

Modelling Estonia's concentrated HIV epidemic

A case study

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Acronyms

AIDS	acquired immune deficiency syndrome
ART	antiretroviral treatment
CD4	cluster of differentiation 4 (<i>T-cell coreceptor</i>)
EEK	kroon(i) (<i>1 euro = 15.65 krooni</i>)
EHIF	Estonian Health Insurance Fund
GBV-C	GB virus C (<i>formerly known as the hepatitis G virus</i>)
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HIV-1	HIV subtype 1
IDU	injecting drug user
MDR-TB	multidrug-resistant tuberculosis
MSM	men who have sex with men
NGO	nongovernmental organization
NIHD	National Institute for Health Development
PLHIV	person/people living with HIV
TB	tuberculosis
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

Executive summary

There are various sources of data on HIV in Estonia, and several studies have been carried out as well. However, little has been done to collect this information and summarize it for policy purposes.

The present modelling exercise seeks to assemble a comprehensive summary from the available data to better understand the HIV epidemic in Estonia, identify data gaps, support planning and implementation of the national HIV prevention strategy and foster discussion among national experts. It began with a meeting of such experts, which formed the basis for the informal working group that authored this report and the broader network that helped gather data and validate the modelling results. Additionally, this report can also be used as an introductory theoretical manual for the modelling framework and process of the model used in this study.

Since injecting drug users (IDUs) are the population most affected by HIV in Estonia, we used the UNAIDS/WHO model of concentrated HIV epidemics. Most previous epidemiological modelling of HIV in Estonia has been based on this framework, and Estonian experts are relatively familiar with UNAIDS/WHO estimates.

The total number of Estonians living with HIV was approximately 11 000 in 2008. This estimate is based on studies conducted among IDUs and other risk groups. As of April 2009, the cumulative number of diagnosed cases is approximately 7000, which indicates about 4000 undiagnosed cases.

Comparing the modelled and diagnosed incidence rates over time shows that the diagnosis gap was probably largest in the beginning of the epidemic. Our results suggest that the diagnosis gap has decreased to approximately 10%. In addition, the actual incidence of HIV is decreasing due to high saturation of the major risk groups.

The size of the total HIV-positive population and the magnitude of the diagnosis gap profoundly influence prevalence, treatment need and mortality estimates, both current and projected. Our model suggests that the number of infected people who now need antiretroviral treatment (ART) may be as high as 3000. This estimate implies that current ART coverage is less than 50% of need, leaving as many as 1800 people without the treatment they require.

In turn, this suboptimal coverage greatly increases the risk of HIV transmission in the general population, since among people living with HIV (PLHIV), those who receive ART are much less infectious than those who do not. Universal ART coverage is one of the main tools for containing the HIV epidemic.

The treatment gap is also a major source of disease burden and avoidable deaths. In addition, HIV infection is significantly implicated in the spread of several other diseases, of which tuberculosis (TB) is probably the most important for Estonia. Not only does the spread of HIV inevitably lead to increased TB incidence, but the course of TB infection is also more severe among PLHIV.

Finally, our projections indicate that increasing the availability, access and coverage of ART and other HIV services would significantly reduce HIV transmission in high-risk groups, decrease the risk of the disease spreading to low-risk groups and improve the health of PLHIV.

Key findings

The key results of our HIV epidemiology modelling are as follows.

- Our results confirm previous international estimates that in 2008 there were approximately 11 000 PLHIV in Estonia.
- Comparison of the modelled and the diagnosed number of HIV cases indicates that 36% of the 2008 cases were undiagnosed (approximately 4000 cases).
- HIV incidence is stabilizing due to HIV saturation in high-risk populations.
- Approximately 60% of the persons who would benefit from ART do not receive it, either because they are not aware of their HIV status, or because for various reasons they have not accessed health care services.
- The concentrated nature of the HIV epidemic in Estonia influences TB occurrence, probably leading to increased TB incidence in the future. The course of TB is also more severe among PLHIV.
- Increasing the availability, access and coverage of ART and other needed services would significantly reduce HIV transmission among high-risk groups, decrease the spread of HIV to low-risk groups and improve the health of PLHIV.

Objectives

There is a wealth of information on the Estonian HIV situation that has been produced by the national surveillance system, research facilities, clinical institutions and similar sources. All this information can be and is used to improve policies and programmes to fight HIV in the country. Disease modelling, however, has received relatively little attention over the years. The essence of disease modelling is to collate available data in a comprehensive system that enables one to more effectively assess current knowledge, discuss it and plan for future developments. Disease modelling also has the added bonus of allowing one to use projections of the best available knowledge to compare the effects of competing actions.

Our main areas of interest for this project have been as follows.

- **Description and analysis of the progress of the HIV epidemic.** It is important to acquire a better overview of the incidence and prevalence of HIV in Estonia. Better knowledge is also needed about the interventions that are currently implemented (in both prevention and treatment), the organizations that are active in the field and the resources involved in current activities.
- **Unified understanding.** It is critical to foster communication and discussion among the major stakeholders – including the Ministry of Social Affairs, academic research groups, nongovernmental organizations (NGOs), community-based organizations like networks of people living with HIV (PLHIV) and United Nations agencies – on the provision and monitoring of interventions. Our goal is to achieve consensus on the best course of action for preventing and treating HIV in the country.
- **Tools.** HIV epidemiology models that have been updated and contextualized for the Estonian situation would be invaluable to health policy- and decision-makers. Such models could serve as tools for improved targeting and provision of HIV prevention and treatment interventions, as well as for better resource planning.
- **Information dissemination.** Lastly, we aim to improve communication on HIV with this project by making information more visible and accessible to risk groups and the general public.

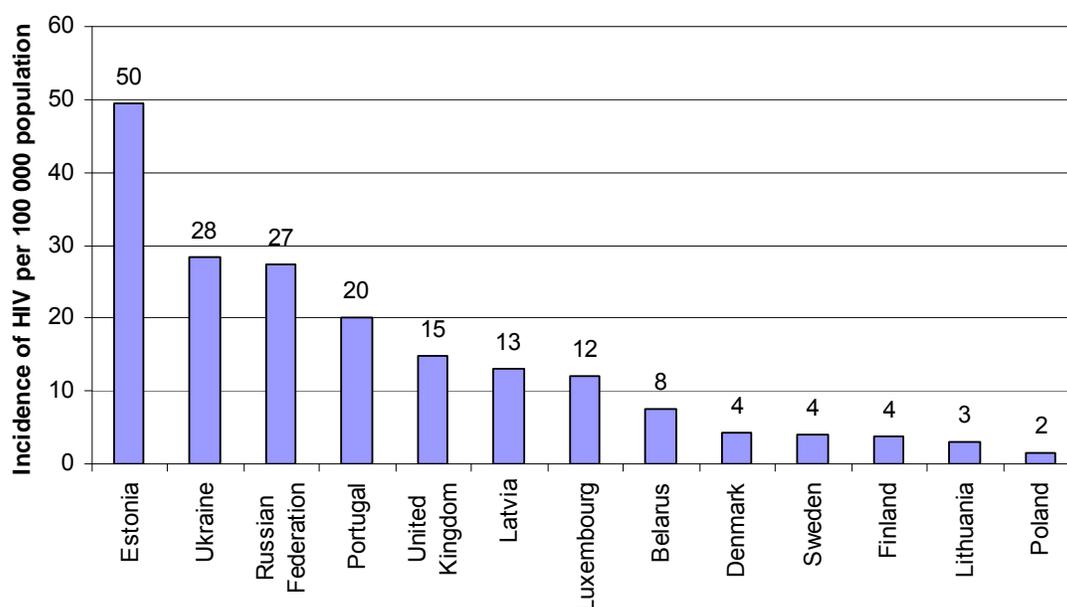
Our specific objectives are to:

- provide updated epidemiological estimates of the HIV epidemic in Estonia using internationally available tools;
- provide epidemiological projections of possible future epidemic developments in relation to targets in the national HIV prevention strategy;
- facilitate discussions among national experts on the HIV situation in Estonia, supported by the latest data; and
- provide a planning tool to support the development and implementation of the national HIV prevention strategy.

1. Epidemiological overview of the Estonian HIV epidemic

During the third decade of the HIV era, new national epidemics have continued to appear. Among the world's regions, the most rapid recent increase in HIV incidence has emerged in eastern Europe. The major political, social, cultural and economic upheavals that the region has seen in the last 20 years have been associated with epidemics of HIV and sexually transmitted infections (STIs), declines in health and life expectancy, and growth of the informal economy, including prostitution and the dealing of recreational drugs (1–5). Together, these developments have led to large increases in morbidity and mortality (6, 7). HIV in eastern Europe is predominantly transmitted by injecting drug use, which accounts for up to 80% of all the region's HIV infections (8). Within eastern Europe, the HIV incidence rate in 2006 was highest in Estonia, where it was 50 per 100 000 population (see Fig. 1.1) (9).

Fig. 1.1 HIV incidence in selected European countries, 2006

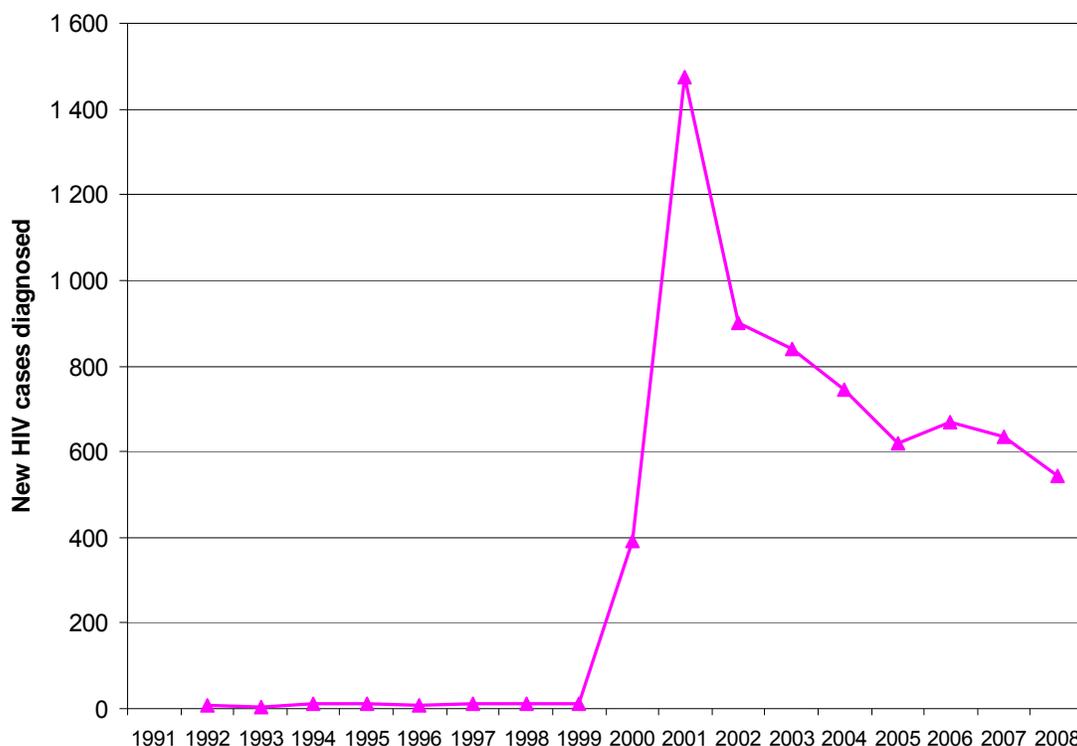


1.1 The course of the HIV epidemic in Estonia

By the end of 2008, the cumulative number of HIV cases registered in Estonia was 6909, while the country's total population of the country was 1.34 million. The first HIV case had been reported in 1988, and a total of 96 cases had been diagnosed by 1999. Men who have sex with men (MSM) accounted for 48% of the registered cases, while heterosexual transmission accounted for 32% and injecting drug use only 4% (10).

The second half of 2000 saw a sudden increase in HIV infections among IDUs. The overall registration of new cases spiked in 2001 with 1474 diagnoses (Fig. 1.2). Since 2000, injecting drug use has been the main route of HIV transmission in Estonia. The first case of mother-to-child HIV transmission (MTCT) was reported in 2001, and the number of such cases has remained low throughout the epidemic, with less than 1% of the infants born to HIV-positive women being infected, and less than 0.5% of all HIV cases being vertically transmitted.

Fig. 1.2 Newly registered HIV cases in Estonia, 1991–2008



Over two thirds of newly diagnosed HIV cases between 2000 and 2007 have been among people younger than 30. The majority of HIV cases have been found among men. However, due to the falling number of newly reported HIV cases for men, the stable number of such cases among women has resulted in an increase in their share of new cases. While women accounted for 20% of all new cases registered in 2000, the figure was 42% in 2008 (11).

Subnationally, the year 2000 saw an explosive increase in HIV case registration in Ida-Viru County, especially in its chief city, Narva. New cases from this county accounted for 92% of the national total in 2000, although its share had declined to approximately 50% by 2008. The second-largest number of newly registered cases is from the capital, Tallinn (Harju County), and together these two areas are responsible today for approximately 94% of the new case registrations. See Fig. 1.3 for the geographic distribution of the cumulative caseload (12).

Fig. 1.3 Cumulative number of registered HIV cases by county, 1988–2008



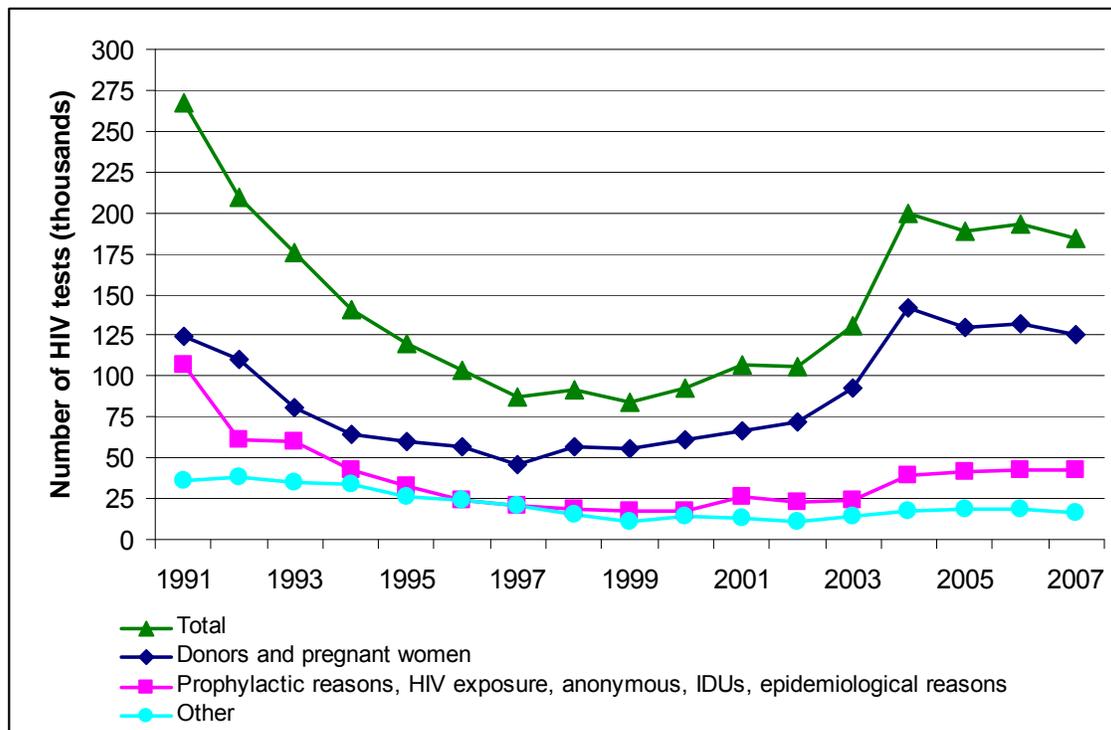
Even though the absolute numbers of new registrations are similar in these two localities, the situation is direr in Ida-Viru, where there were 166 new cases per 100 000 population in 2008 versus 44 per 100 000 in Tallinn. It is also worth mentioning that there has been at least one HIV case registered in each of the 15 counties.

The past few years have seen a decrease in the number of HIV diagnoses, from 899 in 2002 to 545 in 2008. Nevertheless, the estimated national adult prevalence rate of 1.3% (plausibility bound 0.7%–2.5%) (13) in 2007 was still the second highest in the WHO European Region, after Ukraine. Previous estimates indicate that the actual number of PLHIV at the end of 2007 was likely 30%–50% larger than the number of registered cases (14, 15), or about 9900, with an uncertainty range of 5300–18 000 (16).

The first case of AIDS was diagnosed in 1992, four years after the first case of HIV infection. The total number of people diagnosed with AIDS by the end of 2008 was 252. The first AIDS death was registered in 1996, and the cumulative number of deaths attributed primarily to AIDS in the national mortality statistics reached 170 in 2008, with 42 of those deaths occurring in 2007.

In 2001, when registration of new HIV cases reached its peak, the level of HIV testing was at one of its lowest points (Fig. 1.4) (17). Biological surveillance of HIV in Estonia started in 1987, and it is now carried out by 33 screening laboratories, located in the larger health care facilities, and the national HIV reference laboratory in Tallinn. Testing is voluntary and may be performed only with the informed consent of the subjects, except for blood and organ donors, for whom testing is obligatory. The voluntary nature of HIV testing is likely a primary reason why risk-group testing has historically comprised no more than 25% of the total.

Fig. 1.4 Number of HIV tests performed in Estonia, 1991–2007 (in thousands)



PLHIV were diagnosed with tuberculosis on 47 and 39 occasions in 2007 and 2008, respectively. Meanwhile, the proportion of PLHIV among TB patients increased from 6.6% in 2005 to 9.4% in 2007. The prevalence of multidrug-resistant TB (MDR-TB) in Estonia is also quite high by international standards – 14.5% in 2008. Among HIV-positive TB cases, the proportion of MDR-TB is even higher, 25.6% in the same year (18).

Overall, the number of new HIV cases reported each year has been slowly decreasing since it peaked in 2001. The epidemic currently appears to be limited mostly to the IDU communities in two cities, although recent years have seen an increasing proportion of women among the new cases, most likely with IDU contact.

A more detailed description of the recent HIV situation in Estonia can be found in a report by the National Institute for Health Development (NIHD), *Fighting HIV in Estonia 2006–2007* (19).

1.2 Estonian HIV policies and strategies

The Ministry of Social Affairs has used four strategies and programmes to combat HIV since the first HIV case in Estonia was recorded:

- 1992–1996 – National AIDS Prevention Programme 1992–1996;
- 1997–2001 – National Development Plan for the Prevention of HIV/AIDS and Other Sexually Transmitted Diseases until 2001 (20);
- 2002–2005 – National HIV/AIDS Prevention Programme 2002–2006 (21); and
- 2006–2015 – Estonian National HIV and AIDS Strategy for 2006–2015 (22).

The current HIV strategy describes the previous programmes' key achievements as increased awareness of HIV, the provision of harm-reduction and counselling services, the creation of a state-financed HIV testing system, free access to ART and good cooperation among stakeholders. It lists as their main shortcomings little change in lifestyle and risk-taking behaviour, insufficient involvement of local communities, insufficient integration of activities, the lack of strong central management and low levels of funding (23).

This strategy aims to achieve a permanent decline in the spread of HIV in Estonia by prioritizing the following areas of action:

- containing the epidemic among IDUs using harm-reduction measures;
- focusing on young people in risk groups and providing prevention services to them, their sexual partners and their parents; and
- ensuring the availability of health care services to PLHIV (22).

This strategy, which runs through 2015, identifies various activities in these priority areas and sets measurable targets for most of them. Its main goal is to achieve a permanent reduction in HIV incidence, bringing it down to 20 new infections per 100 000 by 2015, with an intermediate target of reducing it to 30 new infections per 100 000 by 2009.

Its strategic targets include HIV incidence rates for specific age and risk groups, vertical transmission rates and STI incidence rates. Box 1 contains the full list of strategy goals.

Box 1. Objectives and main indicators of the current HIV strategy in Estonia

General objective

HIV-spread has permanent decline tendency.

General target indicators

- New HIV cases per 100,000 people 30 in 2009 and 20 in 2015.
- Share of pregnant women infected with HIV among all pregnant women <1% in 2009 and 2015.

Strategic objectives

1. Decrease in the number of injecting drug users and permanent decrease in the spread of the HIV infection among injecting drug users.
2. Permanent decrease in the number of new HIV cases among 15-29-year-olds.
3. Zero increase in the spread of the HIV infection among sex workers; decrease in the spread of STI.
4. Increase in the knowledge of the ways of HIV transmission and the skill of assessing the risk of infection among general population; decrease in negative attitude towards people living with HIV or AIDS.
5. Zero spread of the HIV infection in places of detention (incl. jails).
6. Decrease in vertical HIV infection <2% for HIV+ mothers in both 2009 and 2015.
7. Zero increase in the spread of the HIV infection among MSM.
8. Decrease in the spread of STI among the population.
9. Zero cases of HIV infection in the course of professional activities.
10. Increase in availability of HIV testing and counselling.
11. Guaranteed safety of donor blood/organ/tissue transfer to recipients.
12. Improvement in the quality of life of the people living with HIV and AIDS.
13. Enhanced use of verifiable data for the planning.
14. Increase in competent organisational and human resources actively involved with HIV prevention.
15. Increase in the number of services rendered on the basis of the service description approved by the specialists in the field.

Source: Ministry of Social Affairs, 2005 [official translation] (22).

Implementation of the national strategy is coordinated by the HIV/AIDS Committee of the Government of the Republic, which includes deputy secretaries general of relevant ministries and representatives of key public institutions, NGOs, hospitals, local governments, strategy creation workgroups and PLHIV. The ministries involved in the implementation of the strategy include the Ministry of Social Affairs, the Ministry of Justice, the Ministry of Education and Research, the Ministry of Defence and the Ministry of the Interior. These ministries prepare

annual action plans and budgets for achieving the strategic objectives in their respective areas of governance. Activity plans and implementation reports are both approved by the HIV/AIDS Committee.

The majority of the activities in the strategy framework excluding health care services for PLHIV) are implemented through the National Institute for Health Development (NIHD), a body in the Ministry of Social Affairs that coordinates the activities of the various actors.

HIV prevention on the local level is carried out by local governments, county health and prevention councils, various NGOs, private limited companies and hospitals. It thus depends on the active participation of these same entities.

1.3 Budget of HIV activities in Estonia

There are three main components to the HIV budget in Estonia:

1. resources in the NIHD for implementing the national HIV strategy;
2. resources in the Ministry of Social Affairs for procuring ART; and
3. resources in the Estonian Health Insurance Fund (EHIF) to cover health care system costs.

More than half of the national strategy expenditures in 2006 and 2007 were for PLHIV services, as shown in Table 1.1. Of the strategy expenditures listed, 37%, or EEK 96 million (about €6 million) was spent on antiretroviral drugs. One quarter of the expenditures were associated with IDU services and prevention work among youth. About two thirds of the national strategy budget for 2006 and 2007 was spent through the Ministry of Social Affairs and the NIHD. Another fourth was expended by the EHIF on providing inpatient and outpatient medical care to insured PLHIV and supporting prevention efforts aimed at youth (such as Youth Counselling Centres). Of the remaining ministries, the Ministry of Justice is the largest funder, contributing 2%–3% of the funds for the national strategy.

Table 1.1 National HIV strategy implementation costs, 2006 and 2007 (in EEK) (19)

Target group or activity field	2006	2007	Total	% of total
IDUs	15 762 263	19 457 762	35 220 025	13.5%
Youth	14 603 918	18 493 101	33 097 019	12.7%
Sex workers	845 039	1 334 313	2 179 352	0.8%
General population	1 873 836	3 115 966	4 989 802	1.9%
Prisoners	2 459 903	5 421 375	7 881 278	3.0%
Vertical transmission of HIV ¹	34 612	100 752	135 364	0.1%
MSM	538 906	493 000	1 031 906	0.4%
People at risk due to their profession ²	8 175	760 800	768 975	0.3%
HIV testing	3 695 152	4 168 086	7 863 238	3.0%
PLHIV	54 231 462	100 482 357	154 713 819	59.4%
Surveillance, monitoring and evaluation	1 672 108	1 800 907	3 473 015	1.3%
Coordination, training of partners and development of services ³	3 766 652	5 398 611	9 165 263	3.5%
Total	99 492 026	161 027 030	260 519 056	100.0%

¹ These amounts include expenditures on the training of health care and social workers. It does not include spending on services for pregnant women, which are part of general health care system expenditures.

² The 2006 expenditure does not include spending to ensure the availability of safety equipment and vaccination against hepatitis B in the administrative parts of the Police and Rescue Board; the 2007 expenditure does.

³ The 2006 expenditure listed for this item includes only the Global Fund programme coordination costs, while the state-funded coordination costs have been divided among the other expenditure items. The 2007 figure includes all coordination costs of the NIHD, which coordinates strategy activities.

In addition to the state budget, an important source of funding from October 2003 to September 2007 was the Global Fund to Fight AIDS, Tuberculosis and Malaria. Global Fund financing amounted to EEK 39 million in 2006 and EEK 36 million in 2007. Other financial contributions have been made by the Gambling Tax Council, the Integration Foundation, WHO, the United Nations Office on Drugs and Crime (UNODC), the European Union's Public Health Programme, the Nordic Council of Ministers, some local governments and some embassies.

EHIF is the main purchaser of health care services for the country's insured population. The HIV-related services that EHIF pays for form part of the national HIV strategy and strategy budget. In 2007, EHIF's expenditures for PLHIV care amounted to EEK 28.3 million (about a 60% increase from 2006). These expenditures were divided between inpatient and outpatient care, which comprised EEK 20.1 million (70%) and EEK 8.3 million (30%), respectively.

Between 2006 and 2007, EHIF expenditures on HIV increased by one third. The main reasons for the rise were the increase in the reference prices of health care services in 2007, as well as a 6% increase in the number of PLHIV who required medical interventions.

In addition to health care services, EHIF finances youth awareness activities in the form of reproductive health counselling. In 2007, such activities accounted for EEK 10 million, a 29% increase from the previous year.

2. Disease modelling

2.1 History of disease modelling

Mathematical models have been used in epidemiology for at least 250 years, taking as a somewhat arbitrary starting point Daniel Bernoulli's study, published in 1760, on the advantages of smallpox vaccination. Mathematical models are commonly understood to have two distinct roles: to predict and to facilitate understanding (24).

Prediction has different meanings according to context, but it is important to note that it does not always – or even often – refer to the future: prediction can merely mean the ability of a model to accurately reproduce a set of observed phenomena. In addition, prediction often means the ability of a model to give valid insights into the relative desirability of several competing courses of action (for instance in Bernoulli's discussion about the advantages of vaccination).

In this latter context, which can be thought of as “what if” analysis, the more accurate term *projection*, which has mainly been used in the ecological sciences (25) but is now also being used in standard works on population demography (26), serves to draw a useful distinction between analysing the implications of different hypotheses (which models can and should do) and making statements about the future. (Despite the fact that models can make such statements, modellers are best advised to refrain from this activity on the principle that predictions, especially those regarding the future, are usually wrong.)

Models are formal statements, often mathematically or algorithmically expressed, that describe our understanding of certain observed features of the world. As such, they are abstractions that help to make our assumptions explicit and provide a tool for testing hypotheses. Since this report is concerned with the response to an HIV epidemic – and secondarily, a TB epidemic – what we describe below applies mainly to models of infectious disease.

Within this broad field, we can further distinguish between diseases that are transmissible indirectly, through an environmental mechanism like soil or water, and those that are only transmissible directly from person to person. What we will be discussing here is mainly relevant to diseases like HIV and TB that are directly transmissible by person-to-person contact. Furthermore, among the directly transmissible disease models, we can use the models for diseases transmitted by microorganisms – in this case a virus and a bacterium, rather than for those transmitted by macroorganisms such as worms and flukes (24).

By far the largest, best-understood group of models are deterministic and expressed in terms of differential equations. These can be simple models – such as the so-called SI, SIR or SEIR models, which consist of one, two and three equations, respectively – or more complicated aggregations of states. These deterministic models model the behaviour of epidemiologically relevant classes. These classes are sometimes referred to as compartments and this type of model as compartmental models. The SI model, for example, models two states, a susceptible state (S) and an infectious state (I). The SIR model adds a recovered state (R), to which the SEIR model adds an exposed state (E) for those who are exposed but not yet infectious.

Usually the choice between such models is dictated by the natural history of the disease: for example, is there a recovered state that is immune? Is there an exposed state that is not infectious? Generally, the simpler the model is, the more transparent its behaviour and the more understandable its results. Simplicity is, other things being equal, an aid to the modelling goal of facilitating understanding. At the same time, too much simplicity can obviously be a barrier to the accuracy of prediction (for example, the accuracy of prediction may depend on accounting for a state that is latently infected but not yet infectious).

Other classes of models add other dimensions of complexity: for example, heterogeneities among hosts in terms of either their infectiousness or susceptibility; heterogeneities among

microbes, such as competing bacterial or viral strains; temporal variations due to seasonal events, such as school being in or out of session; the presence of a random element in infectiousness or susceptibility; and the impact of spatial diversity on the number of hosts or microbes (24). The art of modelling thus often consists in determining how much complexity is needed for the question at hand and adapting a model to fit.

2.2 WHO/UNAIDS modelling framework for HIV

Even in the countries with the best HIV surveillance and registration, the precise numbers of people who have HIV, who have been newly infected or who have died of AIDS are not known. Achieving exact figures would entail the logistically impossible – and unethical – task of testing every inhabitant.

One of the main data collection methods used for HIV is case reporting. It generally tends to underestimate the number of PLHIV. Case reporting also tends to focus data collection on specific risk groups, often missing other groups. Case reporting sometimes also relies heavily on contact with government authorities (for example when people are arrested or attend drug treatment clinics). Even though extensive voluntary counselling and testing programmes can greatly increase the precision of case reporting, they are unlikely to capture recent HIV infections when there are no obvious symptoms. For these reasons, case reports can only indicate a minimum number of PLHIV.

On the other hand, sentinel surveillance of risk groups can lead to overestimation of prevalence in these groups. That is because such surveillance often favours individuals who are at highest risk of HIV infection. For example, sentinel surveillance of sex workers or their clients often focuses on those who seek treatment at STI clinics and tend to have more unprotected sex (and STIs), while the ones who practise safer sex are less likely to be included.

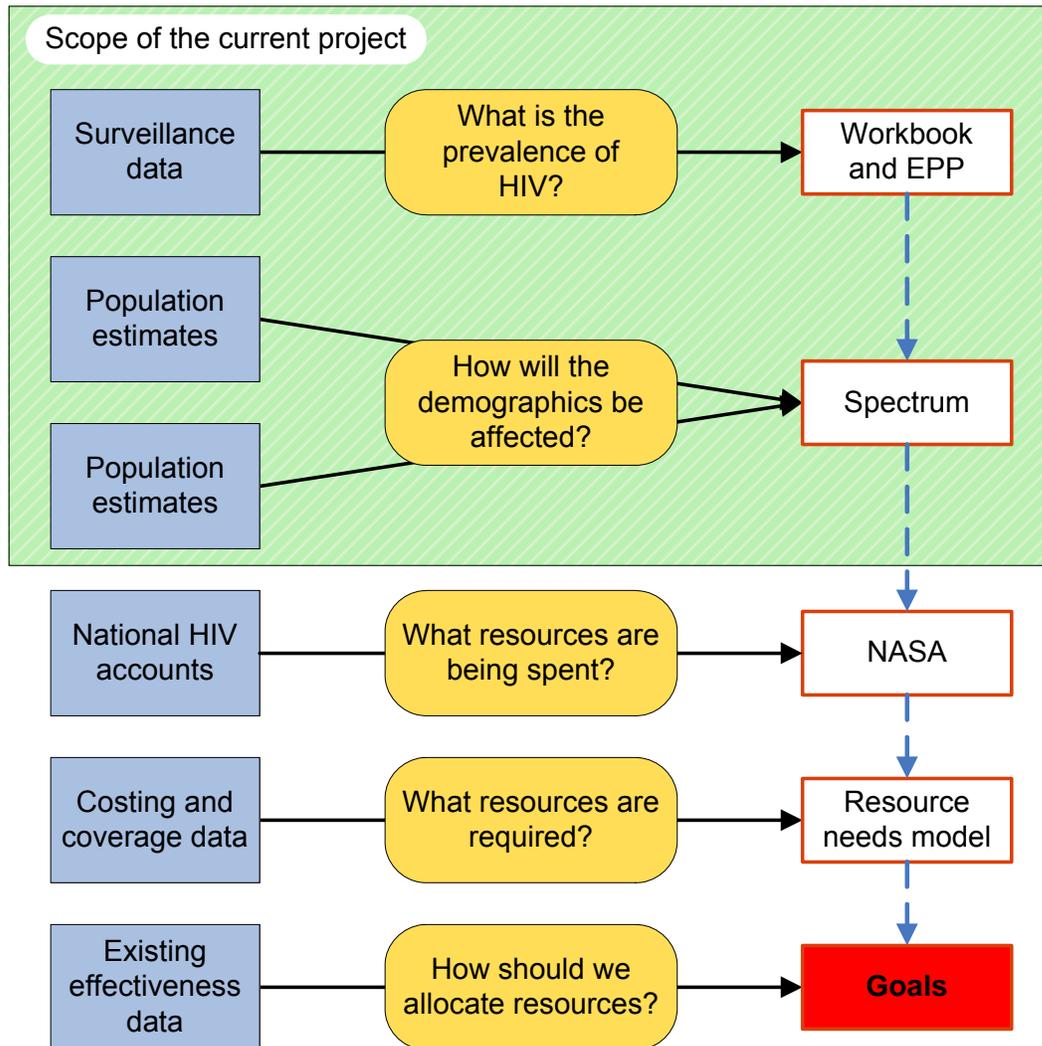
Once data has been gathered, estimation becomes a critical tool for generalizing and making sense of the data. It should be noted that in many cases, epidemiological modelling is only the first step in developing a larger health policy framework. Fig. 2.1 depicts the role of disease epidemiology modelling in relation to possible next steps on the road to formulating strategic goals.

As an example, countries with concentrated epidemics should focus prevention efforts on the populations at greatest risk. To reduce the likelihood of epidemic generalization, prevention programmes should also focus on potential epidemiological “bridges”, such as the sex partners of IDUs and the female partners of MSM (16). High coverage for prevention initiatives that address the general population (e.g. mass media awareness campaigns, school-based education and workplace prevention programmes) is needed mostly in countries with generalized epidemics while more focus on targeted initiatives are required in concentrated epidemics. In general, prevention efforts should focus more strategically on sexual relationships (16), since serodiscordant and multiple concurrent relationships are important risk factors in the generalization of an HIV epidemic. By specifically tailoring programmes to reach people in specific kinds of partnerships, HIV prevention efforts may achieve greater impact than if they only sought to affect the behaviours of individuals (16).

For Estonia, the strategic goals are described in the Estonian National HIV and AIDS Strategy for 2006–2015, as detailed in Box 1 of the previous chapter, while resource use issues are mapped out both there and in the report *Financing HIV/AIDS and TB interventions in Estonia* by Politi and Tõrvand (27).

Unfortunately, national HIV expenditures rarely match national needs. Countries often opt for broad prevention programmes for general population, rather than more effective – and cost-effective – interventions targeting the populations at greatest risk. In Estonia, the only parts missing from the comprehensive policy support framework shown in the Fig 2.1 are the modelling of resource needs and intervention cost–effectiveness would selection of most appropriate action against HIV.

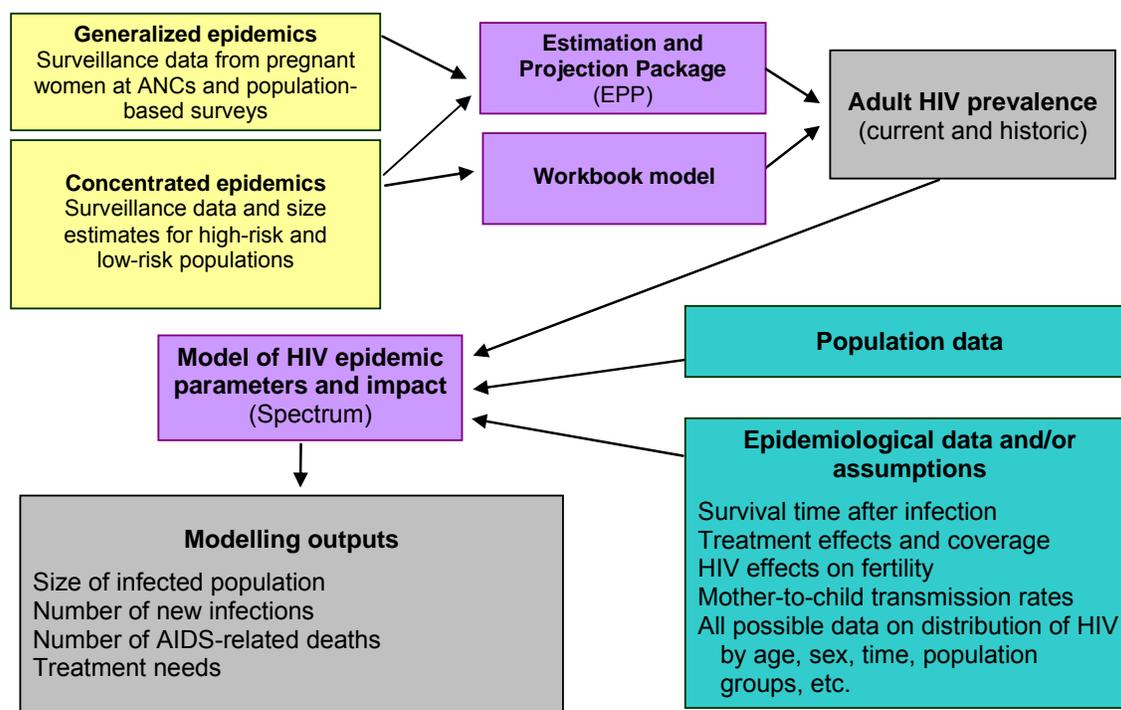
Fig. 2.1 The scope of the current project within the WHO/UNAIDS health policy support framework for HIV



EPP: Estimation and Projection Package; NASA: National AIDS Spending Assessment (a resource tracking methodology).

The UNAIDS/WHO modelling framework for reaching global, regional or national HIV epidemiology estimates is depicted below in Fig. 2.2, along with descriptions of input and output data. The framework uses different sets of data to calculate estimates of HIV prevalence for generalized epidemics, where HIV is firmly established in the general population, and low-level or concentrated HIV epidemics, where they are concentrated in risk groups such as IDUs, sex workers or MSM.

Fig. 2.2 Overview of the WHO/UNAIDS modelling tools for HIV, and the flow of data between the different tools



Purple: modelling packages; yellow: initial data input; grey: modelling output; turquoise: additional data input. ANCs: antenatal clinics.

The Estimation and Projection Package (EPP) is used to estimate and project adult HIV prevalence from surveillance data. In countries with generalized epidemics, input to EPP includes surveillance data from antenatal clinics and national population-based surveys. In concentrated epidemics, the input includes the population size and HIV prevalence of key subpopulations. EPP is used to fit available epidemiological data from various geographic sites to a simple epidemic model (28).

The Workbook Method is a spreadsheet model used to estimate adult HIV prevalence from surveillance data in countries with low-level or concentrated epidemics. Estimates are based on the size and HIV prevalence rates of different subpopulations.

Output from either of these two packages can be imported into Spectrum to calculate numbers of PLHIV, new HIV infections, AIDS cases, AIDS deaths and AIDS orphans, as well as treatment need, etc. Spectrum is a suite of several interlinked policy models that produce these projections for both past and future. It also includes a section for estimating the uncertainty of estimates.

These modelling tools and their underlying methodology are continually updated to improve the accuracy of estimates. The other two ways to improve HIV estimates are by obtaining better input data and increasing stakeholder involvement.

The Workbook Method

Concentrated epidemics are defined as those where HIV prevalence is greater than 5% in at least one subpopulation, but where HIV is not well established in the general population (29). The future course of the epidemic is determined by the frequency and nature of links between these infected subpopulations and the general population. The Workbook Method enables point prevalence estimates and includes a curve-fitting feature. It requires making several decisions in defining the geographical structure of the HIV epidemic, identifying the groups most exposed to HIV and describing the spread of HIV to groups at lower risk of HIV.

Point prevalence estimates

The Workbook tool lets users estimate several geographically distinct epidemics, which may be chosen for a mix of political, practical and epidemiological considerations. Population size data must be available for each area for these estimates to be meaningful.

In addition, the subpopulations most at risk for HIV must be defined for each geographic area, along with low and high estimates of each group's size and HIV prevalence. By default, the Workbook defines four risk groups: MSM, IDUs, sex workers and clients of sex workers. Additional risk groups can be added (e.g. prisoners, military personnel and migrants), and the default groups can be replaced if, for example, there are no IDUs in the country. It is important to define the risk groups as mutually exclusive, to avoid double-counting people at risk. Thus, people who both inject drugs and sell sexual services should only be included in one category – preferably the one with the greatest risk of HIV transmission – which in this example would probably be the IDUs. It is also possible to make a new category for drug-injecting sex workers and then exclude its members from the IDU and sex worker categories.

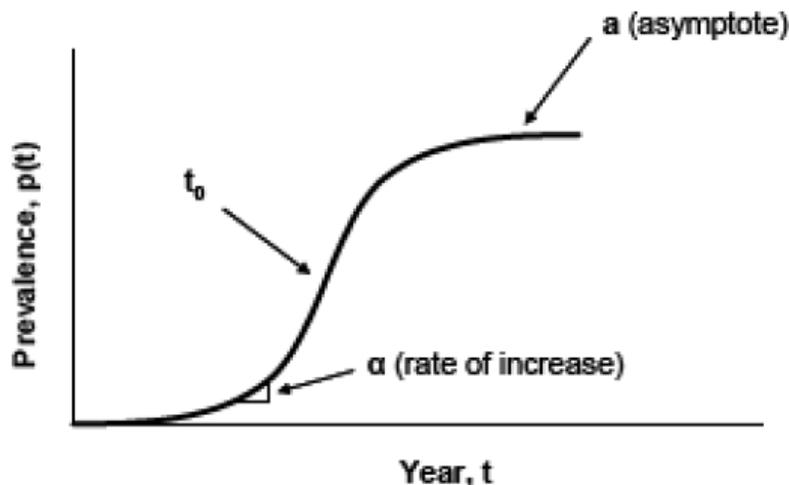
Finally, one must select an approach to estimating HIV prevalence in the low-risk population (typically the general population). The default is to use the low-risk sexual partners of risk group members. This approach implies that the risk of sexual transmission of HIV between two individuals from the low-risk population can be ignored. The other approach is to use data on HIV among pregnant women to estimate prevalence in the general population.

Projection scenarios

Scenarios for the future course of the epidemic, as well as an epidemic curve of adult HIV prevalence, can be generated from the point prevalence estimates. These types of predictions require additional estimates of changes in the size of the general population and of all risk subpopulations used in the point prevalence part of Workbook. Peak prevalence levels for each of these populations are also needed, along with the year those levels are reached. These data will produce a scenario for each population group with adult prevalence and incidence rates, plus numbers infected over time.

For each scenario, Workbook fits a prevalence curve that asymptotically approaches saturation. It fits this curve to the historical prevalence data using either a single or double logistic function, which allows for the definition of increasing, stabilizing or declining trends. Single logistic curves are better suited to situations with increasing or stabilizing prevalences (see Figs 2.3 and 2.4).

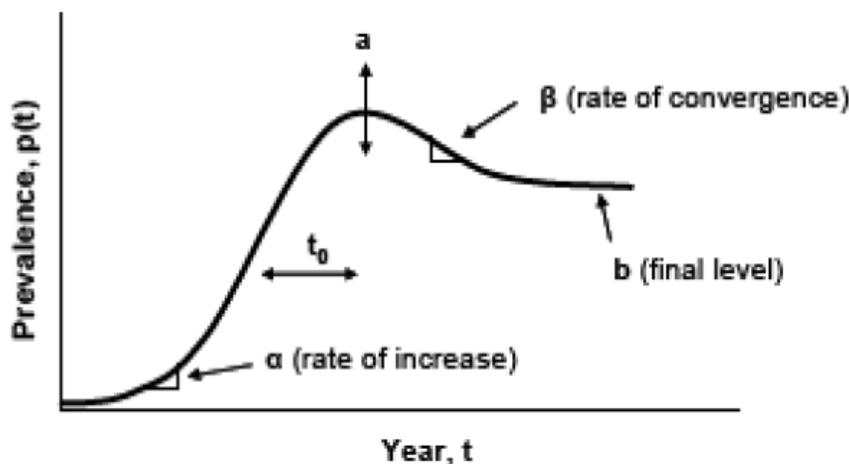
Fig. 2.3 Single logistic curve fitted on historical prevalence points



a = asymptote (i.e., the level at which the epidemic is expected to level off); α = the rate of increase at the start of the epidemic; t_0 = the time at which the epidemic reaches half its asymptotic value

Source: UNAIDS, 2008 (35).

Fig. 2.4 Double logistic curve fitted on historical prevalence points



α = the rate of increase at the start of the epidemic; a = determines the peak value; β = the rate of convergence; b = final prevalence level; t_0 = turn-over time (shifts the whole curve backward or forward)

Source: UNAIDS, 2008 (35).

This fitting process generates a yearly national prevalence rate, using the national population for the base year and projected growth rates that can be used as input for Spectrum. Although the Workbook fitting process can theoretically extend to 2030 (to allow for saturation in the various populations), the prevalence curve is only fitted through the current year. Future projections can be made in Spectrum, though it is recommended that one not look farther than five years into the future. The reason that the Workbook does not make future predictions is that it is not intended to capture the dynamics of the various sub-epidemics among risk groups that would make that possible. However, it does allow one to specify possible saturation levels and time to reach saturation to create future scenarios in Spectrum.

Strengths

The primary strength of the Workbook approach is the transparency of the process of making estimates and creating future scenarios. It is easy to trace the assumptions used in making estimates – which population groups are most exposed to HIV, how large those groups are, and their current and projected prevalence rates. This feature forces the user to rethink all available evidence, reconsider values that fall outside the usual range and examine assumptions. It also highlights data gaps clearly, which is invaluable for planning and (re)designing surveillance systems. Such planning processes are particularly effective when the major stakeholders participate and discuss the data.

A second strength of the approach is that it emphasizes ranges for the estimates instead of single point estimates, reflecting the uncertainty of the input data. In addition, it encourages review and analysis of the behavioural and serological data needed to make good estimates. In some ways, the analysis required in making the estimate can be more important than the estimate itself, since it not only requires a review of all available data, but also helps identify information gaps and ways to improve surveillance.

Weaknesses and limitations

The primary weakness of the Workbook Method is the variable quality of input data – there are always data gaps, and some data may be based on proxy assessment (e.g. using STI treatment rates to estimate the size of the client population for female sex workers estimated from) or expert opinion. Other possible drawbacks are that interactions among groups are not dealt with directly, and that the epidemic is pictured as static succession of separate states.

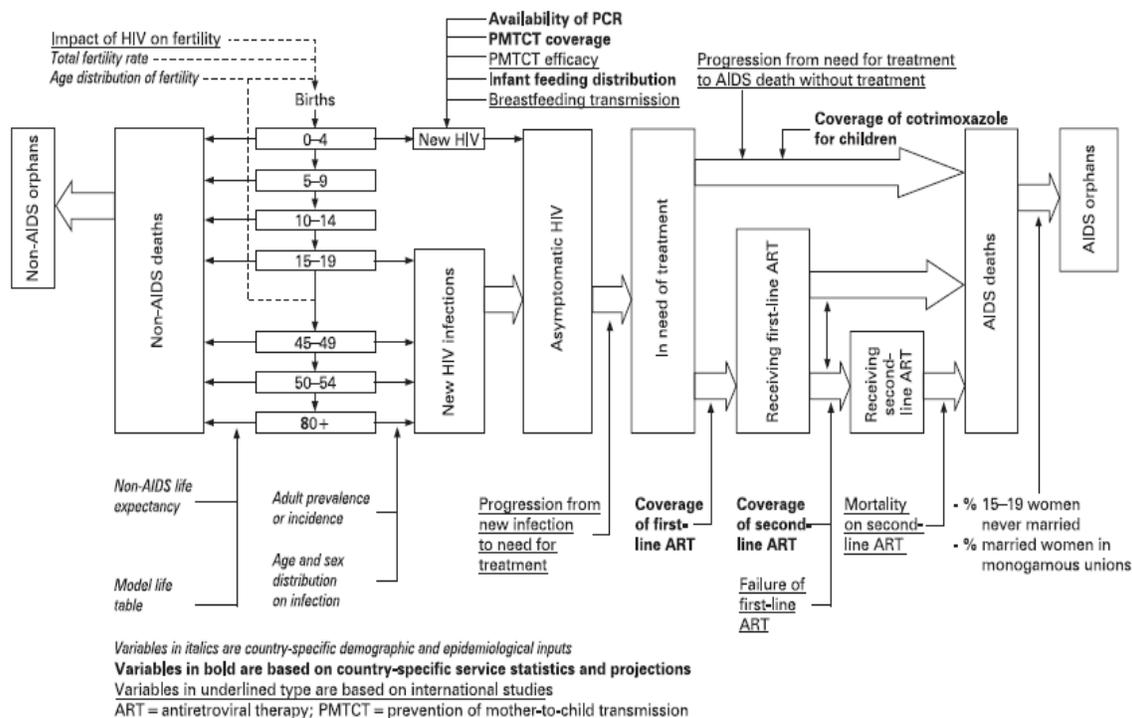
In addition, the methodology used to calculate the uncertainty (the plausibility bounds) of the national HIV prevalence estimate is based on an overall categorization of the quality of the national surveillance system. That means that the uncertainty estimates do not directly reflect the quality of the input data.

Another weakness is that these static representations of various time points in the epidemic cannot capture the dynamic membership of the risk groups. Finally, the curve generated is necessarily a simplification that will never exactly follow the actual epidemic curve, which can have multiple inflection points over time (30, 31).

The Spectrum projection package

The Spectrum package takes prevalence projections and calculates some of their key statistical implications, including the numbers of new infections, PLHIV disaggregated by age and sex, AIDS deaths and AIDS orphans, as well as the need for treatment and the impact of treatment. It also estimates other demographic indicators of interest, such as life expectancy and under-5 mortality. Fig. 2.5 shows a flow chart with the major inputs and outputs in the program's demographics and AIDS modules, which is used to examine the consequences of current trends and future programme interventions in reproductive health.

Fig. 2.5 Inputs, outputs and process of the demographic and AIDS modules in Spectrum.



Source: Stover et al., 2008 (32).

Demographic projections

The demographic projection component of Spectrum is a full-featured cohort projection model. Demographic projections are based on user input or projections prepared by the United Nations Population Division.

Regardless of the progress of the disease, PLHIV are subject to non-HIV mortality at the same rates as those who are not infected. The demographic projections in Spectrum rely on life tables to describe age-specific patterns of mortality corresponding to assumed levels of life expectancy at birth. Complete single-year life tables are used, instead of the more common age-group life tables, to capture the rapidly changing dynamics of HIV epidemics.

The HIV projections begin with an estimate and projection of adult prevalence, which is combined with information on the age and sex distribution of prevalence and of progression to death to estimate the number of new adult infections by age and sex. New infant infections are estimated from prevalence among pregnant women and the rate of mother-to-child transmission, which is dependent on infant feeding practices and the coverage of antiretroviral prophylaxis.

New infections progress over time, and at some point the PLHIV will require ART. Those who receive first-line and, if needed, second-line ART survive longer than those who do not. AIDS deaths of adults also result in AIDS orphans if both parents of a child die of AIDS.

Age and sex distribution of HIV

Adult HIV prevalence trends estimated in the first stage of modelling, using the Workbook Method, refer to the percentage of adults age 15–49 infected with HIV. For use in Spectrum these infections need to be distributed by age and sex – the adult HIV prevalence is disaggregated into female and male prevalence by specifying the ratio of female to male prevalence. It is assumed that the ratio is strongly weighted towards males in the start of a concentrated epidemic, but if it becomes generalized, more and more females are infected, and after ten years into the epidemic, the female-male ratio in the model reaches a plateau of 3:2 .

The age composition of the infected will change over time as well, due to saturation in higher-risk age groups, aging of PLHIV and probable changes in sexual behaviour. Spectrum takes account of these factors in describing the increases typically observed in the mean age of new and existing infections during the course of an HIV epidemic.

Progression from infection to AIDS deaths in the absence of treatment

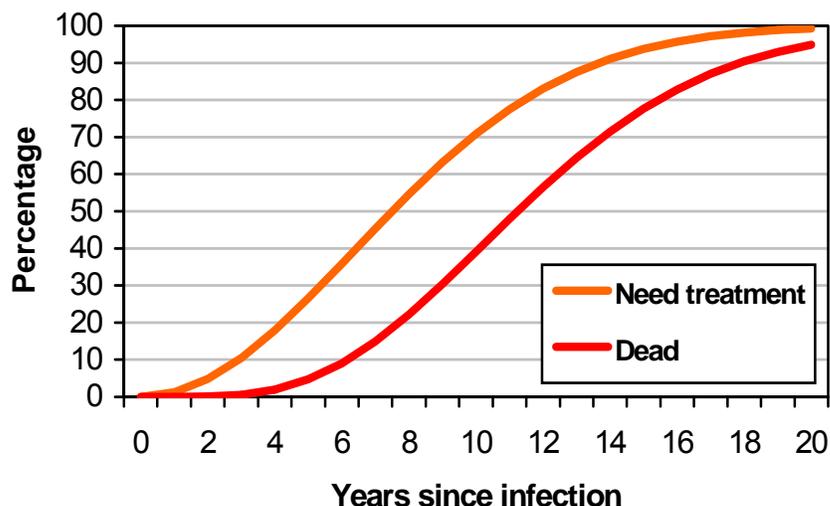
The survival time calculation in the Spectrum model is based on several studies and meta-analyses from around the world. In most countries, untreated male and female PLHIV have median survival times of approximately 10.5 and 11.5 years respectively. The difference is ascribable to males' older mean age at infection.

Time to eligibility for antiretroviral treatment

For a rising proportion of PLHIV, the progression to AIDS death described above is delayed or avoided by ART. Before 2007, Spectrum calculated ART eligibility as occurring two years before untreated AIDS death, but based on a number of cohort studies this estimate was increased from 2.1 to 4.0 years for the various eligibility criteria.

ART eligibility criteria usually states that a PLHIV is eligible if he or she has either less than 200 CD4 cells/mm³, WHO Stage 4 disease or a combination of 200–350 CD4 cells/mm³ and Stage 3 disease. However, due to data scarcity it is not possible to calculate the time to eligibility for ART for the full criteria, and the Spectrum model instead uses a duration average for the available criteria (see example in Fig. 2.7), which results in a longer time between seroconversion and ART eligibility, and a shorter time between ART eligibility and death in the absence of ART if compared to the full ART eligibility criteria.

Fig. 2.7 Sample progression to ART need and death without ART for adult male PLHIV



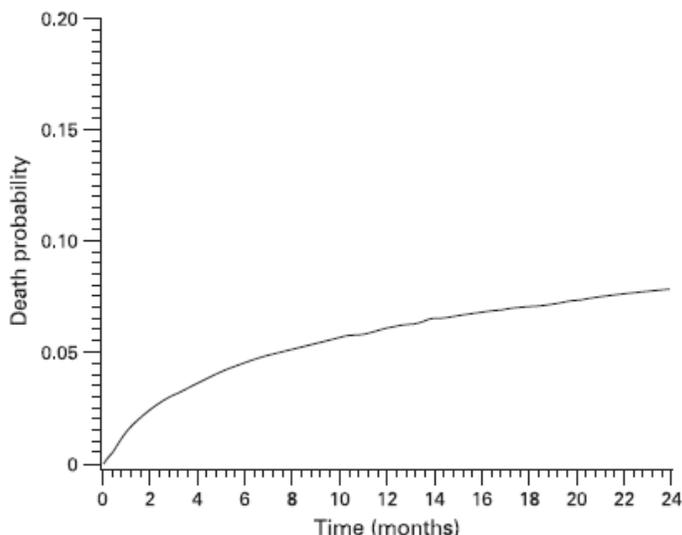
Source: UNAIDS, 2008 (35).

Survival on ART

The literature review that UNAIDS model developers performed to elicit default values for survival on ART to use in the Spectrum model, indicated that after 12 months on ART, the overall adult mortality rate ranged from 6% to 26%, or a survival rate of 74%–94%. Factors associated with poorer survival among adults were low CD4 counts (especially initial counts below 50 cells/mm³), advanced WHO Stage 3 or 4, low body mass index, low haemoglobinaemia, male gender and poor adherence. The death rate was the highest in the first three months after the initiation of ART (from 5.1 to 37.3 deaths per 100 person-years) (33). For children, the six-month survival after ART initiation varied from 91% to 95%, and a low CD4 count was associated with poorer survival, as it was in adults. Little or no data was available on survival rates for different first-line regimens or treatment switches in the first year of ART.

Fig. 2.8 plots a combined probability of death for people on ART from one of the reviewed studies. The survival probability is estimated at 93.9% after one year of treatment and 92.9% after two. However, the proportion of patients lost to follow-up is of serious concern in fully interpreting the survival/mortality findings, as almost 16% of the study sample was already lost to follow-up during the first six months.

Fig. 2.8 Probability of death among 36 615 adult ART patients in 17 cohorts in Africa, Asia and South America (33)



Source: Stover et al., 2006 (33).

Based on these figures, the default probabilities of adult survival on ART in the Spectrum model were set at 85% for the first year and 95% for each subsequent year. The default value of annual survival for children older than 1 year was set at 90% for the first year of ART and 95% subsequently, while for children who began ART before age 1 the first year survival of 80% was used.

Uncertainty analysis

A special module in Spectrum can be used to produce uncertainty bounds around the usual point estimates for each indicator for each year. The Spectrum uncertainty analysis consists of a large number of Monte Carlo runs that each randomly select a prevalence curve from the Workbook fits and input values for other parameters from a range that can be set by the user. The results are stored and then sorted to determine the ranges for any percentile selected.

Strengths

The main strength of the Spectrum package lies in its continually updated default values based on literature reviews, in the transparency of the input data and model assumptions, in the flexibility of its output options and in the ease with which the user can construct different scenarios. Spectrum output includes some of the most important indicators for understanding the scope and magnitude of an HIV epidemic – including numbers of people infected, new infections and AIDS deaths – and for planning a response, such as the number of people needing treatment or interventions to prevent mother-to-child transmission. All these factors make Spectrum a useful tool for countries planning and managing their HIV programmes, as well as for international agencies mobilizing commitment and resources.

Weaknesses and limitations

The main weakness of the Spectrum package is that many of the default assumptions are derived from a small number of studies that may not be representative of all populations,

especially as many more studies are available for African populations than for those in other regions (32–36).

Literature on the UNAIDS/WHO framework for HIV modelling

For more details on the UNAIDS/WHO modelling framework for HIV, please consult the following resources, which are available free online.

- Ward H, Walker N, Ghys PD, eds. Methods and tools for HIV/AIDS estimates and projections [special issue]. *Sexually Transmitted Infections*, 2004, 80(Suppl. 1) (http://sti.bmj.com/content/vol80/suppl_1, accessed 13 May 2009).
- Ghys P et al., eds. Improved methods and tools for HIV/AIDS estimates and projections [special issue]. *Sexually Transmitted Infections*, 2006, 82(Suppl. 3) (http://sti.bmj.com/content/vol82/suppl_3, accessed 13 May 2009).
- Improved data, methods and tools for the 2007 HIV and AIDS estimates and projections [special issue]. *Sexually Transmitted Infections*, 2008, 84(Suppl. 1) (http://sti.bmj.com/content/vol84/Suppl_1, accessed 13 May 2009).
- Epidemiological software and tools (2007) [web page]. Geneva, UNAIDS, 2008 (http://www.unaids.org/en/KnowledgeCentre/HIVData/Epidemiology/epi_software2007.asp, accessed 13 May 2009). Includes the latest downloadable versions of EPP, the Workbook Method and the Spectrum package, as well as manuals.
- Methods and assumptions for estimates [web page]. Geneva, UNAIDS, 2009 (<http://www.unaids.org/en/KnowledgeCentre/HIVData/Methodology>, accessed 13 May 2009).

3. Estonian HIV data sources

3.1 *Epidemiological information*

Estonian Health Protection Inspectorate

The Estonian Health Protection Inspectorate is responsible for the passive surveillance of communicable diseases, including HIV (37). The Inspectorate receives data on new HIV cases from the HIV Reference Laboratory. The data are anonymous and include the age, gender, transmission category and place of testing.

National HIV Reference Laboratory

HIV serological surveillance in Estonia is performed by 33 primary diagnostic laboratories, located in all the larger medical institutions. Samples with positive results are sent to the National HIV Reference Laboratory, located in West Tallinn Central Hospital (17).

By legal requirement, all samples sent for HIV testing have to be categorized and coded. Some of the coding categories reflect transmission modes (such as types of sexual contacts or injecting drug use), some the type of institution where the person was tested (such as prison or an anonymous facility) and some why the person was tested (such as blood donation, pregnancy or STI). There are a total of 14 categories, and a person tested may feature in several categories simultaneously (e.g. an IDU tested in an anonymous facility). For each sample, the Reference Laboratory assigns a primary code for inclusion in its HIV database, which contains data on all HIV tests performed in Estonia, with personal identifiers if they exist. About 30% of the tests cannot be associated with any individual, as they stem from anonymous testing facilities.

The Reference Laboratory also collects data from all primary diagnostic laboratories on the number of HIV tests they performed and the number of people they test. These data are cumulative and anonymous.

National Institute for Health Development (NIHD)

The NIHD is an independent national research and development agency under the jurisdiction of the Ministry of Social Affairs (38). It is responsible for implementing the national public health strategies, including the national HIV prevention strategy, the national drug abuse prevention strategy and the national TB prevention programme. It is also responsible for the active serological and behavioural surveillance of HIV in risk groups – IDUs, commercial sex workers, MSM, et al. – and the general population. Finally, the NIHD is active in monitoring and evaluating national public health strategies, and in collecting and disseminating information on HIV-related topics.

Estonian Health Insurance Fund (EHIF)

Health insurance in Estonia relies on the principle of solidarity, and the relevant legislation has been in force since 1992.

Health insurance is organized by the EHIF, the only organization in Estonia that handles compulsory health insurance (39). The EHIF has four regional departments that cover the whole country. The purpose of health insurance is to cover the costs of health services provided to insured persons, prevent and cure diseases, finance the purchase of medicinal products and technical aids, provide benefits when medical problems cause a temporary inability to work, and provide other benefits. While health care services for the uninsured are funded by the state budget, they are also administered by the EHIF.

EHIF contracts with health care providers for different types of health care services such as primary care, specialist care (both outpatient and inpatient), nursing care etc.

EHIF has a database of everyone who has ever received any kind of health care services. This database includes general information such as gender and date of birth, as well as information about disorders, diseases and services received. These data are sent to EHIF by health care providers electronically.

National Tuberculosis Registry

The National Tuberculosis Registry is currently operating as part of the North Estonian Regional Hospital (18). The Registry has been collecting data on individual TB cases and treatment from doctors and mycobacteriology laboratories via a compulsory notification system for the last 20 years.

Ministry of Justice

The Ministry of Justice provides health care services – including HIV testing, treatment and care as well as TB diagnostics and treatment – in prisons and other penitentiary institutions (40). The Ministry collects data on the number of newly diagnosed HIV cases in prison, the cumulative number of incarcerated PLHIV and the number of people under its jurisdiction who receive ART or treatment for TB.

Ministry of Social Affairs

The Ministry of Social Affairs is responsible for procuring antiretrovirals (41). It collects and aggregates monthly data on ART usage from the hospitals. The data include the total number of people in each treatment regimen in each hospital, with the proportion of children, pregnant women and other adults treated, as well as the proportion of drug-resistant cases.

Statistics Estonia

Statistics Estonia is a government agency under the Ministry of Finance (42). Its main task is to provide public institutions, business, the research sector, international organizations and private individuals with reliable and objective information service on economic, demographic, social and environmental situations and trends in Estonia. With regard to HIV, the primary data of interest that it provides are official mortality and population statistics.

3.2 Previous research and studies

There are numerous sources of HIV data in Estonia since all the institutions named in the previous section are involved in collecting and analysing data as well as evidence generation more generally. In addition, all HIV service providers, including both hospitals and numerous NGOs, collect data on their activities. Several research groups at Estonian universities are also working on HIV-related issues that span from epidemiology to genetics to vaccine development. The most prominent academic research on HIV epidemiology is conducted by the Department of Public Health at the University of Tartu (43), which along with the NIHD is the main Estonian institution carrying out HIV epidemiological and behavioural studies.

The following overview briefly describes the chief epidemiological surveys conducted in the country in recent years. It should provide an initial sense of the epidemiological research that exists on HIV and populations at risk in Estonia.

Injecting drug users (IDUs)

- *Prevalence of HIV, other infections and risk-taking behaviour among injecting drug users.* The original survey was performed in 2005, with a follow-up in 2007. It was carried out in collaboration with the NIHD and the University of Tartu using a respondent-driven sampling methodology. Structured interviews and blood samples were used for collecting the data (44, 45).
- The NIHD has conducted an annual knowledge and behaviour survey of new and returning clients of needle exchange points since 2003. The survey is carried out in cooperation with the service providers via a self-administered questionnaire (46–49).
- There also exist a number of research papers on HIV among Estonian IDUs (15, 50–54).

Female sex workers

- *HIV prevalence and risk-taking behaviour among female sex workers in Tallinn.* This survey was carried out during 2005 and 2006 by the NIHD, using structured interviews and saliva samples. It utilized respondent-driven sampling together with other approaches (55, 56).
- A study has also been conducted of sex workers who had contact with STI diagnostic or treatment services. Using a self-administered questionnaire, the study was carried out annually among new and returning clients of the services in 2004–2007, in cooperation with the NIHD and the service providers (57–60).
- *Prostitution in Estonia: overview of the situation of women involved in prostitution.* This 2006 study was part of the Employment, Social Affairs and Equal Opportunities (EQUAL) project financed by the European Commission. It was carried out by the Estonian Institute for Open Society (61).
- *Meaning of prostitution in Estonian society: internal security or economic benefit.* This study was also carried out in 2006 by the Estonian Institute for Open Society as part of the EQUAL project (62).

Prisoners

- *Inmates' knowledge, attitudes and behaviour related to HIV and illicit drug use.* This study has been carried out three times so far (in 2004, 2006 and 2008), in cooperation with the NIHD and the Ministry of Justice. It uses random sampling and a self-administered questionnaire (63–65).

Men who have sex with men (MSM)

- *HIV prevalence and risk-taking behaviour among MSM in Tallinn and Harju County.* This pilot study used respondent-driven sampling. Data were collected from self-administered questionnaires and blood samples. The NIHD carried out this study in 2007 (66).
- *HIV-related knowledge and behaviour among MSM visiting gay websites.* This web-based study was carried out in 2004, 2005 and 2007 by the NIHD using a self-administered questionnaire (67–69).

PLHIV

- *Quality of life and HIV-related discrimination of HIV-infected people visiting infectious disease clinics.* This study was carried out by the NIHD in cooperation with three hospitals using a self-administered questionnaire. The first wave of data collection took place in 2005–2006 and the second in 2008 (70, 71).

- *Qualitative research on access barriers for people living with HIV/AIDS in Estonia and Kaliningrad.* This one-time study was carried out in 2007 by the NIHD and the Russian Public Opinion Research Center (VCIOM) and financed by the United Nations Development Programme (UNDP).

Young people

- *HIV-related knowledge, attitudes and behaviour among Estonian youth.* This survey used random sampling and self-administered questionnaires and has been carried out every other year (2003, 2005 and 2007) by the NIHD. The data are collected during visits to schools (for surveying those aged 10–18) and by mail (for those aged 19–29) (72–74).
- The European School Survey Project on Alcohol and Other Drugs (ESPAD) is a collaborative effort of independent research teams in about 40 European countries. Data are collected every fourth year, and Estonia has been taking part since the survey started in 1995. The study population is schoolchildren aged 15 and 16. It covers knowledge, attitudes and behaviour regarding illicit drugs, among other issues. The survey in Estonia is carried out by the Institute of International and Social Studies and financed through the NIHD (75, 76).
- Health Behaviour in School-aged Children (HBSC) is a cross-national research study that is conducted in 35 countries and targets young people attending school, aged 11, 13 and 15 years. Data are collected through self-completed questionnaires administered in the classroom. The survey covers background factors, individual and social resources, health behaviours (e.g. alcohol use, cannabis use and sexual behaviour) and health outcomes among the target populations. The study has been carried out by NIHD every three years since 1993 (77).

Adults

- *Health behaviour survey of the Estonian adult population.* This survey is part of the FinBalt Health Monitor, a collaborative surveillance project conducted in Finland, Estonia, Latvia and Lithuania, which Estonia has participated in since 1990. The biennial postal survey covers many health behaviour topics (including some questions on HIV awareness, beliefs and related behaviour) and targets the population aged 16–64 years of age. The NIHD conducts the survey in Estonia (78, 79).

Other

- The NIHD has been continuously surveying the clients of seven HIV counselling facilities since 2004 with a self-administered questionnaire covering HIV risk behaviours (80). Analogous data are also collected from IDUs and their sexual partners who use STI diagnostic services.
- In 1994 and 1999, the KISS survey – KISS being an acronym for “maturation, relations, friends and sexuality” in Estonian – examined sexual maturation and reproductive health risks among ninth-graders, primarily aged 15–16. The study was carried out by the Estonian Family Planning Union (81).

4. Previous modelling of the HIV epidemic in Estonia

Over the years there have been several efforts to model the HIV epidemic in Estonia and estimate its likely future progression to inform policy. The focus of these modelling projects has varied, as has the output. The results of these efforts have not reached a wider audience, however, because the individual projects were never finalized or were intended for internal use only. The following sections briefly describe the chief HIV modelling activities of recent years that we have been able to identify for Estonia.

4.1 *Use of WHO/UNAIDS modelling tools in the Ministry of Social Affairs*

In 2005, the Estonian Ministry of Social Affairs started to use the WHO/UNAIDS HIV estimation model – specifically, the Workbook and Spectrum components – in developing the National HIV and AIDS Strategy for 2006–2015.

Initially, the Ministry used earlier versions of these modelling tools. It primarily used the international data provided with the toolset, with some adjustments based on the opinion of national experts. However, by the end of the year the Ministry produced new estimates that relied more on national survey data. It continually updated the estimates with new national data, compared different scenarios and began estimating the need for ART. Table 4.1 presents an overview of its progress in using the WHO/UNAIDS model.

By the end of 2007, the model's output was being used in policy (and budget) planning. Contextualization of the input data had improved, the data were more rigorously verified and the use of different model features had expanded. However, there are still input data that could be profitably contextualized (e.g. general population demographics), and new evidence from national sentinel surveys could be used to refine the overall accuracy of the model.

Table 4.1 Recent use of UNAIDS/WHO HIV models by the Ministry of Social Affairs

Year	Data	Different scenarios modelled?	ART need estimates?
2005	<ul style="list-style-type: none"> • Chiefly default model data from the United Nations Population Division and UNAIDS • Country-specific data on HIV prevalence and peak incidence based on expert opinion • Risk group sizes based on expert opinion 	No	No
2005	<ul style="list-style-type: none"> • Chiefly default model data from United Nations Population Division and UNAIDS • Country-specific data on HIV prevalence and peak incidence based on HIV diagnosis statistics • Risk group sizes based mainly on national studies and international estimates reviewed by national experts 	<p><i>First scenario</i> No change in incidence but slower progression to AIDS and increased survival with AIDS due to an assumed increase in ART coverage</p> <p><i>Second scenario</i> Reduction of annual HIV incidence by 8% starting in 2006 (based on the latest trend in HIV diagnosis)</p> <p><i>Third scenario</i> Reduction of annual HIV incidence by 8% starting in 2006 (based on the latest trend in HIV diagnosis), along with slower progression to AIDS and increased survival with AIDS due to the assumed increase in ART coverage</p>	No
2007	<ul style="list-style-type: none"> • Risk group sizes based mainly on national studies and international estimates reviewed by national experts • HIV prevalence estimates for risk groups taken from national sentinel surveys • National ART treatment volumes incorporated • Model defaults (based on United Nations Population Division and UNAIDS estimates) for population structure, migration, life expectancies and fertility rates 	<p><i>First scenario</i> Modelled as if no ART was in place</p> <p><i>Second scenario</i> Modelled with current ART volumes</p>	Yes

4.2 Earlier modelling of HIV resource needs in the Ministry of Social Affairs

In 2005 and 2006, before it began using the WHO/UNAIDS model to assess HIV resource needs, the Ministry of Social Affairs had developed a model to estimate the probable size of various resources and costs in relation to the HIV epidemic, with a time horizon of approximately 10 years. The model was mainly a resource planning tool that relied on disease data from specialized epidemiology modelling tools.

The main model inputs were HIV incidence, time until treatment need, survival probability and unit prices for HIV prevention- and treatment-related resources. The model calculated HIV surveillance, treatment and medication resource needs, and expenses. This planning tool was also able to perform cost-effectiveness calculations for different interventions, provided that effectiveness data were available (*Madis Aben, personal communication, 8 October 2008*).

4.3 Organization and financing models developed with WHO of HIV and TB services

Since 2005, the WHO Regional Office for Europe has been carrying out a project to scale up HIV and TB treatment, care and prevention in the Baltic states, a project supported financially by the French government.

Besides preparing guidelines, developing case management systems and facilitating the exchange of experience among the three countries, the project also carried out two analyses that provide useful insights for modelling the HIV and TB epidemics in Estonia.

The first report was entitled *Scaling up treatment and care for HIV/AIDS and TB and accelerating prevention within the health system in the Baltic States (Estonia, Latvia, Lithuania): economic, health financing and health system implications (82)*. It was prepared by Anita Alban and Joe Kutzin and finalized in 2006.

While the focus of the study was mainly on national health financing, it also included a comprehensive review of HIV and TB services in each country. The analysis of service organization and financing was grounded in the WHO financing framework, which enabled a systematic approach to the issue as well as comparison with other areas of the health system. The framework is based on the three main functions of health financing:

1. *collection*: integrating funding sources, contribution mechanisms and collection entities;
2. *pooling*: arranging to accumulate collected funds for specific populations and services; and
3. *purchasing*: allocating funds to service providers, specifying the structure and content of expenditures.

The second and more detailed analysis, *Financing HIV/AIDS and TB interventions in Estonia*, was prepared by Claudio Politi and Triin Tõrvand and finalized in 2007 (27). This report furthered the analysis of Alban and Kutzin. Of particular interest was its detailed cost analysis of public health programmes, covering all the main sources of financing and services that Estonia provided to the target populations. The authors presented the results using charts that showed the flow of funds and highlighted relevant organizational and financial links among the various health system components, which helped them address the issue of fragmentation and the need for client focus.

It is also worth mentioning that the WHO health financing framework was developed as a tool for modelling alternative scenarios and then analysing and assessing their financial and organizational impacts. The flow of funds in this framework provides baseline information for various scenarios and projections and facilitates joint planning and budgeting processes.

4.4 HIV epidemiology and economic impact models developed by international experts

In 2004, Rifat Atun and colleagues used a system dynamics model to simulate the transmission dynamics of HIV and TB in Estonia (83). This type of model takes into account the complexities of infectious disease transmission, including different interconnected systems with feedback loops, time delays and non-linear relationships, which makes this approach invaluable in developing effective policy.

The model estimated the average daily drug injection frequency among IDUs and the proportion of IDUs who share needles as the two main parameters for simulation, since these measures represent the key behaviours that drive HIV transmission in Estonia. Moreover, these behaviours can be influenced by effective harm-reduction interventions, which the authors modelled for impact in five policy scenarios.

They used data from both international literature (e.g. transmission rates) and national sources (for official HIV and TB notifications and other surveillance data). Their starting point for the simulation was the beginning of 2003, and the model was simulated for a period of 20 years. The outputs of the model were cumulative HIV-associated deaths and cumulative TB-associated deaths.

In 2005, another HIV epidemiology and economic impact model began to be developed in collaboration between the PRAXIS Center for Policy Studies and international experts (*Tom Novotny, personal communication, 13 August 2008*). This project sought to examine a 10-year time period for HIV and TB in Estonia using an interactive simulation model that would calculate HIV prevalence, incidence and mortality for four groups (IDUs, drug-injecting sex workers, non-injecting sex workers and low-risk adults), along with the microeconomic impact of the increased need for ART and the macroeconomic consequences of HIV, particularly for economic performance and the labour force. The project also sought to analyse the impact of HIV and HIV prevention on the TB epidemic, including the effects of prevention efforts on mortality and the economy. In addition, it modelled best and worst case scenarios for each of the project's key research objectives. Unfortunately, the project was never finalized and the results never published.

4.5 WHO/UNAIDS estimates for Estonia

WHO and UNAIDS have produced HIV/AIDS estimates on the Estonian situation for a number of years (16, 84), as detailed in previous sections of this report. These international estimates have used the locally collected data that the Ministry of Social Affairs also uses to produce national estimates.

Recent WHO/UNAIDS estimates for Estonia have directly involved national experts who prepared the data in collaboration with the agencies. WHO/UNAIDS has later performed consistency checks on the material and produced the final results. Nonetheless, using the toolset in Estonia itself has permitted more flexibility in reacting to observed demographic changes, more extensive contextualization and thus better suitability for policy use.

5. Modelling inputs, process and scenarios

5.1 The modelling process in general

For the present study, we used the following two-stage modelling approach.

1. We fitted and calibrated the model for Estonia in three steps:
 1. collecting and analysing available epidemiological data to calculate total 2007 HIV prevalence (with uncertainty margins);
 2. modelling alternative scenarios to identify the year of peak incidence; and
 3. modelling alternative scenarios to identify the rate at which the HIV epidemic expanded through 2007.
2. Based on the calibrated model and assuming attainment of national HIV strategy goals, we projected HIV prevalence, ART need and AIDS-related deaths through 2015.

Each of these steps involved alternative scenarios, which we evaluated against available data and for overall plausibility. Each step was based on the best-fitted scenario from the previous step. This report thus only presents results for the overall best-fitting scenario, providing examples of intermediate alternatives only to illustrate the modelling process. The one deviation from this approach is found in Section 5.5, which presents the possible impact of falling short of and of surpassing the incidence reduction goal at the centre of the national HIV strategy and thus contains three scenarios.

5.2 Data for model input

General population characteristics

General population data are used in modelling HIV prevalence and HIV impact in every component of the WHO/UNAIDS modelling framework. Table 5.1 presents a cursory overview of the population data we used. Although such aggregate population data are used for estimating HIV prevalence, modelling the impact of HIV on the population in Spectrum requires full population data, both historical and projected, stratified by age and gender. All the population data we utilized were provided by Statistics Estonia (42).

We also used Statistics Estonia data on life expectancy at birth, male:female ratio at birth and total fertility for all years, and United Nations data on international migration.

Table 5.1 Summary population data and HIV diagnosis statistics for Estonia, 2007

	Indicator	Datum or estimate	Data source
Population	Total population	1 341 672	Statistics Estonia (2007)
	Adult population (age 15–49)	671 524	Statistics Estonia (2007)
	% living in urban areas	71%	Statistics Estonia (2007)
HIV registration	Total number of new HIV cases reported in 2007	Females: 260	Health Protection Inspectorate (2008)
		Males: 373	
		Total: 633	

HIV prevalence data for high- and low-risk populations

HIV prevalence data was collected separately for low- and high-risk populations to estimate the total HIV point prevalence in the country. As described in Section 2.2 of this report, the HIV prevalence curve over time is anchored to one or more reference points with the best point prevalence estimates of HIV. The suitability of a particular yearly prevalence estimate to function as a reference point is linked to data availability. The latest and most comprehensive data coverage at the time we reached this modelling step was for the year 2007. Hence we used 2007 as our main reference point, with secondary reference points in 2000 and 1996. Table 5.2 presents an overview of the population groups, principles of prevalence calculation and data sources for the 2007 HIV prevalence point estimate.

Table 5.2 Overview of data used to estimate HIV prevalence for 2007

	Population size	HIV prevalence	Female statistics		Total HIV+	UNAIDS guidance values on population size	Source of data or estimate	Comments
			% female	HIV+ females				
1. Populations at higher risk								
IDUs	8 000–20 000	50%–70%	15%	1 260	8 400	EMCDDA estimate 10 000–30 000	Population size: Uusküla et al., 2007 (52) Prevalence: Löhmus et al., 2007 (45)	
MSM	7 500–19 000	2%–5%	0%	0%	464	2%–5% of adult male population	Population size: UNAIDS guidance value Prevalence: Trummal et al., 2007 (66) and expert opinion	
Female sex workers	1 600–4 000	4.6%–12.5%	100%	239	239	0.4%–1.4% of adult female population	Population size: expert opinions Prevalence: Uusküla et al., 2008 (56)	IDUs (20% of female sex workers) excluded
Male clients of female sex workers	10 000–30 000	0.5%–2.0%	0%	0%	250	2%–7% of adult male population, or five times the female sex worker population	Population size: Uusküla et al., 2008 (56) Prevalence: expert opinion	IDUs (5% of clients) excluded. Prevalence among female sex workers in Tallinn about 80%, prevalence among their clients about 0.5% (56)
Prisoners	4 500	10%	—	—	450	—	Population: Ministry of Justice (2008) Prevalence: Ministry of Justice (2004)	IDUs (30% of prisoners) excluded (64) HIV prevalence based on inmate testing (81% coverage)
2. Populations at lower risk (excludes risk group members)								
Urban females	233 421–236 403	0.03%–0.05%	100%	106	106	—	Population: Statistics Estonia (2008) Prevalence: National HIV Reference Laboratory and Health Protection Inspectorate (2008)	HIV prevalences of pregnant women, neonates and women receiving abortions used to estimate prevalence among low-risk women
Rural females	95 341–96 559	0.01%–0.02%	100%	14	14	—	Population: Statistics Estonia (2008) Prevalence: National HIV Reference Laboratory and Health Protection Inspectorate (2008)	

EMCDDA: European Monitoring Centre for Drugs and Drug Addiction.

Current ART coverage for HIV impact modelling

Modelling of HIV impact uses current ART levels as a main input value, together with the HIV prevalence estimates from the Workbook tool. The Ministry of Social Affairs provided us with information on historic and current ART coverage (41). We projected the ART trends through 2015 to estimate future coverage levels (Table 5.3). We did not use second-line ART in our modelling.

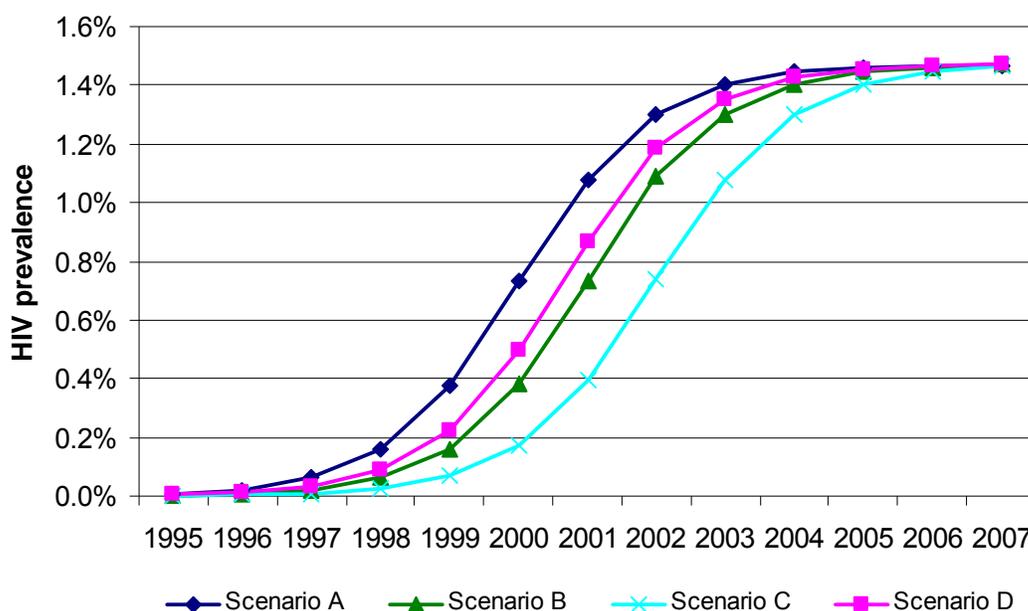
Table 5.3 First-line ART coverage in Estonia, historic and predicted

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Number of people on ART	1	2	3	4	10	20	30	40	55	100	250	460	720
Year	2008	2009	2010	2011	2012	2013	2014	2015					
Predicted number of people on ART	1 100	1 500	2 000	2 500	3 100	3 900	4 400	4 900					

5.3 Modelling the year of peak incidence

Detection of new HIV cases peaked in 2001, with approximately 1500 new cases registered that year. However, there is of course a time lag between infection and detection. We prepared four scenarios to estimate the time lag. The scenarios differed only by the time of peak incidence, which we set at the beginning of 2000 (Scenario A), 2001 (Scenario B) and 2002 (Scenario C), as well as mid-year 2000 (Scenario D). The model assumes that highest incidence is reached when prevalence has reached half its highest value (the epidemic's half-peak). Hence, the incidence peak was set using two parameters – the time when HIV prevalence started to increase in the population and the time when the prevalence plateau was reached (see Fig. 2.3). The distance between the beginning and end of the increase in incidence was held constant among the scenarios, as were the other epidemiological characteristics. The resulting four scenarios are presented in Fig. 5.1.

Fig. 5.1 HIV prevalence for scenarios used to model different peak incidence points



Note: peak incidence defined as occurring when half the maximum observed prevalence is reached.

We scrutinized the prevalence, incidence and mortality results from these four scenarios against all available data, including both national evidence on the epidemic as well as international evidence on typical HIV epidemic progressions, registration patterns and prevention effectiveness. After thus evaluating the scenarios and consulting experts, we selected Scenario D, with peak incidence occurring in mid-2000, as the most plausible. According to this scenario, the average time lag between infection and registration at the time of highest incidence was less than six months.

5.4 Modelling the rate of infection spread

Epidemiological data collected in the first step of our modelling indicated that the total number of PLHIV in Estonia at the beginning of 2007 was approximately 10 000 (see Table 5.3), while the cumulative number of registered cases was less than 7000.

There are two main possibilities for the detection (or diagnosis) gap:

1. the true epidemiological HIV incidence curve has the same shape as the curve of registered cases, but at a higher level; or
2. the true incidence curve has a different shape than the detection curve.

In the next modelling step we sought to compare the plausibility of each possibility. The previous step had indicated that the incidence peak was approximately in line with the diagnosis peak and assigned it to mid-2000. We now introduced variation in the rate of HIV prevalence increase to assess how fast HIV was spreading among high-risk populations, creating two new scenarios, D1 and D2. We changed the rate of prevalence increase by changing the period between the start and end of the increase. The shorter the time between these two points, the faster the increase and the higher the number of new infections at peak incidence. If most of the infection spread occurred over two years, as the graph of detected cases suggests, the number of new infections would have to be several times the number of newly registered infections. Conversely, if the two numbers were the same at peak incidence, the infection spread would have had to last several years longer. As in the previous step, we used the same ART levels for both scenarios.

Scenario D2 assumes an earlier start to the prevalence increase (1992) and an average yearly increase of 675 PLHIV over the course of its rise. D1 assumes that prevalence begins rising somewhat later (1996), with an average annual increase of 901 PLHIV (Fig. 5.2), thus following the shape of the registered incidence curve more closely (Fig. 5.3). Of course, these are just two scenarios, and there are an infinite number of possible scenarios – though in this case they are unlikely to contribute much more to understanding the question at hand.

Fig. 5.2 Two scenarios for the total number of PLHIV in Estonia

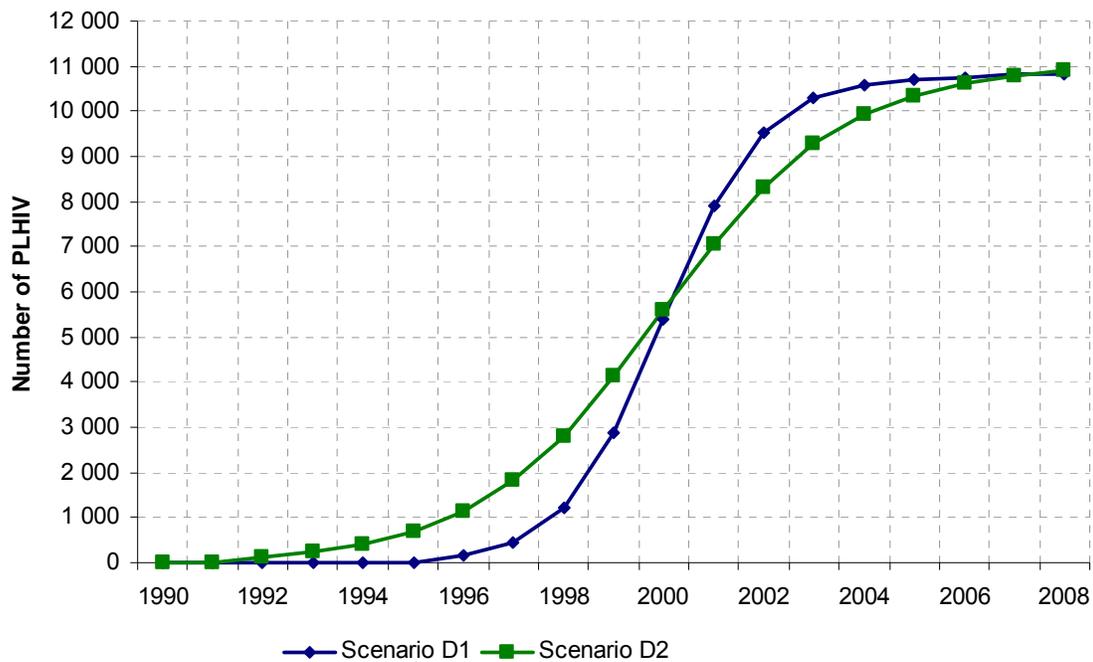
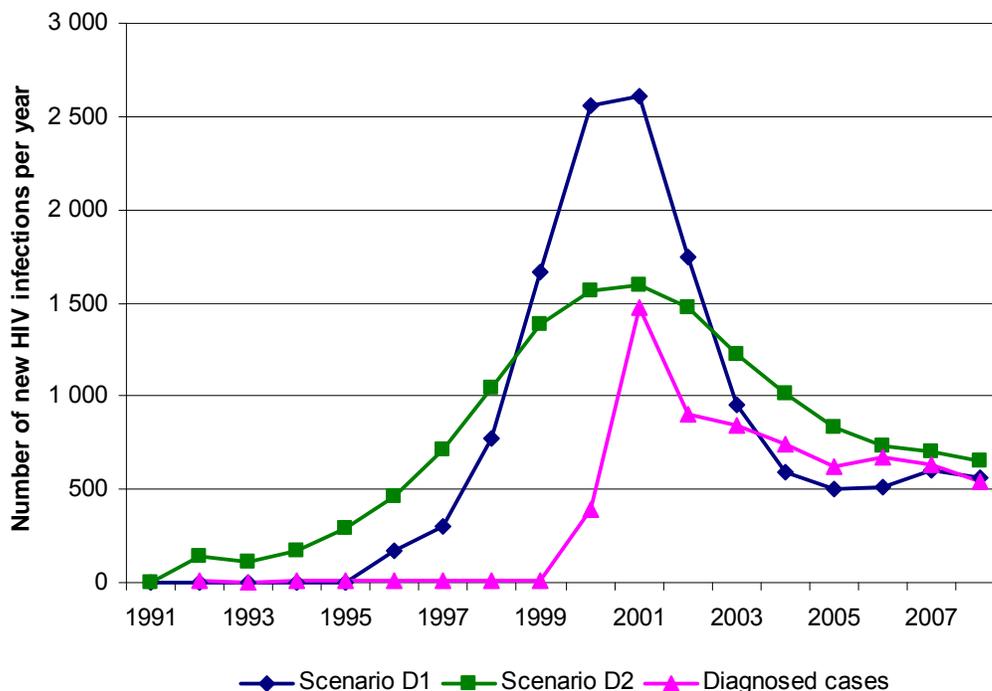


Fig. 5.3 New HIV infections in the two scenarios and as actually registered



Once again, we again compared the number and distribution of new infections and existing infections over time and among different population groups against available national and international research findings, taking particular account of current knowledge on the evolution of HIV epidemics in different population groups. Based on this review, we decided to use Scenario D2, with its slower HIV spread, as our baseline in the next modelling steps and in generating our final results.

5.5 Modelling the impact of attaining the main national strategy goal

In our final modelling step, we focused on possible courses of the HIV epidemic after 2007. We constructed future scenarios using Scenario D2, with an incidence peak in mid-2000 and a relatively gradual spread, since we found it to best fit the probable dynamics of the epidemic to date.

Although there are several approaches to constructing future scenarios, they can be loosely categorized in two categories: those that are purely epidemiological and those that are tied to public health action. The first kind examine what would happen if the epidemic were left to run its course, while the second look at the effects of interventions – in this case, interventions to implement the national HIV strategy and attain its primary goal.

As the results of the previous modelling steps show, the incidence targets for Estonia's national HIV strategy are close to the incidence rates that would likely occur if the epidemic were to follow its natural course, assuming no explosive HIV spread among the country's general population. The HIV saturation of high-risk populations, particularly IDUs, will lead to declining incidence as long as the epidemic is confined to these groups. Hence, we felt it reasonable to select the second approach in constructing future scenarios.

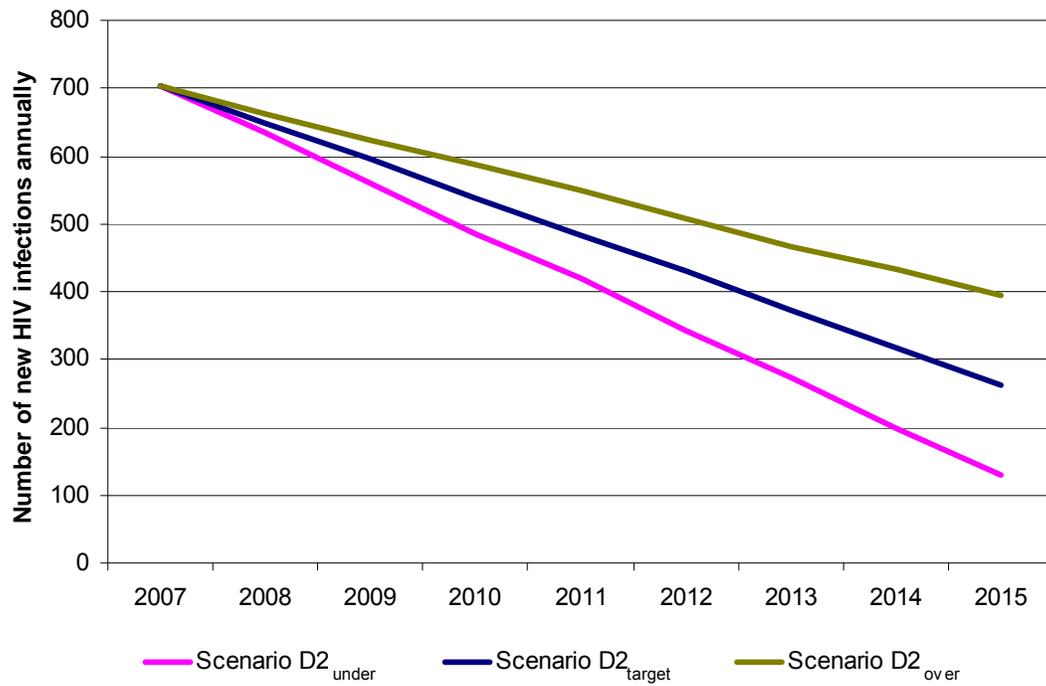
We proceeded by creating three scenarios based on the national strategic targets in order to explore the likely effects of meeting, surpassing and falling short of the main incidence target.

In interpreting the results of these future scenarios, it is important to keep in mind that the authors of the WHO/UNAIDS modelling toolset do not advise making predictions farther than five years into the future (33). Nonetheless, we defined our modelling horizon as 2015, eight years into the future, because the primary national strategy targets fall in that year.

We used incidence as the base indicator in constructing these three scenarios, since the main target is bringing the incidence rate down to 20 new registered cases per 100 000 population by 2015.

All three scenarios start with the same initial HIV incidence in 2007, but the incidence gradually diverges. The first scenario reaches the 2015 incidence target exactly and is designated Scenario D2_{target}. We constructed the second one, Scenario D2_{over}, to model overachievement, bringing incidence all the way down to just 50% of the 2015 target (10 new cases per 100 000). Similarly, we constructed the third scenario, Scenario D2_{under}, to fall short of the target, only reducing the incidence rate down to 150% of the target (30 per 100 000). We assumed an identical incidence history for all three scenarios through 2007, and modelled the subsequent trends in new infections as linear progressions (see Fig. 5.4). We also assumed the same level of ART, as described in Table 5.3 above, for all three.

Fig. 5.4 Projection scenarios modelling the effects of achieving, surpassing and falling short of the 2015 national HIV incidence target for Estonia



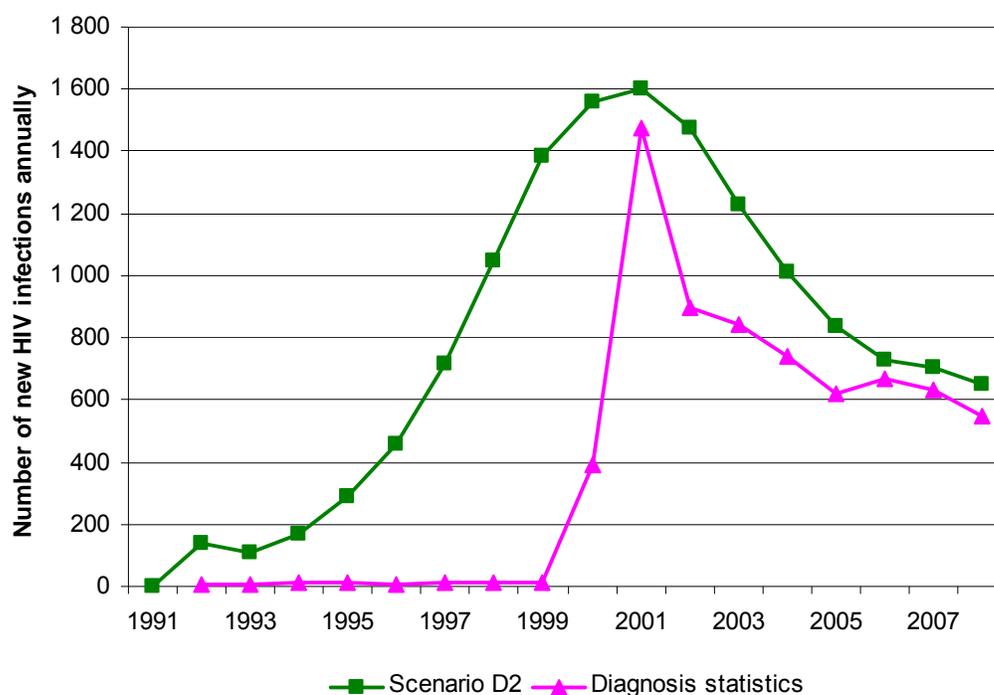
6. Results

6.1 Course of the HIV epidemic through 2008

New HIV cases

According to Scenario D2, our scenario with the best historical fit, the HIV epidemic in Estonia began in 1992 (Fig. 6.1). The annual number of new cases remained below 200 for several years, but around 1995 the number of new cases, according to this scenario, started to increase. HIV incidence reached its peak by the end of 2001 and has been decreasing ever since. The main differences between this modelled scenario and actual diagnosis statistics fall in the period 1994–2001, while the difference after 2004 is minimal (most likely indicating improved detection over time).

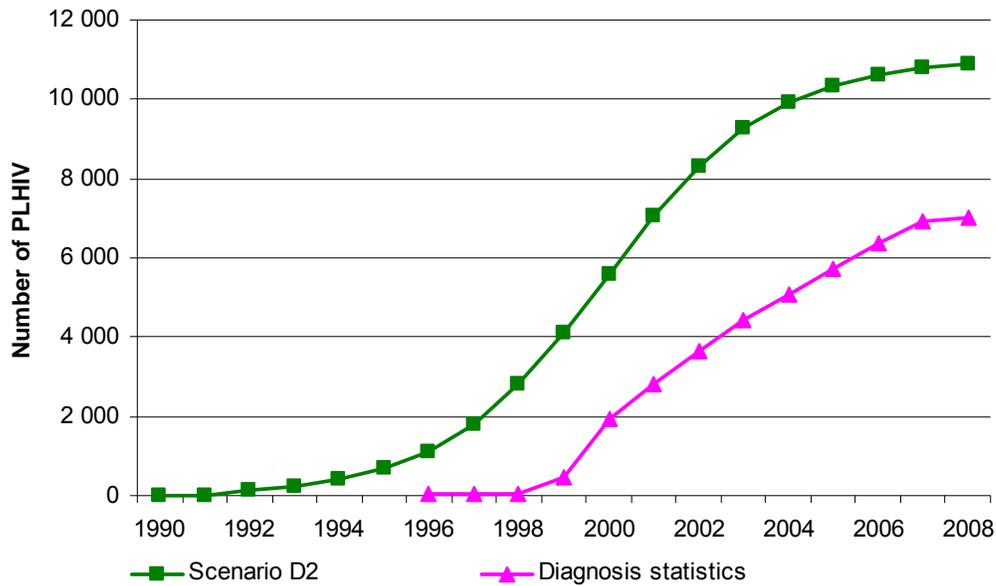
Fig. 6.1 Annual number of new HIV infections in Estonia, modelled vs. diagnosed



Total number of HIV cases

Based on the latest epidemiological data, there were approximately 11 000 PLHIV in Estonia in 2007. The number of registered HIV cases in Estonia was approximately 7000, which included people who had died from AIDS or other causes and a fraction of cases which were double-registered due to anonymous testing. Both the modelled scenario and case registration show similar rates of increase in the cumulative number of PLHIV, although the model shows almost twice as many (Fig. 6.2). It is worth noting that the size of these two curves would differ even more if HIV-related deaths were included in the modelled figures, as they were in the registration data.

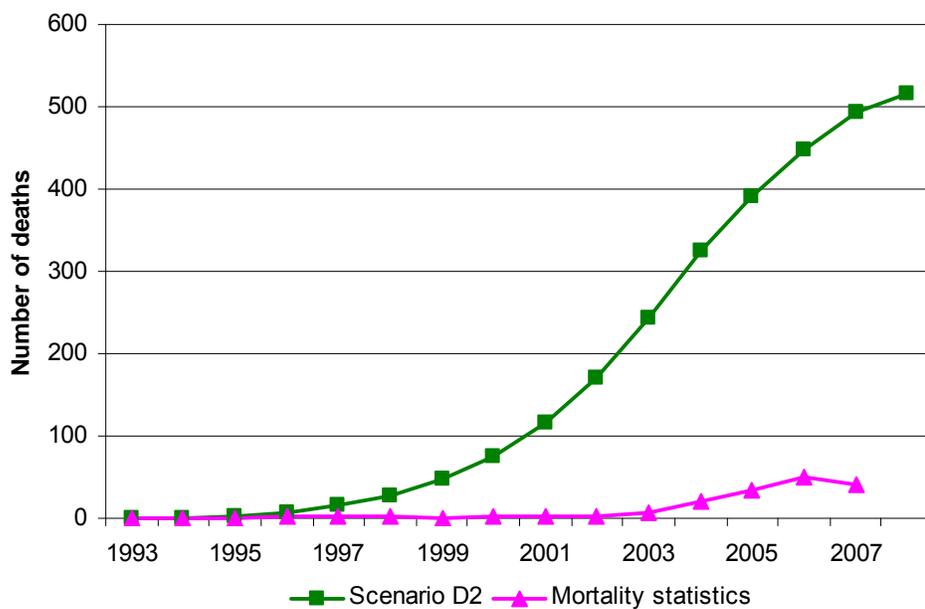
Fig. 6.2 Modelled number of PLHIV in Estonia vs. cumulative number of registered HIV cases



HIV-related deaths

Fig. 6.3 presents the number of HIV-related deaths, showing approximately 500 in 2007 in the modelled scenario. The registration data in Fig. 6.3 are drawn from mortality statistics from Statistics Estonia, and they indicate 49 deaths officially attributed to HIV in 2007 and 191 throughout the history of the epidemic.

Fig. 6.3 HIV-related deaths per year, modelled vs. registered

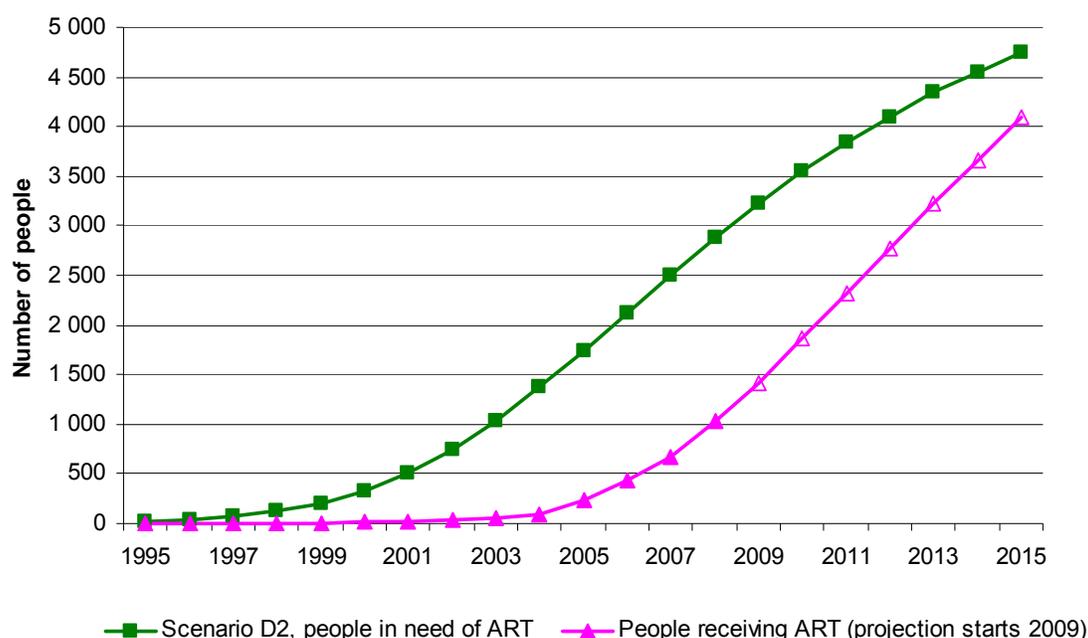


6.2 Projections of the HIV epidemic in Estonia

Treatment need

Scenario D2 predicts that approximately 3000 persons needed ART in 2008 and projects that this figure would increase to almost 5000 by 2015. According to this scenario, the first need for ART would have arisen in 1995, when approximately 10 people needed it. In reality, the number of Estonians on ART only reached 10 in 2001. Comparison of the modelled need and the actual provision of treatment indicates that approximately 30% of the need is being met. Our projections of current trends suggest that coverage will increase in the coming years. Ironically, this coverage improvement will be due chiefly to the rise in HIV-related deaths that will occur as a result of historically low ART coverage.

Fig. 6.4 Modelled need for first-line ART, compared to observed ART provision and linear projection of the most recent provision trend

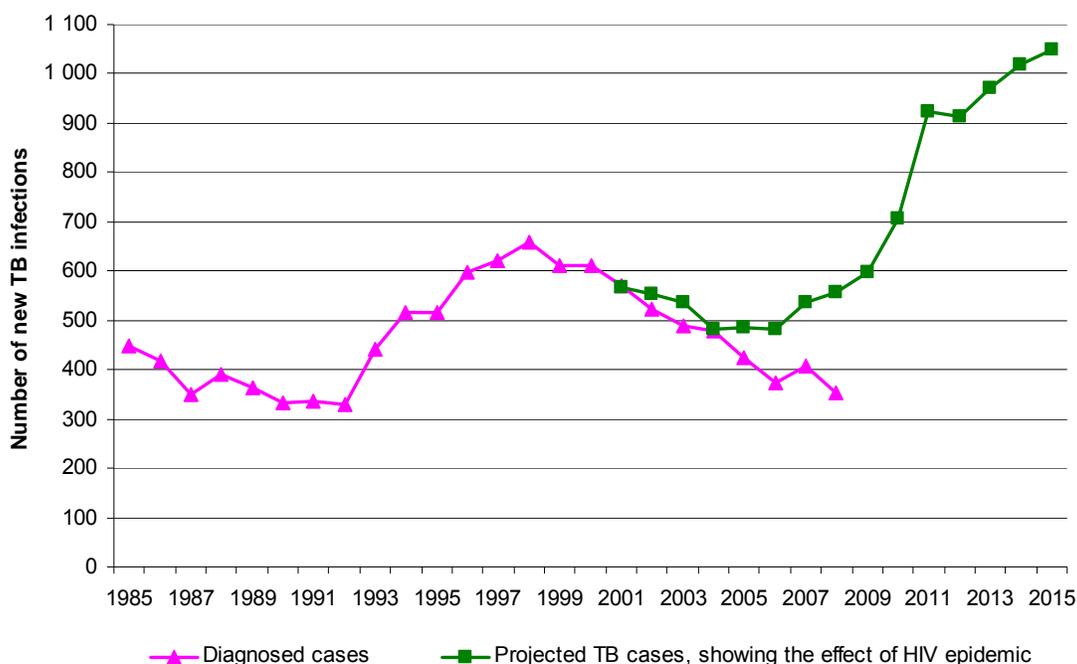


Impact of the HIV epidemic on TB

HIV infection also influences the incidence of other diseases due to its suppression of the body's immune response. There is abundant evidence that PLHIV are vulnerable to a variety of renal and rheumatological autoimmune diseases, while some cancers, such as Kaposi sarcoma, are almost exclusively linked to HIV. And there are of course a multitude of other infections that are usually suppressed by an intact immune system.

Fig. 6.5 presents the number of new TB cases diagnosed in Estonia over time, along with a modelled scenario of that shows the increasing effect of HIV on TB incidence in the coming years. We calculated this scenario using our historical HIV model, official TB notifications, ART coverage, the estimated size of the population with latent TB and the proportion of HIV coinfection among TB cases, and assuming a six-year lag between increased HIV incidence and increased TB incidence. According to this model, HIV began to affect the number of new TB cases in 2004. At present, there may be as many as 130–150 undetected new TB infections each year, and the total number of annual TB cases could reach 1000 in 2015 due to the spread of TB among PLHIV.

Fig. 6.5 Number of new TB diagnoses per year, compared to modelled number of new TB cases

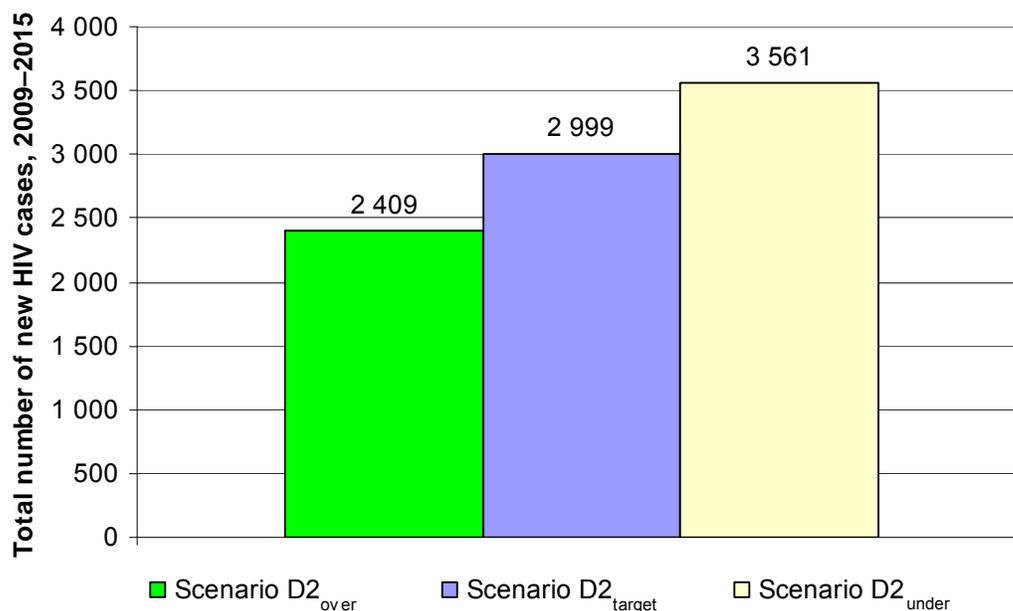


The impact of different incidence reductions

Estonia’s national HIV prevention strategy aims to reduce the number of new HIV cases diagnosed annually to 20 per 100 000 population by 2015. As mentioned above, our modelling shows that the number of new HIV infections will decrease to this target level in the natural course of the epidemic. The decline will be mostly due to high HIV saturation in Estonian risk groups, which leaves little room for major changes in incidence trends – so long as an explosive expansion into low-risk populations can be prevented.

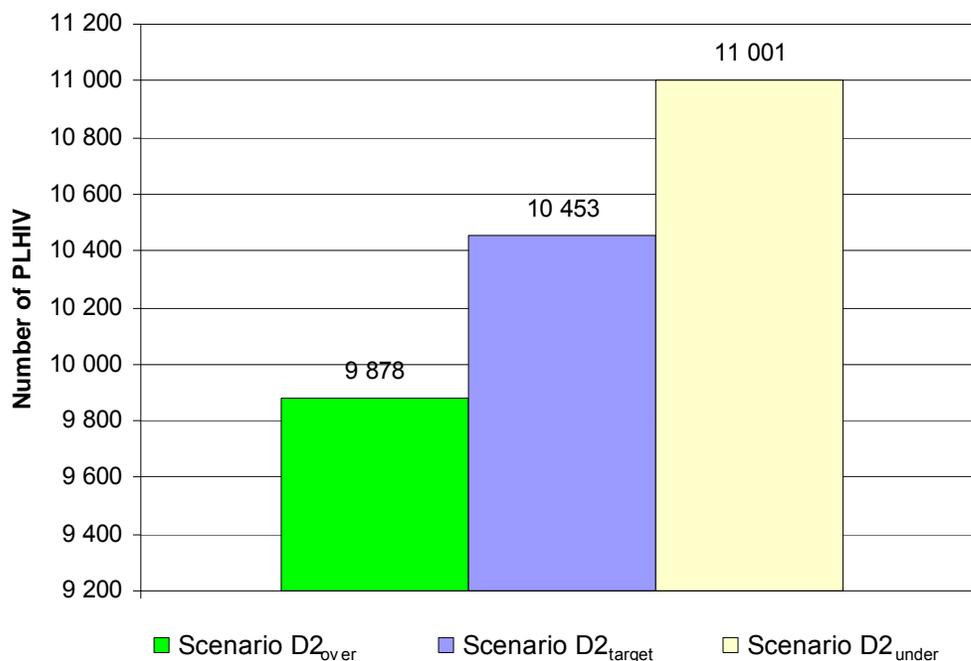
As described in Section 5.5, we constructed three scenarios to assess the impact of various reductions in HIV incidence during the strategy period. Meeting the incidence target would mean approximately 3000 new HIV cases in 2009–2015. Reducing the incidence only to 30 per 100 000 population in 2015 would translate to approximately 3600 new cases during the same period, while reducing the incidence to 10 per 100 000 would result in about 2400 new cases (see Fig. 6.6).

Fig. 6.6 Total number of new HIV cases in three incidence-reduction scenarios, 2009–2015



Reducing incidence to 30 per 100 000 would sustain the country's PLHIV population at its current level (Fig. 6.7), since HIV deaths would be balanced by new infections. In the two other scenarios, prevalence will drop due to HIV deaths that will increase if current trends of ART coverage hold.

Fig. 6.7 Projected size of PLHIV population in 2015



The successfulness of efforts to meet the incidence target will have very little effect on the number of HIV-related deaths in 2009–2015, since almost all such deaths in that period will stem from HIV infections acquired previously. On the other hand, increased ART coverage during the same period would have a profound effect on HIV mortality.

The actual levels of ART need in these years will also be mainly influenced by the incidence history of the previous seven years. The number of people who need ART is likely to increase to 5000 by 2015 if current trends in treatment coverage and HIV-related deaths continue.

6.3 Discussion of results

The previous sections present epidemiological data on HIV in Estonia from a modelled scenario. That particular scenario emerged from a long modelling process as one of the most likely representations of the national epidemic. However, we would like to emphasize that these results do not represent “the final truth”; rather, the scenario is merely one attempt to find a middle ground among the sometimes conflicting data that are currently available on HIV in Estonia. Moreover, the particular results are just a single snapshot in a long process of disease modelling, in which any new data incorporated into the knowledge base and the model would invariably produce different results. As such, the results presented in the previous sections should be regarded as illustrative, a tool for improving our understanding of the intricacies of HIV epidemiology and the Estonian epidemic.

Below, we discuss some possible explanations for and implications of the results, as well as indicating some areas for improvement in future epidemiological modelling of HIV.

HIV incidence and prevalence

Trends in HIV incidence and prevalence present intriguing epidemiological issues. Understanding these trends is critical for planning prevention, care and treatment services.

The last two historical scenarios we modelled in this study differed substantially with respect to incidence and prevalence over time. In Scenario D1 (“faster”), the epidemic spread of HIV started in the late 1990s and peaked around 2000–2001, resembling the official diagnosis statistics, albeit with significantly lower peak incidence in the latter (Fig. 5.3). This scenario is strongly supported by data from molecular epidemiological studies of people newly diagnosed with HIV in 2000–2002, which show the recentness of the epidemic’s origin (85).

A very rapid spread of HIV among risk groups has been witnessed in other parts of the world too. Several regions have experienced very rapid spread of HIV among IDUs, with prevalence of HIV rising to 40% or more extremely rapidly, sometimes within a half year of the virus’s introduction. Evidence suggests that, once HIV prevalence among IDUs reaches a level of about 10%–20%, HIV epidemics can become self-perpetuating, and even modest levels of risk behaviour lead to substantial rates of infection (86, 87). In Estonia, several studies have found that prevalence rates were already high (40%–60%) among IDUs in 2003–2004 (88). In 2005, a 54% prevalence rate was observed among 350 IDUs in Tallinn and a 90% rate among 100 IDUs in Kohtla-Järve (51). In 2007, a prevalence of 55% was found among Tallinn IDUs and a prevalence of 70% among Kohtla-Järve IDUs (45).

In Scenario D2 (“slower”), the epidemic spread started earlier, in the mid-1990s, and the incidence curve is flatter. Several arguments favour this scenario. The first HIV case in Estonia was diagnosed in 1988 (time of infection unknown), and the first AIDS death was registered in 1992 (a different person). Current evidence shows that on average, progression from infection to AIDS takes seven years without ART, and from there to death another three years (32). Progression from infection to death was likely faster than 10 years in the early days of the HIV epidemic (89). We can also argue about whether the infections diagnosed in Estonia in the late 1980s were the only ones, or whether the proportion of undiagnosed PLHIV was 30%–50% even then.

As this report clearly illustrates, modelled scenarios are approximations based on available data. As an example, data on the stage of the HIV infection at the time of diagnosis would facilitate the selection and development of accurate models. Unfortunately, the stage of the HIV infection is not ascertained in Estonia during the initial diagnosis. However, there is evidence from epidemiological research that despite the advances in antiretroviral treatment

and improved access to HIV-related health services, including HIV testing, a large proportion of newly diagnosed PLHIV are identified with symptomatic, often late-stage HIV infection. Existing evidence points to high rates of late diagnosis across Europe – approximately 15%–38% of all HIV cases present in later stages of infection (late presenters being usually defined as cases in which AIDS is diagnosed less than a year after HIV diagnosis) (90). According to Estonian data, 43% of AIDS cases diagnosed in 2001–2007 were late HIV diagnoses (*Kai Zilmer, personal communication, 16 April 2009*). Even though this epidemiological evidence suggests late diagnosis to be a persistent issue in Estonia, the data is not yet comprehensive enough to use for the systematic improvement of model accuracy..

HIV incidence started to decrease after 2001, when high-risk populations reached half-peak. It will probably decrease further, a prediction based on the assumption that public awareness of HIV is increasing in Estonia, as are the coverage and effectiveness of prevention interventions.

Another important subject to address is the possibility of a generalized epidemic, in which HIV would be firmly established in the general population. While risk groups may continue to contribute disproportionately to the spread of HIV, the network of sexual contacts in the general population is sufficient to sustain an epidemic independent of these groups (16).

For Estonia, the available data suggest that it is still in the concentrated epidemic phase. According to the Health Protection Inspectorate (12), the HIV prevalence among blood donors is less than 0.1% and among pregnant women less than 1%.

In a concentrated epidemic, HIV spreads rapidly in a defined subpopulation, suggesting active networks of risk. The future course of the epidemic is determined by the frequency and nature of links between highly infected subpopulations and the general population (16). Several studies have found that Estonian IDUs are sexually active with both injecting and non-injecting partners but use condoms infrequently (51, 54, 91). Their sexual partners who are not IDUs are thus at substantial risk for HIV infection. The documented high prevalence of HIV among IDUs, coupled with the high prevalence of injecting drug use reported in Estonia (2.4% of the adult population) (52) may lead to a substantial and self-sustaining epidemic in this “bridge population” of IDU partners (14).

Whether a bridge epidemic will spread to the general heterosexual population is arguable. Outside sub-Saharan Africa, most epidemics are either low-level or concentrated, being predominantly associated with high levels of risk behaviour in specific groups. In almost every case, the members of these groups are exposed to HIV through unprotected sex or exposure to contaminated injecting equipment (16). In sub-Saharan Africa, the sexual spread of HIV is believed to be facilitated by a broad combination of biological, behavioural, cultural, socioeconomic, structural and other factors. Although the data are limited, they suggest that the potential for concurrent sexual relationships to accelerate HIV transmission is especially pronounced where there is high background prevalence or high population mobility. Both factors are common in southern Africa, where concurrent relationships have been cited as a potential reason for the region’s uniquely high levels of HIV infection (16).

According to several studies over the years, unsafe sexual behaviour is widespread in the Estonian population. The level of concurrency, which is considered a critical factor in the transmission of HIV and other STIs, is not known, however. Research in this area is needed in order to better estimate the risk of HIV spreading heterosexually in the general population, and to plan and provide appropriate interventions.

Coinfections and opportunistic infections

Coinfection with one or more forms of viral hepatitis is common among PLHIV in many regions of the world. HCV prevalence rates among IDUs as high as 92% have been observed in eastern Europe (92). Studies in the United States suggest that 50%–90% of HIV-positive IDUs are also infected with hepatitis C virus (HCV) (93). The HCV coinfection rate among HIV-infected IDUs in Estonia is also high – in the most recent survey, all HIV-infected IDUs in Tallinn and close to 99% in Kohtla-Järve tested positive for HCV-antibodies (45).

Approximately 80% of the people infected with HCV become chronic carriers, and HCV is readily transmitted through sharing of injection equipment. For the minority of infected persons who develop severe disease, the estimated period from initial HCV infection to the development of end-stage liver disease is 20–30 years (86). HIV infection significantly increases the risk of death from liver disease in individuals infected with HCV (94). Although it is possible to achieve excellent clinical outcomes for individuals coinfecting with HIV and HCV, simultaneous medical management of both conditions can be complex due to potential drug interactions and toxicities (95).

Coinfection with HIV and the hepatitis B virus (HBV) similarly exacerbates both conditions. Coinfected adults progress to chronic HBV infection five times faster than adults who have HBV but not HIV. And PLHIV with HBV often have difficulty tolerating antiretroviral drugs (96).

In settings where antiretroviral drugs have been in widespread use since the mid-1990s, treatment has radically altered the natural course of HIV infection, inadvertently expanding the spectrum of health problems PLHIV present with and altering their most common causes of death (97). In particular, chronic illnesses and comorbidities cause an increasingly large percentage of deaths among PLHIV in places where antiretroviral drugs have been used extensively for more than a decade. Between 1995 and 2006, the percentage of non-HIV-related deaths among PLHIV in New York City increased from 8% to 32%, with cardiovascular conditions and non-AIDS-defining cancers accounting for nearly half of such deaths. In Norway, although the risk of HIV-related death has declined 80% with the advent of combination therapy, the mortality rate for individuals living with HIV is still four times higher than for the general population (16).

As people living with HIV live longer due to increased access to antiretroviral drugs, evidence indicates that the range and prevalence of HIV-related opportunistic infections changes. For instance, three types of cancer that occur in HIV-positive individuals – Kaposi sarcoma, non-Hodgkin lymphoma and invasive cervical cancer – are currently included in the clinical definition of AIDS. However, in high-income countries where antiretrovirals have been widely available since the mid-1990s, other cancers have also become increasingly significant complications of HIV infection (16), particularly Hodgkin lymphoma and cancers of the anus, lung and liver (98).

In Italy, to take a specific example, the incidence ratio for Kaposi sarcoma and non-Hodgkin lymphoma among PLHIV fell considerably between the 1986–1996 period and the 1997–2004 period, yet a high incidence of Kaposi sarcoma persisted in the increasingly large fraction of PLHIV who were late presenters. A significant excess of liver cancer also emerged among Italian PLHIV in 1997–2004, whereas the incidence of cervical, anal, pulmonary, brain and skin (non-melanoma) cancers, as well as Hodgkin lymphoma, myeloma and other non-AIDS-defining cancers, were similarly elevated in both periods. The excess incidence of liver cancer among the PLHIV was linked to their high prevalence rates of HBV and, more notably, HCV (99).

Nonetheless, TB remains the most common opportunistic infection among PLHIV, whether or not they are on ART, and a leading cause of death for PLHIV in low- and middle-income countries (16). Potential drug–drug interactions, as well as the difficulty of adhering to multiple treatment regimens, can complicate the simultaneous treatment of TB and HIV. Among TB patients, PLHIV have also been shown to be twice as likely as HIV-negative people to be infected with multidrug-resistant TB (100).

HIV-related deaths and treatment needs

Knowing when the HIV epidemic began to spread is crucial because it helps determine subsequent prevalence and HIV-related mortality. So far the number of officially registered HIV-related deaths remains very low in Estonia – a cumulative total of only 191 through the end of 2007 – despite the low ART coverage. Our modelling, however, suggests that in the year 2007 alone there were about 500 HIV-related deaths in country (see Fig. 6.3 above).

The low official HIV mortality rate may be partly attributed to poor registration of deaths and causes of death among PLHIV. HIV-infected people may die due to many causes besides HIV-related illnesses, of course, including reasons related to HIV risk behaviours. For example, in 2005–2006 an exceptional epidemic of overdoses with 3-methylfentanyl, a highly potent opioid designer drug, occurred among Estonian drug users (101). Yet these factors do not fully explain the major differences we found in the registered versus modelled death rates. One possible reason could be a slower spread of HIV, such as seen in Scenario D1, in which case the number of AIDS-related deaths to date would be lower than shown by Scenario D2. Another reason for the very large discrepancy is that the Estonian authorities register deaths as HIV-related only when HIV is the main cause of death, while our model assumes that every PLHIV death is counted as HIV-related death, regardless of the main cause of death.

However important such factors may be, the potential misclassification of HIV-related deaths still warrants discussion and attention from the authorities. It is possible that some HIV-related deaths are wrongly coded as being due to external causes, cardiovascular causes, etc. On the other hand, it could also be the case that faster disease progression without ART in the early days of the epidemic actually resulted in a higher number of HIV-related deaths than shown in the model, which does not address this likelihood.

A final factor that may contribute to the difference between the modelled and registered number of HIV deaths is the possibility that the actual survival of HIV-infected persons in Estonia is longer than 10 years, the model default. Some studies have shown that people who are coinfecting with HIV subtype 1 (HIV-1) and GB virus C (GBV-C) may have better AIDS-free survival rates and higher CD4 counts than those who are infected only with HIV-1. Limited research in Estonia shows that GBV-C infection was detected in 33 of 95 (35%) subjects, all with genotype 2. GBV-C infection was associated with injecting drug use, as 41% of the past or current IDUs in the study had the virus, versus 33% of the non-IDUs (102).

If actual survival is longer than 10 years, the number of HIV-related deaths in the model should be lower, and as a result the HIV incidence required to achieve the prevalence level indicated by epidemiological studies would decrease. In turn, the lower incidence rate would reduce the time of infection spread, or the difference in peak incidence between modelled and registered cases. An increase in the modelled survival time would also postpone ART need and would thus reduce the number of people estimated as needing ART today. We are considering constructing and comparing scenarios based on different survival rates for future models if more data emerge.

Regardless of such possible contributing factors, the main reason for the large number of HIV-related deaths in the model remains the HIV detection gap. A high proportion of PLHIV have avoided HIV testing, which means they were unable to receive ART or other HIV services. The large treatment gap translates in turn to a high number of HIV-related deaths. But even though the detection gap explains much of the low ART coverage, it does not fully explain why more than 60% of the people who need ART do not receive it. The most likely of the other reasons for the ART gap relate to treatment access, such as geographically inconvenient treatment provision, poor integration of treatment services, a scarcity of treatment resources and problems with adherence.

One example of such access barriers is the fact that, unlike TB patients, HIV patients in Estonia must pay visitation fees in order to access specialist care (or at least they must in theory) (103). On the other hand, Estonians on ART have quite high adherence rates compared to some other countries (*Kai Zilmer, personal communication, 16 April 2009*), since to qualify most of them have had to navigate the referral system and have already proven themselves by adhering to methadone substitution treatment. Yet these same requirements can themselves be barriers to access.

For the individual, the immediate effects of ART include dramatic improvement in health, quality of life and life expectancy. From a public health point of view, however, its most important outcome lies in reducing the infectiousness of PLHIV by reducing their viral load.

High ART coverage has thus become an essential tool in containing an HIV epidemic and preventing it from becoming generalized.

ART coverage is also a key factor in addressing the spread and severity of TB, which HIV contributes to. As Fig. 6.5 illustrates, after years of decline, the TB incidence rate rose again in 2007, a likely result of the HIV epidemic. Although TB incidence again fell in 2008, the proportion of PLHIV among TB patients has exceeded 10% in last couple years. Moreover, according to data from the Estonian TB registry, TB cases are much more severe when HIV coinfection is present. Fortunately, ART can diminish the severity of TB among PLHIV.

National HIV strategy

WHO and UNAIDS suggest that the modelling tools we employed in this report not be used to make projections longer than five years into the future. Nevertheless, we chose to project seven years forward in order to utilize the main target in the Estonian national HIV strategy as a reference point.

This target involves reducing HIV incidence by 2015. In fact, given the seven-year time lag between HIV infection and typical need for ART, it seems possible to assess the effects of meeting this target only 7–10 years *after* the 2015 target date. As shown in Fig. 6.6, the consequences of failing to meet this target, even by 50%, would be relatively minor during 2009–2015 in comparison to the size of Estonia’s PLHIV population, but the effects of such failure would become more substantial after 2015.

While achieving the national strategy’s main target seems quite likely, our model suggests that the large gap in ART coverage is a much greater cause for concern. This treatment gap poses probably the greatest danger to HIV containment, threatening to let the disease spread to the general population. Substantial scaling up of ART coverage thus seems pertinent.

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