ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

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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.

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4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

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Section 1. Identifying Information

1. Given Name (First Name): Fan
2. Surname (Last Name): Wu
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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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Generate Disclosure Statement

Dr. Wu has nothing to disclose.

Evaluation and Feedback

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Section 1. Identifying Information

1. Given Name (First Name): Kuan-Yu
2. Surname (Last Name): Wang
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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

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Section 1. Identifying Information

1. Given Name (First Name): Guan-Zhang
2. Surname (Last Name): Li
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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1. Given Name (First Name): Yuan-Hao
2. Surname (Last Name): Chang
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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2. Surname (Last Name): Wang
3. Date: 03-August-2019

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Corresponding Author's Name: Yong-Zhi Wang

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Section 1. Identifying Information

1. Given Name (First Name): Zheng
2. Surname (Last Name): Zhao
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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

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Section 1. Identifying Information

1. Given Name (First Name): Yu-Qing
2. Surname (Last Name): Liu
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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Section 1. Identifying Information

1. Given Name (First Name): Yu-Zhou
2. Surname (Last Name): Chang
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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

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Section 1. Identifying Information

1. Given Name (First Name): Ke-Nan
2. Surname (Last Name): Zhang
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

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Section 1. Identifying Information

1. Given Name (First Name): Yi-Ming
2. Surname (Last Name): Li
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

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Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting , lectures, speakers bureaus, expert testimony, employment, or other affiliations
Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.
Other: Anything not covered under the previous three boxes
Pending: The patent has been filed but not issued
Issued: The patent has been issued by the agency
Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

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Section 1. Identifying Information

1. Given Name (First Name): Rui-Chao
2. Surname (Last Name): Chai
3. Date: 03-August-2019

4. Are you the corresponding author? ☐ Yes ☑ No

Corresponding Author's Name: Yong-Zhi Wang

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-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

ADD

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

ADD

Section 4. Intellectual Property -- Patents & Copyrights

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

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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?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):

☑ No other relationships/conditions/circumstances that present a potential conflict of interest

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement

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

Generate Disclosure Statement

Dr. Chai has nothing to disclose.

Evaluation and Feedback

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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.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report 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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Section 1. Identifying Information

1. Given Name (First Name): Yong-Zhi
2. Surname (Last Name): Wang
3. Date: 01-August-2019

4. Are you the corresponding author? ☑ Yes ☐ No

5. Manuscript Title: RNA processing genes characterize RNA splicing and further stratify lower-grade glioma

6. Manuscript Identifying Number (if you know it): 130591-INS-CMED-RV-2

Section 2. The Work Under Consideration for Publication

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

ADD

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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.

Generate Disclosure Statement

Dr. Wang has nothing to disclose.

Evaluation and Feedback

Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT		**RNA processing genes characterize RNA splicing and further stratify lower-grade glioma**	
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	AUC was used.
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	Yes
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	Included
	4	Study objectives and hypotheses	Included
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	Retrospective study
Participants	**6**	Eligibility criteria	Included
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	LGGs with molecular , survival and pathological information
	8	Where and when potentially eligible participants were identified (setting, location and dates)	NA
	9	Whether participants formed a consecutive, random or convenience series	convenience series
Test methods	**10a**	Index test, in sufficient detail to allow replication	Yes
	10b	Reference standard, in sufficient detail to allow replication	Yes
	11	Rationale for choosing the reference standard (if alternatives exist)	NA
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	Yes
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	NA
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	Yes
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	Yes
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	Kaplan–Meier method, ROC curves, univariate and multivariate Cox regression analysis
	15	How indeterminate index test or reference standard results were handled	NA
	16	How missing data on the index test and reference standard were handled	NA
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	NA
	18	Intended sample size and how it was determined	NA
RESULTS			
Participants	**19**	Flow of participants, using a diagram	Figure1
	20	Baseline demographic and clinical characteristics of participants	Supplementary table 14
	21a	Distribution of severity of disease in those with the target condition	Figure 2
	21b	Distribution of alternative diagnoses in those without the target condition	NA
	22	Time interval and any clinical interventions between index test and reference standard	Table 1
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Table1
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	Table1, Figure 2 and 3
	25	Any adverse events from performing the index test or the reference standard	NA
DISCUSSION			

	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	NA
	27	Implications for practice, including the intended use and clinical role of the index test	The last paragraph of discussion
OTHER INFORMATION			
	28	Registration number and name of registry	NA
	29	Where the full study protocol can be accessed	Yes
	30	Sources of funding and other support; role of funders	The funding information is included

STARD 2015

AIM

STARD stands for "Standards for Reporting Diagnostic accuracy studies". This list of items was developed to contribute to the completeness and transparency of reporting of diagnostic accuracy studies. Authors can use the list to write informative study reports. Editors and peer-reviewers can use it to evaluate whether the information has been included in manuscripts submitted for publication.

EXPLANATION

A **diagnostic accuracy study** evaluates the ability of one or more medical tests to correctly classify study participants as having a **target condition.** This can be a disease, a disease stage, response or benefit from therapy, or an event or condition in the future. A medical test can be an imaging procedure, a laboratory test, elements from history and physical examination, a combination of these, or any other method for collecting information about the current health status of a patient.

The test whose accuracy is evaluated is called **index test.** A study can evaluate the accuracy of one or more index tests. Evaluating the ability of a medical test to correctly classify patients is typically done by comparing the distribution of the index test results with those of the **reference standard**. The reference standard is the best available method for establishing the presence or absence of the target condition. An accuracy study can rely on one or more reference standards.

If test results are categorized as either positive or negative, the cross tabulation of the index test results against those of the reference standard can be used to estimate the **sensitivity** of the index test (the proportion of participants *with* the target condition who have a positive index test), and its **specificity** (the proportion *without* the target condition who have a negative index test). From this cross tabulation (sometimes referred to as the contingency or "2x2" table), several other accuracy statistics can be estimated, such as the positive and negative **predictive values** of the test. Confidence intervals around estimates of accuracy can then be calculated to quantify the statistical **precision** of the measurements.

If the index test results can take more than two values, categorization of test results as positive or negative requires a **test positivity cut-off**. When multiple such cut-offs can be defined, authors can report a receiver operating characteristic (ROC) curve which graphically represents the combination of sensitivity and specificity for each possible test positivity cut-off. The **area under the ROC curve** informs in a single numerical value about the overall diagnostic accuracy of the index test.

The **intended use** of a medical test can be diagnosis, screening, staging, monitoring, surveillance, prediction or prognosis. The **clinical role** of a test explains its position relative to existing tests in the clinical pathway. A replacement test, for example, replaces an existing test. A triage test is used before an existing test; an add-on test is used after an existing test.

Besides diagnostic accuracy, several other outcomes and statistics may be relevant in the evaluation of medical tests. Medical tests can also be used to classify patients for purposes other than diagnosis, such as staging or prognosis. The STARD list was not explicitly developed for these other outcomes, statistics, and study types, although most STARD items would still apply.

DEVELOPMENT

This STARD list was released in 2015. The 30 items were identified by an international expert group of methodologists, researchers, and editors. The guiding principle in the development of STARD was to select items that, when reported, would help readers to judge the potential for bias in the study, to appraise the applicability of the study findings and the validity of conclusions and recommendations. The list represents an update of the first version, which was published in 2003.

More information can be found on http://www.equator-network.org/reporting-guidelines/stard.