

Reacting to an outbreak



ARISTOTLE

Professor Angelos Hatzakis, together with **Professor Meni Malliori**, recently led a pioneering programme in Greece to curb an outbreak of HIV among injecting drug users. Here, he discusses its concept, implementation and benefits



In 2011, Greece experienced an unprecedented increase in the number of HIV-1 infections among injecting drug users (IDUs). How did this lead to the development of the ARISTOTLE programme?

Until 2010, the HIV epidemic was concentrated among men who had sex with men, with only a few sporadic cases among IDUs. In fact, between 2002 and 2010, only 2-4 per cent of newly diagnosed HIV infections per year were reported within this population. In 2011, however, this number increased sharply from 11 to 260 cases – more than 16 times the incidence in 2010. For the first time in over 10 years, intravenous drug use was the main route of transmission among newly diagnosed HIV cases.

It was then that the National Retrovirus Reference Center of Athens University Medical School and the Organisation Against Drugs launched the ARISTOTLE programme, a 'seek, test, treat and retain' intervention that managed to curb the virus' expansion and in so doing gained European and international recognition.

How was the idea behind ARISTOTLE born?

In mid-2011, we recognised the sudden HIV outbreak amongst IDUs in the Athens Metropolitan Area through case reporting and molecular surveillance. It was then that

our team decided to create ARISTOTLE. We wanted to rigorously apply research to inform interventions, while rapidly expanding prevention, care and treatment services, as recommended by the World Health Organization, the Joint United Nations Programme on HIV/AIDS, the European Monitoring Centre for Drugs and Drug Addiction, and the European Centre for Disease Prevention and Control.

Could you outline the ways in which the programme combined lab and field work?

ARISTOTLE was unique in that it was developed using hypotheses formulated in the lab, while at the same time expanding prevention, harm reduction, treatment and care services to control transmission of the virus on the street. When we started, time was of the essence to effectively address the outbreak, but it was also a luxury we could not afford. Therefore, we had to think outside of the traditional 'public health box' and very much within the 'evidence-based interventions box'. We had no time to run a pilot, assess its findings, and then design an intervention. We had to act immediately, while the outbreak was speeding out of control, but at the same time our actions had to be scientifically valid and economically cost-effective.

What do you consider the major success of ARISTOTLE?

The success of ARISTOTLE was, first and foremost, its contribution to the expansion of service provision, as well as its impact on changing risk behaviour and reducing HIV transmission among the injecting population. Rapid enrollment was secured with response-driven sampling and monetary incentives. ARISTOTLE contributed to achieving a moderate increase in sterile needles, syringes and condoms

distribution, and an increase in the number of persons receiving opiate substitution treatment (OST). Moreover, it linked 400 HIV seropositive IDUs to HIV care and documented decreasing risk behaviours through the programme.

How has ARISTOTLE contributed to long-term control of HIV amongst IDUs in the Athens Metropolitan Area?

The programme tried to urgently bring care to people in need, and because of its timeliness and user-friendliness, it had a very high participation rate and an equally high satisfaction rate. Through engagement in the programme's repeated rounds, participants were exposed to various and repetitive risk behaviour information, and by the latest rounds had started to engage in safer behaviours. Findings confirm that, following the programme, HIV prevalence stabilised at around 16 per cent, incidence of HIV infection was reduced by 78-88 per cent, and injecting risk behaviour declined from 11 to 5 per cent. Yet we must stay vigilant: these impressive results will need to be sustained in the long run, and this may require repeating the intervention.

It is said that for every dollar spent on prevention, five are saved in later healthcare costs. Did ARISTOTLE confirm the return on investment of preventive public health strategies?

Yes, we far surpassed the 1:5 ratio. Preliminary results confirm that for a total cost of €6.5 million – which includes the cost of needles, syringes and OST – ARISTOTLE managed to avert 2,000 new infections that would have required over €95 million for antiretroviral treatment over the next five years. We are very proud to confirm that for every €1 spent on the project, we have averted a future spend of approximately €14.

Seek, test, treat, **retain**

By combining laboratory testing with education and linkage to treatment, the **ARISTOTLE** programme has successfully curbed an HIV outbreak among injecting drug users, significantly reducing incidence of infection in this population and demonstrating the potential and cost effectiveness of harm reduction strategies

ACCORDING TO THE World Health Organization (WHO), around 16 million people across the world inject drugs, and almost 20 per cent of these individuals are living with HIV. Sharing equipment for drug taking, particularly unsterilised needles, carries a high risk of virus transmission. On average, one in every 10 new HIV infections is the result of injecting drugs.

HIV infection among injecting drug users (IDUs) is an important public health challenge. This problem became particularly acute in Greece in 2011, when there was a surge of new HIV cases reported among IDUs. In fact, in the first seven months of the year, 266 IDUs were diagnosed with HIV – a figure 16 times higher than in 2010.

In concert with austerity cuts, the economic downturn and limited resources, this

unprecedented increase created the perfect storm for an HIV epidemic in this vulnerable subgroup, with huge medical, social and economic consequences. The need for preventive interventions and epidemiological monitoring was urgent, and an effective response was needed quickly.

Dr Angelos Hatzakis, Professor of Epidemiology and Preventive Medicine and Head of the National Retrovirus Reference Centre at Athens University Medical School, works on the diagnosis, epidemiology, prevention and treatment of viral diseases. At the time, Professor Meni Malliori was leading an effort to open up access to opioid substitution treatment (OST) and needle and syringe exchange programmes (NSP). Observing this outbreak, they knew they had to act to stop the impending HIV epidemic in Greece. After conducting preliminary epidemiological

investigations, the group established the ARISTOTLE programme to rapidly diagnose and provide information, care and treatment to those in need, and ultimately decrease HIV incidence among IDUs in the Athens Metropolitan Area.

MOLECULAR SURVEILLANCE

Due to the rapid spread of HIV among IDUs in Greece, it was important to act promptly to study the characteristics and possible causes of the outbreak. As a 'seek, test, treat, retain' intervention programme, ARISTOTLE screened for HIV in IDUs in the Athens Metropolitan Area, and provided a prevention, linkage to care and treatment package to all those who tested positive.

From August 2012 to December 2013, respondent-driven sampling was used to recruit



ARISTOTLE: The process

- 1 Participant arrives at the ARISTOTLE site
- 2 Participant is screened for eligibility (must have injected drugs in the past year, live in Athens, and be 18 years old or over)
- 3 Consent is acquired
- 4 An interview is conducted and blood sample obtained for HIV testing
- 5 At the end of the process, each participant is paid a primary incentive, provided with coupons, and given leaflets on syringe use

Just three days later, the participant receives the HIV test result, a secondary incentive payment and, for those who have tested positive, counselling and referral for antiretroviral treatment and opioid substitution treatment.

ARISTOTLE

OBJECTIVES

To curb an HIV-1 outbreak among injecting drug users in the Athens Metropolitan Area by combining work in the lab with work in the field.

KEY COLLABORATORS

Dr Meni Malliori; Dr Dimitrios Paraskevis; Dr Vana Sypsa; Dr Maria Kantzanou; Dr Ada Katsoulidou, Athens University Medical School, Greece • **Dr George Nikolopoulos**, Transmission Reduction Intervention Project, Greece • **Tasos Panopoulos**, Organisation Against Drugs, Greece

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ANGELOS HATZAKIS trained in internal medicine and epidemiology. He has served as Director of the Department of Hygiene, Epidemiology and Medical Statistics at Athens University Medical School (2008-14) and in many executive committees, including the Hellenic CDC, of which he was President, and the Hepatitis B and C Public Policy Association, of which he is co-Chair and Founder. Hatzakis' research interests cover epidemiology, virology, and the prevention of viral diseases and oncogenic viruses. He is the author or co-author of more than 250 scientific papers.

participants. In order to increase the chances of containing the outbreak, ARISTOTLE needed to screen as many HIV-infected IDUs as possible in the shortest feasible period of time. Therefore, the team provided candidates with financial incentives. "The sampling technique began with a few initial recruits (seeds), who were asked to draw from their existing social networks to identify potential recruits and give them referral coupons," Hatzakis explains. Participants were rewarded for taking part themselves (primary incentives) as well as for recruiting others (secondary incentives), and they could also be involved in multiple sampling rounds. "Through this process, we succeeded in meeting (and even surpassing) our initial recruitment aim, recruiting 3,320 IDUs in total," explains Hatzakis. Around half of these recruits participated in multiple rounds, allowing the team to collect a rich dataset.

First, blood samples were collected from participants in order to test for HIV. Indeed, molecular biology techniques were crucial to achieving the programme's goals and directing its interventions, as Hatzakis elucidates: "Molecular surveillance validated the importance of migrant populations in the transmission of the virus. This was essential to further target awareness and outreach activities and so intercept the outbreak and optimise return on investment". To determine at what point in time participants acquired the virus, ARISTOTLE also used a limiting antigen avidity assay to identify recent infections. During the programme, 45 seroconversions were detected; in other words, HIV antibodies developed and become detectable in 45 individuals during the course of the programme.

SELF-REPORTING

The researchers complemented information from blood tests with behavioural information, obtained from interviews based on the questionnaire of the National HIV Behavioural Surveillance System. In the five rounds of ARISTOTLE, over 7,000 questionnaires and blood samples were obtained.

ARISTOTLE connected all those who tested positive for HIV to antiretroviral treatment, as well as treatment for drug dependence in the form of OST. "The idea was to offer people information on HIV/AIDS to engage them quickly in harm reducing behaviours, and then link them to care that they could sustain," Hatzakis adds. Furthermore, because ARISTOTLE was conducted in five sampling rounds, the same patients could

ARISTOTLE screened for HIV in injecting drug users in the Athens Metropolitan Area, and provided a prevention, linkage to care and treatment package

return for additional consultations. "Repeat consultations and ongoing support helped minimise high-risk behaviours and succeeded in reducing new cases," comments Hatzakis.

A RAPID DECLINE

As well as being used for treatment referral, the patient data allowed the ARISTOTLE team to assess trends in HIV incidence. Using data from repeat blood testing, the team was able to assess the impact of their interventions. Overall, HIV incidence among IDUs decreased by at least 78 per cent. Moreover, modelling suggests that IDU HIV incidence rates are now a striking 88 per cent lower than if the programme had not been implemented. The speed at which this change took place – little over a year – makes it even more astounding.

Adherence to OST also increased during ARISTOTLE. The proportion of participants who reported being on OST increased from 10 to 20 per cent over the five rounds. However, no scale-up was observed in the NSP. Although the proportion of participants receiving OST did increase, this alone cannot explain the dramatic decline in incidence rates.

WORLDWIDE ROLL-OUT

Through its multipronged approach, ARISTOTLE had significant impact in Greece. Of course, the large decline in rates of HIV infection could be the result of multiple factors, including the scale-up of HIV screening and OST, improved antiretroviral treatment coverage and increased awareness on high-risk behaviours. Separating the effect of the programme on incidence rates from other factors is complex. Nevertheless, it seems that ARISTOTLE acted as an induction network, stimulating interactions between IDUs (peers within the network) to encourage them to adopt similar behaviours (behavioural diffusion). There was also a notable increase in knowledge of HIV status. In the first round, only 20 per cent of those who were HIV positive were aware; this figure had risen to almost 90 per cent by the final round.