The role of pharmacology in TB treatment and research: experience from Bandung, Indonesia

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LIV TB
Liverpool TB Research Group
VIRTUAL SESSION!

Rovina Ruslami, MD, PhD
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Indonesia TB Research Network (*JetSet TB* Indonesia)

Thursday 16th June 2022, 12.00 – 13.00
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The role of pharmacology in TB treatment & research

Speaker: Rovina (Nina) Ruslami is an internal medicine specialist and clinical pharmacologist from Faculty of Medicine, UNPAD, Bandung, Indonesia. She is the head of the Dept. of Biomedical Science in FoM UNPAD. Her teaching focused on pharmacology, clinical pharmacology, research methodology, and research ethics. Started form her PhD at Radboud UMC Nijmegen, the Netherlands 18 years ago, she continues working focusing on pharmacology of anti-TB treatment. She acts as principle investigator for several international studies. Currently she is the head of Indonesia TB Research Network, called as "*JetSet (Jejaring Riset = research network) TB Indonesia*. Since 2018, she also works voluntarily for the International Union Against Tuberculosis and Lung Disease (The Union) as the scientific liaison for the TB Section, and starting 2021 as the TB Conference Programme Lead.

Topic: Nina will be presenting the overview of pharmacology of TB treatment and the importance of pharmacokinetic studies as the path to TB elimination, its historical background, existing condition with regards to TB treatment, and new insight about optimizing TB treatment by understanding pharmacology of anti TB drugs, especially rifampicin, the cornerstone for TB treatment. She will share several works on different type of Tuberculosis: TB Meningitis, TB Infection, and Pulmonary TB. She will also highlight the importance of research collaboration in providing best evidence, transfer knowledge, and in building professional as well as academic capacity.

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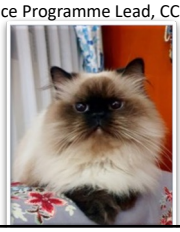
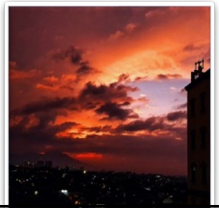
Who am I?

- Name : Prof. Rovina Ruslami, MD, PhD
- Occupation : Faculty of Medicine, UNPAD, Dept. of Biomedical Sciences, Division of Pharmacology & Therapy
- Office : Jl. Prof. Eijkman no. 38, Bandung
- E-mail address : rovina.ruslami@unpad.ac.id

- **Education & Training:**
  - 1991 Medical Doctor FoM Unpad, Bandung
  - 2001 Internal Medicine specialist FoM Unpad, Bandung
  - 2009 PhD in Clinical Pharmacology Radboud University Nijemegen, The Netherlands
- **Position:**
  - 2010 - present TB-HIV Research Group
  - 2012 - present Head of Dept. of Biomedical Sciences, Div of Pharmacology & Therapy
  - 2012 - present Health Research Ethics Committee, FoM, Unpad
  - 2015 - present Member of Tuberculous Meningitis International Research Consortium
  - 2017 - present Member of JetSet TB (Indonesian TB Researcher Netwrok)
  - 2018 - present Member of A-TRACTION (Asian Tuberculosis Research and Clinical trial Organisational Network)
  - 2018 - 2021 Scientific Liaison of the TB Section, The Union
  - 2021 – present Conference Programme Lead, CCSA, The Union

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Where do I work?




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Tuberculosis at glance

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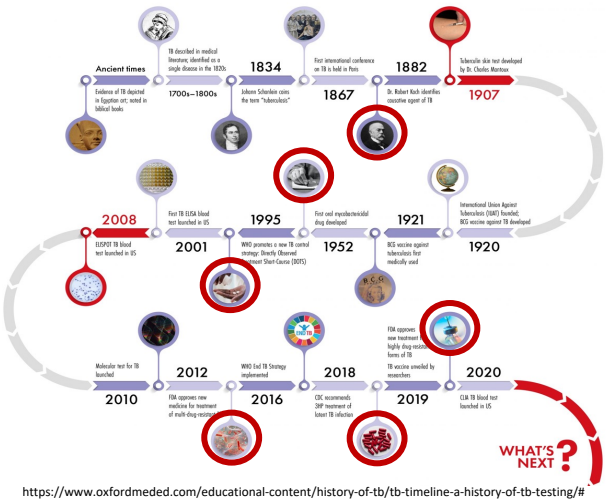
A History of Tuberculosis: From Ancient Times to Today



https://www.oxfordmeded.com/educational-content/history-of-tb/tb-timeline-a-history-of-tb-testing/#

A very old disease

Treatment:

- It took ~50 years to find the first TB drug - since the agent (*M.tb)* was identified

Before that? …it's a plague: a white plague

- It took another 40 years until TB treatment being implemented.
- Treatment: complex & long → *not user-friendly*
- After that…less and less enthusiasm in finding new drug for TB (*very expensive*)
  - More for resistant-TB
  - Novel regimen instead of new drugs (using available drugs with different dose and/combination)

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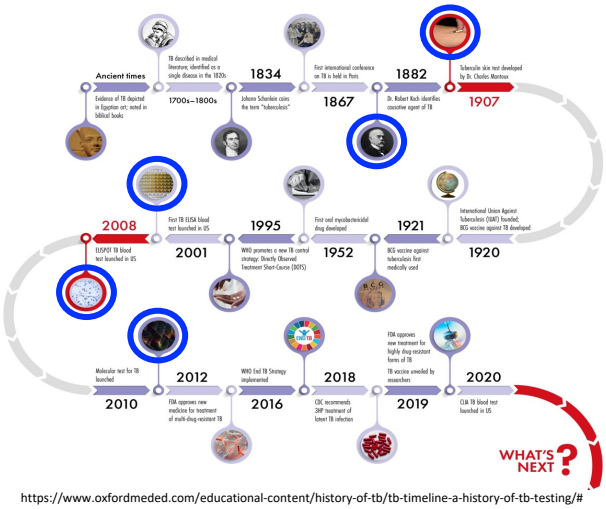
A History of Tuberculosis: From Ancient Times to Today



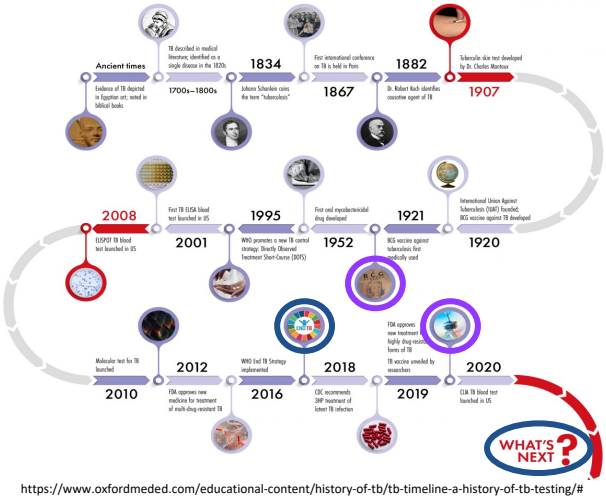
https://www.oxfordmeded.com/educational-content/history-of-tb/tb-timeline-a-history-of-tb-testing/#

A very old disease

Diagnosis

- AFB (*M.tb* in the sputum) & culture → ~ 2 months
- Tuberculin skin test (TST) → immunological reaction → infected by *M.tb*
- TB blood test
- Molecular test → faster → ~2 hours
- …
- …
- …

A History of Tuberculosis: From Ancient Times to Today



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~~A very old disease~~

we want to eliminate TB

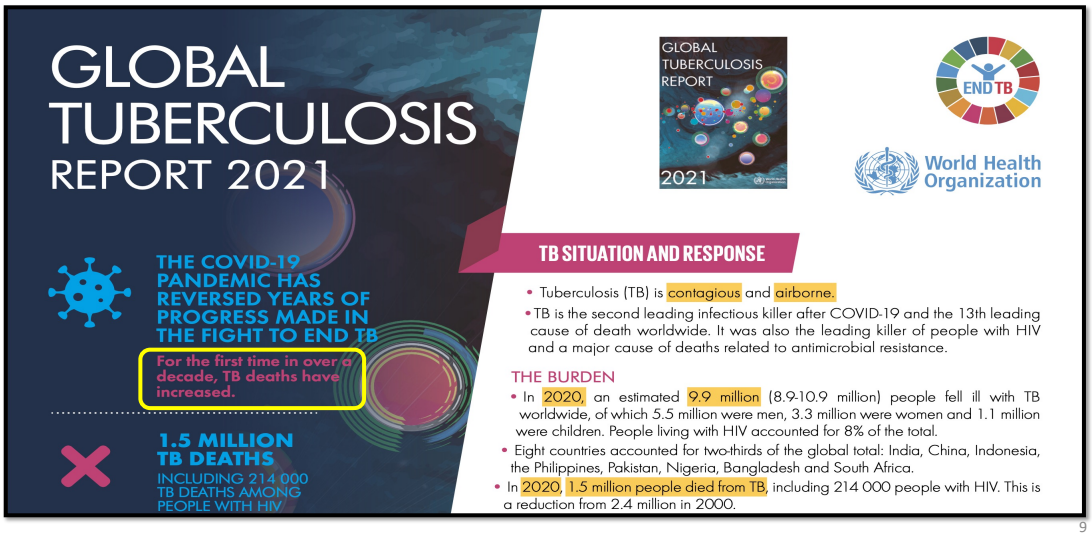
Prevention

- TB Vaccine: first 1921 – unveiled (wake up): 2020
- TPT: from infection to disease

End TB Strategy

- Comprehensive & massive approach!

TB in 2020



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TB in 2020

RESEARCH AND INNOVATION

- The diagnostic pipeline remains robust in terms of the number of tests, products or methods in development. These include newer skin tests for TB infection that have better performance than tuberculin skin tests; next-generation lateral-flow lipoarabinomannan (LF-LAM) assays that perform better than currently mar- keted assays; amplification- based targeted next-gen- eration sequencing assays for detecting drug-resistant TB directly from sputum specimens; and an expanding pipeline of new interferon gamma release assays to test for TB infection.
- Fourteen vaccine candidates are in clinical trials: two in Phase I, eight in Phase II and four in Phase III. They include candidates to prevent TB infection and TB disease, and candidates to help improve the outcomes of treatment for TB disease.
- There are 25 drugs and several combination treatment regimens in clinical trials.
- Progress in the development of new TB diagnostics, drugs and vaccines, is constrained by the overall level of investment, which at US$ 0.9 billion in 2019 falls far short of the global target of US$ 2 billion per year.

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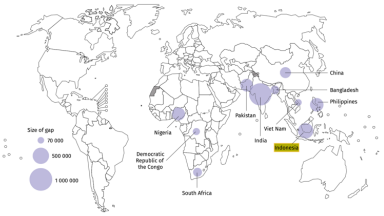
What about Indonesia?

High TB burden: India (26%), China (8.5%), and **Indonesia (8.4%)**
Covid-19 pandemic affects mostly India, **Indonesia** & Philippines

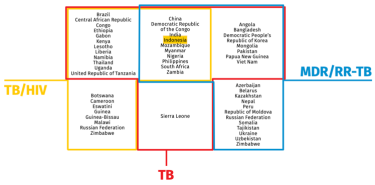
FIG. 22
The ten countries with the largest gaps between notifications of new and relapse (incident) TB cases and the best estimates of TB incidence, 2020*



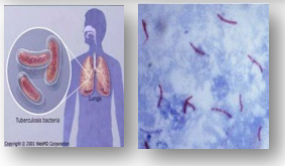
* The ten countries ranked in order of the size of the gap between notified cases and the best estimates of TB incidence in 2020 are: India, Indonesia, Philippines, Nigeria, Pakistan, China, South Africa, Bangladesh, Democratic Republic of the Congo and Viet Nam.

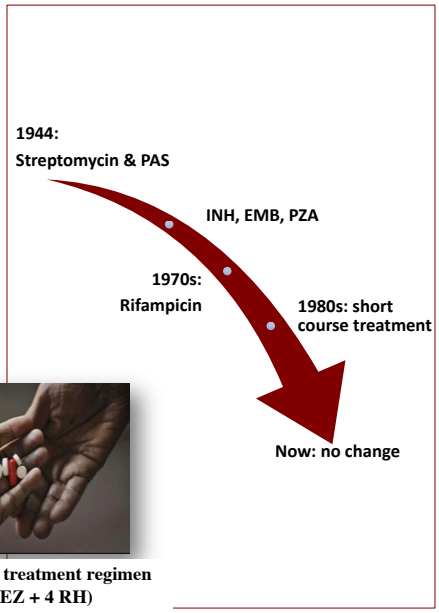
FIG. 11
Estimated TB incidence in 2020, for countries with at least 100 000 incident cases
The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2020, are labelled.

FIG. A3.1
The three global lists of high-burden countries for TB, HIV-associated TB and MDR/RR-TB to be used by WHO in the period 2021–2025, and their areas of overlap



TB treatment





Short course treatment regimen
(2RHEZ + 4 RH)

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TB treatment: complex and long

4 drugs must be taken daily for 2 months
& 2 drugs for the next 4 months (at least)

- Complex & long (+ potency of AEs)
- Non-adherence/Drop Out
- Treatment Failure
- Drug Resistance
- Continuously spreading the disease

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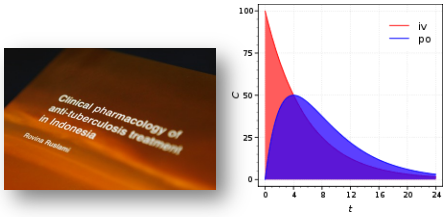
How can we optimize TB treatment
by understanding pharmacology of their drugs?



Pulmonary TBC TB Meningitis *TBI*

TBC in children **TB – DM**

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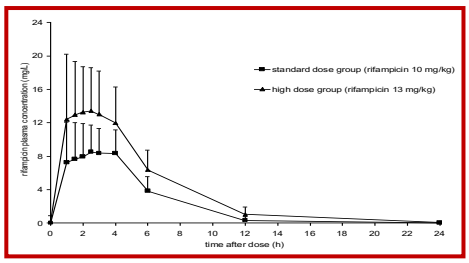
Higher dose rifampicin (13mg/kg) *in Indonesia*

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2007, p. 2546–2551 Vol. 51, No. 7
0066-4804/07/$08.00+0 doi:10.1128/AAC.01550-06

Pharmacokinetics and Tolerability of a Higher Rifampin Dose versus the Standard Dose in Pulmonary Tuberculosis Patients▽

Rovina Ruslami,[1]† Hanneke M. J. Nijland,[2]† Bachti Alisjahbana,[3] Ida Parwati,[4] Reinout van Crevel,[2] and Rob E. Aarnoutse[2]*



Ruslami et al, AAC 2007

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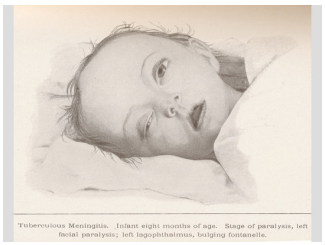
TB Meningitis



https://www.historyofvaccines.org/content/tb-meningitis

- ~10% of TB, *most severe form & deadly* (~30-50-% mortality)
- Affects all age (mainly children <5 years old and young adults)
- Develops slowly, not specific symptoms (headache, low-grade fever, etc.)

- Slowly progress → *difficult to diagnose* & the *advance stage before treatment*
- HIV (+) makes it worse (probability & prognosis)

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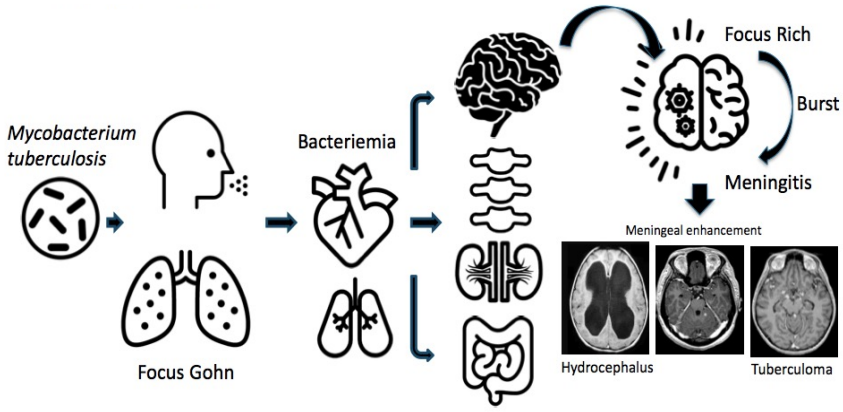
TB Meningitis, how?



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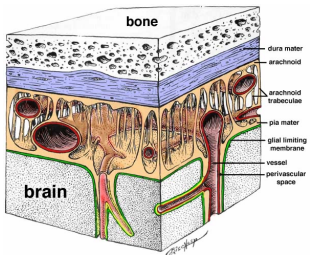
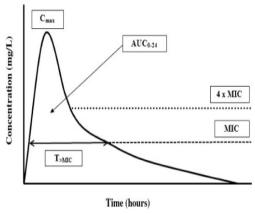
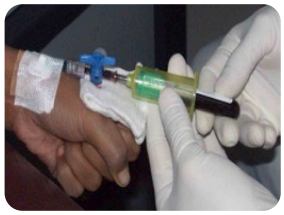
Optimal treatment: not defined



Drugs must past the Blood Brain Barrier
(very difficult!)





Research is needed

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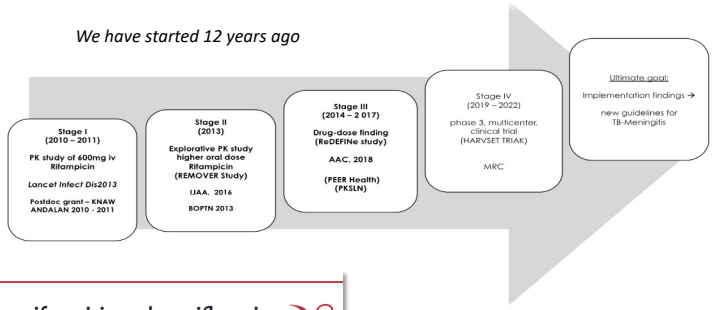
We have started 12 years ago



Intensified regimen containing rifampicin and moxifloxacin for tuberculous meningitis: an open-label, randomised controlled phase 2 trial

Rovina Ruslami*, A Rizal Ganiem*, Sofiati Dian, Lika Apriani, Tri Hanggono Achmad, Andre J van der Ven, Geesje Borm, Rob F Aarnoutse, Reinout van Crevel

Pharmacokinetics and safety/tolerability of higher oral and intravenous doses of rifampicin in adult tuberculous meningitis patients

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Double-Blind, Randomized, Placebo-Controlled Phase II Dose-Finding Study To Evaluate High-Dose Rifampin for Tuberculous Meningitis

S. Dian,[a,c,g] V. Yunivita,[d,g] A. R. Ganiem,[c,g] T. Pramaesya,[g] L. Chaidir,[c,g] K. Wahyudi,[f] T. H. Achmad,[e] A. Colbers,[b] L. te Brake,[b] R. van Crevel,[a] R. Ruslami,[d,g] R. Aarnoutse[b]

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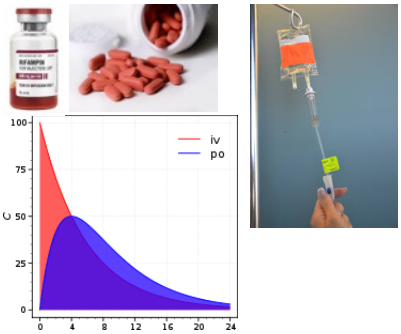
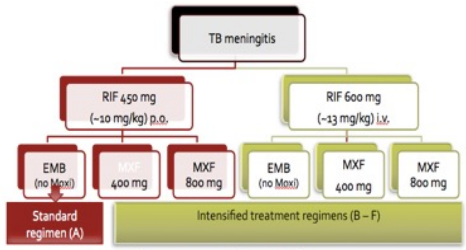
First study (2010)

- Rifampicin (RIF): ***concentration-dependent killing activity***
- Modifying the RIF dosage
  - Higher dose (600 mg)
  - Intravenous – 14 days
- 60 adult TB M patients in an open-label, phase 2, RCT
- Data collected:
  - PK of the drug (plasma & CSF)
  - Safety/tolerability
  - Efficacy





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Patients' characteristics

	All patients (n=60)	Oral rifampicin 450 mg (n=31)			Intravenous rifampicin 600 mg (n=29)		
		No moxifloxacin (n=12)	Moxifloxacin 400 mg (n=10)	Moxifloxacin 800 mg (n=9)	No moxifloxacin (n=10)	Moxifloxacin 400 mg (n=9)	Moxifloxacin 800 mg (n=10)
Sex, male	33 (55%)	8 (67%)	6 (60%)	4 (44%)	4 (40%)	3 (33%)	8 (80%)
Age (years)	28 (16-64)	34 (19-47)	33 (19-50)	27 (18-57)	29 (16-49)	27 (18-60)	27 (19-64)
Bodyweight (kg)	48 (34-75)	50 (35-57)	49 (40-55)	48 (40-58)	46 (34-54)	47 (42-62)	49 (40-75)
Body-mass index (kg/m²)	18·4 (15·1-26·0)	18·0 (16·0-23·3)	18·6 (15·6-22·9)	18·3 (15·4-23·3)	18·1 (15·1-21·6)	18·4 (16·3-24·7)	19·9 (16·5-26·0)
Tuberculous meningitis (grade)							
1	4 (7%)	0	0	1 (11%)	2 (20%)	1 (11%)	0
2	49 (82%)	12 (100%)	10 (100%)	5 (56%)	7 (70%)	7 (78%)	8 (80%)
3	7 (12%)	0	0	3 (33%)	1 (10%)	1 (11%)	2 (20%)
Infected with HIV	7 (12%)	2 (17%)	1 (10%)	1 (11%)	1 (10%)	1 (11%)	1 (10%)
Glasgow Coma Scale <14 on presentation	46 (77%)	11 (92%)	8 (80%)	8 (89%)	5 (50%)	5 (56%)	9 (90%)
Drug dose (mg/kg)							
Rifampicin (n=60)	10·8 (7·8-17·6)	9·0 (7·9-12·9)	9·2 (8·2-11·3)	9·4 (7·8-11·3)	13·1 (11·2-17·6)	12·8 (10·0-14·3)	12·2 (8·0-15·0)
Isoniazid (n=60)	6·3 (4·0-8·8)	6·0 (5·3-8·6)	6·2 (5·5-7·5)	6·3 (5·2-7·5)	6·5 (5·6-8·8)	6·4 (5·0-35·7)	6·1 (4·0-7·5)
Pyrazinamide (n=60)	31·3 (20·0-44·1)	30·0 (26·3-42·9)	30·6 (27·3-37·5)	31·2 (25·9-37·5)	32·6 (27·8-44·1)	31·9 (25·0-35·7)	30·6 (20·0-37·5)
Ethambutol (n=22)	15·6 (13·2-22·1)	15·0 (13·2-21·4)	..	..	16·3 (13·9-22·1)	..	..
Moxifloxacin (n=38)	10·3 (6·7-20·0)	..	8·2 (7·3-10·0)	16·7 (13·8-20·0)	..	8·5 (6·7-9·5)	16·3 (10·7-20·0)
Initial oral treatment through nasogastric tube	46 (77%)	11 (92%)	8 (80%)	8 (89%)	5 (50%)	5 (56%)	9 (90%)

Data are number (%) or median (range).

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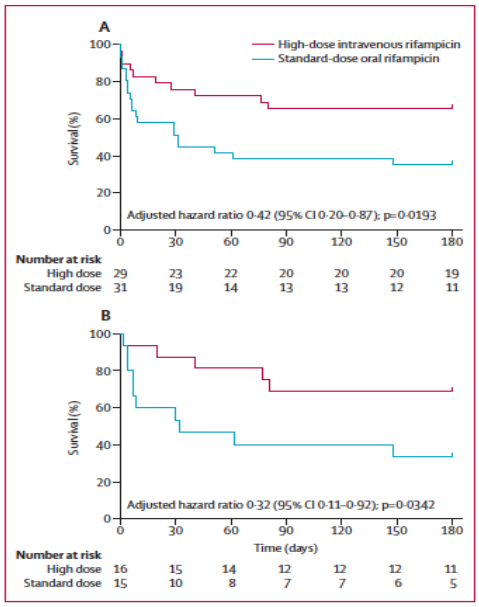
Results

	600 mg, intravenous (n=26)	450 mg, oral (n=26)	Ratio of intravenous to oral	p value
Plasma				
AUC_{0-6} (mg.h/L)	78·7 (71·0–87·3)	26·0 (19·0–35·6)	3·0 (2·2–4·2)	<0·0001*
C_{max} (mg/L)	22·1 (19·9–24·6)	6·3 (4·9–8·3)	3·5 (2·6–4·8)	<0·0001*
C_{max} (≥8 mg/L)	26 (100%)	13 (50%)	..	<0·0001†
T_{max} (h; median, range)	2 (1–2)	2 (1–6)	..	0·048‡
CSF				
C_{max} (mg/L)§	0·60 (0·46–0·78)	0·21 (0·16–0·27)	2·92 (2·03–4·20)	<0·0001*

- Safe & tolerated well by the patients
- 50% died within 6-m; 22 (73%) in the first month

  Main causes:
  - respiratory failure (9)
  - neurological deterioration (7)
  - others (6)
- **Mortality was much lower in the high-dose RIF group**
  - (All 60 pts.) adjusted HR 0.42 (95%CI 0.2-0.87), p=0.0193



(Ruslami et al, Lancet ID, 2013)

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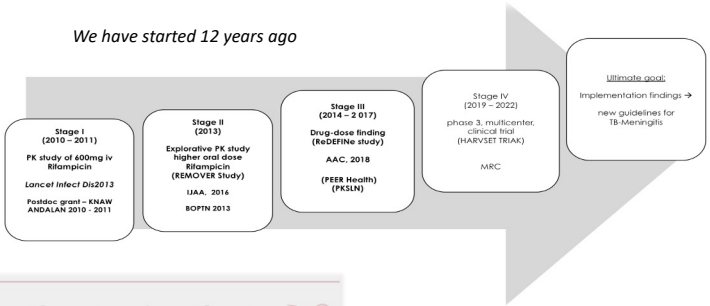
We have started 12 years ago



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Intravenous Rifampicin:
- Expensive
- Invasive

Not always feasible

Double-Blind, Randomized, Placebo-Controlled Phase II Dose-Finding Study To Evaluate High-Dose Rifampin for Tuberculous Meningitis

S. Dian,[a,c,g] V. Yunivita,[d,g] A. R. Ganiem,[c,g] T. Pramaesya,[g] L. Chaidir,[e,g] K. Wahyudi,[f] T. H. Achmad,[e] A. Colbers,[b] L. te Brake,[b] R. van Crevel,[a] R. Ruslami,[d,g] R. Aarnoutse[b]

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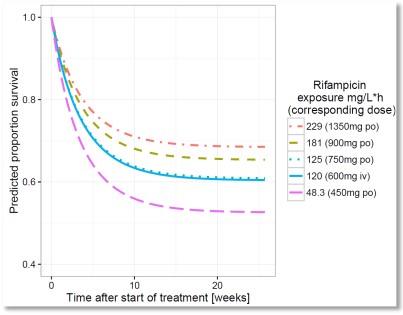
Combined analysis of Indonesian data

Clinical Infectious Diseases
MAJOR ARTICLE

Model-Based Meta-analysis of Rifampicin Exposure and Mortality in Indonesian Tuberculous Meningitis Trials

Elin M. Svensson,[1,6] Sofiati Dian,[3,4] Lindsey te Brake,[1] Ahmad Rizal Ganiem,[3,4] Wycke Yunivita,[4,5] Arjan van Laarhoven,[4] Reinout van Crevel,[4] Rovina Ruslami,[4,5] and Rob E. Aarnoutse[1]

(Svensson E, et al, CID, 2019)



Plasma $AUC_{0\text{-}24h}$ (day 2±1) stronger predictor than C_{max} or CSF exposure

Conclusions:

- Higher Rifampicin exposure substantially decreased the risk of death
- Maximal effect not reached within the study range (10 – 30 mg/kg or 450 – 1350 mg) → ***at least 30 mg/kg (~1350 mg)***
- No PK/PD relationship for toxicity

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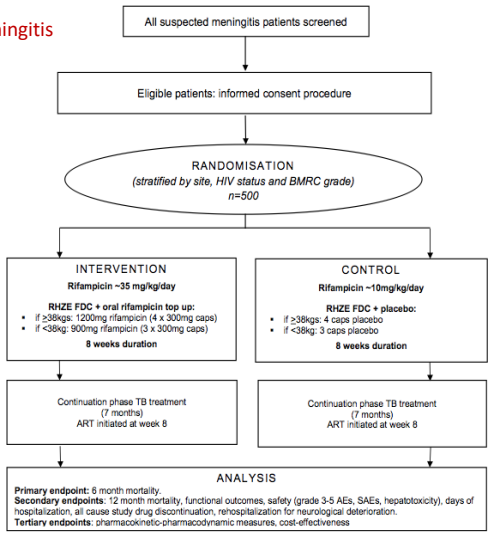
Harvest Trial

High Dose Oral Rifampicin to Improve Survival from Adult Tuberculous Meningitis

- Double-blinded Randomized Phase III Trial
  - Oral RIF (~35mg/kg/d) 8 weeks vs. standard care (~10mg/kg/d)
  - 8 weeks intervention + 7 months cont. & 12-m follow up
- Subject: adult TBM patients (> 18 y-o)
  - N = 500 participants
- Sites: South Africa, Uganda (Mbarara & Kampala) & Indonesia (Jakarta & Bandung)



Radboudumc university medical center
University of Minnesota
Harvest
HIGH DOSE ORAL RIFAMPICIN FOR IMPROVED SURVIVAL OF TB MENINGITIS

26/06/22 26

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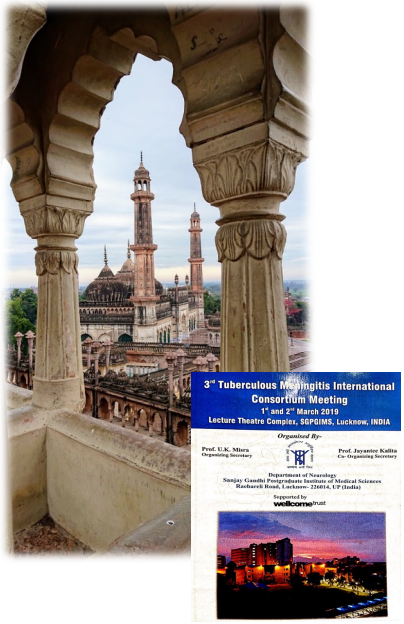

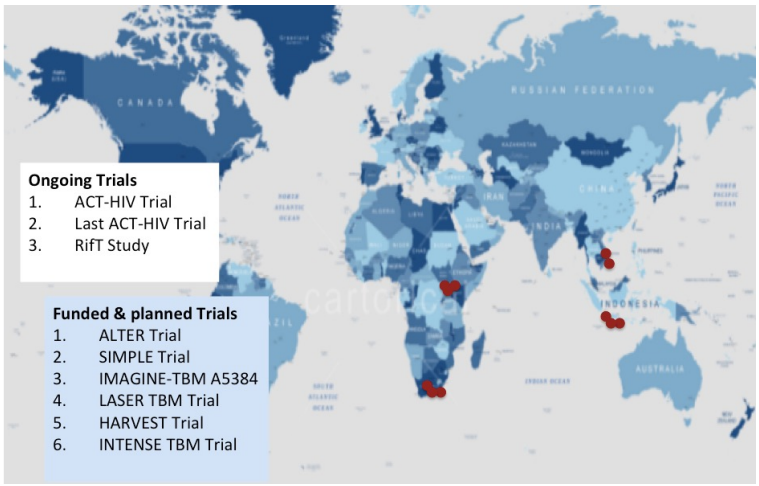

Ongoing Trials
1. ACT-HIV Trial
2. Last ACT-HIV Trial
3. RifT Study

Funded & planned Trials
1. ALTER Trial
2. SIMPLE Trial
3. IMAGINE-TBM A5384
4. LASER TBM Trial
5. HARVEST Trial
6. INTENSE TBM Trial

Higher dose of Rifampicin (35 mg/kg/d) for TBM

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And now…
High-dose of Rifampicin
in the regimens being tested for TB Meningitis

with PK parameters → PK/PD analysis

Upcoming or current TBM clinical trials of intensified therapy

Trial name	Start	Country	Trial design/ population	Sample size	Regimens to be examined	Duration of intervention	Outcome measures
RifT study ISRCTN42218549	2018	Uganda	Phase II RCT 3 arm, parallel group (95–100% HIV-positive)	60	A: Standard of care R (R~10 mg/kg) B: Intravenous R 20 mg/kg C: Oral R 35 mg/kg H, Z and E given at standard doses in all arms	8 weeks	1. PK parameters in plasma and CSF (C_{max}, AUC, T > MIC) 2. Safety 3. 8 and 24-week mortality 4. Functional status (Rankin scale) at 2 and 24 weeks 5. Incidence of TBM-IRIS
TBM-KIDS NCT02958709	2018	India Malawi	Phase II RCT paediatric	120	A: high dose R (standard dose H, Z, E) B: high dose R and levofloxacin (standard dose H and Z) C: standard of care	8 weeks	1. PK parameters (plasma, CSF) 2. Functional outcome (Modified Rankin Scale) 3. Safety 4. Neurocognitve (Mullen Scales of Early Learning)
Simple NCT03537495	2018	Indonesia	Phase II RCT	36	Rifampicin 1350 mg (~30 mg/kg) with A: no LZD B: LZD 600 mg daily C: LZD 1200 mg daily H, Z and E given at standard doses to all participants	14 days	1. PK parameters in plasma and CSF 2. Safety 3. Clinical response 4. Neurological response 5. Mortality 6. Blood and CSF inflammatory response
Harvest	2019	Indonesia South Africa Uganda	Phase III RCT 2 arm, parallel design	600	A: Standard of care B: R 1500 mg (Asia) or 1800 mg (Africa), equivalent to ~35 mg/kg. H, Z and E given at standard doses	8 weeks	1. 6 month survival time 2. Time to normalisation of consciousness (GCS 15) 3. Neurocognitive outcomes 4. safety and tolerability endpoints 5. PK-PD endpoints 6. Cost effectiveness
ACTG A5384	2019	TBD	Phase II RCT 2 arm, parallel design	300	A: 2 months $R_{35}H_{10}$ $LZD_{1200}Z$, 4 months $R_{35}H_{10}$ B: Standard of care	6 months	1. 18 month survival time 2. Modified Rankin scale at week 12, 24, 26, 48 and 72 3. Grade 3–5 adverse events 4. Neurocognitive function 5. Time to GCS = 15 6. Pharmacokinetic parameters

(Cresswell et al, ERCP, 2019)

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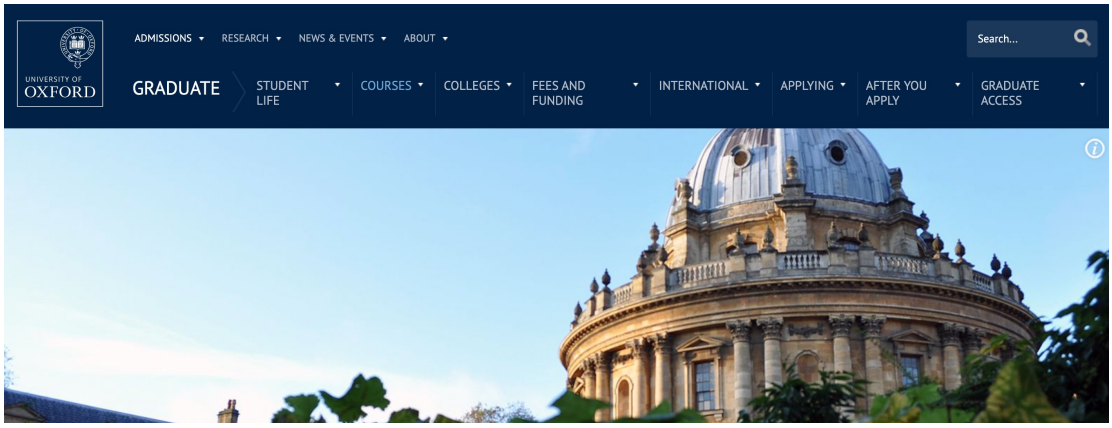
4th International TB Meningitis Consortium Meeting 2022
September 1-2, 2022



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Higher dose of Rifampicin for other Tuberculosis

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TRUNCATE-TB Trial

- Multi-center, multi-country phase 2-3 RCT (MAMS approach) for adult DS-PTB (Philippine, Thailand, India, Indonesia, and Uganda)
- N: 672, Funded by MRC, Chief PI: Nick Paton
- 4 novel short regimens (2 month) vs. standard regimen (standard dose RIF, 6 months)
  - 2 of them using High dose Rif: 35 mg/kg/d among other drugs
  - Population PK sub study → very rich! (~4000 samples)

- Current status:
  - Result meeting (June 2, 2022)
  - Bio-analysis: Univ of Liverpool (Prof. Saye Kho)

"Bersatu melawan TBC"

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2R² Trial

- Three-arm, superiority, phase 2b, partially-blind, (cluster) randomized trial for TBI
- Funded by Canadian Institute of Health Research
- Vietnam, Indonesia and Canada. N = 1359
- Design:
  - **2-m higher dose (20 or 30 mg/kg) vs 4-m standard dose (10 mg/kg) of rifampicin**
  - Endpoint: safety/tolerability
  - PK sub study:
    - Intensive PK sampling (from children and adult with TBI, Indonesian site only, n=18 per arm)
    - Population PK sampling (N = 400)
- Current status:
  - Recruitment: 1124 (85%)

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Reflection

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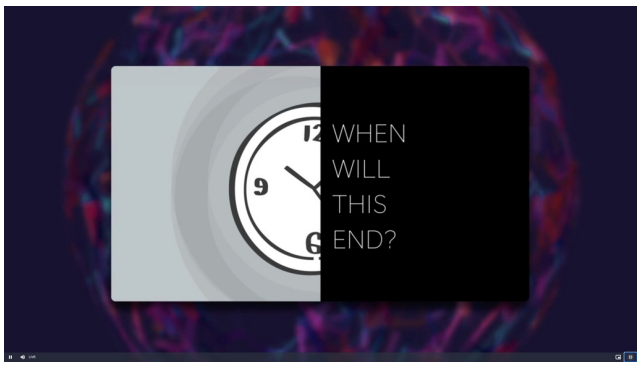
Tuberculosis

We are running out of the time

Clock is ticking

It's time for urgent action to end TB

How can we participate in this battle?



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PK Lab, Bandung

Radboud UMC, Nijmegen, the Netherlands

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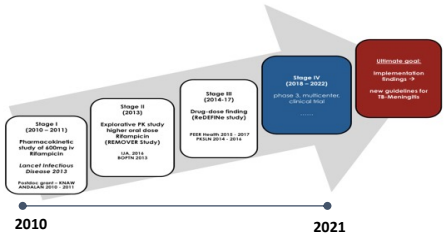
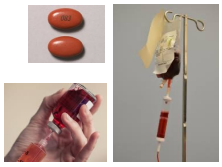
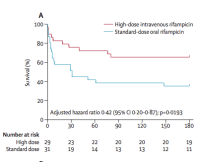
Work on TB Meningitis, as an example..



Modification of the drug (rifampicin) dosage (dose and delivery methods)

KNAW USAID FROM THE AMERICAN PEOPLE rshs Radboudumc

Problems:
severe, deadly, difficult to diagnose
treatment management: not yet optimized

Improving treatment for Tuberculous Meningitis

- antibiotics
  - Rob Aarnoutse
  - Ahmad Rizal Ganiem
  - Lindsey te Brake
  - Vycke Yunivita
  - ReDEFINe Study
  - SPICE Study
- diagnosis
  - Lidya Chaidir
  - Reinout van Crevel
  - Evaluation & strengthening diagnostics of TBM
- immunopathogenesis
  - Arjan van Laarhoven
  - Safiatt Dian
  - Immunophenotyping, flowcitrometry Metabolomic

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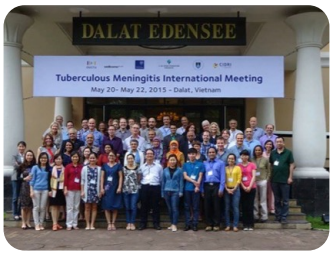
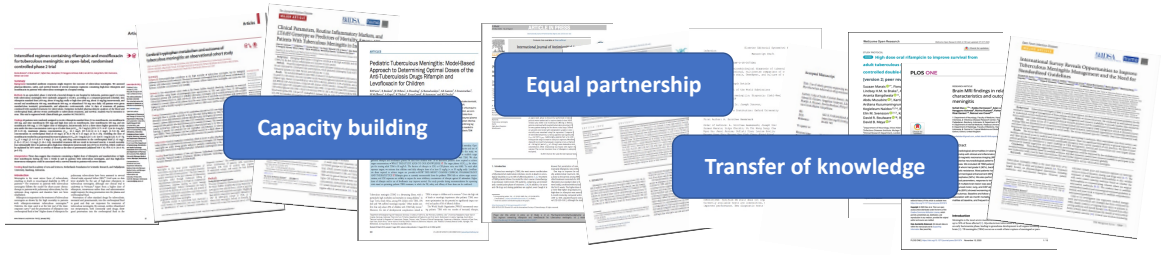
Our achievement so far:

Pave for the future research in TB Meningitis & other forms of TB



TB Meningitis International Research Consortium



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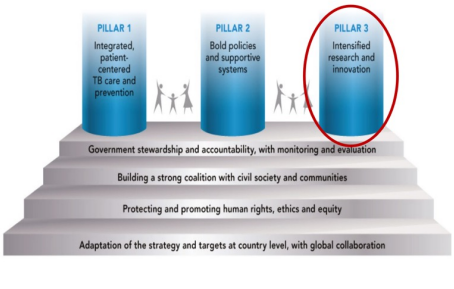
Let's work together..



Dr Tedros Adhanom Ghebreyesus
Director-General
World Health Organization

Ending this debilitating disease remains a priority for WHO, and in recent years, we have made encouraging progress globally. But the COVID-19 pandemic has put these gains at risk. Not only does the virus pose an increased risk to people with TB, it has also caused severe disruption to services.

I want to remind you that the struggle to end TB is not just a struggle against a single disease. It's also the struggle to end poverty, inequity, unsafe housing, discrimination and stigma, and to extend social protection and universal health coverage. If the pandemic has taught us anything, it's that health is a human right, not a luxury for those who can afford it.

With solidarity, determination and the equitable use of tools, we will defeat COVID-19. And with the same solidarity, determination and equitable use of tools, we can end TB.

WHO Global TB Report, 2021

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Acknowledgement

- All TB patients
- TB-HIV Research Center, Bandung
- Pharmacokinetic Lab, Bandung
- Radboud University, Nijmegen, NL
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- KNAW, VIDI grant
- CIHR grant
- McGill University, Montreal, Canada

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• Vycke Yunivita
• Sofiati Dian
• Lidya Chaidir
• Tri Hanggono Achmad
• Sofia Imaculata

Dutch Collaborators:
• Reinout van Crevel
• Rob Aarnoutse
• Arjan van Laarhoven
• Lindsey te Brake

McGill University Collaborators:
•Dick Menzies
• Federica Fregonese

NIH collaborators:
• H. Clifford Lane
• Sophia Siddiqui

• Prof. Nick Paton
• Prof. Philip Hill, Otago University, New Zealand

rshs unpad universitas padjadjaran Radboudumc

CIHR IRSC USAID FROM THE AMERICAN PEOPLE KNAW

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Thank you…

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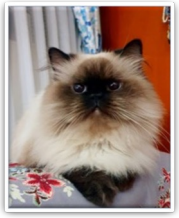
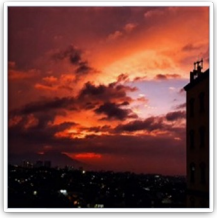
  - 1991 Medical Doctor FoM Unpad, Bandung
  - 2001 Internal Medicine specialist FoM Unpad, Bandung
  - 2009 PhD in Clinical Pharmacology Radboud University Nijemegen, The Netherlands

- **Position:**
  - 2010 - present TB-HIV Research Group
  - 2012 - present Head of Dept. of Biomedical Sciences, Div of Pharmacology & Therapy
  - 2012 - present Health Research Ethics Committee, FoM, Unpad
  - 2015 - present Member of Tuberculous Meningitis International Research Consortium
  - 2017 - present Member of JetSet TB (Indonesian TB Researcher Netwrok)
  - 2018 - present Member of A-TRACTION (Asian Tuberculosis Research and Clinical trial Organisational Network)
  - 2018 - present Scientific Liaison of the TB Section, The Union

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