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EDITORIAL

Research in GP: side effects of "large researches"

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The word "research" nowadays is having an undoubted fortune among GPs. Each Gp believes he/she is a beneficiary of researches or a researcher. Without contact with the Sacred Grail of trial, chi-square tests, t tests and NNT the GP feels "poor" and an "outsider". Besides, it seems foregone that the GP who wants to orient his work towards research must be connected to universities, organize researches that avoid small scale surveys; that try to publish on journals that are index-linked on medline[1,2]. In this context, Italian GPs and from many Mediterranean countries, deprived of an academic and institutional carrier, should give up. In order to develop a discussion, even if this means breaking a taboo, I think that a useful approach could be that of discussing the negative aspects of "research" in a GP's profession, and principally of those having larger dimensions or logistics. And we think it is congenial that an audit and research newsletter in GP has the will of describing the side effects of research in GP, in order to be able to identify the laws of "downfall", and build a research that is able to "soar" with major confidence, in the complex and difficult context of GP.

The HYPOTHESIS: ***bigger researches have greater side effects.***

I would like to develop a hypothesis: side effects are greater, the greater the adhesion of GPs to the systems of large researches. Actually, the productive machine of modern science seems to affirm the following equivalences: research = large numbers; research = large organization; research = hyper-planned experimentation. If it is unquestionable that these equivalences seem to grant an operative power to research, at the same time, a suspicion arises to whether they can actually produce considerable side effects to the GP's profession and to our discipline.

And a matter of fact, large numbers, an efficient and centralized organization, the complex "hierarchical" apparatus of Trials, risks separating us from tradition and from the context of our professional practice, in which every GP's attention must never be distracted from the single case, the single family, and from horizontal types of relational contexts, which are more qualitative than quantitative. From an organizational point of view, the GP always dwells in the shadow of an office with one or few GPs, while researches with large databases and large trials, assume founding virtual offices with hundreds if not thousands of GPs. GP, in the end, is lived on an economy of scale that is more similar to an artisan's store than to a medium size entrepreneurial logics that large researches imply, with relative financial aspects connected to private sponsoring or public financing. Large researches in GP, besides, request to GP researchers a strong informatics and/or bureaucratic standardization and homogenization, which many times stimulates an early quantification and/or codification of the patient's problems, dangerous for the decisional and welfare process in GP -creative and adaptive – which instead must respect the high-frequency of problems having a faint logics, "open" and psychosocial. The great quantity of codes, standstills and summons -required by such researches – many times risks becoming "cosmetics" and the decimation of imperfections, which is the real "fuel" of an Audit; it also risks worsening the ergonomic dimension of our work.

What strategies to minimize side effects?

The previous mass of side effects may induce more than one person to affirm that research is not recommended in GP. But in my opinion, this is a rash conclusion. Audit and

research are added values that cannot be renounced in modern GP, where informatics and telematics made many GPs emerge from a cultural isolation. The problem is not in the dilemma yes/no to research, but lies in part in the reduction of the "technological" "bureaucratic" commitment required to the single researcher GP, and on the other side, in the intensification of the discussion on "strategic" and "political" choices in large researches. Majority of the GPs whom organize researches and Audits must first of all ask to continue being a doctor at best, and only after, he/she can import the small modifications that a research, which respects the profession, requires; for example, it is useless to ask a GP to be a perfect machine and create coded problems or to "fill out" fields in his/her computerized clinical records: most of the time, this work can be carried out – in backstage – by computerized systems that are less rigid and of more quality. At the same time, GPs that participate in large databases should require clear decisional and democratic mechanisms, to be involved in discussions that regard the relationship between research and practical practice; among financers/ consignors and GPs; among the managers of the Databases and GPs that are on the bottom-line; between "GPs whom are authors of scientific articles" and GPs whom just "send the data". Each GP that participates in large trials or in large databases should at the same time, keep a tight healthy relationship with the self-audit and perhaps with circuits as ours, Netaudit, where the focus is on a pragmatic change of the professional quality level and "the scale" is deliberately limited: the rule "less than three hours of work" and generally no more than 20-25 cases (which should be evaluated one by one) for the Netaudit, guarantee a greater osmosis between a "collection" of data and return to the single clinical record, to the single case. Among other things, lately our circuit has timidly launched a section with "netauditstories" (http://www.netauditstorie.blogspot.com/), with the subtitle "colours among numbers", in which we try to exercise creating a relationship between numbers and quality in each Netaudit.

If, for example, we notice on the papers that in many Netaudits, there are too many empty fields in the laboratory tests, we try to fill-out the counts, and also to identify the various "case reports" or moments and places in which quality was missing. Continuing with examples, we have not transcribed the laboratory tests, even if the patient brought them in? Or the patients did not bring them back? And what would happen to the empty fields if the laboratories, in a new organizational context, sent via postal mail or e-mail the tests results, directly to us GPs? Well, in GP every respectful Audit and research must develop osmosis among "qualitative" and "quantitative" questions. Therefore, we ask ourselves: how can large trials and large databases respect this task? Maybe in this sense, the pilot experience in research, as our Netaudit, may supply some solutions to bigger researches … In short, "small is not only beautiful, but also indispensable in GP research" and "large research" can become a collective power only if every single GP in the trial network will be able to influence the power games that, frequently, remain the prerogative of a limited number of GPs, in growing contact with academics and universities or influent editorial groups, or with a "strong power" in informatics and public and private institutions and sometimes in decreasing contact with the "base". I am convinced that the side effects of large trial databases will be lesser and lesser, the more the GP group will develop an independence in its thoughts, alternative solutions (see i.e. our article on "Participated Consensus" in the "RP"3 Trial), democratic participation and collaboration on equal terms with more authentic professional researchers, which prefer the experience of a "transformational" to that of an academic carrier or a climb to power. For those like us in Italy and Europe that promote self-audit and researches that are sponsored on a voluntary basis and on a small scale, remains the need to carry out a complementary task, with a "setting" that is more refractory to side effects, but not without the danger of coming across the schism between scientific research and professional mandate. Research in GP also means to monitor and fill-in the distance between discoveries and quantitative knowledges and the "tastes" of our praxis.

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What is a Sensitivity Analysis?

Alessandro Battaggia; Lia Battaglia; Stefano Berardi; Anna Longobardi; Isabella Fracasso; Giuditta Motta; Giulio Rigon; Alberto Vaona: *E.Q.M. Association*

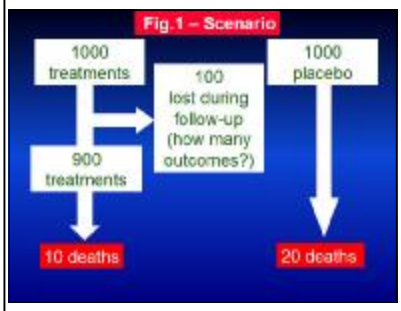
Preliminary Introduction

The E.Q.M. Association (*Evidence, Quality and Method in General Practice*) was constituted to produce services for quality Medicine <EBM-based> calibrated on the operative needs of Primary Care settings ands is opened to anybody that wants to actively participate in that sense. For information:
evidenzaqualitametodo@yahoo.it

The big problem of losses in the follow-up period.

In the previous number of the QQ journal we began treating the analysis of the quality during the follow-up period, an important

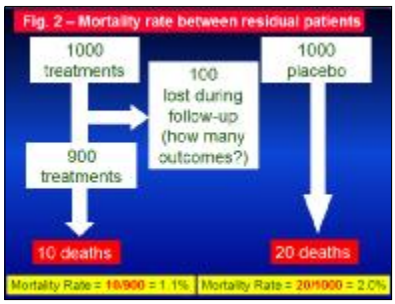
element in the methodological validity in a research. In order to exemplify this complex subject, we separated the problem of <non compliant> patients (examined in the previous number while discussing the Intention-To-Treat Analysis) from the problem of patients <lost during the follow-up> , which means patients of which we do not know the outcome. This article is dedicated to the analysis of this phenomenon. Just to make an example, let's imagine we conducted a RCT with the aim of studying the effects of a new medication drug on a disease that still does not have an identified therapy. In our trial we enrolled 2000 patients, 1000 of which were assigned randomly to the medication drug and 1000 to the placebo (**Fig. 1**).



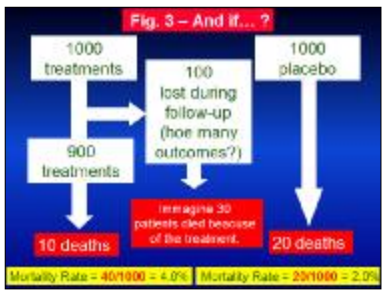
Among the patients assigned to the medication drug during the follow-up period, 100 left the experimentation and we know nothing about them. If we do not know the outcome it is obviously impossible to calculate with precision, the frequency of the event in the group in which these losses were recorded (in this case: the mortality in the intervention group).

Let's imagine that at the end of the experimentation, we had recorded 10 deaths in the group treated with the medication drug and 20 deaths in the group treated with the placebo. How do we carry out our calculations? It is natural to think that we should consider only those patients that remained in the trial, of which we know the outcome, ignoring the losses during the follow-up period. In this case, the mortality (Absolute Risk of Increase) recorded in the intervention group is equal to ARi = 10/900 = 1.1%, while in the control group ARC = 20/100 = 2.0%-up periodem of lost patients during er only those patients that remained in the study.

We therefore can conclude that in this disease that is usually fatal, the new medication drug is advantageous (it reduces mortality rate respect to the control group) (**Fig. 2**).



But what would happen if by hypothesis all patients lost during the follow-up period, all died for a side effect of the medication drug? (we do not know this, therefore cannot exclude it). The calculations in this case would be different because mortality in the intervention group would be greater than the one recorded in the control group. In fact: ARI = 40/1000 = 4%; ARC =20/1000 = 2%. (**Fig. 3**).



This simple example suggests how insidious it is not to fear, in calculating the frequency of an outcome, the serious problem of patient's loss during the follow-up period.

Theoretically and using an extreme logic, a study in which there are losses during the follow-up period, should not be taken into consideration. Not knowing the outcome of part of the patients we enrolled, we cannot in fact, correctly compare the frequency of the event in the two groups. Nevertheless, reality clashes with these "extreme" decisions.

Long trials will never lack losses during the the control groupoupsrt of the patients, in factiont during the follow-up period. ifferent because mortality in the int follow-up period: even if we exert maximum surveillance it is inevitable that part of the case study will get lost "along the road".

How do we manage losses in the follow-up period? Introduction to the Sensitivity Analysis.

It is convenient to underline, since there is a lot of confusion on these subjects, that the Intention-To-Treat Analysis (ITT) –treated in the last number – is not a system to manage the losses during the follow-up period, but rather it is a system *to manage the violations to the protocol*. An Intention-To-Treat Analysis assumes that at the end of the experimentation the outcome of all patients should be known; both of those patients that respected the protocol and those that violated it in some way (see the previous QQ number).

The only way to deal with unknown data is to make believe we know them, which means analysing them within "extreme" scenarios. This approach is defined in a quite general way as a **Sensitivity Analysis**. *A Sensitivity Analysis* allows to confirm or less the "weight" of the conclusions of the trials in which we had significant losses during the follow-up period.

It is important to say that modest losses during the follow-up period are considered "acceptable" and do not require further detailed analysis.

For example a loss during the follow-up period of 2-3% is considered quite as "physiological" in long-term large trials: losses of this type are not considered as dangerous and that may cause dangerous interpretative distortions. A practical example is, in the

ALLHAT study (considered an RCT having a good methodological quality) were randomized in the four experimentation groups of more than 40.000 people and the losses during the follow-up period in each group were approximately 3%; no *Sensitivity Analysis* was carried out in this study. Losses greater than 10% are considered a serious problem for most authors.

Some, as Sackett himself, "tolerates" losses up to 20%, but this type of attitude is definitely a minority. Probably (nobody knows, that's sure, the truth) it would be worth carrying out a *Sensitivity Analysis* only if the losses are greater 3% and less than 10%. In presence of losses that are greater than 10% of the cases enrolled, it probably would be opportune not to consider the conclusions of a trial as accurate. The cut-offs proposed here are absolutely arbitrary and must therefore be used cautiously.

In a *Sensitivity Analysis* applied to losses during the follow-up period, we usually imagine four extreme scenarios.

For each scenario the frequency of the outcome is calculated in one of the two groups and it is compared with the same datum recorded in the other group. For practical reasons, we will avoid using here an efficient measure that expresses this comparison in an aggregated manner (subject that shall be dealt with one of the following QQ numbers) and we shall therefore, only express the results by illustrating the frequency of the event recorded in the two groups and by signalling the "statistical significance" or less of the differences.

The four "extreme" scenarios are the following:

a)All patients lost during the follow-up period had an outcome, both in the intervention group and in the control group (scenario I)

b) None of the patients lost during the follow-up period had an outcome (scenario II).

c) Only patients lost during the follow-up period control group had an outcome (scenario III)

d) Only patients lost during the follow-up period intervention group had an outcome (scenario IV)

When the authors of a research do not carry out any *Sensitivity Analysis* it is simply that they ignored the problem of the patients lost during the follow-up period and this approach is called a "Complete Case Analysis".

A real scenario: Stent or Angioplasty after aorto-coronary bypass restenosis?

A study published a few years ago on the NEJM brilliantly highlights the problems associated to significant losses during the follow-up period (in this case: 22% of the entire cases). This research shall supply a real example that illustrates a *Sensitivity Analysis*.

Title: *Stent placement compared with balloon angioplasty for obstructed coronary bypass grafts. Saphenous Vein De Novo Trial Investigators. Savage MP, Douglas JS Jr, Fischman DL, Pepine CJ, King SB 3rd, Werner JA, Bailey SR, Overlie PA, Fenton SH, Brinker JA, Leon MB, Goldberg S.N Engl J Med. 1997 Sep 11; 337(11): 740-7.*

Methods: *The purpose of this study was to compare the effects of Stent placement with those of balloon angioplasty in patients with obstructive disease of aorto-coronary bypass. A total of 220 patients with new lesions in aortocoronary-venous bypass grafts were randomly assigned to placement of Palmaz-Schatz Stents (n = 110) or standard balloon angioplasty (n = 110). Coronary angiography was performed during the index procedure and six months later (….).*

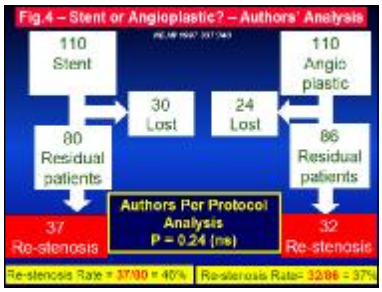
Results: *It was possible to examine the coronarography after six months in 6 80 patients that underwent Angioplasty and in 86 patients that underwent a Stent placement (…) Restenosis occurred in 37 percent of the patients in the Stent group and in 46 percent of the patients in the angioplasty group (P=0.24).*

Conclusions: *(…..) In patients with obstructive disease of aorto-coronary bypass that underwent a Stent placement* ***there was no*** *significant benefit in the rate of angiographic restenosis comparing the results of this group with the outcome of patients that underwent standard coronary angioplasty (…..).*

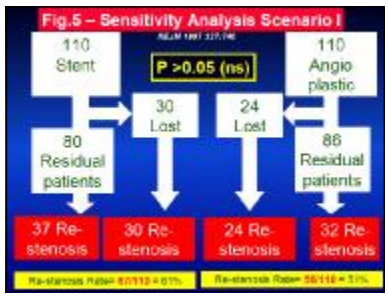
The possibilities of calculating our PTCA Stent in the trial are the following:

	Stent	**PTCA**
Restenosis yes	37	32
Restenosis no	43	54
Restenosis?	30	24
Tot	110	110

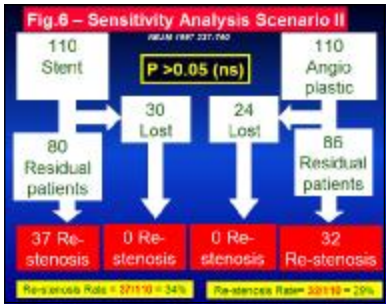
Complete case analysis (the losses during the follow-up period are ignored) (**Fig. 4**)
ARI = 32/86 =37%
ARC = 37/80 =46%
Insignificant result P>0.05



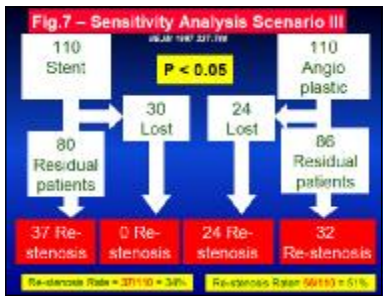
Sensitivity analysis (Scenario I: all patients lost underwent a restenosis) (**Fig. 5**)
ARI = (32+24)/(32+54+24) = 56-/110 =51% ARC = (37+30)/ (37+43+30) =67/110 = 61%
Insignificant result P>0.05



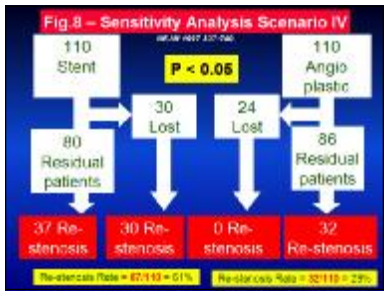
Sensitivity analysis (Scenario II: no patient lost underwent a restenosis): **Fig. 6***:*
ARI = (32)/(32+54+24) = 32/110 =29% ARC = (37)/(37+43+30) = 37/110 =34%
Insignificant result P>0.05



Sensitivity analysis (Scenario III: only patients lost in the control group underwent a restenosis) (**Fig. 7**)
ARI = (32)/(32+54+24) = 32/110 =29% ARC = (37+30)/(37+43+30) = 67/110 = 61%
Significant result P<0.05 in favour of the Stent



Sensitivity analysis (Scenario IV: only patients lost in the intervention group underwent a restenosis): **Fig. 8***:*
ARI = (32+24)/(32+54 +24) = 56/110 =51%
ARC = (37)/(37+43+30) =37/110 = 34%
Significant result P<0.05 in favour of Angioplasty



In this study it was not possible to establish the outcome in 54 patients (30 in the control group, 24 in the intervention group), which corresponds to 54/220 = 24, 5% of the entire cases. In presence of such a high percentage of "missing data" the validity within the experimentation results is quite compromised. The authors followed the procedure called "Complete Case Analysis" completely ignoring the missing data and evaluating the outcome (= number of coronary restenosis cases) on two outcomes (respectively: 37+ 43 = 80 patients in the control group; and 32+54= 86 patients in the intervention group) (**Fig. 4**).
In presence of losses in the follow-up period, the conclusions of an article can be, as mentioned, quite mystifying. In fact, where did the 54 patients end up? Admitting (extreme hypothesis in favour of the Stent) that all patients that underwent a Stent of whom we have no outcome (n°=24), did not have restenosis and that at the same time, all patients that underwent angioplasty, of whom we have no outcome (n°=30) suffered a stenosis, the trial result would be strongly in favour of the Stent: ARI=29% ARC=61% (P<0.05) (**Fig. 7**).

Imaging an opposite scenario, which means admitting (extreme hypothesis in favour of angioplasty) that all patients that underwent an angioplasty and of whom we do not know the outcome (n°=30) did not have a restenosis, and that at the same time all patients that underwent a Stent of whom we do not know the outcome (n°=24), suffered a stenosis, trial result would be strongly in favour of angioplasty: ARI=51% ARC=34% (P>0.05) (see Figure 8).

How is the missing data used?

Hollis analysed all the RCT reports published in 1997 on four prestigious journals (BMJ, Lancet, JAMA, NEJM): in presence of "missing data" the most common method of analysis is represented by not considering the missing data (complete case analysis: 44.49%).
It is clear that there still is a lot of work to do in the methodological field! In the next numbers we will study the meaning of the most common efficiency measures used in trials.

Underuse of NHS prescriptions by public specialists

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1) Context of our research
In the summer of 1991, the Regional Council of the Lombard region approved a resolution (DGR n 5/12317 dated 30 July 1991 "Acts that address access procedures to health services of the Lombard region"), with the aim of simplifying the bureaucratic procedures in occasion of a specialist consultancy; it prescribed that " the specialist of a Public Health Service, both working in a hospital and an office, may carry out further diagnostic tests, if deemed as necessary, to answer the questions of the GP, prescribing them directly on his/her prescription book without further interventions of the family doctor ". The following National Collective Agreements, both of GPs and of Specialists operating within the National Health Service, accepted the spirit and substance of the dispositions anticipated by the Lombard Council, up to the last national agreement signed in January 2005, which came into force the following spring.

2) Aims, instruments and method
This research proposes to verify, after almost 15 years, how the Lombard resolutions were applied by the public health specialists. Two GPs, which had an overall

		A	B	C
Prescriptions	Tot. Prescr.	Prescr. Suggested by public Spec.	Prescr. Suggested by private Spec.	Tests preswcribed by others (E.R. = 148)
Admissions	205	54 (26.3%)	61 (29.7%)	55
Examinations	1158	310 (26.8%)	164 (14.2%)	104
RX	640	90 (14.1%)	95 (14.8%)	119
TC	170	40 (23.5%)	51 (30.0%)	15
Eco	509	140 (27.5%)	99 (19.4%)	39
NMR	84	19 (22.6%)	39 (46.4%)	4
ECG	225	39 (17.3%)	37 (16.4%)	35
Tests various	467	94 (20.1%)	63 (13.5%)	18
Tot	3458	786 (22.7%)	609 (17.6%)	389

population of 3000 patients residing in the suburbs of Brescia and in the neighbouring towns, participated in this study. The observations lasted 6 months, from January to June 2005, during which the GPs "marked" the prescriptions for diagnostic tests and specialist visits (excluding biohumoral stic visitsdiagJunering towns0 assisted patientsnticipated by the Lombard Council tests, laboratory and cytological tests) in order to divide the prescriptions in these following categories:

A - GP prescriptions suggested by public health specialists,

B - GP prescriptions suggested by private or accredited specialists,

C –tests prescribed directly by other NHS professionals (public office specialists during a consultancy, patients in the anti-diabetes centre, tests and specialist visits prescribed and carried out in E.R., etc).

In order to assign the prescriptionsionalsalists tegories to one of the categories, the "expense origin" function was used of MilleWin management software, created by the Florentine *Datamat* informatics company.

3) Results

Table 1 reports the typology of the GP prescriptions made by public and private specialists, both overall and disaggregated per test typology, besides the tests prescribed directly by the specialist. The low number of samples was partially compensated by the six-month period of observation, during, which they recorded the following: -7626 direct office contacts between GP and patient - 1818 indirect office contacts -148 accesses in E.R. that patients did, without a request coming from the GP.

Table:

Number of Tests, Visits and Hospitalisations (the % of prescriptions made by specialists on the overall number that GPs made on their prescription books).

What must be underlined is that the type C prescriptions could be underestimated because of a sort of recording bias, since not all tests prescribed by the specialist on their NHS prescription books, reach the GP soon, and because of recordings on the computerised clinical record. We must also highlight that the overall tests suggested by the public health specialists, and transcribed by the GP on his/her own NHS prescription book (type A), must be subtracted by the prescriptions that are charged to the GP, since they are not part of the subjects regulated by the 5/12317 resolutions (hospitalisation proposals, tests suggested upon hospital dismissal, after an access in the E.R. or for distance follow-ups, etc).

4) Conclusions

During the period the data was collected, the specialists directly prescribed 389 tests and specialist visits, requested and carried out in about 50% of the cases in the E.R. (148 overall accesses), while the prescriptions transcribed by the GP (786 equivalent to 23% of the overall GP "prescriptions") after receiving a "suggestion" by a specialist were almost double, while they should have been charged to the specialists themselves, as the Lombard resolutions of July 1991 specifies. The results of the research, even if only partial, supply a scene of the situation that certainly is not reassuring. After almost fifteen years from the 5/12317 resolution, abouter almost fifteen years from theng specialists themselvesrescribed health specialistshe GP in a short time, and because of th 20% of the prescriptions for visits and tests attributed to GPs, should be drawn-up by public health specialists on their NHS prescription book.

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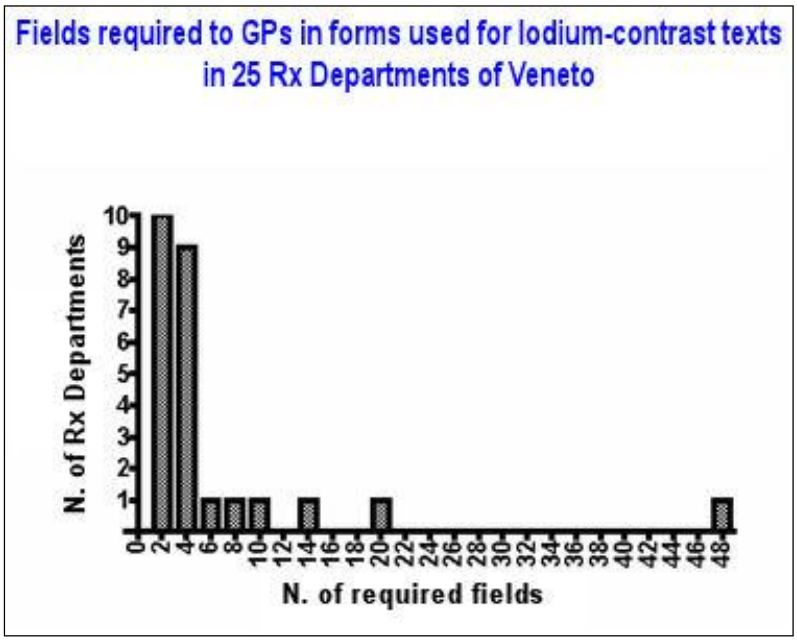
Contrasts on Contrast Media

Research by 12 GPs of List SIMG - Veneto
Baruchello M., Bianchin G., Cancian M., Del Zotti F.*, Fanton L., Fassina R., Gasparotto A.,Mazzi M., Negrini A., Ometto G., Pastori C., Pegoraro R.

Background
GPs often request radiological examinations with iodinated contrast media. In any case, even if there are clear guidelines that suggest only a small number of clinical-anamnestic evaluations and not to carry out laboratory tests, as GPs we have the feeling that the behaviour of some radiology departments is characterised by an excessive variability.

Method
The GPs in the SIMG-Veneto Mailing List were invited to send to one of the authors via fax, the printed forms that the different radiology departments use for examinations with iodinated contrast media. 12 GPs participated in this study and sent 25 forms belonging to 25 different departments of all the provinces of the region. For each printed form, we counted the number of clinical or laboratory fields, which were required to be filled out by the GP.



Results and conclusions
As you can see in the figure, there still is a moderate variability in the number of fields per form. The median is 3, but the average is 5.8 fields per form, with a standard deviation that isn't so small of 9.6 and consequent Variation Coefficient of 60%. Respect to the growing number of radiology departments that tend to be fairly closer to the guideline recommendations, principally in the province where the Medical Association that most intervened (Padua), there still is a number of radiology departments that resist and request even 14, 19, 20 and actually, in 1 case (in Bassano), 47 fields! We hope that this simple survey we carried out, will stimulate professional unions, GP associations, specialists and patients to reduce and standardise this field excess and these useless fields, which tend to compromise both the GP's job and our patient's everyday life.

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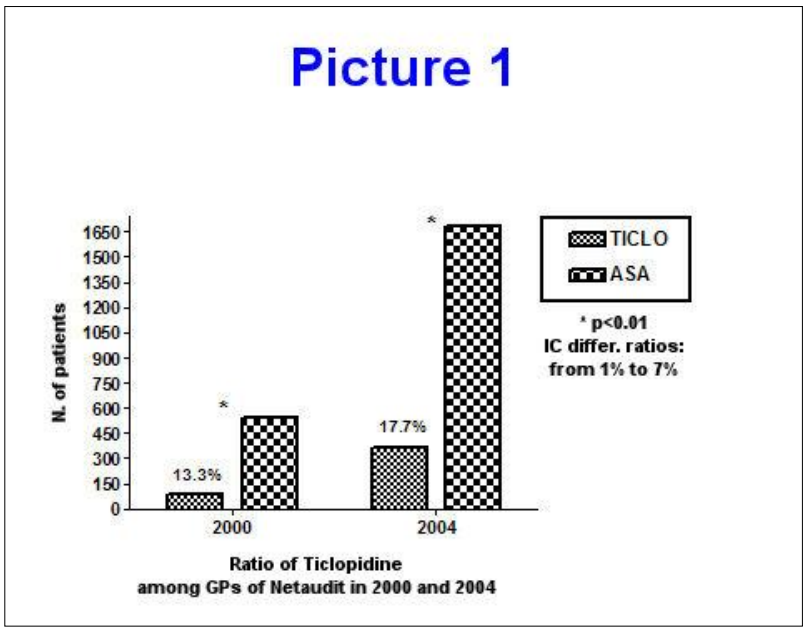
Tamburrini - Gavelli - De Ferrari - Perotti: Raccomandazioni all'uso dei mezzi di contrasto organo-iodati e per Risonanza Magnetica per via iniettiva - Considerazioni radiologiche e medico-legali - Radiol. Med. 107 (Suppl 1 al N. 4): 53-64, 2004 - http://sirm.org/documenti/agg_profess/mdc/10.pdf

Ticlopidine in GP despite the risks

Net-Audit List
(www.netaudit.org)

Introduction
In these last few years the use of Ticlopidine has been more and more object of attention and preoccupying notices. Actually this medication drug is under special surveillance since it causes dangerous reactions in a large number of cases. According to Mosby[4], the estimate is that a neutropenia can appear (less than 1200 mmc) in 2.4% of the patients treated; a new case of thrombocytopenic purpura every 2000 patients treated; a new case of aplastic anaemia every 4000 treated. To reduce these risks, frequent blood tests are suggested every 15 days, principally in the first 3 months, tests that many times risk not to be carried out or are forgotten by GPs and patients. For all the previous reasons, the most accredited pharmacologists and epidemiologists [1,2] suggest to avoid the medication drug, using it



only in case of real intolerance to acetylsalicylic acid (ASA) drugs. Compressed between a broad and consolidated use of ASA drugs and the arrival on the market of Clopidogrel and new inhibitors of glycoproteins (limited to some niche indications), this medication drug finds less space in certain European nations: for example it seems to have disappeared from the British National Formulary (www.bnf.org). In any case, after these considerations, the GPs belonging to the Netaudit wanted to analyse the following widespread sensation: the medication drug in Italy continues having a significant diffusion and therefore, could be used in an improper manner.

Method

In a first moment, the Italian GPs belonging to the Netaudit List evaluated the proportion between Ticlopidine drugs respect to antiaggregating drugs in their database in the year 2004 and they compared it to another Netaudit, on heart strokes during 2002. In a second moment, they evaluated the number of tablets used (only one or two pro/die 250 mg?) and then evaluated in a prospective study the first 5 patients that came to repeat the prescriptions.

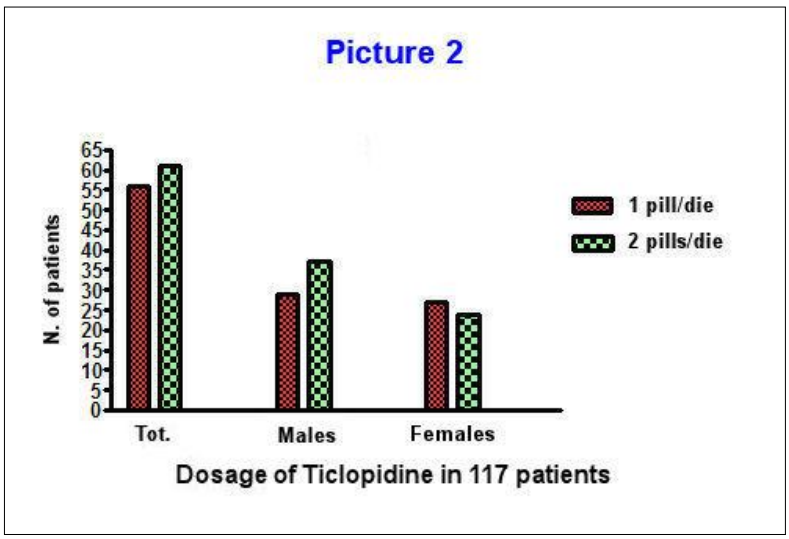
Results

How many patients are under treatment with Ticlopidine respect to the overall number of patients treated with platelet antiaggregating drugs? What is the temporal trend in the use of Ticlopidine among the GPs of the Netaudit list?

(Pict. 1) 19 GP in the Netaudit list evaluated in a retrospective study of the year 2004, the number of patients undergoing Ticlopidine respect to the overall number of patients in therapy with ASA: 350 (17.6%) were undergoing Ticlopidine treatment and 1636 were undergoing ASA treatment, in a total number of 1986. In a Netaudit prior to the year 2002 on after-heart stroke we found that 83 patients were undergoing Ticlopidine treatment and 540 were undergoing ASA treatment, which means 13.3% Ticlopidine respect to the total number of 623.

The difference between the 2 proportions, of 4%, is significant (p=0.01) and with a confidence interval of the difference, according to Miettinen, which goes from 7% to 1% more in 2004 respect to 2002. The dosage of Ticlopidine used (Fig. 2)

24 GPs of the Netaudit list had the responsibility of recording the number of tablets that patients took daily for at least six months (97 patients for more than a year; 20 patients from 6 months), in the first 5 cases that came into the office for re-prescriptions. GPs enrolled and analised 117 cases (51 female; 66 male). In 47.9% (confidence interval from 38% to 64%) the patients took only one 250 mg tablet. There is a small and insignificant difference between the two genders: in females, the percentage of cases with only one tablet exceeds the one with two tablets: (27/51; 52.9% with only one tab.); visa versa in males, this proportion is lower (29/66 equivalent to 43.9% cases with only one tablet).



Conclusions

The data we possess seems to indicate that among Italian GPs of the Netaudit list, the use of Ticlopidine respect to acetylsalicylic acid is not reducing: approximately 1 patient out of 5

takes Ticlopidine, a medication drug that has always been discussed among pharmacologists, whom indicate it as to be used II – III choice after ASA drugs (which on the other hand is easier to use, because taken only once a day), because of rather frequent cases of severe blood diseases. The matter becomes even more preoccupying if you analyse in our samples the high frequency (a little less than half) of under-dosages: one tablet per day instead of two. Actually, a little less than half of our patients risk twice for: inefficiency because of the half dosage and the side effects, which are typical of this molecule. An indicative datum, yet not significant, of the underuse of the dosage in females – in line with the well-known underestimation of cardiovascular diagnosis and therapy among women – is worth being studied in-depth in studies having a greater statistic power. What remains to be understood in the following studies, is the reason of the above-mentioned results. Maybe what important was: the preferences among the numerous specialists for this medication drug; the new indications (use for Stents in cardio-surgery); the possibility for GPs of using generic prescriptions, thus reducing pharmaceutical costs. The quite frequent use of Ticlopidine gives us GPs the urgency and need to have more attention towards clinical and laboratory monitoring procedures, in order to limit as much as possible severe side effects.
It also gives the Italian Public Authorities the duty of better weighing cost/benefits of the different antiaggregating drugs and the criteria for their refundability.

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Members of Netaudit taking part in I stage (proportion of Ticlopidina respect to antiaggregating drugs):
Augruso A., Baruchello M., Bonetti D., Brizio E., Cervone A., Covanti M., Del Zotti F., Fantini M., Farinaro C., Lazzari G., Nebiacolombo C., Nicolosi M., Rinaldi V., Scala A., Schianchi P., Tondi L., Ubaldi E., Vantaggi G., Visentini E.

Members of Netaudit taking part in II stage (1 or 2 pills?):
Arzenton E., Augruso A., Baruchello M., Brasesco P., Brizio E., Carosino C:, De Bari A., De Mola C., Del Zotti F:, Di Febo E., Di Pasquale A., Dolci A., Farinaro C., Granzotto S., Lippa L., Marchetto B., Murari T., Nicolosi M., Scala A., Schianchi P., Valletta D., Vantaggi G.