Uncontrolled proliferation of the co-authors of clinical and observational studies, and inter-cohort analyses, in the field of clinical management of HIV disease

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In a previous article [1], we expressed concern about methods of conduction of the most important studies, related to the most significant publications about HIV natural history and its management, which, since 2008, have been based on studies conducted on a consistent number of patients from all over the world, with the main aim to obtain, in relatively short time, statistical significant data (not always synonymous of statistical clinical meaning). Moreover, these mega-studies (often retrospective analyses, or post-hoc experiences) were signed by hundreds of the so called "collaborators", all of them "elevated" to the rank of true Authors, through the placement of each single name in all major databases and search engines of the international scientific literature, right since 2008 [1].

In the following years (2009-2010) this phenomenon has, if possible, increased exponentially, leading to a multiplication of these "collaborators", who, until that date, were just listed in a note in the Acknowledgments section of the article, and were not considered as real authors. The current situation seems to lead to a somewhat unacceptable inflation of the author's role itself in biomedical publications, based on the well-known statement that should be considered as author one that has given a substantial supply to the design of the study, data results and evaluation, while those who contribute to data collection cannot be included among the Authors.

As a specialist in infective diseases, here I would like only to highlight the situation of the most relevant studies in HIV infection, but obviously the same "infection" is contaminating (to use a word common in my field) the whole world of biomedical literature. Even though it is necessary to have wide databases aiming at evaluating the events that happen less frequently, to examine consistent long-term endpoints or pharmacologic safety profiles, nonetheless considerable bias and distortions happen, as a consequence of the extremely high number of the Centres and of the investigators, recruited in a planetary scale [1].

As an example, in Table I are listed the most significant and recent studies (published in 2009-2010) that have also affected the guidelines of the management of HIV-related comorbidities. These studies appear to be burdened by an enormous number of authors and collaborators that clashes especially if compared with the number of patients of cases followed, and with the times of observation and inter-

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Main outcome and main endpoints of the study	Sample (n. pz.)	Study period	Main authors (n.)	"Co-authors" (fully indexed in PubMed - Medline) (n.)	Reference
Mortality of HIV-related events	31,620	43 months	19	855	*Clin Infect Dis* 2009; 48: 1138
HIV infection therapy with interleukin-2	5,806	7-8 years	18	949	*N Engl J Med* 2009; 361: 1548
Efficacy and safety of etravirin	1,203	48 weeks	12	181	*AIDS* 2009; 23: 2289
Accumulation rate of viral mutation during NRTI therapy	538 pt./ year	4.3 years	10	176	*J Infect Dis* 2009; 200: 687
Virologic outcome based on genotipic resistance that determines therapeutic variation	634	24 weeks	15	102	*J Antimicrob Chemother* 2009; 64: 616
Viral interferences in HIV-positive patients co-infected with HBV, and/or HDV, and/or HCV	72	N.D.	12	147	*J AIDS* 2009; 51: 574
Mortality rate for HIV-infection and tubercular co-infection	1,075	3 years	19	353	*AIDS* 2009; 23: 2485
Response to interferon-ribavirin therapy in patients HIV-HCV co-infected	100	24-72 weeks	11	41	*Curr HIV Res* 2009; 7: 447
Co-infection with HCV and CD4+ lymphocites count	4,208	< 3 years	10	148	*J AIDS* 2009; 50: 457
Interruption of nevirapine because of toxicity, or patient's or physician's choice	16,733	N.D.	11	435	*AIDS* 2009; 23: 1689
Effects of the antiretroviral therapy on overall mortality	62,760	3.3 years	0	1,179	*AIDS* 2010; 24: 123
Life-expectancy in case of HIV-infection of recent diagnosis	17,580 pt./year	6 months	5	130	*AIDS* 2010; 24: 1527
Definition of metabolic syndrome in HIV-infected patients	178,835 pt./year	7 years	10	596	*AIDS* 2010; 24: 427
Mortality rate in patients naïve to antiretrovirals with CD4+ lymphocytes count > 350 cells/µl	80,682 pt./year	N.D.	24	353	*Lancet* 2010; 376: 340
Duration of the HIV replicative suppression as predictor of virologic failure after therapeutic switch	451	N.D.	10	194	*HIV Med* 2010; 11: 469
Increase of CD4+ lymphocites count during viremic suppression, in relation to previous virologic failure	3,537	Up to 51 months	15	118	*Clin Infect Dis* 2010; 51: 456
Incidence of malignant carcinoma and prognostic role of CD4+ lymphocytes count	6,695	58 months	12	143	*Clin Infect Dis* 2010; 50: 1316
Renal toxicity in HIV-positive patients treated with antiretroviral drugs	21,482 pt./year	N.D.	10	197	*AIDS* 2010; 24: 1667
Plasmatic concentrations of raltegravir with and without administration of maraviroc	54	6 months	13	80	*Ann Pharmacother* 2010; 44: 838
Tolerability of atazanavir-ritonavir versus lopinavir-ritonavir	599	6 months	7	105	*AIDS Care* 2010; 22: 677
Correlation between genotype and HBV viraemia during chronic hepatitis in HIV-positive patients	16,505	N.D.	10	196	*J Antimicrob Chemother* 2010; 65: 548

Table I. Highly relevant studies published in 2009-2010 about the natural history and management of HIV infection and related complications, listed highlighting the number of authors and co-authors, as cited in PubMed-Medline database

ND = transversal studies or investigations performed with follow-up times different for each group of patients

vention. In these studies about HIV infection and AIDS, the so-called collaborators represent in reality the responsible of the Clinical Centres involved, all over the world, in the study, and in addition some sub-investigators of the belonging to the same Centres, who, in most of the cases, are responsible for the enrolling or the registration of a very little number of patients or events for each Centre or each investigator. For example, a trial published in 2010 has been signed by 13 principle authors and 80 collaborators, all indexed on PubMed-Medline. These authors examined the pharmacokinetic characteristics of an antiretroviral agent administered in association with another anti-HIV drug in no more than 54 patients, followed for 6 months [2]: it is therefore evident that each collaborator has followed an avarage of 0.58 patients, and nonetheless is included among the authors of a relevant scientific publication, included in PubMed with its update in 2008.

Likewise, a total of 204 authors and collaborators analysed the temporal suppression of HIV viraemia as a predictive factor of virologic failure in 451 patients (that is to say, an avarage of 2.21 patients enrolled by each collaborator or author) [3]. A previous trial, published in 2009, examined the role of interleukin-2 in 5,806 patients followed for 7 years, but the total number of authors plus collaborators is 967 (an avarage of 6 patients, thanks to which every collaborator has been listed as author of the prestigious *New England Journal of Medicine*) [4].

At the same time, all these mega-trials that have an extreme high power in affecting clinical practice, because their results are included in international clinical guidelines about HIV management, can lead to distortions, and in particular the possibility that a sort of hyperinflation of the number of the samples have been made in favour of statistic evaluations: a high number of patients or events or post-hoc analysis are usually made on data coming from hundreds of Centres disseminated all over the world, aiming at reaching a sufficient statistical power, without taking into consideration the possible bias regarding enrolling, measurement, and registration of extremely sensible data, of the time passed in long term studies, and of the inter-human differences about gender, race, BMI, and genetic and pharmacogenomic features, only to cite some of the most evident examples [1].

Parallely, in the same studies there is, as previously described, the phenomenon of the inflation of the number of the so called co-authors (in reality, nothing more than collaborators), that introduces other distortions during the evaluation of the scientific production of each investigator. Unavoidable consequences are then possible in the evaluation of academic curricula and in the consequent recognitions, for the obtainment of institutional funds, or external sponsorships, or the prestige of the institutions themselves.

In reality, the problem of the proliferation (sometimes inadequate) of the authorship is a well known phenomenon since twenty years and concerns all the fields of the research and clinical medicine, but nonetheless is and remains a scarcely debated topic, as emerged from the few articles published [5-9].

In my opinion, all the involved authorities, starting form scientific associations and biomedical journals and publishers, should become aware of this increasing problem and of the implicit distortion and scientific, technical, and ethical related consequences, with the goal of developing some rules that can guarantee the maintenance of the central and critical role of the authorship, as currently intended, and of preventing and avoiding the main bias related to the conduction of mega-trials and inter-cohort analyses, often signed by a disproportionate number of co-authors. Probably, it appears correct to list an adequate number of authors that contributed in first person in conceiving, following, writing and discussing the study (the so called "steering committee"). The remaining co-investigators should better be represented using an acronym or a "corporate" denomination, that comprehends in a single abbreviation all the co-investigators that took part in the study, that can be then listed in a specific appendix, or in the standard Acknowledgement section, as it happened before 2008 (and as reported in the recent HIV-Causal Collaboration study which, even if not listing any author, allowed the inclusion in PubMed of even 1.179 presumed "co-authors") [10].

Scientific and practical consequences related to the publication and diffusion of these mega-trials deserve the maximum attention of all the scientific community.

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