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# Beyond journal publications – a new format for the publication of clinical trials

## *Das Ende der Zeitschriftenpublikation – ein neues Format für die Veröffentlichung klinischer Studien*

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ABSTRACT

Journal publications are the major route to communicate methods and results of clinical trials. However, the shortcomings of this format are well known, including insufficient quality of the information provided as well as publication and outcome reporting bias. Attempts to improve the situation via peer review, reporting guidelines or study registration did not solve the problem. Currently, new ways of data presentation in electronic databases, increased access to previously confidential documents, and the potential use of anonymized individual patient data from clinical trials beyond the individual trial, have led to discussions about new publication formats for clinical trials. The current paper describes the components required for full information on a clinical trial and discusses a new format to provide this information.

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ZUSAMMENFASSUNG

Zeitschriftenpublikationen gelten als Standardquelle für Informationen zu Methoden und Ergebnissen klinischer Studien. Die Schwächen dieser Publikationen sind allerdings gut dokumentiert. Dabei geht es wesentlich um eine mangelnde Qualität der in Publikationen enthaltenen Information sowie um Publikations- und Outcome-Reporting-Bias. Versuche, die Situation durch Begutachtung von Manuskripten, durch Publikationsrichtlinien oder durch Studienregistrierung zu verbessern, haben die Probleme nicht gelöst. Neue Wege der Datenpräsentation in Datenbanken, der zunehmende Zugriff auf bisher als vertraulich eingestufte Dokumente zu klinischen Studien und die Möglichkeiten der Analyse anonymisierter individueller Patientendaten über die einzelne klinische Studie hinaus haben eine Diskussion zu neuen Formaten zur Veröffentlichung von klinischen Studien angestoßen. Die vorliegende Publikation beschreibt die Komponenten, die eine vollständige Information zu klinischen Studien sicherstellen, und diskutiert ein neues Format zur Bereitstellung dieser Informationen.

## Introduction

Historically, publications in scientific journals have been the major route to communicate methods and results of clinical trials. Since evidence-based medicine started systematically using study results for decision making, the completeness and quality of

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journal publications and the availability of full information on study methods and results have become more and more important. Therefore, since its establishment in 2004, the German Institute for Quality and Efficiency in Health Care (IQWiG) has participated in efforts to improve data transparency.

Although difficulties with study publication and the risk of bias in the published literature have been discussed for more than 30 years [1,2], the general idea of journal publications being the main instrument of dissemination of study methods and results has not been challenged until recently: New ways of data presentation, e.g. in electronic databases with fewer limitations on the volume of information to be presented, have become a standard approach. Furthermore, there is increasing access to documents and data previously considered confidential, such as documents from regulatory authorities or individual patient data (IPD). Given these newer formats of study information and changes in policies on data transparency, it seems even more questionable whether journal publications are still an appropriate format to communicate information on clinical trials.

The current paper describes the problems with journal publications using examples from IQWiG's work, reviews attempts to solve the problem, and discusses an alternative approach for the dissemination of study results by means of newer formats.

## An example from IQWiG's daily work

The relevance of the problem of insufficient study information from journal publications can be demonstrated by an example from IQWiG's daily work. In 2012, IQWiG was commissioned to assess the potential added benefit of the new antidiabetic drug linagliptin versus sulphonylureas. The assessment was mainly based on Study 1218.20 (ClinicalTrials.gov number NCT00622284), published in the Lancet in 2012 [3]. However, in addition to the journal publication, IQWiG had access to the clinical study report (CSR) prepared according to the International Conference on Harmonization Guideline ICH E3 [4].

According to the journal publication, the study demonstrated the non-inferiority of linagliptin to the sulphonylurea glimepiride for the primary outcome "change in HbA1c from baseline up to week 104" ("reductions in HbA1c were similar, meeting the pre-defined non-inferiority criterion" [3]). This finding was accompanied by a figure showing the time course of HbA1c in a completers' cohort, i.e. in the per-protocol analysis set (N = 504 patients), rather than in the intention-to-treat (ITT) analysis set used for the analysis of the primary outcome (N = 1551 patients).

Moreover, in the analysis of a key secondary outcome (occurrence of hypoglycaemic episodes up to 104 weeks) the authors pointed out that fewer patients had experienced hypoglycaemia with linagliptin than with glimepiride (58 [7%] of 776 vs. 280 [36%] of 775, $p < 0.0001$). These data suggest advantages of linagliptin over glimepiride and the authors concluded that "the results of this long-term randomized active-controlled trial advance the clinical evidence and comparative effectiveness bases for treatment options available to patients with type 2 diabetes mellitus. The findings could improve decision making for clinical treatment when metformin alone is insufficient" [3].

On the basis of the information available from the CSR, IQWiG's conclusion on the study was quite different [4]. When the time course of HbA1c in the ITT analysis set available in the CSR was analysed, it became apparent that at the beginning of the study a sharp decrease in HbA1c was observed in the glimepiride, but not in the linagliptin group (Figure 1). This was probably due to

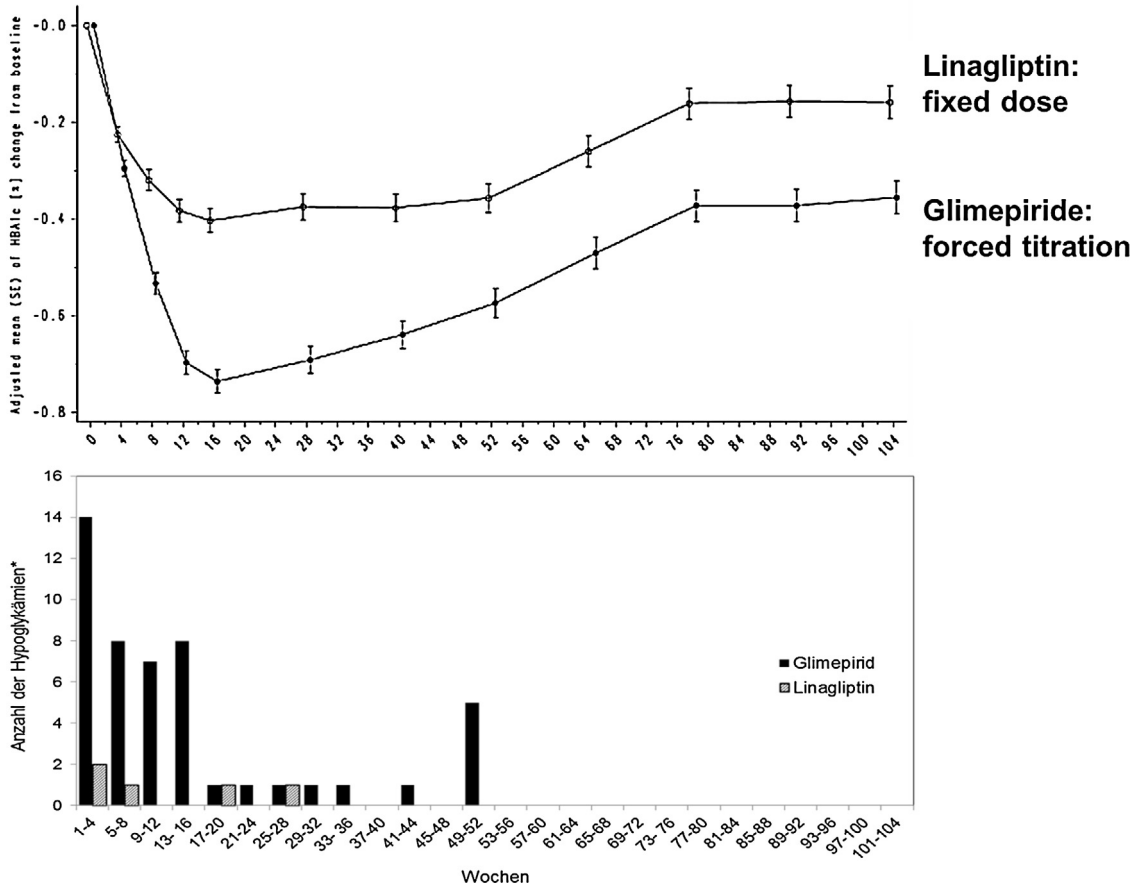


**Figure 1.** Time course of change in HbA1c (upper panel) and frequency of hypoglycemic episodes (lower panel) in study 1218.20 comparing linagliptin and glimepiride (reproduced from [4]).