

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.

Identifying information.

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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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Pending: The patent has been filed but not issued **Issued:** The patent has been issued by the agency

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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

Morales 1



Section 1.	Identifying Inform	nation		
1. Given Name (Fi Blanca M.	rst Name)	2. Surname (Last Name) Morales	3. Date 03-October-2018	
4. Are you the corresponding author?		☐ Yes ✓ No	Corresponding Author's Name Emilie Barruet, PhD	
5. Manuscript Title NFkB/MAPK Acti		I-mediated Inflammation i	n Human Heterotopic Ossification	
6. Manuscript Ide	ntifying Number (if you kr	now it)		
			-	
Section 2.	The Work Under Co	onsideration for Public	ation	
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 Your				
	_			
Section 3.	Relevant financial	activities outside the s	ubmitted work.	
of compensation clicking the "Add	n) with entities as descri	ibed in the instructions. Us port relationships that wer	ether you have financial relationships (regardless of amount se one line for each entity; add as many lines as you need by e present during the 36 months prior to publication.	
Section 4.	Intellectual Prope	rty Patents & Copyri <u>c</u>	phts	
Do you have any	patents, whether plan	ned, pending or issued, br	oadly relevant to the work? Yes V No	

Morales 2



Section 5.				
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Dr. Morales has	nothing to disclose.			

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Morales 3



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Hsiao 1



Cartinus					
Section 1. Identifying Inform	ation				
Given Name (First Name) Edward	2. Surname (Last Nar Hsiao	ne)		3. Date 03-October-2018	
4. Are you the corresponding author? Yes No					
5. Manuscript Title NFkB/MAPK Activation Underlie ACVR1-	-mediated Inflammat	ion in Human He	terotopic Os	sification	
6. Manuscript Identifying Number (if you kn 122958-INS-CMED-RV-3	ow it)				
Section 2. The Work Under Co	onsideration for P	ublication			
Did you or your institution at any time recei any aspect of the submitted work (including statistical analysis, etc.)? Are there any relevant conflicts of interei If yes, please fill out the appropriate info Excess rows can be removed by pressing	but not limited to grands: st? Yes ormation below. If you	its, data monitoring	g board, study	design, manuscript preparation,	
Name of Institution/Company	Grant? Personal Fees?	Non-Financial Support?	Other?	Comments	
National Institutes of Health	✓				
Doris Duke Charitable Foundation	✓				
University of California Department of Medicine					
Radiant Hope Foundation	✓				
March of Dimes	\checkmark				
Section 3. Relevant financial and Place a check in the appropriate boxes in				relationships (regardless of amount	
of compensation) with entities as descri clicking the "Add +" box. You should rep	bed in the instruction oort relationships tha	ns. Use one line fo	or each entity	y; add as many lines as you need by	
Are there any relevant conflicts of intere		No			
If yes, please fill out the appropriate information below.					

Hsiao 2



Name of Entity		Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Clementia Pharmaceuticals		√				Clinical Trials Support via Sponsored Resaerch Agreement
						nesaeren Agreement
Section 4.	Intellectual Propert	ty Pater	nts & Cop	yrights		
Do you have any	y patents, whether planr	ned, pendin	g or issue	d, broadly releva	nt to the	work? ☐ Yes ✓ No
Section 5.	Relationships not o	overed a	bove			
	relationships or activities encing, what you wrote		-		nfluence	d, or that give the appearance of
✓ Yes, the follo	owing relationships/conc	ditions/circu	umstance	s are present (exp	olain belo	w):
No other rela	No other relationships/conditions/circumstances that present a potential conflict of interest					
International Cli		d on the Fil				al Registry Advisory Board, on the I Advisory Board. These activities
	anuscript acceptance, jo Irnals may ask authors to					sary, update their disclosure statements. elationships.
Section 6.	Disclosure Stateme	ent				
Based on the abo	ove disclosures, this forn	n will autor	matically g	generate a disclos	sure state	ment, which will appear in the box
						ritable Foundation, grants from n, grants from March of Dimes,

Hsiao 3

during the conduct of the study; grants from Clementia Pharmaceuticals, outside the submitted work; and Edward Hsiao serves in an unpaid capacity on the International FOP Association Medical Registry Advisory Board, on the International Clinical Council on FOP, and on the Fibrous Dysplasia Foundation Medical Advisory Board. These activities pose no conflicts

for the presented research..



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Hsiao 4



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Hellman 1



Section 1. Identifying Inform	nation	
1. Given Name (First Name) Judith	2. Surname (Last Name) Hellman	3. Date 02-October-2018
4. Are you the corresponding author?	☐ Yes 🗸 No	Corresponding Author's Name Emilie Barruet
5. Manuscript Title NFkB/MAPK Activation Underlie ACVR1	-mediated Inflammation in	n Human Heterotopic Ossification
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Section 2. The Work Under C	onsideration for Public	cation
	g but not limited to grants, da	a third party (government, commercial, private foundation, etc.) for ta monitoring board, study design, manuscript preparation,
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Do you have any patents, whether plan		

Hellman 2



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Ottenhoff 1



Section 1. Identifying Inform	nation			
1. Given Name (First Name) THM	2. Surname (Last Name) Ottenhoff	3. Date 04-October-2018		
4. Are you the corresponding author?	☐ Yes ✓ No	Corresponding Author's Name Emilie Barruet, PhD Edward Hsiao, MD, PhD		
5. Manuscript Title NFkB/MAPK Activation Underlie ACVR1	-mediated Inflammation i	n Human Heterotopic Ossification		
6. Manuscript Identifying Number (if you kr	now it)			
		-		
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Do you have any patents, whether plan	ned, pending or issued, br	roadly relevant to the work? Yes V No		

Ottenhoff 2



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Dr. Ottenhoff ha	s nothing to disclose.

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Moody 1



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Moody 2



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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

Wentworth 1



Section 1.	Identifying Inform	nation					
1. Given Name (First Name) Kelly		2. Surname (Last Nam Wentworth	ne)	3. Date 03-October-2018			
4. Are you the cor	4. Are you the corresponding author?			Corresponding Author's Name Emilie Barruet			
5. Manuscript Title NFkB/MAPK Acti	e vation Underlie ACVR1	-mediated Inflammati	on in Human He	terotopic Ossification	١		
6. Manuscript Ide 122958-INS-CME	ntifying Number (if you kr ED-RV-3	now it)					
Section 2.	The Work Under Co	onsideration for Pu	ublication				
any aspect of the s statistical analysis, Are there any rel If yes, please fill o	submitted work (including etc.)? evant conflicts of intere	g but not limited to gran est? Yes 1 ormation below. If you	ts, data monitoring No	board, study design, n	cial, private foundation, etc.) for nanuscript preparation, "ADD" button to add a row.		
Name of Institut	cion/Company	Grant? Personal Fees?	Non-Financial Support	Other? Commen	ts		
lementia Pharmaceuticals				✓ I am a sub-ir clinical trial	nvestigator on their		
Section 3.	Relevant financial	activities outside t	he submitted v	work.			
of compensatior clicking the "Adc Are there any rel		ibed in the instruction port relationships that	s. Use one line fo were present d	or each entity; add as	thips (regardless of amount many lines as you need by sprior to publication.		
Section 4.	Intellectual Proper	rty Patents & Cop	yrights				
Do you have any	patents, whether plan	ned, pending or issue	d, broadly releva	nt to the work?	Yes ✓ No		

Wentworth 2



Section 5. Polationships not savared above
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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Disclosure statement
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Dr. Wentworth reports other from Clementia Pharmaceuticals, during the conduct of the study; .

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Wentworth 3



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

Ton 1



Section 1. Identifying Inform	nation	
1. Given Name (First Name) Amy	2. Surname (Last Name) Ton	3. Date 03-October-2018
4. Are you the corresponding author?	☐ Yes ✓ No	Corresponding Author's Name Emilie Barruet
5. Manuscript Title NFkB/MAPK Activation Underlies ACVR	1- mediated Inflammation	in Human Heterotopic Ossification
6. Manuscript Identifying Number (if you k	now it)	
Section 2. The Work Under C	onsideration for Public	cation
	g but not limited to grants, da	a third party (government, commercial, private foundation, etc.) for ita monitoring board, study design, manuscript preparation,
Are there any relevant connicts of litter	est: Tes 🚺 140	
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of compensation) with entities as descr	ibed in the instructions. Us	ether you have financial relationships (regardless of amount se one line for each entity; add as many lines as you need by the present during the 36 months prior to publication.
Are there any relevant conflicts of interest	est? ☐ Yes ✓ No	
Section 4. Intellectual Prope	rty Patents & Copyric	ghts
Do you have any patents, whether plan	ned, pending or issued, br	oadly relevant to the work? Yes V No

Ton 2



Section 5. Relationships not sovered above
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):
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Section 6. Disclosure Statement
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Amy Ton has nothing to disclose.

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Haks 1



Section 1.	Identifying Inform	nation					
1. Given Name (Fi Marielle	rst Name)	2. Surname (Last Name) Haks	3. Date 05-October-2018				
4. Are you the cor	responding author?	onding author? Yes V No Corresponding Author's Name Emilie Barruet, PhD and Edward Hsiao, MD, PhD					
5. Manuscript Title NFkB/MAPK Acti		-mediated Inflammation ir	n Human Heterotopic Ossification				
6. Manuscript Ide 122958-INS-CME	ntifying Number (if you kr ED-RV-3	now it)	_				
Section 2.							
Section 2.	The Work Under C	onsideration for Public	ation				
any aspect of the s statistical analysis,	ubmitted work (including	g but not limited to grants, da	a third party (government, commercial, private foundation, etc.) for ta monitoring board, study design, manuscript preparation,				
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Section 4.	Intellectual Prope	rty Patents & Copyrig	phts				
Do you have any	patents, whether plan	ned, pending or issued, br	oadly relevant to the work? Yes V No				

Haks 2



Section 5. Relationships not covered above
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patent

Cain 1



Section 1. Identifying Inform	nation	
Given Name (First Name) Corey	2. Surname (Last Name) Cain	3. Date 03-October-2018
4. Are you the corresponding author?	☐ Yes ✓ No	Corresponding Author's Name Edward Hsiao
5. Manuscript Title NFkB/MAPK Activation Underlie ACVR1	-mediated Inflammation i	n Human Heterotopic Ossification
6. Manuscript Identifying Number (if you kr 122958-INS-CMED-RV-3	now it)	
Section 2. The Work Under Co	onsideration for Public	ation
	g but not limited to grants, da	a third party (government, commercial, private foundation, etc.) for ta monitoring board, study design, manuscript preparation,
Section 3. Relevant financial	activities outside the s	ubmitted work.
Place a check in the appropriate boxes of compensation) with entities as descr	in the table to indicate whole in the instructions. Use port relationships that wer	ether you have financial relationships (regardless of amount se one line for each entity; add as many lines as you need by e present during the 36 months prior to publication.
Section 4. Intellectual Proper	rty Patents & Copyrig	yhts
Do you have any patents, whether plan		

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Section 5.	
Section 5.	Relationships not covered above
	elationships or activities that readers could perceive to have influenced, or that give the appearance of ncing, what you wrote in the submitted work?
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Chan 1



Section 1.	Identifying Inform	nation			
1. Given Name (Fii Tea	rst Name)	2. Surname (Last Name) Chan		3. Date 05-October-2018	
4. Are you the cor	responding author?	☐ Yes ✓ No	Corresponding Auth Emilie Barruet, PhE	or's Name O and Edward Hsiao, MD, PhD	
5. Manuscript Title NFkB/MAPK Acti		-mediated Inflammation	n in Human Heterotopi	c Ossification	
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of compensation) with entities as descr	ibed in the instructions.	Use one line for each e	cial relationships (regardless of amo ntity; add as many lines as you need e 36 months prior to publication .	
•	evant conflicts of intere				
If yes, please fill o	out the appropriate info	ormation below.			
Name of Entity		Grant? Personal N	on-Financial Support? Other	Comments	
Clementia Pharmace	uticals			Research grant support for clinical trial, Edward Hsiao (PI)	
Section 4.	Intellectual Prope	rty Patents & Copy	rights		
Do you have any	patents, whether plan	ned, pending or issued,	broadly relevant to the	work? Yes Vo	

Chan 2



Section 5. Polationships not savared above
Relationships not covered above
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Ms. Chan reports other from Clementia Pharmaceuticals, outside the submitted work; .

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Barruet 1



Section 1.	Identifying Inform	nation				
1. Given Name (Fi		2. Surname (Last Na Barruet	me)		3. Date 03-October-201	8
4. Are you the cor	responding author?	✓ Yes No				
5. Manuscript Titk NFkB/MAPK Acti	e vation Underlie ACVR1	-mediated Inflamma	tion in Human He	eterotopic Oss	sification	
6. Manuscript Ider 122958-INS-CME	ntifying Number (if you kr :D-TR-2	now it)				
Section 2.	The Work Under Co	onsideration for F	Publication			
any aspect of the s statistical analysis, Are there any rel If yes, please fill o	stitution at any time rece ubmitted work (including etc.)? evant conflicts of intere out the appropriate info be removed by pressin	g but not limited to gracest? Yes promation below. If you	nts, data monitorin No	g board, study	design, manuscript p	oreparation,
Name of Institut	ion/Company	Grant? Personal Fees?	Non-Financial Support?	Other? Co	omments	
California Institute fo Fellowship Program t	r Regenerative Medicine to UCSF	✓				
Section 3.	Relevant financial	activities outside	the submitted	work.		
of compensation clicking the "Adc Are there any rel	the appropriate boxes i) with entities as descri I +" box. You should rep evant conflicts of intere	ibed in the instructic port relationships th	ns. Use one line f	or each entity	/; add as many lines	as you need by
Section 4.	Intellectual Proper	rty Patents & Co	pyrights			
Do you have any	patents, whether plan	ned, pending or issu	ed, broadly releva	ant to the wor	rk? Yes	No

Barruet 2



Section 5.	Relationships not covered above
	relationships or activities that readers could perceive to have influenced, or that give the appearance of encing, what you wrote in the submitted work?
Yes, the follo	wing relationships/conditions/circumstances are present (explain below):
✓ No other rela	tionships/conditions/circumstances that present a potential conflict of interest
	anuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements rnals may ask authors to disclose further information about reported relationships.
Section 6.	Disclosure Statement
Based on the abo	ove disclosures, this form will automatically generate a disclosure statement, which will appear in the box
Emilie Barruet h	as 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.

Identifying information.

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.

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.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.

Grant: A grant from an entity, generally [but not always] paid to your organization

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

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Section 1.	Identifying Inform	nation	
1. Given Name (Fii Mary	rst Name)	2. Surname (Last Name) Nakamura	3. Date 02-October-2018
4. Are you the cor	Are you the corresponding author? Yes V No Corresponding Author's N Emilie Barruet		Corresponding Author's Name Emilie Barruet
5. Manuscript Title NFkB/MAPK Acti		-mediated Inflammation ir	n Human Heterotopic Ossification
6. Manuscript Ider 122958-INS-CME	ntifying Number (if you kr :D-RV-3	now it)	
Section 2.	The Work Under Co	onsideration for Public	ation
any aspect of the s statistical analysis,	ubmitted work (including	g but not limited to grants, da	a third party (government, commercial, private foundation, etc.) for ta monitoring board, study design, manuscript preparation,
Section 3.	Relevant financial	activities outside the s	ubmitted work.
of compensation clicking the "Add) with entities as descri	ibed in the instructions. Us port relationships that wer	ether you have financial relationships (regardless of amount e one line for each entity; add as many lines as you need by e present during the 36 months prior to publication .
Section 4.	Intellectual Proper	rty Patents & Copyrig	ıhts
Do you have any	patents, whether plan	ned, pending or issued, br	oadly relevant to the work? Yes V No

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Section 5.	Relationships not covered above
	relationships or activities that readers could perceive to have influenced, or that give the appearance of encing, what you wrote in the submitted work?
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	anuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements rnals may ask authors to disclose further information about reported relationships.
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Dr. Nakamura h	as nothing to disclose.

Evaluation and Feedback

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or	1
		the abstract	
		(b) Provide in the abstract an informative and balanced summary of what	3
		was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation	4
		being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	20
Setting	5	Describe the setting, locations, and relevant dates, including periods of	6
Č		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection	6
		of participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed	NA
		and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	Supplemental
		confounders, and effect modifiers. Give diagnostic criteria, if applicable	Tables
Data sources/	8*	For each variable of interest, give sources of data and details of methods	20
measurement		of assessment (measurement). Describe comparability of assessment	
		methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	20
Study size	10	Explain how the study size was arrived at	20
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If	20
		applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	23
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(\underline{e}) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	Figure 1
_		potentially eligible, examined for eligibility, confirmed eligible, included	
		in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical,	Supplemental
		social) and information on exposures and potential confounders	Tables
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental Tables
		(c) Summarise follow-up time (eg, average and total amount)	NA
		(-),	Figures 2-8

Main results 16		(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates	NA
		and their precision (eg, 95% confidence interval). Make clear which confounders	
		were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a	NA
		meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and	NA
		sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or	18
		imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	14-18
		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	24
		applicable, for the original study on which the present article is based	

^{*}Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.