

Paul Martini and the development of clinical epidemiology in Germany

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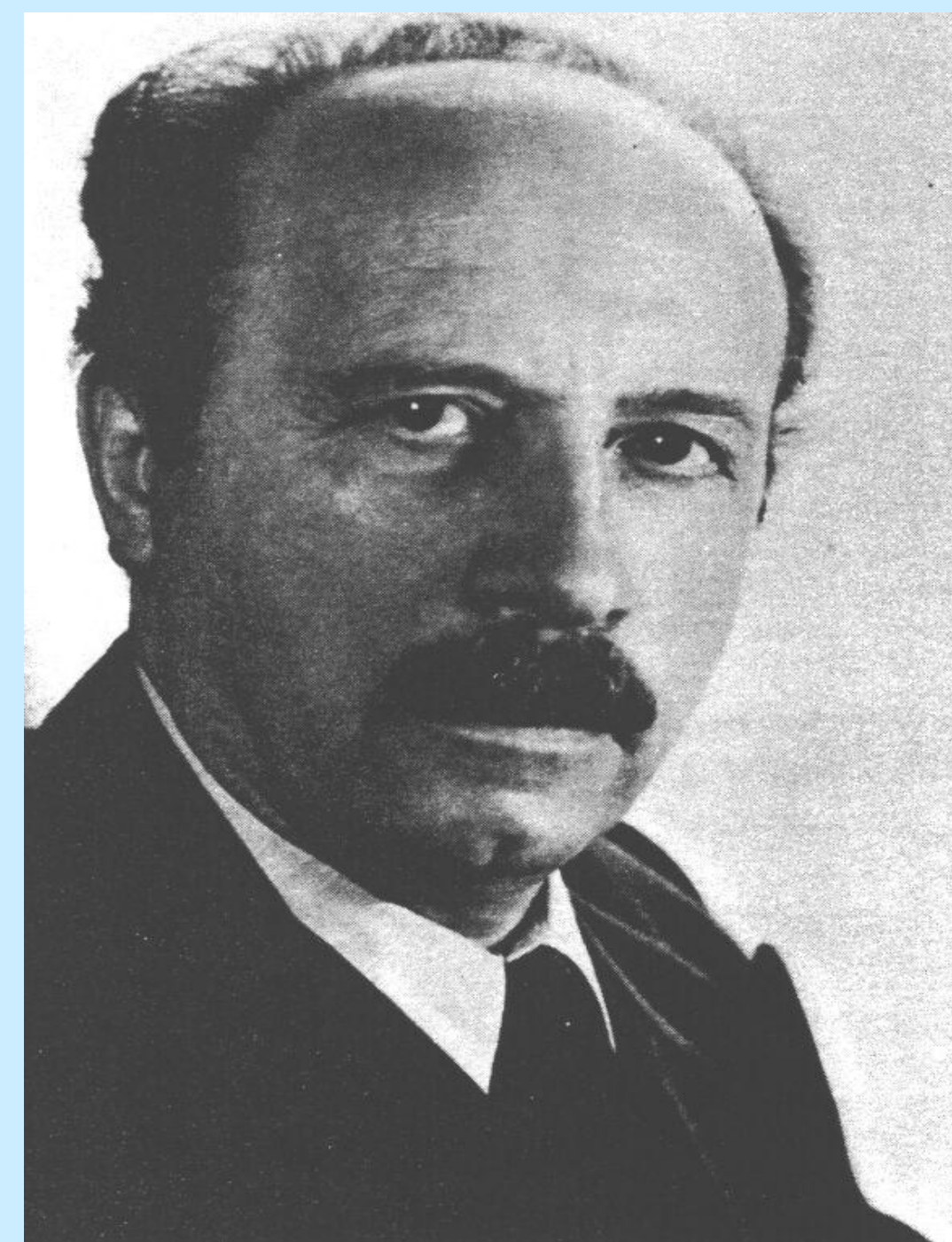
“Three years, in which I had the chance to head the medical section of the St. Hedwig’s Hospital in Berlin, were filled with looking for satisfying methods of therapeutic investigation. The results presented are still not perfect. However, I will publish them, as it seems to me that a change of the current situation is not to be postponed any longer.”¹

Paul Martini, April 1932

Martini’s biography

Paul Martini absolved his medical studies in Munich where he graduated in 1922.

Mainly the development of criteria to measure therapeutic outcomes was one of his aims when he moved to Berlin in 1927. There the basic studies for his „Methodology of Therapeutic Investigation“ („Methodenlehre der therapeutischen Untersuchung“) were established and published in 1932 just after he had become professor of medicine at the University of Bonn where he stayed until his retirement in 1959.



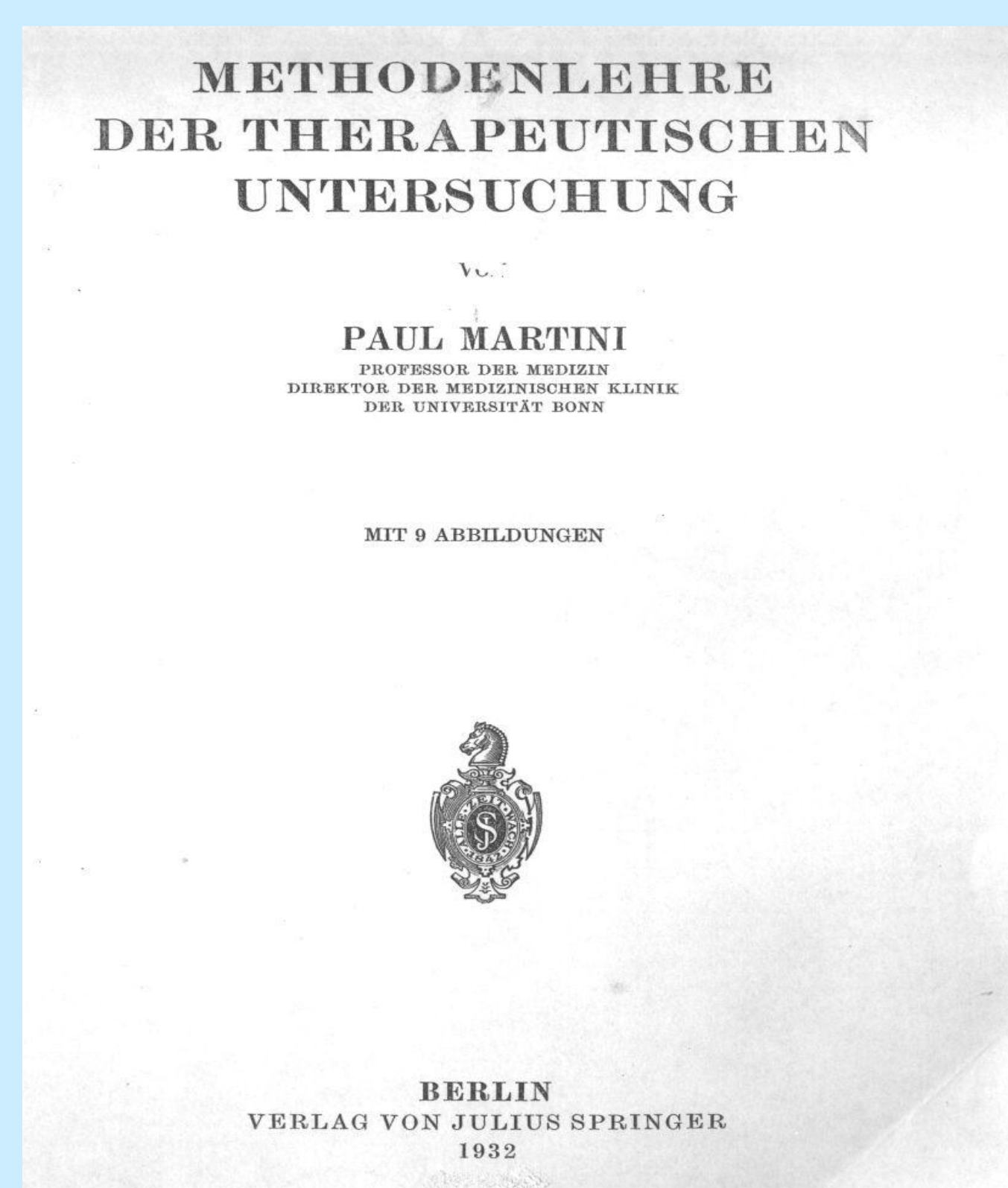
Paul Martini (1889-1964)

However, not only did he demand the improvement of methodological thinking, he also reflected his work by raising ethical issues of clinical investigation.

During Nazi times in Germany, Martini (a confessing catholic) never was a member of the national-socialist party, but was able to keep his position as a university lecturer although he was in trouble with the regime more than once.

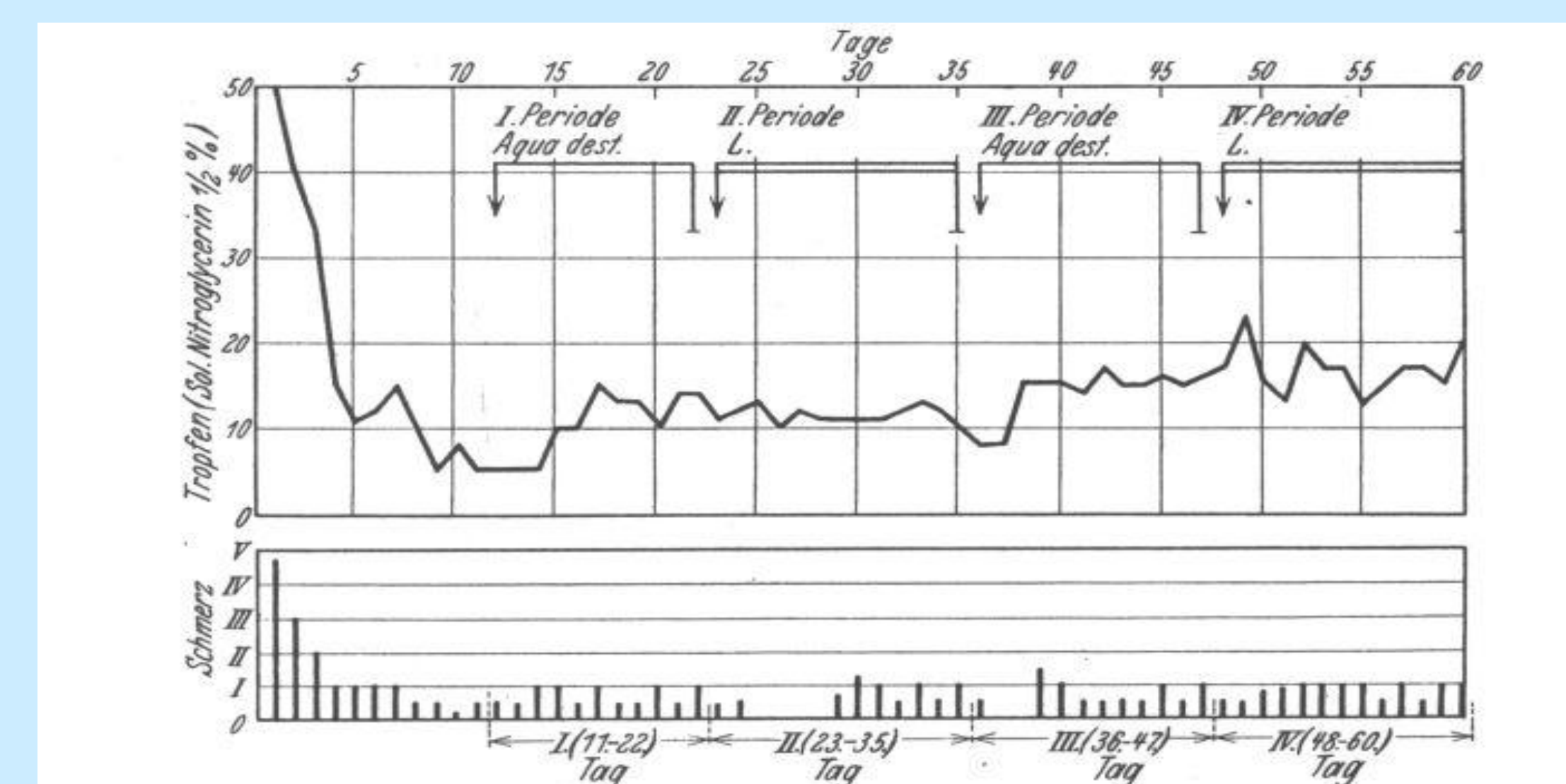
One of the most honourable judgements of his character, which was mentioned by his friend Siegfried Thannhauser, may be the description as “the conscience of German medicine”².

Paul Martini’s “Methodology of Therapeutic Investigation” in its first edition 1932³. As the first and only textbook of clinical epidemiology in Germany it is an early, major and original contribution to the development of the discipline in Germany.



Martini’s criticism of contemporary therapeutic investigation

- Neglect of methodology in clinical-therapeutic investigation with, consequently, invalid study results and in the best case unnecessary, but more often even harmful medical treatments.
- Neglect of publication of methodological details and results of therapeutic interventions in studies which are supposed to give evidence for therapeutic effects.
- Neglect of clinical-therapeutic investigation in general in comparison to diagnostic studies and basic research.



Treatment periods in Angina therapy. Given were Aqua dest. and the „cardiac hormone“ L. Criteria of the patient’s progress were the amount of Nitroglycerin needed and a rating scale for pain containing five grades⁴.

Martini’s Principles of Therapeutic Investigation (summary)

1. Comparison as the basis of therapeutic investigation by observing the course, duration and result of a disease without and under specific treatment:
 - a) definition of a control group without specific treatment or
 - b) design of a n=1-study by observing a single patient during a longer time with defined periods (pre-treatment, under treatment, post-treatment)
2. Homogeneity of the patients observed:
 - a) Comparability of cases – not only based on the diagnosis
 - b) Comparability of other characteristics such as age, sex and physical condition.
3. Use of an alternation scheme by treating one patient without specific remedy and every other patient with the specific treatment.
4. Number of cases and duration of the observation depend on the quality (reliability, validity) of the observational criteria;
 - a) use of criteria which are as objective, as exact, as much countable in numbers as possible;
 - b) introduction of numeric rating scales where subjective criteria cannot be avoided.
5. Blinding of the experimental design:
 - a) Equality of different remedies in shape, colour and taste to conceal their special character or purpose
 - b) Use of placebo during the pre-treatment period (in n=1-studies)
 - c) Disclosure of the start of treatment, maybe even of the fact of giving a specific treatment.
6. Minimisation of artefacts (eg physical / psychological factors, different remedies at one time, changes in nursing care).
7. Statistical methods to describe the outcomes; if necessary division of the sample into sub-groups (stratification).
8. Analysis of the outcomes by referring to probability theory.

Bibliography:

1. Martini P: Methodenlehre der therapeutischen Untersuchung, Springer 1932, Vorwort
2. Thannhauser SJ: Paul Martini zum 70. Geburtstag, Deutsche Medizinische Wochenschrift 84 (1959) 154-155
3. Martini P: Methodenlehre der therapeutischen Untersuchung, Springer 1932, Deckblatt
4. Martini P: Methodenlehre der therapeutischen Untersuchung, Springer 1932, S 50

Evidence based Medicine - Is there a German History?

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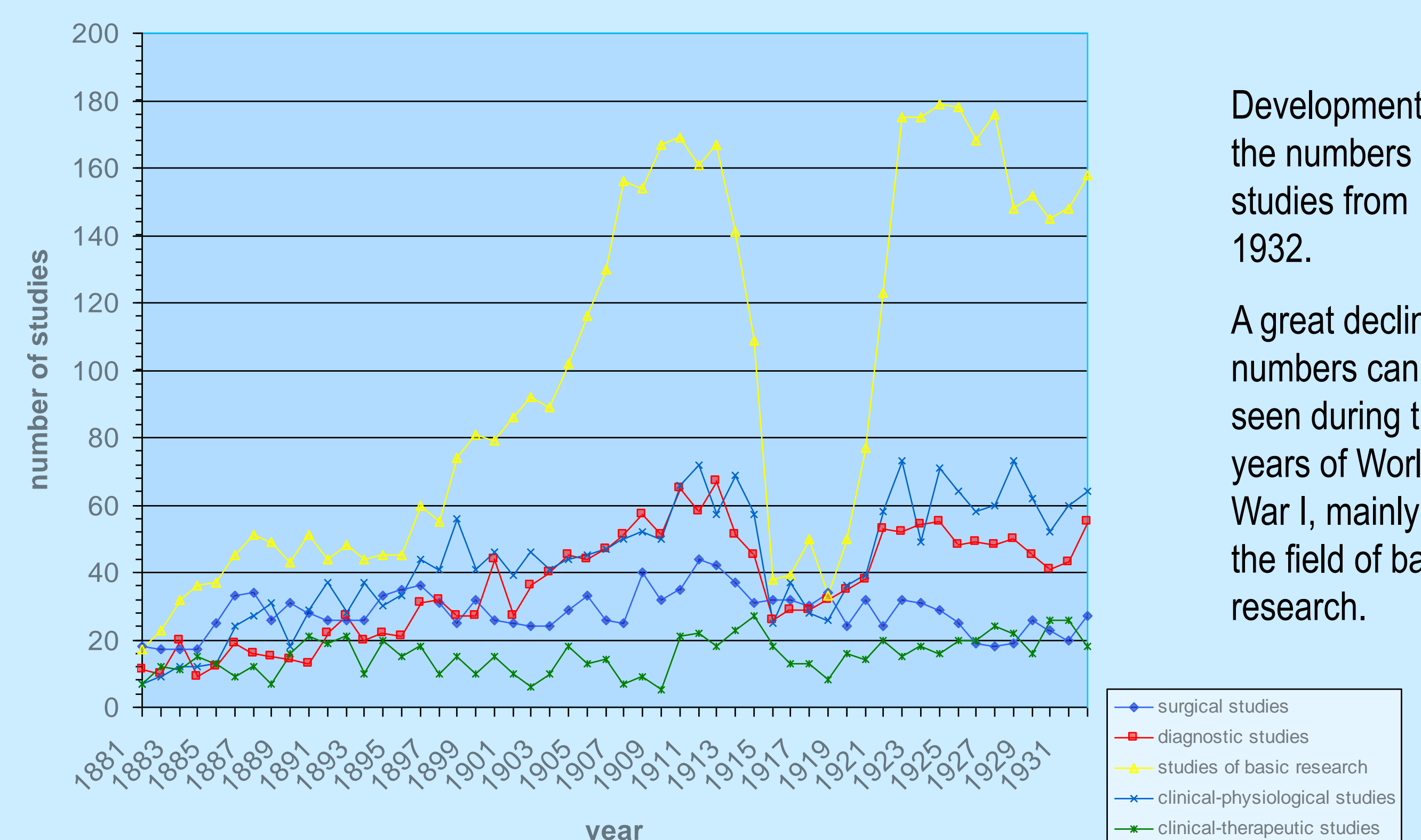
“If you brush through a dozen volumes of our medical journals, you can be lucky if you find altogether two dozens of therapeutical studies which will resist critical judgement. In the “Clinical Archives” even therapeutical studies can be found in an infinitely small number; 100 studies of basic research or diagnostic studies will here be met by maybe 3 or 4 therapeutical ones – which – by the way – will not be sufficient concerning methodological quality in a high percentage. You will not be in fundamental error by thinking that the majority of the authors of therapeutic studies does not feel well in a scientific context of stricter criteria.”¹

Paul Martini, 1932

Bearing in mind Paul Martini’s words an analysis of five important German medical journals from 1881 (foundation of the German Society of Internal Medicine) to 1932 (publishing year of Paul Martini’s “Methodology of Therapeutic Investigation”) was performed to identify publications of early therapeutic trials in internal medicine and to describe the general development of clinical investigation in Germany.

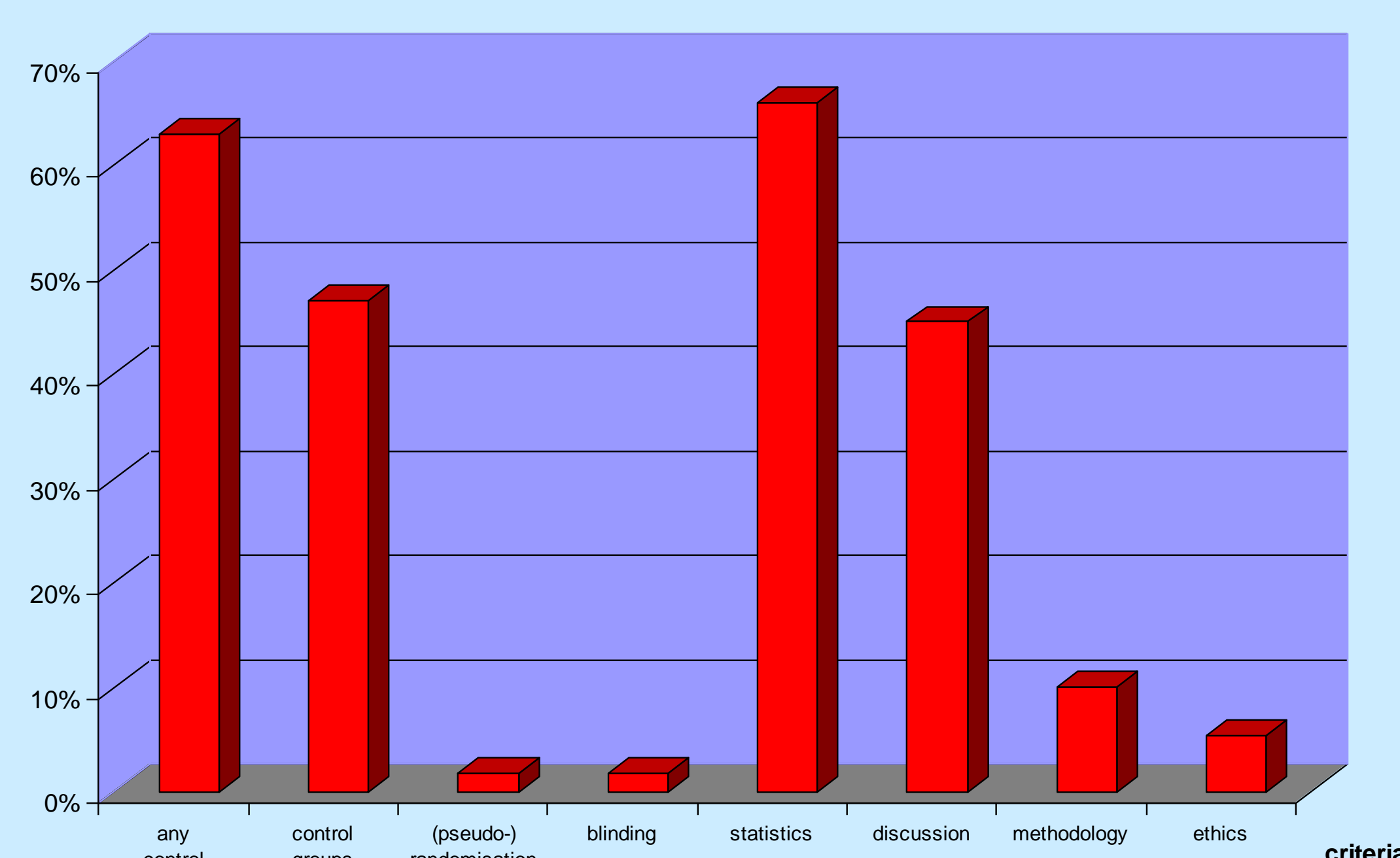
A total number of 11401 empirical studies was identified. Studies of basic research (laboratory or animal studies) 44%, 19,7% clinical-physiological, 16,5% diagnostic, 12,8% surgical and 7% clinical-therapeutic studies.

In the next step a period from 1918 (end of World War I) till 1932 was chosen to carry out a systematic analysis and reconstruction of clinical-therapeutic studies in internal medicine by predefined criteria. A selection of the criteria can be seen below.



Between 1918 and 1932 a total number of 279 clinical-therapeutic studies was found.

In 66% a mechanism of control was described, the use control groups was reported in 47%, methods of (pseudo)randomisation in 1,8% (all alternating schemes), blinding in 1,8%. Medical statistics (descriptive in most cases) were used in 66%. In 45% the results were critically discussed, aspects of methodology appeared in 10% and consideration of ethical aspects in 5,4% of all discussions.



| Criteria | Percentage |
|--|------------|
| 1. Was a mechanism of control reported? | 66% |
| 2. Was the use of control groups reported? | 47% |
| 3. Was a method of randomisation described? | 1,8% |
| 4. Was blinding reported? | 1,8% |
| 5. Were methods of quantification / medical statistics used? | 66% |
| 6. Was there a critical discussion of the results? | 45% |
| 7. Were aspects of methodology mentioned? | 10% |
| 8. Were aspects of medical ethics considered? | 5,4% |

Conclusion:

While there was a strong development of the studies of basic research, the number of clinical-therapeutic studies was constantly low and their quality, with very few exceptions, poor – thus corroborating Paul Martini’s complaints and his intention to improve the situation by publishing his “Methodology of Therapeutic investigation” as early as in 1932.