

Responses of institutions to wide-ranging concerns about research reported by a group of researchers with multiple retracted publications: a narrative review

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Conflict of interest statement

- None of the authors has a conflict of interest to disclose
- All authors wish to improve the integrity of the research literature in order to minimise the impact of research misconduct on patient care

Background

November 2016, systematic review of 33 RCTs published by a group of researchers identified pervasive compromise of integrity

By early 2017, 12 retractions but no evidence that a systematic investigation of integrity of > 200 other publications by the same researchers was underway

We assessed some of the other publications by the group of researchers and were concerned about their integrity

Methods

	Institution			
	Hirosaki University	Keio University	Kurume University	NYU-Winthrop
Concerns				
Date(s) concerns raised by our group	14 March 2017	14 March 2017 15 May 2017 11 October 2017 18 November 2017	14 March 2017 18 November 2017	11 October 2017 24 November 2017 3 May 2018
Types of concern	Fabrication Falsification Plagiarism Authorship misconduct Study conduct and governance irregularities Implausible productivity Implausible data Data errors	Fabrication Falsification Plagiarism Duplicate reporting Authorship misconduct Study conduct and governance irregularities Implausible productivity Impossible data Implausible data Data errors Funding unclear	Fabrication Falsification Plagiarism Duplicate reporting Authorship misconduct Study conduct and governance irregularities Implausible productivity Impossible data Implausible data Data errors Funding unclear	Fabrication Plagiarism Duplicate reporting Authorship misconduct Study conduct and governance irregularities Impossible data Data errors Funding unclear
Detailed concerns raised about specific publications	N	Y	Y	Y
Employees affected, N	4	4	6	2
Publications potentially affected, N	49	200	68	34

Methods

Publications ^a	Concerns						
	Authorship misconduct		Duplicate results, unacknowledged		Methodology discrepancies ^b , N	Data/analysis discrepancies ^b , N	Funding statement
Index publication, second publication(s)	Known ^c	Possible ^d	Proportion of data in second publication that was reported in the index paper ^b	Proportion of data from the full parent study that is reported in both publications ^b			
A40, A1	Yes (A1)	Yes	49%	41%	Yes, 4	Yes, 3	None
A39, A3	Yes (A3)	Yes	45%	33%	Yes ^e , 3	Yes, 1	None
A2, A6, A4, A5, A8, A9							
A2, A6	Yes (both)	Yes	79%	29%	No	Yes, 2	None
A2, A4	Yes (both)	Yes	67%	30%	No	Yes, 1	None
A2, A5	Yes (both)	Yes	78%	16%	Yes, 2	Yes, 2	None
A2, A8	Yes (both)	Yes	63%	21%	No	Yes, 2	None
A2, A9	Yes (both)	Yes	71%	32%	No	Yes, 3	None
A6, A4	Yes (both)	Yes	56%	25%	No	Yes, 3	None
A6, A5	Yes (both)	Yes	43%	9%	Yes, 2	Yes, 2	None
A6, A8	Yes (both)	Yes	50%	16%	No	Yes, 3	None
A6, A9	Yes (both)	Yes	32%	14%	No	Yes, 2	None
A4, A5	Yes (both)	Yes	35%	7%	Yes, 2	Yes, 1	None
A4, A8	Yes (both)	Yes	27%	9%	No	Yes, 1	None
A4, A9	Yes (both)	Yes	37%	16%	No	Yes, 3	None
A5, A8	Yes (both)	Yes	12%	4%	Yes, 2	Yes, 3	None
A5, A9	Yes (both)	Yes	37%	16%	Yes, 2	Yes, 4	None
A8, A9	Yes (both)	Yes	50%	16%	No	Yes, 2	None
A7 ^f	Yes	Yes	-	-	-	-	None
A11, A10	Yes (both)	Yes	0%	0%	No	Yes ^e	None
A13, A12	Yes (both)	Yes	45%	39%	Yes, 1	Yes, 3	None
A15, A14	Yes (both)	Yes	50%	43%	Yes, 1	Yes, 4	None
A17, A16	Yes (both)	Yes	28%	19%	No	Yes, 5	None
A18, A21, A20							

Methods

1. Duplicated or inconsistent data

In two papers, there appears to be duplicated/inconsistent data that require explanation.

1. Iwamoto J, Takeda T, Sato Y, Uzawa M. Comparison of effect of treatment with etidronate and alendronate on lumbar bone mineral density in elderly women with osteoporosis. *Yonsei Med J* 2005;46:750-8.
2. Iwamoto J, Takeda T, Sato Y, Uzawa M. Effect of whole-body vibration exercise on lumbar bone mineral density, bone turnover, and chronic back pain in post-menopausal osteoporotic women treated with alendronate. *Aging Clin Exp Res* 2005;17:157-63.

The baseline data from Table 1 in both papers for the alendronate group are shown. The data in both Tables are identical, except for minor differences in 4 variables highlighted.

	Paper 1		Paper 2
	Alendronate group (n = 25)		ALN group (n=25)
Age (yrs)	70.6 ± 8.7	Age (years)	70.6±8.7
Height (m)	1.46 ± 0.07	Height (m)	1.46±0.07
Body weight (kg)	45.4 ± 8.4	Body weight (kg)	44.4±8.4
Body mass index (kg/m ²)	20.8 ± 3.3	Body mass index (kg/m ²)	20.8±3.3
Years since menopause	20.6 ± 8.0	Years since menopause	21.5±8.9
Lumbar BMD (g/cm ²)	0.569 ± 0.107	Lumbar BMD (g/cm ²)	0.569±0.107
% of the YAM	55.6 ± 10.5	T score (%)	55.6±10.5
Number of prevalent vertebral fractures per patient	2.4 ± 3.0	Number of prevalent vertebral fractures per patient	2.4±3.0
Face scale score	4.6 ± 1.2	Face scale score	5.6±1.2
Serum calcium (mg/dL)	9.4 ± 0.3	Serum calcium (mg/dL)	9.4±0.3
Serum phosphorus (mg/dL)	3.4 ± 0.6	Serum phosphorus (mg/dL)	3.4±0.6
Serum ALP (IU/L)	243 ± 114	Serum ALP (IU/L)	244±114
Urinary NTX (nmol BCE/mmol Cr)	75.8 ± 44.9	Urinary NTX (nmol BCE/mmol Cr)	75.8±44.9

Results

Each institution commenced an investigation in response to our concerns

2 institutions had already conducted investigations:

Keio University (March 2016 – January 2017) concluded that its employee (Dr Iwamoto) had engaged in systematic gift authorship with co-author Yoshihiro Sato, which constituted ‘improper scientific conduct’. No notification of affected journals

Hirosaki University (October 2016 – February 2017) conducted a preliminary enquiry → full enquiry March 2017.

Results

	Institution			
	Hirosaki University	Keio University	Kurume University	NYU-Winthrop
Scope	38 (49) papers	7 (200) papers	38 (68) papers	5 (34) papers,
Employees investigated, N	Uncertain	1	Uncertain	Uncertain
Date of report	17 November 2017	23 August 2018	19 December 2018	30 May 2018
Decisions	Research misconduct primary respondent No research misconduct other employees	No misconduct	Research misconduct primary respondent No research misconduct other employees	Duplicate reporting present 'Concerns about integrity of research well-justified'
Recommendations	Retraction of 14 papers, 7 of which were already retracted. Remaining 24 papers, no clear evidence of fraud	Retraction of 2 papers, to be actioned by primary respondent. Noted 1 existing retraction, overlooked 1	Retraction of 7 papers, 2 of which were already retracted. Remaining 32, no clear evidence of research misconduct	No action
Report publicly available	Yes	No	Yes	No

Results

	Hirosaki	Keio	Kurume	NYU-Winthrop
Scope				
Includes executive summary	No	No	No	No
Clear and understandable	In part	In part	No	In part
Allegations clearly presented	In part	No	No	No
Charge to committee clearly described	No	No	No	No
Scope sufficient to address scientific integrity issues	No	No	No	No
Investigative Committee				
Appropriately constituted	Cannot assess	Cannot assess	Cannot assess	Cannot assess
Any external members	Yes	Yes	Yes	Cannot assess
Potential conflicts of interest reviewed	No	No	No	No
Report indicates standards of due process and confidentiality followed	No	No	No	No
Respondent had opportunity to identify conflicts	Cannot assess	Cannot assess	Cannot assess	Cannot assess
Any concern that committee lacked expertise and resources	Yes	Yes	Yes	Yes

Results

6/108 categories
adequately addressed

	Hirosaki	Keio	Kurume	NYU- Winthrop
Evidence				
Report indicates evidence sequestered and protected	No	No	No	No
Description of evidence considered	In part	In part	No	In part
Respondent offered opportunity to respond	Cannot assess	Cannot assess	Cannot assess	Cannot assess
Committee considered and addressed whether important evidence was unavailable	In part	Cannot assess	In part	In part
Explanation for failure to review seemingly pertinent evidence	In part	No	No	No
Need for further evidence or additional analysis	Yes	Yes	Yes	Yes
List of individuals interviewed	No	No	No	No
Should others have been interviewed	Cannot assess	Cannot assess	Yes	Yes
Additional questions that should have been asked or evidence examined to reach a supportable conclusion	Yes	Yes	Yes	Yes
Conclusion				
Report clearly states findings	Yes	In part	No	In part
Report clearly states conclusions	Yes	In part	Yes	In part
Evidence fully support conclusions	Cannot assess	No	No	No
Articulates and applies institutional policies	No	No	No	No
Recommendations clear and supported by report	No	No	No	No
Report describes and addresses requirements of external sponsors' regulations	No	No	No	No
Overall assessment	Not acceptable	Not acceptable	Not acceptable	Not acceptable

Additional comments

- At 3 institutions [Hirosaki University, Kurume University, Keio University] research was purportedly conducted at affiliated hospitals and clinics. No evidence that investigation included, or was undertaken at, these hospitals
- Focus on 'misconduct', narrowly defined as fabrication, falsification or plagiarism, rather than the integrity of the published research
- No response from any institution to detailed specific concerns
- Conclusions of 'improper scientific conduct' [Keio University] and 'concerns about the integrity of research well-justified' [NYU-Winthrop] without action to correct the literature
- Keio University requested that its former employee (Dr Iwamoto) retract his publications. Several months later, the relevant journals had not heard from Dr Iwamoto.

Results

	Institution			
	Hirosaki University	Keio University	Kurume University	NYU-Winthrop
Scope	38 (49) papers, first author primary respondent	7 (200) papers, first author primary respondent	38 (68) papers, first author primary respondent	5 (34) papers, first author primary respondent
Employees investigated, N	Uncertain	1	Uncertain	Uncertain
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Report publicly available	Yes	No	Yes	No
Subsequent response from our group	Raised specific concerns about 18 papers for which the investigation could not determine integrity	Reiterated concerns about >100 papers	Raised specific concerns about 22 papers for which the investigation could not determine integrity	Concerns not addressed or resolved for any publication

Hirosaki University

Among the 15 unretracted papers found to not 'contain instances of fraud', we reported a median (range) 5 (2-8) types of concern

Sato Y, Kanoko T, Satoh K, Iwamoto J. Risk factors for hip fracture among elderly patients with Alzheimer's disease. J Neurol Sci 223(2): 107-12, 2004	Authorship Ethical oversight Implausible recruitment Implausible investigator workload Implausible laboratory testing Duplicate publication Data errors Self-plagiarism
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12. Sato Y, Kanoko T, Satoh K, Iwamoto J. Risk factors for hip fracture among elderly patients with Alzheimer's disease. J Neurol Sci 223(2): 107-12, 2004

Concerns:

Authorship

Drs Sato and Iwamoto engaged in systematic reciprocal authorship misconduct between 2002 and late 2013 (statement by Dr Sato previously provided to Hirosaki University). Dr Iwamoto has publicly acknowledged that he did not participate in Dr Sato's studies.⁶ Drs Kanoko and Satoh were 'honorary authors' on several retracted papers.

Study conduct

The site at which the study was performed is not stated, presumably it was Futase Social Insurance Hospital. That institution has only 55 beds and 4 physicians. It is highly implausible that recruitment of a cohort of 225 women > 70y with Alzheimer's disease, no cardiac, renal or thyroid dysfunction, and no treatment with several medications including calcium and vitamin D could be recruited at such a small institution..

Evaluation of the patients 'was performed by the Chairman of the Human Clinical Study Committee of the Futase Social Insurance Hospital'. We can find no evidence from internet searches that the Human Clinical Study Committee of the Futase Social Insurance Hospital

Kurume University

Of 32 publications about which judgement could not be made, we assessed 20, and found median concerns/paper = 6 [range 1-10].

Sato Y, Kaji M, Tsuru T, Oizumi K. Risk factors for hip fracture among elderly patients with Parkinson's disease. *Journal of the Neurological Sciences*. 2001;182:89-93

Ethical oversight
 Study location uncertain
 Implausible recruitment
 Implausible laboratory testing
 Implausible data
 Impossible data
 Data errors
 Overlapping and duplicate data with other publications
 Self-plagiarism
 Implausible investigator workload

Impossible data

As above, in the text, the mean age of the participants with Parkinson's disease is stated to be 71.9y. However, the calculated mean age of the participants with Parkinson's disease using the subgroups data in Table 1 = 69.9y. Thus $18 \times 73.9 + 86 \times 70.7$ divided by 104 = 69.9y.

These data are mathematically impossible.

Overlapping and duplicate data with other publications

Please refer to the Excel spreadsheet, file entitled 'Sato studies duplicate data'. In that spreadsheet, this paper is listed in row 10.

Please also compare the Results section of this paper with the Results section of Sato et al, *J Neurol Sci* 2004;223:107-12, row 36 in the spreadsheet

In Tables 1 and 2 in the 2004 paper, the mean values of several variables in the control group and the Alzheimer's disease non-fracture group are identical to those in the control group and the Parkinson's disease non-fracture group, respectively, in Table 2 in the 2001 paper

	Controls		Non-fracture group	
	2004 paper	2001 paper	2004 paper	2001 paper
N	200	68	176	86
Age	76.8 ± 5.2	72.0 ± 3.1	76.1 ± 3.9	70.7 ± 3.2
Gender (M/F)	0/200	30/38	0/176	38/48
Disease	-	-	Alzheimer's disease	Parkinson's disease
BMI	23 ± 3	23 ± 3	21 ± 3	22 ± 4
Ionized calcium	1.26 ± 0.04	1.26 ± 0.04*	1.27 ± 0.04	1.27 ± 0.05*
Intact PTH	29 ± 6	29.3 ± 5.7	35 ± 14	35 ± 14
Intact BGP	7.7 ± 3.5	7.7 ± 3.5	8.7 ± 3.8	8.7 ± 3.8
ICTP	3.9 ± 1.4	7.1 ± 1.1	4.2 ± 2.1	7.2 ± 2.2

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Subsequent response from our group	Raised specific concerns about 18 papers for which the investigation could not determine integrity	Reiterated concerns about >100 papers	Raised specific concerns about 22 papers	Concerns not addressed or resolved for any publication
Current status	Further investigation undertaken, no change. Closed	?Ongoing	No further investigation. Closed	Further investigation undertaken, identified multiple examples of duplicate data reporting, journals to be notified, no indication of which ones

Conclusions

Important deficiencies exist in the quality and reporting of institutional investigations of concerns about research integrity

Deficiencies are wide-ranging and include

- **limited scope**
- **uncertain governance**
- **uncertain expertise**
- **limited assessment**
- **inadequate reporting**
- **limited transparency**

Institutional investigations focus on narrowly defined misconduct at the expense of comprehensive assessment of integrity of published research