ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

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Pending: The patent has been filed but not issued

Issued: The patent has been issued by the agency

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Royalties: Funds are coming in to you or your institution due to your patent

Mohammadi
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)
   Alireza

2. Surname (Last Name)
   Mohammadi

3. Date
   07-September-2019

4. Are you the corresponding author?  ☑ No
   Corresponding Author's Name
   Justin Lathia

5. Manuscript Title
   Metronomic capcitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)
   130748-INS-CMED-RV-2

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest?  ☑ No

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Are there any relevant conflicts of interest?  ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work?  ☑ No
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Section 6. Disclosure Statement

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Dr. Mohammadi has nothing to disclose.

Evaluation and Feedback

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Pengjing
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Huang
2. Surname (Last Name) Pengjing
3. Date 10-September-2019

4. Are you the corresponding author? ☑ No
Corresponding Author's Name
Justin Lathia

5. Manuscript Title
Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)
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Are there any relevant conflicts of interest? ☐ Yes ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☑ No

Pengjing
ICMJE Form for Disclosure of Potential Conflicts of Interest

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information
1. Given Name (First Name)
   Justin
2. Surname (Last Name)
   Lathia
3. Date
   07-September-2019
4. Are you the corresponding author? [ ] Yes [ ] No
5. Manuscript Title
   Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells
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Dr. Lathia has nothing to disclose.

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Section 1. Identifying Information

1. Given Name (First Name) Mary
2. Surname (Last Name) McGraw
3. Date 06-September-2019
4. Are you the corresponding author? Yes No Corresponding Author's Name Justin Lathia
5. Manuscript Title Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells
6. Manuscript Identifying Number (if you know it)

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Dr. McGraw has nothing to disclose.

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1. Given Name (First Name)  
   David

2. Surname (Last Name)  
   Peereboom

3. Date  
   06-September-2019

4. Are you the corresponding author?  
   Yes ☑ No
   Corresponding Author's Name  
   Justin Lathia

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Are there any relevant conflicts of interest?  
Yes ☑ No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

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Dr. Peereboom reports grants from Musella Foundation, grants from NIH, grants from Cancer Biology Training Grant, grants from Sontag Foundation, grants from B*CURED, grants from Dr. Miriam and Sheldon G. Adelson Medical Research Foundation, non-financial support from Mylan Pharmaceuticals, during the conduct of the study;

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Alban
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)  
   Tyler

2. Surname (Last Name)  
   Alban

3. Date  
   10-September-2019

4. Are you the corresponding author?  
   ☑ Yes  ☐ No
   Corresponding Author's Name  
   Justin Lathia

5. Manuscript Title  
   Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)  
   130748-INS-CMED-RV-2

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest?  
   ☐ Yes  ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest?  
   ☐ Yes  ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work?  
   ☑ Yes  ☐ No
ICMJE Form for Disclosure of Potential Conflicts of Interest

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Dr. Alban has nothing to disclose.

Evaluation and Feedback

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Vogelbaum
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)  
   Michael

2. Surname (Last Name)  
   Vogelbaum

3. Date  
   08-September-2019

4. Are you the corresponding author?  
   □ Yes  ✔ No
   Corresponding Author’s Name  
   Tyler Alban

5. Manuscript Title

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest?  
   □ Yes  ✔ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest?  ✔ Yes  □ No

If yes, please fill out the appropriate information below.

<table>
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<th>Name of Entity</th>
<th>Grant?</th>
<th>Personal Fees?</th>
<th>Non-Financial Support?</th>
<th>Other?</th>
<th>Comments</th>
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<td>□</td>
<td>□</td>
<td>□</td>
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<td>□</td>
<td></td>
</tr>
</tbody>
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ICMJE Form for Disclosure of Potential Conflicts of Interest

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Section 6. Disclosure Statement
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Dr. Vogelbaum reports other from Infuseon Therapeutics, Inc, personal fees from Tocagen, personal fees from Celgene, personal fees from Blue Earth Diagnostics, outside the submitted work.

Evaluation and Feedback
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Radivoyevitch
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)  
Tomas

2. Surname (Last Name)  
Radivoyevitch

3. Date  
06-September-2019

4. Are you the corresponding author?  
[ ] Yes  [x] No

Corresponding Author's Name  
Justin D. Lathia

5. Manuscript Title  
Metronomic capcitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)

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Do you have any patents, whether planned, pending or issued, broadly relevant to the work?  
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Radivoyevitch
ICMJE Form for Disclosure of Potential Conflicts of Interest

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Dr. Radivoyevitch has nothing to disclose.

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Alvarado
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Alvaro
2. Surname (Last Name) Alvarado
3. Date 08-September-2019
4. Are you the corresponding author? ☑ No
   Corresponding Author’s Name Justin D. Lathia
5. Manuscript Title Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells
6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☑ No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? ☑ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☑ No
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Dr. Alvarado has nothing to disclose.

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Otvos
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)
   Balint

2. Surname (Last Name)
   Otvos

3. Date
   06-September-2019

4. Are you the corresponding author? □ Yes  ✔ No
   Corresponding Author's Name
   Justin D Lathia

5. Manuscript Title
   Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)

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Are there any relevant conflicts of interest? □ Yes  ✔ No

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Section 4. Intellectual Property -- Patents & Copyrights

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Dr. Otvos has nothing to disclose.

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Otvos
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Royalties: Funds are coming in to you or your institution due to your patent
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)  
   Defne

2. Surname (Last Name)  
   Bayik

3. Date  
   06-September-2019

4. Are you the corresponding author?  
   ☐ Yes  ✔ No  
   Corresponding Author’s Name  
   Justin D. Lathia

5. Manuscript Title  
   Metronomic capcitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (If you know it)

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest?  
   ☐ Yes  ✔ No

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Are there any relevant conflicts of interest?  
   ☐ Yes  ✔ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work?  
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ICMJE Form for Disclosure of Potential Conflicts of Interest

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Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Bayik has nothing to disclose.

Evaluation and Feedback

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Kornblum
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)  
   Harley

2. Surname (Last Name)  
   Kornblum

3. Date  
   06-September-2019

4. Are you the corresponding author?  
   □ Yes  ✔ No
   Corresponding Author’s Name

5. Manuscript Title

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest?  
   □ Yes  ✔ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity, add as many lines as you need by clicking the “Add +” box. You should report relationships that were present during the 36 months prior to publication.

Are there any relevant conflicts of interest?  
   □ Yes  ✔ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work?  
   □ Yes  ✔ No
Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

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Grabowski
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)
   Matthew

2. Surname (Last Name)
   Grabowski

3. Date
   06-September-2019

4. Are you the corresponding author?
   ☑ No
   Corresponding Author’s Name

5. Manuscript Title
   Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)
   130748-INS-RG-1

Section 2. The Work Under Consideration for Publication

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)  
   Gustavo

2. Surname (Last Name)  
   Roversi

3. Date  
   07-September-2019

4. Are you the corresponding author?  
   [ ] Yes  [ ] No  
   Corresponding Author’s Name  
   Justin Lathia

5. Manuscript Title  
   Metronomic capecitabine as an immune modulator in glioblastoma patients reduces myeloid-derived suppressor cells

6. Manuscript Identifying Number (if you know it)

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## TREDN Statement Checklist

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<tr>
<th>Paper Section/Topic</th>
<th>Item</th>
<th>Descriptor</th>
<th>Reported?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title and Abstract</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title and Abstract</td>
<td>1</td>
<td>• Information on how unit were allocated to interventions</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Structured abstract recommended</td>
<td>✓</td>
</tr>
</tbody>
</table>
|                     |      | • Information on target population or study sample                          | ✓         | 14, 15
| **Introduction**    | 2    | • Scientific background and explanation of rationale                        | ✓         | 3, 14
|                     |      | • Theories used in designing behavioral interventions                        | ✓         | 14, 15
| **Methods**         | 3    | • Eligibility criteria for participants, including criteria at different levels in recruitment/sampling plan (e.g., cities, clinics, subjects) | ✓         | 14
|                     |      | • Method of recruitment (e.g., referral, self-selection), including the sampling method if a systematic sampling plan was implemented | ✓         | 14, 15
|                     |      | • Recruitment setting                                                       | ✓         | 14, 15
|                     |      | • Settings and locations where the data were collected                       | ✓         | 1, 14, 15
|                     | 4    | • Details of the interventions intended for each study condition and how and when they were actually administered, specifically including: | ✓         | 14, 15
|                     |      |   o Content: what was given?                                                | ✓         | 14, 15
|                     |      |   o Delivery method: how was the content given?                             | ✓         | 14, 15
|                     |      |   o Unit of delivery: how were the subjects grouped during delivery?        | ✓         | 14, 15
|                     |      |   o Deliverer: who delivered the intervention?                              | ✓         | 14, 15
|                     |      |   o Setting: where was the intervention delivered?                          | ✓         | 14, 15
|                     |      |   o Exposure quantity and duration: how many sessions or episodes or events were intended to be delivered? How long were they intended to last? | ✓         | 14, 15
|                     |      |   o Time span: how long was it intended to take to deliver the intervention to each unit? | ✓         | 14, 15
|                     |      |   o Activities to increase compliance or adherence (e.g., incentives)       | ✓         | 14, 15
| **Objectives**      | 5    | • Specific objectives and hypotheses                                        | ✓         | 3, 14
| **Outcomes**        | 6    | • Clearly defined primary and secondary outcome measures                    | ✓         | 16
|                     |      | • Methods used to collect data and any methods used to enhance the quality of measurements | ✓         | 16, 17
|                     |      | • Information on validated instruments such as psychometric and biometric properties | ✓         | 16
| **Sample Size**     | 7    | • How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules | ✓         | 5
| **Assignment Method** | 8   | • Unit of assignment (the unit being assigned to study condition, e.g., individual, group, community) | ✓         | 5
|                     |      | • Method used to assign units to study conditions, including details of any restriction (e.g., blocking, stratification, minimization) | ✓         | 14, 15
|                     |      | • Inclusion of aspects employed to help minimize potential bias induced due to non-randomization (e.g., matching) | ✓         | 14, 15
**TREND Statement Checklist**

<table>
<thead>
<tr>
<th>Blinding (masking)</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to study condition assignment; if so, statement regarding how the blinding was accomplished and how it was assessed.</td>
<td>√ 17</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unit of Analysis</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Description of the smallest unit that is being analyzed to assess intervention effects (e.g., individual, group, or community)</td>
<td>√ 6,7,8</td>
</tr>
<tr>
<td>• If the unit of analysis differs from the unit of assignment, the analytical method used to account for this (e.g., adjusting the standard error estimates by the design effect or using multilevel analysis)</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statistical Methods</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Statistical methods used to compare study groups for primary methods outcome(s), including complex methods of correlated data</td>
<td>√ 6,7,8,17</td>
</tr>
<tr>
<td>• Statistical methods used for additional analyses, such as a subgroup analyses and adjusted analysis</td>
<td>√ 17</td>
</tr>
<tr>
<td>• Methods for imputing missing data, if used</td>
<td>NA 17</td>
</tr>
<tr>
<td>• Statistical software or programs used</td>
<td>√ 17</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>Participant flow</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Flow of participants through each stage of the study: enrollment, assignment, allocation, and intervention exposure, follow-up, analysis (a diagram is strongly recommended)</td>
<td>√ 5,14,15</td>
</tr>
<tr>
<td>o Enrollment: the numbers of participants screened for eligibility, found to be eligible or not eligible, declined to be enrolled, and enrolled in the study</td>
<td>NA</td>
</tr>
<tr>
<td>o Assignment: the numbers of participants assigned to a study condition</td>
<td>√ 5</td>
</tr>
<tr>
<td>o Allocation and intervention exposure: the number of participants assigned to each study condition and the number of participants who received each intervention</td>
<td>√ 5</td>
</tr>
<tr>
<td>o Follow-up: the number of participants who completed the follow-up or did not complete the follow-up (i.e., lost to follow-up), by study condition</td>
<td>√ 5,14</td>
</tr>
<tr>
<td>o Analysis: the number of participants included in or excluded from the main analysis, by study condition</td>
<td>√ 5,14,15</td>
</tr>
<tr>
<td>• Description of protocol deviations from study as planned, along with reasons</td>
<td>√ 17</td>
</tr>
</tbody>
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<thead>
<tr>
<th>Recruitment</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dates defining the periods of recruitment and follow-up</td>
<td>√ 5,14</td>
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<table>
<thead>
<tr>
<th>Baseline Data</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Baseline demographic and clinical characteristics of participants in each study condition</td>
<td>√ 5</td>
</tr>
<tr>
<td>• Baseline characteristics for each study condition relevant to specific disease prevention research</td>
<td>NA 78</td>
</tr>
<tr>
<td>• Baseline comparisons of those lost to follow-up and those retained, overall and by study condition</td>
<td>NA</td>
</tr>
<tr>
<td>• Comparison between study population at baseline and target population of interest</td>
<td>√ 5,78</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline equivalence</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Data on study group equivalence at baseline and statistical methods used to control for baseline differences</td>
<td>√ 5,17</td>
</tr>
</tbody>
</table>
### TREND Statement Checklist

| Numbers analyzed | 16 | • Number of participants (denominator) included in each analysis for each study condition, particularly when the denominators change for different outcomes; statement of the results in absolute numbers when feasible | ✓ ✔️ |
|                 |    | • Indication of whether the analysis strategy was “intention to treat” or, if not, description of how non-compliers were treated in the analyses | ✔️ |
| Outcomes and estimation | 17 | • For each primary and secondary outcome, a summary of results for each estimation study condition, and the estimated effect size and a confidence interval to indicate the precision | ✓ ✔️ ✔️ ✔️ |
|                 |    | • Inclusion of null and negative findings | ✔️ ✔️ ✔️ |
|                 |    | • Inclusion of results from testing pre-specified causal pathways through which the intervention was intended to operate, if any | ✔️ |
| Ancillary analyses | 18 | • Summary of other analyses performed, including subgroup or restricted analyses, indicating which are pre-specified or exploratory | ✓ ✔️ ✔️ |
| Adverse events | 19 | • Summary of all important adverse events or unintended effects in each study condition (including summary measures, effect size estimates, and confidence intervals) | ✓ ✔️ |

### DISCUSSION

| Interpretation | 20 | • Interpretation of the results, taking into account study hypotheses, sources of potential bias, imprecision of measures, multiplicative analyses, and other limitations or weaknesses of the study | ✓ ✔️ 10-13 |
|                |    | • Discussion of results taking into account the mechanism by which the intervention was intended to work (causal pathways) or alternative mechanisms or explanations | ✔️ 10-13 |
|                |    | • Discussion of the success of and barriers to implementing the intervention, fidelity of implementation | ✔️ 10-13 |
|                |    | • Discussion of research, programmatic, or policy implications | ✓ ✔️ 10-13 |
| Generalizability | 21 | • Generalizability (external validity) of the trial findings, taking into account the study population, the characteristics of the intervention, length of follow-up, incentives, compliance rates, specific sites/settings involved in the study, and other contextual issues | ✓ ✔️ 10-13 |
| Overall Evidence | 22 | • General interpretation of the results in the context of current evidence and current theory | ✓ ✔️ 10-13 |