

Respiratory tract infections

Dr hab. med. Tadeusz M Zielonka

**Medical University of Warsaw
Department of Family Medicine**

Respiratory tract infections - key questions

- 1. An interactive case of a respiratory infection**
- 2. Respiratory tract infections - how important is this problem?**
- 3. How to recognize the disease?**
- 4. Who to hospitalize?**
- 5. How to heal?**
- 6. How to control?**
- 7. What to do if there is no improvement?**
- 8. Tuberculosis epidemiology**
- 9. Tuberculosis diagnosis**
- 10. Treatment and prevention of tuberculosis**

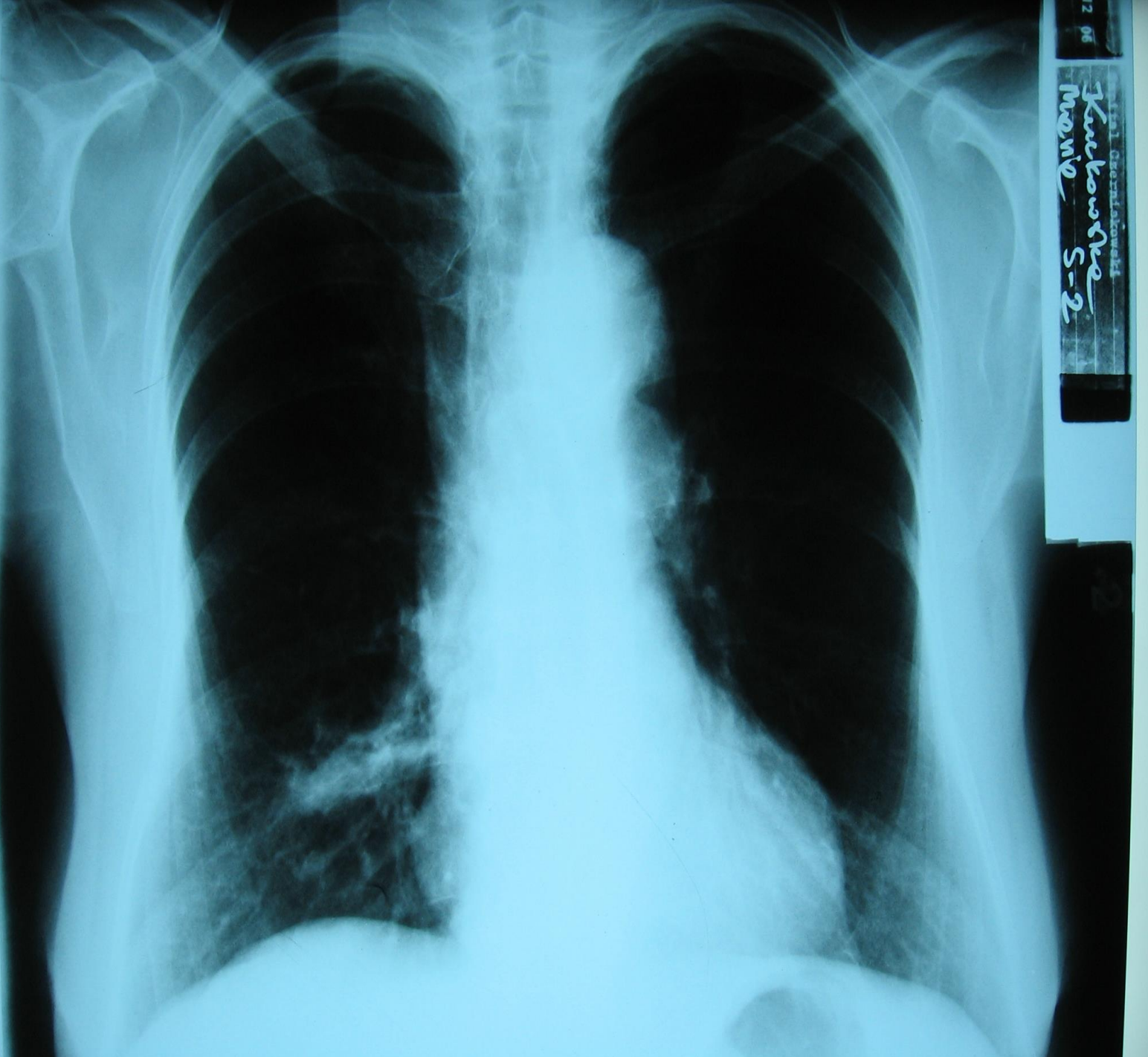
Symptoms

A 79-year-old woman in good general condition was referred by a family doctor due to severe hemoptysis lasting for 3 days, which was not accompanied by fever or symptoms of upper and lower respiratory tract infection.

In the physical examination: crackles at the base of the right lung, enlarged of liver, pulse 88/min, RR 150/90

Medical history

- 1. Hepatitis C type C for 30 years**
- 2. Hypothyroidism - hormonal substitution**
- 3. Hypertension (beta blocker and diuretic)**
- 4. Ovary removed 30 years ago (large cyst)**
- 5. Right breast lump (cyst) was removed 35 years ago**
- 6. Nicotine 3 years in adolescence until pregnancy**



Chest

X-ray

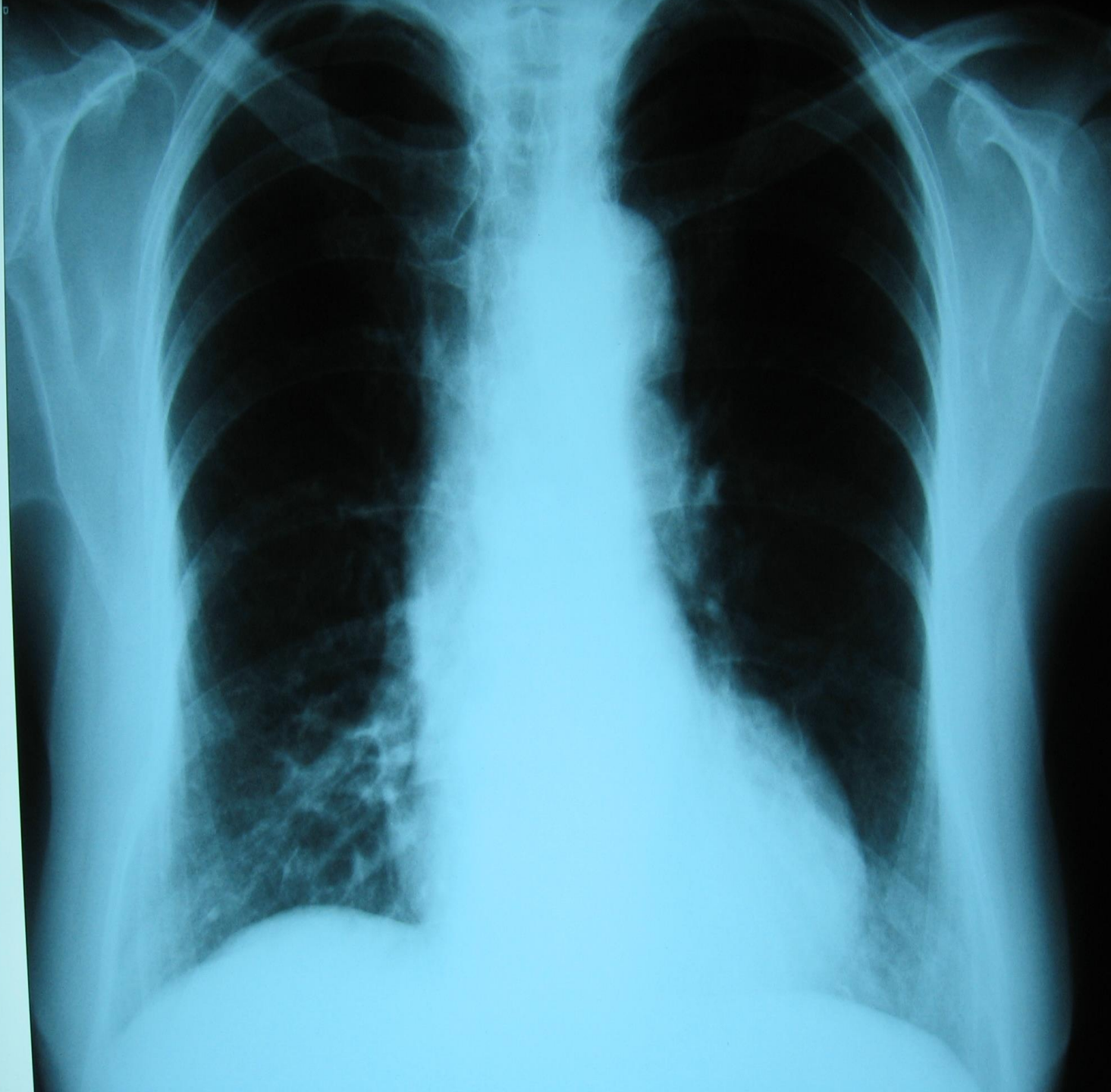
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Prescriptions

- **She was not admitted to hospital**
- **Treatment with clarithromycin twice 500 mg a day was prescribed**
- **Radiological control was recommended in 10 days**

How do you evaluate these recommendations?

- 1. It was perfectly correct**
- 2. Correctly selected antibiotic, but hospitalization was necessary**
- 3. Incorrectly selected antibiotic and necessary hospitalization**
- 4. Incorrectly selected antibiotic and indications for hospitalization were not assessed**



Chest

X-ray

2

Hemoptysis

completely reseeded

PHYSICAL EXAMINATION

- temperature was 36.6°C;
- heart rate 88 bpm;
- arterial blood pressure 180/100 mm Hg;
- respiratory rate 19 breaths/min;
- SaO₂ was 96% on room air;
- crackles on the base of right lung;
- enlargement of liver (6 cm on midclavicular line)

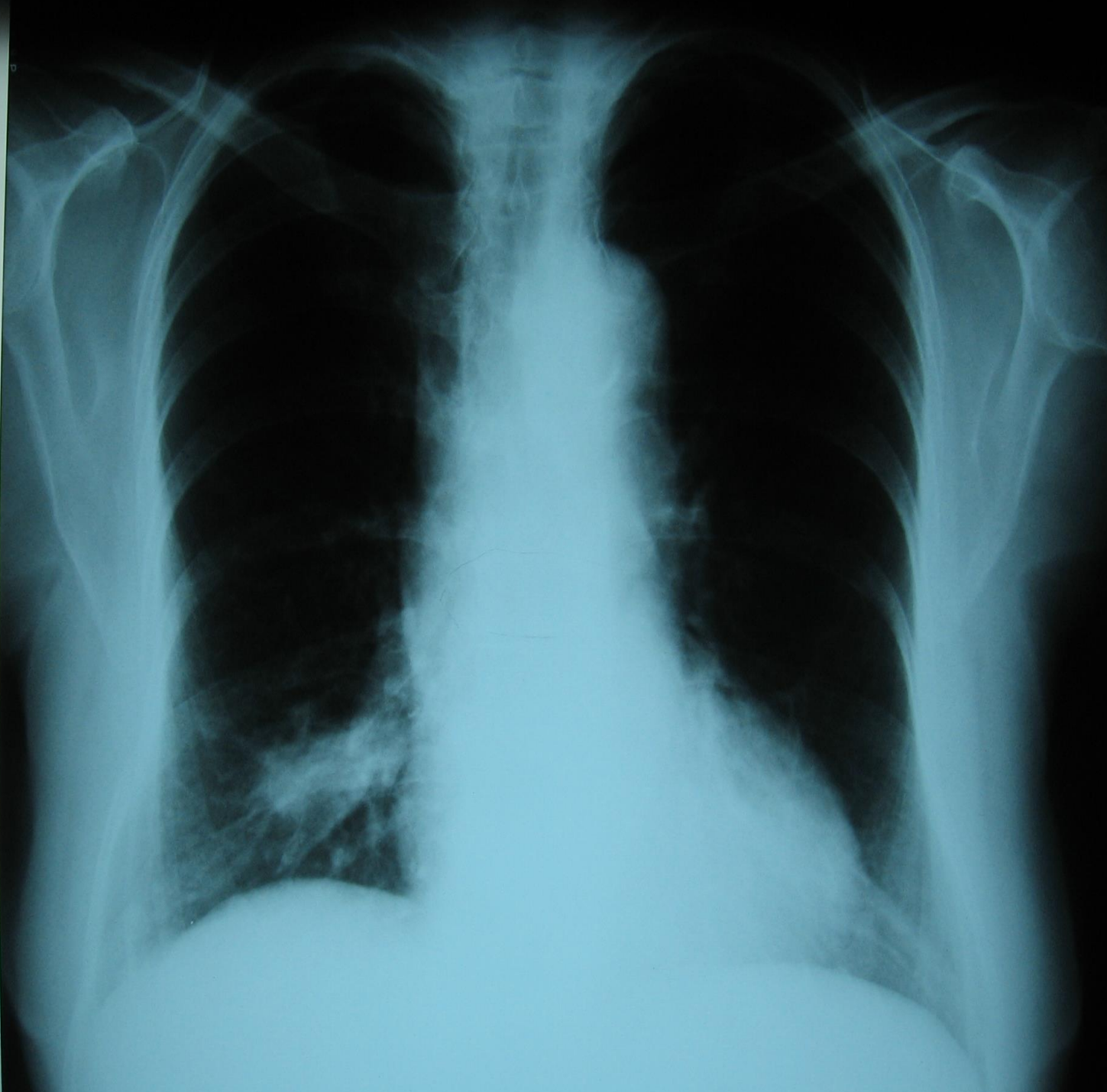
LABORATORY TESTS

- **AspAT 150 IU, AlAT 97 IU; GGTP 26 IU, FA 74 IU;**
- **protein 6.8 g/L, albumin 3.5 g/L;**
- **ESR - 12 mm/h, CRP 0.05; WBC $5.38 \times 10^3 / \mu\text{l}$**
(N-50%, E-4%, B-1%, M-10%, L-34%);
- **INR 1.2, APTT 30 s, PLT $159 \times 10^3 / \mu\text{l}$, RBC $4.57 \times 10^6 / \mu\text{l}$;**
- **cholesterol 126 mg/dL, glucose 74 mg/dL;**
- **creatinine 0,7 mg/dl, urea 42 mg/dL**

Chest

X-ray

3



Consultations

- **Laryngological evaluation not demonstrated the source of bleeding; blood was observed in the region of larynx; atrophic inflammation of nasopharynx;**
- **Gastroscopy was demonstrated small oesophageal varices (II grade) without bleeding, and pyloritis; urease test was negative**

What examination do you propose as first?

- 1. Tuberculin skin test**
- 2. Serological assay to *Aspergillus* sp.**
- 3. Bronchochography**
- 4. Bronchoscopy**
- 5. Computed tomography**

What disease do you suspect?

- 1. Bronchiectasis**
- 2. Broncho-pleural fistula**
- 3. Pulmonary embolia**
- 4. Aspergilloma**
- 5. Tuberculosis**

CONCLUSIONS

- **Infected bronchiectasis are important cause of hemoptysis**
- **HRCT is the method of choice for diagnosis bronchiectasis**

Respiratory infections - the scale of the problem

- 1. Respiratory infections are the most common human diseases.**
- 2. Acute pharyngitis is the most common reason for visiting your GP.**
- 3. Every year 1 / 5-1 / 3 children and 5% of adults have 1 episode of bronchitis. Peak school-age cases.**
- 4. About 90 percent these infections are caused by viruses (adeno-, corona-, rhino-, RSViruses)**
- 5. Pneumonia accounts for 5% of respiratory infections.**

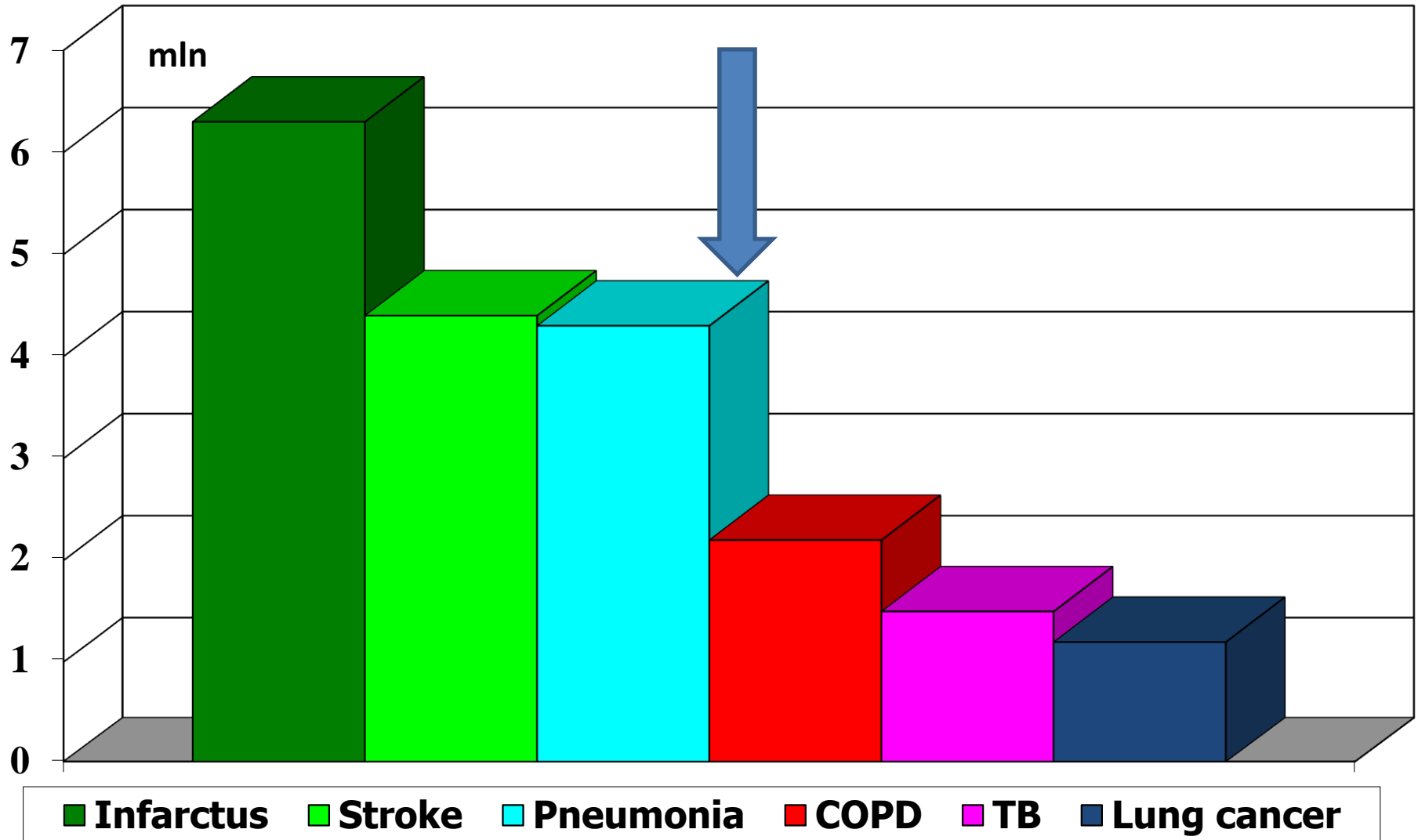
Principles of antibiotic therapy

- **Empirical therapy based on the most likely etiological factor and presumed sensitivity. Based on local epidemiological studies.**
- **Adjusted treatment for failure in the absence of improvement 48-72 hours after taking the first antibiotic.**
- **Targeted treatment after obtaining an antibiogram.**
- **Sequential treatment is parenteral administration of the same drug followed by oral administration.**

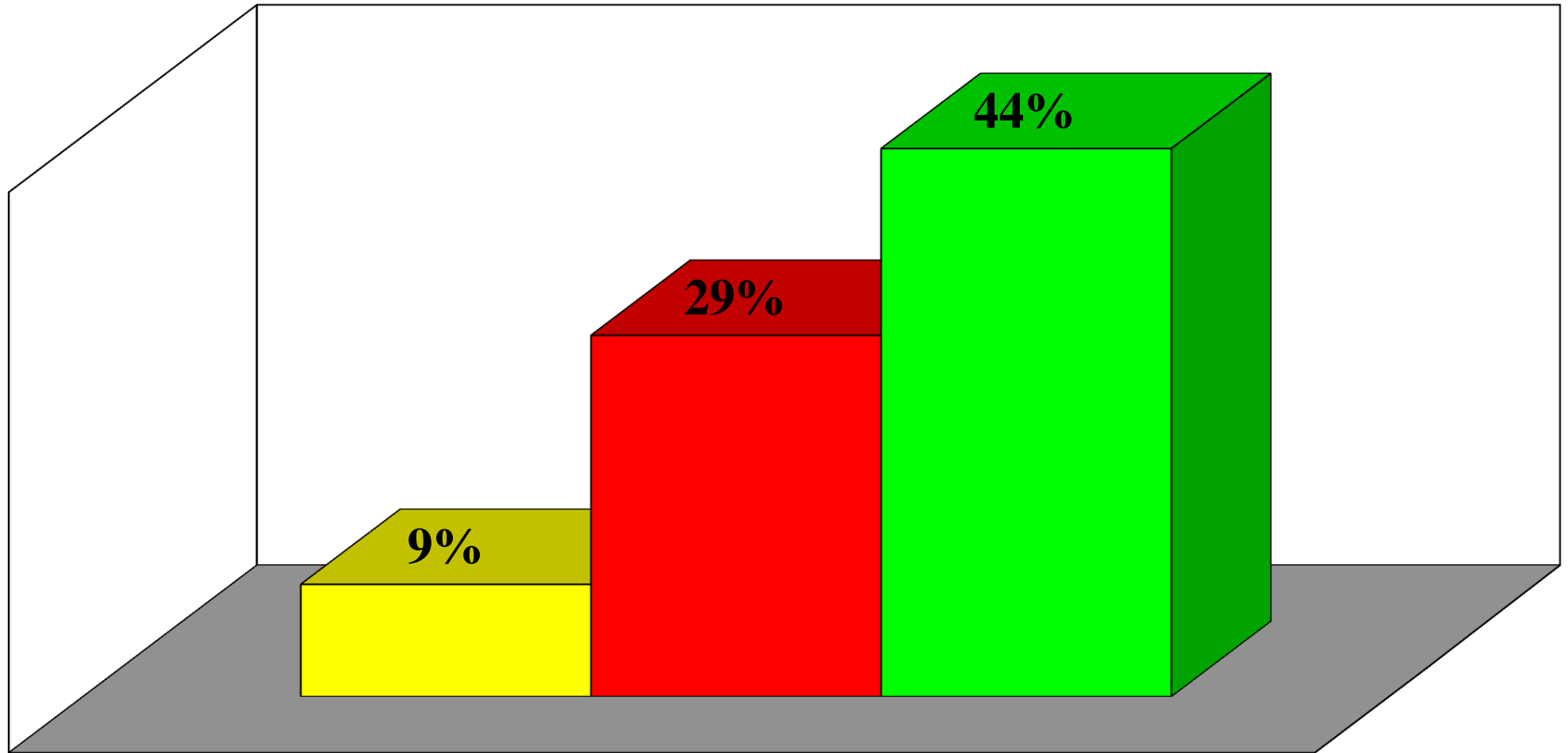
Problems with antibiotic therapy

- 1. Increasing antibiotic resistance**
- 2. Disturbances in the bacterial flora of the digestive tract**
- 3. Overuse of antibiotics without indications, especially in viral infections**
- 4. Too long use of low-dose antibiotics**
- 5. Too late culture in the event of treatment failure**
- 6. No new drugs**

TOP list of the main causes of death



Mortality from pneumonia

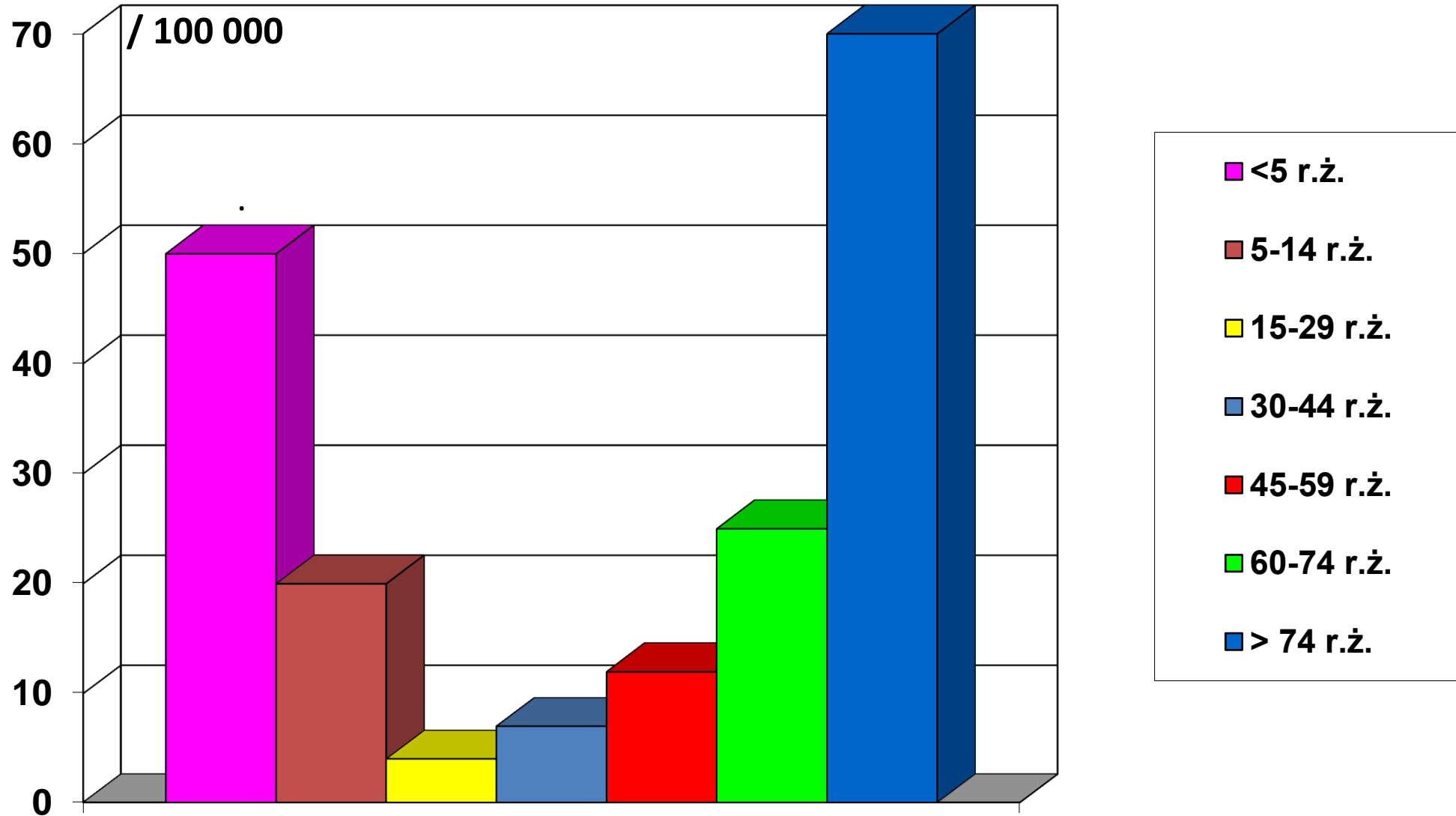


■ out-patient

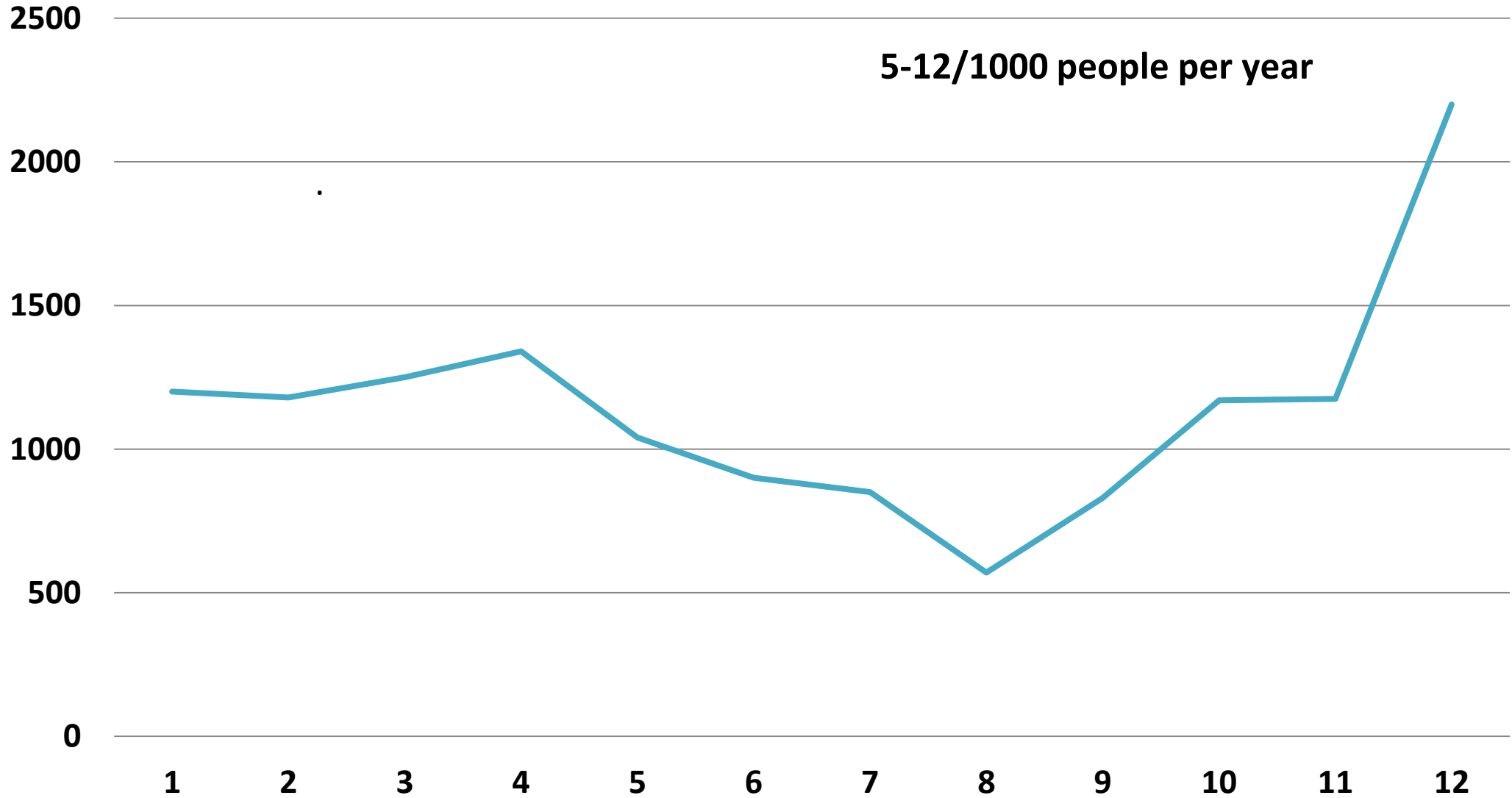
■ in-patient

■ Ventilator-associated

Hospitalization due to pneumonia



Seasonality of pneumonia in Europe



British and Polish education

Pneumonia diagnosis (*Wielka interna*)

History (symptoms, cough, expectoration, dyspnoea, fever, comorbidities, risk factors, family history)

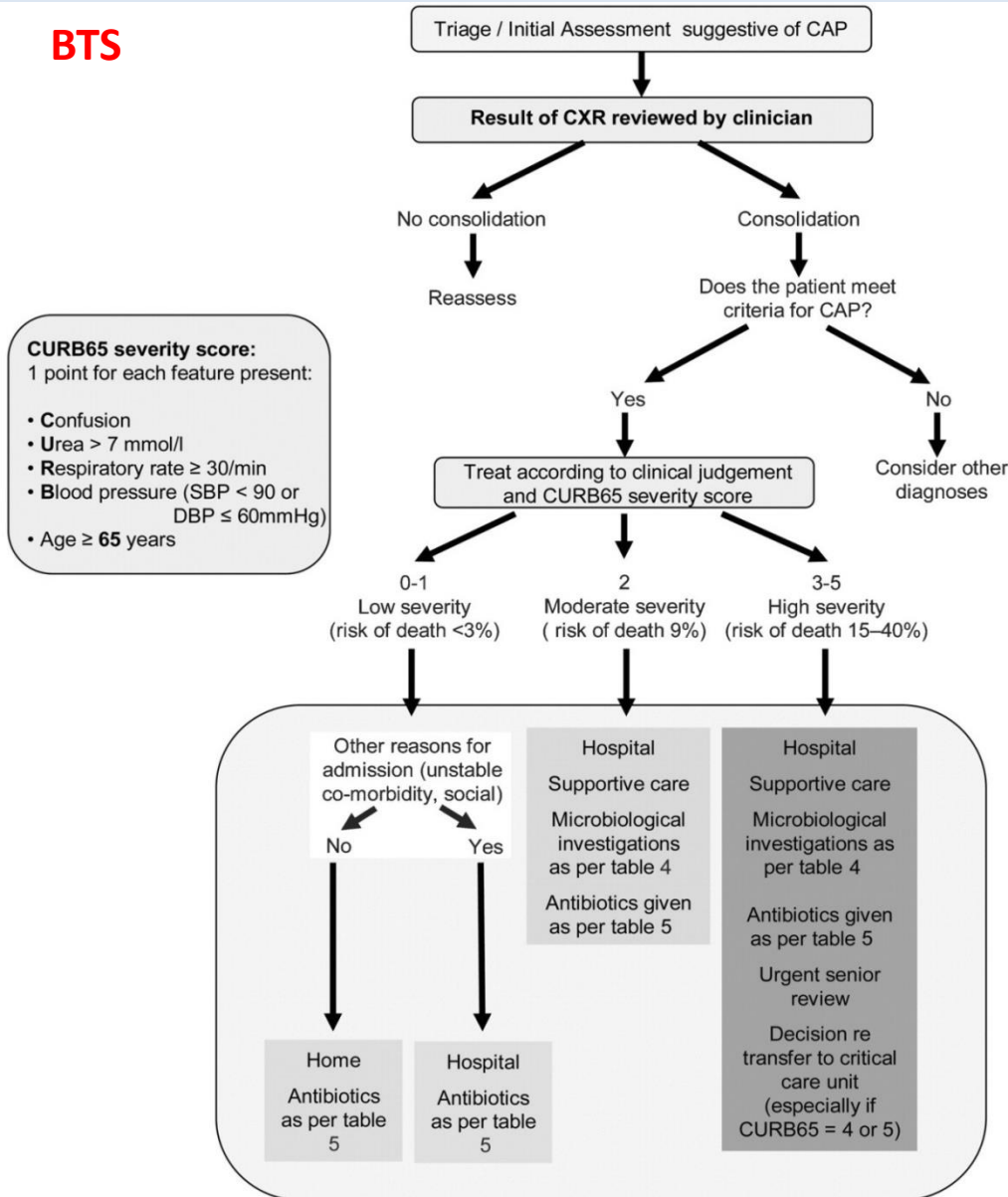
Physical examination

(bubble murmur, crackling noise percussion suppression, tremor, heart rate, respiratory rate, blood pressure, state of consciousness)

Additional examinations

(inflammatory markers, CRP, morphology, sputum culture, chest x-ray).

BTS



Aim by 4 hours: diagnosis made and management including antibiotics started

Symptoms of pneumonia

- cough with purulent sputum
- fever > 38°C
- tachypnea and tachycardia
- limited auscultation and percussion changes

Less often

- dyspnea
- chest pain
- hemoptysis
- deterioration of the mental state

Clinical symptoms in pneumonia

In the group of patients who were referred to the emergency room with symptoms of lower respiratory tract infection, only 7% of pneumonia was radiologically confirmed.

[J Chronic Dis 1984; 37: 215]

In patients presenting to their GP with symptoms of acute cough, pneumonia was reported in 3-6%.

[Am J Emerg Med 2007; 25]

In patients who experience crackling or suppression of percussion sound, the likelihood of pneumonia is 8-10% and 10-18%, respectively.

[J Emerg Med 1989; 7: 26]

The appearance of purulent sputum does not prejudge either a bacterial infection or a diagnosis of pneumonia.

[Am J Emerg Med 2007; 25: 631]

The most important abnormalities indicating pneumonia in people presenting to a physician for acute cough are: fever, hypoxemia, tachycardia and tachypnea.

[Arch Intern Med 2003; 138: 109]

The value of clinical symptoms in the diagnosis of pneumonia

There are no pathognomonic signs or symptoms for pneumonia.

The clinical examination is characterized by high sensitivity and low specificity in the diagnosis of community-acquired pneumonia.

Significant differences in the interpretation of chest auscultation and peripheral changes by different physicians are reported, with agreement of 76-79%.

Pneumonia diagnostics

Pneumonia cannot be diagnosed on the basis of clinical examination alone, as the signs and symptoms are not specific enough [EII]. (nor sensitive in the elderly > 75 years of age)

Chest x-ray is the method of choice for diagnosing adult pneumonia [AII].

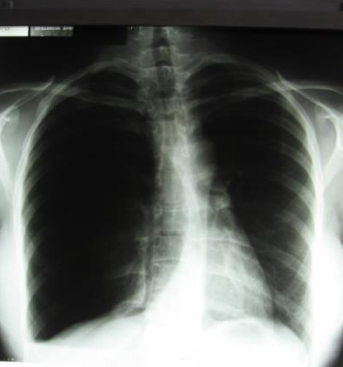
The diagnosis of pneumonia and the implementation of antibiotic treatment without performing a radiological examination exposes the patient to adverse effects of the drugs used and contributes to the increase in drug resistance [BI].

Indications for X-ray examination

The indication for chest X-ray examination is the presence of symptoms of lower respiratory tract infection and the presence of at least one of the following disorders: tachycardia above 100/min. tachypnea above 24/min, fever above 38°C or focal auscultation changes over the lungs [**BII**].

These symptoms often do not occur in the elderly!

Chest radiography



- confirms infiltrative changes in the lung parenchyma the location and extent of the changes in the lung
- multifocal changes
- desintegration of the infiltrate – cavities
- fluid or air in the pleural cavity
- enlargement of the chest lymph nodes
- lung assessment (emphysema, atelectasis, pulmonary fibrosis interstitial changes)
- assessment of the heart and circulation
- assessment of the chest wall
- assessment of the diaphragm and abdominal organs

The value of microbiological tests in the diagnosis of pneumonia

The analysis of the usefulness of microbiological diagnostics in outpatient patients with CAP showed that the pathogen causing pneumonia was established in sputum tests only in 5% of patients with mild CAP.

[Acad Emerg Med 1996; 3: 768]

The necessity to perform the examination within 2 hours of collecting the material makes it difficult to perform it outside the hospital; a positive blood culture was found in 2% of patients admitted to the emergency room for whom the decision to use outpatient pneumonia was made, and the result influenced the course of treatment in only 0.5% of patients.

[Emer Med J 2003; 20: 521]

Cultures in patients receiving antibiotics are rarely helpful in establishing the etiology of pneumonia.

[BTS 2009]

Microbiological diagnostics

Clinical, radiological and laboratory tests do not allow to differentiate the etiology of pneumonia sufficiently to select the appropriate antibiotic [DII].

Routine culture is not recommended for patients with mild community-acquired pneumonia for whom hospitalization is not indicated [EII].

Sputum culture should be performed in patients hospitalized for moderate or severe CAP [AII].

Blood culture may also be performed [CIII].

Rekomendacje postępowania w pozaszpitalnych zakażeniach układu oddechowego 2017

Clinical indications for microbiological testing prior to antibiotic administration are age, comorbidities, rates of serious illness, and epidemiological indications.

Indications for hospitalization

Indications for hospitalization in patients with community acquired pneumonia should be established on the basis of the death risk score, and in doubtful situations based on individual patient assessment [BI].

CURB 65 SCALE - BTS

- **Confusion**
- **Urea** (urea concentration > 7 mmol/L)
- **Respiratory rate** (tachypnoea > 30 /min)
- **Blood pressure**
 - systolic pressure < 90 mmHg
 - diastolic pressure < 60 mmHg
- **65 years** (age > 65)

0-1 points outpatient treatment (risk of death $< 3\%$)

2 points hospitalization (risk of death 9%)

3-5 points, possible treatment in the ICU (risk of death $15-40\%$)

PORT scale - interview

Age of men	Points = age
Age of women	Points = age - 10
Stay in a nursing home	+ 10
Cancer	+30
Liver diseases affecting its function	+20
Congestive heart failure	+10
Cerebral circulation disease (stroke)	+10
Diseases leading to kidney failure	+10

PORT scale - physical examination

Physical examination	
A disturbance of consciousness known to be non-chronic (lack of orientation as to place and time)	+20
Respiratory rate > 30/min	+20
Systolic pressure < 90 mmHg	+20
Body temperature < 35°C or > 40°C	+15
Pulse > 125/min	+10

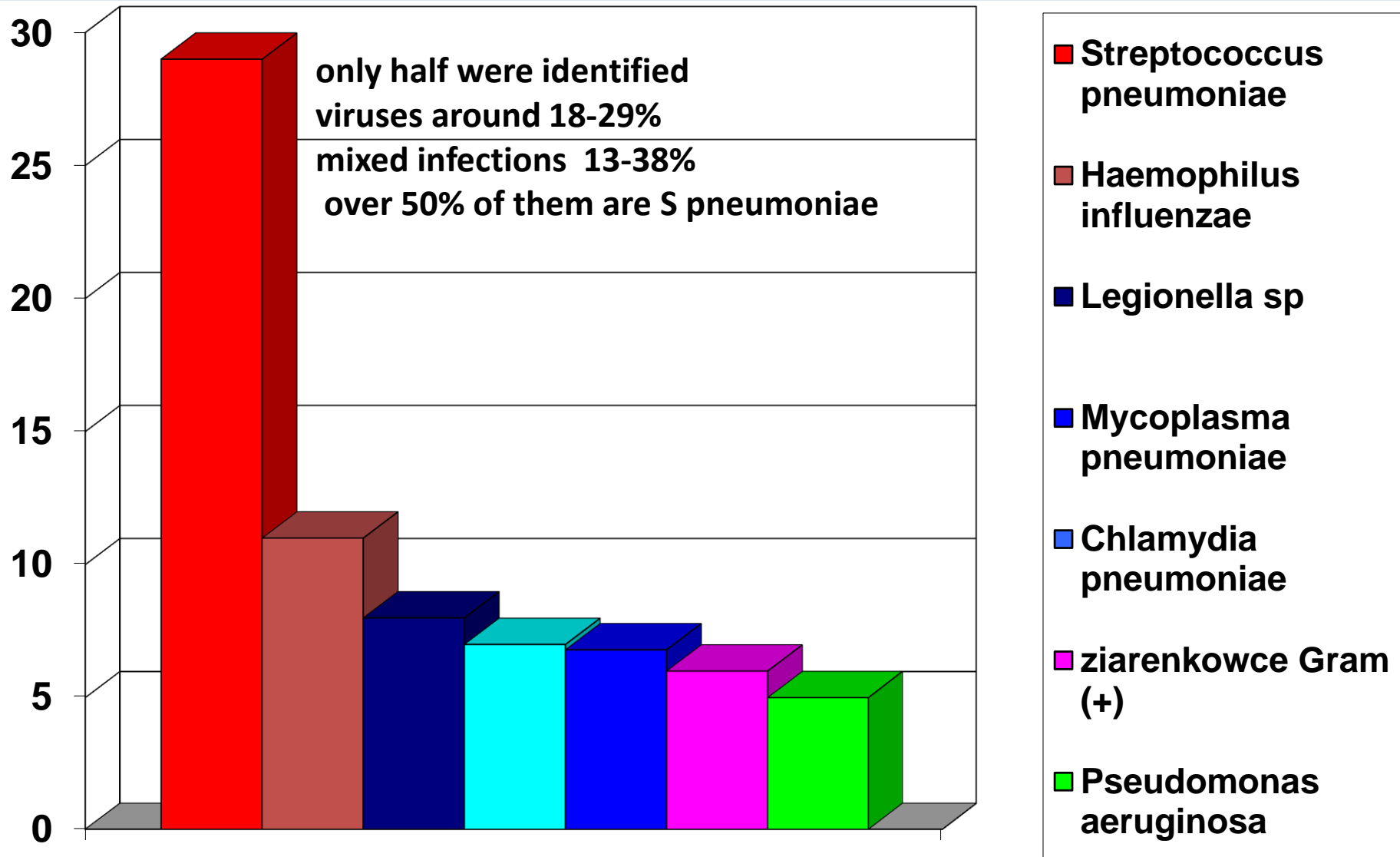
PORT scale - additional tests

Additional tests	
Arterial blood pH <7.35	+30
Increased levels of urea or creatinine	+20
Serum Na + decreased <130 mmol / L	+20
Increased serum glucose > 250 mg / dL	+10
Haematocrit <30%	+10
PaO₂ < 60 mmHg	+10
Pleural effusion	+10

The risk of death on the PORT scale

Category	Number of points	Risk of death	Recommended treatment site
I	age <50 years, without medical conditions and deviations in the table	0,1-0,4%	outpatient
II	< 70	0,6-0,7%	outpatient
III	71-90	0,9-2,8%	place of treatment determined individually
IV	91-130	8,2-9,3%	hospital
V	>130	27-31,1%	intensive care unit

The main causes of pneumonia



Treatment in primary health care

In the first flare of community-acquired pneumonia, it is recommended to use an antibiotic effective against *Streptococcus pneumoniae*, mainly amoxicillin 3 x 1 g or 2 x 1.5-2 g per os [AI].

In young adults with a mild course of pneumonia, without coexisting diseases, it is possible to use macrolide in the first line [BI] .

Treatment in the hospital

In the first line of community-acquired pneumonia, it is recommended to use an antibiotic effective against **Streptococcus pneumoniae, especially amoxicillin 3 x 1 g i.v or ampicillin in a dose of 4 x 1 g i.v. Benzylpenicillin 4-6 x 1-4 million units can also be used intravenously. [AI]**

In the case of severe pneumonia requiring treatment in an intensive care unit, the use of ceftriaxone or cefotaxime with macrolide is recommended [BI].

Allergy to beta-lactams

- 1. Immediate allergic reaction** (urticaria, Quincke's edema, bronchospasm, anaphylactic shock) **macrolide** should be used: clarithromycin 2 x 500 mg, azithromycin 500 mg once a day and then 250 mg for 4 days; fluoroquinolones can also be used
- 2. Non-immediate allergic reactions** (e.g. maculo-papular rash) cefotaxime at a dose of 1-2 g three times a day every 8 hours; ceftriaxone at a dose of 1-2 g once a day depending on severity

Treatment of aspiration pneumonia

1 Treatment of patients without accompanying diseases:

amoxicillin / ampicillin + beta-lactamase inhibitor ceftriaxone + metronidazole or clindamycin

2 Treatment of patients staying in nursing homes:

piperacillin with tazobactam ceftazidime/cefepime with metronidazole

3 Treatment of alcoholics with periodontal changes:

**piperacillin with tazobactam, imipenem or meropenem
ceftriaxone + clindamycin or metronidazole**

Expectorants and mucolytics

- In acute lower respiratory tract infections, short-term use of erdosteine is recommended in the period of productive cough [**BI**].
- In CAP, levodropropizine may be used for a short time in the period of acute dry cough, and erdosteine in the period of productive cough [**CIII**].

Rekomendacje postępowania w pozaszpitalnych zakażeniach układu oddechowego 2017

Physical therapy, respiratory gymnastics and mucolytics, in case of high difficulty in expectoration of sputum.

How long to cure pneumonia?

Treatment of community-acquired pneumonia in mild to moderate adults should be approximately 7 days or approximately 3 days from clinical stabilization [**AII**].

- resolution of fever
- tachypnea <24 / min.
- SaO₂ > 92% heart
- systolic RR > 90 mmHg
- rate <100 / min.

Rekomendacje postępowania w pozaszpitalnych zakażeniach układu oddechowego 2017

7 days light and moderate pneumonia

BTS 2009

7-10 days severe pneumonia (up to 14-21 days can be)

2-6 weeks in special cases - staphylococcus, legionellosis, abscess, empyema

Control tests

In case of rapid clinical improvement in patients with community acquired pneumonia, routine evaluation of the response to treatment with additional tests is not necessary [BII].

Control chest radiography is recommended in the absence of clinical improvement and in patients with cancer risk factors [DIII].

Rekomendacje postępowania w pozaszpitalnych zakażeniach układu oddechowego 2017

Clinical control after 48 hours of antibiotic therapy in primary care and hospitalization is indicated if no improvement is seen.

CRP and chest x-ray control in the absence of clinical improvement after 3 days of antibiotic. Clinical control after 6 weeks in primary health care or in a treatment hospital.

What determines the success of pneumonia treatment



4 hours



UK



1 hour



Germany



Reasons for treatment failure

1. Infectious causes (approx. 40%)

- infection with a microorganism resistant to the antibiotic used
- infection with a microorganism that is difficult to treat (Staphylococcus aureus, Legionella spp., S. pneumoniae resistant for drugs, gram negative rods, superinfection with hospital strain)
- occurrence of complications in the form of lung abscess, pleural empyema

2. Non-infectious causes (16%)

- alveolar haemorrhage
- pulmonary embolism
- side effects of drugs
- circulatory failure tumour

3. Cause unknown (35-45%)

Treatment failure

No improvement after first-line treatment, which cannot be explained by the clinical picture and the results of additional tests performed, is an indication for the immediate implementation of diagnostic tests identifying the cause, such as:

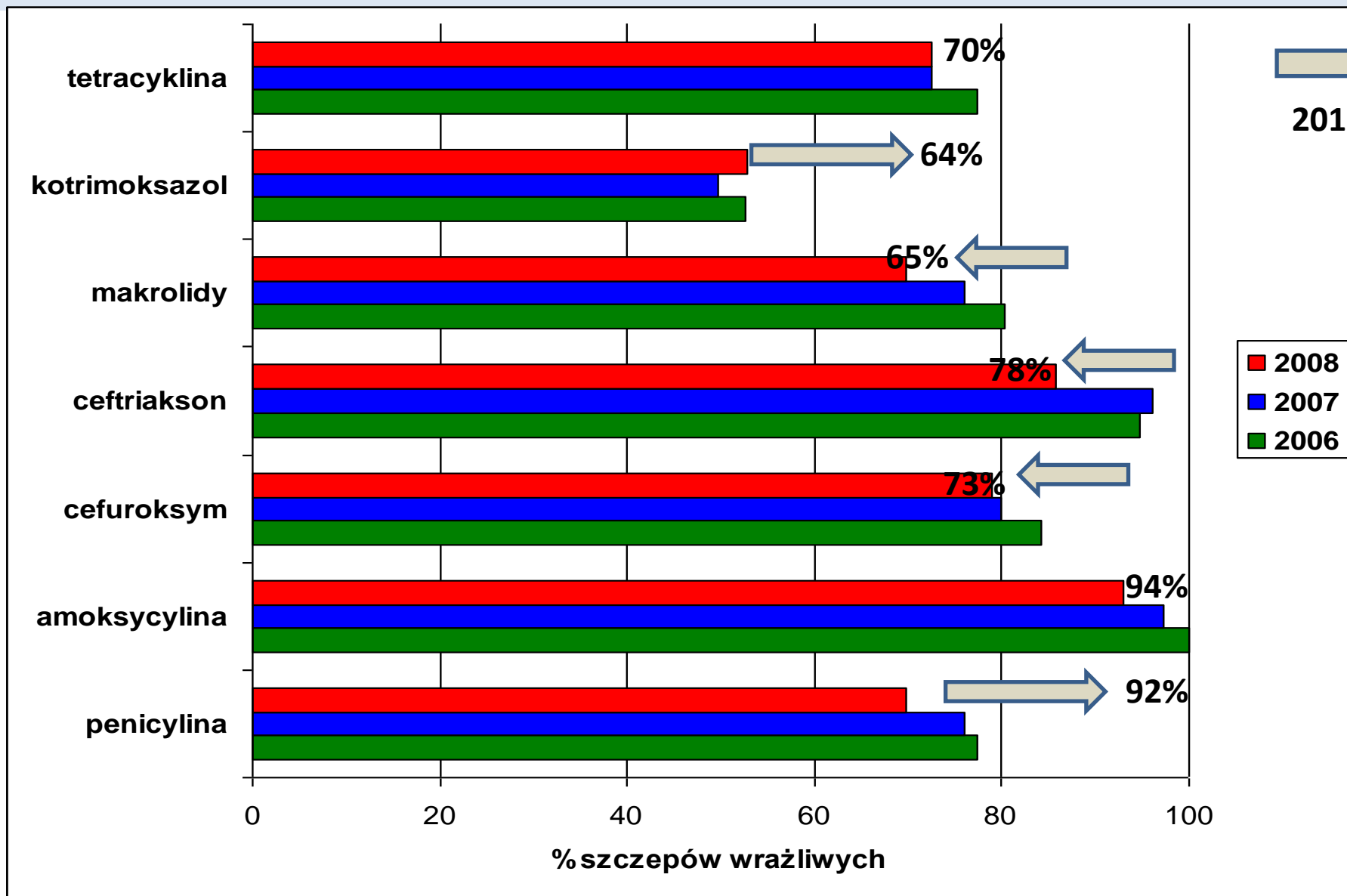
- computed tomography of the chest [CIII]
- microbiological tests: blood or sputum culture, determination of antigens in urine [BIII]
- bronchoscopy to identify infectious and non-infectious causes of the disease, if reliable material for bacteriological tests has not been obtained from sputum [BIII]

Second-line treatment

In the absence of improvement, when amoxicillin was used in the first-line treatment and further antibiotic administration is required, it is recommended to use a third-generation cephalosporin (ceftriaxone or cefotaxime) with macrolide [CIII].

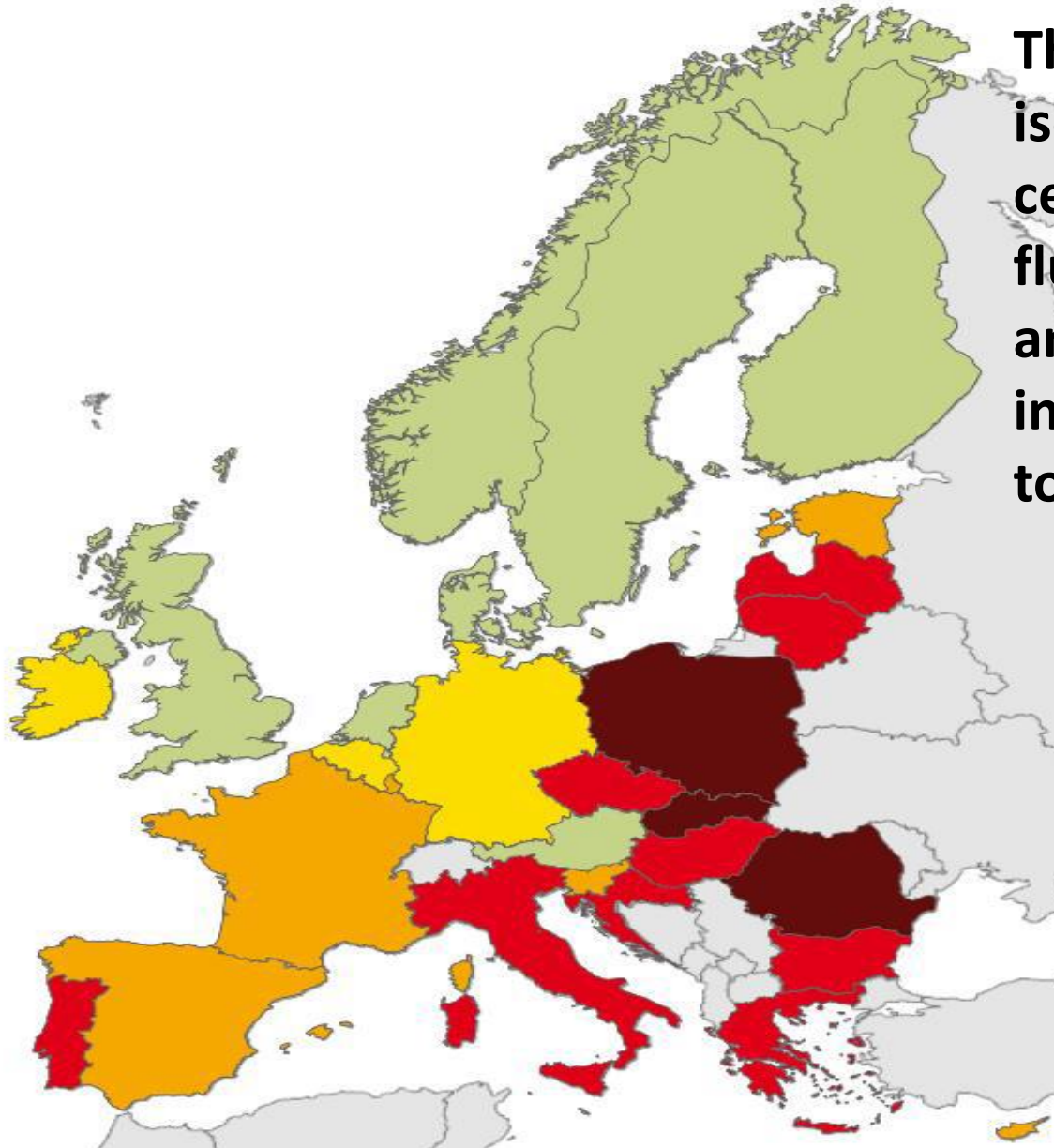
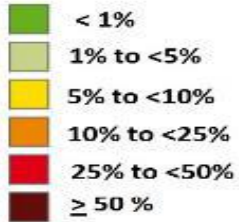
However, these antibiotics are not the optimal choice for *Staphylococcus aureus* and are not effective against non-fermenting Gram negative rods (e.g. *Pseudomonas aeruginosa*).

Pneumococcal resistance in Poland



Resistance of *K. pneumoniae*

2016

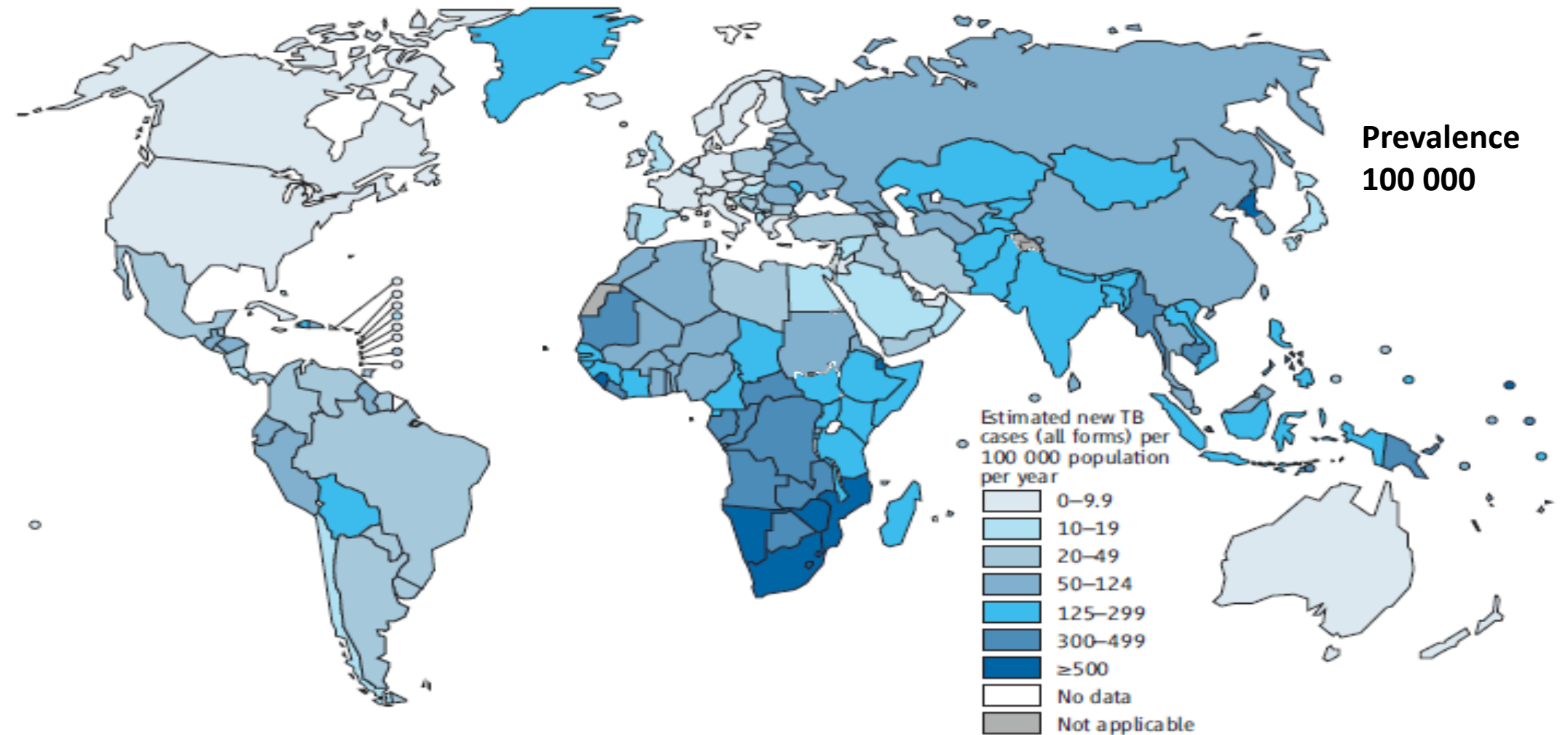


The percentage of invasive isolates resistant to cephalosporins III, fluoroquinolones, aminoglycosides in EU countries according to ECDC

***Clostridium difficile* infections**

High risk	Medium risk	Low risk
Cephalosporins II and III Fluoroquinolones Penicillins with broad spectrum of action with inhibitors Ticarcillin/Clavulanate Piperacillin /Tazobactam	Macrolides Cotrimoxazole Carbapenems Amoxicillin Ampicillin Piperacillin / Tazobactam Ticarcillin / Clavulanate Tigecycline	First-generation cephalosporins Nitrofurantoin Aminoglycosides Rifampicin Metronidazole Vancomycin Tetracycline Penicillin Cloxacillin

Tuberculosis in the world



**10,4 mln new cases, 1,3 mln deaths,
110/100 000 (3-1400/100 000) new cases**

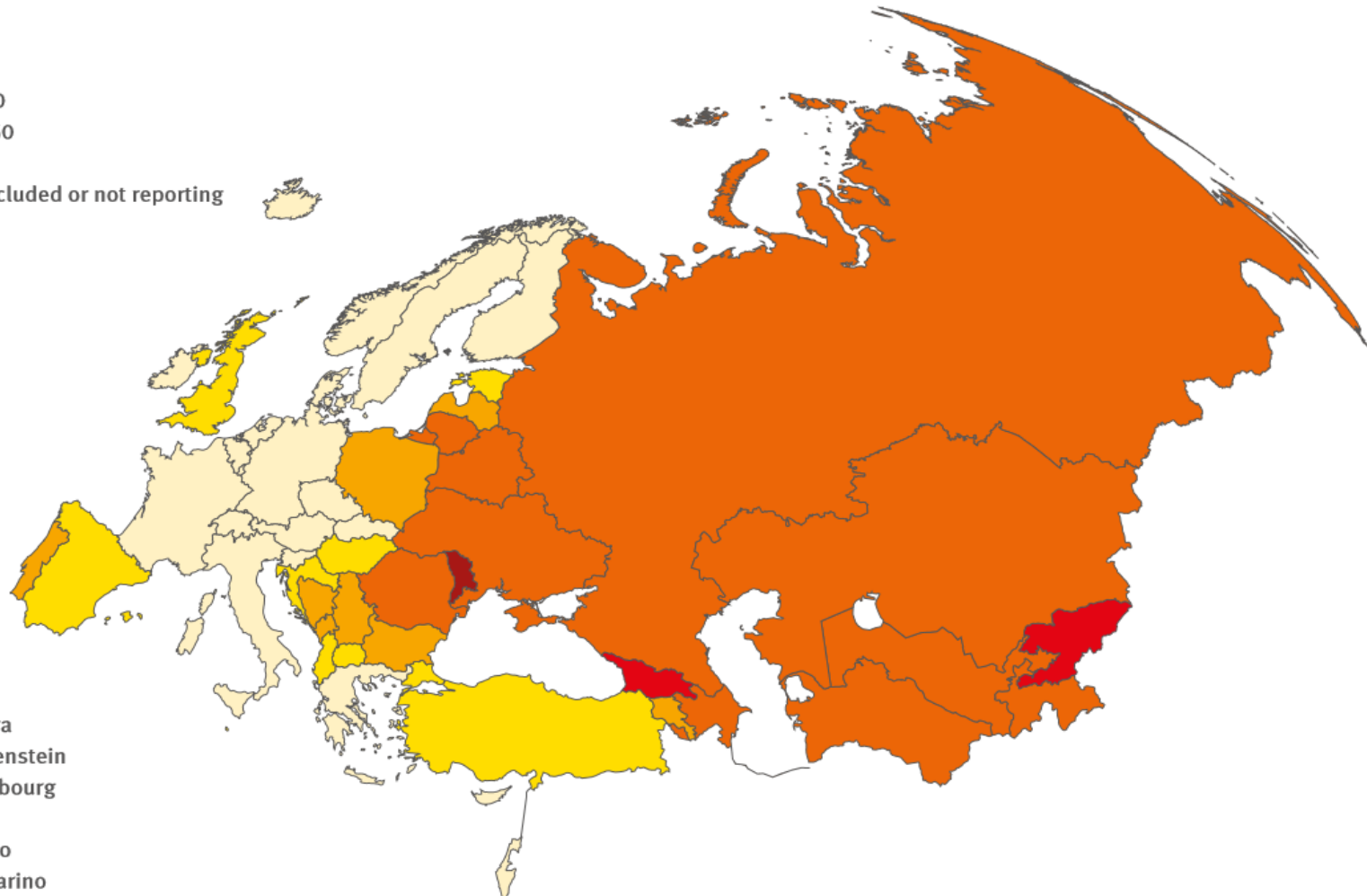
Tuberculosis in Europe

Map 2: Estimated TB incidence per 100 000 population, European Region, 2014

www.ecdc.europa.eu

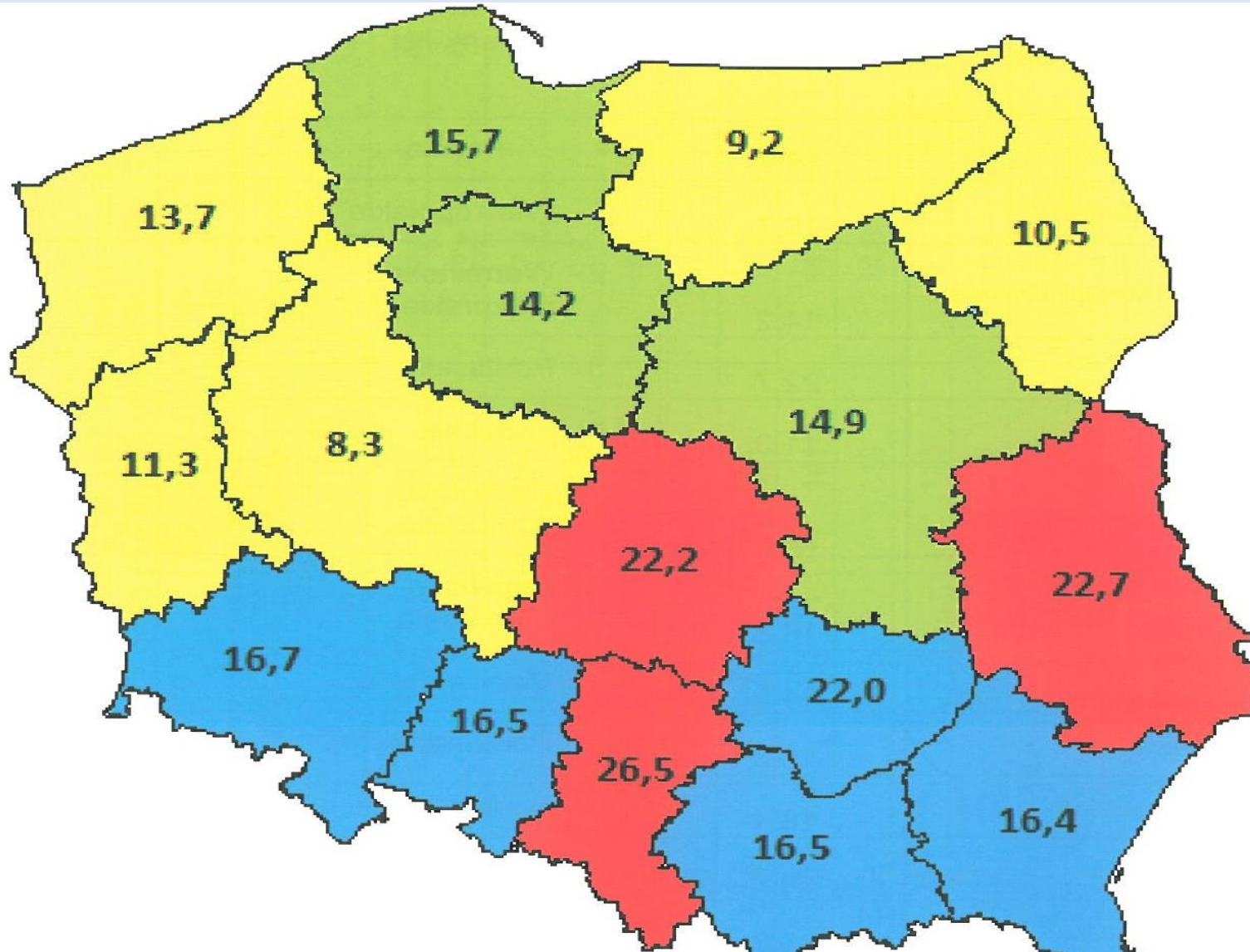


Not included or not reporting



340 000 new cases, 33 000 deaths, 37 000/100 000

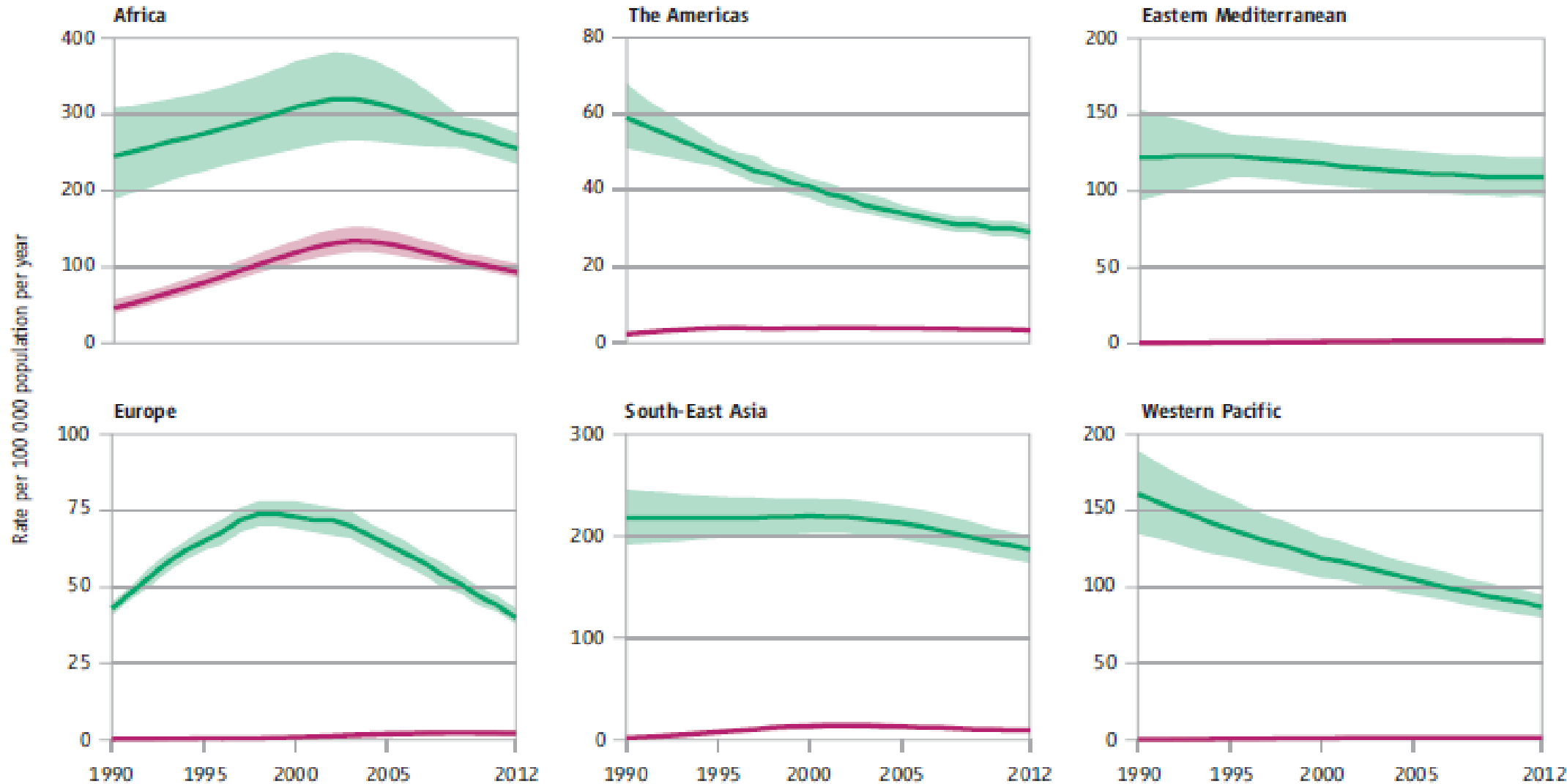
Tuberculosis in Poland



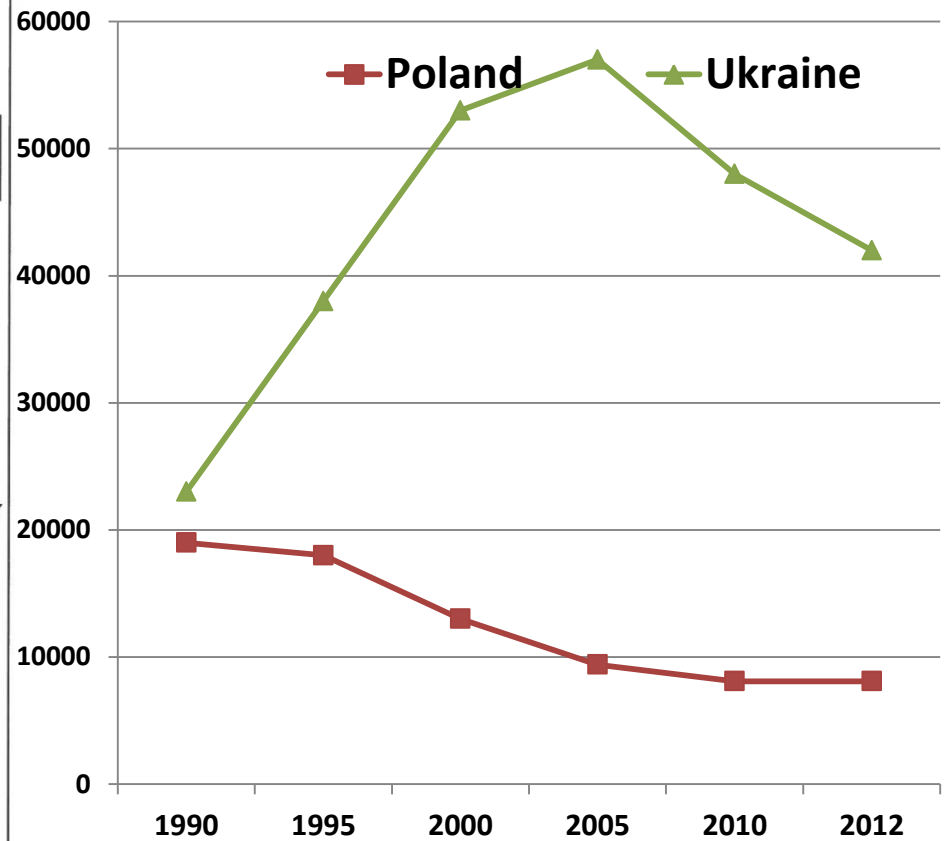
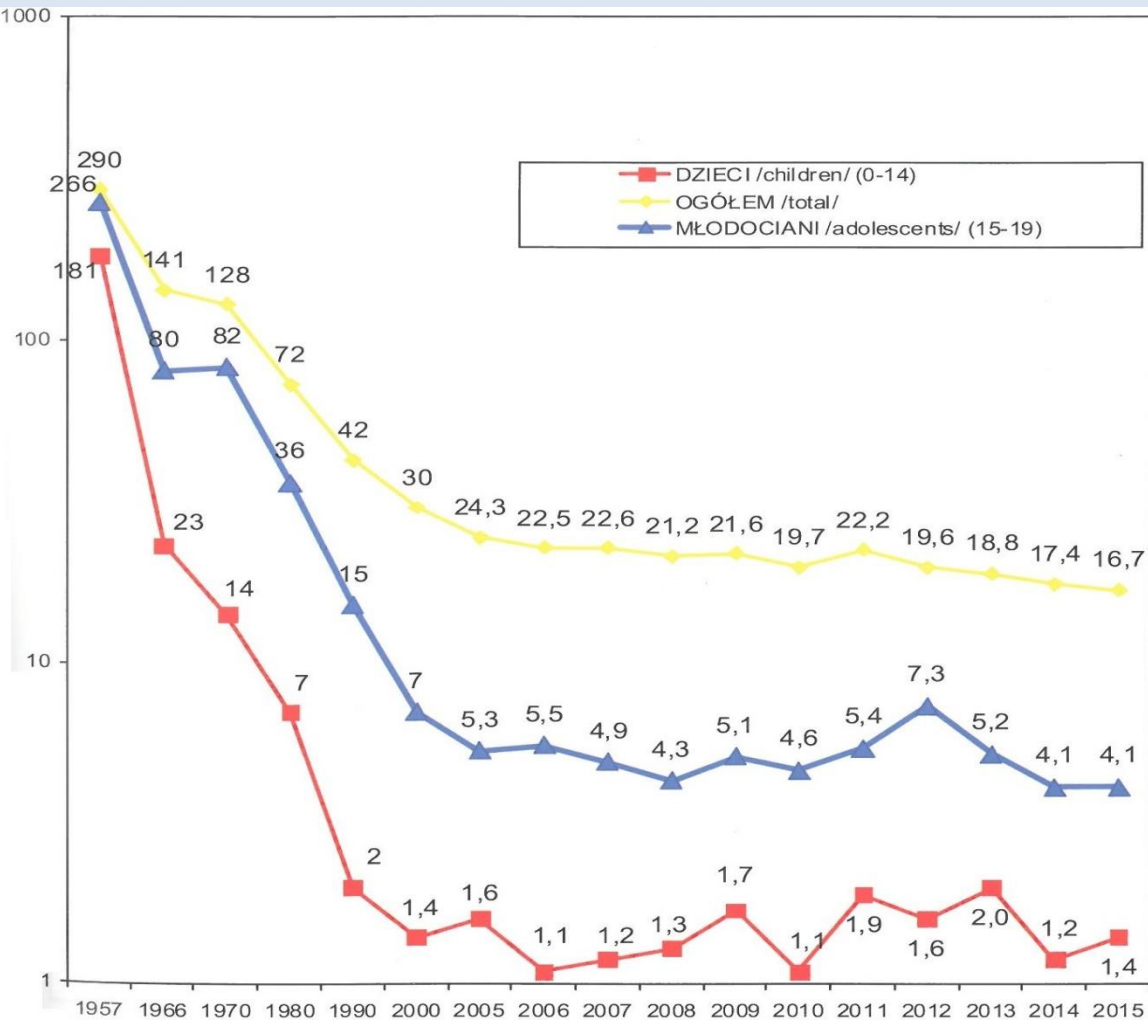
IGICHP 2016

6430 nowych zachorowań, 562 zgony, 16,7/100 000

Regional dynamics of TB epidemiological changes 1990-2012



Dynamics of the changes in Poland

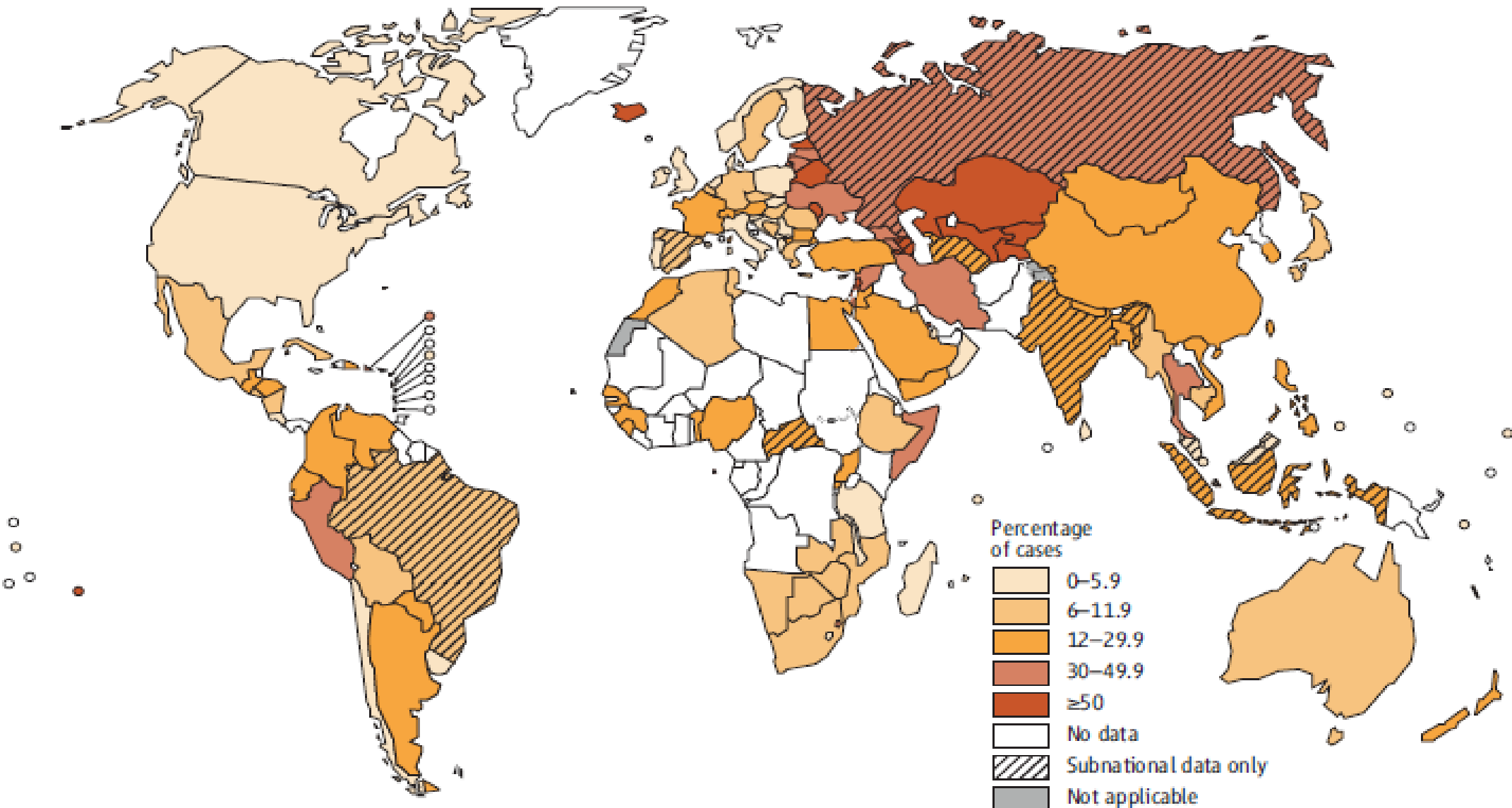


IGICHP 2016

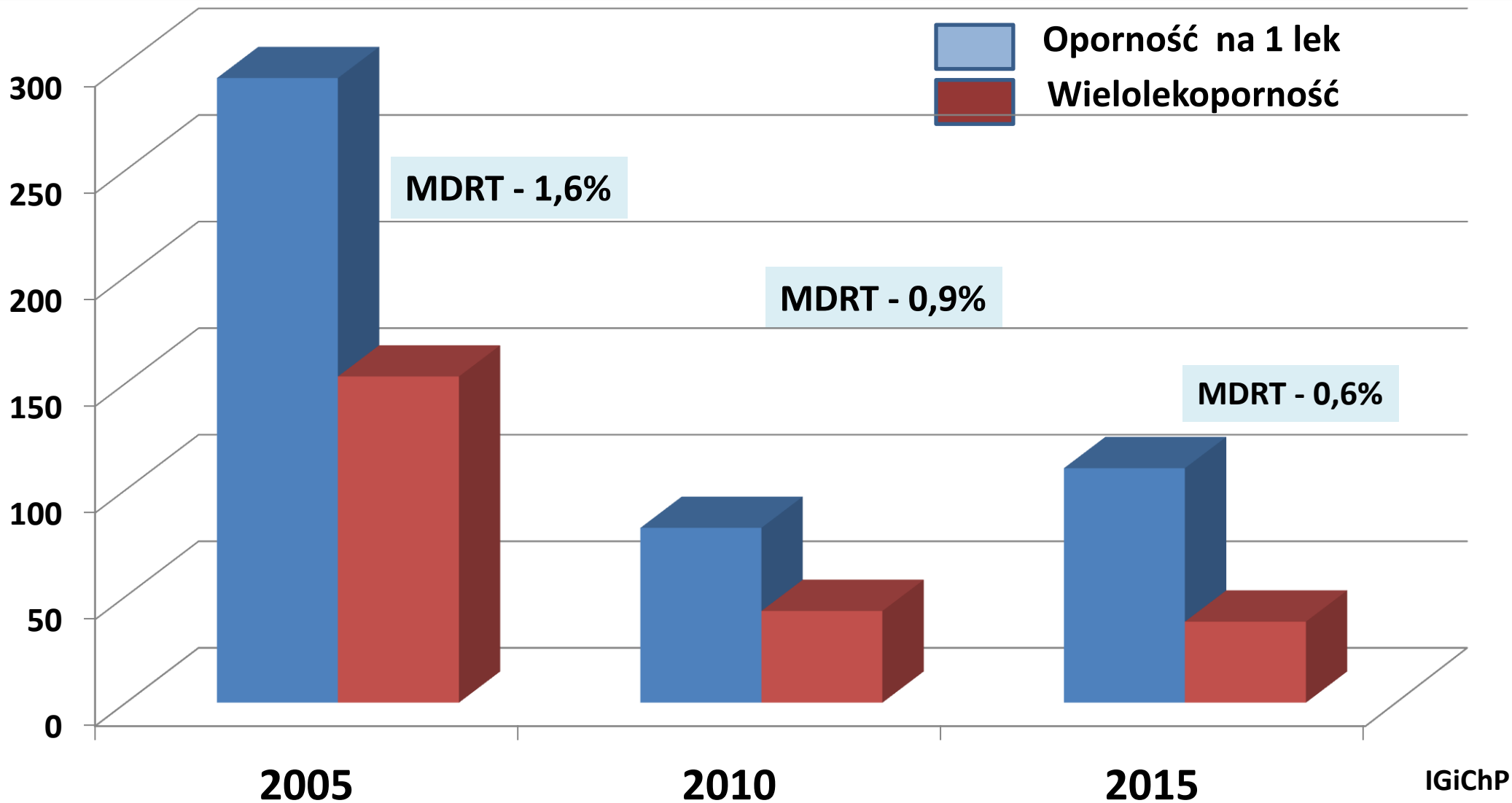
WHO 2016

Multidrug-resistant TB

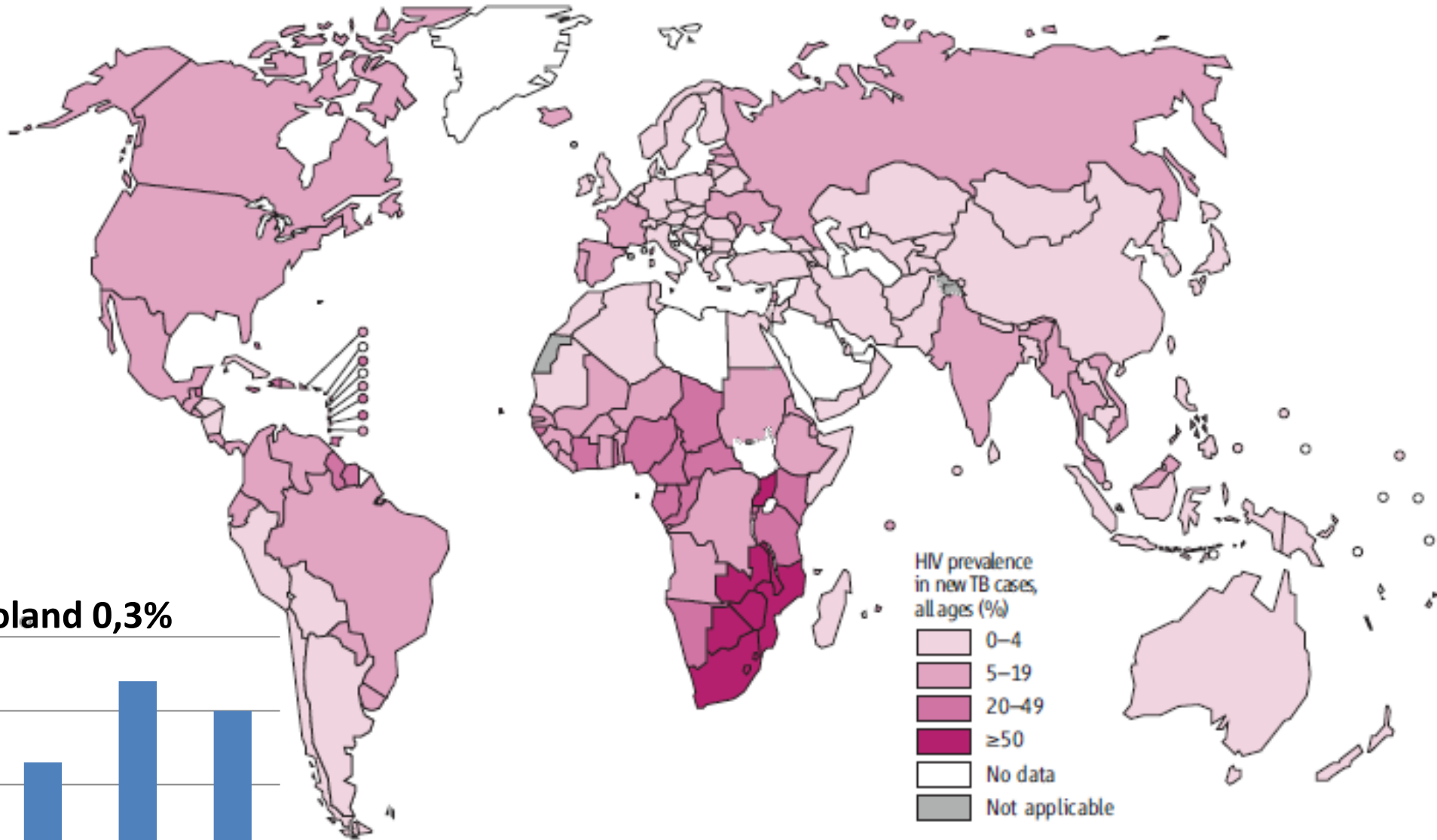
Percentage of previously treated TB cases with MDR-TB^a



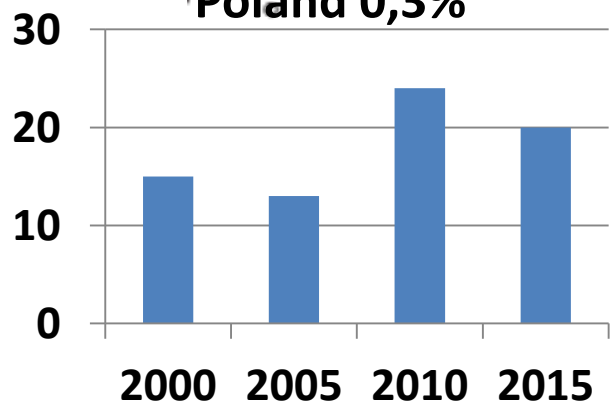
Multidrug-resistant TB in Poland



TB & AIDS



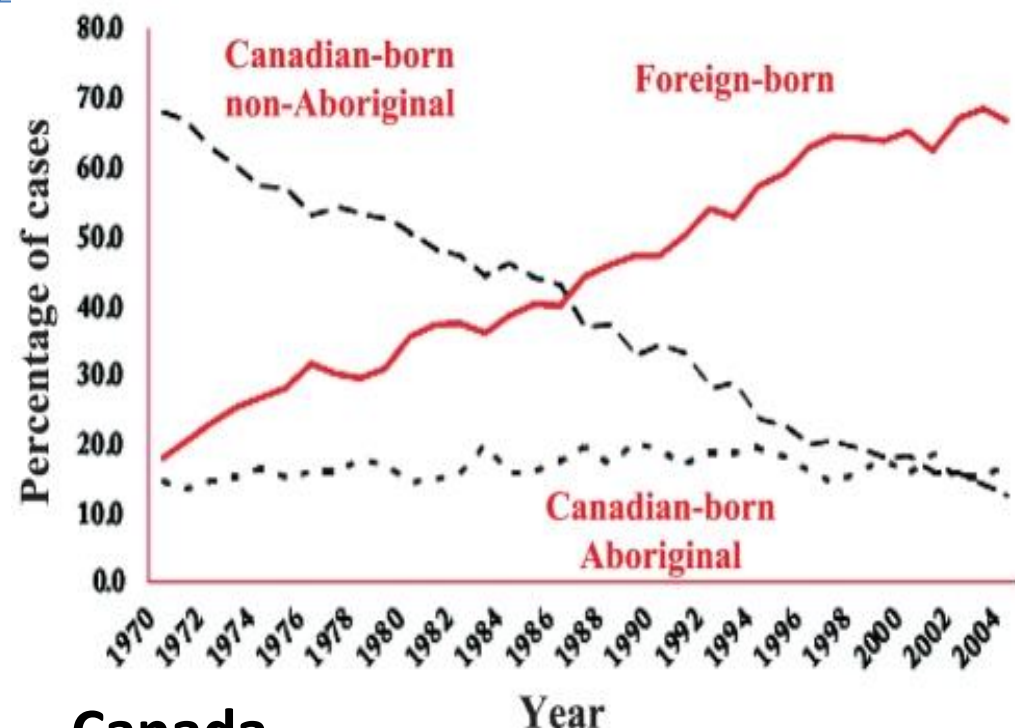
Poland 0,3%



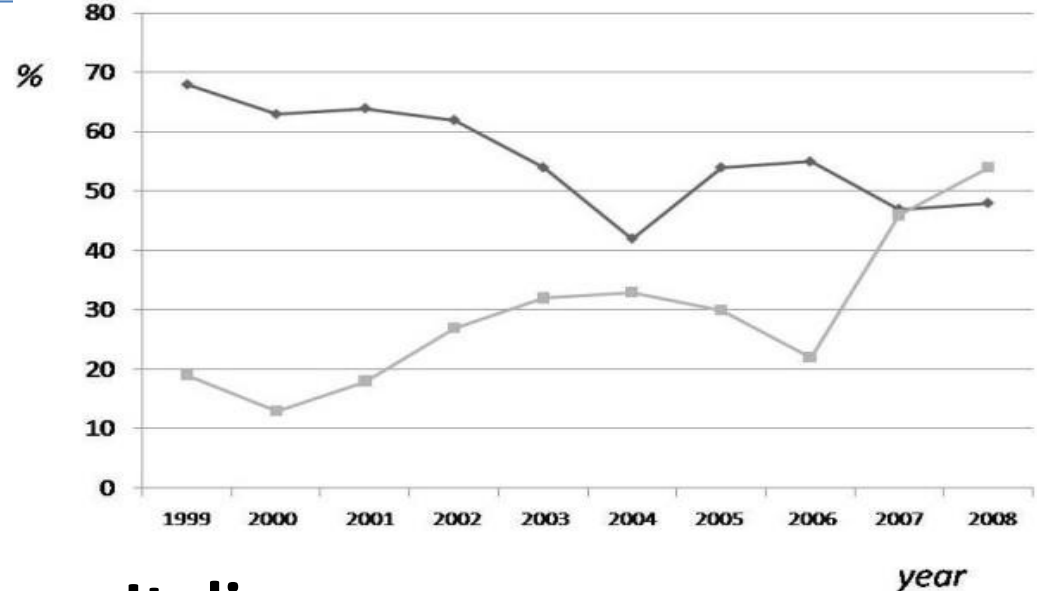


Country	New cases in immigrants	Percentage new cases in immigrants
Luxemburg	21	80.8%
Malta	28	84.8%
Hollande	710	70.5%
Poland	38	0.4%
Portugal	385	15.2%
Romania	50	0.3%
Slovakia	3	0.8%
Slovenia	57	29.7%
Spain	2,138	31.6%
Sweden	524	89.4%
UK	6,287	70.1%
Iceland	7	77.8%
Norway	317	87.8%
USA	6,510	62%
Canada	1,040	66%
Australia	1,141	88%

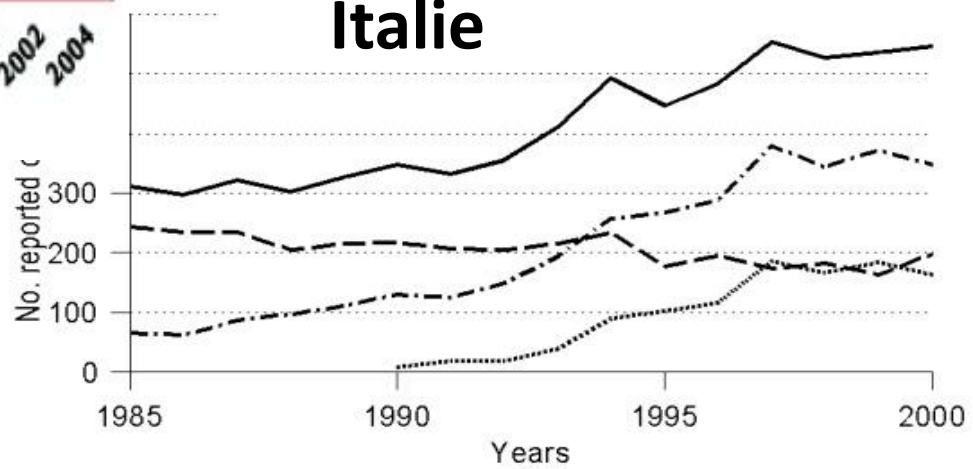
Dynamics of the epidemiological changes in reach countries



Canada



Italie



Danemark

- All
- - - Danes
- · - · Immigrants
- Somalis

Extrapulmonary TB dynamics of the changes

UK

Poland

47%

53%

11%

8%

5%

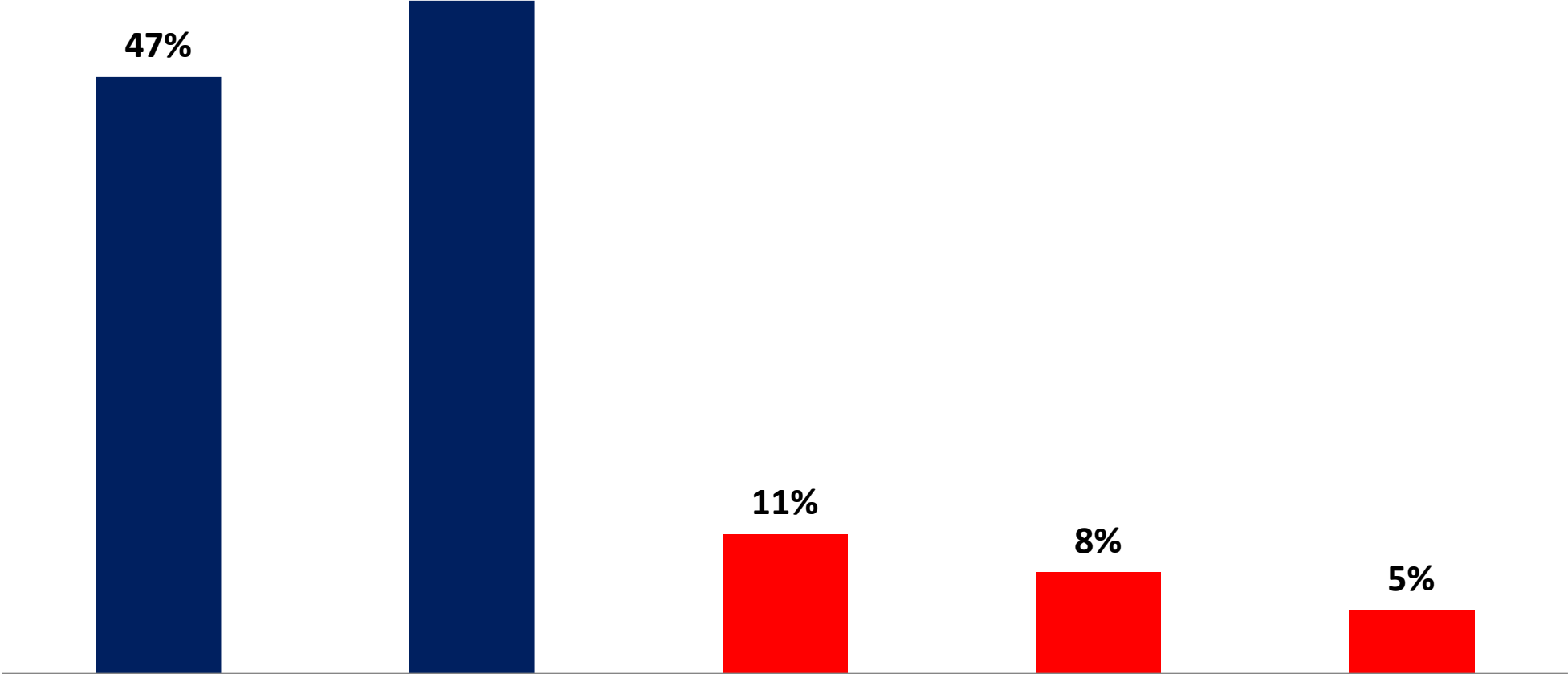
1999

2006

1980

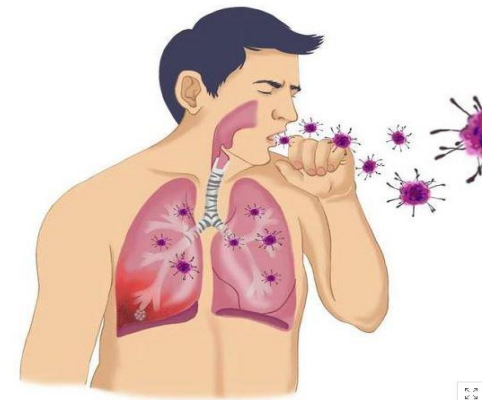
2000

2015



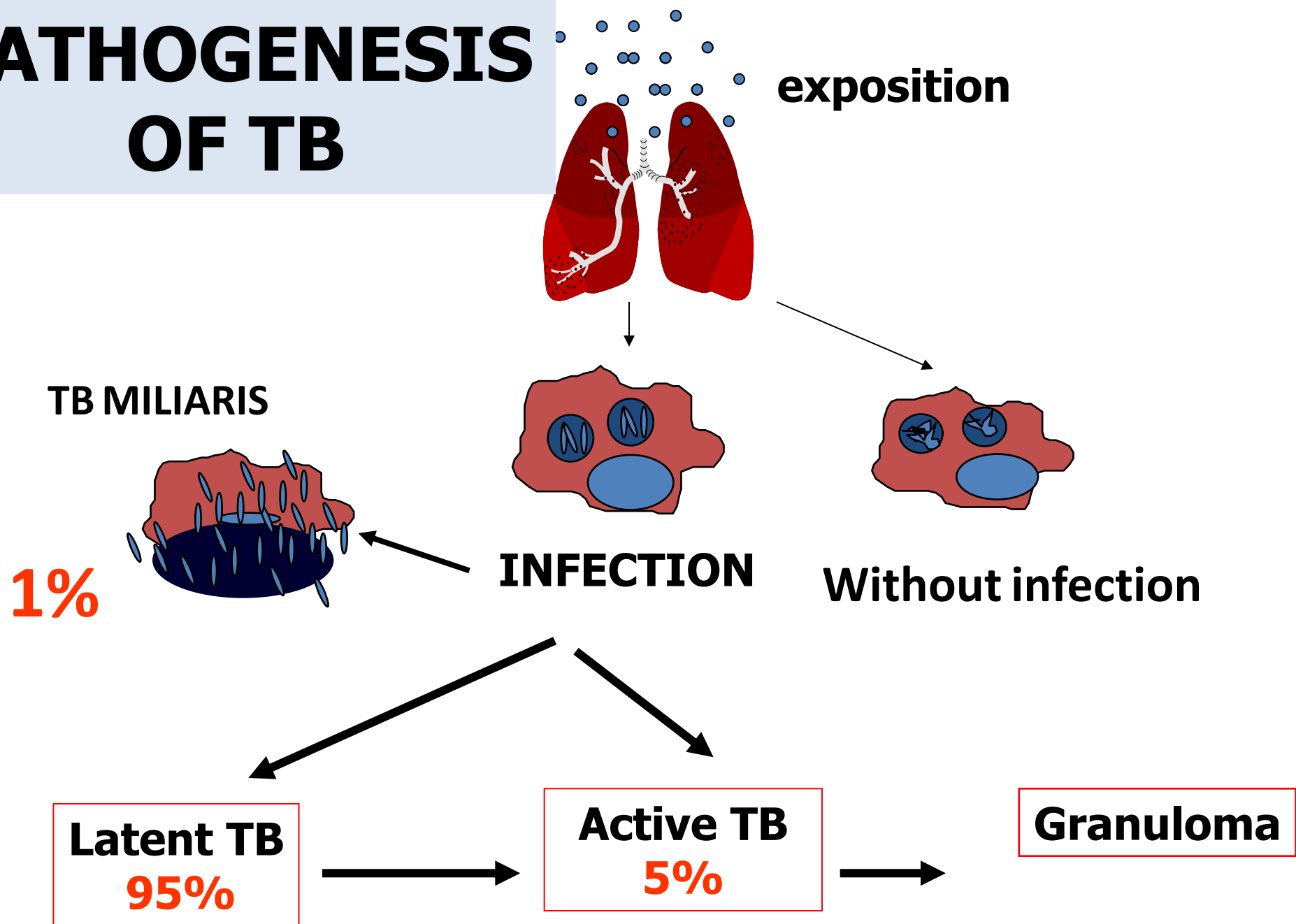
Ways of TB spreading

- **Tuberculosis is an infectious bacterial disease caused by *Mycobacterium tuberculosis* complex transmitted from person to person by airborne droplets.**



- **It is possible to become infected through the ingestion of milk cows suffering from tuberculosis.**
- **Casuistic cases of infection through damaged skin.**

PATHOGENESIS OF TB



TB risk group

- **Immigrants**
- **Prisoners**
- **Homeless**
- **The unemployed**
- **Children**
- **Elderly people**
- **Immunosuppression**

TB symptoms

1. General

fever, nocturnal sweats, loss weight, weakness

2. Pulmonary

cough, sputum, pain of the thorax, dyspnoea, hoopoe

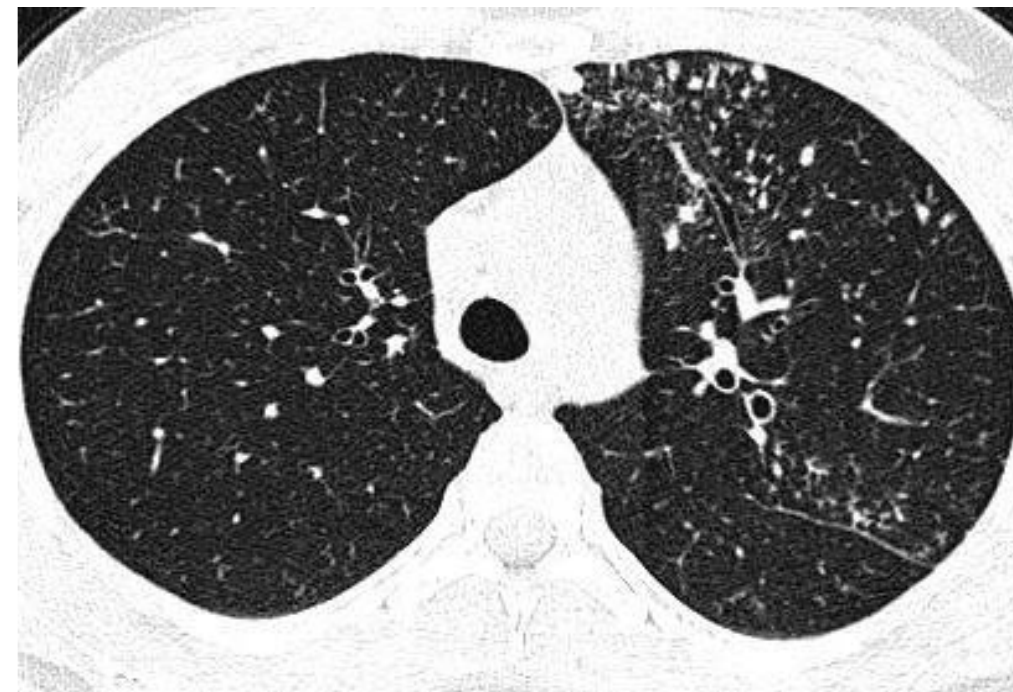
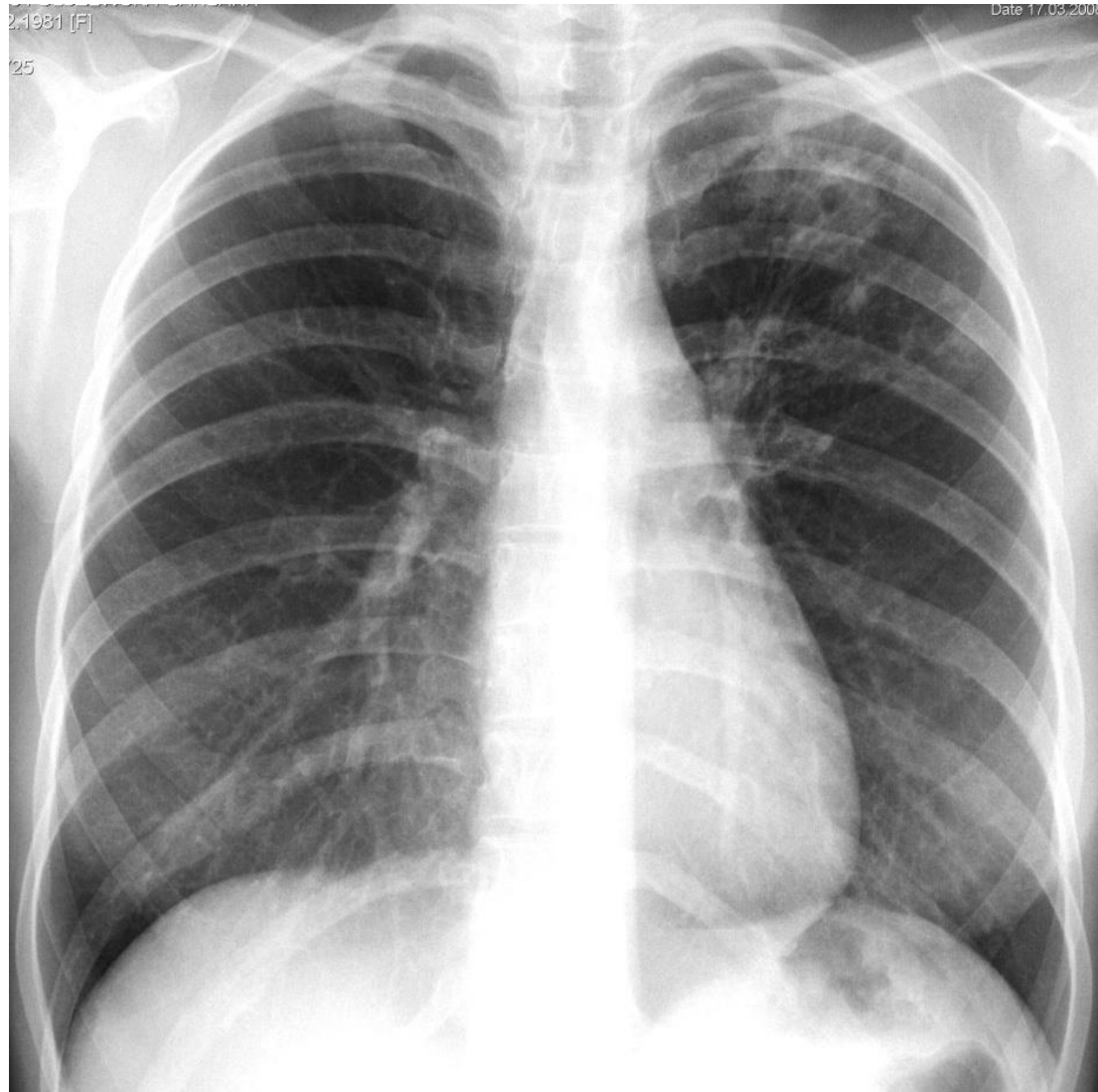
3. Extrapulmonary

meningitis, miliary, bilateral or unilateral exudative pleurisy, pericarditis, peritonitis, tuberculosis of the intestines, spine, liver, adrenal glands, lymph nodes, bones, spine, skin, ear,

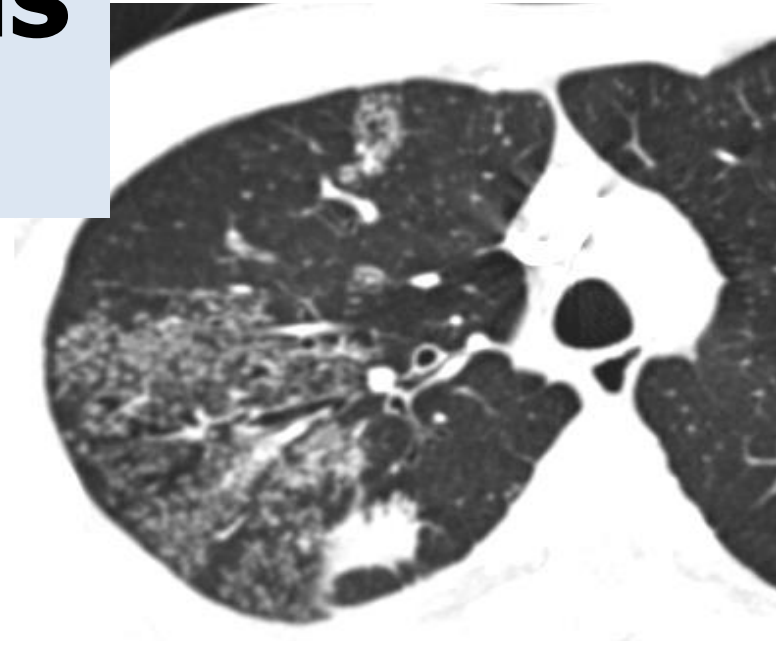
Laboratory changes in TB

- **inflammatory markers**
(ESR, leukocytosis, leukopenia)
- **electrolytes**
(hypercalcemia and hyponatremie)
- **urinal analysis**
(chronic leukocyturie)
- **pleural exudate**
(lymphocytes, increase in ADA, decrees in glucose)

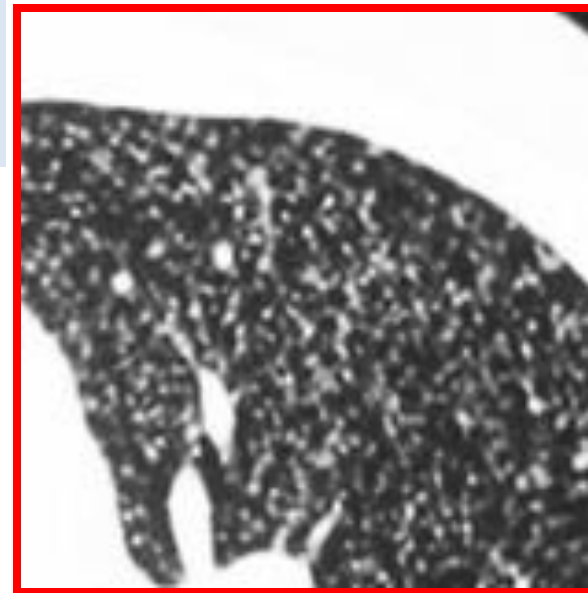
TB - chest X-ray



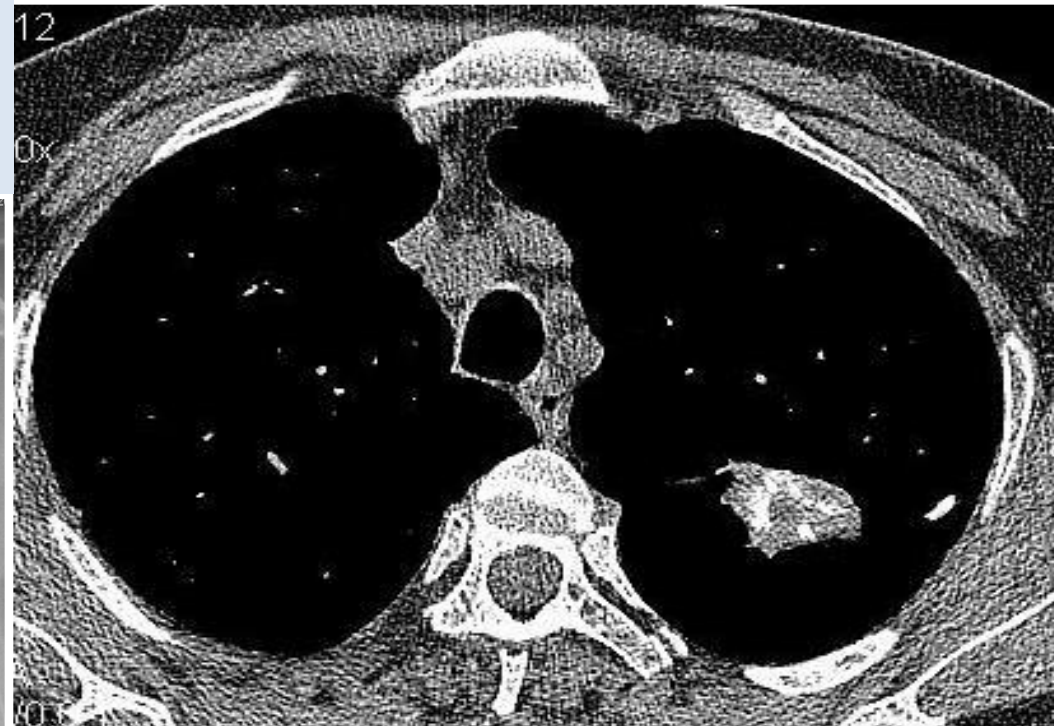
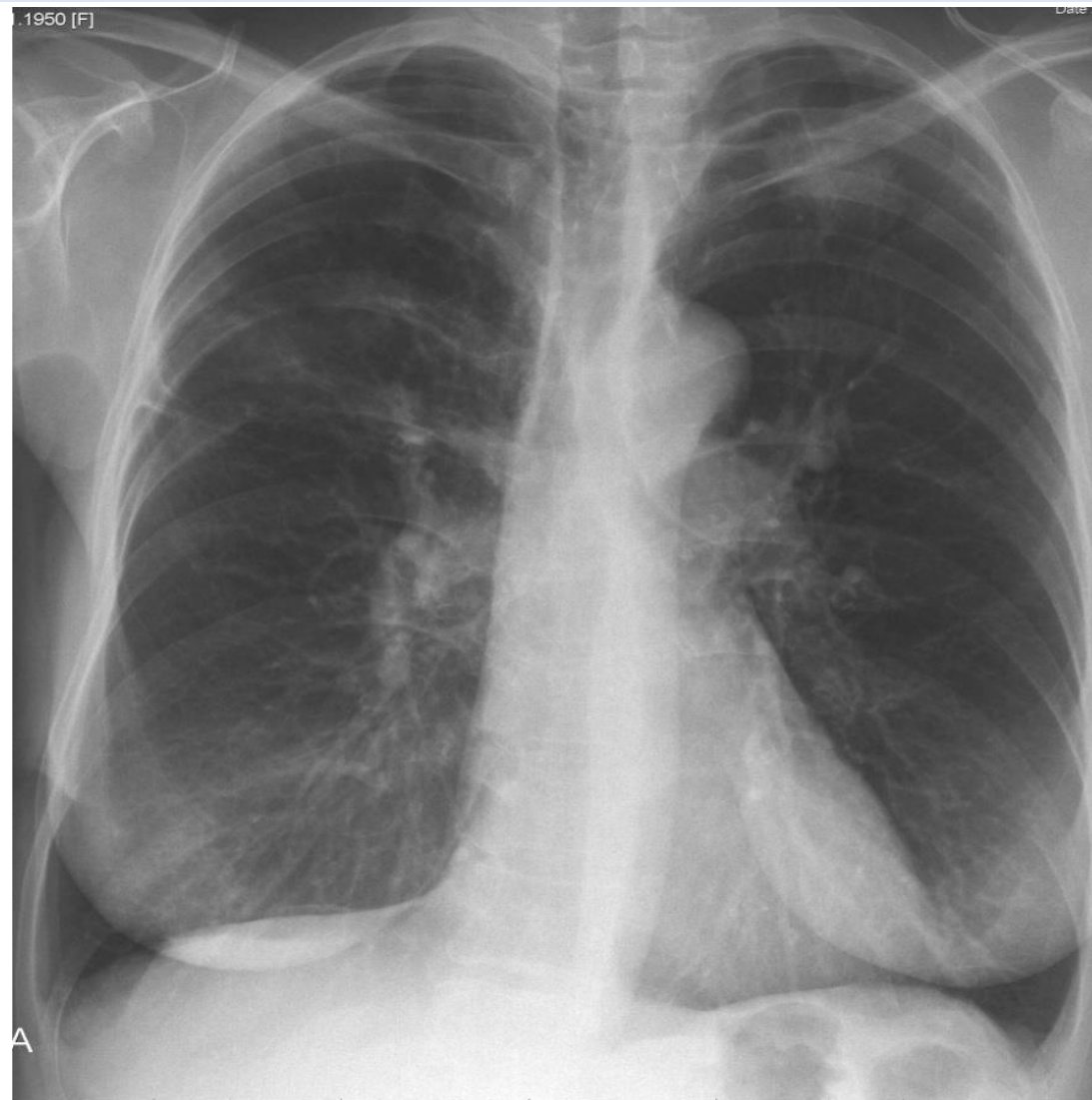
Pulmonary tuberculosis with pleural exudate



Tuberculosis miliaris



Tuberculoma



TB diagnosis

Diagnosis of tuberculosis bases on clinico-radiological symptoms and on identification of mycobacteria.

Accuracy of both methods is limited

Gold standard in TB diagnosis is culture

The criteria for the diagnosis of tuberculosis according to WHO

Certain diagnosis

- ✓ Culture (+)
- ✓ AFB (+) Genetic test (+)
- ✓ Histopathology (+) Genetic testing (+)

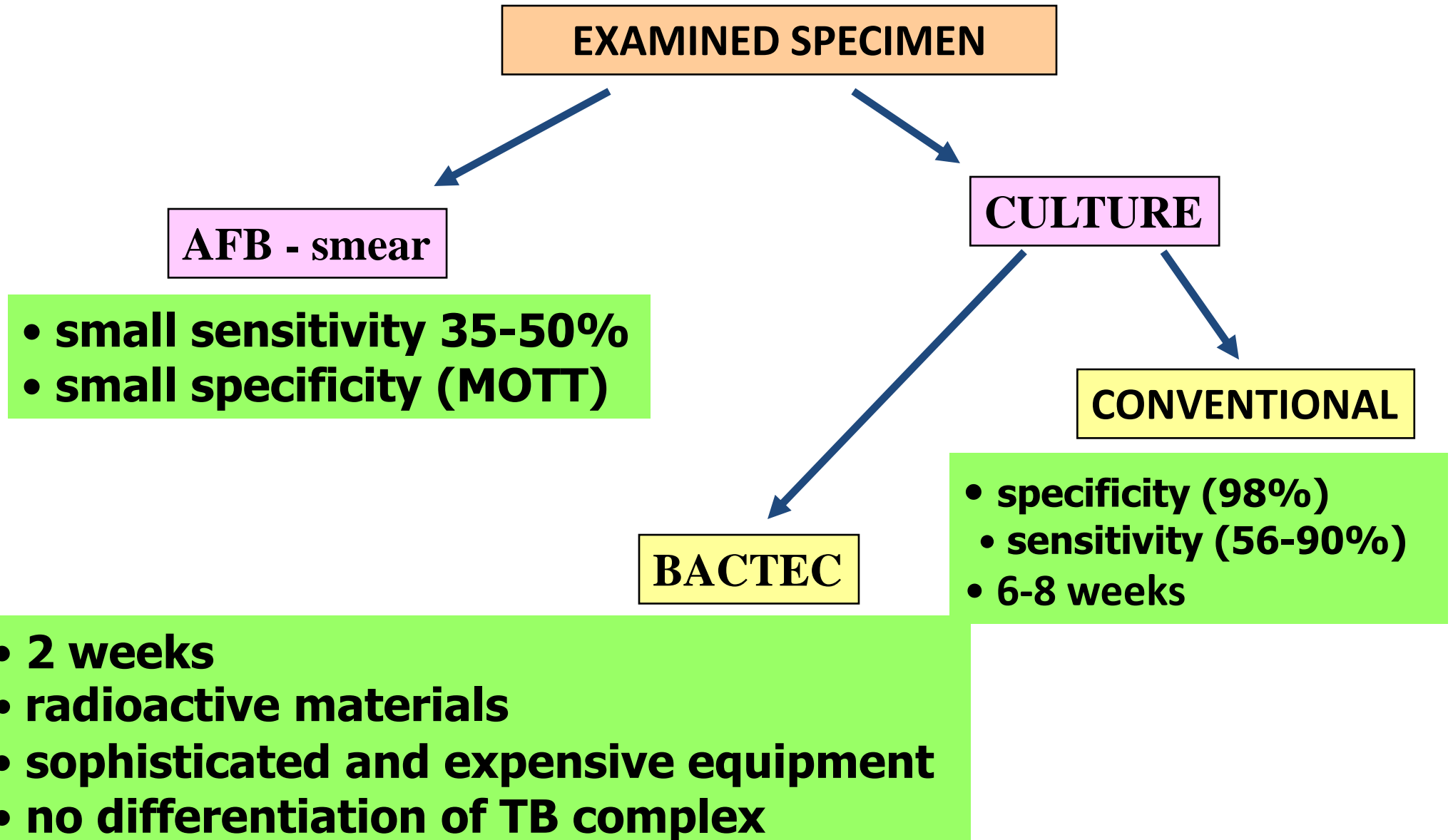
Probable diagnosis

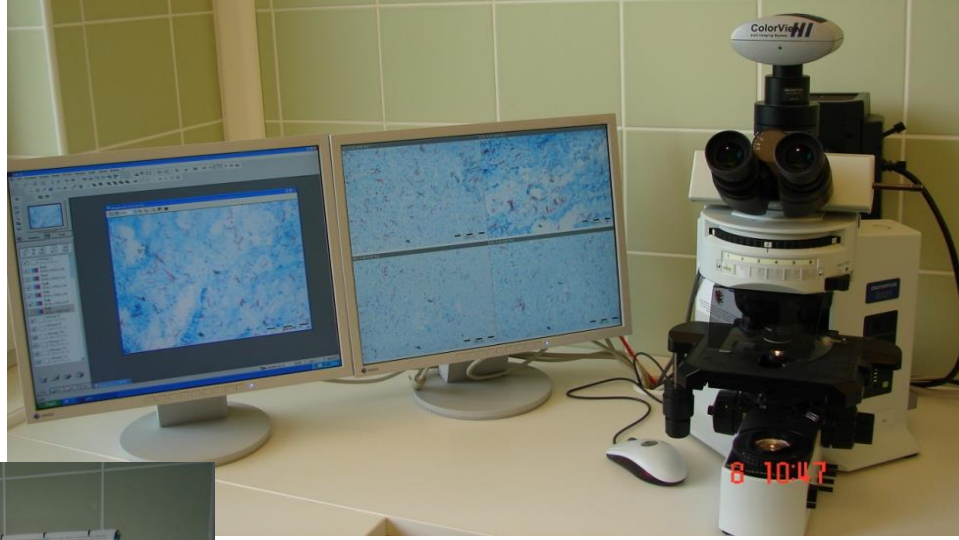
- ✓ AFB (+)
- ✓ Genetic test (+)
- ✓ Histopathology (+)

Possible diagnosis

- ✓ Clinical picture
- ✓ Radiological examination

MICROBIOLOGICAL METHODS



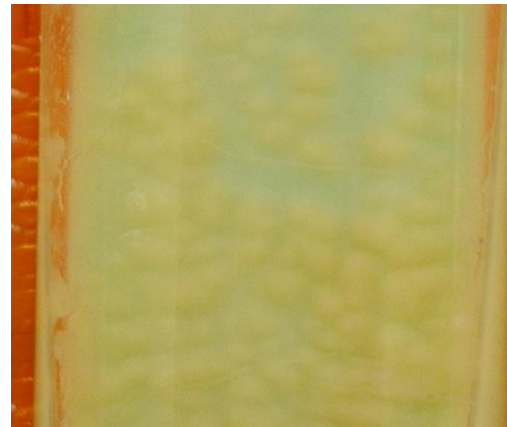


Hours

How long does TB diagnostics take?



Days



Months

TB diagnostics of minimal changes

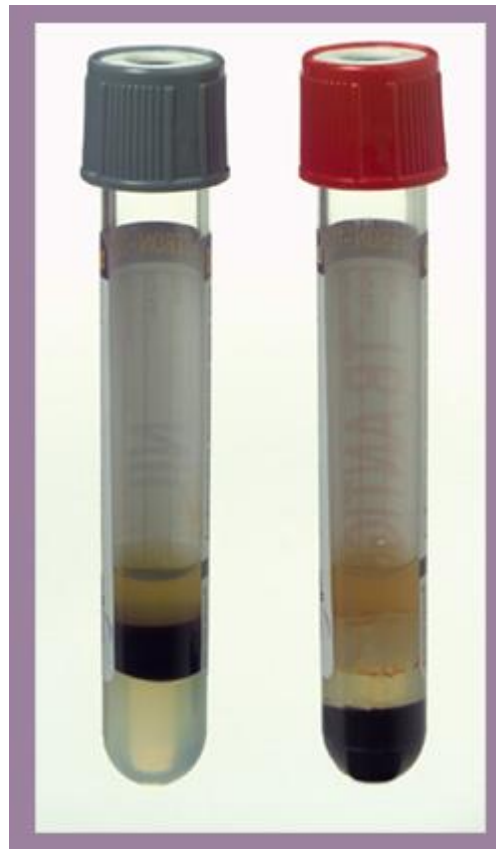
Method	Sensitivity	Specificity
BACTEC	73%	100%
PCR	42%	100%
X ray	67%	66%
PT	94%	20%
Serology	33%	87%

IMMUNOLOGICAL DIAGNOSTICS OF TUBERCULOSIS

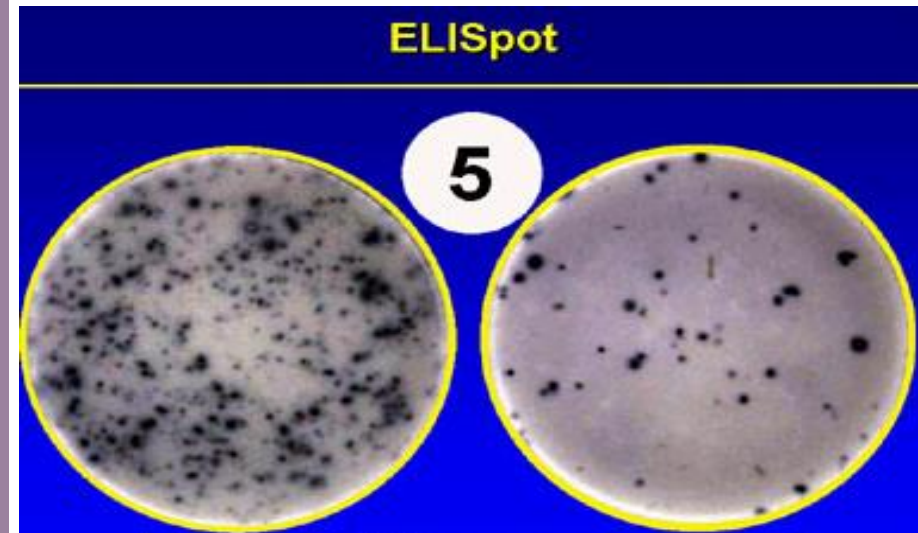
Tuberculin reaction



Quantiferon



T-spot TB



Tuberculin reaction - indications

according to SPLF, BTS, ERS, ATS

- children before BCG vaccination (> 4-12 weeks)**
- control of personnel exposed to TB**
- after contact with TB patients**
- diagnosis of latent TB (before chemoprophylaxis)**
- diagnosis of sarcoidosis**

There is no justification for performing OT in people who were certainly ill and were treated for TB !!!

TB categorisation

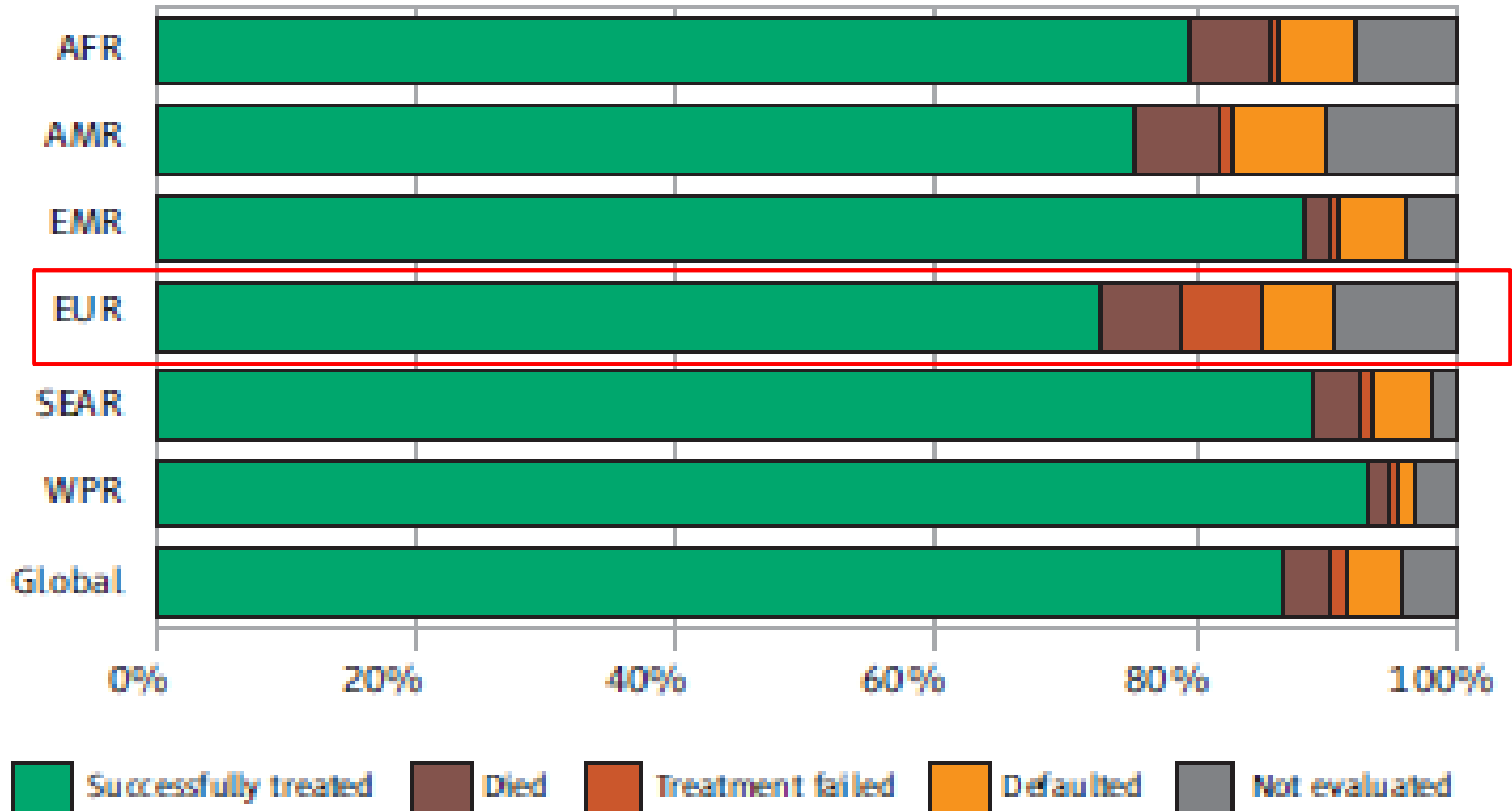
- **I category – new cases, AFB positive**
 - massive radiological changes in lungs**
 - sever course of extrapulmonary cases;**
- **II category – TB relapse,**
 - failure of treatment,**
 - treatment after break (AFB +);**
- **III category – new cases, AFB negative**
 - extrapulmonary slight course;**
- **IV category – chronic AFB positive**

TB treatment

Kat.	Intensive phase	Supportive phase
I	2 months RMP + INH + PZA + EMB (SM)	4 months RMP and INH
II	2 months RMP + INH + PZA + EMB + SM and 1 month RMP + INH + PZA + EMB	5 months RMP and INH
III	2 months RMP + INH + PZA	4 months RMP and INH
IV	according to antibiogram in special centres	12 -24 months 5-7 drugs

Treatment effects according to WHO

b. All new cases



New drugs in TB treatment

✓ **Bedaquiline**

✓ **Linezolid**

✓ **Delamanid**

Chemoprophylaxis

Protection against transfer latent infection to active

- **INH 6 for months 5 mg/kg/day**
- **INH for 12 months**
- **RMP and INH for 3 months**
- **RMP and PZA for 2 months**

BCG vaccination

- **obligatory**
- **only newborns**
- **alive attenuated strain of BCG**
- **limited protection**
(sever disseminated cases, miliary TB, and acute meningitis)

TB prevention

- **early diagnosis and treatment**
- **isolation – 2 weeks ???**
- **surgical mask – patients**
- **mask with HEPA filter - personnel**
- **ventilation**
- **UV radiation**