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Lessons learned from the ARISTOTLE Study

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HELLENIC REPUBLIC
National and Kapodistrian University of Athens

Outline of the presentation

- Short background information
- Aims & design of ARISTOTLE program
- Main findings
- Lessons learned from the outbreak & the implementation of ARISTOTLE
- ARISTOTLE in epidemic & non epidemic settings

Short background information

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ARISTOTLE in epidemic & non epidemic settings

Greece – background info

Located at the crossroads of Europe and Asia

~11M population

Economic recession since 2009

- National surveillance system for HIV/AIDS (Hellenic Centre for Disease Control and Prevention)
- Low-level HIV epidemic, mainly concentrated among MSM. In 2010:
  - Approx. 600 newly diagnosed HIV-1 cases
  - MSM → ~72% of cases with known transmission route

People who inject drugs (PWID) in Greece

Size of the population
In 2010: 22,200 high risk drug users
10,100 in Athens

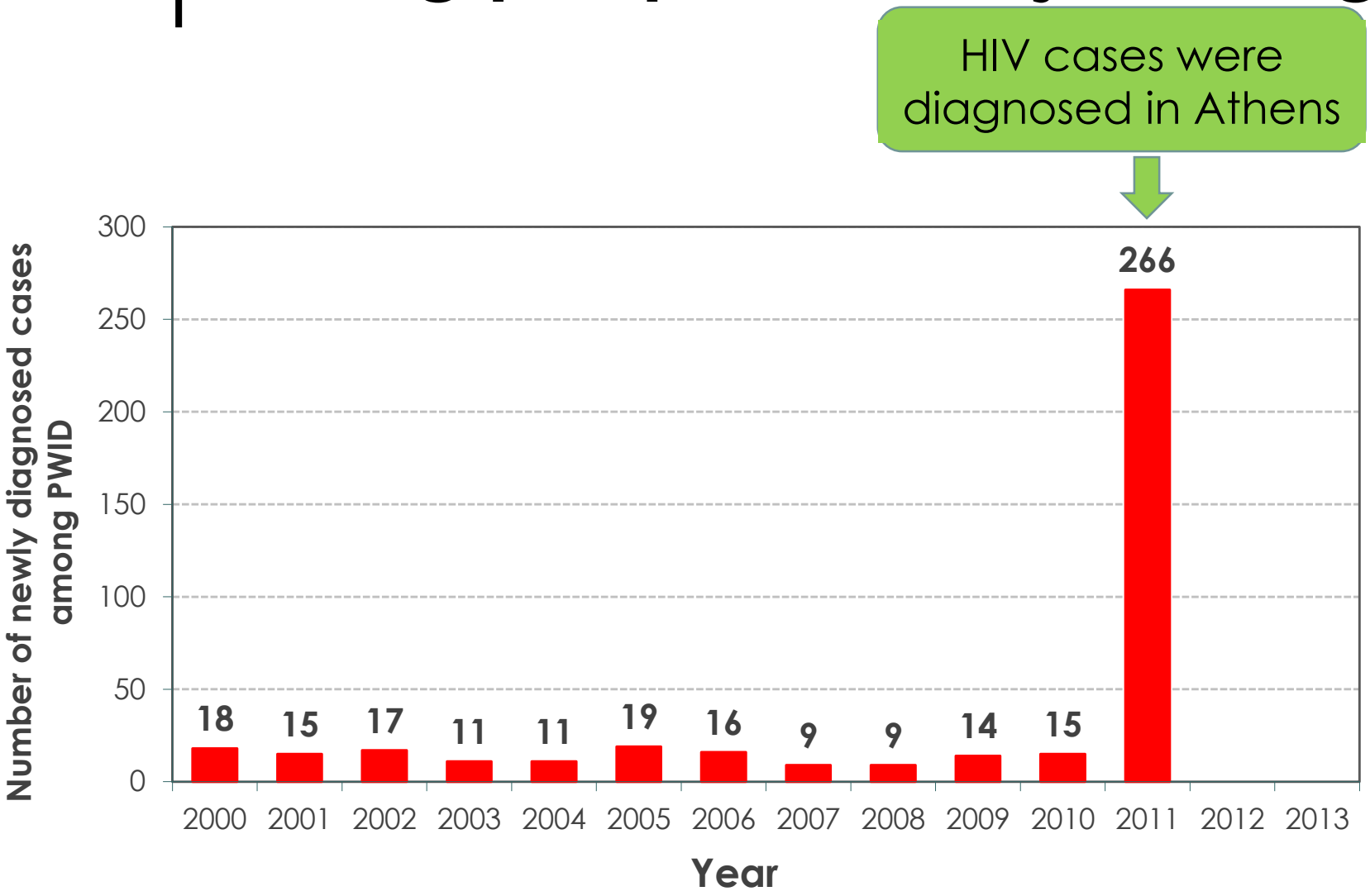
HIV infection
Low number of reported HIV cases
BUT
increasing prevalence of HCV infection

Coverage of harm reduction in Athens (2010):
More than 5.500 opioid users were waiting to enter opioid substitution treatment programs
→ waiting time ~7.5 years

On average 16 syringes per PWID per year

Greek Reitox Focal Point
Malliori et al, Addiction, 2013

The beginning of an HIV outbreak among people who inject drugs



Surveillance data from the Hellenic Centre for Disease Control & Prevention

First steps

The Greek Organisation Against Drugs:

- Increased the number of centers providing opioid substitution treatment

  25 units (Aug 2011) → 58 units (Dec 2012)

- In cooperation with NGOs & the Hellenic Centre for Disease Control and Prevention: Scale up of needle and syringe programs
- Introduction of low dead-space syringes

University of Athens

- Analysis of sequences from newly HIV-infected PWID
- Proposal to get a grant to implement ARISTOTLE

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Aims of ARISTOTLE

Primary Aims

- To screen for anti-HIV the population of PWID in Athens Metropolitan Area.
- To provide the WHO/ UNODC/ UNAIDS and EMCDDA/ECDC prevention, treatment and care package.
- To contribute to the decrease of HIV-1 incidence among PWID.

Secondary Aims

- To provide an estimate of anti-HIV prevalence among PWID during the course of study.
- To monitor the linkage to and retention in care and treatment.
- To describe phylogenetic and injection networks.

Seek-test-treat design

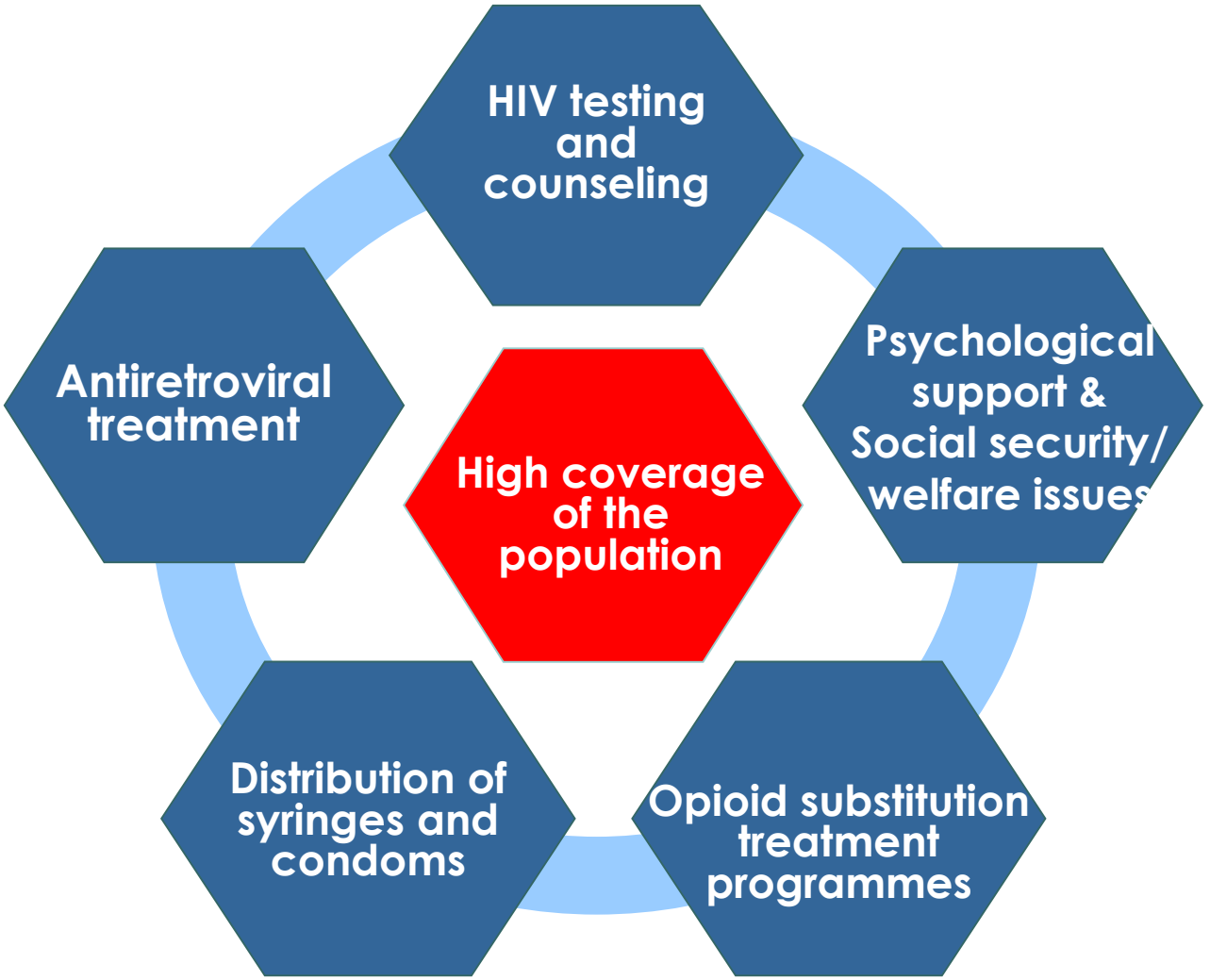
Seek — Rapid identification of as many PWID as possible

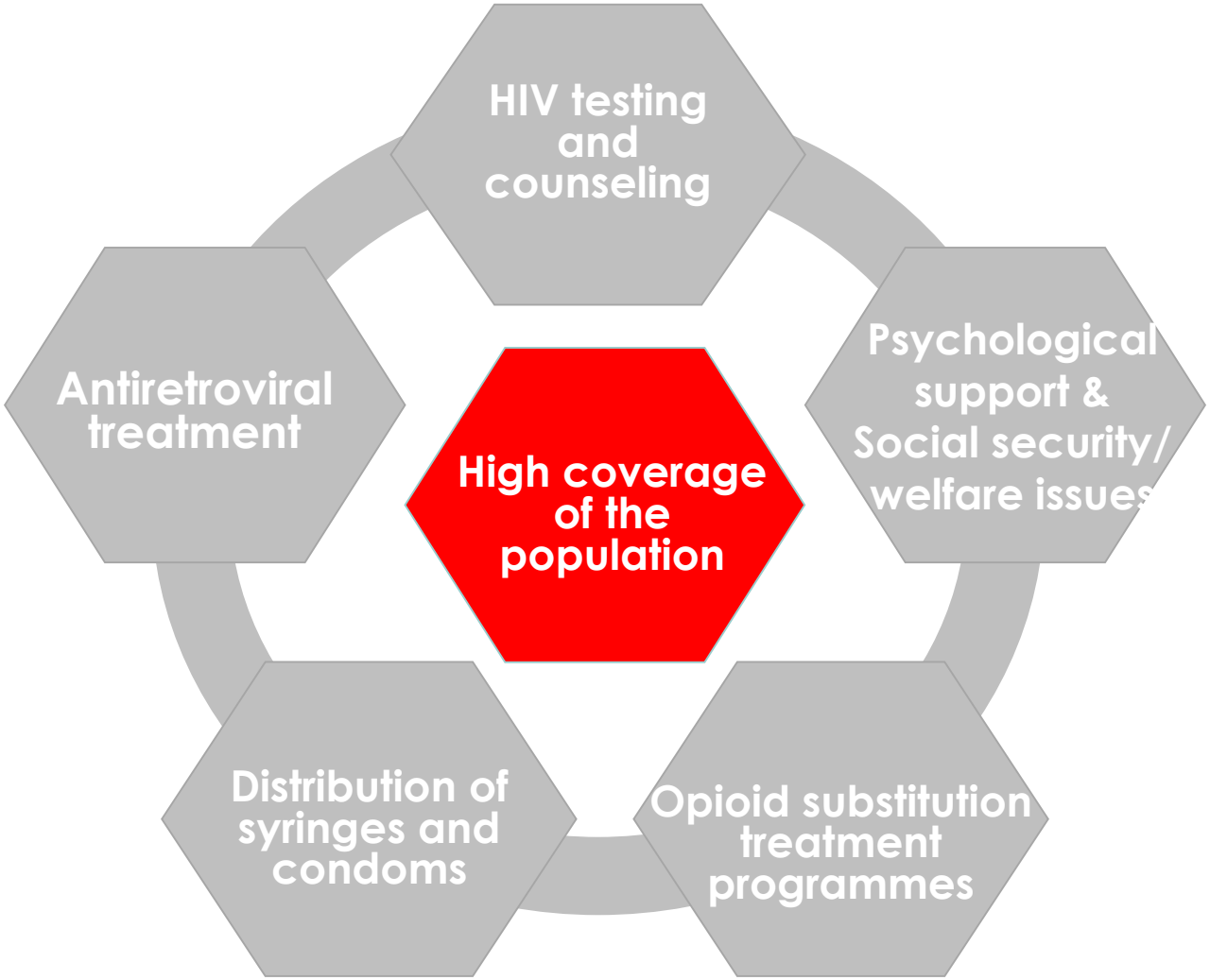
Test — HIV testing

Treat — Linkage to HIV care, antiretroviral therapy & opioid substitution treatment programme (OST)

5 sampling rounds to recruit PWID (August 2012-December 2013)

ARISTOTLE: A combination prevention programme




HIV testing and counseling
Psychological support & Social security/ welfare issues
Opioid substitution treatment programmes
Distribution of syringes and condoms
Antiretroviral treatment
High coverage of the population

Achieving high coverage

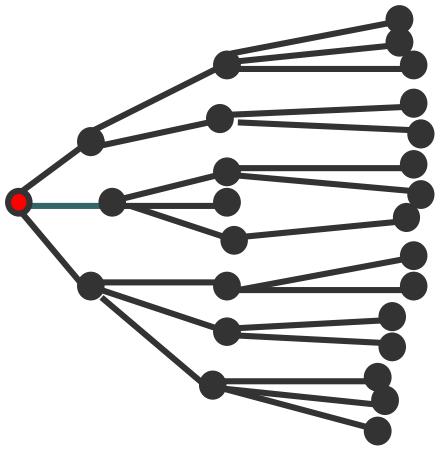
- PWID → **hard-to-reach population**
  - Subgroups even more hard-to-reach:
    e.g. immigrants without documents

- Need to implement the intervention **as rapidly as possible** during the evolving epidemic and to achieve **high coverage** in the screening of the target population

- In addition, **a representative sample** of the target population was desirable to estimate anti-HIV prevalence

Overcoming this challenge: Respondent-driven sampling (RDS)

- An initial number of recruits (seeds) from the target population receive coupons and are asked to draw from their existing social networks to identify up to 3 potential recruits → Chains of recruits are accrued



- Monetary incentives to:
  - participate
  - to recruit others

Heckathorn et al, Social Problems 1997

Advantages of RDS

- Participants are limited in the number of respondents they can recruit
  - → final sample independent of the initial seeds
  - → long recruitment chains which allow increased 'reach' of the sample into more hidden pockets of the population

- It is based on financial reward in combination with peer pressure → as those who would not participate for financial reasons alone may do so as a favor to a friend → lower nonresponse bias

- There are appropriate methods that allow to adjust estimates for the RDS sampling design

Heckathorn et al, Social Problems 1997
Magnani et al, AIDS 2005

Implementation of RDS in ARISTOTLE

Respondent Driven Sampling (RDS) using coupons

- RDS carried out in 5 rounds over the period August 2012-December 2013 (16 months)
- PWID could participate in multiple rounds but only once in each round
- The aim was to recruit approximately 1400 PWID per round

Seeds:

- Non-randomly selected PWID (selected by the staff of the Greek Organisation Against Drugs)
- 5-10 seeds per round
- The selection was based on the basis of diversity concerning gender, age, ethnicity and HIV status.

Implementation of RDS in ARISTOTLE

Incentives:

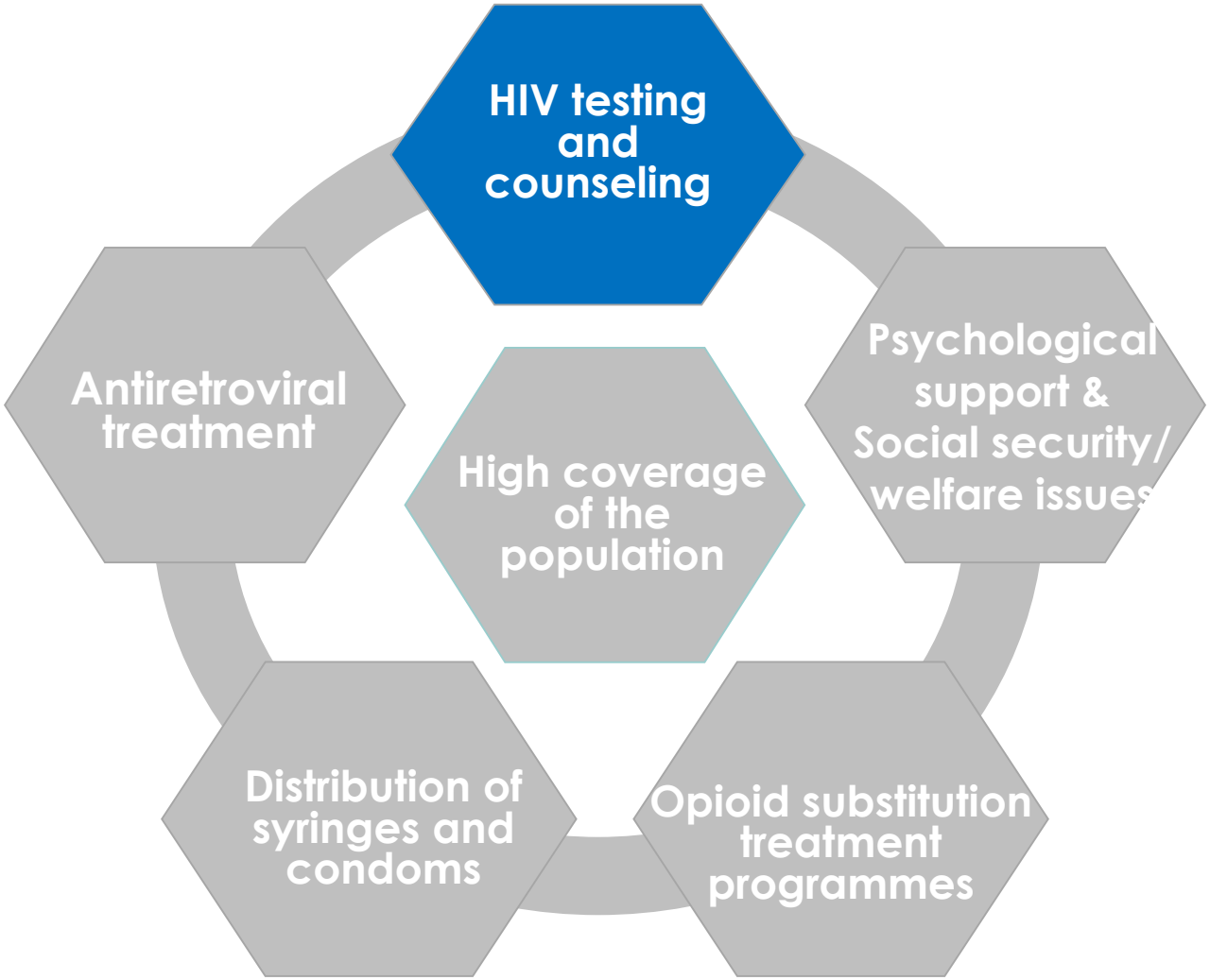
- Primary incentives (to participate)
- Secondary incentives (to recruit others)

Cultural mediators

- to attract migrants, with a focus on people from Iran/Afghanistan)
- 6 languages (Greek and Farsi, English, French, Arab and Kurdish)

- A useful manual on how to deal with all the practical aspects concerning the set-up of RDS:

  Johnston LG. Behavioural Surveillance: Introduction to Respondent Driven Sampling (Participant Manual). 2008
  Centers for Disease Control and Prevention, Atlanta, GA.
  http://globalhealthsciences.ucsf.edu/PPHG/surveillance/other_modules.html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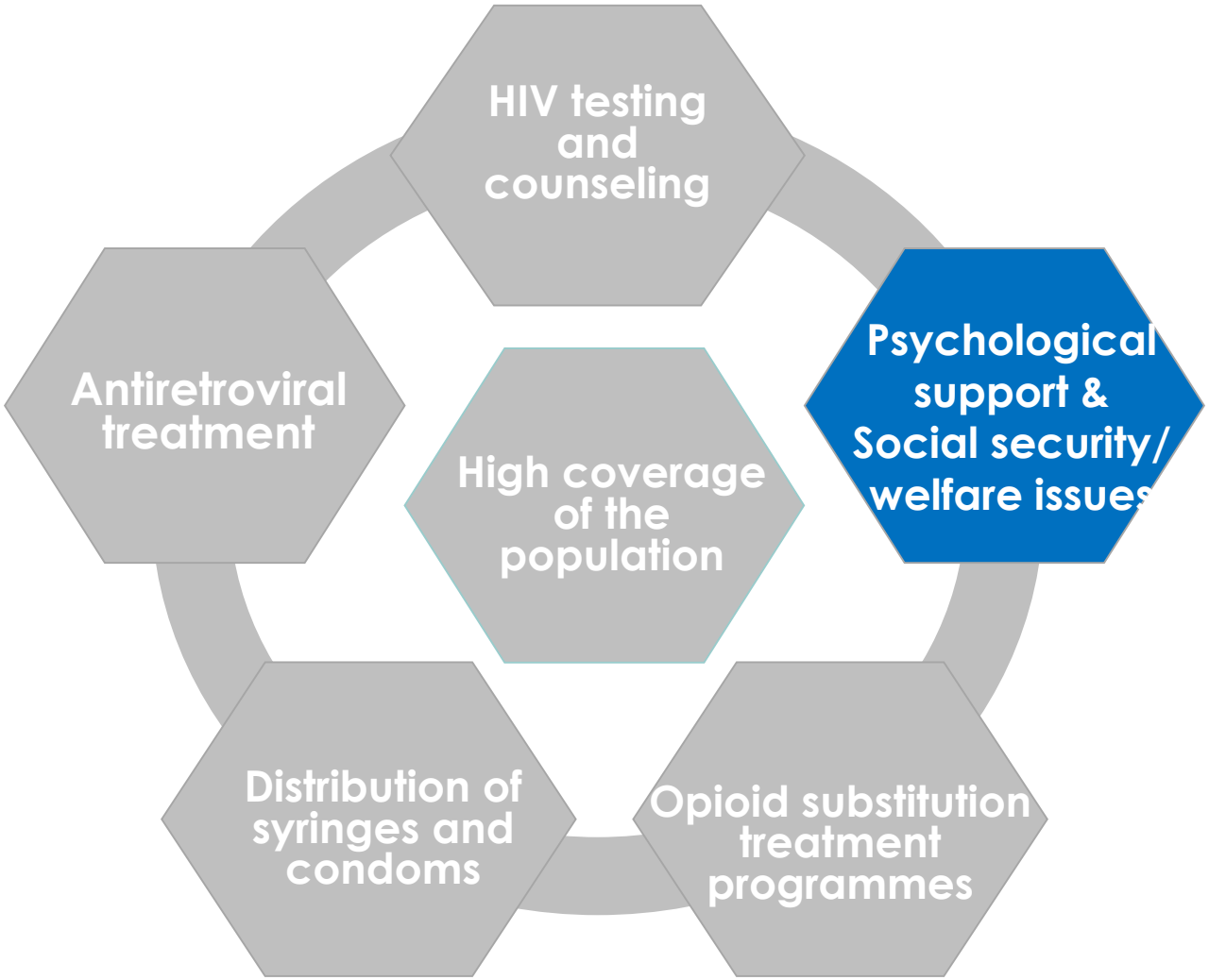
Blood sampling-Laboratory testing

- Collected blood samples (10 ml) were transported on a daily basis to the lab.
  - HIV tests were performed with a microparticle EIA anti-HIV-1/2 (AxSYM HIV-1/2 gO, Abbott)
  - HIV-1 and HIV-2 confirmation by Western Blot (MP Diagnostics)
  - Molecular HIV-1 typing conducted with deep-sequencing and phylogenetic analysis to identify transmission networks.
  - LAg-Avidity EIA for anti-HIV1/2 positive samples (in selected cases)

HIV testing & counseling

- Pre-test counseling & blood sample collection at the program site
- Leaflets

- Post-test counseling
  - The doctor announced the results to the participants and provided a brief counseling on HIV
  - The psychologist was present in the announcement of a new HIV positive result & had a counseling session with the participant
  - An experienced volunteer from NGO "Positive Voice" was located in the same building to assist the counseling of seropositive PWID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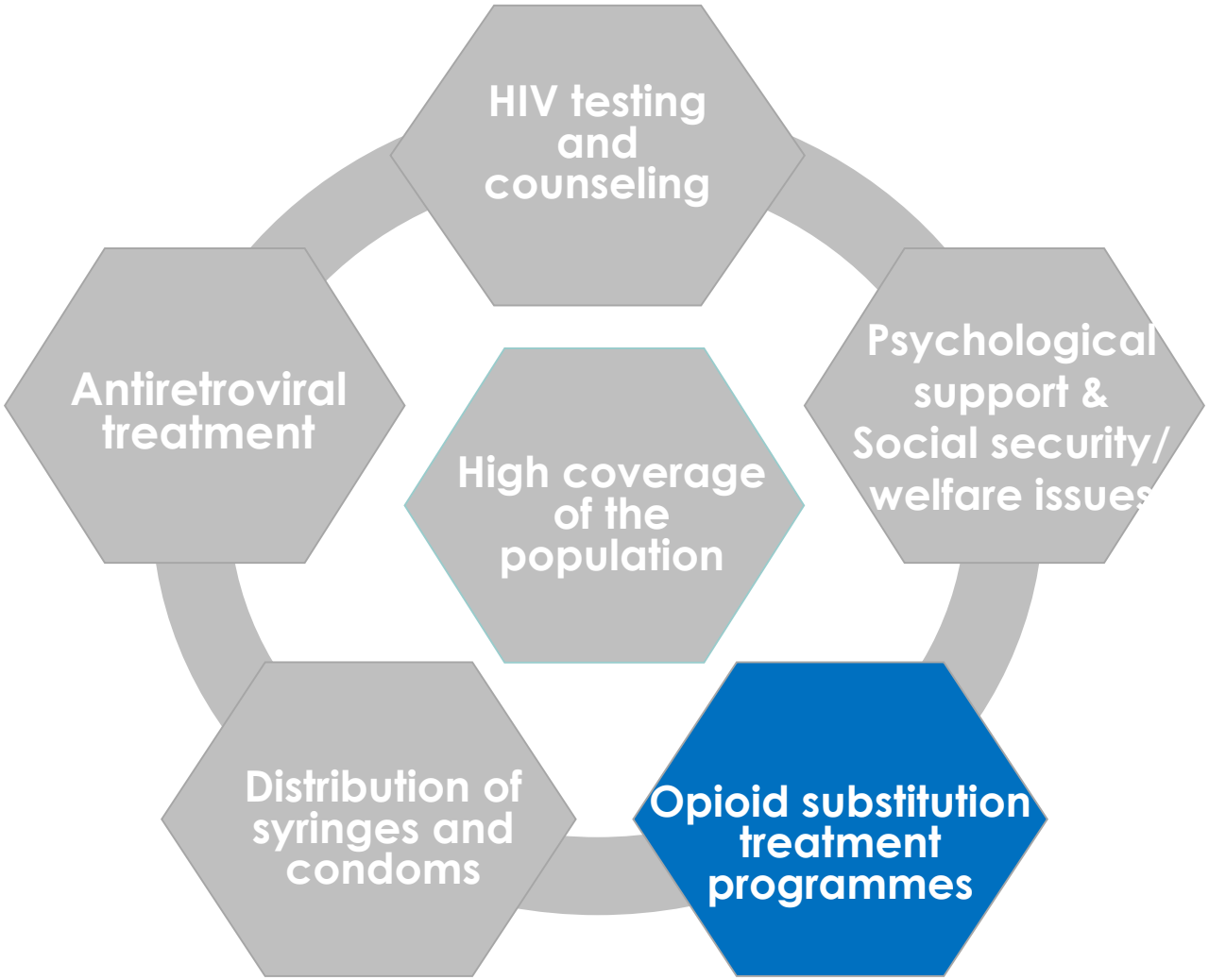
Psychological support & Social security/welfare issues

- A psychologist and 2 social workers worked on counselling & help on other issues too (e.g. health insurance, psychological support)
  - Linkage to the appropriate service of the Greek Organisation Against Drugs and to NGOs
- The staff had prepared leaflets with information concerning:
  - Info on the required documents to apply for OST or to get health coverage
  - Places proving services such as laundry, shower, food, clothes, counseling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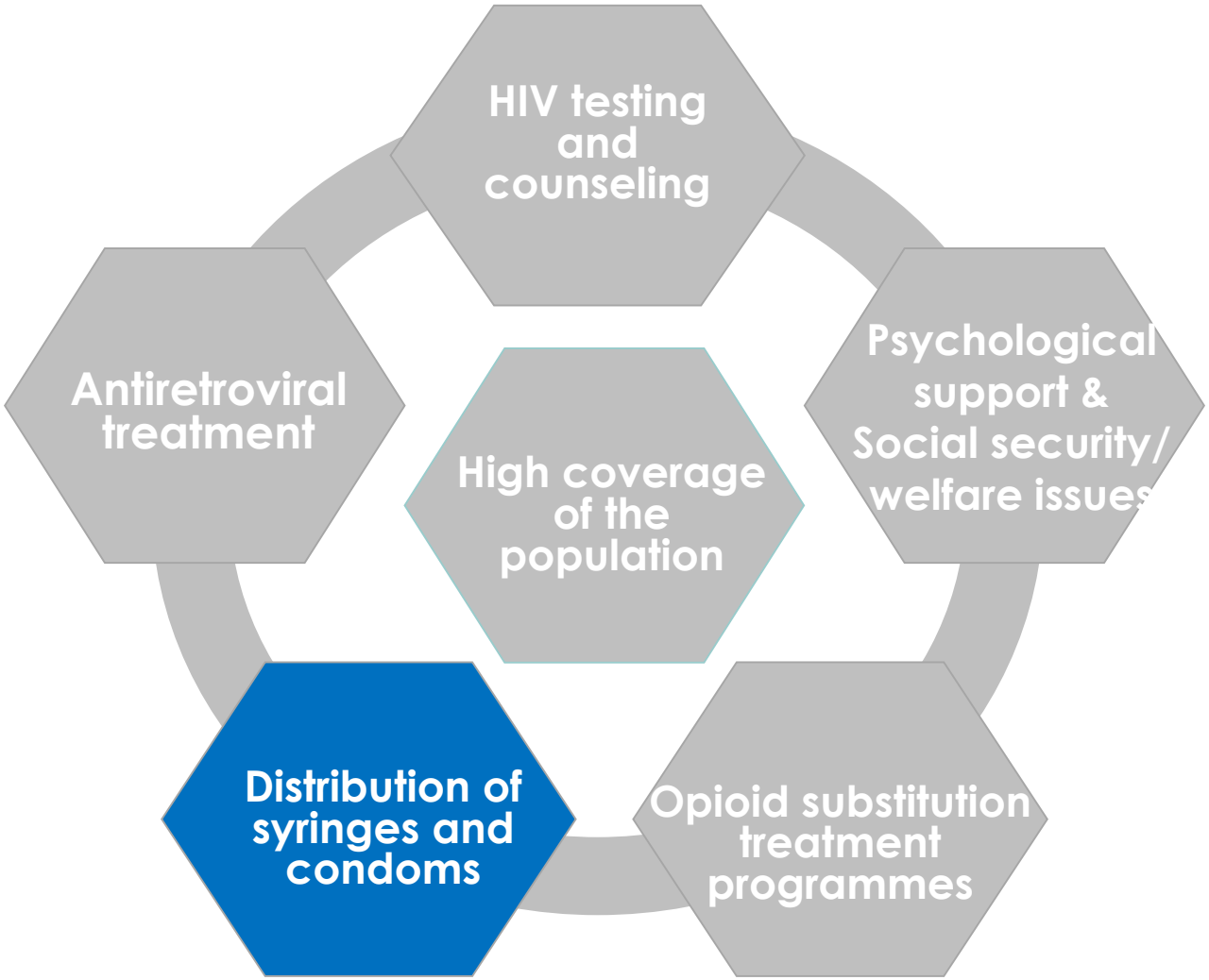
Linkage to Opioid Substitution Treatment programs

- A psychologist and 2 social workers worked on linking PWID to OST
- Linkage to the Greek Organisation Against Drugs (the organization offering OST) which was located in the same building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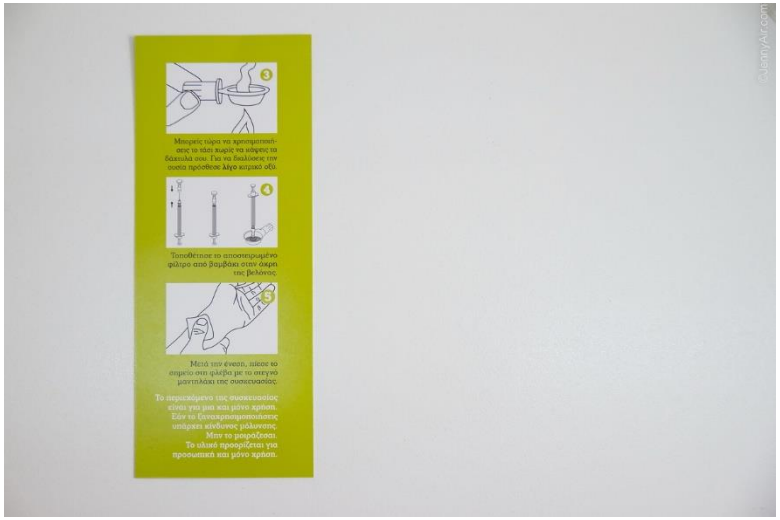
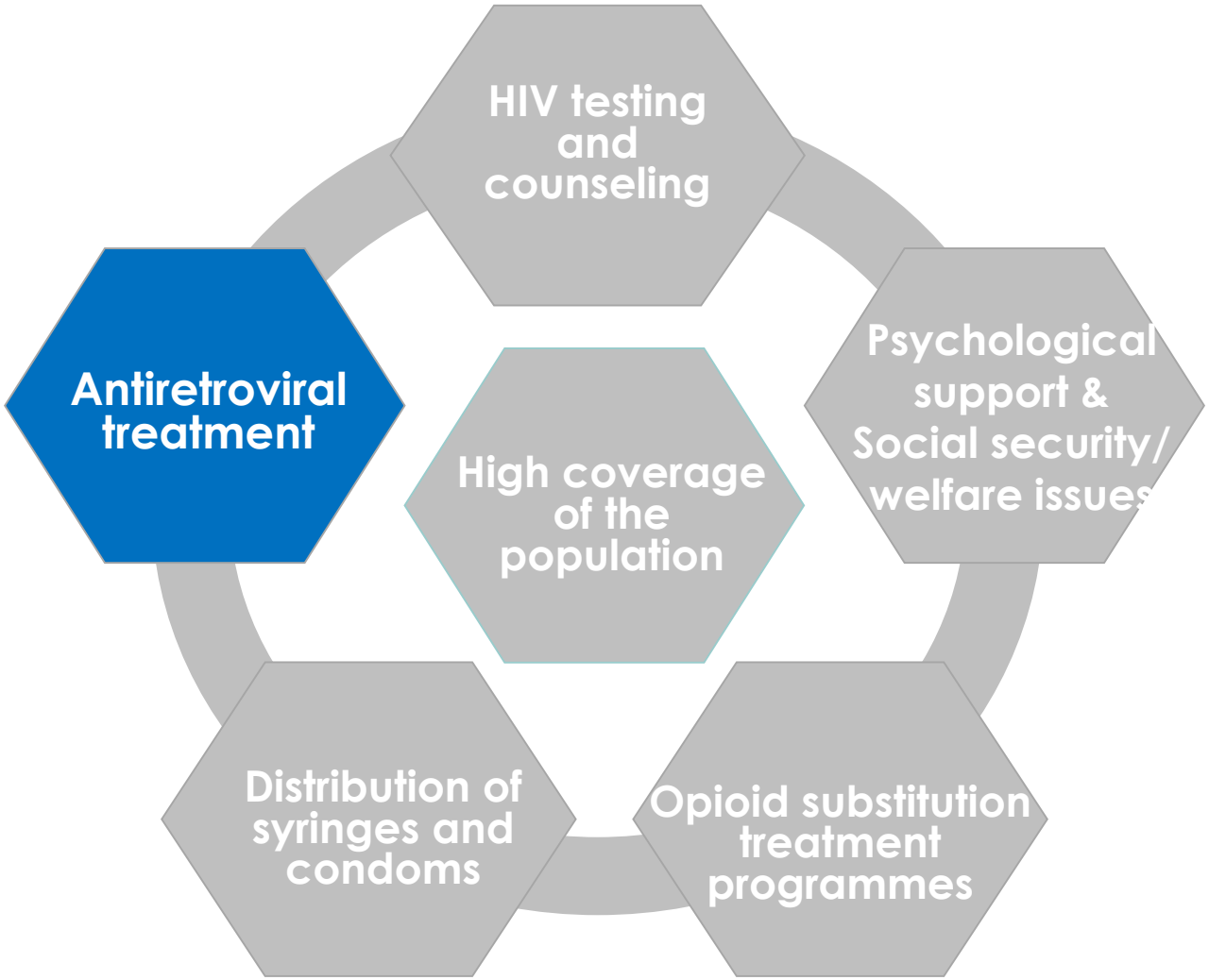
Distribution of free syringes

- Participants were given syringes (a kit of 25 low dead-space syringes & injection paraphernalia), condoms and leaflets with information about how to prevent blood borne infections.

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Linkage to antiretroviral treatment

- The psychologist and 2 social workers worked on referrals
  - Arranged the appointments with the doctors of the infectious diseases units for HIV(+) participants
  - Reminded appointments – arranged again missed appointments
- Seropositive migrants without documents were referred to NGO Praksis

Eligibility criteria - ARISTOTLE site & staff

Eligibility criteria for participants

Persons who:

- Have injected drugs in the past 12 months
- Live in the area of Athens
- ≥18 years old

- **Site:**
  A building of the Organisation Against Drugs located in the centre of Athens

- **Staff:**
  Ex-PWID, social workers, phsychologist, cultural mediators, one medical doctor

Questionnaire

- The questionnaire of the National HIV Behavioral Surveillance System (NHBS)-IDU3 was used as the basis for the core questionnaire of ARISTOTLE - modified as appropriate in order to be used in Greek PWID

- It included sections on:
  - Network size
  - Sexual behavior (past 12 months & last partner)
  - Injecting & non-injecting drug use (past 12 months & last time)
  - Alcohol use
  - Alcohol and drug treatment
  - HIV testing experience
  - Health condition
  - Assessment of prevention activities
  - Knowledge/Attitude on recent HIV Infection
  - Food insecurity

Description of the process

Participant arrives at interview site

If valid coupon:
Eligibility screening

If eligible:
Consent process

If consent obtained:
Interview & blood sample collection for HIV testing

At the end of the process:

- Payment of primary incentive
- 3 coupons are provided
- Syringes-leaflets are provided

Approximately 3 days later:

- HIV test result
- Payment of secondary incentive(s)
- For HIV (+) participants: Referral to ARV treatment - Priority referral to OST

Short background information

Aims & design of ARISTOTLE program

Main findings

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ARISTOTLE in epidemic & non epidemic settings

The 5 rounds of ARISTOTLE

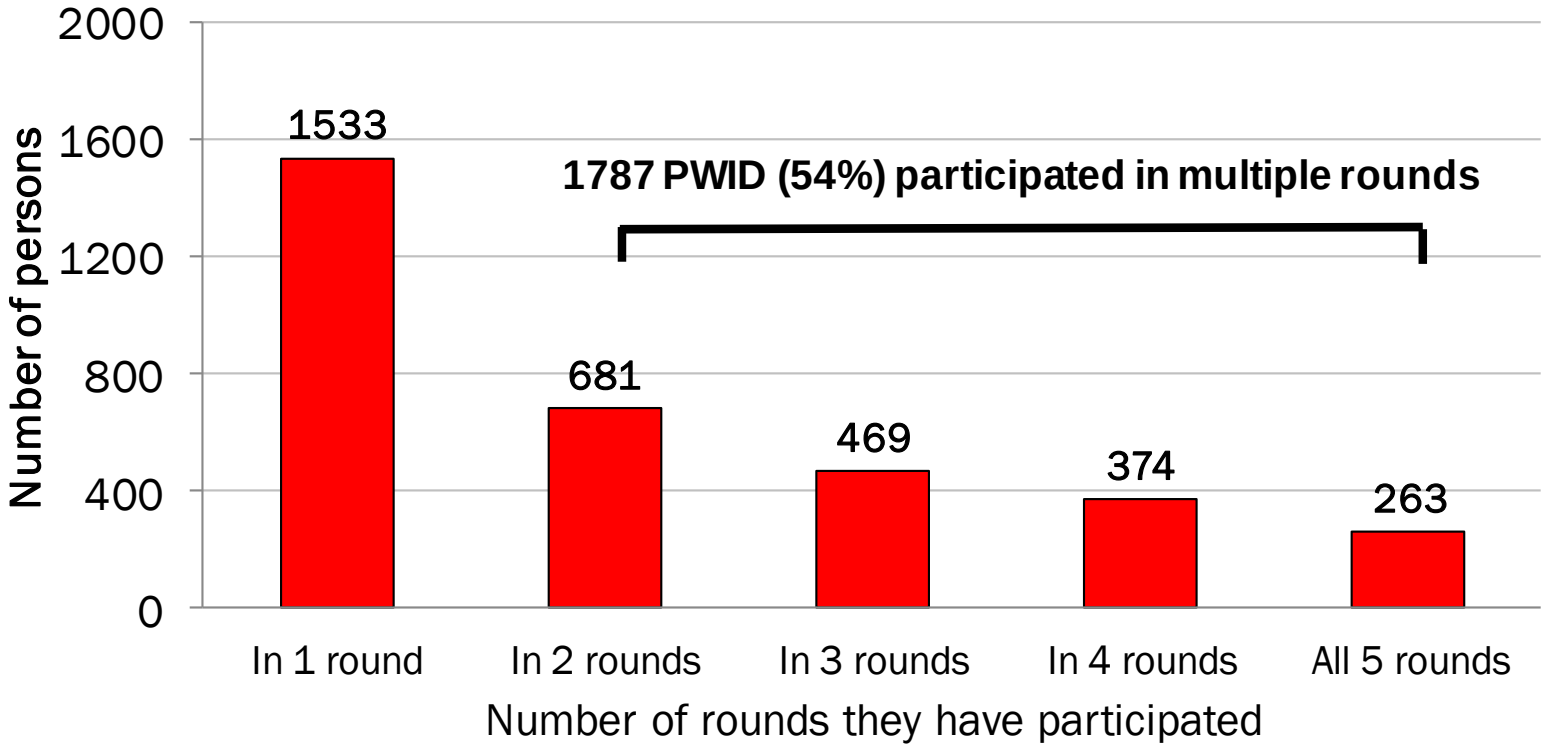
Round	Time period	Duration of recruitment (weeks)	Total number of participants
A	Aug2012 - Oct2012	**10.0**	**1,415**
B	Dec2012 - Mar2013	**12.4**	**1,444**
C	Mar2013 - Jun2013	**11.4**	**1,434**
D	Jun2013 - Sep2012	**12.3**	**1,413**
E	Sep2013 - Dec2013	**12.6**	**1,407**

Median (25th, 75th) number of participants per day :
28 (20,21)

Total number of participants (20Aug2012 – 23Dec2013)

- During these 5 rounds :
  - 3,320 unique persons participated to the program
  - 7,110 questionnaires and blood samples were obtained

Multiple participations

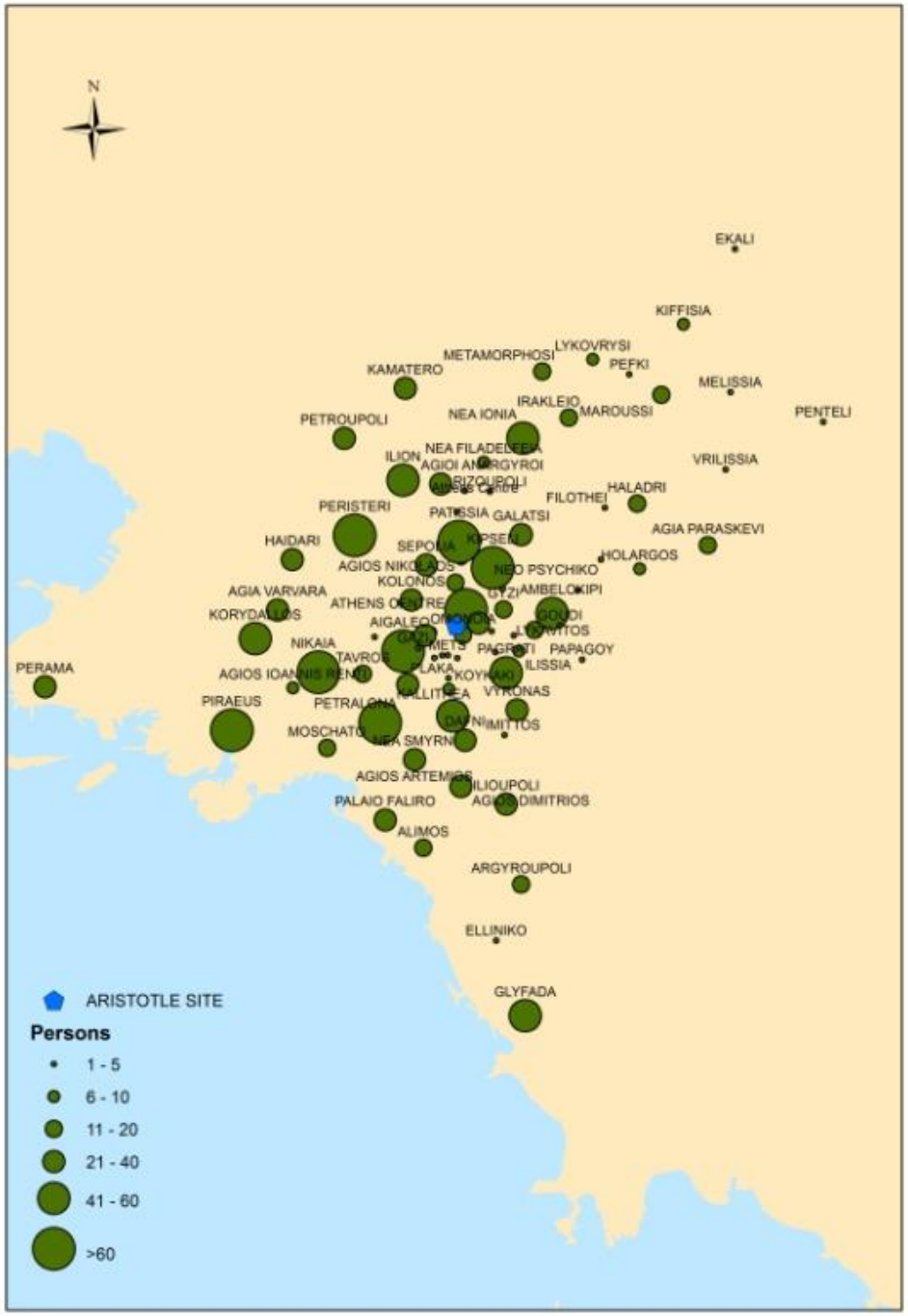


Population coverage

In total: 3,320 unique PWID during 16 months

Population coverage: 88% (71%-100%)

Coverage based on the number of persons who had injected drugs in the past month:
2689 participants in ARISTOTLE
3069 estimated population size (capture-recapture)



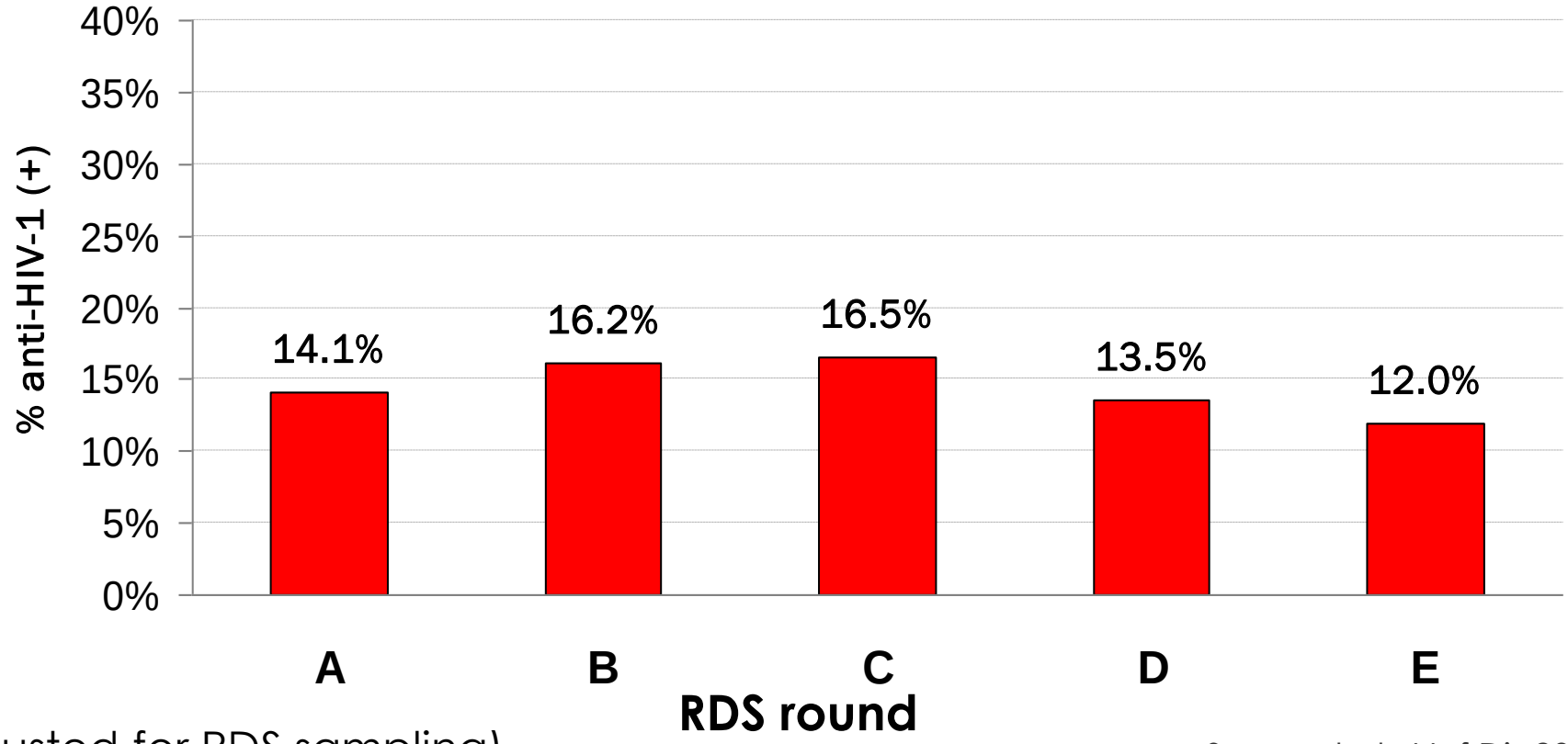
Geographical coverage:
Map of Athens marked with the **areas where PWID reported that they live in** (green circles) –

The blue symbol indicates the **location of the Aristotle site**

Sypsa et al, Am J Public Health 2015

Estimated HIV prevalence during the program

In total, 547 out of 3320 participants were HIV positive (16.5%)



(adjusted for RDS sampling)

Sypsa et al, J Inf Dis 2017

HIV prevalence among PWID in Athens

2010

0.8%

2012-2013

16.5%
(15.2%–17.8%)

Sypsa et al, J Inf Dis, 2017

Risk factors for anti-HIV positivity

Men (N=2797)

- Cocaine or speedball as main substance of use
- Injecting more than once per day
- Sharing syringes
- Currently homeless
- Low educational level

Women (N=510)

- Cocaine or speedball as main substance of use
- Dividing drugs with a used syringe
- History of imprisonment
- More than 5 sexual partners in the past year

Hatzakis et al, Addiction 2015

Incidence of HIV infection during ARISTOTLE

Time period	Incidence /100 pyrs (95% CI)
Aug 2012-Dec2012	**7.76** (4.60, 13.4)
Dec2012-Apr2013	**5.88** (3.70, 9.33)
Apr2013-Aug2013	**2.91** (1.57, 5.41)
Aug2013-Dec2013	**1.71** (0.55, 5.31)

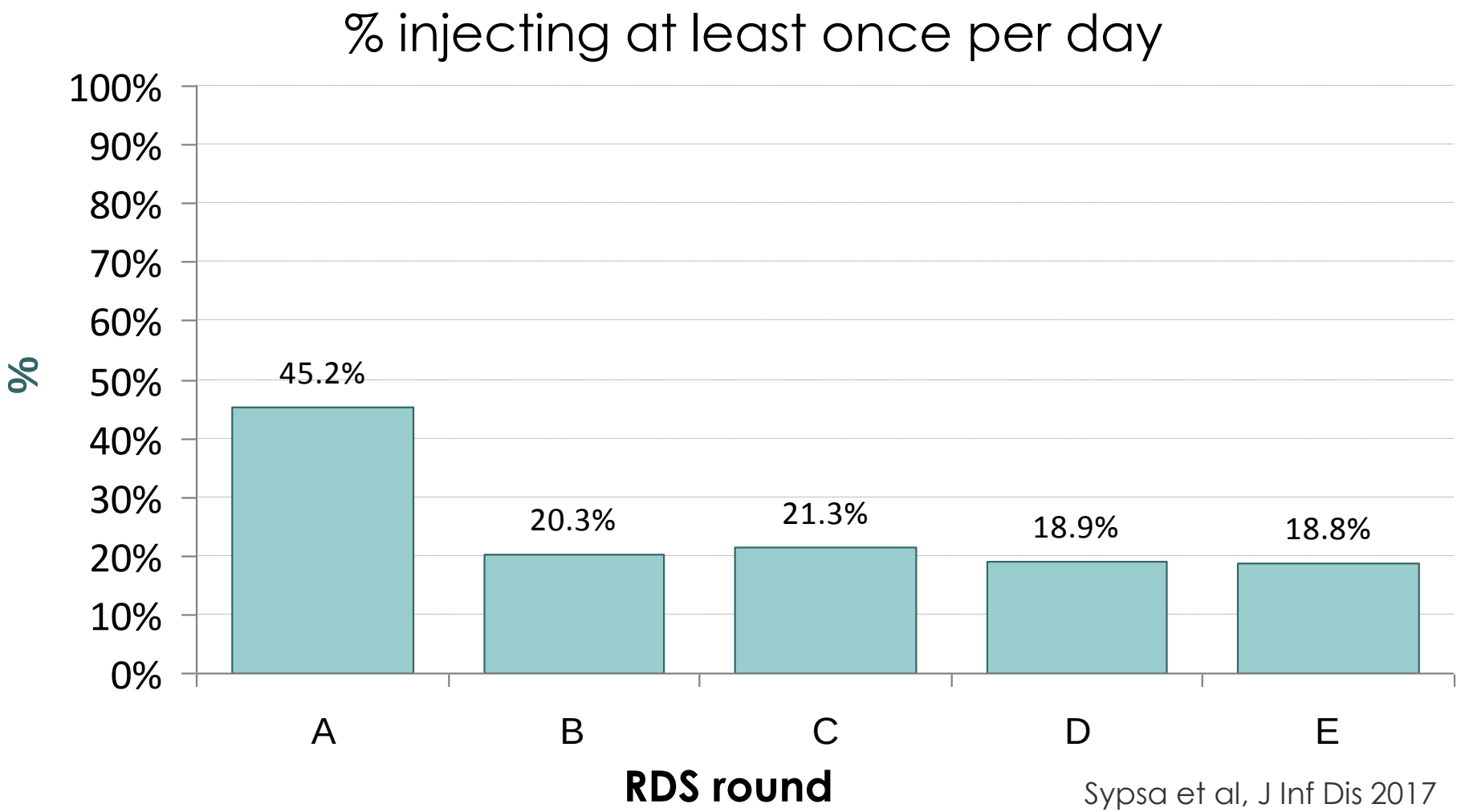
78% decline

Risk factors for HIV seroconversion

- Injecting drugs at least once per week
- History of imprisonment
- Being currently homeless

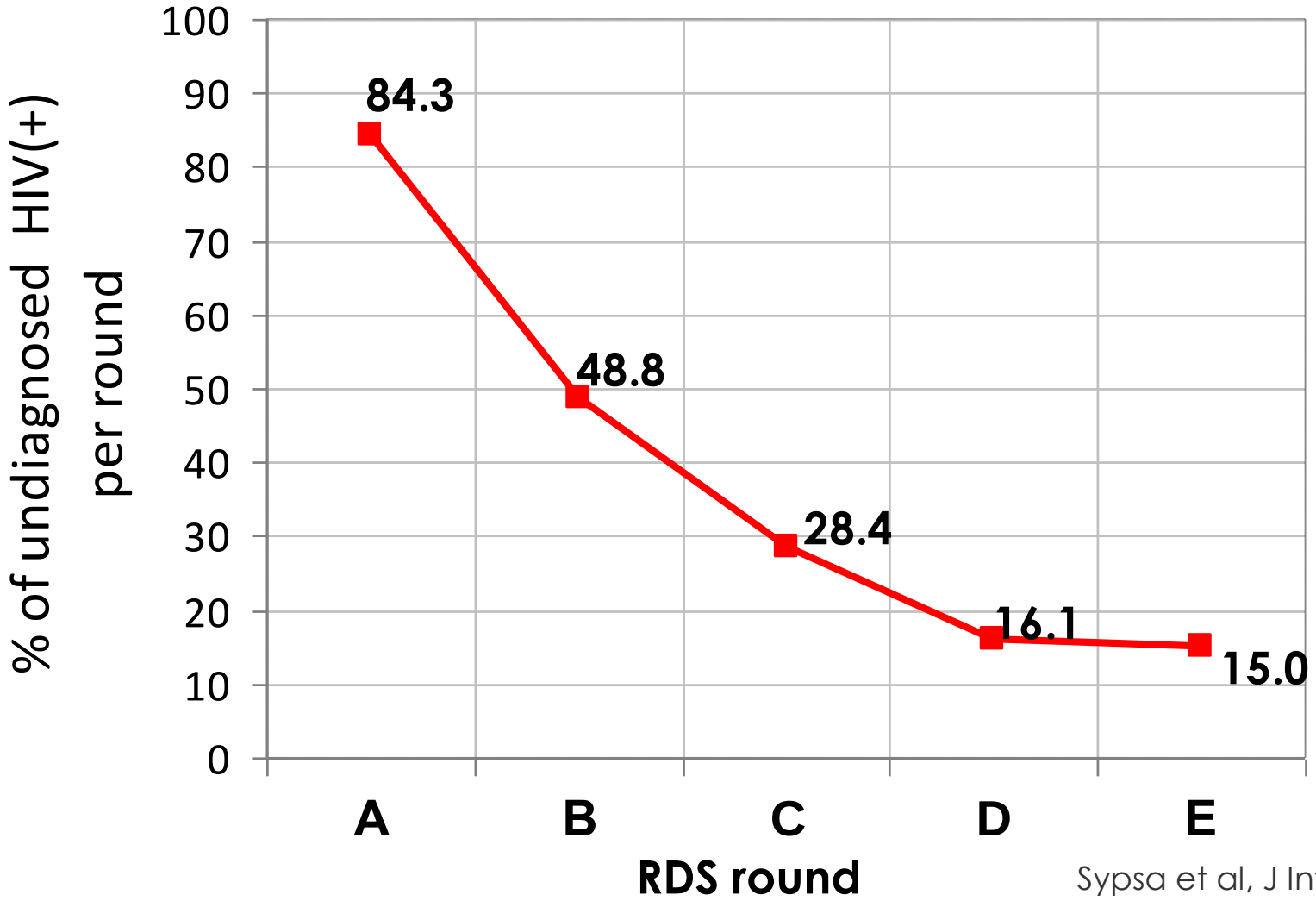
Sypsa et al,
J Inf Dis,2017

Decrease in the prevalence of high-risk behaviours



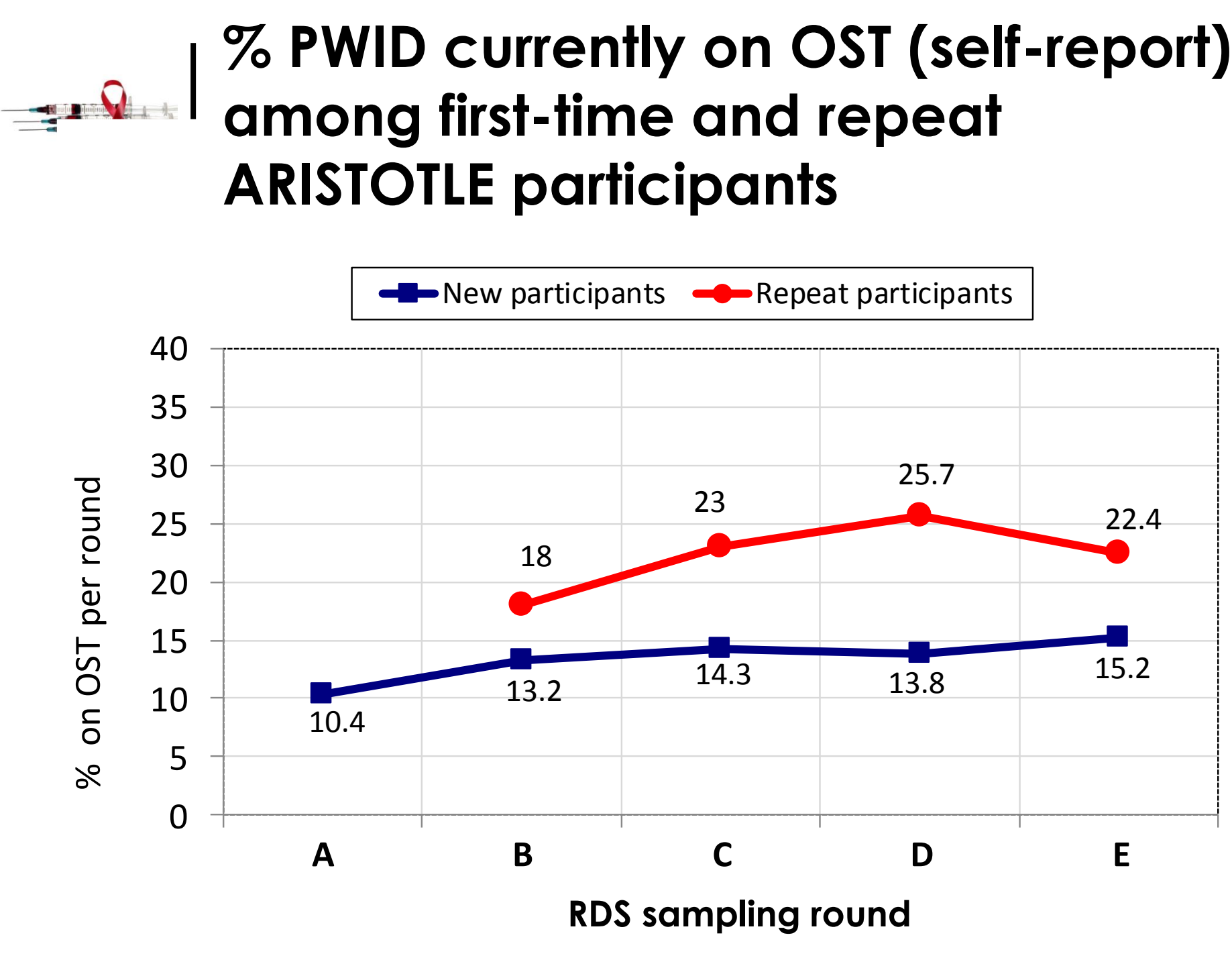
Sypsa et al, J Inf Dis 2017

Decrease in the % of HIV (+) who were not aware of their infection (undiagnosed fraction)



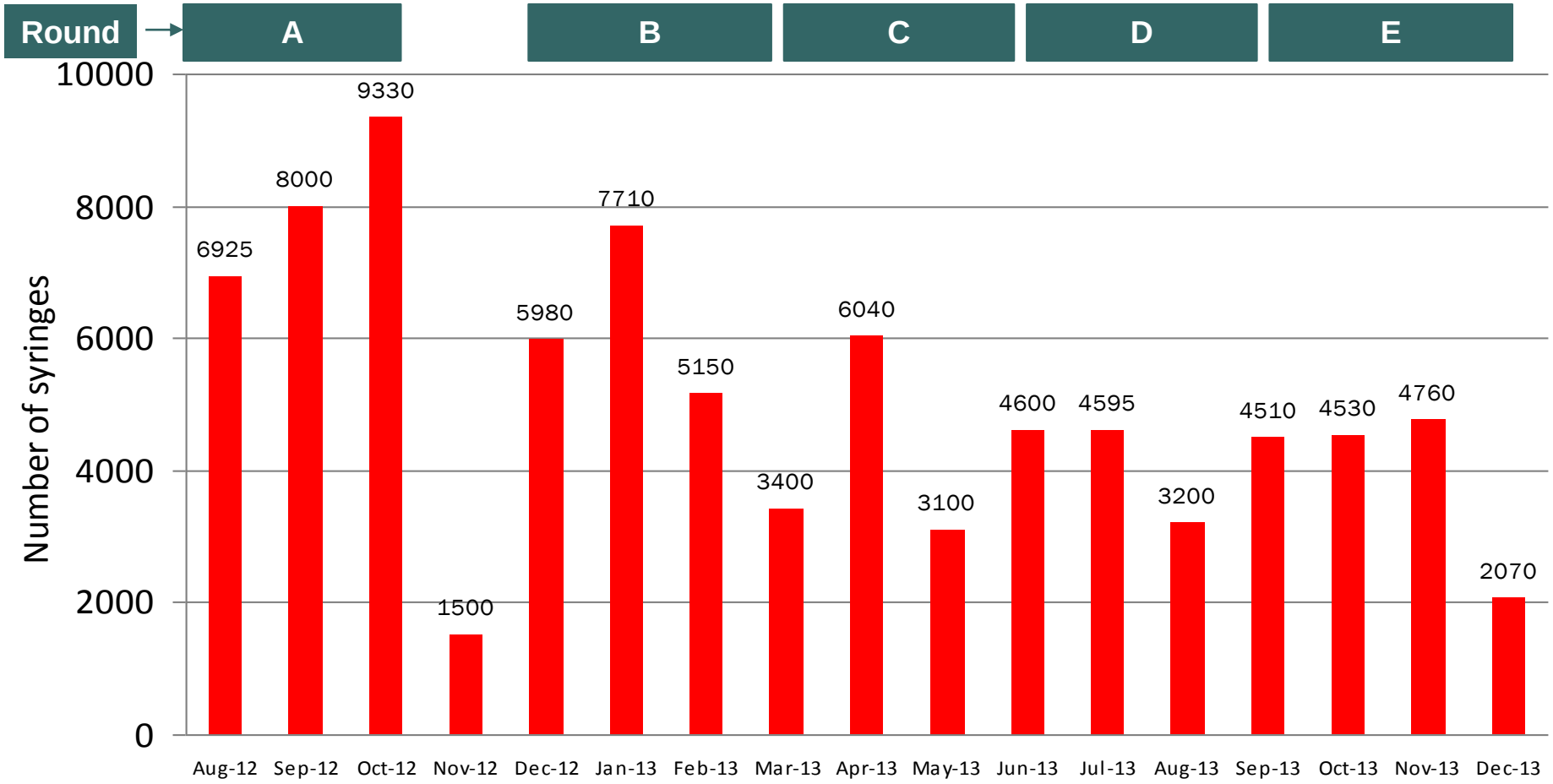
Sypsa et al, J Inf Dis 2017

% PWID currently on OST (self-report) among first-time and repeat ARISTOTLE participants

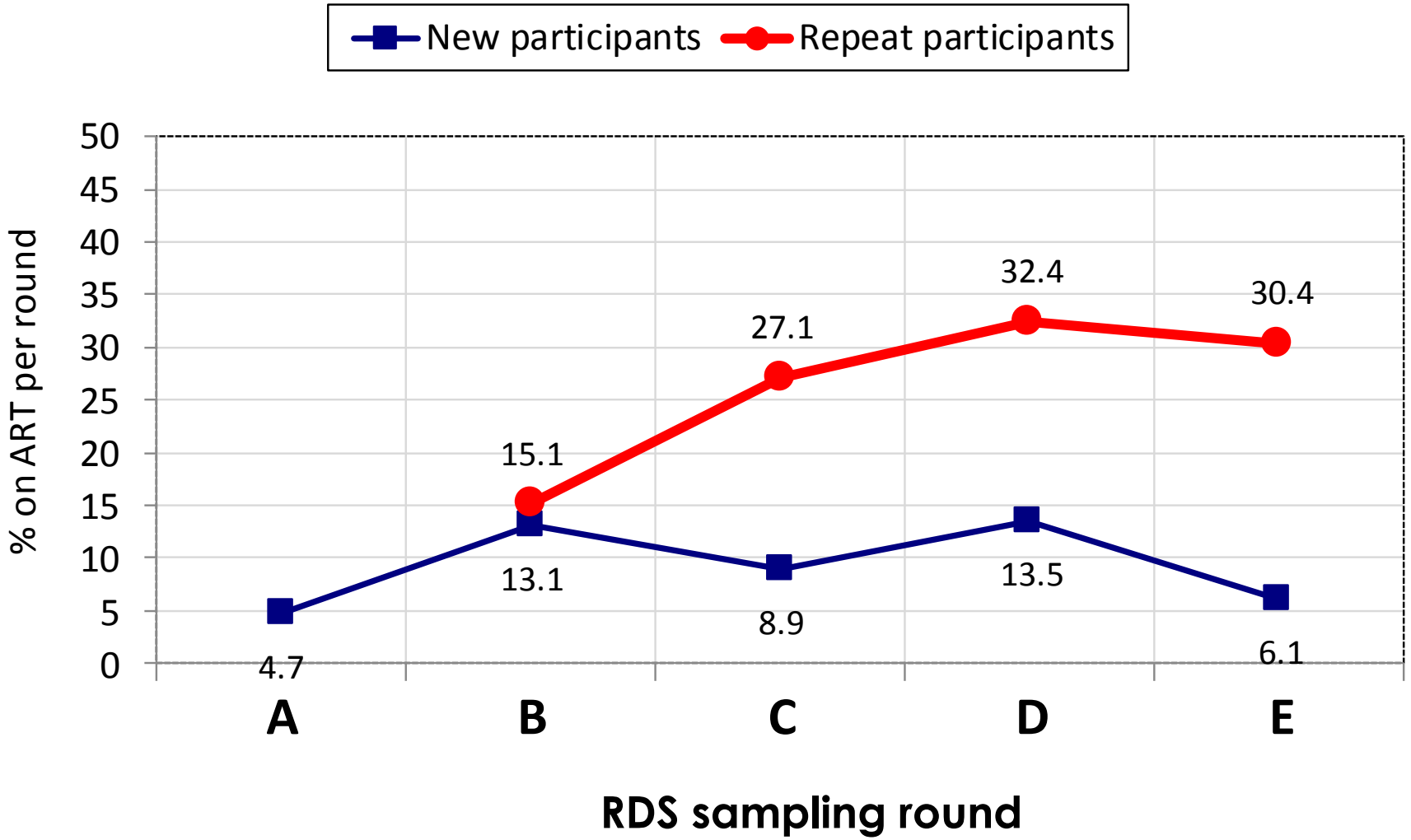


Syringes distributed to the participants of the program (Aug 2012- Dec 2013)

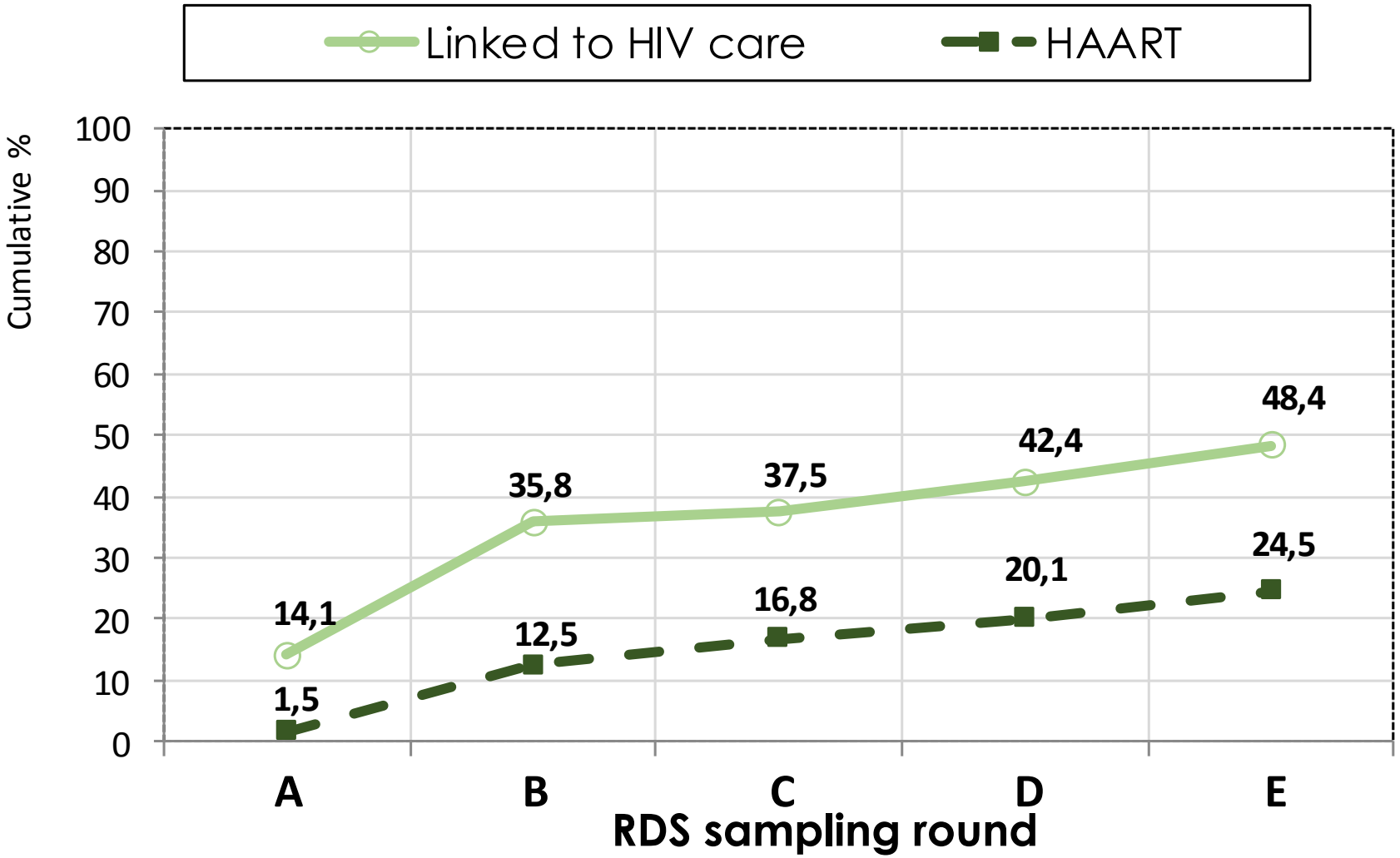
In total, 85,400 syringes were distributed in these 16 months



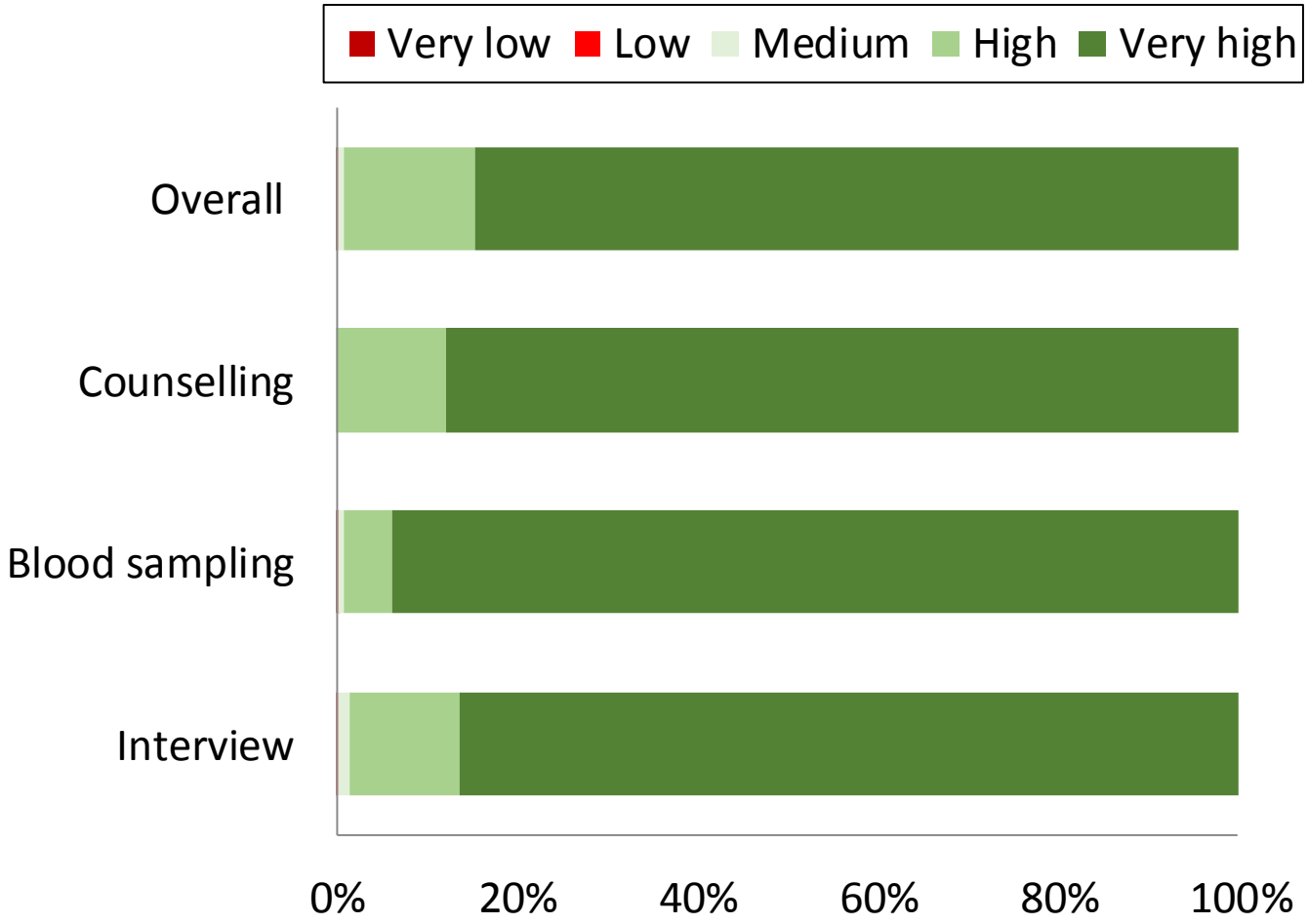
% of HIV positive currently on antiretroviral treatment among first-time and repeat ARISTOTLE participants



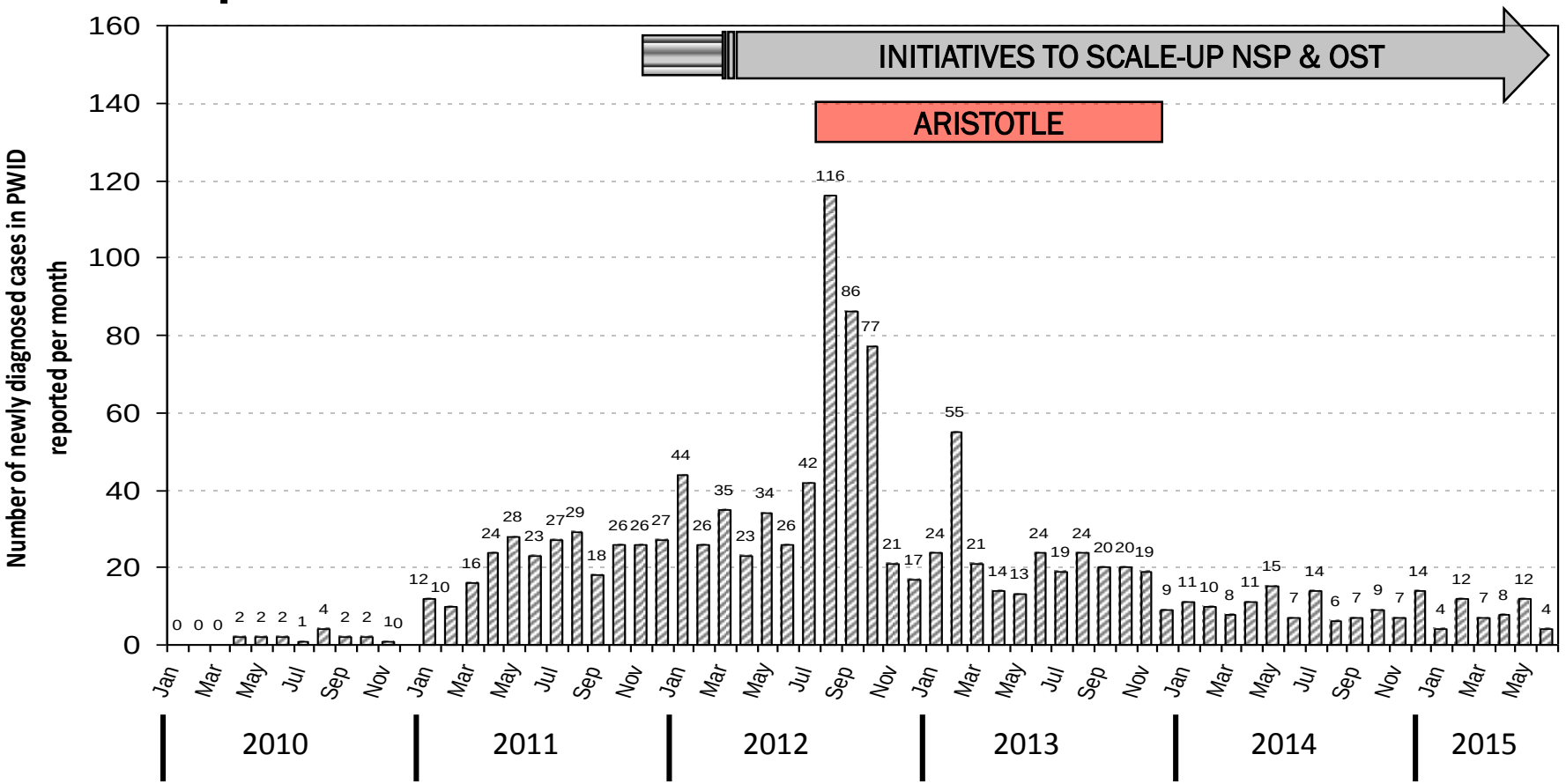
Cumulative proportion of previously unlinked HIV-positive PWID who were linked to HIV care and started HAART by the end of ARISTOTLE



Evaluation of the program by the participants: Level of satisfaction



1200 newly diagnosed PWID during 2011-2014 (data from the Hellenic Centre for Disease Control and Prevention)



Further decrease in the reported number of new HIV diagnoses among PWID (81 in 2016) but still higher than in pre-outbreak years

Short background information

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Lessons learned from the outbreak & the implementation of ARISTOTLE

ARISTOTLE in epidemic & non epidemic settings

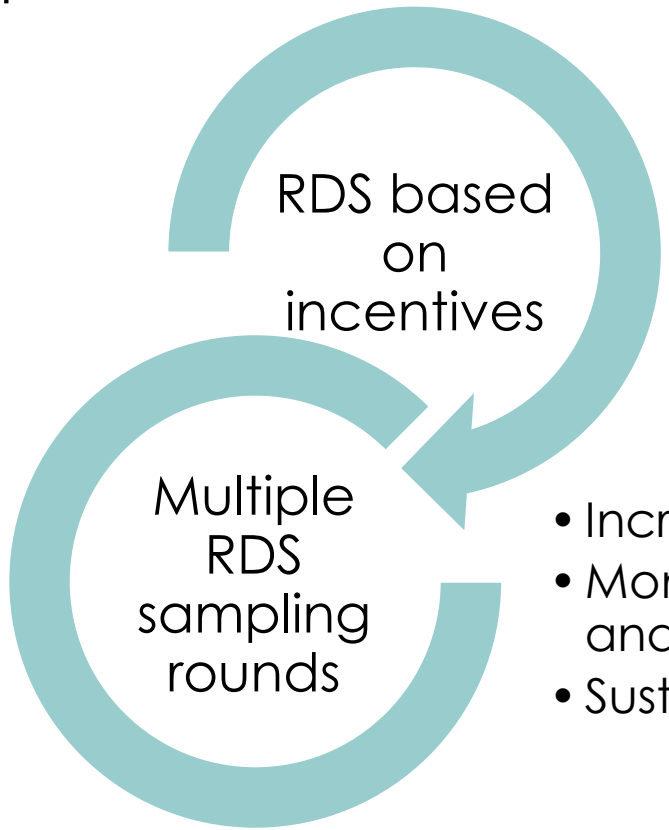
Lessons learned - 1

- HIV outbreaks among PWID could be triggered in settings with low coverage of harm reduction programmes, high prevalence of unsafe injecting practices and economic recession

- Apart from PWID practicing risky injecting behaviours, other vulnerable sub-groups:
  - Homeless
  - With history of imprisonment
  - Women with multiple sex partners
  - Migrants - due to high prevalence of homelessness and risky injection behaviours

Lessons learned - 2

- ARISTOTLE as public health intervention had unique characteristics:



- Effective & efficient recruitment
- High coverage
- Valid key population estimates (e.g. prevalence)

- Increased coverage
- Monitoring prevalence, incidence and risk behaviors
- Sustainability of intervention

In similar programs, ways to increase linkage to care should be considered

Why was ARISTOTLE successful?
(Chan & Flanigan, J Inf Dis 2017, Editorial)

1. Rapid mobilization
2. Focused on the entire HIV care continuum, including prevention, diagnosis, linkage to care, and treatment
3. Included community involvement and mobilization of PWIDs.
4. Incorporated a robust evaluation and monitoring component. Outcomes were rigorously measured, and the intervention was adapted accordingly

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In epidemic settings

Similar interventions

→ **timely and effective implementation of structural-level HIV prevention approaches.**

- Rapid mobilization
- Access to syringes, opioid replacement therapy, HIV testing, and linkage to care and treatment.

"As the HIV epidemic matures, rapid response and implementation of appropriate interventions to stem outbreaks is needed, especially among at-risk populations, such as PWID and MSM"

Chan & Flanigan, J Inf Dis 2017

In non-epidemic settings

The implementation of similar programs can help:

To recognize early the risk of an outbreak

To provide prevention, screening & linkage to care

To asses:
Retention to treatment
Undiagnosed fraction
Community viral load

Related papers

- Sypsa V, Psichogiou M, Paraskevis D, et al. Rapid Decline in HIV Incidence Among Persons Who Inject Drugs During a Fast-Track Combination Prevention Program After an HIV Outbreak in Athens. **J Infect Dis. 2017**;215(10):1496-505.
  - Editorial: Chan PA, Flanigan TP. Effective HIV Prevention Interventions and the Need for Rapid Mobilization to Address HIV Outbreaks Among At-Risk Populations. **J Infect Dis. 2017;215(10)**:1491-2
- Sypsa V, Paraskevis D, Malliori M, et al. Homelessness and Other Risk Factors for HIV Infection in the Current Outbreak Among Injection Drug Users in Athens, Greece. **Am J Public Health. 2015;105(1)**:196-204.
- Hatzakis A, Sypsa V, Paraskevis D, et al. Design and baseline findings of a large-scale rapid response to an HIV outbreak in people who inject drugs in Athens, Greece: the ARISTOTLE programme. **Addiction. 2015**;110(9):1453-67.
- Tsang MA, Schneider JA, Sypsa V, et al. Network Characteristics of People Who Inject Drugs Within a New HIV Epidemic Following Austerity in Athens, Greece. **Journal of AIDS**. 2015;69(4):499-508.
- Paraskevis D, Nikolopoulos G, Fotiou A, et al. Economic recession and emergence of an HIV-1 outbreak among drug injectors in Athens metropolitan area: a longitudinal study. **PLoS One 2013**; 8:e78941.
- Paraskevis D, Nikolopoulos G, Tsiara C, et al. HIV-1 outbreak among injecting drug users in Greece, 2011: a preliminary report. **Euro Surveill. 2011**;16(36).

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"ARISTOTLE" Advisory Board:

- S. Friedman, NDRI/New York
- D. Des Jarlais, Beth Israel/New York
- M. van de Laar, ECDC/Stockholm
- A. Pharris, ECDC/Stockholm
- L. Wiessing, EMCDDA/Lisbon
- M. Donoghoe, WHO-Europe/Copenhagen
- K. Gazgalidis, OKANA/Thessaloniki, Greece

- NGO PRAKSIS

PRAKSIS

- NGO Positive Voice

PositiveVoice
people+HIV

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