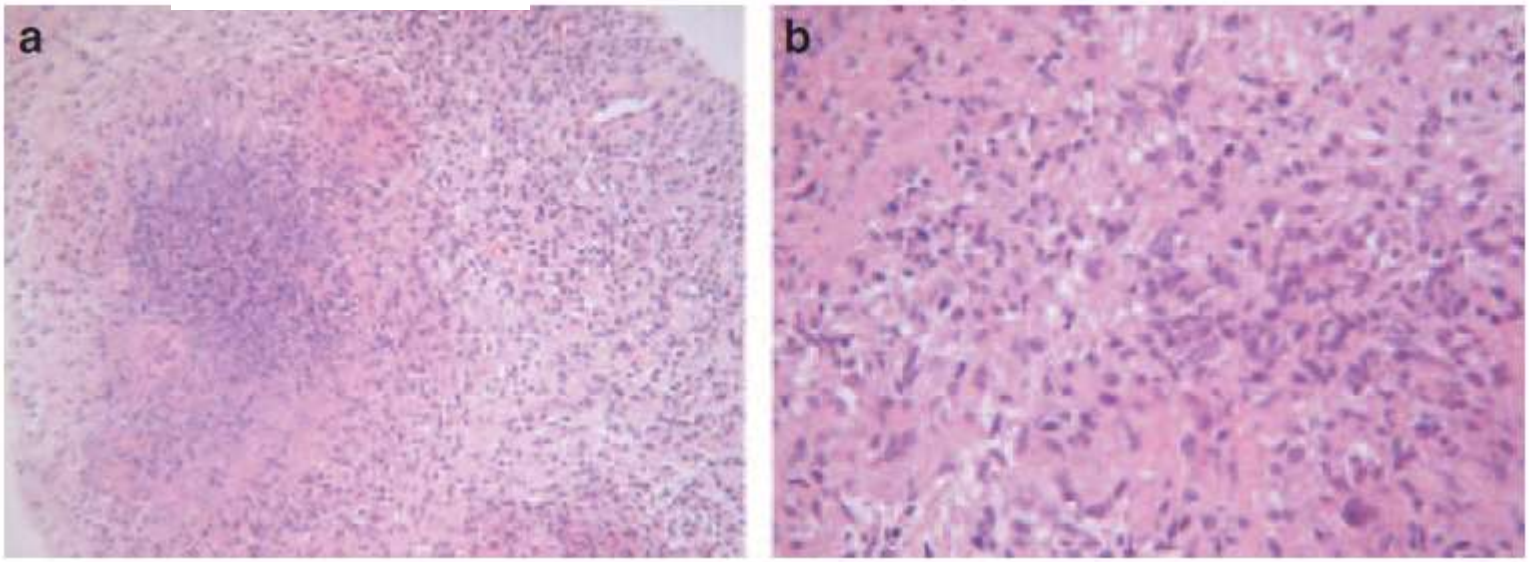
Table 1 | Demographics of patients with tubercular interstitial nephritis

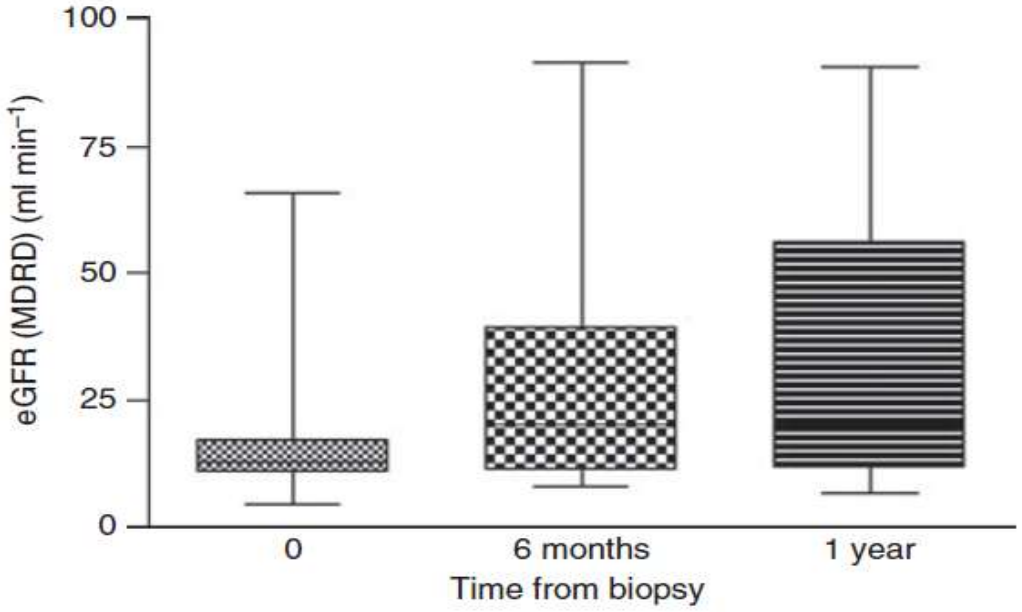
Parameter	Value
Median age (range)	40 (20–75)
Male gender (%)	44
Race and country of birth	
Black/African	6
Somalia	3
Zambia	1
Uganda	1
Ethiopia	1
Indo-Asian	19
South Asian	13
Kenya	3
United Kingdom	3
Median follow-up (range)	36 months (6–72 months)

South Asian patients included patients born in India, Pakistan, and Bangladesh.

Caseating granuloma

Langhans giant cell formation.





4 patients with ESKD

9 patients ESKD from 2 to 5 years

Sarcoid tubulo-interstitial nephritis: Long-term outcome and response to corticosteroid therapy

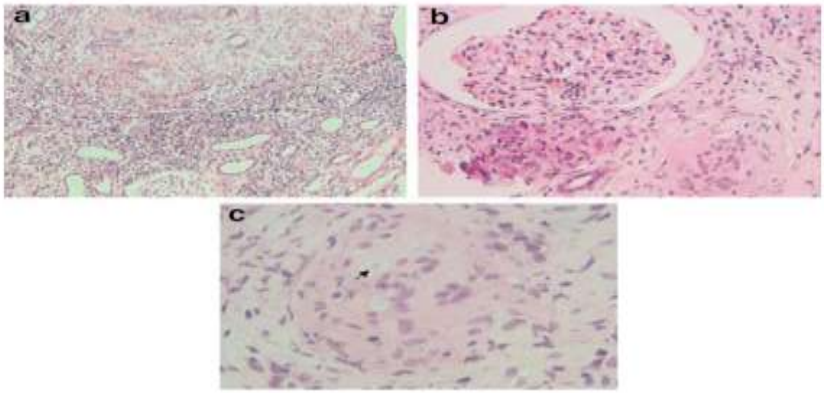
R Rajakariar[1,3], EJ Sharples[1,3], MJ Raftery[1], M Sheaff[2] and MM Yaqoob[1]

Kidney International (2006) **70,** 165–169.

Table 1 | Demographics of patients with confirmed sarcoid interstitial nephritis on renal biopsy

		%
Age	44±15.8	
Sex		
Male	8	47
Female	9	53
Race		
Black	9	53
White	6	35
Indo-Asian	2	12
Clinical features		
Chest	8	47
Lymph nodes	4	24
Uveitis	6	35
Hypercalcemia	4	24
Elevated SACE	3	18
Creatinine (mean±s.d.)	366±299 μmol/l	
eGFR (mean±s.d.)	26.8±14 ml/min	
Follow-up (mean±s.d.)	88±73	

SACE, serum angiotensin-converting enzyme; eGFR, estimated glomerular filtration rate; s.d., standard deviation.



DIFFERENCES BETWEEN GRANULOMA OF TB and SARCOIDOSIS

	TUBERCULOSIS	SARCOIDOSIS
EPITHELOID CELLS	PRESENT	PRESENT
NECROSIS	COMMON	ABSENT
CONFLUENT GRANULOMA	USUAL	DISCRETE
GIANT CELLS	MULTIPLE	FEW
RETICULIN IN GRANULOMA	LOST	PRESERVED
AFB	MAY BE PRESENT	ABSENT

Sarcoid tubulo-interstitial nephritis: Long-term outcome and response to corticosteroid therapy

R Rajakariar[1,3], EJ Sharples[1,3], MJ Raftery[1], M Sheaff[2] and MM Yaqoob[1]

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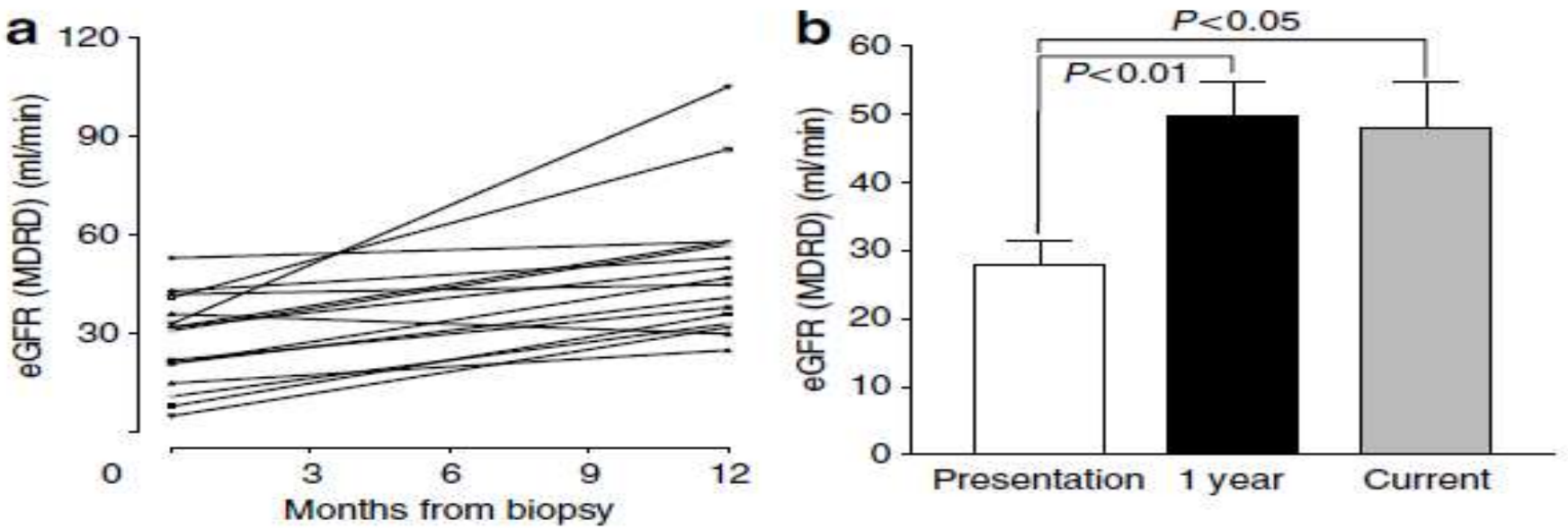


Figure 3 | Response to corticosteroid treatment. (**a**) Individual eGFRs at presentation and at 1 year in patients with sarcoid TIN. (**b**) Mean eGFR at presentation, 1 year and at last follow-up in the same group. The mean eGFR improved from 26.8 ± 14 to 49.6 ± 5.2 ml/min ($P < 0.01$) at 1 year, and 47.9 ± 6.8 ml/min ($P < 0.05$) at last follow-up.

Progression of chronic kidney disease in a multi-ethnic community cohort of patients with diabetes mellitus

G. Dreyer[1], S. Hull[2], R. Mathur[2], A. Chesser[1] and M. M. Yaqoob[1]

Diabet. Med. 30, 956–963 (2013)

Total population with diabetes in 2010
n = 48 406

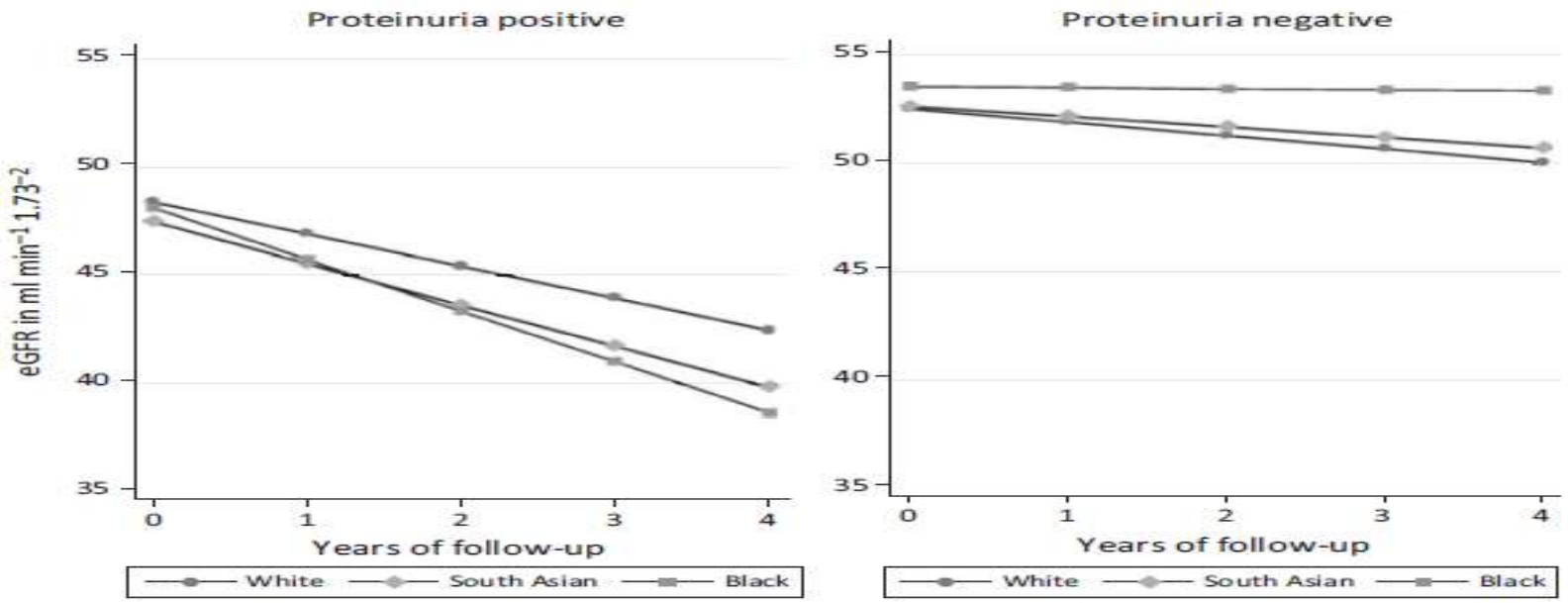
Included in the study analysis
n = 3855 (95.3%)

eGFR < 60

White
n = 1509 (39.1%)

South Asian
n = 1725 (44.7%)

Black African/Caribbean
n = 621 (16.1%)



Accelerated Decline of GFR in Diabetic Nephropathy Predicted by Interferon Release Assay to Tuberculosis Antigens

Catherine Lane[a] Anthony Ashcroft[b] Graham Bothamley[b] Magdi M. Yaqoob[a]
Stanley L.-S. Fan[a]

Nephron Clin Pract 2011;117:c266–c269

Table 1. Comparison of characteristics of QFT-positive and QFT-negative diabetic patients: mean (SEM) values

	QFT-positive	QFT-negative	Significance (t test)
Patients, n	18	20	–
Age, years	73.0 (1.67)	65.5 (2.57)	NS
Proportion ethnic origin non-white	0.71 (0.11)	0.74 (0.10)	NS
Systolic BP, mm Hg	135 (4)	138 (4)	NS
Diastolic BP, mm Hg	74 (2)	78 (3)	NS
MAP, mm Hg	95 (2)	98 (2.7)	NS
Presenting GFR, ml/min	21.2 (2.7)	28.9 (4.7)	NS
Serum 25-vitamin D, nM	24.3 (12.3)	31.9 (14.0)	NS
CRP, mg/l	4.22 (2.02)	7.90 (2.92)	NS
HbA1c, %	7.85 (0.49)	7.55 (0.41)	NS
Total cholesterol, mM	3.88 (0.23)	3.91 (0.17)	NS
Protein:creatinine ratio mg/mmol	498 (167)	246 (61.8)	NS
Number treated with ACEi/ARB	14	14	NS
Number treated with statins	16	15	NS

Nephron Clin Pract 2011;117:c266–c269

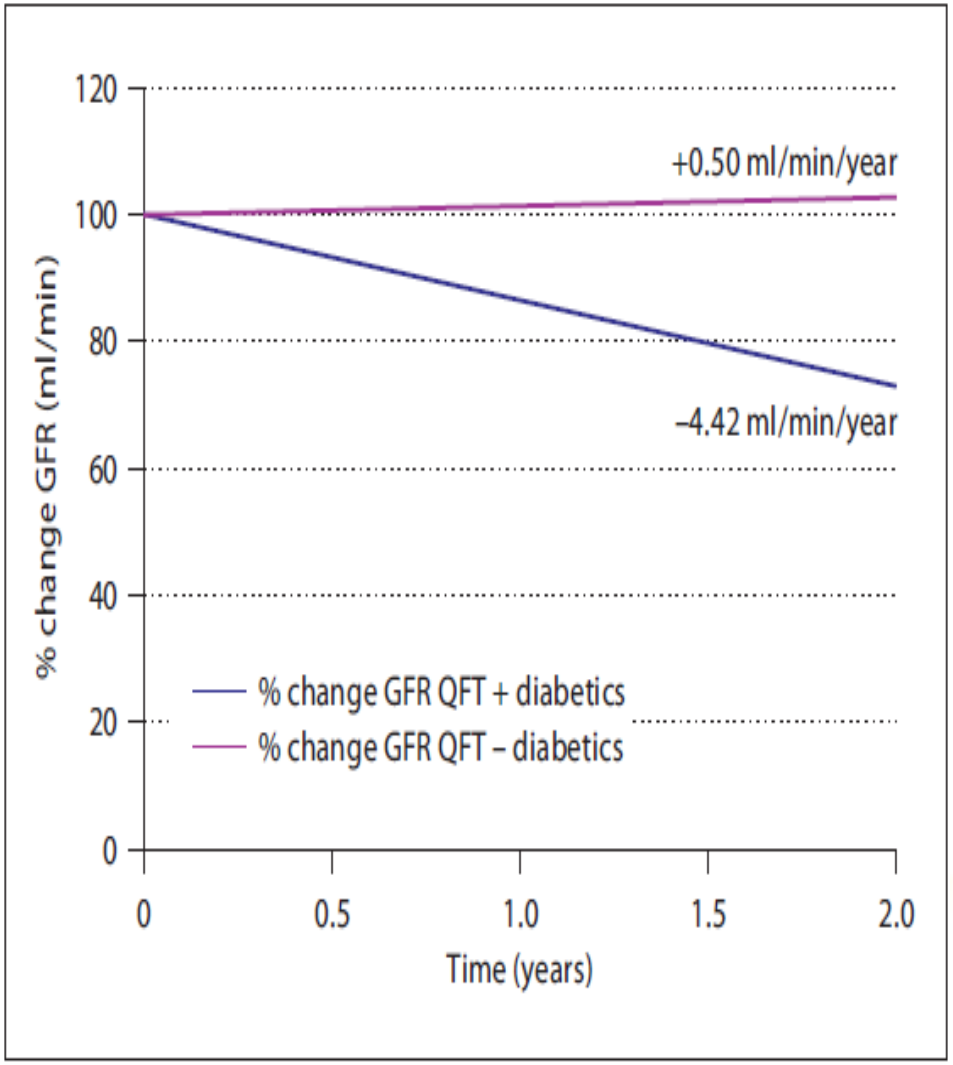


Table 2. Multivariate general linear model examining factors that might affect rate of change of eGFR

Source	Type III sum of squares	d.f.	Mean square	F	p
MAP, mm Hg	0.410	1	0.410	1.512	0.229
HbA1c, %	0.034	1	0.034	0.125	0.727
T-chol, mM	0.244	1	0.244	0.899	0.351
Age, years	0.475	1	0.475	1.755	0.196
QFT positivity	1.168	1	1.168	4.311	0.048
Use of ACEi/ARB	0.109	1	0.109	0.402	0.531

BMJ open
accessible medical research
2013;3:e001855.

A cohort study on the rate of progression of diabetic chronic kidney disease in different ethnic groups

Omer Ali,[1] Atif Mohiuddin,[1] Rohini Mathur,[2] Gavin Dreyer,[1] Sally Hull,[2] Muhammad M Yaqoob[1]

Table 3 Adjusted linear regression for annual change in eGFR (n=329)

	Annual change (ml/min/1.73^2)	95% CI	p Value
Predictor variables			
Years of follow-up (slope in reference pop)	−1.93	−2.31 to −1.56	<0.001
Coefficients for ethnicity interaction (additional decline in ml/min/1.73^2 per year)			
Additional decline in Black population	−0.19	−0.68 to 0.30	0.438
Additional decline in south Asian population	0.08	−0.31 to 0.48	0.676
Time-varying variables			
BP ≤ 130/80 mm Hg × time in years	0.62	0.27 to 0.98	<0.001
HbA1c ≤ 7.5%×time in years	0.03	−0.33 to 0.39	0.883
Constant variables			
Ethnicity (White is reference category)			
Black ethnicity	−1.67	−4.97 to 1.64	0.322
South Asian ethnicity	−0.51	−3.25 to 2.23	0.716
Age	0.03	−0.06 to 0.13	0.466
Gender (female is reference category)	−2.64	−4.87 to −0.40	0.021
SBP target at baseline	−2.31	−3.89 to −0.73	0.004
HbA1c value at baseline	−0.66	−2.37 to 1.06	0.454
Vascular disease ever (PVD, CVD, IHD)	−1.44	−3.66 to 0.79	0.206
Drug treatment ever (ACE, ARB, dual block)	0.02	−4.46 to 4.50	0.993
Proteinuria at baseline (PCR>15)	0.173	−1.99 to 2.33	0.875
Baseline eGFR	1.05	0.99 to 1.11	<0.001
Constant	−3.18	−11.26 to 4.89	0.440

The annual decline in the reference population (White) is −1.93 ml/min.
The annual decline in Black patients is −2.12 ml/min.
The annual decline in south Asian patients is −1.85 ml/min.

NIELS FINSEN

- ***FATHER OF PHOTOTHERAPY:***

- Won Nobel Prize in Physiology & Medicine in 1903 "In recognition of his contribution to the treatment of diseases, especially Lupus Vulgaris, with concentrated light radiation, whereby he has opened a new avenue for medical science"
- Dr. Finsen's contribution to medicine is unparallel. He treated 300 patients with Lupus Vulgaris and demonstrated, 100% success rates. Today, we have nothing in our arsenal of medications that can produce such results.

Science

AAAS

Toll-Like Receptor Triggering of a Vitamin D-Mediated Human Antimicrobial Response

Philip T. Liu *et al.*

Science **311**, 1770 (2006);

DOI: 10.1126/science.1123933

High-dose vitamin D_3 during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial

Lancet 2011; 377: 242–50

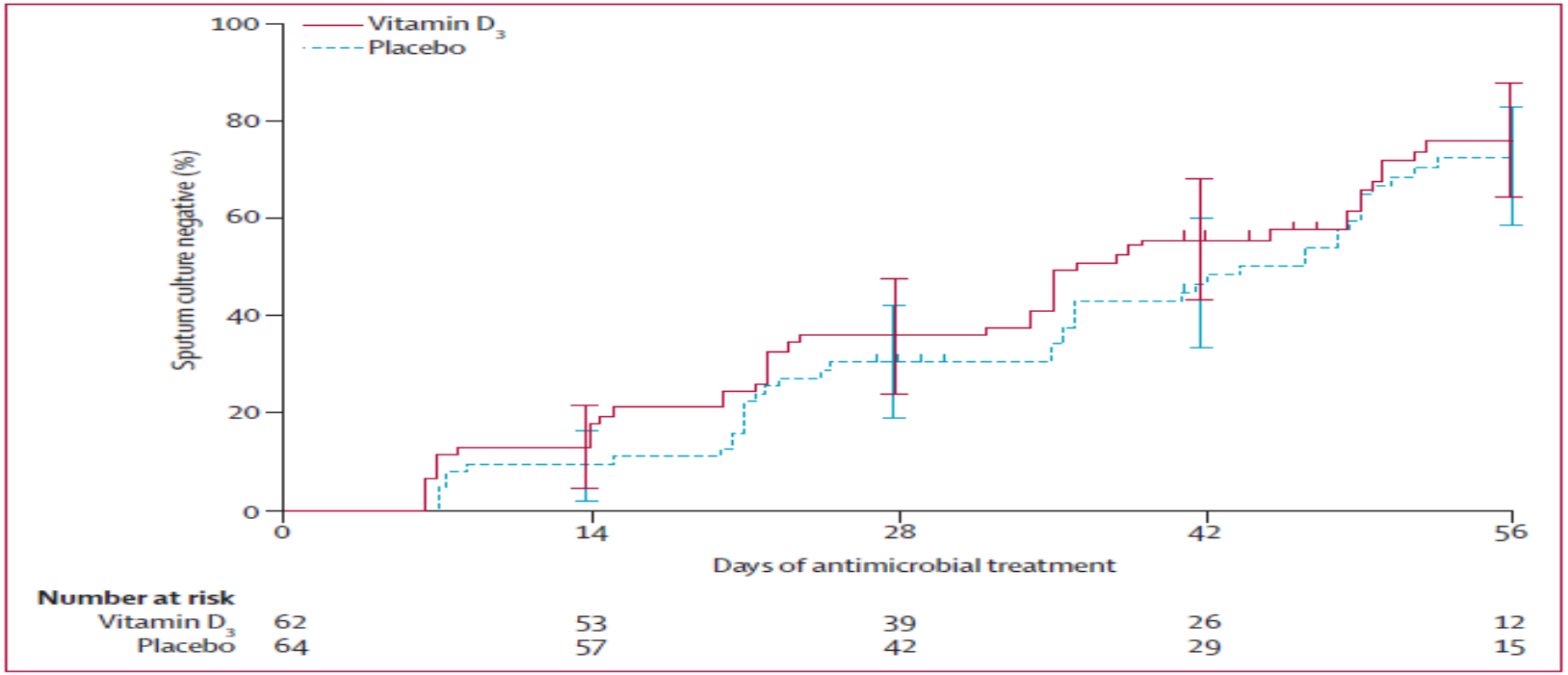
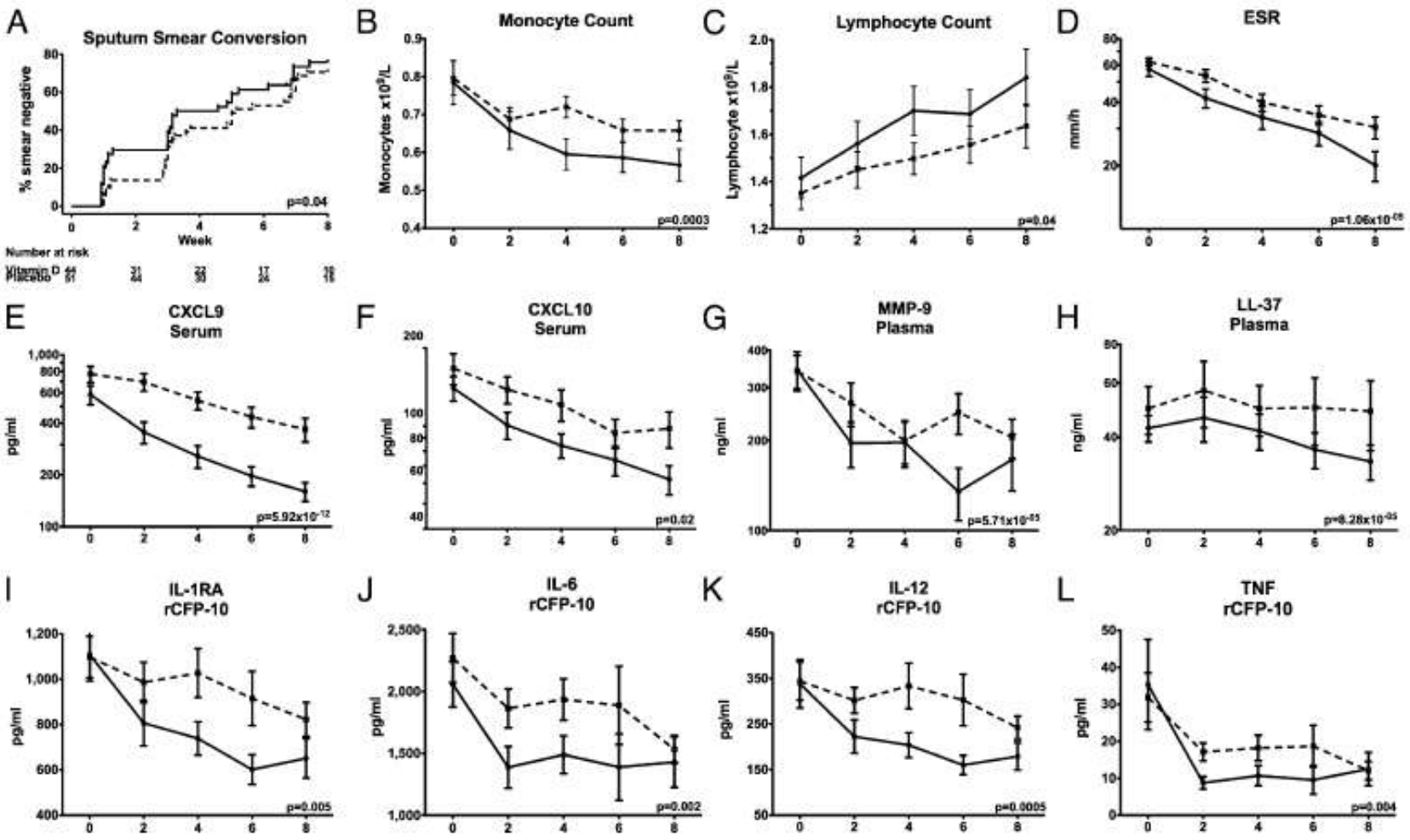


Figure 2: **Time to sputum culture conversion by allocation**
Error bars, 95% CI. Numbers of patients with positive sputum culture remaining in follow-up (number at risk) at 0, 14, 28, 42, and 56 days are shown.[27]

Interpretation Administration of four doses of 2·5 mg vitamin D_3 increased serum 25-hydroxyvitamin D concentrations in patients receiving intensive-phase treatment for pulmonary tuberculosis. Vitamin D did not significantly affect time to sputum culture conversion in the whole study population, but it did significantly hasten sputum culture conversion in participants with the *tt* genotype of the *TaqI* vitamin D receptor polymorphism.

Vitamin D accelerates resolution of inflammatory responses during tuberculosis treatment

www.pnas.org/cgi/doi/10.1073/pnas.1200072109



Nouvelles formes de tuberculoses avec atteinte rénale:

New aspects of tuberculosis involving the kidneys

THANK YOU