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## ESPACOMP Medication Adherence Reporting Guidelines (EMERGE): A Reactive-Delphi Study Protocol

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# ESPACOMP Medication Adherence Reporting Guidelines (EMERGE): A Reactive-Delphi Study Protocol

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## Abstract

### Introduction

Medication adherence is fundamental to achieving optimal patient outcomes. Reporting research on medication adherence suffers from some issues – including conceptualization, measurement, and data analysis – that thwart its advancement. Using the ABC taxonomy for medication adherence as the conceptual basis, a steering committee of members of the European Society for Patient Adherence, COMpliance, and Persistence (**ESPACOMP**) launched an initiative to develop the ESPACOMP medication adherence reporting guidelines (**EMERGE**). This paper reports on a Delphi study that aims to build consensus among a group of topic experts regarding an item list that will support developing EMERGE.

### Methods and analysis

This study uses a reactive-Delphi design where a group of topic experts will be asked to rate the relevance and clarity of an initial list of items, in addition to providing suggestions for further items and/or modifications of the initial items. The initial item list, generated by the EMERGE steering committee through a structured process, consists of 26 items distributed in 2 sections; 4 items representing the taxonomy-based minimum reporting criteria, and 22 items organized according to the common reporting sections. A purposive sample of experts will be selected from relevant disciplines and diverse geographical locations. Consensus will be achieved through pre-defined decision rules to keep, delete, or modify the items. An iterative process of online survey rounds will be carried out until consensus is reached.

### Ethics and dissemination

An ethics approval was not required for the study according to the Swiss federal act on research involving human beings. Participating experts will be asked to give an informed consent. The results of this Delphi study will feed into EMERGE, which will be disseminated through peer-reviewed publications and presentations at conferences. Additionally, the steering committee will encourage its endorsement by registering the guidelines at the **EQUATOR** network and other relevant organizations.

**Strengths of the study**

- Builds on the conceptualization of medication adherence as put forward by the ABC taxonomy
- Incorporates the input of many topic experts across various disciplines and geographical areas
- Preserves subject anonymity and reduces the effect of dominant individuals
- Controls the feedback and reduces the effect of noise compared to face-to-face discussions
- Uses statistical analysis techniques to further reduce the potential of group pressure for conformity

**Limitations of the study**

- The sample of experts and the decision rules are the most critical components of the study and any compromise in their quality can affect the results
- Potential of low response rates due to the nature of the study of having multiple feedback rounds
- Consumption of large blocks of time to administer several survey rounds and consolidate their output
- Potential of molding opinions based on the received aggregate feedback

## INTRODUCTION

Reporting research on medication adherence is suboptimal. Confusion prevails regarding the conceptual underpinning, adequate measurement, and analysis of medication adherence data, hindering scientific progress in this field[1, 2, 3]. The *ABC taxonomy for medication adherence*[4] was developed to enhance the conceptualization of medication adherence. This taxonomy defines medication adherence as *'the process by which patients take their medications as prescribed'*. It divides this process into three interrelated phases: (1) initiation; (2) implementation; and (3) persistence, each demanding a clear operational definition and appropriate measurement and data analysis.

Guidelines on the reporting of health research aim at enhancing publication quality and may focus on specific study designs, research areas, or sections of a report. Examples of such guidelines can be found on the website of the Enhancing the QUALity and Transparency Of health Research (**EQUATOR**) network (<http://www.equator-network.org>), and include STROBE[5] (for observational studies in epidemiology), CONSORT[6] (for trials), and TIDieR[7] (for description and replication of interventions) guidelines. The introduction of such guidelines and their endorsement by professional societies and journals have proven to be helpful in enhancing the transparency and accuracy of health research reporting[8, 9].

There are existing published guidelines and recommendations focusing on medication adherence research[1, 10-13]. However, these guidelines overlap considerably with those developed for general clinical research and are, thus, not particularly specific for medication adherence research[10, 11]. Additionally, they do not build on a clear conceptualization of medication adherence[1, 10, 11, 13] such as the *ABC taxonomy for medication adherence*, and focus on study design rather than reporting[1, 12, 13]. For these reasons, medication adherence science would benefit from specific guidelines for reporting medication adherence research that complement the existing general guidelines for health research reporting (e.g. STROBE, CONSORT, TIDieR) to boost the quality of reporting of medication adherence research.

Developing reporting guidelines requires input by experts from various scientific backgrounds and needs to be relevant across geographical regions. This is particularly applicable in the context of medication adherence, which is a multidisciplinary science ranging from behavioural sciences through statistics and clinical medicine to economics. Delphi methodology, as a means for consensus building[14], enables integration of input from a wide variety of experts. It achieves consensus through an iterative process of survey rounds, providing the opportunity for participants to revise their input in subsequent rounds based on collective group feedback from previous rounds. This method enables the neutral and efficient integration of feedback from different experts, is suggested as one of the 18 steps put forward by the EQUATOR network in their guidance on developing health research reporting guidelines[15] and has been used in developing many similar guidelines[16, 17].

This approach has many benefits[18, 19, 20]. First, the iterative nature of the study and the feedback process allows participants to reassess their initial judgments. Thus, consensus is reached through a gradual stepwise process based on rational thinking and input. Second, participants do not

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3 interact directly and remain anonymous to each other until the survey rounds end. Hence, group  
4 domination by the views of certain individuals is avoided. Third, when participants consider changing  
5 or sticking to their original opinion after checking group response, this decision is not affected by the  
6 desire to be seen concordant with senior or dominant individuals. Fourth, experts can participate  
7 asynchronously and do not need to be present together while answering surveys as they receive  
8 collective feedback along with new surveys, which can be conducted through a web-based platform.  
9 Accordingly, it is feasible to use this approach to involve geographically distant participants.  
10 Moreover, the controlled feedback minimizes the effect of noise, which can happen in face-to-face  
11 group discussions. Finally, the ability to use statistical analysis facilitates reaching a more objective  
12 consensus than that usually reached through face-to-face conversations. Consequently, the Delphi  
13 method is an appropriate method to include the knowledge of many experts to cover the numerous  
14 aspects of the medication adherence subject.  
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## 20 21 **AIM**

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24 The aim of this Delphi study is to build consensus among a group of topic experts regarding  
25 an item list that will support developing guidelines for medication adherence research reporting.  
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## 28 **METHODS AND ANALYSIS**

### 29 30 **Overview of the study design**

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33 The study implements a reactive-Delphi design[21] where a group of medication adherence  
34 experts will be provided, in the first survey round, with an initial list of 26 items that are specific to  
35 medication adherence research. They will be asked to rate the relevance and clarity of the items (on a  
36 scale from 1 to 4; 1 is the lowest relevance/clarity, 4 is the highest relevance/clarity), with a possibility  
37 of providing suggestions of modifications of the initial items, or new items to be added. After each  
38 round of survey, pre-defined decision rules will be applied to keep, delete, or modify the items. This  
39 reactive-Delphi design allows for reduction of effort needed from the experts and faster arrival at  
40 consensus compared to the traditional Delphi design where experts are asked to come up with all  
41 items themselves.  
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### 47 **The steering committee**

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50 The committee driving this initiative to develop guidelines for reporting research on medication  
51 adherence (also the authors of this study protocol) are members and founding members of the  
52 European Society for Patient Adherence, COMpliance, and Persistence (**ESPACOMP**,  
53 [www.espacomp.eu](http://www.espacomp.eu)). One of their major research interests is medication adherence. They represent a  
54 diversity of disciplines including biostatistics, health economics, health policy and management,  
55 health services research, medicine, nursing, pharmacy, pharmacology, and psychology. Some  
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members of the committee were involved in development of the *ABC taxonomy for medication adherence* (BV, DH, and SDG).

### Role of the steering committee

The steering committee developed the initial items and will select the sample of experts for this study. Based on the decision rules, the steering committee will also apply the corresponding actions after each survey round: (i) keeping or deleting an item based on relevance scores, and (ii) modifying the wording of items based on clarity scores and the suggestions provided by the experts. For items that will not have achieved consensus on relevance after the survey rounds will be stopped, the steering committee will decide on each item individually based on internal consensus among its members, taking into consideration the aggregate input provided by the expert panel. All of the abovementioned tasks of the steering committee are further detailed later in this protocol.

### Sample and sampling procedures

A purposive sample of medication adherence experts will be included in the study. The size of the group of experts needed for participation in any Delphi study does not depend on statistical power as representativeness in such studies is assessed based on the quality of the sample rather than its size[20]. Accordingly, the steering committee identified medication adherence experts based on the representation of disciplines and geographical locations. In concordance with other similar projects aiming at developing guidelines for reporting of health research[16, 17], the goal is to include a minimum of 20 experts in the final survey round. To compensate for possible initial refusal or attrition over rounds, oversampling was considered with a rate of 25% per round. With a literature-based average[22] of three rounds until consensus is achieved, the starting sample will be a minimum of 40 experts.

More specifically, the Delphi participants need to be established experts in the field of medication adherence and satisfy all the following main selection criteria:

- 1) having a minimum experience of five years in the field of medication adherence;
- 2) having an established international profile in this field, recognized by scientific publications, policy reports and/or extensive participation in specialized topic conferences, meetings, or interest groups; and
- 3) having good English proficiency to complete the surveys

To ensure representativeness of all relevant disciplines and geographical locations, the following variability selection criteria will be applied:

1. The starting sample will include participants from each of the following disciplines:
  - a. Health services research
  - b. Clinical research
  - c. Statistics
  - d. Medicine
  - e. Nursing



- f. Pharmacy/pharmaceutical sciences
- g. Pharmaceutical industry
- h. Clinical pharmacology
- i. Pharmacoepidemiology
- j. Behavioural medicine/health psychology
- k. Journal editing
- l. Public health
- m. Health policy

2. Geographical representation will be ensured by selecting experts from all continents.

Each of the steering committee members will provide suggestions for experts to be included on the expert panel for the Delphi study based on the aforementioned criteria. Feedback and agreement on the proposed list by the whole steering committee will be sought before experts are invited to participate. The final choice of the experts to be included will be based on an optimal distribution and representation of experts in view of the sample selection criteria (main & variability criteria) and will be moderated by two members of the steering committee (SDG, RH). Delphi participants who will complete all rounds of the study will be listed in the final publication of the reporting guidelines in an acknowledgment section. However, the study will be fully anonymized and participants will not be known to each other during the survey rounds.

### Generation of the initial item list

The initial item list was developed and fine-tuned by the steering committee. First, a literature review was performed to identify existing medication adherence research guidelines[10-12] and recommendations[1, 13] by two members of the steering committee (RH, SDG). This information was summarized and discussed in an in-person meeting in Prague in November 2015 among all of the steering committee members. This discussion, guided by the *ABC taxonomy for medication adherence* as well as by a review of common sections of the existing reporting guidelines for health research reporting (e.g. STROBE, CONSORT), led to generating a pool of items.

Using a stepwise review process, the steering committee reviewed and further fine-tuned the items in view of relevance and clarity over four feedback rounds via e-mail and conference calls. Items were gradually enhanced and revised to focus exclusively on aspects relevant to medication adherence. Redundancy between items of the existing reporting guidelines for health research (e.g. STROBE, CONSORT) and items for reporting research on medication adherence was scrutinized and eliminated where needed.

The resulting initial item list consists of 26 items distributed in two sections. The first section includes 4 items that reflect the conceptualization of medication adherence as put forward by the *ABC taxonomy for medication adherence* and represent the taxonomy-based minimum reporting criteria. The second section includes 22 items specific to medication adherence research reporting and organized in a way congruent with common sections of reporting guidelines for major study types (e.g. STROBE, CONSORT).



## Decision rules and definition of consensus on relevance and clarity of items

Since the definition of consensus varies among Delphi studies according to the aims of each study, rating scales along with consensus rules for this study were inspired by the content validity index[23] as it simplifies the decision-making process as explained below. **Rectangle (A)** in **figure (1)** shows how the below decision rules will work together and their possible outcomes.

### Item-level decision-making rules

Scores for *relevance* will be used to decide on keeping or deleting an item. Consensus on relevance of an item is defined as 70% of the experts in the sample giving this item a score of three or more on a scale from one to four (1: not relevant; 2: somewhat relevant; 3: quite relevant; 4: highly relevant) during any survey round. Hence, this item will be kept on the final item list. Consensus on irrelevance of an item is defined as 70% of the respondents giving this item a score of two or less during any survey round. Consequently, this item will be deleted from the item list.

Scores for *clarity* of wording will subsequently guide fine-tuning of the wording of the respective items to be included on the list. For simplifying the procedures, only one rule will be used for consensus on lack of clarity, defined as 70% of the respondents giving this item a score of two or less on a scale from one to four (1: not clear; 2: somewhat clear; 3: quite clear; 4: highly clear) during any survey round. Consensus on lack of clarity for any item will further lead to using comments provided by the experts to modify the wording of each corresponding item. This will be done by the steering committee after the rounds end.

### List-level decision-making rule

One of the key methodologic criteria of Delphi studies is having a stoppage rule on when the survey rounds will stop[23]. For this purpose, a stoppage rule of having a consensus on relevance for 80% of all items on the list will be used. In other words, the Delphi rounds will be stopped once 80% of the items on the list at that point of time receive consensus on relevance (i.e. 80% of the items received a score  $\geq 3$  by 70% of the experts). This rule will be applied from the first round if no new items will be suggested or from the second round after the experts will have provided scores for any suggested new items.

### Study procedures

Once the initial item list and the participants sample are ready, the study will start with a preparatory period of two weeks to set up the online environment of the survey and test its functionality. Afterwards, survey rounds will start and continue until the stoppage rule is fulfilled. An invitation for a feedback round will be sent to the expert group with a response deadline of two weeks after the invitation day. Reminders will be sent to those who won't respond, or will respond partially. Each round will be followed by an additional period for summarizing and analysing the responses and integrating the results into the following version of the survey. An invitation for a next feedback round

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2  
3 will be sent out as described before to experts who will have completed all rounds from the beginning  
4 until then.

5  
6 The surveys will be conducted and the responses will be collected online via a survey  
7 platform (SurveyMonkey®). Two member of the steering committee (SDG, RH) will be responsible for  
8 data collection and responding to possible inquiries from the experts. In case substantial issues are  
9 addressed by any member of the expert group, the other members of the committee will be consulted  
10 for advice and problem resolution.  
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14 A more detailed explanation of the process is provided below:

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16 **1. First survey round** will consist of:

- 17  
18 a. providing a score for each of the items in view of *relevance* to the topic and *clarity* of  
19 wording  
20 b. justifying the scores chosen and/or suggesting modifications for each item – (*optional*  
21 – free-form text)  
22 c. suggesting additional new items – (*optional* – free-form text)  
23

24 Additionally, experts will provide information on their demographics, professional  
25 background, and specific areas of expertise in adherence research for descriptive purposes  
26 as well as confirming their eligibility in the first survey round.  
27

28 Scores provided for the items will be summarized by their percentages and frequency  
29 distribution and inclusion or deletion of items in the following version of the survey will be  
30 guided by the aforementioned decision rules. Comments on potential adaptations of item  
31 wording will be summarized and integrated by the steering committee where deemed  
32 relevant.  
33

34 If no new items are suggested and consensus on relevance is reached for 80% of the  
35 items on the initial item list, the survey rounds will be stopped. Otherwise, the scores and  
36 comments of items that will not have reached consensus on relevance will be presented in  
37 the following round and/or suggestions of new items will be summarized and integrated into  
38 the following version of the survey. Further evaluation and decision making will follow the  
39 methodology described before.  
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45 **2. Second round:** An adapted item list including the scores and comments of the initial items as  
46 well as any new items from the 1<sup>st</sup> round will be sent to the experts. They will be invited to:

- 47  
48 a. revise their opinion with new *relevance* and *clarity* scores, on the same scale as  
49 mentioned before, and comments for items that did not achieve consensus on  
50 relevance in the 1<sup>st</sup> round  
51 b. score each of the new items in view of *relevance* to the topic and *clarity* of wording,  
52 on the same scale as mentioned before  
53 c. justify the scores chosen and/or suggest modifications for each item – (optional –  
54 free-form text)  
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3 If list-level consensus is not reached by the 2<sup>nd</sup> round, scores and comments will be  
4 summarized as described in the 1<sup>st</sup> round and integrated into the item list to be presented in  
5 further rounds until consensus is reached.  
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3. **Further rounds** will consist of presenting consolidated feedback for all items that will not have achieved consensus on relevance in previous rounds with a chance for experts to revise their opinion accordingly with:
- a. new *relevance* and *clarity* scores for the remaining items
  - b. justification for the scores chosen and/or modifications for each item – (optional – free-form text)

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Finally, results of the final round will be consolidated and presented to the steering committee for proceeding with further steps. The flowchart in **figure (1)** delineates the survey rounds based on the input and output of each round.

## 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38

### ETHICAL AND LEGAL CONSIDERATIONS

Since this study does not use health data of individuals, an ethics approval is not required according to the Swiss federal act on research involving human beings. Participants in the Delphi study will be asked to provide informed consent to have their responses included in further analysis and dissemination of the results. Furthermore, they will be informed about confidentiality of the data and the corresponding legal obligations of not exposing such data to third parties. Additionally, they will be asked whether they would like to be acknowledged in the corresponding publications and dissemination of the guidelines. All data relevant to the study will be kept on password-encrypted computers which can be accessed by the steering committee only.

### 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60

### FURTHER PLANNING OF GUIDELINES DEVELOPMENT

The list of items reached through this study will be integrated by the steering committee into the planned ESPACOMP medication adherence reporting guidelines (**EMERGE**). The guidelines will be disseminated through peer-reviewed publications, presentations at conferences of ESPACOMP and other relevant organizations, and registration of the guidelines with the EQUATOR Network. Endorsement of the guidelines by journals and relevant professional organizations will be encouraged. Two members of the steering committee (SDG, RH) will remain available to receive feedback and criticism after publication. Accordingly, further updates and revisions of the guidelines will be considered on an annual basis during ESPACOMP annual meetings, based on the EQUATOR guidance for developers of health research reporting guidelines.

## OUTLOOK

Medication nonadherence is a public health threat that causes poor patient outcomes and increased economic burden[24, 25]. The quality of medication adherence research as well as the quality of its reporting will determine the development and testing of effective and innovative solutions to enhance patients' adherence to medications and is therefore of paramount importance to many stakeholders. EMERGE aim at guiding researchers to report relevant aspects of medication adherence research in a standard manner. The use of the guidelines, in combination with other existing guidelines like STROBE or CONSORT, is expected to facilitate this task and, subsequently, help research in medication adherence field advance towards achieving its ultimate goal of improved outcomes.

## DELPHI STUDY STATUS

The initial item list was developed and the online survey environment was set up and tested by the steering committee. The sample of experts was chosen and data collection (1<sup>st</sup> round) started in June 2016.

## CONTRIBUTORSHIP STATEMENT

No person other than the authors listed contributed significantly to the manuscript preparation. All persons listed as authors contributed to preparing the manuscript and the International Committee of Medical Journal Editors (ICMJE) criteria for authorship were met. Specifically, the following contributions were made by the respective authors:

- **RH:**

1. Contributed substantially to the conception and design of the study, and the acquisition, analysis, and interpretation of data for the work
2. Drafted the work and revised it critically
3. Approved the final version to be published
4. Agrees to be accountable for all aspects of the work

- **JDJ, DH, BV, IBW, LLZ:**

1. Contributed substantially to the acquisition, analysis, and interpretation of data for the work
2. Revised the work critically
3. Approved the final version to be published
4. Agree to be accountable for all aspects of the work

- **SDG:**

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1. Is the project's principal investigator who contributed substantially to the conception and design of the study, and the acquisition, analysis, and interpretation of data for the work
  2. Drafted the work and revised it critically
  3. Approved the final version to be published
  4. Agrees to be accountable for all aspects of the work

## COMPETING INTERESTS STATEMENT

The authors have declared no competing interests regarding their work on the current study.

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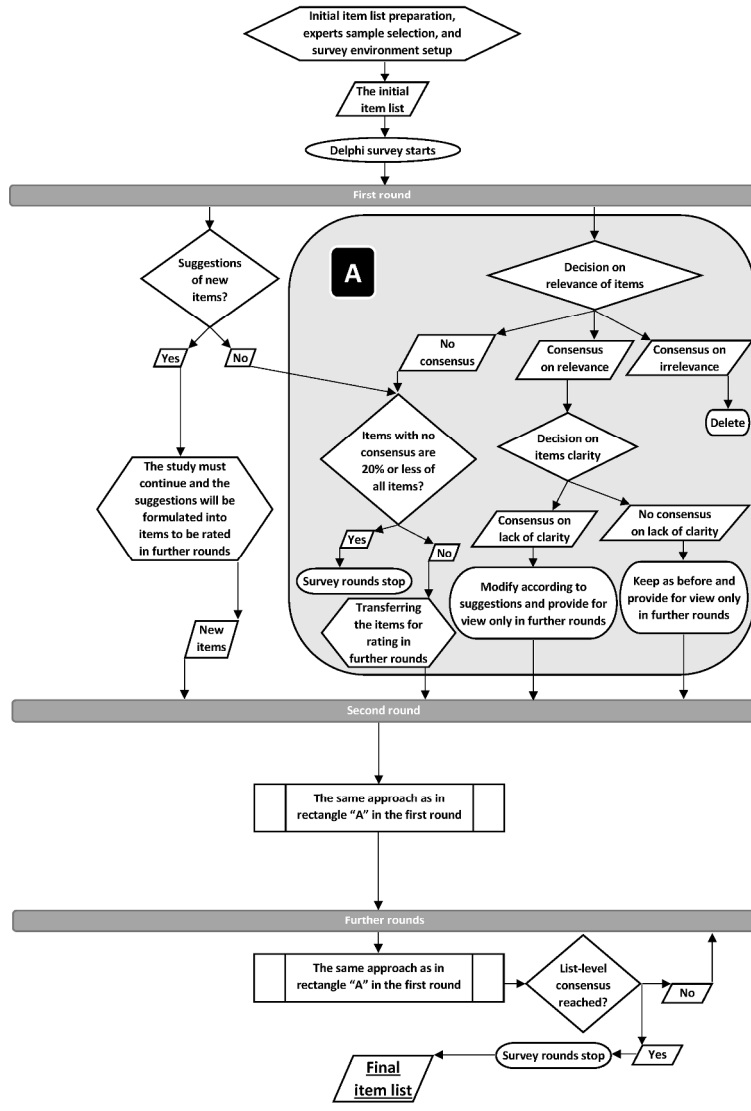


Figure 1: Flowchart of the survey rounds  
210x297mm (300 x 300 DPI)

# BMJ Open

## ESPAComp Medication Adherence Reporting Guidelines (EMERGE): A Reactive-Delphi Study Protocol

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Keywords:	Medication adherence, Medication compliance, Health research reporting guidelines, Delphi method, Study protocol

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# ESPACOMP Medication Adherence Reporting Guidelines (EMERGE): A Reactive-Delphi Study Protocol

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## Abstract

### Introduction

Medication adherence is fundamental to achieving optimal patient outcomes. Reporting research on medication adherence suffers from some issues – including conceptualization, measurement, and data analysis – that thwart its advancement. Using the ABC taxonomy for medication adherence as the conceptual basis, a steering committee of members of the European Society for Patient Adherence, COMpliance, and Persistence (**ESPACOMP**) launched an initiative to develop ESPACOMP medication adherence reporting guidelines (**EMERGE**). This paper reports on a Delphi study that aims to build consensus among a group of topic experts regarding an item list that will support developing EMERGE.

### Methods and analysis

This study uses a reactive-Delphi design where a group of topic experts will be asked to rate the relevance and clarity of an initial list of items, in addition to providing suggestions for further items and/or modifications of the initial items. The initial item list, generated by the EMERGE steering committee through a structured process, consists of 26 items distributed in 2 sections; 4 items representing the taxonomy-based minimum reporting criteria, and 22 items organized according to the common reporting sections. A purposive sample of experts will be selected from relevant disciplines and diverse geographical locations. Consensus will be achieved through pre-defined decision rules to keep, delete, or modify the items. An iterative process of online survey rounds will be carried out until consensus is reached.

### Ethics and dissemination

An ethics approval was not required for the study according to the Swiss federal act on research involving human beings. Participating experts will be asked to give an informed consent. The results of this Delphi study will feed into EMERGE, which will be disseminated through peer-reviewed publications and presentations at conferences. Additionally, the steering committee will encourage its endorsement by registering the guidelines at the **EQUATOR** network and other relevant organizations.

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<p><b>Strengths of the study</b></p> <ul style="list-style-type: none"><li>• Incorporates the input of many topic experts across various disciplines and geographical areas</li><li>• Preserves subject anonymity and reduces the effect of dominant individuals</li><li>• Uses statistical analysis techniques to reduce the potential of group pressure for conformity</li></ul> <p><b>Limitations of the study</b></p> <ul style="list-style-type: none"><li>• Requires large blocks of time to administer several survey rounds and consolidate their output</li><li>• Has potential to mold opinions based on the received aggregate feedback</li></ul>
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For peer review only

## INTRODUCTION

Reporting research on medication adherence is suboptimal. Confusion prevails regarding the conceptual underpinning, adequate measurement, and analysis of medication adherence data, hindering scientific progress in this field[1, 2, 3]. Guidelines on the reporting of health research aim at enhancing publication quality and may focus on specific study designs, research areas, or sections of a report. Examples of such guidelines can be found on the website of the Enhancing the QUALity and Transparency Of health Research (**EQUATOR**) network ([www.equator-network.org](http://www.equator-network.org)), and include STROBE[4] (for observational studies in epidemiology), CONSORT[5] (for trials), and TIDieR[6] (for description and replication of interventions) guidelines. The introduction of such guidelines and their endorsement by professional societies and journals have proven to be helpful in enhancing the transparency and accuracy of health research reporting[7, 8].

There are existing published guidelines and recommendations focusing on medication adherence research[1, 9-12]. However, these guidelines overlap considerably with those developed for general clinical research and are, thus, not particularly specific for medication adherence research[9, 10]. Additionally, they do not build on a clear conceptualization of medication adherence[1, 9, 10, 12], and focus on study design rather than reporting[1, 11, 12]. Considering the shortcomings of the existing guidelines and the aforementioned deficits in the quality of medication adherence research, this field would benefit from specific reporting guidelines to boost the quality of reporting medication adherence research.

A steering committee of members of the European Society for Patient Adherence, COMpliance, and Persistence (**ESPACOMP**, [www.espacomp.eu](http://www.espacomp.eu)) launched an initiative to develop ESPACOMP medication adherence reporting guidelines (**EMERGE**) that will tackle the abovementioned shortcomings in the following manner. Considering the conceptualization of medication adherence, the anticipated guidelines will build on the *ABC taxonomy for medication adherence*[13]. This taxonomy defines medication adherence as *'the process by which patients take their medications as prescribed'*. It divides this process into three interrelated phases: (1) initiation; (2) implementation; and (3) persistence, each demanding a clear operational definition and appropriate measurement and data analysis. Hence, setting this conceptualization as a standard for reporting medication adherence research is anticipated to remove the ambiguity surrounding medication adherence as a concept. Additionally, designing the guidelines attentively to avoid overlapping with the existing guidelines for general clinical research has a twofold benefit. First, it will steer clear of redundancy and, thus, any confusion that might arise accordingly. Second, it will allow the new guidelines to be applied to the different study designs and used in parallel with the general guidelines available for the corresponding study design. Finally, developing the guidelines as reporting guidelines will help both the authors in figuring out the important elements to be reported about their research and the reviewers in critically appraising the quality of the studies.

Developing reporting guidelines, however, requires input by experts from various scientific backgrounds and needs to be relevant across geographical regions. This is particularly applicable in the context of medication adherence, which is a multidisciplinary science ranging from behavioural

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3 sciences through statistics and clinical medicine to economics. Delphi methodology, as a means for  
4 consensus building[14], enables integration of input from a wide variety of experts. It achieves  
5 consensus through an iterative process of survey rounds, providing the opportunity for participants to  
6 revise their input in subsequent rounds based on collective group feedback from previous rounds.  
7 This method enables the neutral and efficient integration of feedback from different experts, is  
8 suggested as one of the 18 steps put forward by the EQUATOR network in their guidance on  
9 developing health research reporting guidelines[15] and has been used in developing many similar  
10 guidelines[16, 17].

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14 This approach has many benefits[18, 19, 20]. First, the iterative nature of the study and the  
15 feedback process allows participants to reassess their initial judgments. Thus, consensus is reached  
16 through a gradual stepwise process based on rational thinking and input. Second, participants do not  
17 interact directly and remain anonymous to each other until the survey rounds end. Hence, group  
18 domination by the views of certain individuals is avoided. Third, when participants consider changing  
19 or sticking to their original opinion after checking group response, this decision is not affected by the  
20 desire to be seen concordant with senior or dominant individuals. Fourth, experts can participate  
21 asynchronously and do not need to be present together while answering surveys as they receive  
22 collective feedback along with new surveys, which can be conducted through a web-based platform.  
23 Accordingly, it is feasible to use this approach to involve geographically distant participants.  
24 Moreover, the controlled feedback minimizes the effect of noise, which can happen in face-to-face  
25 group discussions. Finally, the ability to use statistical analysis facilitates reaching a more objective  
26 consensus than that usually reached through face-to-face conversations. Consequently, the Delphi  
27 method is an appropriate method to include the knowledge of many experts to cover the numerous  
28 aspects of the medication adherence subject.  
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## 36 AIM

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39 The aim of this Delphi study is to build consensus among a group of topic experts regarding  
40 an item list that will support developing guidelines for medication adherence research reporting.  
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## 43 METHODS AND ANALYSIS

### 44 Overview of the study design

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48 The study implements a reactive-Delphi design[21] where a group of medication adherence  
49 experts will be provided, in the first survey round, with an initial list of 26 items that are specific to  
50 medication adherence research. They will be asked to rate the relevance and clarity of the items (on a  
51 scale from 1 to 4; 1 is the lowest relevance/clarity, 4 is the highest relevance/clarity), with a possibility  
52 of providing suggestions of modifications of the initial items, or new items to be added. After each  
53 round of survey, pre-defined decision rules will be applied to keep, delete, or modify the items. This  
54 reactive-Delphi design allows for reduction of effort needed from the experts and faster arrival at  
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consensus compared to the traditional Delphi design where experts are asked to come up with all items themselves.

### **The steering committee**

The committee driving this initiative to develop guidelines for reporting research on medication adherence (also the authors of this study protocol) are members and founding members of ESPACOMP. One of their major research interests is medication adherence. They represent a diversity of disciplines including biostatistics, health economics, health policy and management, health services research, medicine, nursing, pharmacy, pharmacology, and psychology. Some members of the committee were involved in development of the *ABC taxonomy for medication adherence* (BV, DH, and SDG).

### **Role of the steering committee**

The steering committee developed the initial items and will select the sample of experts for this study. Based on the decision rules, the steering committee will also apply the corresponding actions after each survey round: (i) keeping or deleting an item based on relevance scores, and (ii) modifying the wording of items based on clarity scores and the suggestions provided by the experts. For items that will not have achieved consensus on relevance after the survey rounds will be stopped, the steering committee will decide on each item individually based on internal consensus among its members, taking into consideration the aggregate input provided by the expert panel. All of the abovementioned tasks of the steering committee are further detailed later in this protocol.

### **Sample and sampling procedures**

A purposive sample of medication adherence experts will be included in the study. The size of the group of experts needed for participation in any Delphi study does not depend on statistical power as representativeness in such studies is assessed based on the quality of the sample rather than its size[20]. Accordingly, the steering committee identified medication adherence experts based on the representation of disciplines and geographical locations. In concordance with other similar projects aiming at developing guidelines for reporting of health research[16, 17], the goal is to include a minimum of 20 experts in the final survey round. To compensate for possible initial refusal or attrition over rounds, oversampling was considered with a rate of 25% per round. With a literature-based average[22] of three rounds until consensus is achieved, the starting sample will be a minimum of 40 experts.

More specifically, the Delphi participants need to be established experts in the field of medication adherence and satisfy all the following main selection criteria:

- 1) having a minimum experience of five years in the field of medication adherence;

- 2) having an established international profile in this field, recognized by scientific publications, policy reports and/or extensive participation in specialized topic conferences, meetings, or interest groups; and
- 3) having good English proficiency to complete the surveys

To ensure representativeness of all relevant disciplines and geographical locations, the following variability selection criteria will be applied:

1. The starting sample will include participants from each of the following disciplines:
  - a. Health services research
  - b. Clinical research
  - c. Statistics
  - d. Medicine
  - e. Nursing
  - f. Pharmacy/pharmaceutical sciences
  - g. Pharmaceutical industry
  - h. Clinical pharmacology
  - i. Pharmacoepidemiology
  - j. Behavioural medicine/health psychology
  - k. Journal editing
  - l. Public health
  - m. Health policy
2. Geographical representation will be ensured by selecting experts from all continents.

Each of the steering committee members will provide suggestions for experts to be included on the expert panel for the Delphi study based on the aforementioned criteria. Feedback and agreement on the proposed list by the whole steering committee will be sought before experts are invited to participate. The final choice of the experts to be included will be based on an optimal distribution and representation of experts in view of the sample selection criteria (main & variability criteria) and will be moderated by two members of the steering committee (SDG, RH). Delphi participants who will complete all rounds of the study will be listed in the final publication of the reporting guidelines in an acknowledgment section. However, the study will be fully anonymized and participants will not be known to each other during the survey rounds.

### Generation of the initial item list

The initial item list was developed and fine-tuned by the steering committee. First, a literature review was performed to identify existing medication adherence research guidelines[9-11] and recommendations[1, 12] by two members of the steering committee (RH, SDG). This information was summarized and discussed in an in-person meeting in Prague in November 2015 among all of the steering committee members. This discussion, guided by the *ABC taxonomy for medication adherence* as well as by a review of common sections of the existing reporting guidelines for health research reporting (e.g. STROBE, CONSORT), led to generating a pool of items.

Using a stepwise review process, the steering committee reviewed and further fine-tuned the items in view of relevance and clarity over four feedback rounds via e-mail and conference calls. Items were gradually enhanced and revised to focus exclusively on aspects relevant to medication adherence. Redundancy between items of the existing reporting guidelines for health research (e.g. STROBE, CONSORT) and items for reporting research on medication adherence was scrutinized and eliminated where needed.

The resulting initial item list consists of 26 items distributed in two sections. The first section includes 4 items that reflect the conceptualization of medication adherence as put forward by the *ABC taxonomy for medication adherence* and represent the taxonomy-based minimum reporting criteria. The second section includes 22 items specific to medication adherence research reporting and organized in a way congruent with common sections of reporting guidelines for major study types (e.g. STROBE, CONSORT).

### **Decision rules and definition of consensus on relevance and clarity of items**

Since the definition of consensus varies among Delphi studies according to the aims of each study, rating scales along with consensus rules for this study were inspired by the content validity index[23] as it simplifies the decision-making process as explained below. **Square (A) in figure (1)** shows how the below decision rules will work together and their possible outcomes.

#### **Item-level decision-making rules**

Scores for *relevance* will be used to decide on keeping or deleting an item. Consensus on relevance of an item is defined as 70% of the experts in the sample giving this item a score of three or more on a scale from one to four (1: not relevant; 2: somewhat relevant; 3: quite relevant; 4: highly relevant) during any survey round. Hence, this item will be kept on the final item list. Consensus on irrelevance of an item is defined as 70% of the respondents giving this item a score of two or less during any survey round. Consequently, this item will be deleted from the item list.

Scores for *clarity* of wording will subsequently guide fine-tuning of the wording of the respective items to be included on the list. For simplifying the procedures, only one rule will be used for consensus on lack of clarity, defined as 70% of the respondents giving this item a score of two or less on a scale from one to four (1: not clear; 2: somewhat clear; 3: quite clear; 4: highly clear) during any survey round. Consensus on lack of clarity for any item will further lead to using comments provided by the experts to modify the wording of each corresponding item. This will be done by the steering committee after the rounds end.

#### **List-level decision-making rule**

One of the key methodologic criteria of Delphi studies is having a stoppage rule on when the survey rounds will stop[22]. For this purpose, a stoppage rule of having a consensus on relevance for 80% of all items on the list will be used. In other words, the Delphi rounds will be stopped once 80% of the items on the list at that point of time receive consensus on relevance (i.e. 80% of the items received a score  $\geq 3$  by 70% of the experts). This rule will be applied from the first round if no new

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3 items will be suggested or from the second round after the experts will have provided scores for any  
4 suggested new items.  
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## 7 **Study procedures**

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10 Once the initial item list and the participants sample are ready, the study will start with a  
11 preparatory period of two weeks to set up the online environment of the survey and test its  
12 functionality. Afterwards, survey rounds will start and continue until the stoppage rule is fulfilled. An  
13 invitation for a feedback round will be sent to the expert group with a response deadline of two weeks  
14 after the invitation day. Reminders will be sent to those who won't respond, or will respond partially.  
15 Each round will be followed by an additional period for summarizing and analysing the responses and  
16 integrating the results into the following version of the survey. An invitation for a next feedback round  
17 will be sent out as described before to experts who will have completed all rounds from the beginning  
18 until then.  
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22 The surveys will be conducted and the responses will be collected online via a survey  
23 platform (SurveyMonkey®). Two member of the steering committee (SDG, RH) will be responsible for  
24 data collection and responding to possible inquiries from the experts. In case substantial issues are  
25 addressed by any member of the expert group, the other members of the committee will be consulted  
26 for advice and problem resolution.  
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30 A more detailed explanation of the process is provided below:

### 31 **1. First survey round** will consist of:

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33 a. providing a score for each of the items in view of *relevance* to the topic and *clarity* of  
34 wording  
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36 b. justifying the scores chosen and/or suggesting modifications for each item – (*optional*  
37 – free-form text)  
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39 c. suggesting additional new items – (*optional* – free-form text)

40 Additionally, experts will provide information on their demographics, professional  
41 background, and specific areas of expertise in adherence research for descriptive purposes  
42 as well as confirming their eligibility in the first survey round.  
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44 Scores provided for the items will be summarized by their percentages and frequency  
45 distribution and inclusion or deletion of items in the following version of the survey will be  
46 guided by the aforementioned decision rules. Comments on potential adaptations of item  
47 wording will be summarized and integrated by the steering committee where deemed  
48 relevant.  
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51 If no new items are suggested and consensus on relevance is reached for 80% of the  
52 items on the initial item list, the survey rounds will be stopped. Otherwise, the scores and  
53 comments of items that will not have reached consensus on relevance will be presented in  
54 the following round and/or suggestions of new items will be summarized and integrated into  
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the following version of the survey. Further evaluation and decision making will follow the methodology described before.

**2. Second round:** An adapted item list including the scores and comments of the initial items as well as any new items from the 1<sup>st</sup> round will be sent to the experts. They will be invited to:

- a. revise their opinion with new *relevance* and *clarity* scores, on the same scale as mentioned before, and comments for items that did not achieve consensus on relevance in the 1<sup>st</sup> round
- b. score each of the new items in view of *relevance* to the topic and *clarity* of wording, on the same scale as mentioned before
- c. justify the scores chosen and/or suggest modifications for each item – (optional – free-form text)

If list-level consensus is not reached by the 2<sup>nd</sup> round, scores and comments will be summarized as described in the 1<sup>st</sup> round and integrated into the item list to be presented in further rounds until consensus is reached.

**3. Further rounds** will consist of presenting consolidated feedback for all items that will not have achieved consensus on relevance in previous rounds with a chance for experts to revise their opinion accordingly with:

- a. new *relevance* and *clarity* scores for the remaining items
- b. justification for the scores chosen and/or modifications for each item – (optional – free-form text)

Finally, results of the final round will be consolidated and presented to the steering committee for proceeding with further steps. The flowchart in **figure (1)** delineates the survey rounds based on the input and output of each round.

## ETHICAL AND LEGAL CONSIDERATIONS

Since this study does not use health data of individuals, an ethics approval is not required according to the Swiss federal act on research involving human beings. Participants in the Delphi study will be asked to provide informed consent to have their responses included in further analysis and dissemination of the results. Furthermore, they will be informed about confidentiality of the data and the corresponding legal obligations of not exposing such data to third parties. Additionally, they will be asked whether they would like to be acknowledged in the corresponding publications and dissemination of the guidelines. All data relevant to the study will be kept on password-encrypted computers which can be accessed by the steering committee only.

## FURTHER PLANNING OF GUIDELINES DEVELOPMENT

The list of items reached through this study will be integrated by the steering committee into the planned ESPACOMP medication adherence reporting guidelines (**EMERGE**). The guidelines will be disseminated through peer-reviewed publications, presentations at conferences of ESPACOMP and other relevant organizations, and registration of the guidelines with the EQUATOR Network. Endorsement of the guidelines by journals and relevant professional organizations will be encouraged. Two members of the steering committee (SDG, RH) will remain available to receive feedback and criticism after publication. Accordingly, further updates and revisions of the guidelines will be considered on an annual basis during ESPACOMP annual meetings, based on the EQUATOR guidance for developers of health research reporting guidelines.

## OUTLOOK

Medication nonadherence is a public health threat that causes poor patient outcomes and increased economic burden[24, 25]. The quality of medication adherence research as well as the quality of its reporting will determine the development and testing of effective and innovative solutions to enhance patients' adherence to medications and is therefore of paramount importance to many stakeholders. EMERGE aim at guiding researchers to report relevant aspects of medication adherence research in a standard manner. The use of the guidelines, in combination with other existing guidelines like STROBE or CONSORT, is expected to facilitate this task and, subsequently, help research in medication adherence field advance towards achieving its ultimate goal of improved outcomes.

## DELPHI STUDY STATUS

The initial item list was developed and the online survey environment was set up and tested by the steering committee. The sample of experts was chosen and data collection (1<sup>st</sup> round) started in June 2016.

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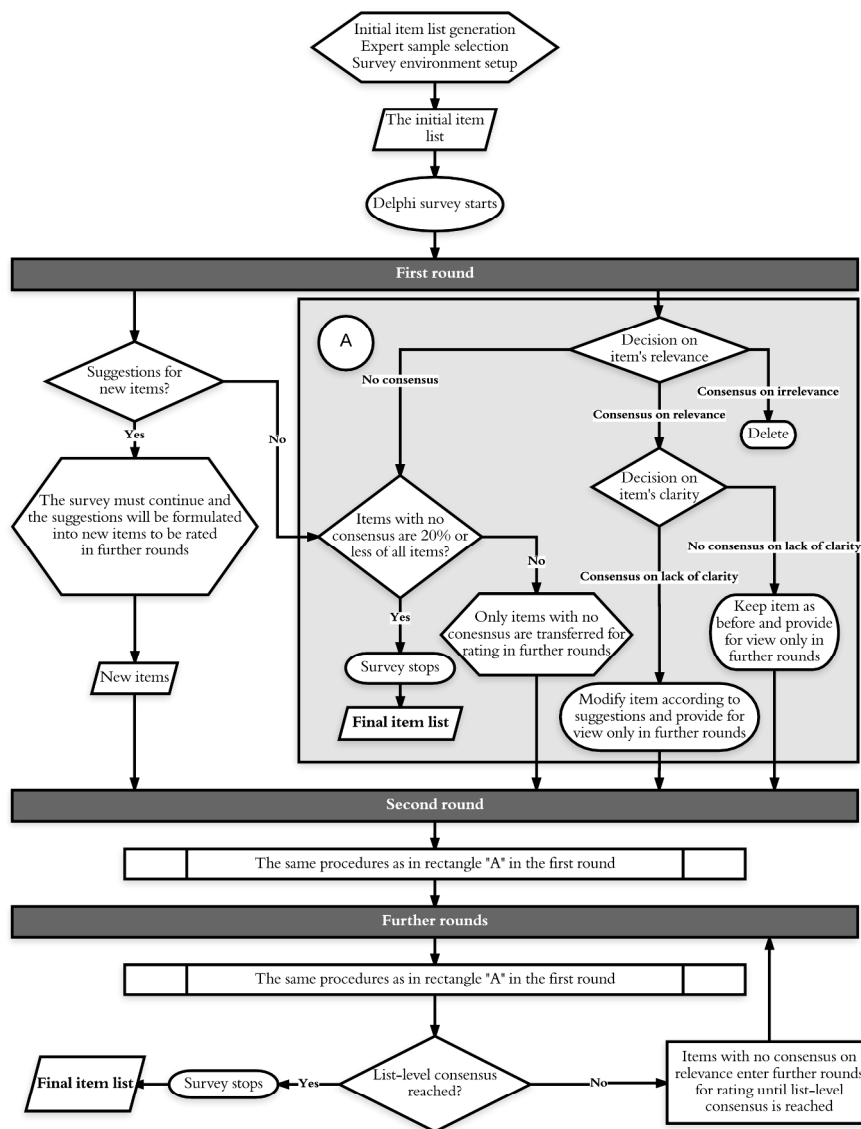


Figure 1: An overview of the Delphi process  
 figure (1)  
 215x279mm (300 x 300 DPI)

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