



German HIV-1 seroconverter study and HIV-1 incidence study Robert Koch-Institute



Berlin, Germany

Outline

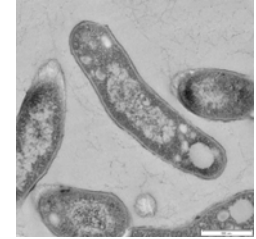
- 1. Robert Koch Institute**
- 2. Epidemiological fact sheets**
HIV and TBC in Germany
- 3. HIV research at the RKI**
- 4. HIV-1 seroconverter study**
- 5. HIV-1 incidence study**
- (6. Research on mycobacterial infections at the RKI, M. bovis and M. avium)**
- 7. Future objectives / potential collaboration**



R. Koch.

Robert Koch-Institute

<http://www.rki.de>



- **Federal institute of the Ministry of Health**
- **Major tasks**
 - **Diagnostic, surveillance and prevention of infectious and non-infectious diseases**
 - **Records of infectious diseases in Germany (Protection against Infection Act, IfSG 2001)**
 - **health report (e.g. health survey of children and adolescents)**
 - **Cancer registry, experimental use of stem cell etc.**

Research at the Robert Koch-Institute

- **Basic and applied biomedical research**
- **Focused on**
 - **New pathogens**
 - **Acquisition of new properties of known pathogens**
 - **Outbreaks of pathogens**
 - **Development of concepts for prevention**
- **Cooperation with ECDC**

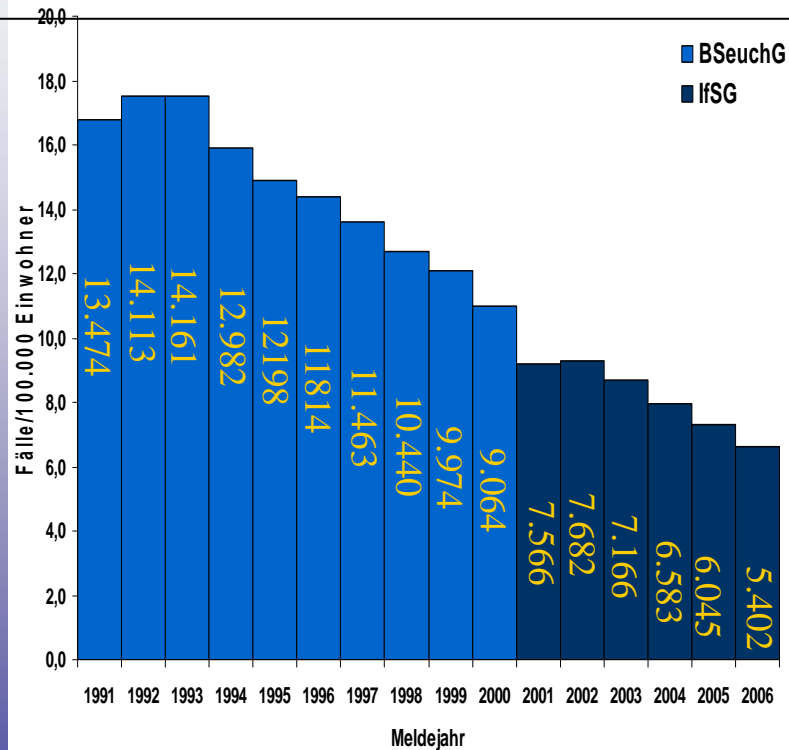


HIV epidemic in Germany

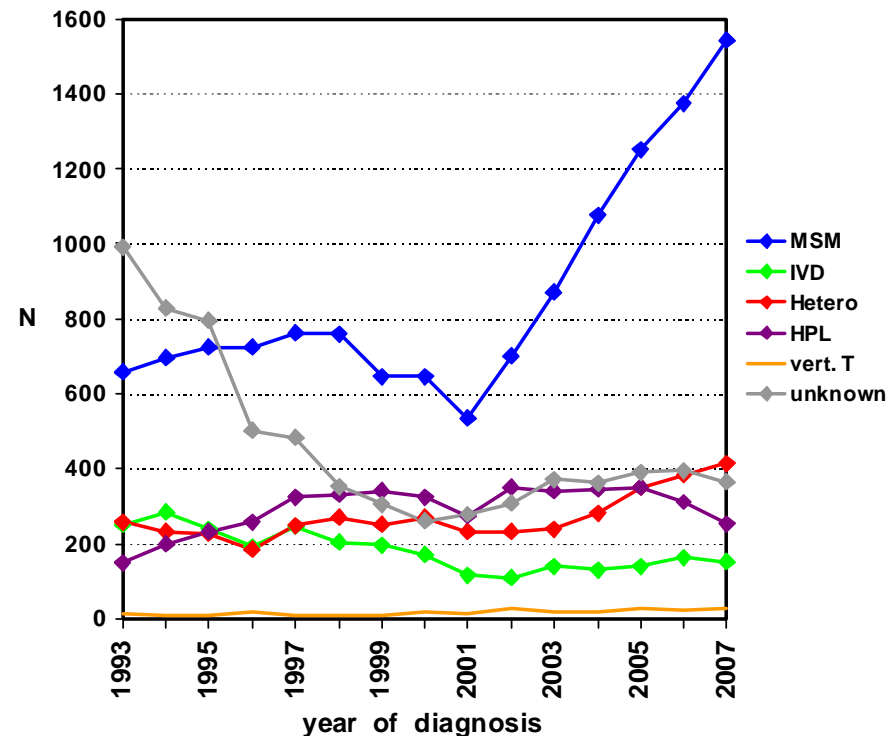
- **Newly diagnosed HIV infections, 2007:** ~ 3.000
 - **men:** ~ 2.400
 - **women:** ~ 600
 - **children:** ~ 25
- **Transmission routes (estimated):**
 - **MSM:** 70 %
 - **Heterosexual contacts:** 20 %
 - **i.v. drug abuse:** 9 %
 - **Mother-to-child transmission:** <1 %
- **New AIDS diagnoses, 2007:** ~ 1.100
- **Deaths HIV infected patients, 2007:** ~ 650
- **HIV infected cumulated:** ~ 86.000
- **AIDS diagnoses, cumulated:** ~ 33.800
- **Deaths HIV infected, cumulated :** ~ 27.000

Tuberculosis and HIV in Germany

TBC incidence



Newly diagnosed HIV



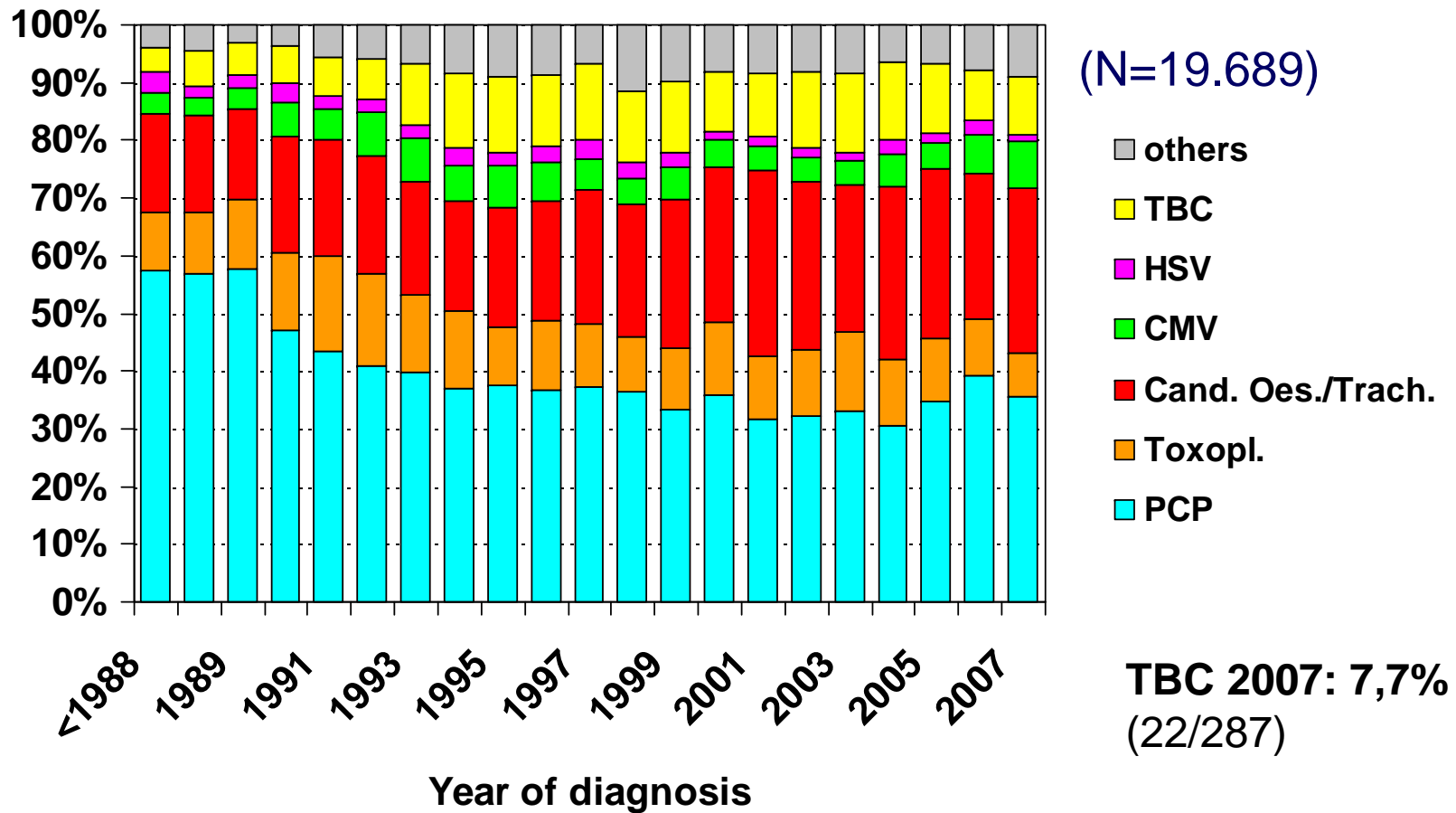
- 57% decrease of incidence (1992-2006)
(Respiratorically transmitted diseases; FG36)

- 62% increase of newly diagnosed infections (2001-2007)
(Epidemiol. Bull. II/2007)

First manifestation of AIDS in Germany

Opportunistic infections / TBC

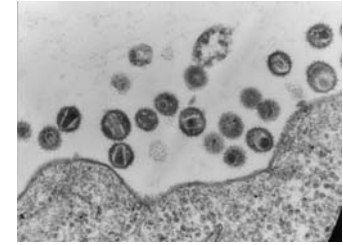
- 75-78 % of first AIDS manifestations are OI*



*RKI AIDS case registry: 11/2007, Christian Kollan



HIV research at the RKI

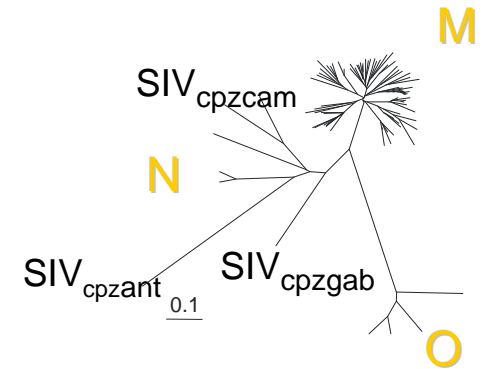


- Department of HIV/AIDS and other sexually transmitted or blood-borne diseases (Osamah Hamouda, FG 34)
AIDS case registry and newly diagnosed HIV-infections

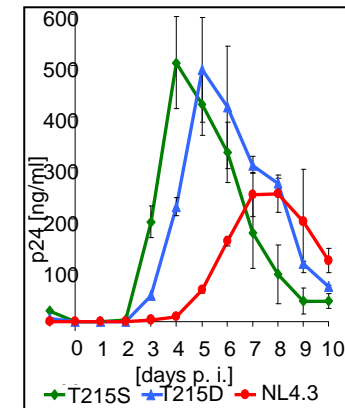
Project groups

- AIDS immunopathogenesis and vaccine development
(Stephen Norley, P12)
- Retrovirus induced immunosuppression
(Joachim Denner, P13)
- HIV variability and molecular epidemiology
(Claudia Kücherer, P11)

HIV variability and molecular epidemiology (P11)



- Spread of HIV subtypes
- Transmission dynamics of resistant HIV (phylogenetic analysis)
- Inter- and intra-patient evolution of HIV
- Persistence and viral fitness of resistant HIV (replication capacity of recombinant HIV)
- Differentiation of recent and chronic HIV infections (serological HIV incidence assays)
- Drug resistance in non-B strains (PMTCT-project, cooperation GTZ)
- Establishment of resistance tests for new drugs (Coreceptor antagonists, fusion inhibitors, integrase inhibitors)
- Evolution of Coreceptor usage (CCR5 deficient HIV infected patients, virus isolation, GHOST panel)



German HIV-1 seroconverter study

Aims

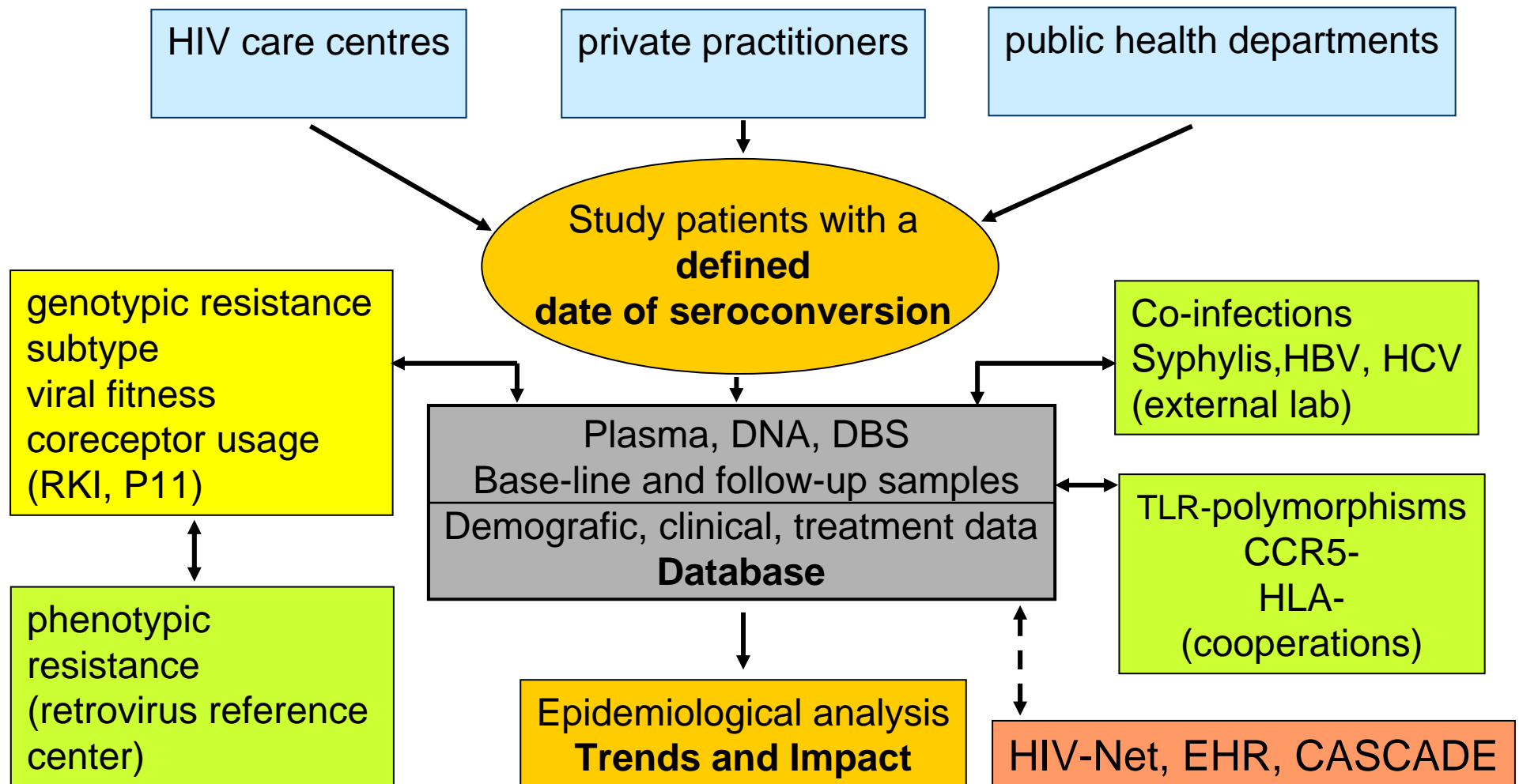
- Identification of factors influencing progression of disease
 - Viral factors (Subtype, drug resistance, Coreceptor usage)
 - Genetic host markers (HLA-, TLR-, Coreceptor polymorphisms)
- Trends in transmission of
 - Subtype
 - Resistant HIV
- Impact of transmitted resistant HIV on treatment success

Study design

Prospective nation-wide observational open study cohort (1997)

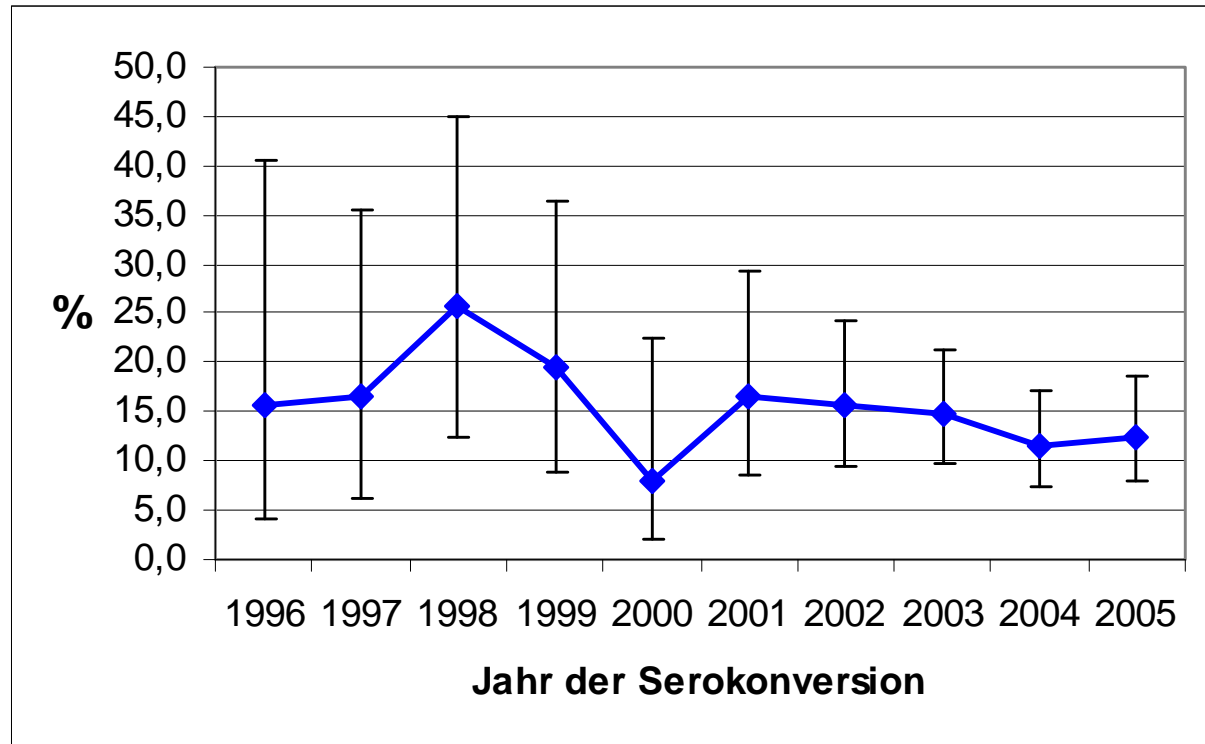
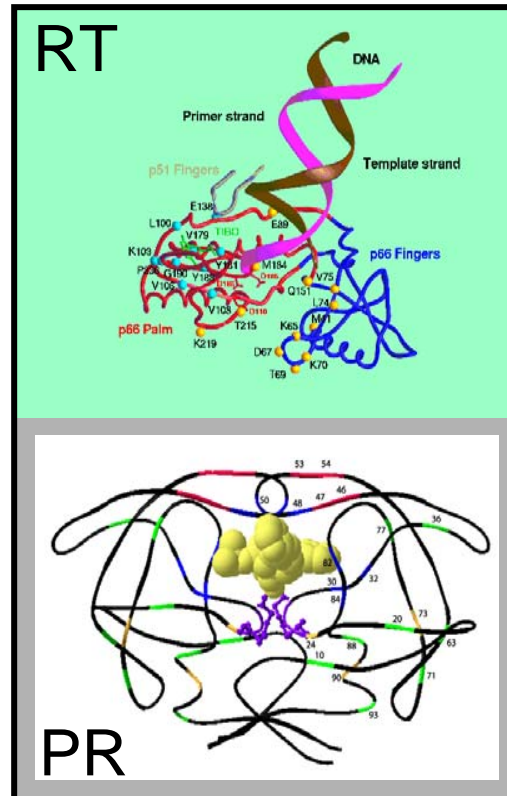
Continuous enrolment of

„acute“ or „documented“ seroconverters



Prevalence of transmitted resistant HIV

Drug-naïve HIV-seroconverters 1996-2005



- Mean prevalence: 12,0% (CI 95% 11,9-16,8), 117/827
- No significant increase or decrease (p for trend = 0.09)
- Application of surveillance resistance mutation list (SRM), Shafer et al, 2007

(Duwe et al, 2001; Poggensee et al, 2007, Kuecherer et al. meeting abstract 2008)

HIV-1 incidence study

Aims

- Improving HIV incidence data in Germany
newly diagnosed infections: unknown duration of infection; invalid back calculation models from AIDS data since introduction of HAART
- Identification of subpopulations contributing to spread HIV to improve prevention

Methods

- serological incidence assay
- collection of information on knowledge, attitude and behaviour (KAB, second generation surveillance)

Pilot incidence study in Berlin

Aims

- Validation of serological incidence assays to select the appropriate test a nation-wide study
- Development of questionnaire to adress KAB issues

Methods

- Comparison of sensitivity and specificity of the BED-Capture-ELISA and the avidity method
- Cross-sectional reference sample panel (seroconverter cohort) with known duration of seroconversion until blood sampling
- Use of dried blood/plasma spots (DBS)

Results pilot study

- **BED-ELISA comparable to avidity method**

BED-Peptide-EIA: gp41-specific antibodies,
normalized to IgG content (Calypte)

Avidity method: AxSym HIV1/2gO (Abbott) +/- GuHCL

Test	% sensitivity (95% CI)	% specificity (95% CI)	Duration of sero- conversion (wk)
→ BED-CEIA	80 (68-89)	86 (76-92)	20
Avidity method	74 (62-84)	82 (72-89)	20

- **53% incident infections among MSM** (n=114)

- lower age (20-29 y)
- higher viral load
- acute infection syndrome
- higher number of previous tests

- **Filter-dried specimens:** comparable results

German HIV-1 incidence study

▪ Laboratory study arm

- 70 representatively selected labs (from 200)
- DPS of newly diagnosed infections
- Protection against infection act
- ca. 1.600 samples annually

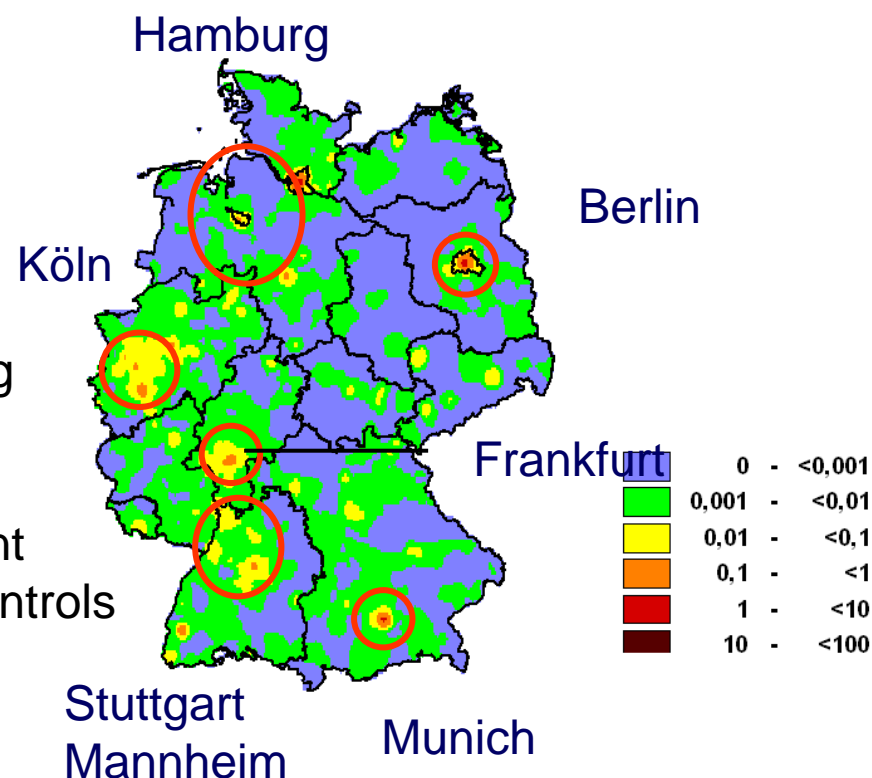
▪ Clinical study arm

- private practitioners, clinics, counseling centers
- DBS from volunteers
- anonymous, unlinked, informed consent
- ca. 600 infections and HIV-negative controls

▪ Filter-dried samples

- mailed to the RKI
- BED-EIA
- started in April 2008, 2 sampling periods
- adjustment and calculation of HIV incidence /Jörg Bätzing-Feigenbaum (FG34)

▪ Six sentinel KAB areas



TBC research at the RKI

- Department of respiratorically transmitted diseases (Haas, FG36)
- Project group: „Immune response during infection with mycobacteria“ (Hubert Schäfer, Astrid Lewin, Albrecht Kiderlen, P22)
 - M. bovis and M. avium mainly
 - Latency-associated genes of M. bovis
 - Identification of virulence genes of M. avium
 - Comparison of clinical M. avium isolates to environmental strains
 - Methods: functional analysis by overexpression and antisense RNA
 - Comparison of growth kinetics of mutants, proteome analysis (2D-gels), cytokine expression and persistence in MØ, granuloma formation

Future objectives / potential cooperation

- Influence of coinfections on transmission of HIV and course of infection
- Role of minor HIV variants for development of resistance during antiretroviral treatment
 - ultra deep genome sequencing will be established at RKI
 - analysis of transmission chains
- Relevance of protease *Gag* cleavage site mutations to develop resistance to antiretroviral drugs (p7/p1; p1/p6)
 - Occurrence in non-B subtypes from drug-naive and treated patients

In the tradition
of Robert Koch:



Open house for
international collaborations

Acknowledgement

- Department „HIV/AIDS and other sexually transmitted or blood-borne pathogens“ (FG34)
Osamah Hamouda
Barbara Gunsenheimer-Bartmeyer (seroconverter study)
Jörg Bätzing-Feigenbaum (incidence study)
- Project group „HIV variability and Molecular epidemiology“ (P11)
Kathrin Keeren (seroconverter study)
Stephan Loschen (incidence study)
- Project group „Cellular immune defense“ (P22)
Hubert Schäfer
Astrid Lewin (*M. avium* ssp.)
Albrecht Kiderlen

External partners

- Study patients and medical doctors
- Diagnostic laboratories
- University of Köln (Rolf Kaiser, Jens Verheyen)
- University of Düsseldorf (Stefan Reuter)
- Krankenhaus Köln (Marc Oette)
- Paul Ehrlich-Institute (Barbara Schnierle)
- German HIV/AIDS competence net (coordinator Norbert Brockmeyer)
- Europe HIV Resistance (coordinator Charles Boucher)
- CASCADE (coordinator Kholoud Porter)