

ICAR 2011: Abstracts

CO 01

THE LOWEST X4 GENO2PHENO-FALSE POSITIVE RATE IS ASSOCIATED WITH GREATER CD4-DEPLETION

M.M. Santoro¹, D. Armenia¹, L. Fabeni², M. Santoro¹, C. Gori², F. Forbici², V. Cento¹, V. Svicher¹, A. Bertoli¹, L. Dori¹, M. Andreoni¹, P. Narciso², A. Antinori², F. Ceccherini-Silberstein¹, C.F. Perno^{1,2}

¹University of Tor Vergata, Rome, Italy; ²I.N.M.I. “L. Spallanzani”, Rome, Italy

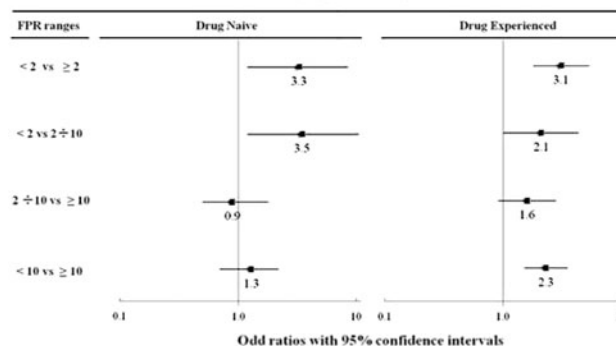
Background: CXCR4 phenotype has been associated with increased severity of HIV disease, higher viral load, and decreased CD4 T-cell counts. We thus evaluated whether a genotypic analysis of coreceptor tropism impacts on HIV-related markers such as CD4-cell counts.

Methods: 960 HIV-1 B subtype infected patients (all maraviro-naive) with an available V3 sequence were analyzed. Tropism determination was performed by using Geno2Pheno algorithm. All V3 mutations, including the mutations used for tropism prediction (Sing T et al., Antiviral Therapy 2007), with prevalence >1% were considered. The associations of CD4 cell counts with false positive rate (FPR) ranges and V3 mutations were evaluated by Mann–Whitney test, Chi-squared test for trend and Fisher exact test, as appropriate. The Benjamini–Hochberg method was used to identify results that were statistically significant in the presence of multiple-hypothesis testing. A false discovery rate of 0.05 was used to determine statistical significance.

Results: Overall, 26% of patients (either drug-naive or drug-experienced) were infected by X4 tropic viruses (using the classical 10% FPR cutoff). Among patients with available CD4 cell-counts at V3 genotypic test, 321 were drug-naive and 490 drug-experienced (median [IQR] CD4-cell counts: 331 [201–448] vs. 282 [138–422] cells/mm³, $p = 0.004$). CD4 cell-count <200 cells/mm³ was observed in 80 drug-naive patients and in 169 drug-experienced patients. For different CD4 cell count ranges, FPR <2% was mostly associated, in experienced patients, with CD4 cell-counts <200 cells/mm³ (<200 vs. 200–350 vs. 350–500 vs. >500 cells/mm³: 21.3 vs. 7.6 vs. 9.0 vs. 8.0%, respectively, $p = 0.0005$). This finding was also observed in drug-naive patients, even if with less significance (11.3 vs. 6 vs. 2.6 vs. 1.5%, respectively, $p = 0.040$). A deeper analysis showed that patients with FPR <2% (both naive and drug-experienced) carried a significantly greater risk of having CD4 counts <200 cells/mm³ (see figure). Among all V3 mutations analyzed (87 in naive patients and 88 in experienced patients), in drug-experienced patients the X4-related S11R was the only mutation found associated with CD4 cell count <200 cells/mm³ (17.8 vs. 5.6% in <200 vs. >200 CD4, respectively, $p < 0.001$). This significance was confirmed after correction for multiple comparisons.

Conclusions: Within the context of genotypically-defined CXCR4 tropism, FPR <2% and the X4-related mutation S11R are associated with low CD4 rank, and thus may be related with a greater risk of disease progression. These findings suggest that FPR, beyond tropism prediction, can be used also as a marker to evaluate the immunological status of HIV-1 infected patients.

Risk to have CD4 cell count ≤ 200 by false positive rate ranges in naive and drug experienced patients



CO 02

A GLYCOMIMETIC COMPOUND INHIBITS DC-SIGN MEDIATED HIV INFECTION IN CELLULAR AND CERVICAL EXPLANT MODELS

A. Berzi¹, S. Sattin², J. Reina², M. Sanchez-Navarro³, J. Rojo³, D. Trabattini¹, P. Antonazzo⁴, I. Cetin⁴, A. Bernardi², M. Clerici⁵

¹Department of Clinical Science L. Sacco, University of Milan, Milan, Italy;

²Department of Organic and Industrial Chemistry, University of Milan, Milan, Italy;

³Instituto de Investigacion Quimicas, University of Sevilla, Sevilla, Spain;

⁴Unit of Obstetrics and Gynecology, Hospital L. Sacco, Milan, Italy;

⁵Air of Immunology, University of Milan, Milan, Italy

Background: Development of topical microbicides and entry inhibitors is a promising approach to prevent sexually transmitted HIV infection. Mucosal dendritic cells (DCs) internalize HIV through DC-SIGN and, on arrival to lymphoid tissues, transmit the virus in trans to CD4 T lymphocytes, promoting HIV dissemination. DC-SIGN, thus, is a potential therapeutic target and the inhibition of HIV interaction with DC-SIGN may efficiently prevent the early stages of HIV infection. The DC-SIGN ligand is the HIV gp120 high mannose glycan Man9. We synthesized structural analogues of this glycan (using polyvalent presentations of di- and tri-mannoside mimics) in the attempt to compete with binding of DC-SIGN to HIV gp120.

Methods: Different experimental models were designed: (1) inhibition of trans infection was assessed by using B-THP-1/DC-SIGN cells. Ability of compounds to block lab and primary HIV-1 strains transmission to CD4 T cells was evaluated; (2) human endocervical explant tissues were treated with the compounds and then exposed to different HIV-1 strains in a non polarised manner. Infection was determined by measuring p24 levels in co-culture and in explant culture supernatants; (3) cytokines and chemokines production following stimulation of monocyte-derived DCs was analyzed. Toxicity of the compounds was evaluated in cellular and tissue models.

Results: One of the compounds tested, a tetravalent dendron containing four copies of a linear trimannoside mimic (compound 12), almost completely (>98%) abrogated the transmission of R5- and

PO 86

20-YEAR (1990–2009) CHANGING PATTERN OF PERSONS ATTENDING AT ITALIAN NATIONAL INSTITUTE FOR INFECTIOUS DISEASES (INMI) “LAZZARO SPALLANZANI” FOR HIV COUNSELLING AND TESTING IN ROME

F.M. Fusco¹, S. Pittalis¹, A. Navarra¹, G. De Carli¹, N. Orchi¹, P. Scognamiglio¹, C. Angeletti¹, E. Girardi¹, V. Puro¹, G. Nurra¹, G. Ippolito¹
¹Istituto Nazionale per le Malattie Infettive “Lazzaro Spallanzani”, Rome, Italy

Background: In Italy, since 1985, confidential and voluntary HIV counselling and testing (CT) can be obtained free of charge and, when requested, anonymously, in publicly funded sites by person self-referral (SR) or referred by a physician (PR). The HIV-CT site of the Italian National Institute for Infectious Diseases “L. Spallanzani”, Rome, is one of the largest in Italy and represents the regional referral centre.

Methods: In order to evaluate if reasons (not risk factors) for attending CT site and demographic characteristics vary over time, we retrospectively analyse data from 29,326 adults (54% women) receiving first lifetime HIV-CT divided into 5-year period each (1990–1994, 1995–1999, 2000–2004, 2005–2009).

Results: The number of persons seeking first lifetime HIV-CT progressively decreases (8,786, 8,311, 5,840, 6,384). The average age progressively increases (32, 33, 34, 36 years, overall median 31), as the proportion of foreign persons (6, 8, 15, 17%). About reasons for testing, heterosexual intercourse with partner of unknown serostatus (Het), that is the first motivation in 1990–1999 (36%), significantly decreases in 2000–2009 (26%), when the first reason becomes pregnancy/family planning (Preg). The proportion of persons stating the use of injecting drugs (ID) as reason for HIV-CT decreases considerably (3, 1.5, 0.6, 0.4%), while an upward trend emerges in the proportion of persons who require HIV-CT because of clinical symptoms considered as HIV-related (6, 8, 9, 11%). Other main reasons for testing, i.e. sexual intercourse with a known HIV+ partner (SP+) and homosexual intercourse with partner of unknown serostatus (Hom), remain stable. Among those PR, main reasons are Preg and suggestive symptoms, while sexual intercourse is the main reason among SR. Overall, HIV prevalence is 3.2% in men, 1.4% in women: no significant time trend is noted. HIV prevalence do not vary among foreign persons (5.1 overall). The highest prevalence is among SP+ (14.9 overall) and Hom (11.3 overall; 9.4 in 2005–2009). HIV prevalence among Het decreases (1.2, 0.9, 1.2, 0.6), as Preg (1.9, 0.4, 0.3, 0.3) and ID (12 in 1990–1994, 0 in 2005–2009); conversely, HIV prevalence increases in persons who require HIV-CT for symptoms (3.2, 2.6, 7.4, 5.2), both in SR and PR.

Conclusions: our data highlights a changing pattern of persons attending CT site. The decrease of proportion of Het is in contrast with the increase of HIV-positivity among heterosexuals in Italy, and suggests that risk awareness among this population is decreasing. The increase of persons who require HIV-CT for symptoms may indicate an improved awareness of physicians and patients, or a higher proportion of late presenters. The advances in prevention, treatment and care of HIV infection support the need to optimise HIV CT programs: a better knowledge about reasons for testing should be used to develop targeted counselling and testing prevention strategies.

PO 87

RESULTS OF EPIDEMIOLOGICAL SURVEILLANCE OF AIDS CASES IN TUSCANY

J.J.V. Branca^{*2}, S. Pacini², M. Ruggiero³

²Department of Anatomy, Histology and Forensic Medicine, University of Firenze, Florence, Italy; ³Department of Experimental Pathology and Oncology, University of Firenze, Florence, Italy

The Regional Public Health System of Tuscany recently achieved remarkable successes in fighting AIDS with fewer than 10 deaths per year of diagnosis in 2008 and 2009 in a population of almost 4 million residents. Of the many factors that contributed to this success, here we shall focus on results obtained by accurate epidemiological surveillance conducted by the Regional Agency for Health (Agenzia Regionale di Sanità). It is worth noting that a regional registry of new HIV infections is not yet available; therefore the data reported here refer only to new AIDS cases. However, the very low numbers of AIDS deaths (2 in 2008 and 7 in 2009) seem to indicate that surveillance of new AIDS cases is probably the most effective epidemiological tool in fighting AIDS. In fact, data from the regional registry of new AIDS cases reveals that the male-to-female ratio for the incidence of AIDS has been essentially constant from 1985 to 2008 at ~3.6, whereas the purported mode of transmission changed drastically: from ~8% of HIV being transmitted heterosexually in 1985–1990, to ~44% being transmitted in that way in 2006–2008. Consistent with these data, in recent years (updated to 2009), 44.5% HIV-positive heterosexuals reported being aware of their serostatus before the diagnosis of AIDS, and 17.8% had been treated with antiretroviral drugs prior to the diagnosis of AIDS. Conversely, about 90% HIV-positive intravenous drug users reported knowing their serostatus before the diagnosis of AIDS, and 57% of them were treated with antiretroviral drugs before the diagnosis of AIDS. Regrettably, however, the probability of survival in the HIV-positive intravenous drug user population has been constantly lower than that observed in the other categories since 1996. Drug-associated multi-organ toxicity might have contributed to this phenomenon. Also the age trend for new AIDS cases shows interesting changes that might have contributed to the decline in AIDS mortality in Tuscany. In 1988, the mean age for new AIDS cases was 31 for males and 28 for females, whereas in 2009 the mean ages were 44.5 and 40, respectively. We believe that information strategies focussed on risky sexual behaviours might have contributed to this trend. In fact, a recent survey of teenagers' sexual behaviour (Indagine EDIT 2008) showed that 43.5% of teenagers had had actual sexual intercourse and only 37.9% (males) and 26.4% (females) teenagers reported more than three partners. Among female teenagers reporting more than three partners, 45% reported using condoms. Taken together, these most recent data are consistent with previous observations on AIDS epidemiology (Ital J Anat Embryol. 2009 Apr–Sep;114 (2–3): 97–108. Oct–Dec;114 (4):179–91), and may suggest that further improvement in AIDS patient survival could be achieved by focussing efforts on reducing or eliminating drug-associated toxicity.

PO 88**HIV/AIDS: UNA MALATTIA DIMENTICATA**

S. Corso^{*1}, A. Poggi², D. Romeo³, A. Alecci⁴, S. Franciolini⁵, A. Campani⁵, C. Bartolozzi⁵, F. Bacherini⁵, B. Di Giacomo⁵, F. Polverini⁶, S. Lo Caputo², F. Mazzotta²

¹LILA-Toscana, Florence, Italy; ²UOC Malattie Infettive-Azienda Sanitaria Firenze, Florence, Italy; ³UO Medicina di Comunità-Azienda Sanitaria Firenze, Florence, Italy; ⁴Dipartimento di Patologia Clinica-Azienda Sanitaria Firenze, Florence, Italy; ⁵UO Assistenza Infermieristica Territoriale-Azienda Sanitaria Firenze, Florence, Italy; ⁶Dipartimento di Statistica-Università di Firenze, Florence, Italy

The great progress in antiretroviral therapy have dramatically changed the evolution of HIV disease in the general population contributing to perceive the problem as solved: but the HIV epidemic continues to be present. The absence of effective public awareness campaigns and information on how to prevent infection, have led to a reduction in the number of HIV tests carried out. In order to promote information-educational intervention in Florence was designed a study to raise awareness and offer HIV testing to the general population. This epidemiological survey is designed to provide information on the prevalence of HIV in the Florence area. Assuming a prevalence of 1/1,000 in this area you need to performed 10,000 tests. The project began in March 2010 with an information campaign on 'HIV with material and brochures available in the main venues of the population, in the sites of medical general practices and in the collection centers where you can have the HIV test. The second phase of the study began in April 2010 after a period of training of nurses working in the collecting centres in Florence with the offer of the HIV test to all those who perform a general blood examinations. Blood samples collected were processed in the laboratory of serology in SM Annunziata Hospital in Florence. The HIV test is made after signing the informed consent from the patient is free of charge, in respect of privacy and if the patient so wishes, with full anonymity. The target population of this study is mainly composed of adults, were deliberately excluded the infectious diseases clinics and those of SERT in order to avoid selection bias. The time of the collection will continue until you reach the amount required but not later than October 2011. At December 31, 2010 patients who have joined the initiative have been 4,539. Only one patient resulted HIV positive and he has been sent to the Infectious Diseases Unit of SM Annunziata Hospital, where he began the routine specialist checks. The relevance of such awareness campaigns to increase the offer to the test is of great importance not only in the aspect of health education, but also in the early diagnosis of HIV-infected patients by ensuring an appropriate treatment.

PO 89**TOWARD IMPROVEMENTS IN HIV EPIDEMIOLOGY**

M. Prayer Galletti^{*1}, S. Pacini², G. Morucci², H.H. Bauer³

¹Department of Experimental Pathology and Oncology, University of Firenze, Florence, Italy; ²Department of Anatomy, Histology and Forensic Medicine, University of Firenze, Florence, Italy; ³Virginia Polytechnic Institute & State University, Blacksburg, VA, USA

Considerable efforts are expended for prevention of HIV infections and for treatment of HIV-positive individuals, and it is widely agreed that improvements in both areas would be highly desirable. Observing and understanding the epidemiology of HIV are centrally necessary for the design of strategies for both prevention and for

treatment. The way to improvement is to focus not on successes but on gaps to be filled or missteps to be corrected, so we discuss weaknesses of current practices and conundrums, why expected successes have not materialized. The fundamental uncertainty stems from the lack of a gold-standard HIV test. As a result, one cannot accurately compare HIV data from different global regions that use different testing protocols, for example, varying criteria for what constitutes a positive Western Blot or the availability or non-availability of PCR or culture tests, or drawing inferences about HIV infection based on the Bangui definition of AIDS. In addition to uncertainty in cross-country comparisons, lack of the gold standard entails a fundamental inability to detect, analyze, and correct for false-negative and false-positive test-results by direct means rather than indirect inferences. Therefore, considerable effort would seem to be warranted to prepare pure samples of HIV for establishment of a true gold-standard HIV test. The weaknesses in testing practices may well account for at least some of the troubling conundrums and mutually contradictory data that seem inexplicable. These troubling conundrums include: conflicting estimates of HIV infections and of HIV-disease deaths from equally authoritative sources; apparently drastically different primary modes of transmission in different geographic regions (primarily among drug injectors in Russia and Eastern Europe, primarily among married couples in sub-Saharan Africa, primarily among gay men and drug addicts in the United States and Western Europe); extreme racial disparities in HIV infection, with Asians and Asian Americans consistently less affected, by about one-third, than white Americans, while black Americans are affected by as much as an order of magnitude more than white Americans. Testing uncertainties doubtless also contribute to the confusion as to whether certain conditions (e.g. lipodystrophy or nephropathy) should be described as HIV-associated or as AIDS-associated. Although it is the time-honoured practice in science that such anomalies or conundrums are quarantined in the expectation that progress will eventually resolve them without research focused directly at the anomalies, it would seem in the case of HIV/AIDS that specific efforts would be worth pursuing to resolve at least some of these conundrums, because a better understanding would improve epidemiological data and understanding and help toward the design of better strategies for prevention and treatment.

PO 90**META-ANALYSIS AND UPDATE ON THE GENERAL AIDS EPIDEMICS PREDICTED FOR AFRICA**

P.H. Duesberg¹, D. Mandrioli¹, A. McCormack¹, J.M. Nicholson², C. Del Popolo^{*3}, D. Rasnick⁴, C. Fiala⁵, C. Koehnlein⁶, H.H. Bauer⁷

¹University of California, Berkeley, USA; ²Virginia Tech, Blacksburg, USA;

³Department of Anatomy, Histology and Forensic Medicine, Florence, Italy;

⁴Oakland, California, USA; ⁵Gynmed Ambulatorium, Vienna, Austria;

⁶Internistische Praxis, Kiel, Germany; ⁷Virginia Tech, Blacksburg, USA

Since the discoveries of a presumably new AIDS virus in 1984 and of millions of asymptomatic carriers in subsequent years, no general AIDS epidemic has occurred in the U.S., Europe, South America and Asia by 2010. Recently, however, Chigwedere et al. "estimated" that between the years 2000 and 2005, the new AIDS virus, now called Human Immunodeficiency Virus (HIV), had killed 1.8 million South Africans at a steady rate of 300,000 per year, based on information from the World Health Organization (WHO) (J Acquir Immune Defic Syndr, 2008). Here we investigate the

evidence for these claims in view of the paradoxes that (1) HIV would cause a huge epidemic in Africa, but not in any other continent despite global prevalence since 1985, and that (2) it would cause a steady rather than a classical bell-shaped epidemic, self-limited by immunity like all other new pathogenic viruses. Surprisingly, we found that the WHO does not even list any South African AIDS case from 1996 until 2007, and that Statistics South Africa attributed only about 10,000 deaths per year to HIV between 2000 and 2005, and thus 30-fold less than those reported by Chigwedere et al. In a further effort to find independent evidence for the reportedly new AIDS epidemic, we searched for losses of lives in South African population growth curves. Surprisingly, we found that South Africa had increased by 3 million between 2000 and 2005 extending a steady growth rate of 500,000 per year, based on statistics from South Africa, the US and the World Bank. This gain was an integral part of a monotonic growth trajectory from 29 million in 1980 before the AIDS era to 49 million in 2008. During the same time Uganda increased from 12 to 31 million, and Sub-Saharan Africa as a whole doubled from 400 to 800 million, despite high prevalence of antibodies against HIV. We deduce that the predicted epidemiological pattern of a new killing virus never showed up in Africa, and that HIV cannot be considered a killer virus from the demographic point of view.

PO 91

ACTIVE IN-THE-FIELD SURVEILLANCE REVEALS HIGH RATES OF HIV AND HEPATITIS INFECTION AMONG AN IMMIGRATE POPULATION

G. Stornaiuolo¹, V. Cuniato², G. Cuomo^{*}, E. Nocera², G. Brancaccio¹, M. De Rosa², A. Pontarelli¹, R.F. Natale², G.B. Gaeta¹

¹UOC Malattie Infettive ed Epatiti Virali, Seconda Università degli studi di Napoli, Naples, Italy; ²Associazione di Volontariato "Jerry Essan Masslo", Castelvolturno, CE, Italy

Background and aims: Barriers to access medical care may underestimate the actual number of HIV, HBV, HCV positive subjects among immigrant population.

Methods: We recruited prospectively an immigrant population from the year 1999 to 2009 in a prevalently rural area (Castelvolturno, Naples) with massive, often irregular, immigration. During the first 5 years (1999–2004) an active recruitment was performed using a mobile unit moving through the area. In the second 5 years (2005–2009) only outpatients coming voluntary in the medical centre were recruited. Medical history was collected with the aid of cultural mediators using a pre-coded questionnaire. Each subject was tested for HBsAg, anti-HBs, anti-HBc, HBeAg, anti-HBe, anti-HCV, anti-HIV.

Results: 2,681 subjects were observed (945 and 1736 in the two study periods), having a median length of stay of 3 years. Median age was 31 years (range 2–75), 52.8% were males, 82.3% came from Sub-Saharan Africa; 64.6% had a middle-high school education level; 13.9% of women were sex workers. 129 subjects (5%) were HIV Ab positive. HBV coinfection was present in 17 patients and HCV coinfection in 9 patients. 206 subjects were HBsAg positive (7.6%), 84 (3.6%) anti-HCV positive. 84 patients (3.1%) were drugs addicted, 436 (16.3%) were alcohol abusers. Anti-HBs were present in 28.2%. The prevalences of HBsAg and anti-HCV remained constant throughout the study period while HIV significantly decreased. HIV patients were more frequently women ($p = 0.0001$), sex workers

($p = 0.0006$) and actively recruited ($p = 0.0001$) than HBV and HCV patients. HCV patients were significantly older than HBV patients ($p = 0.0018$), and were more frequently drug and alcohol addicted ($p = 0.0001$ and 0.003 , respectively). At multivariate analysis, HIV infection was independently associated to female gender ($p = 0.01$), drug addiction ($p = 0.008$), and the active way of recruitment ($p = 0.04$), HBV infection to male gender ($p = 0.0001$) and HCV to drug addiction ($p = 0.0001$). Among sex workers about 25% of the subjects referred not to use condom or its sporadic use, but there were no differences in HIV prevalence as compared with those reporting a systematic use of condom.

Conclusions: An active recruitment can demonstrate a substantial prevalence of HIV and hepatitis infections. We can expect an escalation of the economic costs associated to chronic liver disease and HIV management and to educational and prevention campaigns.

PO 92

A WANDERING BUS FOR THE PREVENTION OF HIV AND SEXUALLY TRANSMITTED DISEASES: THE PROJECT "PARLIAMONETOUR" (LET'S TALK TOUR) OF THE COTUGNO HOSPITAL

A. Franco¹, E. Guidetti¹, M. Figoni¹, C. Dell'Isola^{*1}
for "PARLIAMONETOUR" Group co-authors, A. Giordano¹
¹Monaldi-Cotugno-CTO Hospital, Naples, Italy

Introduction: The Cotugno Hospital in Naples since some years has been extending its interests beyond the specific mission (diagnosis and treatment of infectious diseases); in view of this, and to coincide with World AIDS Day on 1 December 2010, the same has started throughout Naples a project of information and prevention about sexually transmitted diseases (STDs), focusing especially on HIV, because prevention represents the most important investment in public health.

Materials and methods: The organization has provided for the involvement of all the ten municipalities of Naples, with the help of an equipped bus travelling (Figure) from 29 of November to December 12 2010. Several stops has been programmed nearby secondary schools to promote encounters with some experts (specialists of infectious disease, psychiatrists), also by answering to dedicated interviews (7 multiple choice quizzes on HIV infection, using a spreadsheet on-line). The operational plan also envisioned the distribution on the same bus of brochures on both HIV infection and the services of the hospital and the presentation of the project for distance learning already made in 2009 by a multidisciplinary team of Cotugno, that offered a full explanation on AIDS and STD to students through the use of a platform for e-learning on the company website (<http://www.ospedalecotugno.it>). The participants at the project received a T-shirt dedicated to the event. The ambitious proposal called "PARLIAMONETOUR" has been designed using an ad hoc logo and a slogan already forwarded by the "Forum of Public Administration 2010" (... health is contagious) and found the adhesion of some sponsors.

Results: The project has involved in 14 days of activity 54 medical trainers (26 from Cotugno Hospital and 28 from public and private hospitals), and 3 facilitators and assistants; the overall respondents were 2,686 (1,385 M, 1,301 F), mostly young people and adolescents (1,712 <20 years), with a good instructional level (1,461 with a college or university education). An evaluation summary of the seven item multiple-choice questions (some of whom had only intended to