



**Chemoprophylaxis for leprosy**

*A long-term follow up of a cohort established in 2000*

Indonesia

- Hasanuddin University, Makassar
- Leprosy control program, Pangkep district

The Netherlands

- KIT Biomedical Research, Amsterdam

**Rationale and research question**

- Decline in global case detection rate, but when looking at individual countries, many still stable: Indonesia!
- New preventive measures still needed to break the transmission chain
- Dapsone chemoprophylaxis studies in the past

**Research question:**  
What is the effect of chemoprophylaxis with rifampicin on the incidence of leprosy?

**Study area:** 5 small, isolated, islands in the Flores Sea, Indonesia

**Study design**

**2000:**

- Active population screening of leprosy
- Treatment of new patients with MDT
- Supply prophylactic treatment to contacts in July **AND** November (6-14 years: 300 mg; ≥15 years: 600 mg rifampicin)

**2001-2006:**

- Yearly active screening of population
- Treatment of new patients with MDT

**2008-2010:**

- Two-yearly active screening of population
- Treatment of new patients with MDT

**Supply of rifampicin prophylaxis**

5 islands → 3 intervention groups

**Compare 2 types of prophylactic regimens:**

- 1. Contact regimen:** prophylaxis **only for contacts** (household contacts, direct neighbors and next neighbors) [1 island]
- 2. Blanket regimen:** prophylaxis for **all eligible persons** [3 islands]

**with**

- 3. Control group:** **no prophylaxis** [1 island]

**Baseline screening and rifampicin supply in 2000**

- Total population on 5 islands in 2000: 4739
- Screened population: 4123 (87%)
- New patients detected: 85

**Overall Case Detection Rate: 206/10,000**

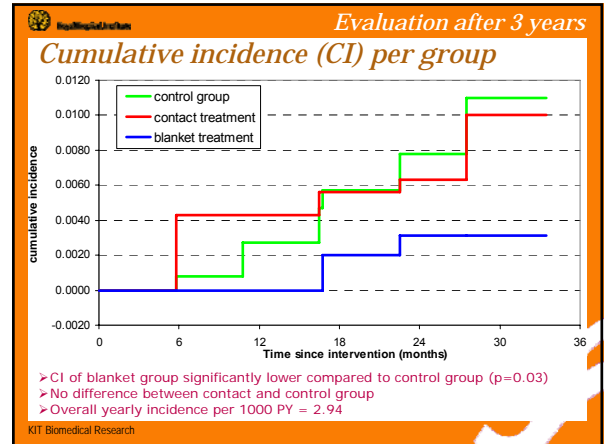
- **Cohort:** 3963 persons without leprosy included
- In control group 0% received rifampicin
- In contact group 18% of population received rifampicin
- In blanket group 82% of population received rifampicin

- 10% took RIF unsupervised (no difference between contact and blanket)
- 200 ps not eligible for RIF: mainly children < 5 and pregnant women



*Evaluation after 3 years*  
*(33.5 months)*

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*Evaluation after 3 years*  
*Summary figures of blanket approach*

		95% CI:
Effectiveness	74.6%	5.4-93.2
Number needed to treat (NNT)	127	65-1878
Benefit per 1000 persons	8	0.5-15.3

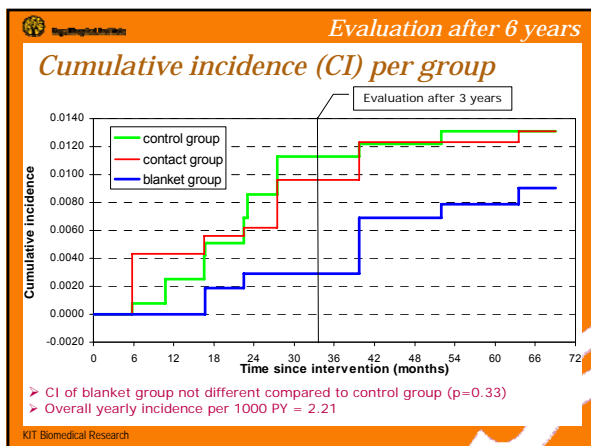
- > Population-based treatment with rifampicin of the population of a high endemic area seems to prevent the development of leprosy
- > Longer follow-up needed to determine whether due to delayed development of leprosy or complete clearance of infection

*Figures based on population data, so including children <5 who did not receive prophylaxis*

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*Evaluation after 6 years*  
*(69 months)*

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*Evaluation after 6 years*  
*Summary figures of blanket approach*

		95% CI:
Effectiveness	57%	-3-82
Number needed to treat (NNT)	244	
Benefit per 1000 persons	4	-5-13

- > The effect of the blanket approach seems to wane off after three years:  
3 years after the intervention there was a significant effect of the blanket approach, but 6 years after the intervention this effect is not significant anymore.

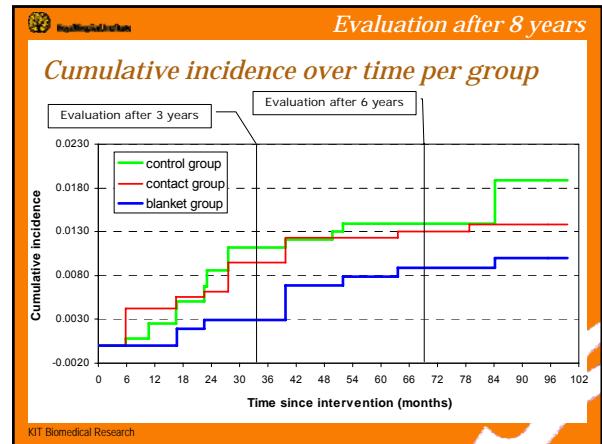
*Effectiveness based on Hazard Ratio adjusted for sex, household size, serological status and contact status in 2000 (no household contact (HHC), HHC of MB, HHC of PB)*

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**Results after 8 years**  
(99.5 months)

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*Evaluation after 8 years*

**Summary figures of blanket approach**

		95% CI:
Effectiveness	67%	24-85
Number needed to treat (NNT)	112	52-773
Benefit per 1000 persons	9	-1-19

- An increase in incidence in the control group has led to an almost significant difference in cum. incidence between the control and blanket group (p=0.09)
- The effect of the blanket approach has increased again compared to the effect after 6 years
- Is this an effect on transmission?

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*Evaluation after 8 years*

**Hazard ratios for developing leprosy by group and by intake of rifampicin**

	Person-Month-at-risk	New patients in cohort	Incidence rate/1000 PY	Adjusted HR (95% CI)
<b>Control</b>	101,800	21	2.48	1.0
<b>Contact</b>	133,287	21	1.89	0.72 (0.39-1.32)
<b>Blanket</b>	93,360	10	1.29	<b>0.34 (0.15-0.76)</b>
<b>Total</b>	328,447	52	1.90	
<i>(below only for age &gt;5)</i>				
<b>No rifampicin</b>	171,432	37	2.59	1.0
<b>Unsupervised rifampicin</b>	8,799	3	4.09	0.69 (0.20-2.40)
<b>1 or 2 times supervised rif</b>	88,645	10	1.35	<b>0.34 (0.16-0.73)</b>
<b>Total</b>	268,876	50	2.23	

- Supervised intake of at least 1 dose of rifampicin against no prophylaxis gave a significant effectiveness of 66%
- Unsupervised rifampicin was not effective (but small numbers)

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*Evaluation after 8 years*

**Characteristics of 52 incident patients**

	MB	PB2-5	PB1	Total
<b>Control group</b>	8	5	8 (38%)	21
<b>Contact group</b>	4	11	6 (29%)	21
<b>Blanket group</b>	3	0	7 (70%)	10

15 patients were detected outside the cohort

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*Evaluation after 8 years*

**Risk factors for leprosy in cohort**

Risk group	Ref. cat	aHR	95% CI
Men	Women	2.1	1.2-3.6
Persons in houses with >7 persons	Persons in houses with 1-4 persons	2.7	1.2-6.1
Persons seropositive in 2000	Persons seronegative in 2000	5.1	2.0-13.2
Household contacts of MB patients in 2000	Non-contacts in 2000	3.2	1.2-8.4

There was no effect of BCG scar

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**Discussion - Conclusion**

- Highly endemic area
- Everybody is a contact
- Not a randomly assigned, placebo-controlled, blinded trial

- Population based prophylaxis was associated with a reduced leprosy incidence in the first 3 years after implementation;
- 6 years after implementation this difference was not significant anymore;
- 8 years after implementation a sudden rise in incidence was seen in the control group.
- Supervised provision of prophylaxis seems to be important

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**TERIMAH KASIH!!**

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**Aim and research questions**

**Overall aim of the study:**  
to identify parameters and tools for early detection and prevention of leprosy that can be applied by routine leprosy control programs in field circumstances.

**Research questions:**

1. What is the long-term effect of chemoprophylaxis on the incidence of leprosy?
2. Is the reduction in the incidence of the more severe forms of leprosy seen in the previous years a true reduction or only a lengthening of the incubation time?
3. Does chemoprophylaxis affect only development of disease in already infected persons or does it also prevent new infections, i.e. have an effect on transmission?
4. What are the effects of repeated active population screening on the incidence of leprosy?
5. What are risk factors for the development of clinical leprosy and how do long-term risk factors compare to short term risk factors?

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**Baseline screening and rifampicin supply in 2000**

	Baseline survey			Rifampicin supply	
	Population	Examined	CDR	Cohort	% received rifampicin
Control	1439	1279	2.1%	1251	0%
Contact	2058	1715	1.4%	1632	18%
Blanket	1242	1129	3.0%	1080	82%
<b>Total</b>	<b>4739</b>	<b>4123</b>	<b>2.1%</b>	<b>3963</b>	<b>30%</b>

- Overall 87% of population screened and 85 new patients detected
- Overall Case Detection Rate: 206/10,000
- 10% took RIF unsupervised (no difference between contact and blanket)
- 200 persons not eligible for RIF: mainly children < 5 and pregnant women

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**Evaluation after 3 years**

**Results of yearly screening**

	Cohort in 2000	Cohort after 3 years	% complete follow-up	New patients in cohort	Cum. Incidence after 3 years
Control	1251	818	65.4%	11	0.0110
Contact	1632	1176	72.1%	15	0.0099
Blanket	1080	874	80.9%	3	0.0031
<b>Total</b>	<b>3963</b>	<b>2868</b>	<b>72.4%</b>	<b>29</b>	

- Cum. incidence of blanket group significantly lower compared to control group (p=0.03)
- No difference between contact and control group
- Overall yearly incidence per 1000 PY = 2.94

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**Evaluation after 6 years**

### Results of yearly screening

	Cohort in 2000	Cohort after 6 years	% complete follow-up	New patients in cohort	Cum. Incidence after 6 years
Control	1251	818	68.5%	15	0.0131
Contact	1632	1176	66.0%	20	0.0131
Blanket	1080	874	73.1%	9	0.0090
<b>Total</b>	<b>3963</b>	<b>2868</b>	<b>68.7%</b>	<b>44</b>	

- **Cum. incidence of blanket group not significantly different compared to control group (p=0.33)**
- Overall yearly incidence per 1000 PY = 2.21

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**Evaluation after 8 years**

### Results of yearly screening

	Cohort in 2000	Cohort after 8 years	% complete follow-up	New patients in cohort	Cum. Incidence after 8 years
Control	1251	693	55.4%	21	0.0189
Contact	1632	947	58.0%	21	0.0138
Blanket	1080	729	67.5%	10	0.0100
<b>Total</b>	<b>3963</b>	<b>2369</b>	<b>59.8%</b>	<b>52</b>	

- **An increase in incidence in the control group has led to an almost significant difference in cum. incidence between the control and blanket group (p=0.09)**
- Overall yearly incidence per 1000 PY = 1.90

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### Results of screening October 2008

- Total population on 5 islands in 2008: 6245
- Overall 69% of population screened (4282) and 9 new patients detected
- **Overall Case Detection Rate: 21/10,000**
- The coverage was 64.9% in the control group, 65.7% in the contact group and 77.5% in the blanket group

Overall 60% of the cohort (2369/3963) screened (55%, 58%, 68%)

Reasons for not being screened:

1. Dead;
2. Moved out of study area;
3. Temporarily not on the island (fishing);
4. reluctant;
5. developed leprosy during previous visits (*they are screened, but are not part of cohort anymore*)

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