Needle-syringe programs are cost-effective in Eastern Europe and Central Asia: data synthesis, modeling, and economics for nine case-study countries

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Abstract

Background: HIV and hepatitis C virus (HCV) are highly prevalent among people who inject drugs (PWID) in Eastern Europe and Central Asia (EECA). This study assessed the cost-effectiveness of needle-syringe programs (NSPs) in this region.

Methods: A comprehensive data collection process was conducted across nine countries in EECA. This informed a mathematical transmission model and health economic analysis. Epidemiological outcomes and costs of NSP coverage were compared with scenarios of no NSPs. For the latter, counterfactual receptive sharing rates were determined by an empirical relationship with syringe availability in each country. Outcomes included numbers of HIV and HCV infections averted, health sector costs, and cost per QALY gained.

Results: Across all countries, financial investments in NSPs increased substantially during 2005-2010. The average number of needle-syringes distributed and proportion of PWID reached increased by over 300%. Reported levels of receptive sharing decreased with increases in per capita distributions of needle-syringes. NSPs were estimated to avert 10-45% of HIV infections; a lower percentage of HCV infections were averted (4-40%). Compared with the WHO-CHOICE willingness-to-pay thresholds, NSPs were found to already be cost-saving or cost-effective with respect to HIV alone in the short-term in seven of the nine countries, borderline cost-effective in one country, but not yet cost-effective in one country. When considering the additional benefits of averted HCV infections, or the lifetime benefits of HIV infections averted, NSPs were very cost-effective to cost-saving in all countries, with median return on investment of 2.1-3.8 times the original investments (with 3% discounting).

Conclusions: NSPs have been effective in reducing risk, leading to reduced incidence of HIV and HCV among PWID, and are a very cost-effective prevention strategy in EECA.

Background

By the time the Berlin Wall fell, HIV had barely affected Eastern Europe and Central Asia (EECA). Now, however, EECA is the only region where HIV prevalence is clearly increasing – by 250% over the past decade [1-4]. Sharing of injecting equipment by people who inject drugs (PWID) is the main mode of HIV transmission in EECA [3]; it is also the dominant mode of transmission of the hepatitis C virus (HCV) [5-10]. HIV prevalence among PWID is high and has exceeded 60% in subnational samples. In 24 countries, more than 20% of all people living with HIV are PWID; of these, 14 are located in EECA [1, 4]. Among PWID, HCV has become the leading cause of death of people living with HIV in Europe [11]. In EECA, the prevalence levels of HIV/HCV co-infection are very high with the majority of people living with HIV also living with HCV [12, 13].

To reverse epidemics of blood-borne viral infections, particularly in a global environment of decreasing HIV/AIDS financial commitments, it is important to identify the most cost-effective interventions. Cost-effectiveness studies evaluate what HIV investments have bought, whether the interventions averted new infections and AIDS deaths, and at what cost. These studies can be used to support decision-making and prioritization of targeted intervention strategies to minimize the burden of disease.

Needle-syringe programs (NSPs) are public health measures designed to reduce the spread of blood-borne infections among PWID through the distribution of sterile injecting equipment. Although there are large differences in HIV epidemics among different PWID populations [5, 6, 14], NSPs have been shown to be safe and effective in reducing HIV transmission in diverse settings [15-20]. Ecological studies suggest that where NSPs are not easily accessible, HIV prevalence tends to be substantially greater than in locations where NSPs are available [1, 19, 21-29]. In contrast to HIV infection, prevalence of HCV among PWID is generally high in all locations regardless of the existence of NSPs, due to its much higher transmissibility via injecting drug use [6, 30]. In this study, we aimed to evaluate NSPs in EECA through (1) development of an HIV/HCV epidemic transmission model that can be applied to any setting when parameterized with local data; (2) development of graphical software as a front-end to the model for modifying key assumptions, model calibration, exploration of epidemiological and economic impacts of NSPs; (3) a regional workshop with data custodians and other experts, emphasizing surveillance, data interpretation, impact evaluation, and health economics; (4) triangulation of country-specific data, including epidemiology, behavior, intervention costs and coverage, and healthcare costs; (5) interpretation of data, arriving at data-informed assumptions and counterfactual scenarios through consensus with country representatives and independent investigators; and (6) analysis of epidemiological and economic outcomes as a regional consortium. Nine countries were evaluated in this study: Armenia, Belarus, Estonia, Georgia, Kazakhstan, Moldova, Tajikistan, Ukraine and Russia; two oblasts within Russia were chosen as separate subnational studies rather than national analyses like the other countries.

Methods

Mathematical transmission model

A mathematical model was developed to describe HIV and HCV transmission among a population of current and former PWID, to track the numbers of people in each HIV or HCV health state associated with the natural history of infection, and to analyze the resulting healthcare costs. Full details of the model are provided in the Supplementary Material. Briefly, the population model consists of a number of compartments defined by infection, diagnosis, disease progression (in terms of CD4 categories for HIV and stages of fibrosis for HCV), and treatment states, as shown in Supplementary Material Figure S1.

One ordinary differential equation (ODE) was used to describe the change in the number of people in each of these compartmental health states over time, for 43 ODEs in total (Figure S1). The rate of change in the numbers of people in each compartment depends on the net effect of rates of people entering the health state and the rate of leaving the health state [31], including rates of initiation of injecting and leaving the population (background death/migration/cessation of injecting, drug-related death, health state-specific death). For example, the ODE representing the rate of change in the number of people uninfected with HIV is

$$\underbrace{\frac{dS}{dt}}_{\substack{\text{Change in} \\ \text{uninfecteds}}} = \underbrace{\pi}_{\substack{\text{Entry into} \\ \text{population}}} - \left(\underbrace{\lambda}_{\substack{\text{Force of} \\ \text{HIV infection}}} + \underbrace{\mu}_{\substack{\text{Background} \\ \text{death}}} + \underbrace{\mu_D}_{\substack{\text{Drug-related} \\ \text{death}}} \right) S$$

where S is the number of uninfected active PWID, π is the annual number of people who commence injecting drugs, μ is the mortality rate among general population, μ_D is the drug-related death rate, and λ is the "force of infection" or per-capita rate at which susceptible PWID acquire infection.

The force of infection is dependent on other health states (namely, numbers of people in the infected health states). To calculate the force of infection, we assume that each PWID injects an average of n times per year and denote the receptive syringe sharing rate (RSS) as s, and the prevalence in the population as *P(t)*. The probability of infection from a contaminated syringe per use is denoted by β. We assume that syringe cleaning has effectiveness ε_c and cleaning occurs in p_c proportion of shared injections. Given these definitions, the force of infections is given mathematically by:

$$\lambda = (1 - (1 - (1 - p_c \varepsilon_c)\beta)^{ns})P(t).$$

The rates of transition between compartments are defined by parameters based on available empirical data (see Supplementary Material). These include biological parameters (HIV and HCV transmission probabilities, HIV- and HCV-related death rates, and treatment effectiveness) and behavioral parameters (number of injections per year, fraction of PWID who receptively share syringes, and needle-syringe cleaning rates) (Table S4, 9,10).

The model is calibrated to the data provided using a mixture of optimization and force-fitting. The model is force-fitted to population size, HIV diagnoses, AIDS diagnoses, and number of

people on HIV/HCV treatment. This method modifies the behavioral parameters to ensure that the model matches thegiven epidemiological data. The model then employs a trust-region-reflective algorithm on the biological model parameters (e.g., disease progression rates) to obtain the best fit to prevalence data. The model estimates the change in the number of PWID in each compartment due to disease progression, treatment initiation, death, and incidence of infection. Expected numbers of new HIV and HCV infections were calculated based on risk behavior probabilities, as described in the Supplementary Material.

Accompanying software

A graphical software package was designed as a front-end to the model. The Needle-Exchange Program Evaluation Model (NEPEM) is open-source and freely available for download at: http://www.natcent.unsw.edu.au/sepph/software.html. In addition, a brief description of this software is provided in the Supplementary Material.

Data collection

An extensive data collection procedure was conducted in each country to parameterize the model. Data inputs included demographics (PWID population sizes), epidemiology (HIV and HCV prevalence, HIV and AIDS diagnoses, testing rates), treatment (numbers of current/former PWID on first- and subsequent-lines of antiretroviral therapy [ART], HCV treatment, and number of HCV-related liver transplants), behavior (frequency of injection, percentage of PWID who receptively share syringes and proportion of their injecting episodes in which they share, syringe cleaning rates), intervention (numbers of needle-syringes distributed, estimated proportion of PWID who access the NSPs), cost of the programs (cost of commodities, distribution, disposal, infrastructural development, personnel, maintenance and other service costs), and healthcare costs for each health state (for the health sector, not including patient costs or productivity losses/gains). All inputs were obtained from different data custodians in the selected countries in collaboration with representatives from government health departments, HIV/AIDS organizations and research institutions. Where data were missing, plausible ranges of values were obtained by combining published estimates from other countries with in-country expert opinion. However, survey methods, sampling frameworks and national/sub-national samples differ between countries and sometimes within countries. Surveillance methods have improved over time in the region but are still less than ideal. To partially ameliorate this limitation, the consortium group went through a rigorous process of in-country data collation and then discussion at a regional level with critical examination of methods and interpretation of data among international experts and local data custodians and national representatives. Thus, while there were some unavoidable data gaps, the model was calibrated using the best data and assumptions available in each setting.

Estimating impact and defining counterfactual scenarios

This study was not able to evaluate the impact of NSPs directly through empirical data collected for evaluation purposes. Incidence data were not available and there were no control groups within groups for direct comparison of changes in prevalence and behavior compared to the intervention group.

To estimate the effect of NSPs, we conducted a theoretical evaluation, informed by all available data, which compared observed conditions with a counterfactual scenario. The counterfactual was based on exposure-response trends in empirical data in each country (i.e., an assumed logistic relationship between sharing rate and needle-syringes received per person-year). Previous studies have concluded that the existence or degree of implementation of NSPs has no effect on the number of PWID or the frequency at which they inject [32-35]. Instead, NSPs aim to reduce the rate of receptive syringe sharing (RSS) among PWID. We assumed the relationship followed a logistic saturation curve defined by four parameters:(initial value, final value, mid-point location, and smoothness. This choice of logistic curve provides a sufficient degree of freedom for curve fitting yet does not over-fit the available data. Therefore, we examined the relationship between needle-syringe distribution and rates of RSS (Figure 1, second column) and used it to interpolate and/or extrapolate the levels of RSS without NSPs. If NSPs did not exist, there may also be increases in purchasing of needle-syringes from other sources. Discussions with stakeholders in each country led to assumptions that most countries would expect only a small increase in purchasing (offsetting ~5% NSP-distributed syringes), but up to 50% in other countries. Therefore, we (conservatively) assumed that in the absence of NSPs, needle-syringe purchasing would compensate for 5-50% of NSP distribution, and that levels of RSS would then be determined by the country-specific relationship between RSS and total needle-syringe availability (Figure 1). We assumed that, in the absence of NSPs, all other conditions would remain unchanged.

We also used the model to estimate expected prevalence levels with pre-NSP syringe sharing behaviors and ascertain whether observed prevalence levels among PWID were plausible without NSPs. We examined these outcomes with and without ART programs (see Supplementary Material).

Model calibration

The model was calibrated to reflect the HIV and HCV epidemics over the period 2000-2010, although most countries only had data from 2005-2010. A trust-region-reflective optimization algorithm [36] was used to find the optimal set of parameter values that match observed conditions (HIV and HCV prevalence, diagnoses, and treatment) in the given setting (within predefined confidence intervals or plausible bounds of parameter values).

Uncertainty analyses

To calculate uncertainty limits on the results, parameters were sampled uniformly over a set of plausible ranges (based on empirical data; ranges are given in Tables S9 and S10 of the Supplementary Material), as determined by using a Latin hypercube algorithm [37, 38] to produce 40 new sets of parameters. The model was then run with each of these parameter

sets. Uncertainty estimates (e.g., those in Figure 3 and Table 1) correspond to the interquartile range of these parameter sets. Subsets of the analyses were run with up to 1000 samples, but there was no significant difference between the results obtained using 1000 samples and those obtained using 40, so the smaller number was used for the full analyses for reasons of computational expediency. The uncertainty in the model is dominated by uncertainty in the RSS, which in turn is dominated by the extent to which needle-syringe purchasing would compensate for lower NSP distribution. This is due to both the sensitivity of the model to the RSS, and the very large uncertainty range for the extent of this compensation (5-50%).

Economic evaluations

Economic analysis was carried out to estimate the cost-effectiveness of NSPs from a health sector perspective. Cost data were sourced directly from the principal recipients and sub-recipients from donors for each country (see Supplementary Material). Patient and family healthcare costs were not included in final analyses. All costs data were presented in 2010 US dollars. Costs were discounted by an annual rate of 3%.

QALYs and healthcare costs for various scenarios were estimated using standard methods from model outputs and health state utilities [39-41]. Incremental cost-effectiveness ratios were calculated and analyses were performed for two time frames: 2000-2010 to study the return obtained over the period of investment, and 2010-2100 to examine lifetime costs and consequences for the population related to investments over the period 2000-2010.

Results

There was a large increase in the number of needle-syringes distributed across all eight countries from 2005 to- 2010; the average annual number of needle-syringes distributed ranged from 73,000 in Armenia to 21,000,000 in Kazakhstan, with an average increase in the six-year period across all countries of more than 300% (Figure 1, first column). Countries also reported increased coverage in the proportion of PWID accessing NSPs, with Ukraine reporting the most significant increase: 12% in 2005 to 59% in 2010; the average increase across all countries was a factor of three. Estonia reported the greatest coverage, reaching 80% in 2010. Armenia and Georgia reported the lowest coverage, with only 10% of the PWID population reached by NSPs in 2010 (which nonetheless represents an increase from 2005 levels). Armenia had the lowest average number of needle-syringes distributed per PWID per year (88 units for those accessing NSPs and 9 units when averaging across all PWID). The greatest distribution was reported by Estonia (135 units per PWID for those accessing NSPs and 108 units when averaging across all PWID). Across all countries, an average of 92 needle-syringes was distributed annually for each PWID accessing NSPs; for all PWID, it was 47.

All countries reported substantially increasing financial investments in NSPs, with the total cost of the programs scaling close to linearly with the distribution of commodities (Figure 1, first column). There was large variation in unit costs in 2005 but were below $0.50 per

needle-syringe distributed in all countries by 2010 with an average cost of $0.32 (Figure 2a). Three countries - Belarus, Moldova and Tajikistan - provided breakdown of costs for NSPs. Across these countries, commodities accounted for 28% of all NSP costs; personnel costs 54%; needle-syringe disposal 3%; maintenance 6%; other costs 9% (Figure 2b). The unit cost of needle-syringe distribution declined with increasing coverage.

The reported level of RSS decreased with increases in the per capita distribution of needle-syringes for all eight countries (Figure 1, second column). The most data were available for Ukraine, where the relationship between NSP scale-up and sharing levels is pronounced, with sharing levels at ~35% prior to the commencement of NSPs and then declining steadily, to ~10%, as the programs scaled up. Other countries also had significant declines in RSS. In no country were there stable or increasing sharing levels.

HIV prevalence levels (Figure 2; third column) have generally been stable but decreased in two countries (Moldova and Ukraine), with no country indicating increasing HIV prevalence. We found that without NSP-associated changes in RSS rates, it was still possible to reproduce trajectories that matched the data due to uncertainty in behavioral and biological parameter estimates; however, the primary effect of ART programs in reducing mortality may have increased prevalence but the extent is likely to be small. It is also estimated that 0.2-2.5% of PWID was on ART in 2010, indicating the preventive effects of ART were small compared with NSPs.

The model, with data-informed counterfactual assumptions, estimated that NSPs have averted significant numbers of HIV and HCV infections in most countries (Table 1). NSPs were estimated to have averted approximately10-45% of HIV infections across the nine countries. The greatest effect was in Russia (42-61%), with the least in Ukraine (8-17%). Compared to HIV, a lower percentage of HCV infections were averted (4-20% for five countries and Russian Lipetsk oblast, ~20-30% for Kazakhstan and Tajikistan, and ~30-40% for Belarus and Russian Kursk oblast, respectively) (Table 1).

There were diverse outcomes in cost-effectiveness across the countries (after standardizing by WHO-CHOICE thresholds [42]). NSPs over the past 5-10 years have already been found to be very cost-effective with respect to HIV alone in six of the countries (Armenia, Belarus, Estonia, Kazakhstan, Ukraine and Russian Lipetsk province); it has been cost-effective in Moldova and Russian Kursk province and borderline cost-effective in Tajikistan, but not yet cost-effective in Georgia (Table 1; Figure 3). Armenia had saved approximately the same health costs as the amount of money invested in NSPs. When considering the health benefits of averted HCV infections as well as HIV, NSPs were cost-effective (Tajikistan) or very cost-effective (Armenia, Belarus, Estonia, Georgia, Kazakhstan, Moldova, Ukraine and Russia) (Table 1; Figure 3).

Infections averted during past program implementation will lead to future benefits of further gains in QALYs and health costs saved. The lifetime benefits of HIV infections averted (with 3% discounting) ranged from very cost-effective (Estonia, Kazakhstan, Tajikistan) to cost-saving (Armenia, Belarus, Georgia, Moldova, Ukraine and Russia)(Table 1; Figure 3). In all countries, modeled scenarios projecting increased program coverage estimated even greater gains in cost-effectiveness.

Discussion

Our study was a theoretical evaluation of the population impact of NSPs in EECA, informed primarily by self-reported RSS and calibrated using other relevant data. If the assumptions underpinning the model are valid, specifically the RSS levels in the PWID population and their modeled association with incidence, then this study suggests that NSPs in EECA may have led to significant health benefits and economic savings. Based on our model estimates, across the countries, the programs ranged from breaking even to not yet cost-effective with respect to the HIV benefits already obtained according to our analyses and assumptions informed by self-reported RSS. When benefits associated with both HIV and HCV are included, NSPs were found to be cost-effective to cost-saving in every country. It is important to note that we compared outcomes with the WHO-CHOICE thresholds for cost-effectiveness; willingness-to-pay thresholds of governments or other donors may be more conservative. However, when lifetime benefits are also considered, NSPs are always either very cost-effective or cost-saving.

Other evaluations in the region support the conclusions presented here. Vickerman et al. previously conducted an evaluation of NSPs in Odessa, Ukraine and determined that the early stage of their implementation was cost-effective at $97 per infection averted [16]. Alistar et al. also evaluated harm reduction programs in Ukraine and found that methadone maintenance therapy is highly cost-effective and should be combined with a strategy that includes ART [43].

Coverage of HIV prevention, treatment, and other services for PWID populations is low, with a recent review suggesting that only 10% of PWID in Eastern Europe and 36% in Central Asia access NSPs, with an average of nine and 92 needle-syringes distributed per PWID per year, respectively [44]. The evidence presented here suggests that NSPs could be further expanded, as saturation is currently far from being reached, and increases in NSP coverage can be cost-effective in the short-term and cost-saving in the long-term. If NSPs were scaled down, our study indicated that there would be resurgences in HIV and HCV incidence among PWID (results not shown). This is supported by external evidence; for example, recently in Canada RSS increased from 10% to 23% following the closure of the only fixed NSP in the city of Victoria, but there was no change in RSS in Vancouver where NSPs remained [45].

Costs of NSPs in EECA are relatively low. There are also economies of scale as programs mature and increase in coverage [46, 47]. Increasing coverage may require expanding infrastructure, capacity, and outreach services. Scale efficiency could be achieved by increasing delivery systems with low fixed operation costs, through drop-in centers and other innovative approaches [48]. Reductions in unit costs can further improve the cost-effectiveness of NSPs, in particular when these are implemented in an overall comprehensive and evidence-informed manner [49]. A previous modeling study has shown that when the incidence of HIV among people who inject drugs is high, such as in many of the countries in EECA, the impact of NSPs is reduced unless their efficacy is optimized, including combining with other evidence-informed, rights-based combination interventions (particularly access to opioid substitution therapy and antiretroviral therapy) [50].

It is important to emphasize that this study is based on model projections and thus the results presented here are unavoidably theoretical. The conclusions of this study are valid if and only if the assumptions behind the model and projections hold. While the assumptions of this analysis were based on the best available data, in some cases the data quality was still poor. Consequently, this study has five major limitations.

First, the most crucial component of our analysis was the assumption that in the absence of NSPs, all factors would remain unchanged except for RSS. It is possible that other factors influenced RSS that are not taken into account in our analysis. In addition, RSS was self-reported and is subject to sampling bias and social desirability bias which may change over time. The large uncertainty in RSS is the primary driver of the considerable uncertainty in our final results (e.g., 4-40% of HCV infections averted). Unfortunately, due to the nonexistence of more reliable data, it is not possible to estimate these results more precisely.

Second, while the model was calibrated against all available data, the optimization procedure did not completely reconcile the diverse data sources. There are heterogeneities in behaviors among PWID, and many individual-level differences could not be captured in this population-based model. Our analysis included ranges of values for population averages. Assumptions of homogeneity may have considerable limitations because the spread of infection may be particularly concentrated among groups of PWID including those within certain mixing networks, geographical locations, demographic subpopulations, behavioral groups and/or groups with particular degrees of access to NSPs and other services. It would not be valid to assume that the same risk of infection and overall reduction in risk due to NSPs applies to every PWID in the population, especially if there is very large heterogeneity. The non-independence of behavioral data, which was included in our model, may likely to lead to bias and increased uncertainties in our results. Assumptions of population rates are often used in modeling evaluations to obtain first-order estimates. Our study did not model the co-infection of both HIV and HCV among some individuals. The effect of HCV on the natural history of HIV is not conclusive whereas HIV leads to more rapid progression of HCV-related liver disease [51]. Exclusion of co-infection may lead to under-estimates of morbidity and mortality for analyses of mono-infections [50]. The absence of incidence data prevents a more accurate calibration of the model to infer the transmission of infections.

Third, we were also unable to quantify uncertainty in the model structure itself; while approaches such as Bayesian model selection [52] or the Akaike information criterion [53] may be used to evaluate between competing models with small numbers of parameters, such approaches become impractical when applied to detailed process models with dozens or hundreds of parameters. However, given that the structure of the model was based primarily on well-established aspects of HIV and HCV disease progression and transmission, and given that there are very large uncertainty ranges for many of the parameters in the model (including, critically, RSS), we believe that uncertainties in the model parameters, rather than uncertainty in the model structure, dominate overall uncertainty.

Fourth, we attempted to account for the possible impact of other programs, specifically ART, but could not directly assess their impact through a biological marker. In addition, this study only assessed the impact of NSPs in averting HIV and HCV infections among PWID, and did not include other benefits of the programs, such as prevention of injecting-related injuries, psychosocial support and referral, and education and prevention. We also did not consider

the effect of NSPs on secondary transmission to other population groups, starting with sexual partners of PWID, as these were not included in this study. Thus, our results may underestimate the full population-level benefits of NSPs.

Fifth, although we strived for consistency across all countries in the types of costs included, the interpretation of model parameters, and the process of data triangulation, there are differences in systems for monitoring and evaluation, and calculations of NSP access rates and population sizes. In particular, as a hidden population, the population size of PWID is hard to estimate. There was variation among countries in costing of personnel, frequency of distribution, and inclusion of counseling and printed materials. One would not expect to observe such large differences in the relationship between NSP coverage and RSS levels between the different countries. However, we found that there were relatively low numbers of needle-syringes distributed per PWID in Belarus but relatively high impact, whereas Estonia has had high coverage for considerable time but relatively low impact. The relative successes of different countries may be partly attributable to differences in economic, political, and social factors that result in a diversity of NSP implementations. Apart from these expected intrinsic differences in implementation and effects in different settings, it is likely that there are inconsistencies in program monitoring and epidemiological and behavioral surveillance systems between the countries.

In summary, the need to reduce the high and increasing rates of HIV (and HCV) transmission throughout this region remains urgent. However, secure funding is a barrier for providing NSPs in EECA [54]. This is becoming increasingly important because many countries in EECA will soon no longer be eligible for international donor assistance [54]. The results presented here provide evidence that NSPs in EECA are generally cost-effective in the short-term and very cost-effective to cost-saving when including long-term benefits. NSPs are among the most cost-effective of any strategy for reducing the incidence of blood-borne infections. Countries in the region may wish to re-examine their HIV prevention strategies and consider how this information might influence future funding allocations. There is a strong rationale for sustaining and further increasing capacity of NSPs in EECA.

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Competing interests

All authors have no financial, personal or professional competing interests to declare.

Author contributions

DPW was the chief investigator of the study, designed the study, facilitated workshops, data collection, and communication among investigators, produced results and wrote the manuscript. LZ implemented the model in computer code, assisted in workshop facilitation, assisted in production of results and provided edits to the manuscript. CCK advanced the computer code implementing the model, including model structure and calibration, generated the software, and assisted with writing of the manuscript. AU led all data collections and evaluations for Estonia, contributed to regional consortium discussions, and provided edits to the manuscript. JAK contributed to the model design and assisted with implementing mathematical and economic computer code. AH assisted in implementing mathematical and economic computer code, calibrating model to data and producing results. OZ coordinated data collation and analyses for Ukraine and contributed to regional consortium discussions. TB coordinated data collation and analyses for Kazakhstan and contributed to regional consortium discussions. AY conducted costing exercises for Belarus and Tajikistan and contributed to analyses in these countries and regional consortium discussions. EG coordinated data collation and analyses for Belarus and contributed to regional consortium discussions. GI coordinated data collation and analyses for Moldova and contributed to regional consortium discussions. DO coordinated data collation and analyses for Georgia and contributed to regional consortium discussions. TG coordinated data collation and analyses for Armenia and contributed to regional consortium discussions. MWS coordinated communication between country teams and managed progress throughout the study as well as assisting in organizing and contributing to regional consortium discussions. LZ coordinated data collation and analyses for Russia. CA proposed the study, coordinated all costing activities across all countries, organized regional consortium meetings, and led economic discussions. MR, KTL and AK collected all relevant data and contributed to analyses for Estonia with input into regional consortium discussions. RH, AY, MM and NS collected all relevant data and contributed to analyses for Armenia with input into regional consortium discussions. IUS, OA, AR, AT and LT collected all relevant data and contributed to analyses for Belarus and assisted in organizing, and providing input into, regional consortium discussions. VT and LT collected all relevant data and contributed to analyses for Georgia with input into regional consortium discussions. OS, ZM and RK collected all relevant data and contributed to analyses for Kazakhstan with input into regional consortium discussions. AI, IS, LG, SP, IO, RP and VS collected all relevant data and contributed to analyses for Moldova and assisted in organizing, and providing input into, regional consortium discussions. AS, TM, UA, MM and MB collected relevant data and contributed to analyses for Tajikistan with input into regional consortium discussions. AI, KS and OV collected all relevant data and contributed to analyses for Ukraine with input into regional consortium discussions. FO, CA, RL, DT and CH contributed to regional consortium discussions.
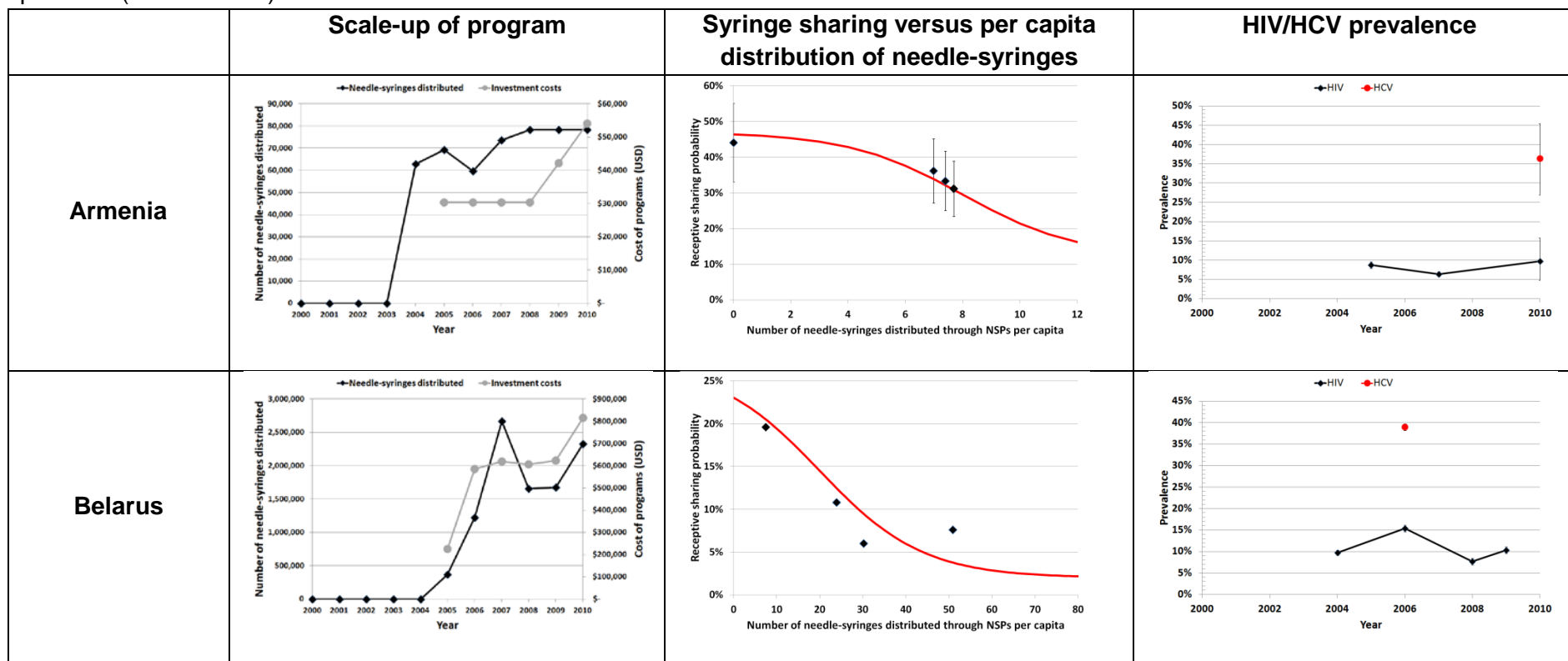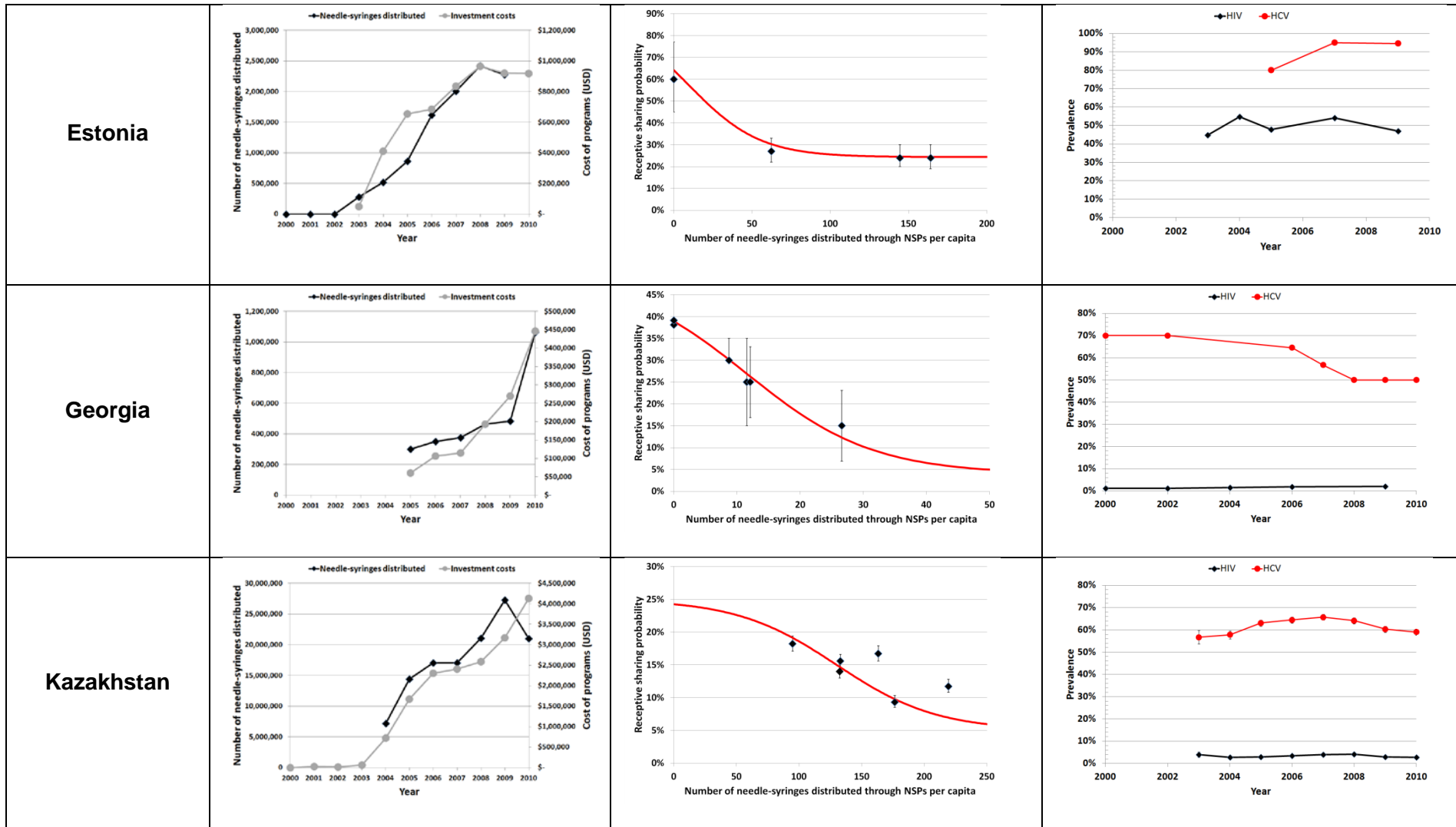
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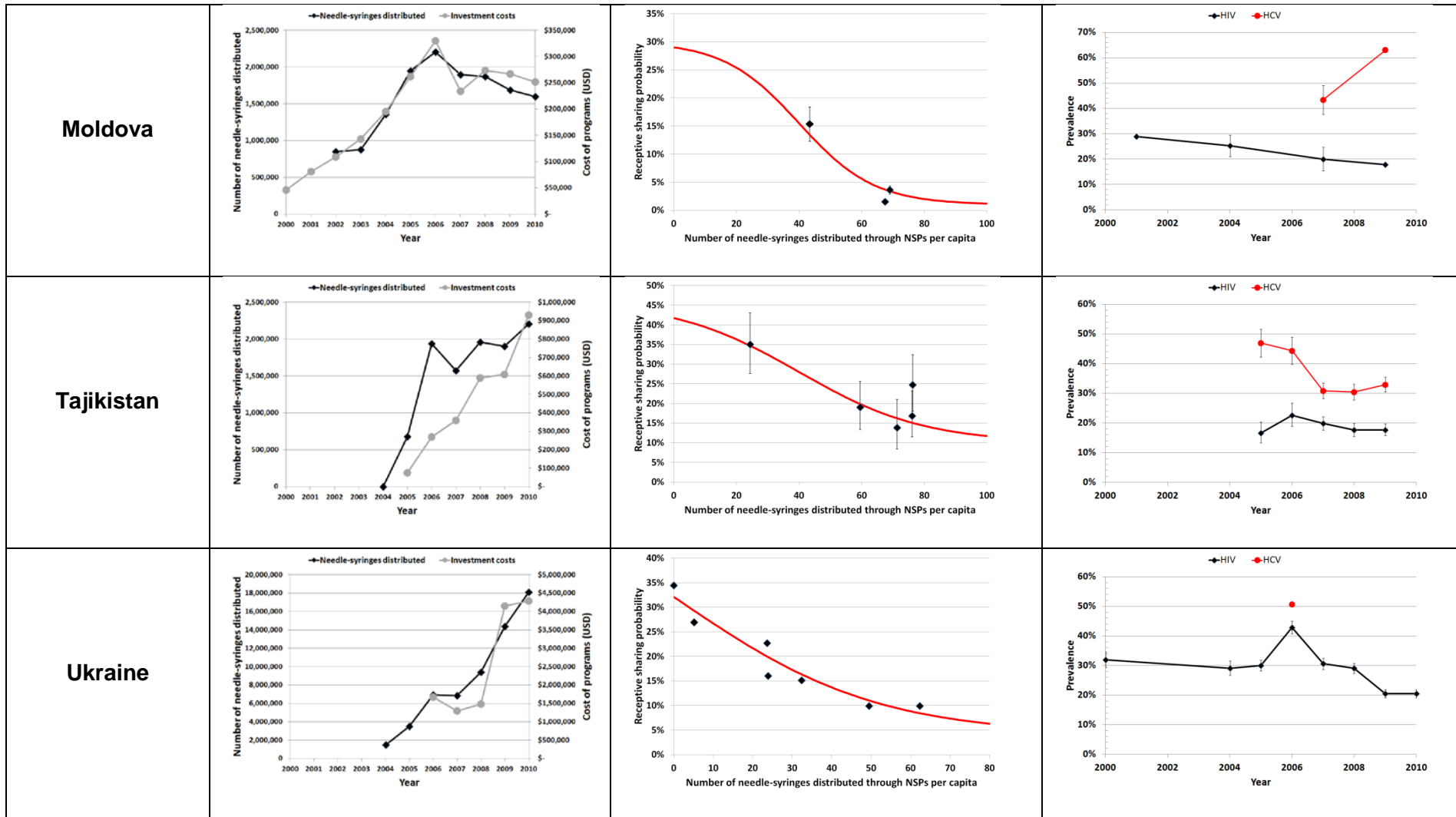
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Figure 1: Plots of data for eight EECA countries on (a) commodities distributed and financial investment in NSPs; (b) the relationship between syringe sharing and the per capita distribution of needle-syringes; and (c) HIV and HCV prevalence among PWID. 95% confidence bounds provided (as error bars) where available.

	Scale-up of program	Syringe sharing versus per capita distribution of needle-syringes	HIV/HCV prevalence
Armenia			
Belarus			

Estonia			
Georgia			
Kazakhstan			

Moldova			
Tajikistan			
Ukraine			

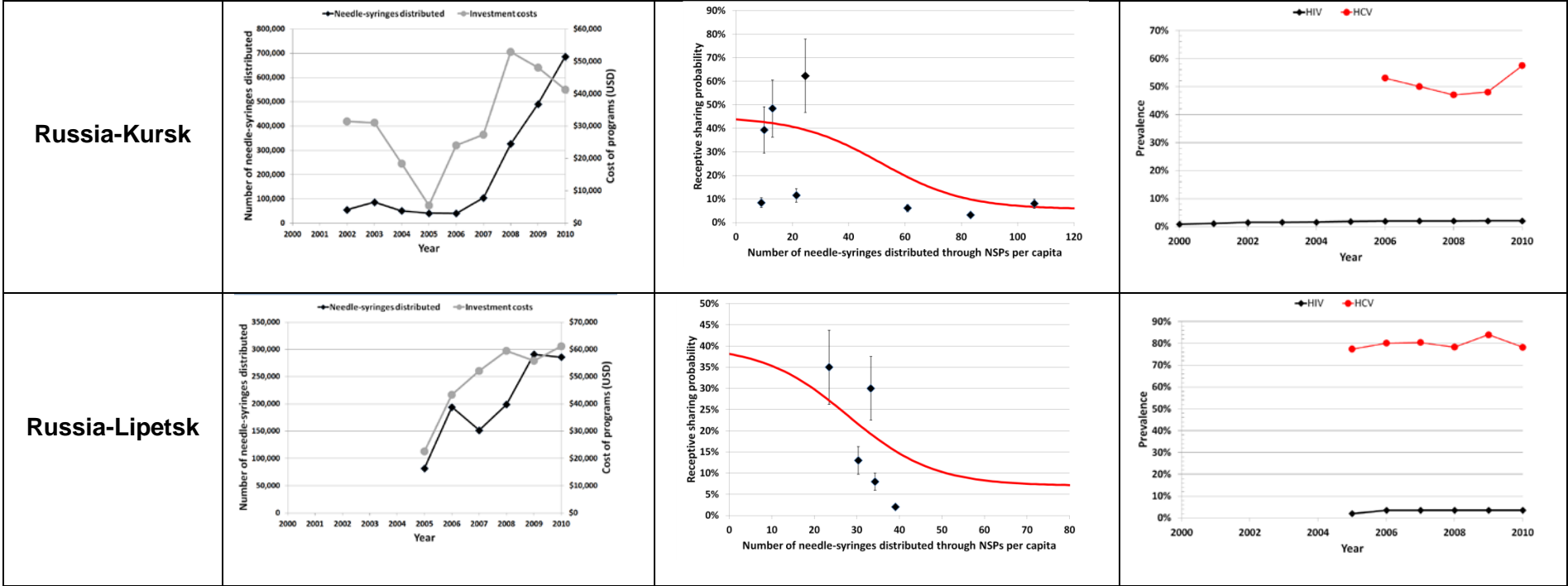|			
Russia-Kursk			
Russia-Lipetsk			

21

Figure 2: (a) Average cost per needle-syringe distributed per country per year; (b) cost components of NSPs for Belarus, Tajikistan, Moldova, and the average of all three countries.

A)
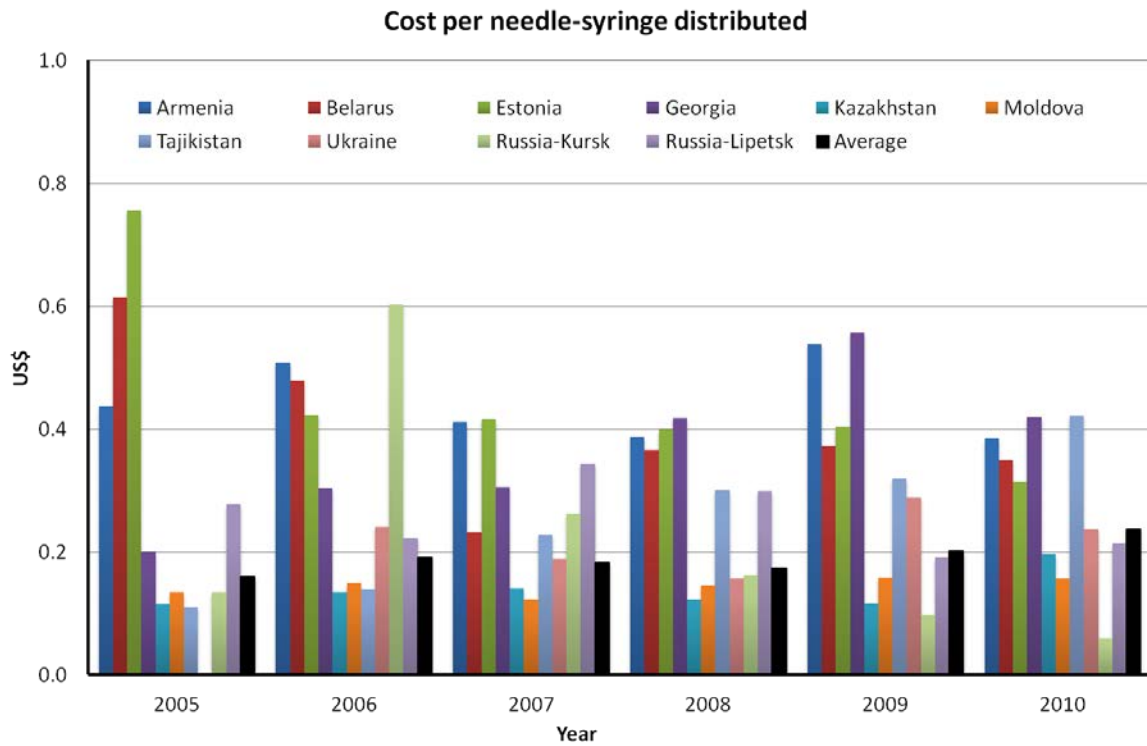
B)
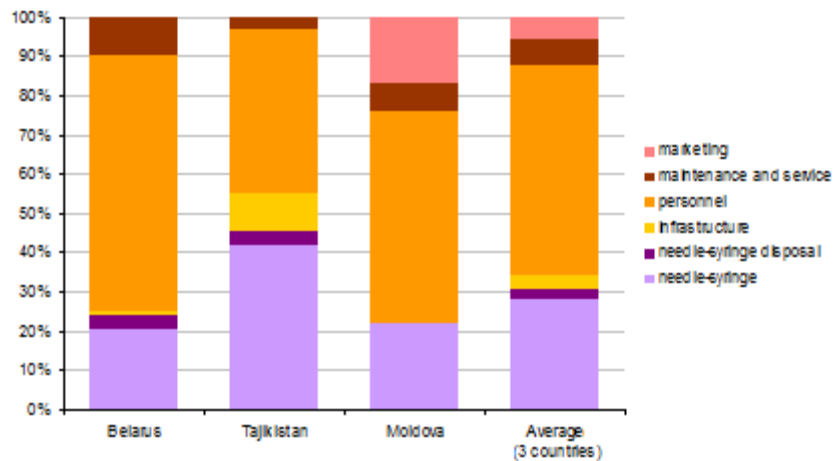
Figure 3: Summary of NSP cost-effectiveness results over the period (a) 2000-2010, considering HIV alone; (b) 2000-2010, considering both HIV and HCV (QALYs, but just HIV costs saved); and (c) life-long time horizons for HIV alone (with HIV-related health costs saved and return on investment (ROI)), for all countries assessed. Error bars show interquartile ranges.

(a)

(b)

Cost-effectiveness (HIV+HCV, 2000-2010)

(c)

Cost-effectiveness (HIV, lifetime)
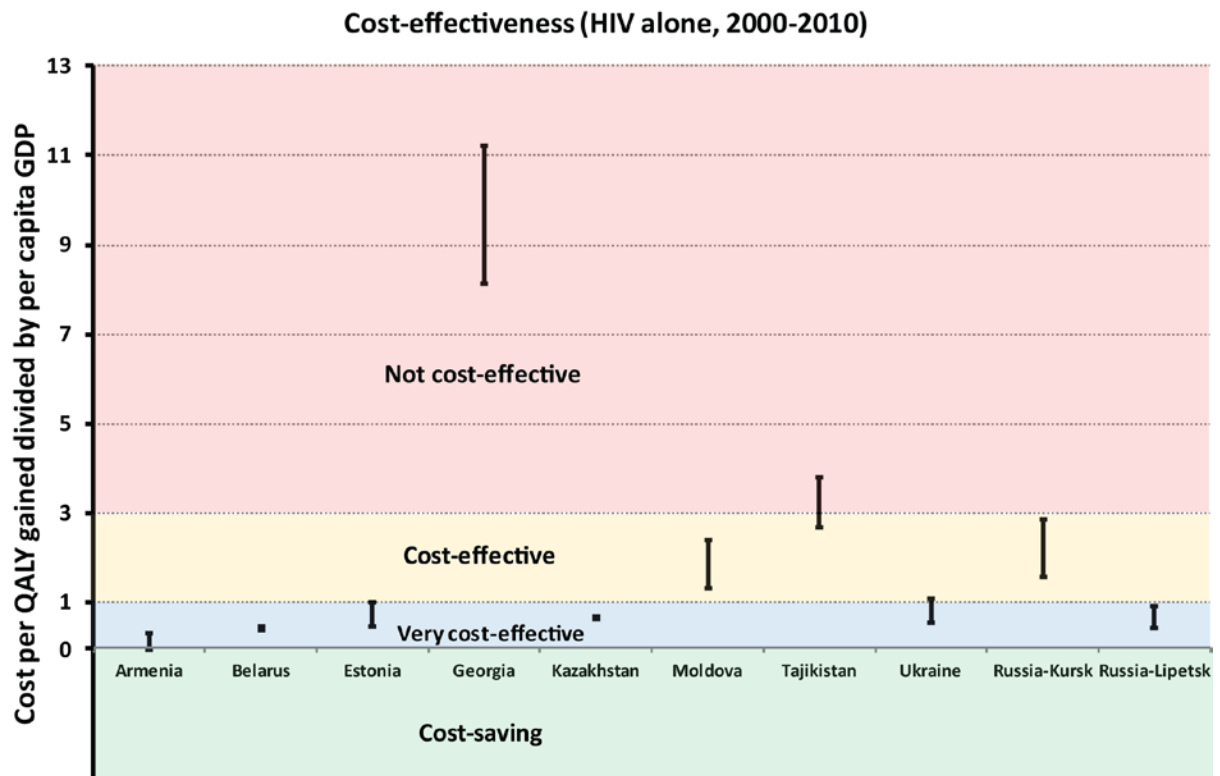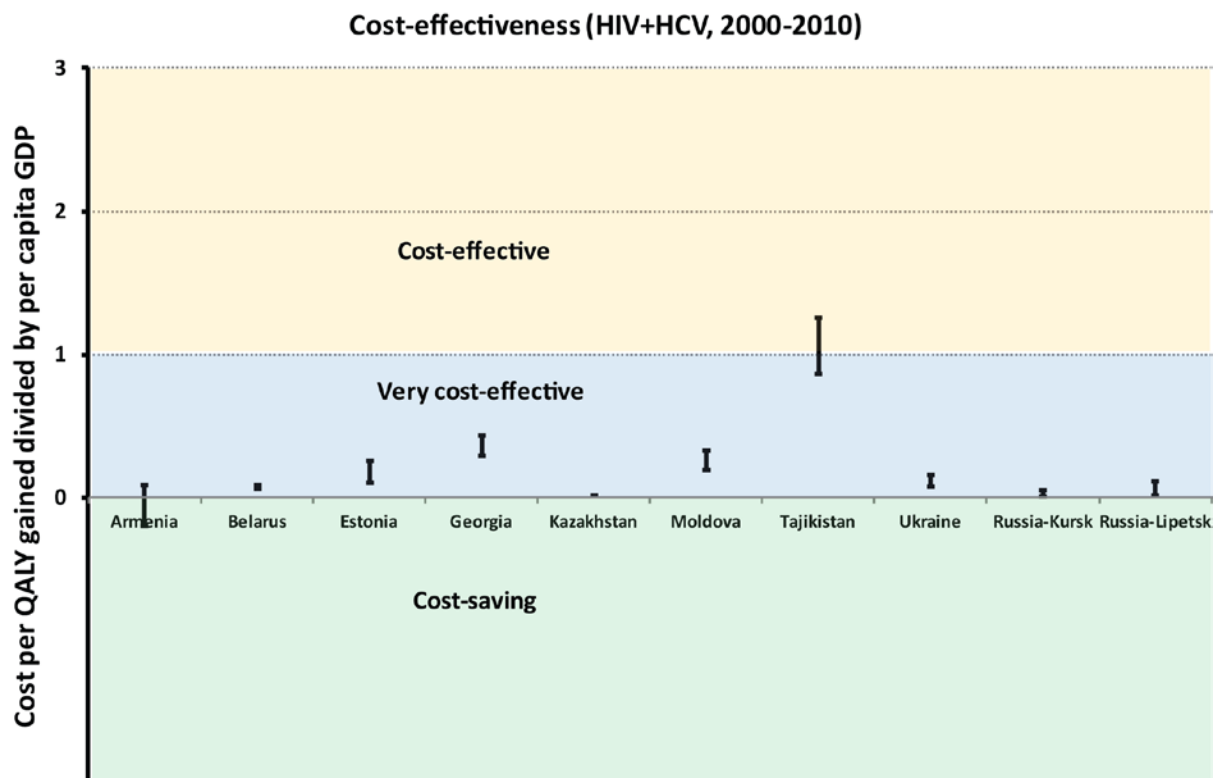
Table 1: Estimated HIV and HCV related epidemiological and economic outcomes (and interquartile ranges) with and without NSPs (2000-2010); all healthcare costs and QALYs have been discounted by 3%.

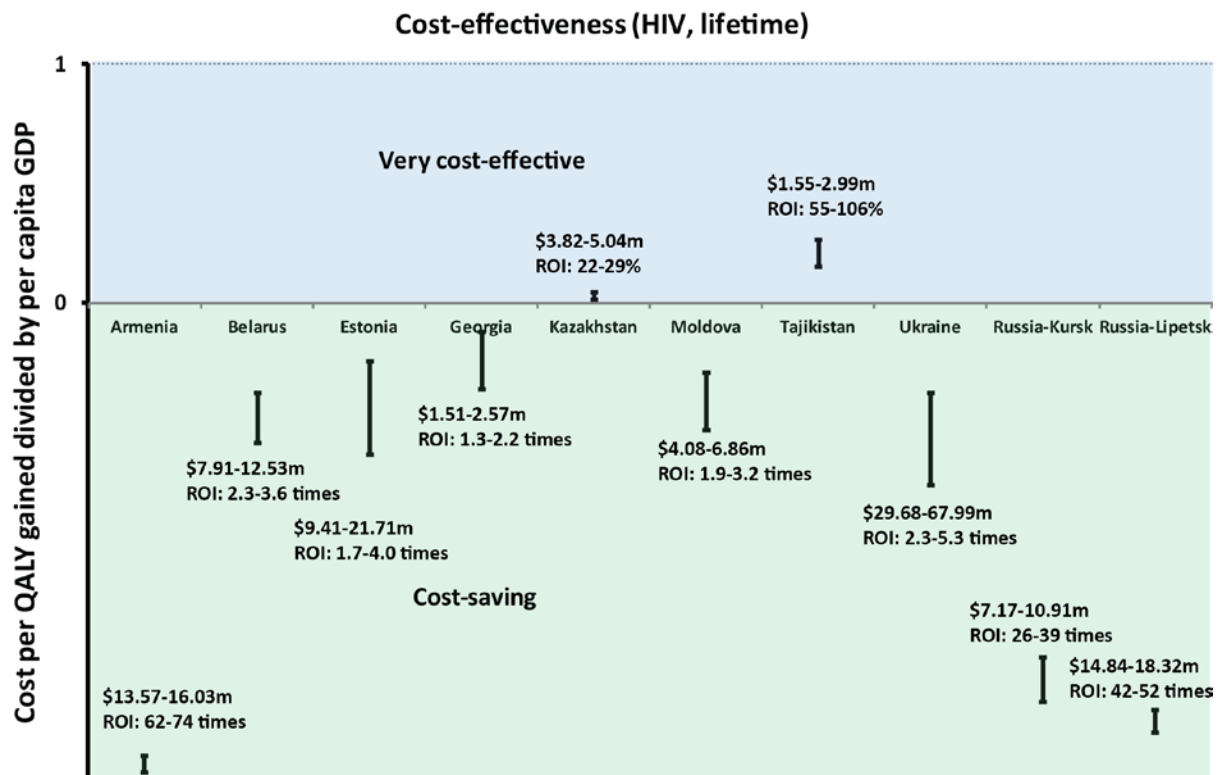|	Armenia		Belarus		Estonia		Georgia		Kazakhstan		Moldova		Tajikistan		Ukraine		Russia-Kursk		Russia-Lipetsk	
	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *	With NSPs	Without NSPs *
Summary of HIV-related outcomes																				
Prevalence of HIV among PWID (2010)	9.2%	11.7-12.3%	11.7%	15.9-18.5%	47.2%	47.8-48.4%	2.1%	2.3-2.5%	3.6%	4.8-5.1%	20.3%	25.5-29.0%	17.7%	25.8-31.8%	24.8%	27.8-31.7%	2.1%	6.9-9.0%	3.5%	9.7-9.9%
Cumulative incidence of HIV infections	776	1,098-1,158	4,831	7,168-8,657	2,543	3,231-4,146	1,042	1,161-1,240	4,546	6,751-7,266	8,477	10,267-11,527	9,206	11,484-13,277	107,142	116,755-128,865	154	282-355	461	282-866
Infections averted	322-382		2,337-3,826		688-1,603		119-198		2,205-2,720		1,790-3,049		2,278-4,071		9,613-21,723		146-219		146-406	
% infections averted	29.3-33.0%		32.6-44.2%		21.3-38.7%		10.2-16.0%		32.7-37.4%		17.4-26.5%		19.8-30.7%		8.2-16.9%		51.8-61.2%		42.1-46.8%	
QALYs gained (2000-2010)	223-251		1,310-1,642		382-820		41-56		2,364-2,518		559-1,026		909-1,283		3,903-7,949		7-13		27-58	
HIV-related health costs (2000-2010)	$4.69m	$4.89-4.92m	$18.29m	$19.28-19.46m	$41.71m	$43.47-45.44m	$2.87m	$2.93-2.96m	$11.18m	$13.49-13.78m	$5.27m	$5.38-5.49m	$2.21m	$2.29-2.34m	$146.2m	$149.2-152.2m	$2.06m	2.06-2.10m	$8.06m	$8.06-8.25m
Health costs saved (2000-2010)	$202,303-228,478		$988,971-1,165,767		$1,757,218-3,736,536		$58,074-81,614		$2,304,057-2,595,243		$111,700-215,701		$83,200-132,484		$2,976,865-5,997,783		$16,866-43,936		$84,464-190,811	
Financial investment in NSPs (2000-2010)	$217,365		$3,472,715		$5,435,005		$1,191,034		$17,093,063		$2,147,014		$2,832,156		$12,890,214		$279,883		$294,581	
Cost per QALY gained (HIV, 2000-2010)	$865-974 Return ~ investment (Extremely cost-effective)		$2,115-2,650 (Very cost-effective)		$6,631-14,214 (Very cost-effective)		$21,337-29,349 (Not cost-effective)		$5,758-6,256 (Very cost-effective)		$2,137-3,926 (Cost-effective)		$2,207-3,117 (Borderline CE)		$1,622-3,302 (Very cost-effective)		$21,903-39,983 (Cost-effective)		$6,036-12,913 (Very cost-effective)	
Lifetime benefits (HIV) from 2000-2010 programs																				
QALYs gained (HIV, lifetime)	7,022-8,254		40,346-64,566		11,098-25,594		877-1,465		33,323-112,742		26,873-45,251		13,088-23,269		197,910-446,142		2,014-3,195		4,032-5,266	
Health costs saved (HIV, lifetime)	$13.57-16.03m		$7.91-12.53m		$9.41-21.71m		$1.51-2.57m		$3.82-5.04m		$4.08-6.86m		$1.55-2.99m		$29.68-67.99m		$7.17-10.91m		$14.84-18.32m	
Cost per QALY gained (HIV, lifetime)	$26-31 (Cost-saving)		$54-86 (Cost-saving)		$211-490 (Very cost-effective)		$813-1,358 (Cost-saving)		$107-398 (Very cost-effective)		$48-82 (Cost-saving)		$122-216 (Cost-saving – Very cost-effective)		$29-65 (Cost-saving)		$88-133 (Cost-saving)		$67-82 (Cost-saving)	
Return on investment	62-74 times		2.3-3.6 times		1.7-4.0 times		1.3-2.2 times		22-29% of investment		1.9-3.2 times		55-106% of investment		2.3-5.3 times		26-39 times		42-52 times	

Additional benefits associated with HCV																				
Prevalence of HCV among PWID (2010)	39.3%	40.7-41.1%	39.0%	42.3-43.9%	89.4%	90.3-90.8%	56.6%	57.6-58.2%	63.9%	73.1-75.4%	63.0%	69.0-72.1%	34.8%	37.4-39.5%	48.9%	51.8-55.4%	57.5%	74.9-77.6%	82.2%	88.0-88.1%
Cumulative incidence of HCV infections	788	951-989	4,158	5,876-6,890	2,784	2,938-3,019	10,994	11,480-11,798	77,777	98,718-102,492	16,415	18,504-19,496	3.807	4,798-5,468	158,688	169,705-183,080	4,111	6,534-6,781	3,961	4,808-4,851
Infections averted	163-201		1,718-2,732		163-585		486-804		20,941-24,715		2,089-3,081		991-1,661		11,017-24,392		2,423-2,670		847-890	
% infections averted	17.1-20.3%		29.2-39.7%		5.1-16.3%		4.2-6.8%		21.2-24.1%		11.3-15.8%		20.7-30.4%		6.49-13.3%		37.1-39.4%		17.6-18.4%	
QALYS gained (HCV, 2000-2010)	605-678		5,707-7,768		1,058-2,861		1,010-1,495		76,242-83,099		3,514-6,835		1,835-2,734		23,756-48,666		3,823-4,153		1,075-1,239	
QALYs gained (HCV, lifetime)	3,456-4,220		30,239-46,631		9,041-31,894		5,127-8,565		174,170-275,633		33,043-47,841		7,179-12,212		92,934-205,478		11,763-12,976		10,105-10,726	
Value for money of NSPs implemented during 2000-2010 (excluding health cost savings due to HCV infections)																				
Cost per QALY gained (HIV + HCV, 2000-2010)	$224-263 (Break even)		$369-495 (Very cost-effective)		$1,477-3,733 (Very cost-effective)		$768-1,134 (Very cost-effective)		$169-188 (Very cost-effective)		$321-538 (Very cost-effective)		$705-1,032 (Cost-effective)		$228-466 (Very cost-effective)		$67-73 (Very cost-effective)		$271-319 (Very cost-effective)	
Cost per QALY gained (HIV + HCV, lifetime)	$12-15 (Cost-saving)		$20-32 (Cost-saving)		$95-270 (Very cost-effective)		$76-127 (Cost-saving)		$31-64 (Very cost-effective)		$15-23 (Cost-saving)		$77-135 (Cost-saving – Very cost-effective)		$17-39 (Cost-saving)		$17-20 (cost-saving)		$22-24 (cost-saving)	
GDP per capita **	$3,031		$5,765		$14,345		$2,620		$9,136		$1,631		$820		$3,007		$14,037		$14,037	

* (50%, 5% offset assumptions)
** According to the World Bank (2010 estimate)