The benefits of introducing IGRAs into contact tracing - the German perspective

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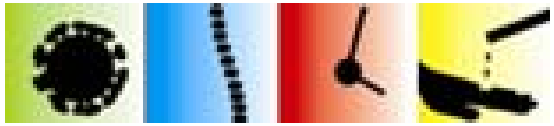
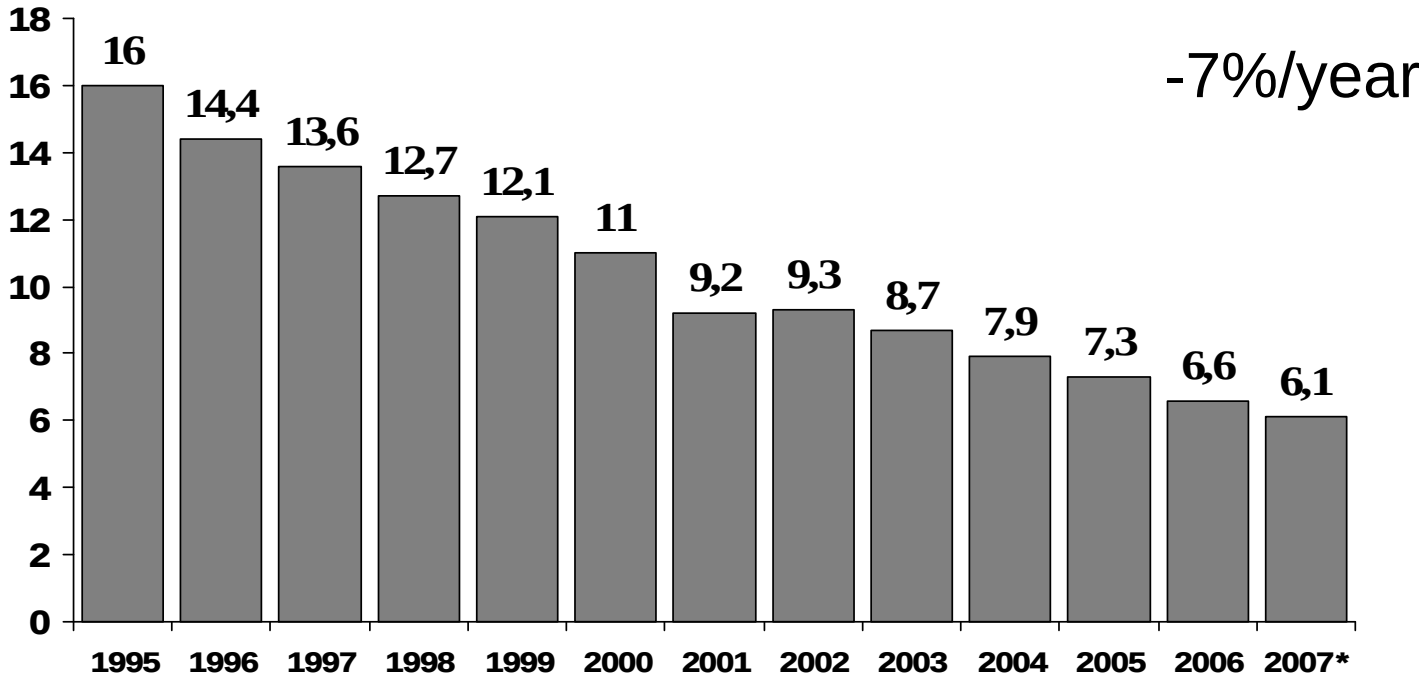


- German Social Security System
  - Health Insurance
  - Retirement Insurance
  - Accidents Insurance
  - founded by Bismark in the 18832qq

Interferon-Gamma Release Assay (IGRA)

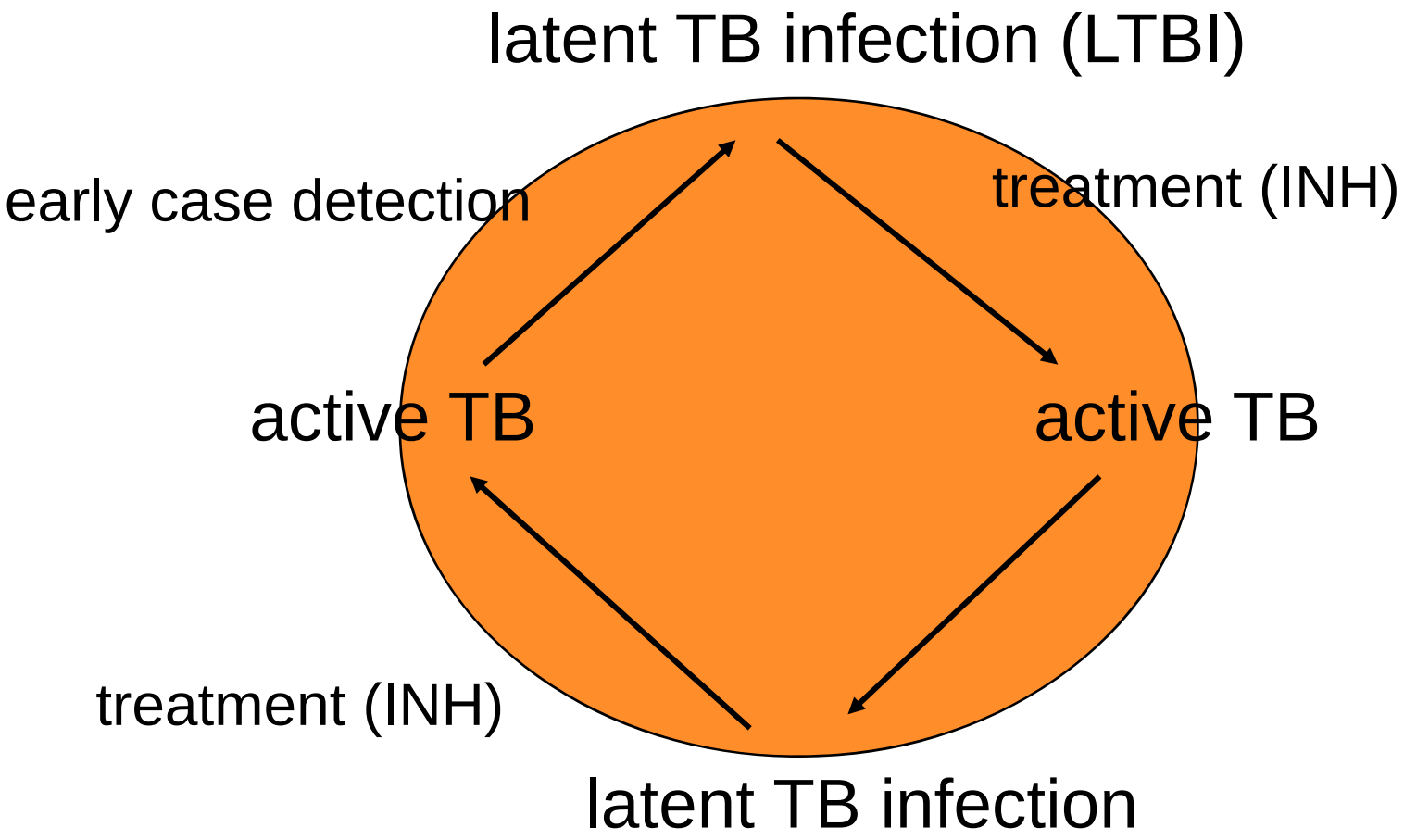
- Why do we screen?
- Agreement between TST and IGRA
- Cost-effectiveness
- Quantiferon and TSPOT.TB
- Contact tracing strategies
- Selection of close contacts

Tuberculosis in the German population thousand cases / 100,000 population



-7%/year

Breaking the cycle of TB transmission: early case detection and treatment of LTBI

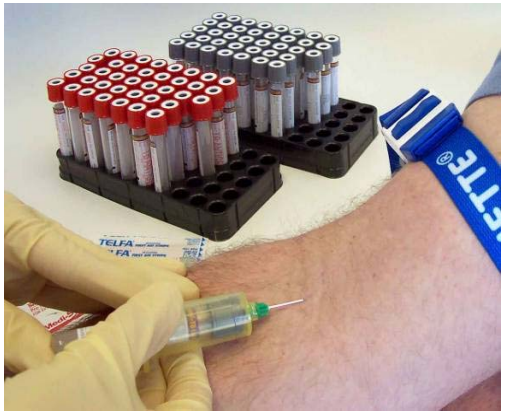


Screening tests

- **tests for diagnosing LTBI in Germany**

multipuncture

TST



IGRA

Mantoux method

strong reaction - necrosis

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Agreement between TST and IGRA

	TST >10mm	IGRA +	TST confirmed
German HCWs	24%	10%	30%
Portuguese HCWs	74%	33%	41%

Portugal	n (%)	positive IGRA
TST 0-4 mm	137 (11)	3%
TST 5-10 mm	178 (15)	12%
TST 11-15 mm	483 (40)	29%
TST >15 mm	420 (34)	55%

- Nienhaus et al IAOEH 2008
- Hospital de São João, Porto, Portugal, unpublished data

Reason for discordant results

Nienhaus et al PloS ONE 2008;3(7):e2665

- **pooled results of 2 German studies**
  - Diel et al Eur Respir J 2006;28(1):16-23
  - Nienhaus et al IAOEH 2008;81:295-300

- **671 observations**
  - IGRA- / TST+ 14.0 % (87.5 % explained by BCG vaccination)
  - IGRA+ / TST- 4.2 % (57.1 % explained by age > 40 years)
  - Agreement 81.8 %

- **corrected for explained discordance**
  - IGRA- / TST+ 3.2 %
  - IGRA+ / TST- 1.8 %
  - Agreement 95.0 %

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Chest X-rays - potentially reduced at University Hospital Nantes after French guidelines

- 85 HCWs with IGRA and TST
  - TST increase >= 10mm 10 IGRA pos 1 (10%)
  - TST >= 15 mm 19 IGRA pos 6 (32%)
  - recent infection 29 IGRA pos 7 (24%)

22 unnecessary X-rays

- Recent infections missed when using TST:
  - no recent infection 56 IGRA pos 14 (25%)
  - Dominique Tripoldi, Nantes unpublished data

Chest X-rays – potentially reduced at the University hospital of Tübingen, Germany

- HCWs with positive TST obtain chest X-ray
  - after contact or every year or every third year
  - contact tracing with 70 HCWs
  - 53 out of 70 (76%) pos in TST >5mm
  - 94 x-ray in history

- after introduction of IGRA: X-ray only when IGRA is pos.
  - 2 (3%) pos. in IGRA
  - 6 (9%) undetermined
    - 3 out of 6 immune-defect, immune-suppressive drugs
  - 86 (91%) X-rays not needed

D Korn in 2nd edition of "TB as Occupational Disease", Germany 2009

Cost-effectiveness for IGRA-based Chemoprevention

- 1,000 contacts followed up for 20 years
- German data on test performance and prevalence of LTBI
- WHO data on disease progression (5% first 2 years, 10% during life)

Strategy:	QFT	QFT if TST>5mm	TST>10mm
Treatment	100	90	207
Cases to treat	22	22	41
Active cases missed	0.58	1.16	2.03
Annual savings in Th US $	2.7	2.4	1.3

Diel et al. CHEST 2007;131:1424-34

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Performance of TST, Quantiferon-Gold in Tube (QFT) and T-Spot.*TB* in 717 close contacts to active TB cases

Results of Interferon-γ-test by diameter of TST

TST	QFT positive		TSPOT positive		Both positive		Discordant	
	N	%	N	%	n	%	N	%
6-10	76	14.8	65	12.7	55	10.7	31	6.0
11-15	89	63.1	86	61.0	80	56.7	15	10.6
> 15	56	88.9	55	87.3	55	87.3	1	1.6
All	221	30.8	206	28.7	190	26.9	47	6.6

Diel,…, Nienhaus CHEST 2009, Vol 135(4): 1010-1018,

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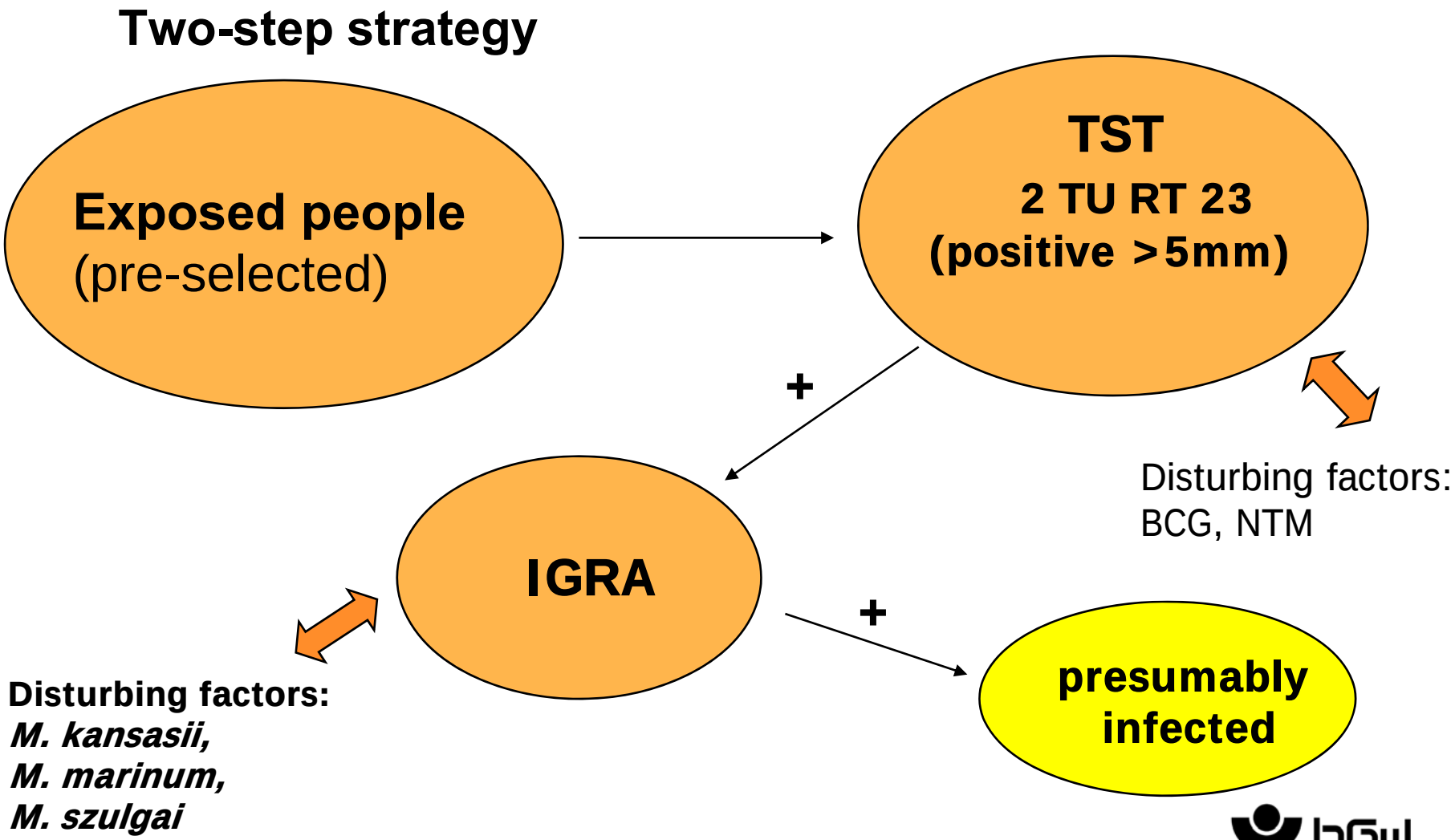
Recommendations for Environmental Contact Tracing in Tuberculosis

German Central Committee against Tuberculosis



Selection of close contacts

- People with **intimate contact** with the index case
  or who **live in the same residence or the same room**

or

- **Intensive contact in Health care:**
  - nursing duties, respiratory physiotherapy, oral inspection,
  - sputum provocation, bronchoscopy ,autopsy

or

- **People with a cumulative exposure time of:**
  - **8 h.** with (AFB+/C+) - index case
  - **40 h.** with (AFB-/C+ or molecular-biologically +) - index case

People not fulfilling one of these criteria only need to be investigated in case of an increased individual risk of illness.

The proportion of recent TB infection in close contacts

	QFT positive OR (95%CI)	attributable risk fraction
Positive smear status of source case	**2.1 (1.5-2.9)**	**52%**
Household or intimate contact	**1.4 (1.0-2.2)**	**29%**
Close contact with coughing index case	**4.0 (2.7-5.8)**	**75%**
Contact time >40h	**5.7 (3.5-9.3)**	**82%**

Diel,…, Nienhaus CHEST 2009, Vol 135(4): 1010-1018,

Recommendations for Environmental Contact Tracing in Tuberculosis

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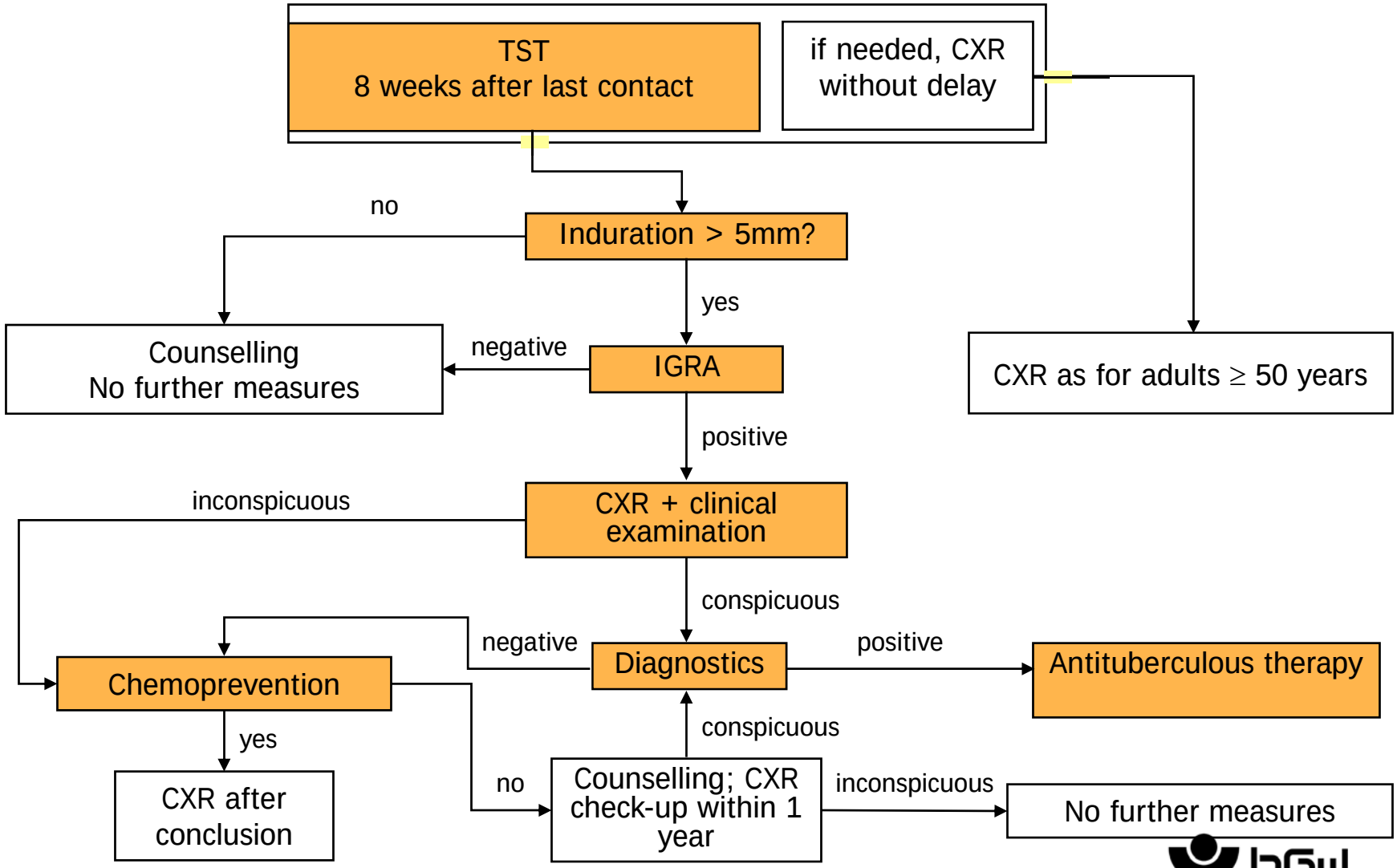
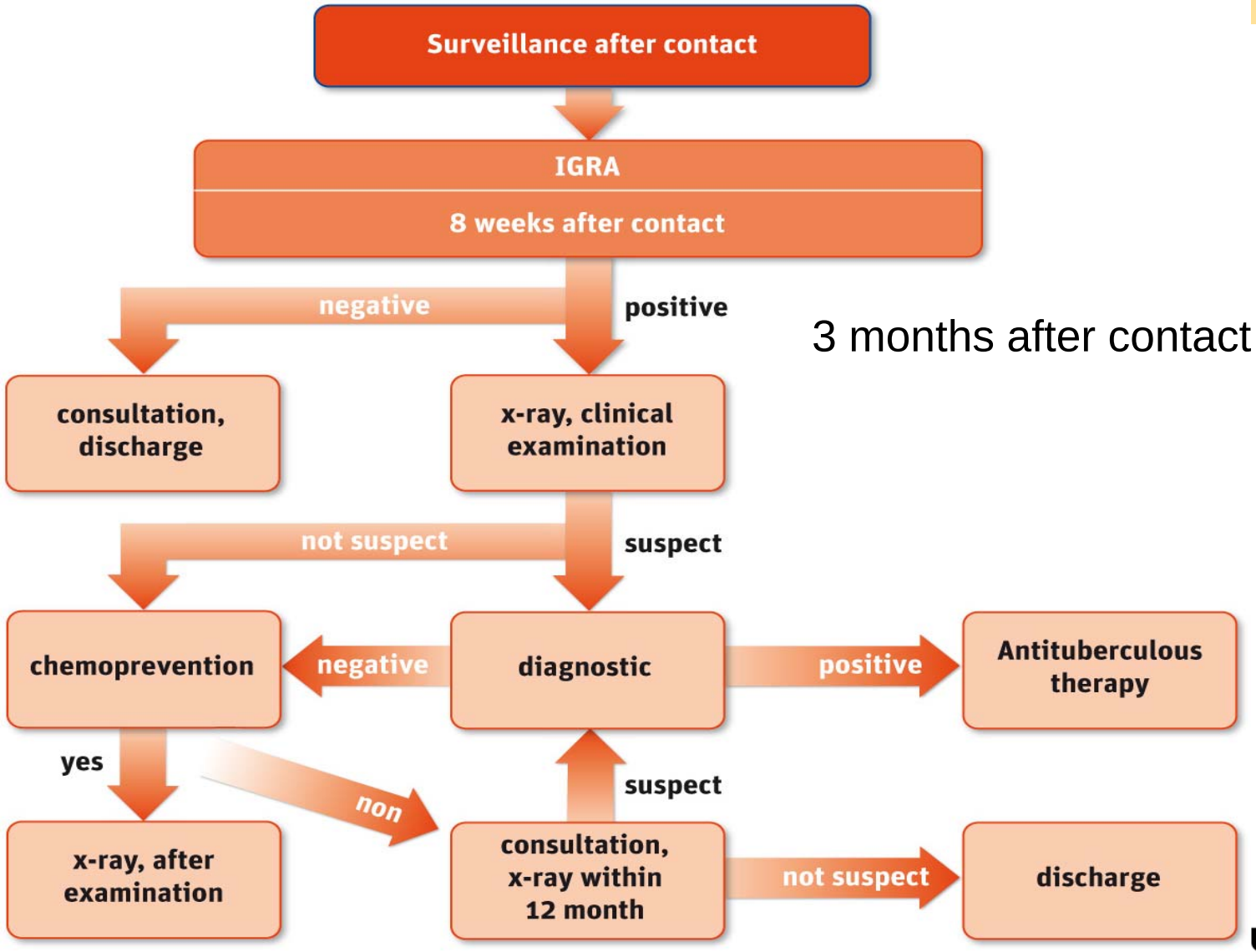


Dubrovnik May 31st 2009

Recommendation for Contact Tracing in health care sector

(Institute of accidents insurance and prevention in the health and welfare services)



Conclusion

- Two step strategy for Environmental Contact Tracing
- IGRA instead of TST in German HCWs
- No X-rays or chemoprevention without IGRA
- Fewer X-rays needed in contact tracing
- Decision of chemoprevention is based on a more specific test
- IGRA in close contacts identifies people who profit from LTBI treatment

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Thank you for your attention