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REPRINTS AND REFLECTIONS

Statistical research on conditions caused by calculi by Doctor Civiale

Messrs. Poisson, Dulong, Larrey and Double

Calculi of the bladder are for the human race, and the more so for male individuals, one of the most intolerable diseases that life can be afflicted with. In addition to the pain and the dangers of the condition, and the pain and dangers of treatment, there are also certain moral feelings, predisposing the soul to sadness, which are closely bound to the affliction, and constitute a complication of varying seriousness to this so distressful state.

The work by Mr Civiale on this matter, of which we are to give an account today, concerns the application of the numerical method to a large number of questions concerning calculi.

Mr Civiale has painstakingly collected a body of research presented in a large number of tables derived from diverse populations, in the main cities, and in the largest hospitals in Europe.

The analysis of these tables, conducted by Mr Civiale, provided him, by using numerical information, with the means of confirming or correcting several of the results derived from general studies of pathogenesis, which were already suggested by inference or very precise summaries in clinical observation. We will report several of these findings to the Academy so that it may better appreciate, by its own judgement, the considerable work done by Mr Civiale.

It had been thought until the present day that in certain families parents transmitted an organic disposition to their children, whereby these children were more inclined than others to contract calculi; and from there, the conclusion drawn was that this disease was hereditary.

On this point a fairly large number of facts, it is true, indicate that the children of individuals suffering from calculi have in turn been affected; but the instances in this category are counterbalanced in a powerful manner by even more numerous instances in the opposite category. In the first instances, indeed, can be found the pressing consideration that the disease may have developed in the children under the influence of the same circumstances that had produced it in the first place in their parents or ancestors, therefore outside any hereditary path. Moreover, to cast as much light on this question as is desirable, it would be necessary to compare, on a large scale, the relative proportion of subjects suffering from calculi whose parents also suffered, and the proportional number of subjects in the reverse case; but information is lacking to cast light on this matter.

It has long been known that calculi are far less frequent among women than among men. In addition, among women, the chances of success after an operation are far greater. The numerical results obtained on this point tend to prove that over an equal number of operations, half as many women as men are lost.

The detailed study of the causes likely to produce calculi disprove a certain number of statements issued in relation to different foods and some beverages that were too hastily declared to be likely to cause the disease. Whatever the research taken into consideration, everything remains obscure, there is nothing but uncertainty on this point.

The numerical relationships established as to the main periods in life more particularly afflicted by this disease show that more than half the sufferers are not more than 14 years of age: in Lyon's hospitals, according to Poutéan, seven to eight children are operated on against one adult. This proposition is not however true in all localities. While demonstrations of this effect are most convincing for Wurtemburg, the Lorraine and Barrois hills, the Italian slopes of the Alps, and some English counties, etc, it appears on the contrary that in other localities, and, for instance, in very hot or very cold countries, adults and old people are more exposed to this condition. It can be added that everywhere the children suffering from calculi belong almost exclusively to the poor classes, while adult and elderly sufferers are evenly distributed over different social classes. Children are almost always free from the genitourinary damage that is such a cruel affliction for the other age groups.

If, in the tables we have before our eyes, we look for the way in which different professions in social life behave, either in favouring or in obstructing the development of calculi, no explicit information is obtained, no conclusive result reached. Indeed it is observed that the disease is encountered in more or less equal manner in individuals belonging to all trades; and this is true when the relative proportions of each profession are taken into account. It is probably true that there is a greater proportion of sufferers in the least well off classes; but it is also unfortunately these classes that are the most numerous; and moreover it is also on these classes that the burdens of material existence weigh most, disease in particular.

The conclusions at which Mr Civiale arrived with respect to professions are similar to those relating to the influence of climates. Calculi have been observed in almost equal manner in all countries. Assertions to the contrary are flawed with exaggeration or inaccuracy. It is true that several circumstances, either unnoticed or ill-assessed, may have contributed to the spread of this error. It suffices that for some reason general attention is drawn here or there to a disease for the examples evidenced of this same disease to increase markedly. In the

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lifetime of the illustrious lithotomist Raw, for instance, it could be thought that calculi were a very common disease in Holland, on the basis of the considerable number of operations performed at the time in Amsterdam hospital. After Raw's death, the number of operations decreased by more than half, and the number today has dropped to around one-third. In the same way the great and useful institutions which have multiplied so much in present times for the benefit of the mentally alienated, as well as the numerous establishments created for the treatment of growth deviations, have brought to light a large number of diseases and illnesses of these sorts which would otherwise have gone unnoticed.

It is however above all, the parallel between methods used to attack and destroy calculi that concerned Mr Civiale, and it is also this crucial part of his work that we will follow with keener attention.

It would be fairly exact to say that the means that have been used successively to control the progress of this cruel disease can be summed up in three general methods. Each of these methods, identical as to their objective, could however involve various series of procedures which we will not enumerate here.

First method

Attempts have been made, but thus far in vain, to dissolve calculi in the bladder by the action of what are claimed to be indirect or direct lithotriptics, general or local.

Second method

Attempts have been made to rid patients of their calculi by incisions and openings, often very varied in their techniques, but always by dieresis or by operation involving cutting instruments.

Third method

The calculi are extracted via the urethra without any incision, and most often accompanied by previous mechanical breaking.

The first method, which aims to dissolve the calculi in the bladder using agents derived from physics, chemistry or medicine, was not broached by Mr Civiale, and we will certainly offer no criticism with respect to this silence. We can however say that at the end of his work Mr Civiale makes a passing disapproving and even disparaging mention of the scientific efforts that have consisted in trying to dissolve the calculi inside the body. We cannot disapprove of this viewpoint, nor make a judgement on it: we would like to keep faith both in the resources of human wit, and in the future of science. Between the thinking of Albucasis, to whom the idea of crushing the calculus within the bladder should very probably be attributed, and this important operation carried out for the first time on a living person and recorded in the annals of science and medical art by Mr Civiale, there is a lapse of time of five or six centuries, during which time there were numerous vain efforts, and no doubt some sarcasm and no less incredulity: none of this prevented the discovery. It will perhaps be so one day for lithotriptics. The academy in the meantime should lead the person who reaches this objective to expect ample reward. It is above all to promote such work that the fruitful generosity of Mr de Montyon was established, and should endure.

It is therefore solely between operation by incision and operations consisting in crushing that Mr Civiale has chosen to establish his comparison.

In the history of this art, the power of figures has already been invoked to assess the relative value of the most prominent procedures used within the scope of the second method, that which always involves an operation by incision. But these comparative calculations, made on not very accurate bases, cannot take the place of science. The 4500 operations attributed to Brother Jacques; the 1547 attributed to Raw, the 316 to Baseillac, the 310 to Lecat, and the 150 to Pouteau, on which the claim that the procedures used by these practitioners were superior was so often based, are for the most part not authenticated, no details or assessments are provided, so that they have no value.

Later other work of similar nature was published. We can mention the publications by Doctors Marcet, Smith, Prout, and Yelloli. But Mr Civiale hastens to recognize that for these facts sufficient detail, desirable accuracy, reasoned critique, and fair assessment are all lacking. And it would be a source of serious error if, on the basis of these tables, we were to claim to determine the numerical proportions of mortality after incision with any degree of accuracy.

In the work which it is our task to present to the Academy, Mr Civiale has succeeded in collecting together a total number of more than 5000 instances, all supplied by the practice of the greatest surgeons alive today in Europe. Here are the general conclusions at which he arrived. Of the 5715 operations by incision that he was able to analyse, he found 1141 deaths, 4478 complete cures, and some 100 infirmities as a result of the operation. Thus, in the only instances where results are well known, mortality is around one-fifth for all ages. It is however noteworthy that more than half the patients had not reached their fourteenth year, and it is known that chances for recovery at that age are doubled at least.

On the other hand, these tables also comprise a total of 257 patients treated by lithotripsy, among whom there were only 6 deaths, and among these there were barely 2 or 3 who were under 14. This gives less than one death for 42 patients treated by lithotripsy.

And to complete the demonstration of the superiority of lithotripsy over lithotomy, it can be added that since the discovery of lithotripsy, among a fairly large number of physicians suffering from calculi, hardly any can be cited as having resorted to lithotomy: all were operated on by lithotripsy.

However, in good logic as in good medicine, it is not on this score that the discussion should dwell today. It is indeed not a question of rejecting lithotomy entirely always to replace it by lithotripsy: nobody disputes the fact that today in a fairly large number of cases lithotripsy is dangerous, difficult, or impossible, and that consequently lithotomy is then preferable or even indispensable. Thus the question is clearly: what are the pathological conditions in which lithotripsy offers more chance of success; what are, conversely, the circumstances in which it will be necessary to resort to cystotomy, in other words, the question is to define the respective indications of lithotripsy and incision. Let us now see what Mr Civiale's tables provide in the way of a solution to this problem.

We hasten to seize this opportunity to broach the question of the application of the calculation of probabilities to medicine. It is above all questions of this nature that physicians should bring

to this institution. Here they can be sure of careful judgement by competent judges.

Medicine, where work is characteristically difficult, slow, lacking in splendour and glory, has all too often sought to hitch on to ideas that are fashionable in the opinion of the day. Thus, at present, statistics are constantly applied to most of the major questions in therapeutics. Yet in this case statistics are no more than an attempt at application of calculation of probabilities. Let us try to see what opinion we should form.

In the field of statistics, that is to say in the various attempts at numerical assessment of facts, the first task is to lose sight of the individual seen in isolation, to consider him only as a fraction of the species. He must be stripped of his individuality so as to eliminate anything accidental that this individuality might introduce into the issue in hand.

In applied medicine, on the contrary, the problem is always individual, facts to which a solution must be found only present themselves one by one; it is always the patient's individual personality that is in question, and in the end it is always a single man with all his idiosyncrasies that the physician must treat. For us, the masses are quite irrelevant to the issue.

Calculations of probability, in general, show that, all other things being equal, the truth or the laws that are to be determined are all the better approached if the observations used embrace a large number of facts or individuals at once. These laws, then, by the very manner in which they are derived, no longer have any individual character; therefore it is impossible to apply them to the individual chances of a single man, without exposing oneself to numerous errors.

All the applications that one might wish to make, even within certain limits, to a particular isolated case would be liable to error. Where would one be, if for instance one were to positively assign the sex of an unborn child from the fairly exact established ratio of the proportional number of male and female births? What result could be expected if one were to try to determine the time when Pierre is to die from general mortality tables?

The calculation of previous or known events for the purpose of reaching a certain degree of probability for circumstances belonging to similar future or unknown events can only provide valid inferences if one does not at all know the nature of the future event which is the object of the calculation. This is assuredly never the situation of the physician at a patient's bedside.

Statistics in practice, which are always, in the end, mechanisms applied to the calculation of probabilities, necessarily require infinite masses, unlimited numbers of facts, not only with a view to coming as close as possible to the truth, but also, using known procedures, to eliminate, as far as possible, the numerous sources of error that are so difficult to avoid.

Everything presents itself differently in medicine: the facts are always very limited for us, by the very nature of things; they are even more so by the fact that we are unable to know and assemble them all. Alongside a few hundred facts published by a small number of men who write profusely, there are thousands of other facts lost in the obscurity of the voiceless clinical practice of that multitude of physicians who, in the midst of practical usefulness of every instant, cannot find time to write at all, and who even hardly have the time to read. Thus, in practical medicine, facts are too few to enter into the field of probability calculation. In addition, the great majority of these facts are not available for calculation, comparison or assessment: and yet what elements, what results would all these lost facts introduce into the issue, into this medical arithmetic? None can presume to say.

The mathematicians who have concerned themselves with the calculation of probabilities have all emphasized the need for the greatest accuracy and care in the classification of facts so as to avoid ill-considered and inaccurate associations which so readily lead to error. They all require that only elements of the same nature, and facts that are comparable one to the other, should be entered into a calculation, in other words facts that have undergone previous examination and analysis, so that as far as possible the conditions of the analogy or dissimilarity that they comprise are fixed.

Observations in the field of medicine are far from being able to comply strictly with these conditions. In medicine the danger is at once the errors that arise from the very nature of the question, and the errors that can be introduced by the men trying to answer the question.

In this sort of subject matter, so many variable conditions, so many diverse circumstances, so many contradictory elements are inevitably involved, and also introduce such a large number of accidental, irregular, and disrupting occurrences that it is impossible to enclose them all inside calculable limits. Experience has proved that in given circumstances a considerable number of patients can be operated on without a single one being lost, while in other circumstances almost all who are operated on are lost.

The diversity of medical constitutions, even in reference to specified seasons, introduces notable differences. Indeed sometimes successes are easy, numerous and assured because the operation and its sequels do not encounter difficulties or obstacles; sometimes on the contrary problems are prompt to occur, frequent and almost inevitable, because severe inflammatory problems, grave bilious complications or violent nervous attacks aggravate the situation.

Further again, everything has an influence on the success or otherwise of the operation: the operative procedure itself, not only considered *per se*, but also in relation to the hand that performs the work—because of the confidence derived from the habit of practising the operation—the season, the climate, and even the place in which the operation is performed. Successes are not at all the same in a large hospital, which is always more or less crowded, in a small hospital where there are usually less people, and in a private house, all other things being equal.

The duration of the illness before the operation, the various forms of damage to the bladder and related organs caused by the presence of the calculus, the general constitution of the patient, his moral and physical disposition at the time of the illness, the ceaseless activity of the organism under the more or less powerful action of life and its functions, all these are among the important circumstances which, for physician, render the cases so variable and unpredictable, so difficult to compare one with another, so open to numerous sources of error, that no law of probabilities can encompass them all. It should also be noted that among all these circumstances none belongs to the category of those which are so small as to be considered negligible in the calculation.

In fact in medicine, even regular circumstances and causes phenomena are most frequently complicated, obscured, unknown, and their action is upset or reversed by such a large number of

accidental factors that they cannot be seized upon by calculations. A calculation could not indeed reach the minute detail of combinations when they are so varied, and when they multiply and involve complication beyond a certain level.

When our famous Morgagni, with all the power of his genius, equally able to collate facts and to deduce from them the most accurate and judicious conclusions, said: *Non numerandae sed perpendendae observationes*, one should not count, but rather weigh the facts, he energetically expressed one of the most important conditions attached to the theory of calculation of numerical probabilities applied to medicine.

This being said, is it because the inflexibility of the calculation and the apparent strictness of figures cannot be applied in an absolute manner to medicine, that our science does not even so possess a series of probabilities that can be assessed? that it cannot reach a certain degree of assurance in its progress? or that there is no form of certainty to be derived from its results? Certainly not, and in this we have with us the agreement of a certain number of eminent mathematicians; the condition of medical sciences, in this respect, is no worse and no different from that of all physical and natural sciences, of jurisprudence, of moral and political sciences, and so forth.

Whenever it is not possible for the human spirit to rise to the mathematical certainty that can be found in astronomy for instance, the consequent requirements of reason are to draw analogies with what strikes the imagination and commands understanding: the logic of the facts turns to the logic of thought. Reasoning then takes on the form of a sort of calculation the result of which acquires ascendancy over our belief, precisely on account of the effect of repetition of judgements or observations. The validity of this calculation depends here, as elsewhere, on the choice of data, and then on the appropriate use of these data. And this appropriate use can only consist in the most detailed examination of the circumstances attendant on each piece of information, in the care taken to break down the information as far as possible, so that pronouncements are made on propositions of an equal degree of simplicity, and of an equal degree of evidence, and so that one guards against any partiality in favour of any particular result.

It should be added that, on almost all points, the calculation will give hardly more than what inference has already provided, and what reason alone might well have suggested.

It can clearly be seen that the main means of reaching the truth are inference, analogy, hypotheses based on facts and continually verified and corrected by new observations, and a sure sense of touch given by nature and strengthened by numerous comparisons between indications it provides and experience which guides it.

After these reflections, for which we might be tempted to apologise to the Academy, we must hasten to do Mr Civiale justice and render the appropriate tribute, that he has already on several occasions deserved and won here. Today we must say that his new work, as it stands, will have provided new evidence for the advantages that in most circumstances are attached to the substitution of an easy, simple operation presenting few dangers for another serious, alarming and painful one which until now constituted the only resource of medical art.

The commissioners invite Mr Civiale to pursue his statistical research to increase the volume of data, and to provide more circumstantial detail to make it more conclusive; at the same time, they are honoured to call for the approval of the Academy for this work.

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Commentary: The Paris Academy of Science report on Jean Civiale's statistical research and the 19th century background to evidence-based medicine

J Rosser Matthews

In 1835, the Paris Academy of Science commissioned a report on the statistical research that had been conducted by the surgeon and urologist Jean Civiale (1792–1867). By collecting statistical data on a wide scale throughout Europe, Civiale argued that a new bloodless procedure for removing bladder stones, a lithotripsy, was superior to the more widely-used technique of surgically cutting to remove the stones known as a lithotomy.[1] Although the specific therapeutic and surgical interventions that motivated the commission's report may no longer be directly relevant to the treatment of bladder stones, the broader issues that this report engaged (namely, the cultural authority of appeals to quantitative evidence) are clearly relevant to the contemporary

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medical world. For this reason, putting this report into a broader historical context illustrates the 19th-century antecedents to *au courant* debates concerning evidence-based medicine.

In order to situate the commission's report historically, it is necessary to realize that, in some respects, Civiale's work builds on research traditions that had developed in the 18th century while, in other respects, it is very culturally specific to the second quarter of the 19th century. As Ulrich Tröhler has demonstrated, the recording of successes and failures in removing bladder stones had been practiced since the beginning of the 18th century; because practitioners received more patients if they had a higher success rate, they began to list the number of their successes and failures annually in tabular form.[2] In this respect, Civiale's method of quantitative comparison was not fundamentally 'new'. However, he was able to carry out his research on a much larger scale than his 18th century predecessors because of support from the French Ministry of Public Instruction.[3] This government support illustrates how the appeal to aggregate data had now come to be seen as key method of settling questions deemed to be 'public issues'.

By the second quarter of the 19th century, several factors had converged that gave quantitative evidence, like that espoused by Civiale, an increasingly high level of cultural cachet. This era in European history was characterized by a marked interest in the collection of numerical information about society—what the philosopher of science Ian Hacking has called the 'avalanche of printed numbers'.[4] Based on the work of reform-minded physicians and political economists, European nations now had at their disposal vast amounts of aggregate data about their citizenry. Also, the political upheavals associated with the French Revolution in the last decade of the 18th century had been the crucible in which modern clinical medicine was formed.[5] In Paris, the new hospital-based methods of instruction placed an emphasis on clinical observation, autopsy, and the use of statistical data—what the French clinician P-C-A Louis famously described as the 'numerical method'.[6] Viewed against the backdrop of these developments, Civiale's report could be seen as another manifestation of this larger focus on quantification to adjudicate questions of medical uncertainty.

In commenting on Civiale's report, however, the Commission of the Academy of Science did more than speculate on whether his statistics were conclusive for the specific issue at hand; they used the report as an occasion to engage the general question of the proper role of statistical reasoning in deciding therapeutic questions. As the report noted, 'We hasten to seize this opportunity to broach the question of the application of the calculation of probabilities to medicine ... Medicine ... has all too often sought to hitch on to ideas that are fashionable in the opinion of the day. Thus, at present, statistics are constantly applied to most of the major questions in therapeutics. Yet in this case statistics are no more than an attempt at application of calculation of probabilities. Let us try to see what opinion we should form'.[7] Although the commission criticized applying the 'calculus of probabilities' to medicine for a myriad of reasons, their main concern was that the clinician (inevitably) focused on the diagnosing and on treating the individual who would present a completely unique and idiosyncratic group of symptoms. By contrast, the commissioners noted that, in statistics, 'the first task is to lose sight of the individual seen in isolation, to consider him only as a fraction of the species. He must be stripped of his individuality so as to eliminate anything accidental that this individuality might introduce into the issue at hand'.[8] It was this fundamental distinction (the individual versus the statistical aggregate) that caused the commission to question the applicability of the numerical method to medicine.

Ultimately, this report is historically significant primarily because it framed the issue of the role of quantification in medicine in ways that still resonate with contemporary medicine at the dawn of the 21st century. Like their 19th-century ancestors Civiale and P-C-A Louis, contemporary supporters of evidence-based medicine herald the use of quantitative methods as the way that medicine will finally be transformed into a science.[9] By contrast, contemporary critics of this approach, like the clinician and commission reporter François Double, question the excessive reliance on such quantitative methods; they still fear that such 'cookbook medicine' may cause physicians to lose sight of the unique and individuating features of the patients under their care.[10]

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Commentary: That was then, this is now

Nick Black

In January 2001, a national newspaper in the UK, the Sunday Times, published a supplement purporting to demonstrate the relative performances of British hospitals in terms of in-hospital mortality.[1] The data were supplied and promoted by a group of researchers from a leading medical school, internationally renowned for its scientific excellence. The publication attracted much public, political and media attention. Hospitals at the 'top of the league' congratulated themselves, while staff working in 'badly performing' hospitals were either demoralized, angry or, more sensibly, dismissed the findings. Here was another example of the misuse of inadequate observational data and yet further ammunition for the critics of such an approach. If only the researchers involved had read the report by FJ Double published 165 years earlier!

That work elegantly highlights the potential shortcomings of using observational data to make meaningful comparisons of clinical effectiveness.[2] While Civiale's claims regarding the aetiology of bladder calculi are measured and show awareness of the limitations of drawing conclusions from selected case series, his interpretation of the relative merits of lithotomy and lithotripsy is highly suspect. This surprises me, given his acknowledgement of the difference between a real and an apparent increase in the incidence of calculi (the latter arising from differences in the judgement and practice of individual clinicians) and the influence of fashion on clinical practice. He also demonstrates his awareness of the vagaries of basing incidence on surgical rates rather than prospective surveys of representative populations. Yet when it comes to comparing surgical techniques, he seems content to use crude post-operative mortality rates (20% versus 2.3%) even though he acknowledges the age mix of the patient populations differed considerably (50% under 14 years compared with 1%).

In contrast, the report by Double and his colleagues recognizes that there are 'numerous sources of error that are so difficult to avoid'. They, rightly, identify the potential confounding factors that might influence the sort of crude comparison carried out by Civiale: seasons, surgical difficulty, inflammation, bilious complications, illness duration, bladder damage and the general constitution of the patient. Not unreasonably, they conclude that the application of numerical methods in medicine is inevitably severely limited and that clinicians should continue to rely on intuition, experience and wisdom in deciding how to treat individual patients. Not unreasonable in 1835, but is such a conclusion reasonable in 2001?

Despite continuing examples of misleading use of observational data, such as that highlighted above, excellent examples do exist that demonstrate the potential application of these techniques.[3] These can only be achieved if the data are accurate (valid and reliable) and complete, and if sufficient steps have been taken to adjust for case-mix or risk differences. Some people believe that the latter is never possible to achieve.[4] If that view is accepted, much of health care will never be evaluated. A more pragmatic view seeks a role for research in improving the quality of health care. This inevitably involves the use of observational data which, if conducted carefully, can make a major contribution.[5] To take two recent examples, the demonstration of the danger of premature discharge from intensive care units at night[6] and the relative merits of surgical procedures to correct stress incontinence in women.[7]

So, while the Parisian Academy was correct in 1835 to treat unadjusted crude comparisons based on selected case series with scepticism, 165 years later we have the information technology to allow us to collect high quality clinical data and the statistical techniques to make meaningful comparisons. The task is to ensure methodological rigour is achieved and that poor analyses do not damage further the reputation of observational approaches.

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Commentary: 'Medical art' versus 'medical science': J Civiale's statistical research on conditions caused by calculi at the Paris Academy of Sciences in 1835

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This report[1] results from an in-depth study of a subject considered sufficiently important by the Paris *Académie des Sciences* to warrant commissioning some members to introduce a formal debate. This was also a normal procedure in the much younger *Académie Royale de Médecine*, which was founded in 1820. The Civiale report, published on 5 October 1835, must be seen in the context of a contest in contemporary French medical literature about the applicability of 'statistics' to medicine.

The issue had been launched in a theoretical way in France by the mathematicians Condorcet and LaPlace in the late 18th and the early 19th centuries. Their successors were now reviving their ideas about probabilistic theory: Siméon-Denis Poisson (1781–1840), for instance, a member of the Civiale Commission, was developing his law of large numbers (to be published in 1837).[2]

Most clinicians, however, lacked a sufficient educational background in mathematics. For them, 'statistics' meant simply counting 'facts', both in nosography and therapeutics. Such quantification as means of improving evidence in medicine had been well developed in 18th century Britain, particularly with respect to therapeutic comparisons. British arithmetic observation and experimentation included designs to avoid selection and/or observer bias.[3] By the 1820s, counting became a feature of the work at the great Paris hospitals where Pierre Charles Alexandre Louis (1787–1872) termed it *méthode numérique*. He championed it with his classical studies on phthisis (1825) and typhoid fever (1828), correlating clinical with post-mortem observations made on hundreds of patients.[4–6]

Jean Civiale (1792–1867) was Louis's contemporary in Paris. His work on the clinical epidemiology and therapy of bladder stones stood in yet another, both international and specifically urological, tradition. Indeed, epidemiological data on bladder stone patients had been collected in various European cities and for various motives. A case in point were the exemplary registers of the Norfolk and Norwich Hospital. In Norwich civic records existed for the whole of the 17th century. Both had been used by British investigators such as Matthew Dobson (1779) and, more recently, Alexander Marcet (1817) or John Yelloli (1821, 1828/29), the latter contributing a sober debate about calculations of average mortalities with his physician-chemist colleague William Prout. As to treatment, arguments for one of the many new technical variations of traditional lithotomy (i.e. extraction of the stone from the bladder) propagated in the 18th century were underpinned throughout Europe in terms of comparative success and failure rates. Such figures were often disclaimed by the proselytes of another method using arguments regarding patient selection, age, lack of precise records or even outright cheating.[3]

Thus, Civiale's approaches were not new, but he had collected data on a considerably larger scale. The sponsorship of the Ministry of Public Instruction after the political changes following the revolution of 1830 had enabled him to do so.[6] This context illustrates the importance attributed to bladder stones in early public health efforts as well as in clinical medicine.

Jean Civiale was a Paris-trained doctor who had been interested in bladder stones since his student days. He had first tried in vain—as so many had before him—to dissolve them chemically. In January 1824 he had been the first to try mechanical intravesical crushing with an instrument introduced via the urethra, in a public demonstration. In 1826 the *Académie des Sciences* awarded him a prize for this lithotripsy. The year after he received the *Prix Montyon*—a highly valued 19th century precursor of the Nobel Prize. In 1828 he was appointed director of a special ward for bladder stone patients at the Necker Hospital in Paris: Civiale was a successful man, indeed.[7,8]

Quite naturally he keenly propagated his innovative method of treatment which he considered much safer, as evidenced by a recovery rate of 98% according to his own results, compared to the 78% he had calculated after aggregating statistics on thousands of lithotomies. But he was not the only inventor of lithotripsy; his procedure would not prevent relapse, and it promoted inflammation. In fact, the history of the treatment of bladder stones in France and Britain over this period corresponds to battles between lithotomists and lithotriptists on the one hand, and among lithotriptists themselves (about the priority of invention) on the other hand, and these battles were often fought with the statistical weapons.

Another aspect of this report,[1] and perhaps the most interesting one from a present day perspective, is that it was used 'to engage the broader issue of the proper function of the medical profession within society as a whole'.[6]

The reporter, Francois-Joseph Double (1777–1842), was a leading physician of the Paris medical establishment, as was the other clinician and member of the Committee, Napoleon's famous surgeon, Dominique-Jean Larrey (1766–1842). Pierre-Louis Dulong (1785–1838) was a physician-chemist along the lines of Marcet, Prout and Yelloli. Poisson, the mathematician,

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was at that time quite sceptical about the applicability of his science to medical issues, as was Double, albeit for quite other reasons: The principal author of the report, Double, held that statistical thinking in terms of masses and groups undermined the notion of the patient's individuality. Furthermore, the clinician's specific *art médical* would be lost by non-medical scientists setting up fixed rules for doctors' decisions about phenomena which were essentially variable. Furthermore, they would do so on the basis of probable results threatening to replace the certain knowledge derived from logical dogmatic systems and personal experience. In short, the clinician was not an empirical scientist but a humanitarian healer.[6]

Poisson criticised the simple cookbook arithmetic used by clinicians, but at the same time formulated reservations about the feasibility of mathematically sound therapeutic comparisons requiring 212 comparable patients in each group (according to his standards).

Civiale, who was considerably younger than the members of the Academy Commission, argued—as his 18th century British predecessors would have done and as would Louis—that only numerical results from pathological observations and all inclusive records of treatment successes and failures could avoid the fallacies of trusting memory alone.

Double made no concessions to the numerists. He claimed that medical knowledge did not suffer from a lack of certitude because it could not meet the rigorous demands of 'the calculus of probability': Morgagni's saying that 'facts need not to be counted but need to be weighed' (1761) was true and decisive. Giovanni Battista Morgagni was the 18th century 'father' of the anatomo-clinical method dear to Paris medicine in the early 19th century. Note that the mathematician Poisson and the clinician Double both used 'calculus of probabilities', but without understanding each other. While Poisson meant it in today's sense, for Double it was a rhetorical expression of opposition to proper medical reasoning by inference from analogies.

Clearly this debate in the Academy of Sciences could neither satisfy Civiale, the urologist, nor the physician Louis and his followers. In 1837 a similar debate arose in the Academy of Medicine about the latter's questioning, with numerical evidence, of the value of bloodletting, highly fashionable in the Paris of that time, to treat typhoid fever. And, of late, the debate is again with us, in the contested claims about evidence-based medicine.

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Commentary: Treatment of bladder stones and probabilistic reasoning in medicine: an 1835 account and its lessons for the present

Jan P Vandenbroucke

The 1835 paper 'by Dr Civiale' (1792–1867) that was translated by Angela Swaine Verdier is an historical gem.[1] Many possible comments are possible about this paper. In the following, I have commented upon the text as such—without the benefit of any comparative study of similar papers, or reactions to this paper in the contemporary literature of the time, except for general historical and medical references that I had immediately at hand.

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In brief, the paper is a narrative commenting upon the work of Dr Civiale that was presented to the 'Académie de Médecine'. The comments were made by four people who were members of the 'Académie' and they present the work of their colleague in the form of a review. The first part of this 'review' describes the numerical data presented by the author, with some remarks on its strengths and weaknesses. The essence of that first part is a comparison of the relative merit of the old treatment of lithotomy (i.e. 'stone cutting' via the perineal route) versus the new transurethral lithotripty, for which new instruments were invented, among others by Dr Civiale. The second, interpretative part, goes beyond the paper and wonders how numerical data and 'probabilistic reasoning' can have a bearing upon the practice of medicine.

My remarks are grouped under several headings: first the disease and its treatment, which are an interesting object of historical epidemiology in itself, second the importance of the mode of presentation of this work in the 'Académie de Médecine', third the interesting remarks of the rapporteurs about the data, and fourth the part where viewpoints are expressed on the relation between probabilistic reasoning and clinical medicine.

Urinary Bladder Stones and their Treatment

Urinary bladder stones is one of those diseases that has disappeared mysteriously, at least from affluent industrialized countries. In the past urinary bladder stones were frequent in the West and they must have caused unbearable suffering as people were prepared to risk their lives in order to get relief. Lithotomy, or 'stone cutting' via the perineal route was the treatment of last recourse before the 1800s—a gruesome procedure with high mortality.

The history as well as the current epidemiology of urinary stones are captured in *The Cambridge World History of Human Diseases* in the chapter on urinary stones: *'The major forms of urolithiasis consist of either upper tract stones within the kidneys or ureters (renal stones) or lower tract stones formed within the bladder. These two forms of urolithiasis have distinct differences in etiology, chemical composition, and epidemiological features, and should therefore be considered two separate diseases. Historical evidence has shown a striking increase in incidence of renal stone in the past 100 years. There has been a simultaneous decrease in bladder stone incidence…'*.[2] The cause of the decline of bladder stones is not known: an interplay of dietary factors (protein versus other nutrition), vitamins, fluid intake and infections is usually mentioned. Equally mysterious, is the rise of the renal stones which still has a socioeconomic gradient, being more prevalent in the higher classes in our society and more in men than in women.[3] However, bladder stones continue to exist as an important medical problem in the developing world, often with the same epidemiology that they had a long time ago in ours. The Cambridge History again: *'The large majority of bladder stones occur in young boys from rural or impoverished areas. In these regions, the disorder is known as endemic bladder stone disease'*.[2] Nowadays, the disease is most prevalent in Middle and Far Eastern countries, North Africa and some other African countries. A brief search in PubMed teaches us that most publications of the past 20 years come from Asia or Africa, with a predominance of publications about children.

Symptoms are pain and (super)infection. The pain of the acute renal colic, of renal stones, is known to be one of the more severe acute pain syndromes in medicine (women have described it as 'worse than the acute phases of childbirth'). The pain of the bladder stone, however, is more or less constant, but can be almost equally excruciating. Samuel Pepys (1633–1703) was a sufferer and marked the anniversary of his surgery for the stone each year with a celebration; Benjamin Franklin (1706–1790) was a fellow sufferer and invented several devices to ease the pain.[4]

The only possible definitive treatment up to the early 1800s was surgery indeed: lithotomy or 'cutting the stone'. Dr Civiale's 1835 paper is a comparative account of this 'old' mode of surgical removal through the perineal route, in comparison with the new 'lithotrypty' by a transurethral instrument. Cutting the stone was literally cutting through the skin, close to the anus into the bladder until the stone could be squeezed out. One 17th century stone sufferer was so much in pain that he applied the procedure upon himself, and was later painted, proudly showing the enormous stone and the knife that he applied to himself (Figure 1).

Early in the 1800s lithotripty was suggested: to enter the bladder via the urethra with instruments that can grasp and then crunch the stone in the bladder. The resulting 'gravel' is later urinated out. Civiale is held to be the inventor of the first lithotripty instrument in 1818, but it did not function well (it drilled a hole through the stone) (Figure 2).

Others made improvements, upon which Civiale improved in turn, until a reasonably practical instrument was developed. This led not only to endless priority debates, but also to debates with the former 'specialists' of stone cutting in the 'Académie'.

Figure 1 Painting of Jan de Dost who applied lithotomy to himself (Dutch, 17th century, courtesy of Prof. H Beukers, Leiden)

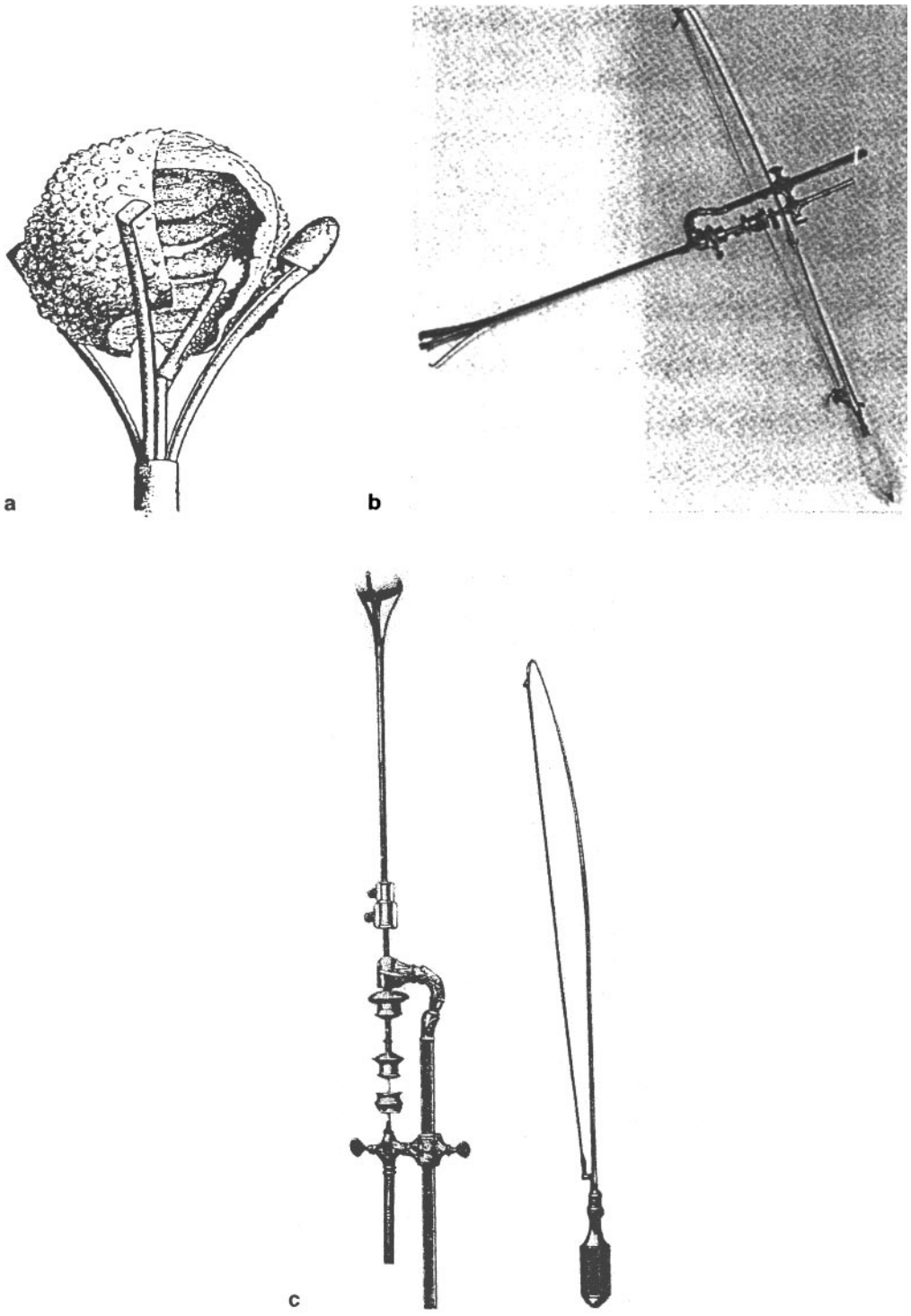

Figure 2 Civiale's instruments for lithotripsy. *a*. Brise-Coque. (From Murphy LJT: *The History of Urology.* Courtesy of Charles C Thomas, Publisher, Springfield, Illinois, 1972.) *b*. Bow type instrument of 1826 to remove stone by drilling. (Museum of Historical Medicine, Copenhagen, in Bennion, 1979.) *c*. Lithontripteur, operated by a bow. (From Collin Collection, in Murphy, 1972.) (Reprinted from Steinbock *et al*.[2] with permission)

However much the lithotripteurs were initially derided, in the end they got the upper hand (after operating upon a famous surgeon), and they became members of the 'Académie' themselves.[5]

One can only shudder at the thought of all these acts being performed without proper anaesthetics. Considerable folklore surrounded 'stone cutting' for centuries. Famous stone cutters travelled from town to town. One of them, named 'Frère Jacques

of Beaulieu (1651–1719)', is also mentioned in Civiale's paper—presumably the well-known children's song refers to him. A glimpse of their results is given in one series by Frère Jacques that was unearthed: 'Of 60 lithotomies performed from April to July 1697, 25 patients died; Mortality rate 42%'.[4] No wonder they travelled from town to town!

There was, of course, little known about the results of lithotomy other than rumour and anecdote that amounted to publicity for the stone cutters. The publication of a true comparative series was an important event, particularly as Civiale had collected patients from centres all over Europe in the early 19th century. Mortality of lithotomy in the series presented by Dr Civiale was a staggering 1 in 5. Usually mortality was less in women, as it was easier to move the cut from the perineum up into the upper vagina—often resulting in lifelong vesico-vaginal urinary incontinence. For men, the discussion was between the medial cut (often through the prostate) and the lateral cut, closer to the leg. The high mortality in Civiale's series was not unusual. The most renowned centre in Britain, at Norfolk and Norwich Hospital, published results obtained between 1772 and 1862 in *The Lancet*, and had a lithotomy mortality of 1 in 8, based on 910 reported cases. Mortality of lithotripty, applied only to 17 people was nil (table republished in ref. 6).

The Presentation of the Work

The presentation of the work to the 'Académie' is an interesting form of peer review. Members of the 'Académie' were a group that perpetuated itself by co-optation of those judged to have outstanding scientific wisdom. Aspiring scientists presented their work to members of the 'Académie', who in turn passed it on—in the form of a commentary. One can only wonder how such papers must have gone back and forth before the content was agreed upon. Interestingly, the present paper was presented by Poisson, Dulong, Larrey and Double (the last one was rapporteur).

One name immediately strikes the epidemiological reader: Poisson (1781–1840). We still use the distribution that bears his name to calculate confidence intervals of counts, as in incidence rates. He was not only a great theoretical mathematician, but sought for practical applications of statistics. His first attempt at practical application was in assessing the correctness of legal decisions. He also became an endorser of numerical medicine, and thereby a supporter of the idea of 'Médicine d'observation' of Charles Pierre Alexandre Louis. The work by Civiale will have suited him well. Larrey (1766–1842) is described as the 'greatest military surgeon of this time', and was intimate with Napoleon.[7] It is probably no accident that a military surgeon wanted to lend his name to the presentation of numerical data. Military medicine often was more 'numerical' than lay medicine, even before the 19th century (after all, it was their responsibility to keep sufficient numbers of men fit to fight).[8] The rapporteur was Double (1776–1842), who is described as representative of the medical establishment of the early 19th century in the account by Rosser Matthews:[9] yes, probabilistic reasoning was useful for scientific comparisons, but in the end the science of medicine rests upon clinical diagnosis, reasoning about cause and effect, and individualized treatment. In the later debates about the merit of 'Médecine d'Observation'—after 1835—Double distanced himself more and more, and eventually became close to antagonistic.[9] Given these names, the second part of the paper, the 'interpretation' of the use of probabilistic reasoning in medicine, is an important historical document. It represents the combined views of one of the most famous mathematicians and one of the most famous surgeons of 19th century France, with proper counterweight from the contemporary medical establishment.

Lithotomy versus Lithotripty

In modern epidemiological language, Civiale's paper might be termed a collaborative follow-up study of the outcome of a surgical procedure—or even a meta-analysis with individual patient data. Apparently, he collected series of patients all over Europe. It must have been an enormous work, and one yearns to know how he might have done it, how he selected the different centres, how he approached surgical colleagues, how he collected and tabulated the numbers, who paid him for doing so, who had the idea, and why. As to the 'who and why', the best guess is that he wanted to make his own point. As mentioned, he is credited with the invention of the first lithotriptic instrument, which he presented in a 1826 treatise 'on lithotriptie'. This was the start of controversies, not only about this new procedure versus the older stone cutting, but also about the priority of the intervention.[10] The presentation in the 'Académie', however, does not mention any of these mundane details. It presents few details of the investigation, and scarcely any numbers—presumably all of this is available in other publications. The 'Académie' devotes itself to high and pure interpretative thought. The interpreters are rather stern about the data: only conclusions from robust numbers with credible backgrounds are discussed, and the remainder is given short shrift. Although details are lacking, a few observations can be made.

It is amusing to read in 2001, in our modern era of 'genomics', that the first topic discussed was the heredity of bladder stones—with equivocal conclusions. The paper then proceeds to general causes, dietary and others, which remain almost as obscure as they are nowadays. Civiale's series consisted predominantly of children, and there is a glimpse from where in Europe he obtained data. The rapporteurs frown upon conclusions without an appropriate denominator. They call attention to what we would call nowadays 'popularity and referral bias'. The main modes of treatment are then discussed, with the 1-in-5 mortality of the lithotomy, versus a much lower mortality of the operation with the new transurethral instruments. It is argued that doctors themselves prefer the latter—an interesting type of argument that is, of course, a double-edged sword. In the 1950s doctors were also enthusiastic to prescribe thalidomide (as it was thought to be free of side effects), and quite recently it was shown that women physicians adopt hormonal replacement therapy more often than other women[11]—a choice that might be rather ill-advised given the higher cardiovascular morbidity recently found in randomized trials.[12]

The rapporteurs stop short of a final verdict on the two modes of treatment. None is possible, as the patients on the two modes of treatment differ too much. However, they fall back on the old adage that it is not a question of absolute superiority, but a matter of relative indication. Given that relative indication (smaller stones, within reach, etc), lithotripty has decidedly lesser mortality.

Probabilistic Reasoning in Medicine

Perhaps of greatest interest to today's epidemiological reader, is the second part, where the rapporteurs discuss the role of probabilistic data in medicine. Again, there must have been reasons for doing so: a few years before the presentation of Dr Civiale's paper, the 'Societé de Médecine d'Observation' was founded in Paris in 1832[5]—a society that is the forebear of our modern 'Evidence Based Medicine' movement.[13] The great debates in the 'Académie' that led to the demise of the society happened between 1835 and 1837.[5,9,14] Those debates centred on the meaning of numerical reasoning for the individual patient, and it was held that *'il n'y a en médecine que des individus…'*.[14] As mentioned, in the course of the debate Double leaned more and more to the latter view.[9] Presumably both the controversy around lithotripty and the emerging discussion about the use of probabilistic reasoning in medicine were reasons for the lengthy discussion and the mixed group of rapporteurs in the 1835 'Académie' report. A definitive description of the function of this paper in contemporary medical literature would almost provide a PhD for a medical historian.[9]

It is interesting to see how cautiously the arguments are made. A great point is made of the fact that probabilities can only be calculated about equal units and about large numbers: think about a large number of perfectly equal fair coins. However, humans are not equal and a physician who treats a patient has information that makes one patient different from the next. By necessity, statistics make people devoid of such characteristics. The usefulness of data from common medical practice is stressed, even if this will never tell the future of the individual patient that the physician is treating. The data offer a kind of 'background': they can yield general comparisons between modes of treatment, and thereby offer general guidelines for treatment. Whether the conclusions from particular data can be accepted is not just a matter of the data (because medical data are imperfect and do not yield probabilities) but also a matter of the logical reasoning behind the data. The rapporteurs mention the old adage of Morgagni: *'Non numerandae sed perpendendae observationes'* (translated as 'one should not count but rather weigh the facts'), which was slightly, but significantly changed for the motto of the 'Societé de Médecine d'Observation' into *'numerandae et perpendendae'*.[14] The rapporteurs clearly steered a most cautious course! One can only guess that this must be due to the discussions between Poisson the mathematician, Larrey the army surgeon, and Double who was distancing himself more and more from the Civiale-like way of doing medical research.[9]

If I understand the rapporteurs well, they hold that judgement enters twice. The first judgement is whether to accept the verdict of the comparative data, which is as much a matter of logical reasoning about the investigation and the principles behind it, as of the data themselves. The second judgement is whether the overall verdict applies to a particular individual patient.

Such themes have been discussed by later writers. Greenwood, the first professor of Epidemiology at the London School of Hygiene wrote in his 1936 account of Pierre Charles Alexandre Louis and the 'Societé de Médecine d'Observation': *'He [the physician] is not an actuary advising a company to accept (or decline) "risks" but a physician called to help a sick man'*.[14] This is an echo, with a distance of a century, of what we read in the report of Civiale's paper: *'What result could be expected if one were to try to determine the time when Pierre is to die from general mortality tables?"*

The debate continues today, it continues about the relative role of numerical, clinical and pathohysiological reasoning in the treatment of an individual patient.[15,16] It also continues when thinking about the relative roles of numerical data and basic scientific insight in accepting arguments.[17]

Conclusions

This important paper that was presented in the French 'Académie de Médecine' presumably played a role in two controversies: the right treatment of bladder stones, and the role of probabilistic reasoning in medicine. The first controversy was soon won by the lithotripteurs: the mortality of removing bladder stones by transurethral instruments was so much less that they triumphed and became members of the 'Académie' themselves. The second needed the passage of more than a century before we saw the rebirth of an interest in numerical reasoning in clinical medicine.[13] Several of the themes of the second controversy still play a role in today's debates about the relative usefulness of numerical, clinical and pathophysiological reasoning, and about the relative role of insight and numerical data in deciding which scientific proposition is true. Indeed, we might conclude that *'The level of debate has not much advanced since Civiale and Double crossed swords…'*[16]—an observation that might be a starting point for self-reflection on all sides, to come to an even better mutual understanding.

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