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## Financial conflicts of interest in clinical practice guidelines for bipolar disorder and major depressive disorder in Japan

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5	37	Abstract
6	38	Abstract
/	30	Clinical practice guidelines (CPGs) are essential for standardizing nations care based on
8	40	evidence based medicine. However, the presence of financial conflicts of interest
10	40	(COIs) among CPC authors can undermine their credibility. This study aimed to
11	41	avaming the extent and size of COIs among authors of neuchistry CPGs in Ispan
12	42 42	examine the extent and size of COIs among authors of psychiatry CPOs in Japan.
13	43	Mathada
14	44	This areas sectional analysis of disalaged normants from abarmacoutical commonies
15	45	This cross-sectional analysis of disclosed payments from pharmaceutical companies
16 17	46	assesses the prevalence and magnitude of personal payments for fecturing, consulting,
17	47	and writing to CPGs for bipolar disorder and major depressive disorder in Japan
19	48	between 2016 and 2020.
20	49	
21	50	Results
22	51	This study found that 93.5% of authors received payments over a five-year period, with
23	52	total payments exceeding \$4 million. The median payment per author was \$49,422
24	53	(interquartile range: $$7,792 - $111,567$ ), with a notable concentration of payments
25	54	among a small number of authors, including the CPG chairperson. Despite these
20 27	55	extensive financial relationships, only a fraction of authors disclosed their COIs in the
27	56	CPGs. These large amounts of personal payments were made by pharmaceutical
29	57	companies manufacturing new antidepressants and sleeping aids listed in the CPGs.
30	58	
31	59	Conclusions
32	60	This study found that more than 93% of authors of Japanese major depressive disorder
33	61	and bipolar disorder CPGs received considerable amounts of personal payments from
34 25	62	the pharmaceutical industry. The findings highlight deviations from international COI
36	63	management standards and suggest a need for more stringent COI policies for
37	64	psychiatry CPGs in Japan.
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## 66 Introduction

67 Clinical practice guidelines (CPGs) have been increasingly used as a tool to endorse 68 evidence-based medicine for healthcare professionals in their clinical practice<sup>12</sup>. CPGs are developed based on the best available evidence and include recommendations for 69 70 diagnosis and treatment of specific diseases. Nevertheless, the integrity and 71 recommendations of CPGs are frequently compromised by conflicts of interest (COIs) between the guideline authors and the pharmaceutical industry, spanning various 72 73 medical specialties. In the field of psychiatry, there is substantial documentation of ghostwriting by pharmaceutical industry<sup>3</sup> and widespread financial COIs between CPG 74 authors and pharmaceutical companies<sup>4-7</sup>. Furthermore, studies showed that financial 75 COIs are associated with a propensity for CPGs to make recommendations favorable to 76 the healthcare industry<sup>48</sup>. This underscores the necessity for rigorous management of 77 78 financial COIs among CPG authors, particularly in psychiatry<sup>6910</sup>. A recent study 79 demonstrated that 60% of panel members of the Diagnostic and Statistical Manual of 80 Mental Disorders (DSM-5), fifth edition, text revision published by the American Psychiatry Association in 2022 received payments from the pharmaceutical industry<sup>11</sup>. 81 82 As the DSM-5 is widely used as a standard for psychiatric disorders' definitions and 83 symptom criteria, influencing treatment selection and approval of new drugs 84 worldwide<sup>11</sup>, the widespread financial COIs among the DSM-5 panel members are concerning. However, financial COIs among psychiatry experts are not unique to 85 86 international criteria and CPGs: they may also be problematic among authors of 87 regional or national CPGs, as these guidelines include specific treatment 88 recommendations that can influence the clinical practice of clinicians in each country or 89 region. 90 91 To enhance the transparency of financial relationships between healthcare professionals 92 and pharmaceutical companies, members of the Japan Pharmaceutical Manufacturers 93 Association have voluntarily disclosed their financial interactions with healthcare 94 professionals and organizations<sup>12</sup>. Subsequent research using this disclosed information 95 has revealed that the vast majority of CPG authors in Japan received personal payments during the CPG development across various medical specialties<sup>12-22</sup>. However, the 96 97 specifics of these financial relationships between pharmaceutical companies and

37 specifies of these financial relationships between pharmaceutical companies and
 38 Japanese CPG authors in psychiatry remain largely unexplored. Considering the
 39 patterns observed in previous studies, we hypothesized that financial COIs are
 30 widespread among psychiatry CPG authors in Japan.

## 102 Methods

103 Study setting, participants, and data collection

This cross-sectional analysis evaluated the extent and prevalence of financial interactions between pharmaceutical companies and authors of CPGs for major depressive disorder and bipolar disorder in Japan. The Japanese Society of Mood Disorders is responsible for the development of the sole CPGs for these conditions, namely Treatment Guideline I: Bipolar Disorder<sup>23</sup> and Treatment Guideline II: Major Depressive Disorder<sup>24</sup>. At the time of this study, the latest versions were published in June 2020 and July 2019, respectively.

- <sup>58</sup> 112 The Japan Pharmaceutical Manufacturers Association, representing over 70 major
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5	113	pharmaceutical companies mandates the disclosure of payments for lectures
6	11/	consultancy and writing to healthcare professionals listing the recipients' names on
/	115	company webgites since 2012 <sup>25-27</sup> . Despite enpuel updates and removal of provious
8	110	company websites since 2013 <sup>22</sup> <sup>27</sup> . Despite annual updates and removal of previous
9	116	years' data by these companies, the Medical Governance Research Institute has
10	117	independently collected and disclosed this payment data on its public online database
17	118	from 2016 to 2020, detailing individual physician and company contributions <sup>28</sup> . As the
12	119	pharmaceutical companies have not individually disclosed other categories of non-
14	120	research payments such as travel and accommodation fees, food and beverage fees, and
15	121	royalties and ownership payments, this study incorporated all personal payments for
16	122	lectures, consultancy, and writing from pharmaceutical companies to the psychiatry
17	123	CPG authors from 2016 to 2020 following the approach of prior studies <sup>29-32</sup>
18	124	
19	121	Data analysis
20	125	The study colculated the properties of CDC outbors receiving personal payments and
21	120	The study calculated the proportion of CFG authors receiving personal payments and
22	127	assessed per-author payment amounts, including median, interquartile range, mean, and
23	128	standard deviation. Payments were converted from Japanese yen to U.S. dollars using
24	129	the 2020 average monthly exchange rate of 106.8 yen per \$1. Data extraction and
25	130	analyses were executed using Python 3.9.12 (Python Software Foundation, Beaverton,
26	131	OR, USA), Microsoft Excel, version 16.0 (Microsoft Corp., Redmond, WA, USA), and
2/	132	Stata version 17.0 (StataCorp, College Station, TX, USA).
20 20	133	
30	134	Use of large language model in the drafting
31	135	During the preparation of this work, the authors used ChatGPT version 4.0 to check and
32	136	correct grammatical and spelling errors. After using this tool, the authors carefully
33	137	reviewed and edited the content as needed and takes full responsibility for the content of
34	138	the publication
35	130	
36	140	Ethical cleanance
37	140	Linical clearance
38	141	As a retrospective analysis of publicity available data, this study was classified as non-
39	142	human subjects research and did not require institutional review board approval in
40	143	accordance with the Japanese Ministry of Health, Labor, and Welfare's Ethical
41	144	Guidelines for Medical and Health Research Involving Human Subjects. The
42 //3	145	methodology adhered to the Strengthening the Reporting of Observational Studies in
44	146	Epidemiology (STROBE) guideline.
45	147	
46	148	Patient and public involvement
47	149	No patients were involved in the preparation of this manuscript or the research project.
48	150	
49	151	Results
50	152	The study included 29 authors for the bipolar disorder CPG and 42 for the major
51	152	depressive disorder CPG, with 25 individuals contributing to both. Consequently, 46
52	153	unique CPG authors were analyzed (Table 1) Disclosure of financial COIs within the
53	154	$CDC_{a}$ was solf reported sololy by the writing sythese. All sythese (1000/ $A$ syst of $A$ )
54	100	Cros was sen-reported solely by the writing authors. All authors (100%, 4 out of 4)
22 56	156	associated with the bipolar disorder CPG and 85./% (12 out of 14) with the major
50 57	157	depressive disorder CPG declared financial COIs with pharmaceutical companies.
58	158	
59	159	A significant majority, 43 authors (93.5%), received personal payments for lectures,
60		4

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5	160	consulting, and writing from pharmaceutical companies between 2016 and 2020 (Table
7	161	2). The cumulative personal payments amounted to \$4,043,436 from 55 pharmaceutical
7 8	162	companies over this period. The median payment per author was \$49,422 (IOR: \$7,792
9	163	- \$111 567) and the mean payment was \$87 901 (SD: \$111 270) indicating a skewed
10	164	distribution where a few outhors received dispropertionately high neumants. Notably
11	104	15 - (1 - (22, 0))
12	165	15 authors (32.6%) received in excess of \$100,000 over five years. The chairperson of
13	166	the guideline development committee received the highest total payment of \$506,108
14	167	for lecturing, consulting, and writing from pharmaceutical companies during this time.
15	168	Payments for lecturing constituted \$2.7 million (65.8% of the total), with consulting and
16	169	writing making up 25.8% (\$1.0 million) and 8.3% (\$337,255), respectively.
17	170	
18	171	Annual analysis revealed a decline in total payments to CPG authors from \$959,503 in
19	172	2016 to \$697 170 in 2020 (Table 2) Correspondingly the median annual payment per
20	173	author decreased from \$11,865 (IOR: $$1,773 - $24,498$ ) in 2016 to \$2,693 (IOR: $$0 - $
21	174	\$22,968 in 2020. The properties of authors receiving payments also fall from $91.3%$ in
22	174	\$22,900) in 2020. The proportion of authors receiving payments also left from 91.570 in
23	175	2017 to 73.9% in 2020, yet a majority still received at least one personal payment
24	176	annually.
25	177	
20	178	Payments from the top 5 and 10 pharmaceutical companies constituted 53.3% (\$2.2
27	179	million) and 83.1% (\$3.4 million) of the total payments, respectively (Table 3).
20	180	Sumitomo Pharma was the most generous, contributing \$695,031 (17.2%), followed by
30	181	Eisai (10.1%, \$408,323), MSD (8.8%, \$357,526), Otsuka Pharmaceutical (8.8%,
31	182	\$354,638), and Takeda Pharmaceutical (8.3%, \$337,370). Among these, MSD, Pfizer
32	183	Japan, and Meiji Seika notably reduced their non-research payments from 2016 to 2020.
33	184	whereas Eisai increased its payments from \$45 779 in 2016 to \$151 856 in 2020
34	185	
35	186	Table 4 presents the types of financial COIs self-reported by the CPG authors within
36	100	and respective guideline. Among the six estagories extracted from the CPC
37	107	dialogurage comparation for locturing was the most frequently dealared (100% for the
38	100	disclosures, compensation for fecturing was the most frequently declared (100% for the
39	189	bipolar disorder CPG and /8.6% for the major depressive disorder CPG). This was
40	190	followed by scholarship donations and participation in pharmaceutical company
41	191	advisory boards. The lack of a specified declaration period precluded the assessment of
42 43	192	the accuracy of each CPG author's self-reported COI status against the payment data
44	193	released by the pharmaceutical companies.
45	194	
46	195	Discussion
47	196	This cross-sectional analysis of publicly disclosed payment data from pharmaceutical
48	197	companies provides a detailed examination of the extent and prevalence of financial
49	198	COIs among authors of the Japanese Society of Mood Disorders' Treatment Guideline I.
50	199	Bipolar Disorder <sup>23</sup> and Treatment Guideline II <sup>1</sup> Major Depressive Disorder <sup>24</sup> These
51	200	CPGs are considered by physicians the authoritative and trustworthy sources for the
52	200 201	treatment of hingler digorder and major depressive disorder in Jener <sup>33</sup> . To the best of
53	201	ure annent of oppoint disorder and major depressive disorder in Japan <sup>33</sup> . To the best of
54	202	our knowledge, this is the first in-depth study to analyze the financial relationships
55	203	between psychiatry CPG authors and pharmaceutical companies in Japan using
50 57	204	disclosed payment data. The findings reveal that a significant majority (93.5%) of CPG
50	205	authors received personal payments for lecturing, consulting, and writing, with a total

- sum of \$4.0 million between 2016 and 2020. The median payment per author was

\$49,422, with a minority, including the CPG chairperson, receiving substantial sums. Nearly all authors involved in writing the CPGs self-reported financial COIs with pharmaceutical companies. Notably, the bulk of personal payments to CPG authors came from companies that manufacture antidepressants and sleeping pills in Japan. However, other CPG authors did not publicly disclose their financial COIs with these companies. When compared to previous studies and international COI policies for CPG authors, these findings raise concerns for physicians, patients, policymakers, and other

The study highlights that over 93% of the authors of CPGs for bipolar disorder and major depressive disorder had financial relationships with pharmaceutical companies. Given the publication dates of the CPGs between 2019 and 2020, these financial

ranged from 86.4% in cardiology<sup>38</sup> to 94.6% in hematology<sup>14</sup>.

relationships likely occurred during the development of the CPGs. This high percentage of authors receiving personal payments aligns with findings from other specialties within Japan<sup>12-15</sup> <sup>17-22</sup> <sup>34-37</sup>, where the proportion of CPG authors with personal payments

In contrast, research from other developed countries, such as the United States, reports lower proportions of CPG authors with financial COIs. For instance, 67% of authors for

pharmaceutical companies<sup>4 10</sup>. In Canada, half of the authors of the CPG for depressive

Moreover, Mooghali et al. reported that 73.7% of physician CPG authors in the United

Furthermore, this investigation revealed that a select group of CPG authors, including

companies. Only authors involved in writing the CPGs were mandated to declare their financial COIs, while other contributors did not publicly disclose any financial COIs with these companies. These results indicate that authors of Japanese CPGs for bipolar disorder and major depressive disorder clearly violate international COI policies on CPG development in several respects. The U.S. National Academy of Medicine's 2011 report and the Guidelines International Network advocate for a majority of CPG authors to be free from financial COIs<sup>12</sup>. These policies also stipulate that the chairperson of CPG development should not hold any COIs<sup>12</sup>. The Guideline Panel Review Working Group's criteria for red flags, as published in the British Medical Journal in 2013, indicate that financial COIs held by a CPG chairperson and multiple authors are significant concerns for the trustworthiness of the CPGs<sup>43</sup>. The prevalence of COIs exceeding 93% in this study is not a marginal discrepancy but a significant deviation from these standards, casting doubt on the objectivity and reliability of the guidelines.

the DSM-5 mood disorders section disclosed financial COIs with the healthcare industry<sup>9</sup>. Additionally, a study by Cosgrove et al. found that only 18% of major depressive disorder CPG authors across eight countries had financial COIs with

disorder developed by the Canadian Network for Mood and Anxiety Treatments reported financial COIs with the healthcare industry<sup>39</sup>. Other specialties in the United States also showed lower percentages, with 53% of gastroenterology CPG authors<sup>40</sup> and

59.3% of urology CPG authors receiving personal and/or research payments<sup>41</sup>.

States received personal and/or research payments from healthcare companies<sup>42</sup>.

the chairperson, received substantial personal payments from pharmaceutical

stakeholders within and beyond Japan.

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Moreover, the study uncovered that substantial payments were made by pharmaceutical

companies marketing new antidepressants and sleep aids in Japan. For example, Sumitomo Pharma, the top paying company, manufactures lurasidone (brand name: Latuda), approved for bipolar disorder and schizophrenia in 2020, and co-promotes venlafaxine hydrochloride (brand name: Effexor) with Pfizer Japan since 2018. MSD, another major payer, produces suvorexant (brand name: Belsomra), the world's first orexin receptor antagonist. Otsuka Pharmaceutical is noted for one of the major manufacturers of atypical antipsychotic medications such as aripiprazole (brand name: Abilify) and brexpiprazole (brand name: Rexulti) which are the most widely prescribed atypical antipsychotic drugs in Japan<sup>44</sup>. Despite these financial ties between the CPG authors and the pharmaceutical companies, the Japanese Society of Mood Disorders actively endorses adherence to these CPGs<sup>45 46</sup>. Considering that the CPGs for bipolar disorder and major depressive disorder include pharmacotherapy recommendations involving drugs from these companies, it is imperative to address the close financial relationships between CPG authors and the pharmaceutical industry. We strongly recommend the Japanese Society of Mood Disorders to enforce more transparent and stringent COI management strategies in the CPG development process for bipolar disorder and major depressive disorder, ensuring the integrity and credibility of these guidelines. 

## 273 Limitations

This study is subject to several limitations. Primarily, the study focus on CPGs for bipolar disorder and major depressive disorder in Japan would limit the generalizability of our findings to other medical fields or countries. Additionally, the payment data were derived from a secondary source, the Medical Governance Research Institute's database, which contains payment information from member companies of the Japan Pharmaceutical Manufacturers Association for the period 2016-2020<sup>26 47</sup>. Absent legal mandates for precise payment disclosures in Japan, the potential for inaccuracies or underreporting in the database cannot be discounted. Furthermore, the voluntary nature of these disclosures means that financial interactions between CPG authors and non-disclosing pharmaceutical entities may remain undetected. Nevertheless, given that the member companies account for 80% of the market share for drugs and medical products in Japan<sup>48</sup>, the impact of financial relationships between the CPG authors and uncovered companies would be minimized. 

## 288 Conclusions

More than 93% of the authors of the Treatment Guidelines for Bipolar Disorder and Major Depressive Disorder developed by the Japanese Society of Mood Disorders received personal payments for the reimbursement of their lecturing, consulting, and writing activities from the pharmaceutical companies manufacturing related drugs. The total amounts of personal payments to the CPG authors were more than \$4.0 million over the five years. Nevertheless, the financial COIs were only declared by the limited group of CPG authors. Further transparent and rigorous COI management strategies must be warranted in the Japanese Society of Mood Disorders. 

## **Conflicts of interest:**

299 The authors declare that there were no conflicts of interest for this study.

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5	301	Funding sources:
0	302	The authors declare that there were no funding sources for this study.
/ 8	303	
9	304	IRB Statement
10	305	As this study was a retrospective analysis of publicly available data and met the
11	206	As this study was a redospective analysis of publicity available data and met the
12	207	users required in accordance with the Isranges Ministry of Health. I shon and Walfers's
13	307	were required in accordance with the Japanese Ministry of Health, Labor, and wenare's
14	308	Etnical Guidelines for Medical and Health Research Involving Human Subjects. This
15	309	study followed the Strengthening the Reporting of Observational Studies in
16	310	Epidemiology (STROBE) guideline.
17	311	
18	312	Declaration of generative AI in scientific writing
19	313	During the preparation of this work, the authors used ChatGPT version 4.0 to check and
20	314	correct grammatical and spelling errors. After using this tool, the authors carefully
21 22	315	reviewed and edited the content as needed and takes full responsibility for the content of
22	316	the publication.
24	317	
25	318	Data availability statement:
26	319	All data used in this study is available from Yen For Docs database run by Medical
27	320	Governance Research Institute (https://wenfordocs.in/) and each pharmaceutical
28	320	companies belonging to the Japan Pharmaceutical Manufacturers Association. Due to
29	321 222	response belonging to the Japan Finalitaceutical Manufacturers Association. Due to
30	322 222	privacy protection, payment data of individual CPG authors will be available from the
31	323	corresponding author upon reasonable request.
32 22	324	
33 34	325	Acknowledgments
35	326	The authors appreciate Ms Megumi Aizawa for her dedicated support of my research
36	327	project. During the preparation of this work, the authors used ChatGPT version 4.0 to
37	328	check and correct grammatical and spelling errors. After using this tool, the authors
38	329	carefully reviewed and edited the content as needed and takes full responsibility for the
39	330	content of the publication.
40	331	
41	332	References
42	333	1. Schunemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: Principles for
43	334	Disclosure of Interests and Management of Conflicts in Guidelines. Ann Intern Med
44 45	335	2015;163(7):548-53. doi: 10.7326/M14-1885 [published Online First: 2015/10/06]
45 46	336 227	2. Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: The National
40 47	338	Academics Press 2011. 3 Roehr B. Professor files complaint of scientific misconduct over allegation of ghostwriting <i>BMI</i>
48	339	2011:343:d4458 doi: 10.1136/bmi d4458 [nublished Online First: 20110713]
49	340	4. Cosgrove L, Shaughnessy AF, Peters SM, et al. Conflicts of Interest and the Presence of
50	341	Methodologists on Guideline Development Panels: A Cross-Sectional Study of Clinical Practice
51	342	Guidelines for Major Depressive Disorder. Psychother Psychosom 2017;86(3):168-70. doi:
52	343	10.1159/000458727 [published Online First: 20170511]
53	344	5. Cosgrove L, Krimsky S, Vijayaraghavan M, Schneider L. Financial fies between DSM-IV panel
54	343 346	members and the pharmaceutical industry. <i>Psychother Psychosom</i> 2006; / 5(3):154-60. doi: 10.1159/000091772 [published Online First: 2006/04/26]
55	347	6 Cosgrove L. Bursztain HJ. Krimsky S. Developing unbiased diagnostic and treatment guidelines in
56 57	348	psychiatry. N Engl J Med 2009:360(19):2035-6. doi: 10.1056/NEJMc0810237
57 58	349	7. Cosgrove L, Bursztajn HJ, Krimsky S, et al. Conflicts of interest and disclosure in the American
50 59	350	Psychiatric Association's Clinical Practice Guidelines. Psychother Psychosom 2009;78(4):228-
60		Ω

4		
5	351	32. doi: 10.1159/000214444 [published Online First: 20090428]
6	352	8. Neistgaard CH. Bero L. Hrobiartsson A. et al. Association between conflicts of interest and favourable
7	353	recommendations in clinical guidelines, advisory committee reports, opinion pieces, and
8	354	narrative reviews: systematic review. <i>BMJ</i> 2020:371:m4234. doi: 10.1136/bmi.m4234
9	355	[published Online First: 20201209]
10	356	9. Cosgrove L. Krimsky S. A comparison of DSM-IV and DSM-5 panel members' financial associations
11	357	with industry: a permicious problem persists <i>PLoS Med</i> 2012:9(3):e1001190 doi:
12	358	10 1371/journal pmed 1001190 [published Online First: 2012/0313]
13	359	10 Cosgrove L. Krimsky S. Wheeler EE, et al. Conflict of Interest Policies and Industry Relationships of
14	360	Guideline Development Group Members: A Cross-Sectional Study of Clinical Practice
15	361	Guidelines for Depression Account Res 2017:24(2):99-115 doi:
16	362	10 1080/08989621 2016 1251319 [published Online First: 20161024]
17	363	11 Davis LC Dijanni AT Drumheller SR et al Undisclosed financial conflicts of interest in DSM-5-
18	364	TR <sup>•</sup> cross sectional analysis <i>BMJ</i> 2024 <sup>•</sup> 384 <sup>•</sup> e076902 doi <sup>•</sup> 10 1136/bmi-2023-076902 [published
10	365	Online First: 20240110]
20	366	12 Murayama A Ozaki A Saito H et al Pharmaceutical company payments to dermatology Clinical
20	367	Practice Guideline authors in Japan <i>PLoS One</i> 2020:15(10):e0239610 doi:
21	368	10 1371/journal pone 0239610 [published Online First: 20201013]
22	369	13 Kida F. Murayama A. Saito H. et al. Pharmaceutical company payments to authors of the Japanese
25	370	Clinical Practice Guidelines for Henatitis C treatment <i>Liver Int</i> 2021:41(3):464-69 doi:
24	371	10.1111/liv.14761 [published Online First: 20201223]
25	372	14. Harada K. Ozaki A. Saito H. et al. Financial payments made by pharmaceutical companies to the
26	373	authors of Japanese hematology clinical practice guidelines between 2016 and 2017. <i>Health</i>
2/	374	<i>Policy</i> 2021:125(3):320-26. doi: 10.1016/j.healthpol.2020.12.005 [published Online First:
28	375	20201217]
29	376	15. Hashimoto T, Murayama A, Mamada H, et al. Evaluation of financial conflicts of interest and drug
30	377	statements in the coronavirus disease 2019 clinical practice guideline in Japan. Clin Microbiol
31	378	Infect 2022;28(3):460-62. doi: 10.1016/j.cmi.2021.11.019 [published Online First: 20211124]
32	379	16. Kamamoto S, Murayama A, Kusumi E, et al. Evaluation of financial relationships between Japanese
33	380	certified pediatric hematologist/oncologists and pharmaceutical companies: a cross-sectional
34	381	analysis of personal payments from pharmaceutical companies between 2016 and 2019. Pediatr
35	382	Blood Cancer 2022;69(10):e29891. doi: 10.1002/pbc.29891 [published Online First: 20220810]
36	383	17. Murayama A, Kida F, Ozaki A, et al. Financial and Intellectual Conflicts of Interest Among Japanese
37	384	Clinical Practice Guidelines Authors for Allergic Rhinitis. Otolaryngol Head Neck Surg
38	385	2022;166(5):869-76. doi: 10.1177/01945998211034724 [published Online First: 20210817]
39	386	18. Murayama A, Yamada K, Yoshida M, et al. Evaluation of Conflicts of Interest among Participants of
40	387	the Japanese Nephrology Clinical Practice Guideline. Clin J Am Soc Nephrol 2022;17(6):819-26.
41	388	doi: 10.2215/CJN.14661121 [published Online First: 2022/05/28]
42	389	19. Mamada H, Murayama A, Kamamoto S, et al. Evaluation of Financial and Nonfinancial Conflicts of
43	390	Interest and Quality of Evidence Underlying Psoriatic Arthritis Clinical Practice Guidelines:
44	391	Analysis of Personal Payments From Pharmaceutical Companies and Authors' Self-Citation Rate
45	392	in Japan and the United States. Arthritis Care Res (Hoboken) 2023;75(6):1278-86. doi:
46	393	10.1002/acr.25032 [published Online First: 20230114]
47	394	20. Murayama A, Kamamoto S, Murata N, et al. Evaluation of financial conflicts of interest and quality
48	395	of evidence in Japanese gastroenterology clinical practice guidelines. J Gastroenterol Hepatol
49	396	2023;38(4):565-73. doi: 10.1111/jgh.16089 [published Online First: 20221229]
50	397	21. Murayama A. Financial Conflicts of Interest Among the Authors of the Clinical Practice Guidelines
51	398	tor Rheumatoid Arthritis in Japan. <i>Cureus</i> 2023;15(10):e46650. doi: 10.7759/cureus.46650
52	399	[published Online First: 20231007]
53	400	22. Yamamoto K, Murayama A, Ozaki A, et al. Financial conflicts of interest between pharmaceutical
54	401	companies and the authors of urology clinical practice guidelines in Japan. Int Urogynecol J
55	402	2021;32(2):443-51. doi: 10.1007/s00192-020-04547-3 [published Online First: 20201105]
56	403	23. Japanese Society of Mood Disorders. Treatment Guideline I: Bipolar Disorder Online: Japanese
57	404	Society of Mood Disorders; 2020 [updated June 16, 2020. 4th edition: [Available from:
58	405	https://www.secretariat.ne.jp/jsmd/iinkai/katsudou/data/guideline_sokyoku2020.pdf accessed
59	400	October 20 2023.
~ ~		

24. Japanese Society of Mood Disorders. Treatment Guideline II: Major Depressive Disorder Or Japanese Society of Mood Disorders; 2019 [2nd edition:[Available from:	line:
https://www.secretariat.ne.jp/jsmd/iinkai/katsudou/data/20190724-02.pdf accessed Octo	ober 20
2023. 25. Ozaki A. Saito H. Senoo Y. et al. Overview and transparency of non-research payments to h	ealthcare
organizations and healthcare professionals from pharmaceutical companies in Japan. A	nalvsis of
payment data in 2016. <i>Health Policy</i> 2020;124(7):727-35. doi: 10.1016/j.healthpol.2020	0.03.011
[published Online First: 20200426]	
26. Murayama A, Kamamoto S, Saito H, et al. Characteristics and Distribution of Scholarship D	onations
From Pharmaceutical Companies to Japanese Healthcare Institutions in 2017: A Cross-	sectional
10 34172/jihpm 2023 7621	otec
27. Murayama A, Kamamoto S, Saito H, et al. Pharmaceutical Payments to Japanese Board-Cert	tified <b>t</b>
Infectious Disease Specialists: A Four-Year Retrospective Analysis of Payments from 9	92 <b>by</b> .
Pharmaceutical Companies between 2016 and 2019. Int J Environ Res Public Health	co ·
2022;19(12):7417. doi: 10.3390/ijerph19127417 [published Online First: 20220616]	aamhar <b>P</b> Y
23. 2023. Available from: https://venfordocs.ip/ accessed March 6, 2024 2024.	in i
29. Murayama A, Kamamoto S, Saito H, Ozaki A. Pharmaceutical payments to Japanese board-	certified 5
dermatologists: a 4-year retrospective analysis of personal payments from pharmaceutic	cal <u>C</u>
companies between 2016 and 2019. <i>Sci Rep</i> 2023;13(1):7425. doi: 10.1038/s41598-023	3-34705-8 <b>d</b> i
[published Online First: 20230308] 30 Murayama A. Saito H. Kamamoto S. et al. Evaluation of non-research navments from pharm	aceutical ດັ
companies to urologists in Japan between 2016 and 2019. Int Urogynecol J 2023;34(6)	:1285-92.
doi: 10.1007/s00192-023-05463-y [published Online First: 20230201]	ses
31. Kusumi E, Murayama A, Kamamoto S, et al. Pharmaceutical payments to Japanese certified	reig
hematologists: a retrospective analysis of personal payments from pharmaceutical comp between 2016 and 2019 Blood Cancer 12022:12(4):54 doi: 10.1038/s/11/08.022.0065	banies a nen
[published Online First: 20220407]	6 - y
32. Murayama A, Hoshi M, Saito H, et al. Nature and Trends in Personal Payments Made to the	e teg
Respiratory Physicians by Pharmaceutical Companies in Japan between 2016 and 2019	. (tape
Respiration 2022;101(12):1088-98. doi: 10.1159/000526576 [published Online First: 2	0221109] det
treatment guidelines for schizonbrenia and major depressive disorder in a nationwide	data
dissemination and implementation study. <i>Neuropsychopharmacol Rep</i> 2021;41(2):199-	206. doi:
10.1002/npr2.12173 [published Online First: 20210311]	inin S)
34. Murayama A, Kamamoto S, Shigeta H, et al. Undisclosed financial conflicts of interest with	, Ģ.
pharmaceutical companies among the authors of the Esophageal Cancer Practice Guide	lines $\mathbf{P}$
35. Muravama A. Mamada H. Shigeta H. et al. Financial Relationships Between Pharmaceutical	
Companies and Rheumatologists in Japan Between 2016 and 2019. J Clin Rheumatol	ing
2023;29(3):118-25. doi: 10.1097/RHU.000000000001922 [published Online First: 20]	221207] e
36. Kamamoto S, Ozaki A, Murayama A. Assessment of Financial Relationships Between	s br
<i>Cureus</i> 2023:15(8):e43633. doi: 10.7759/cureus 43633. [nublished Online First: 202308	<b>1</b> 9. <b>1</b> 7] <b><b>Ž</b>.</b>
37. Murayama A, Shin N, Higuchi K, et al. Financial conflicts of interest between infectious disc	eases ar
clinical practice guideline authors and the pharmaceutical industry in Japan. Infect Dis	(Lond) 🧧
2024:1-5. doi: 10.1080/23744235.2024.2309351 [published Online First: 20240201]	'no
38. Senoo Y, Saito H, Ozaki A, et al. Pharmaceutical company payments to authors of the Japan guidelines for the management of hymotronical <i>Medicine</i> ( <i>Paltimene</i> ) 2021:100(12):22	ese og
doi: 10 1097/MD 00000000024816 [published Online First: 2021/03/26]	4010. <b>e</b> s
39. Elder K, Turner KA, Cosgrove L, et al. Reporting of financial conflicts of interest by Canadi	an .
clinical practice guideline producers: a descriptive study. CMAJ 2020;192(23):E617-E2	25. doi:
10.1503/cmaj.191737 [published Online First: 2020/06/17]	
+U. Comos 1K, Scott J, Jorski A, et al. Evaluation of Industry Relationships Among Authors of Practice Guidelines in Gastroenterology IAMA Intern Med 2018:178(12):1711-12 doi	Unnical
1 nucleo Guidennes in Gustioenterology. SAMA Intern Met 2010,170(12).1711-12. dol	(
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5	160	10 1001/jew sistemas 1 2010 4720 [see 11] hed Outline First 2010/11/02]
6	403	10.1001/jamainternmed.2018.4730 [published Online First: 2018/11/02]
7	464	41. Carlisle A, Bowers A, Wayant C, et al. Financial Conflicts of Interest Among Authors of Urology
8	465	Clinical Practice Guidelines. Eur Urol 2018; $74(3)$ : 348-54. doi: 10.1016/j.eururo.2018.04.023
0	466	[published Online First: 20180507]
9 10	467	42. Mooghali M, Glick L, Ramachandran R, Ross JS. Financial conflicts of interest among US physician
10	468	authors of 2020 clinical practice guidelines: a cross-sectional study. BMJ Open
11	469	2023;13(1):e069115. doi: 10.1136/bmjopen-2022-069115 [published Online First: 20230123]
12	470	43. Lenzer J, Hoffman JR, Furberg CD, et al. Ensuring the integrity of clinical practice guidelines: a tool
13	471	for protecting patients. BMJ 2013;347:f5535. doi: 10.1136/bmj.f5535 [published Online First:
14	472	20130917]
15	473	44. Jiho. Yakuji Handbook 2021: Jiho 2021:522.
16	474	45. Takaesu Y, Watanabe K, Numata S, et al. Improvement of psychiatrists' clinical knowledge of the
17	475	treatment guidelines for schizophrenia and major depressive disorders using the 'Effectiveness of
18	476	Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)' project: A
10	477	nationwide dissemination education and evaluation study. <i>Psychiatry Clin Neurosci</i>
20	478	2019.73(10):642-48 doi: 10.1111/nen.12911 [nublished Online First: 20190822]
20	479	46 Kodaka F. Ohi K. Vasuda V. et al. Relationships Between Adherence to Guideline Recommendations
21	480	for Pharmacological Therapy Among Clinicians and Psychotic Symptoms in Patients With
22	481	Schizonhrenia Int I Neuropsychonharmacol 2023;26(8):557-65. doi: 10.1093/jipn/pyad037
23	482	A7 Ozieranski P. Saita H. Rickard F. et al. International comparison of nharmaceutical industry navment
24	482	disclosures in the UK and Japan; implications for self regulation, public regulation, and
25	405	transporter the UK and Japan. Impleations for sen-regulation, public regulation, and transporter ( <i>Clobal Health</i> 2023:10(1):14, doi: 10.1186/a12002.022.00002.0 [mublished
26	404	Online First 202202021
27	405	Oliline Flist. 20250505] 49. Janan Dharmanautical Manufacturan Acceptation. Data Deals 2022 2022 [Augilable from:
28	400	48. Japan Pharmaceutical Manufacturers Association. Data Book 2023 2023 [Available from:
29	487	https://www.jpma.or.jp/news_room/issue/databook/en/ricmr00000000an3-
30	488	<u>att/DATABOOK2023_en.pdf</u> accessed August 9 2023.
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# 491 Table 1. Demographic characteristics of clinical practice guideline authors for bipolar 492 disorder and major depressive disorder 493

Variables	Guideline dis	sease category	Overall	
	Bipolar disorder	Major depressive disorder		
Number of authors	29	42	46	
Role of guideline authors				
Writing authors	4 (13.8)	14 (33.3)	Not calculated	
Supporting authors	5 (17.2)	11 (26.2)	Not calculated	
Guideline development committee authors	20 (69.0)	17 (40.5)	Not calculated	
Number of authors with self-declared conflicts of interest, n (%) <sup>a</sup>	4 (100)	12 (85.7)	Not calculated	

 <sup>a</sup> Conflicts of interest were only declared by writing authors.

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		yright, i	n-2024-0	
496	Table 2. Summary of personal payments from pharmaceutical companies to psychiatry clinical practi	ncludtb	863961 guid	eline authors between 2016
497 498	and 2020	g for u	n 21 .	

Variables	2016	2017	2018	2019	se Ene	Total amounts
Total amount of payments, \$	959,503	873,288	769,649	743,826	<b>e 6</b> 97,170	4,043,436
Mean payments per author	20,859	18,985	16,732	16,170	at 1 5,156	87,901 (111,270)
(standard deviation), \$	(27,155)	(24,259)	(24,649)	(21,256)		
Median payments per author	11,865 (1,773 –	10,239 (1,517 –	2,294 (521 –	4,476 (531 –	e =2€693 (0 −	49,422 (7,792 –
interquartile range), \$	24,498)	25,058)	6,465)	26,830)	× – (2,968)	111,567)
Aaximum, \$	120,927	100,635	114,153	107,553	an e. a 4,362	506,108
Authors with payments (N=46), n %)					d from eur (A d data	
Any payments	40 (87.0)	42 (91.3)	36 (78.3)	38 (82.6)	<b><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></b>	43 (93.5)
>\$10,000	24 (52.2)	23 (50.0)	20 (43.5)	22 (47.8)		33 (71.7)
>\$50,000	6 (13.0)	5 (10.9)	4 (8.7)	2 (4.4)	<b>(6.5)</b>	23 (50.0)
>\$100,000	1 (2.2)	1 (2.2)	1 (2.2)	1 (2.2)		15 (32.6)
>\$250,000	0 (0)	0 (0)	0 (0)	0 (0)	ai = 0(0)	3 (6.5)
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Page 15 o	of 18			E	3MJ Open		bmjopen 1 by copy	
1 2 3 4 5	501 502	Table 3. Payment amounts by t	op 10 companies.				-2024-086396 on 2 /right, including fo	
7		Variables			Payment am	ounts (%), \$		
8			2016	2017	2018	2019	ອີສັສັສ 2020	Overall
9 10		Total amounts of payments	959,503 (100)	873,288 (100)	769,649 (100)	743,826 (100)	refaner later 170 (100)	4,041,648 (100)
11 12 13		Top 10 companies making the largest payment amounts	K				Downl nent Su d to tey	
14		Sumitomo Pharma	180,436 (18.8)	105,531 (12.1)	127,847 (16.6)	106,975 (14.4)		695,031 (17.2)
15		Eisai	45,779 (4.8)	78,418 (9.0)	52,244 (6.8)	80,026 (10.8)	ag B 856 (21.8)	408,323 (10.1)
16		MSD	122,880 (12.8)	83,528 (9.6)	79,420 (10.3)	57,679 (7.8)	a 14 020 (2.0)	357,526 (8.8)
17 10		Otsuka Pharmaceutical	64,794 (6.8)	73,028 (8.4)	64,161 (8.3)	86,679 (11.7)	<b>3 9 9 76</b> (9.5)	354,638 (8.8)
10 19		Takeda Pharmaceutical	69,017 (7.2)	78,990 (9.0)	45,019 (5.8)	71,206 (9.6)	<b>3 3 3 3 3 3 3 3 3 3</b>	337,370 (8.3)
20		Pfizer Japan	78,269 (8.2)	106,973 (12.2)	65,996 (8.6)	46,086 (6.2)	14 <b>2</b> 247 (2.0)	311,571 (7.7)
21		Mitsubishi Tanabe						
22		Pharma	58,501 (6.1)	47,295 (5.4)	61,056 (7.9)	59,114 (7.9)	a; 25, 789 (3.7)	251,755 (6.2)
23		Eli Lilly Japan	56,337 (5.9)	60,899 (7.0)	59,231 (7.7)	36,314 (4.9)	<b>a</b> 38 130 (5.5)	250,910 (6.2)
24 25		Meiji Seika Pharma	75,608 (7.9)	53,110 (6.1)	57,841 (7.5)	27,228 (3.7)	B 24 235 (3.5)	238,023 (5.9)
26		Mochida Pharmaceutical	35,768 (3.7)	29,405 (3.4)	31,597 (4.1)	41,378 (5.6)	<u><u><u></u></u> 172209 (2.5)</u>	155,356 (3.8)
27 28 29 30 31 32 33	503						on June 11, 2025 at / milar technologies.	

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Table 4. Financial conflicts of interest self-declared by the guideline authors 504 505

Disclosure category	Number of authors report	rting conflicts of interest
	Bipolar disorder (N=4)	Major depressive
		disorder (N=14)
Speaking compensation	4 (100)	11 (78.6)
Scholarship donation	3 (75.0)	6 (42.9)
Consulting payments	0 (0)	4 (28.6)
Collaborative research funds	1 (25.0)	2 (14.3)
Advisory board	2 (50.0)	1 (7.1)
Contracted research funds	1 (25.0)	0 (0)
Legends: Proportion of authors rep	porting conflicts of interes	at were number of authors
reporting conflicts of interest to the	total number of writing au	thors.
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506 Legends: Proportion of authors reporting conflicts of interest were number of authors 507 reporting conflicts of interest to the total number of writing authors.

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STROBE Statemen	ıt—ch	ecklist of items that should be included in reports of observational studies	ght, incluc	024-08639	
	Item No.	Recommendation	ling fo	os 9 Page N No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	ᇦᄪ	<u>ר</u>	<b>_</b>
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	inseign e§'relat	ne 202/	
Introduction			eme ted t		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	to fe	Ň	
Objectives	3	State specific objectives, including any prespecified hypotheses	xfa	loac	
Methods		6	nd o	d d	
Study design	4	Present key elements of study design early in the paper	dafa	from	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure,	min		
		follow-up, and data collection	ning	;p://	
Participants	6	<ul> <li>(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</li> <li>Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</li> <li>Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants</li> </ul>	, Al training, and simi	bmjopen.bmj.com/ on	
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case	lar technologie	June 11, 2025	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	<b>9</b> 4	at Age	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment	4	nce	
measurement		(measurement). Describe comparability of assessment methods if there is more than one group		Bib	
Bias	9	Describe any efforts to address potential sources of bias	n/a	liog	
Study size	10	Explain how the study size was arrived at	3	rap	

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Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which	t, 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1	
variables		groupings were chosen and why	639 clu	
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	6 or	
methods		(b) Describe any methods used to examine subgroups and interactions	ר 21 סיו	
		(c) Explain how missing data were addressed		
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	he 2 sstr	
		Case-control study—If applicable, explain how matching of cases and controls was addressed	elat	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling	ed t	
		strategy	o te	
		( <u>e</u> ) Describe any sensitivity analyses	loac Xta	
Results		5	nd ed	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	date	
1		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		
		(b) Give reasons for non-participation at each stage		
		(c) Consider use of a flow diagram	<u>,                                    </u>	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	ltra	
1		exposures and potential confounders		
		(b) Indicate number of participants with missing data for each variable of interest	μ/a	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	n d	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	sim or	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	ilar Ju	
		Cross-sectional study—Report numbers of outcome events or summary measures	C4-5	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	11, 2	
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	025	
		included	es.	
		(b) Report category boundaries when continuous variables were categorized		
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	n/a Ce	
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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	<u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></u>	
Discussion			5396 Slud	
Key results	18	Summarise key results with reference to study objectives	ing	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	for 21	
		both direction and magnitude of any potential bias	Jun En	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	e 2( sqij s'fe	
		analyses, results from similar studies, and other relevant evidence	)24. Jate	
Generalisability	21	Discuss the generalisability (external validity) of the study results	Do Mệr d'to	
Other informati	tion		wnl ht S	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	upe ad	
		original study on which the present article is based	nd c	
			hiron hata	
*Give informatio	on sena	arately for cases and controls in case-control studies and if applicable, for exposed and unexposed groups	in <b>E</b> and cross-se	ectional studies
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### Cross-sectional analysis of pharmaceutical industry payments to authors of clinical practice guidelines for bipolar disorder and major depressive disorder in Japan

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<b>Primary Subject Heading</b> :	Ethics
Secondary Subject Heading:	Evidence based practice, Ethics, Health policy, Mental health
Keywords:	MEDICAL ETHICS, ETHICS (see Medical Ethics), Depression & mood disorders < PSYCHIATRY, PSYCHIATRY, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT





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6	1	Title: Cross-sectional analysis of pharmaceutical industry payments to authors of
7	2	clinical practice guidelines for bipolar disorder and major depressive disorder in
8	3	Japan
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29	22	Conflicts of interest pharmacoutical companies alinical practice guideling health
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31	23	policy, evidence-based medicine, ethics, depression, bipolar disorder
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5	25	Abstract
6	25 26	Abstract
/	20	Clinical practice guidelines (CPGs) are essential for standardizing nations care based on
o Q	21	avidence based medicine. However, the presence of financial conflicts of interest
10	20	(COIs) among CPC authors can undermine their credibility. This study aimed to
11	29	examine the extent and size of COIs among outhors of neuchistry CDCs in Ispan
12	30 21	examine the extent and size of COIs among authors of psychiatry CPOs in Japan.
13	31 22	Mathada
14	32 22	This areas sectional analysis of displayed normants from abarma contial companies
15	33	This cross-sectional analysis of disclosed payments from pharmaceutical companies
16 17	34	assesses the prevalence and magnitude of personal payments for fecturing, consulting,
17	35	and writing to CPGs for bipolar disorder and major depressive disorder in Japan
10	36	between 2016 and 2020.
20	37	
21	38	Results
22	39	This study found that 93.3% of authors received payments over a five-year period, with
23	40	total payments exceeding \$4 million. The median payment per author was \$51,403
24	41	(interquartile range: $$9,982 - $111,567$ ), with a notable concentration of payments
25	42	among a small number of authors, including the CPG chairperson. Despite these
20 27	43	extensive financial relationships, only a fraction of authors disclosed their COIs in the
27	44	CPGs. These large amounts of personal payments were made by pharmaceutical
29	45	companies manufacturing new antidepressants and sleeping aids listed in the CPGs.
30	46	
31	47	Conclusions
32	48	This study found that more than 93% of authors of Japanese major depressive disorder
33	49	and bipolar disorder CPGs received considerable amounts of personal payments from
34	50	the pharmaceutical industry. The findings highlight deviations from international COI
35 36	51	management standards and suggest a need for more stringent COI policies for
37	52	psychiatry CPGs in Japan.
38	53	
39	54	Strengths and limitations
40	55	This study utilized a publicly accessible database containing all lecturing, consulting,
41	56	and writing payments to physicians disclosed by more than 70 pharmaceutical
42	57	companies in Japan.
43	58	This is the first analysis examining amounts, fraction, and extent of financial ties
44 45	59	between psychiatry guideline authors and pharmaceutical industry in Japan.
46	60	However, the study could not cover financial interactions between the psychiatry
47	61	guideline authors and pharmaceutical companies for research, royalties and licensing
48	62	fees, ownership interests, and other miscellaneous fees.
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64 Introduction

Clinical practice guidelines (CPGs) have been increasingly used as a tool to endorse evidence-based medicine for healthcare professionals in their clinical practice.<sup>12</sup> CPGs aim to summarize the best available evidence and often include recommendations for specific diagnosis and treatment of specific diseases. Nevertheless, the integrity and recommendations of CPGs are frequently compromised by conflicts of interest (COIs) between the guideline authors and the pharmaceutical industry, spanning various medical specialties. In the field of psychiatry, there is documentation of ghostwriting by pharmaceutical industry<sup>3</sup> and widespread financial COIs between CPG authors and pharmaceutical companies.<sup>4-7</sup> Furthermore, studies showed that financial COIs are associated with a propensity for CPGs to make recommendations favorable to the healthcare industry in general.<sup>48</sup> This underscores the necessity for rigorous management of financial COIs among CPG authors, particularly in psychiatry.<sup>6910</sup> A recent study demonstrated that 60% of panel members of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), fifth edition, text revision published by the American Psychiatry Association in 2022 received payments from the pharmaceutical industry.<sup>11</sup> As the DSM-5 is widely used as a standard for psychiatric disorders' definitions and symptom criteria, influencing treatment selection and approval of new drugs worldwide,<sup>11</sup> the widespread financial COIs among the DSM-5 panel members are concerning. However, financial COIs among psychiatry experts are not unique to international criteria and CPGs: they may also be problematic among authors of regional or national CPGs, as these guidelines include specific treatment recommendations that can influence the clinical practice of clinicians in each country or region. To enhance the transparency of financial relationships between healthcare professionals and pharmaceutical companies, members of the Japan Pharmaceutical Manufacturers Association have voluntarily disclosed their financial interactions with healthcare professionals and organizations.<sup>12</sup> Subsequent research using this disclosed information has revealed that the vast majority of CPG authors in Japan received personal payments during the CPG development across various medical specialties.<sup>12-22</sup> However, these financial relationships between pharmaceutical companies and Japanese CPG authors in

psychiatry remain largely unexplored. Considering the patterns observed in previous
 studies, we hypothesized that financial COIs are widespread among psychiatry CPG
 authors in Japan.

## 100 Methods

101 Study setting and participants

This cross-sectional analysis evaluated the extent and prevalence of financial interactions between pharmaceutical companies and authors of CPGs for major depressive disorder and bipolar disorder in Japan. Mood disorders, including bipolar disorder and major depressive disorder, are the most prevalent mental disorders in Japan. According to surveys conducted by the Japanese Ministry of Health, Labor, and Welfare, the number of patients with mood disorders has steadily increased over the past two decades, from 0.4 million in 1999 to 1.7 million in 2020.<sup>23</sup> The Japanese Society of Mood Disorders is responsible for the development of the sole CPGs for these conditions, namely Treatment Guideline I: Bipolar Disorder<sup>24</sup> and Treatment 

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5	111	Guideline II: Major Depressive Disorder. <sup>25</sup> At the time of this study, the most recent
0 7	112	versions were published in June 2020 and July 2019, respectively.
8	113	
9	114	Data collection
10	115	The Japan Pharmaceutical Manufacturers Association representing over 70 major
11	115	nharmacoutical companies, mandates the diselegure of neumants for lectures
12	110	pharmaceutical companies, mandates the disclosure of payments for fectures,
13	117	consultancy, and writing to heatincare professionals, listing the recipients names on
14	118	company websites since 2013. <sup>20-20</sup> Despite annual updates and removal of previous
15	119	years' data by these companies, the Medical Governance Research Institute has
16	120	independently collected and disclosed this payment data on its public online database
17	121	from 2016 to 2020, detailing individual physician and company names. <sup>29</sup>
18	122	
19	123	Information about payments to CPG authors was extracted as follows. First, a list of the
20	124	names of all CPG authors was created and saved as a CSV file. We then searched for
27	125	their names in the payments database and extracted speaking, consulting, and writing
23	126	payments to physicians whose names matched the CPG authors' names from the
24	127	database using Python programming code. After extracting the relevant payment
25	128	information, a manual review was performed to identify and remove any payments
26	129	made to physicians whose names were similar to those of the CPG authors but who
27	130	were actually different individuals as we previously noted <sup>30-33</sup> Finally, we randomly
28	131	selected five CPG authors (representing 11 1% of all authors) and manually searched
29	132	the authors' names in the navments database to ensure that the navment data extracted
30 21	132	using Dython were accurate and complete
21 22	124	using I yulon were accurate and complete.
32	104	As the pharmacoutical companies have not individually disaloged other estagories of
34	100	As the pharmaceutical companies have not individually disclosed other categories of
35	130	non-research payments such as travel and accommodation lees, lood and beverage lees,
36	137	royalties and licensing fees, and ownership interests, this study incorporated all personal
37	138	payments for lectures, consultancy, and writing from pharmaceutical companies to the
38	139	CPG authors from 2016 to 2020, following the approach of prior studies. <sup>30 34-36</sup>
39	140	
40	141	Data analysis
41	142	The study calculated the proportion of CPG authors receiving personal payments and
42 42	143	assessed per-author payment amounts, including median, interquartile range, mean, and
45 44	144	standard deviation.
45	145	We performed a sensitivity analysis examining personal payments to the CPG authors
46	146	from 2016 to 2019, to evaluate financial relationships between the CPG authors and
47	147	pharmaceutical companies before the CPG publication.
48	148	Additionally, we also calculated the proportion of authors receiving payments, total
49	149	payment amounts, and median payment amounts by the roles of CPG authors.
50	150	Payments were converted from Japanese ven to US dollars using the 2020 average
51	151	monthly exchange rate of 106.8 ven per \$1. Data extraction and analyses were executed
52	152	using Python 3.9.12 (Python Software Foundation Beaverton OR USA) Microsoft
55 51	153	Excel version 16.0 (Microsoft Corn Redmond WA USA) and Stata version 17.0
54 55	153	(StateCorn College Station TX USA)
56	154	(StataCorp, Conege Station, TA, USA).
57	155	Ethical clearance
58	100	Ennicul cleur unde
59	157	As a renospective analysis of publicity available data, this study was classified as non-
60		4

human subjects research and did not require institutional review board approval in accordance with the Japanese Ministry of Health, Labor, and Welfare's Ethical Guidelines for Medical and Health Research Involving Human Subjects. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline. Patient and public involvement No patients were involved in the preparation of this manuscript or the research project. **Results** The study included 33 authors for the bipolar disorder CPG and 42 for the major depressive disorder CPG. Of these authors, 30 individual physicians contributed to both CPGs. Consequently, a total of 45 unique CPG authors were analyzed in this study. Of all 45 authors, 42 (93.3%) received personal payments for lectures, consulting, and writing from pharmaceutical companies between 2016 and 2020 (Table 1). The total amount of personal payments received by the 55 pharmaceutical companies over the course of the study period was \$4,041,648. The median payment per author was \$51,403 (IQR: \$9,982 – \$111,567), and the mean payment was \$89,814 (SD: \$111,760), indicating a skewed distribution where a few authors received disproportionately high payments. Notably, 15 authors (33.3%) received in excess of \$100,000 over the five-year period. The majority of payments, constituting 65.8% (\$2.7 million) of the total, were for lecturing fees, with consulting and writing compensations accounting for 25.8% (\$1.0 million) and 8.3% (\$337,255) in total, respectively. All two chairs of each CPG development committee received personal payments from pharmaceutical companies totaling \$506,108 (the highest total) for the chair of the bipolar disorder CPG development committee and \$97,288 for the chair of the major depressive disorder CPG development committee over the five-year period. Annual analysis revealed a decline in total payments to CPG authors from \$959,289 in 2016 to \$697,170 in 2020 (Table 1). Correspondingly, the median annual payment per author decreased from \$11,992 (IQR: \$1,877 - \$24,498) in 2016 to \$2,702 (IQR: \$120 - \$22,968) in 2020. The proportion of authors receiving payments also fell from 91.1% in 2017 to 75.6% in 2020, yet a majority still received at least one personal payment annually. The sensitivity analysis of payments to the CPG authors from 2016 to 2019 showed that 42 (93.2%) authors received at least one payment from pharmaceutical companies. The total amounts of personal payments were \$3,344,478 for the four-year period. Median amounts of four-year payments were \$44,688 (IQR: \$9,325 - \$93,393) per author. Payments from the top 5 and 10 pharmaceutical companies constituted 53.3% (\$2.2 million) and 83.1% (\$3.4 million) of the total payments from 2016 to 2020, respectively (Table 2). Sumitomo Pharma made the largest total amounts of personal payments amounting to \$695,031 (17.2%), followed by Eisai (10.1%, \$408,323), MSD (8.8%, \$357,526), Otsuka Pharmaceutical (8.8%, \$354,638), and Takeda Pharmaceutical (8.3%, \$337,370). Among these companies, MSD, Pfizer Japan, and Meiji Seika notably reduced their personal payments from 2016 to 2020, whereas Eisai increased its 

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5	205	payments from \$45 779 in 2016 to \$151 856 in 2020
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/	200	The two CDCs included three entegories of outher reles: writing outhers, who were
8	207	rimenity responsible for developing the CDCs and making recommendations.
9 10	208	primarily responsible for developing the CPGs and making recommendations;
10	209	supporting authors, who may have contributed to the CPG development in a limited
12	210	capacity, such as identifying relevant evidence, performing literature reviews, and
13	211	making recommendations for specific situations; and guideline development committee
14	212	authors, who did not directly contribute to the creation of CPGs and recommendations
15	213	but critically reviewed the initial CPG drafts and revised the drafts and
16	214	recommendations. The CPGs explicitly indicated that all of these authors were involved
17	215	in the formulation of recommendations.
18	216	Of three categories of author roles all writing authors for both CPGs received personal
19	217	navments from pharmaceutical companies between 2016 and 2020 (Table 3) while
20	217	lower proportion of supporting authors received navments than those for writing authors
21	210	and guideline development committee outhors in both CDCa. Median neument emounts
22	219	and guideline development commutee autions in both CPOS. Median payment amounts
23	220	were the highest for writing authors ( $\$135,867$ (IQK: $\$78,553 - \$187,806$ ) for the
24	221	bipolar disorder CPG and \$87,610 (IQR: \$16,945 – \$111,567) for the major depressive
25	222	disorder CPG).
20	223	
27	224	Disclosure of financial COIs in the CPGs was self-reported only by writing authors.
29	225	There were no COI declaration statements for other types of authors. All authors (100%,
30	226	4 out of 4) of the bipolar disorder CPG and 85.7% (12 out of 14) of the major
31	227	depressive disorder CPG authors declared financial COIs with pharmaceutical
32	228	companies. Table 4 presents the types of financial COIs self-reported by the CPG
33	229	authors within each respective guideline. Among the six categories extracted from the
34	230	disclosure statements in the CPGs, compensation for lecturing was the most frequently
35	231	declared (100% for the bipolar disorder CPG authors and 78 6% for the major
36	232	depressive disorder CPG authors). This was followed by scholarship donations and
3/	232	participation in pharmaceutical company advisory boards. Although there were
38	233	disgraphic in the number of writing outbors receiving neumonts between industry
39 40	234	ansored neuron data and outhous? solf dealand COL statements by
40 //1	235	sponsored payment data and authors self-declared COI statements by
47	236	payment/declaration category (Table 4), the lack of a specified declaration period
43	237	precluded the assessment of the accuracy of each CPG author's self-reported COI
44	238	statements against the payment data reported by the pharmaceutical companies.
45	239	
46	240	Discussion
47	241	This cross-sectional analysis of publicly disclosed payment data from pharmaceutical
48	242	companies provides a detailed examination of the extent and fraction of financial COIs
49	243	among authors of the Japanese Society of Mood Disorders' Treatment Guideline I
50	244	Bipolar Disorder <sup>24</sup> and Treatment Guideline II <sup>.</sup> Major Depressive Disorder <sup>25</sup> These
51	245	CPGs are considered by physicians the authoritative and trustworthy sources for the
52	246	treatment of hinolar disorder and major depressive disorder in Japan <sup>37</sup> To the best of
53	240	our knowledge this is the first in denth study to analyze the financial relationships
54 55	241 210	between neurophistry CDC authors and nharmacoutical companies in Japan using
55	240 240	pharmanautical industry disclosed data. The findings reveal that a large majority
57	249	pharmaccurrent industry-disclosed data. The influings reveal that a large inajority $(02, 20/)$ of CDC such are received where $r_{1}$ is the influence of the interval of th
58	250	(95.5%) of CPG authors received personal payments for lecturing, consulting, and
59	251	writing, with a total sum of \$4.0 million between 2016 and 2020. The median payment
60		6

per author was \$51,403, with a minority, including the CPG chairperson, receiving substantial sums. Nearly all authors involved in writing the CPGs self-reported financial COIs with pharmaceutical companies. Notably, the bulk of personal payments to CPG authors came from companies that manufacture antidepressants and sleeping pills in Japan. However, other CPG authors did not publicly disclose their financial COIs with these companies. When compared to previous studies and international COI policies for CPG authors, these findings raise concerns for physicians, patients, policymakers, and other stakeholders within and beyond Japan. 

The study highlights that over 93% of the authors of CPGs for bipolar disorder and major depressive disorder had financial relationships with pharmaceutical industry. Given the publication dates of the CPGs between 2019 and 2020, these financial relationships likely occurred during the development of the CPGs. This high percentage of authors receiving personal payments aligns with findings from other specialties within Japan, <sup>12-15</sup> <sup>17-22</sup> <sup>31</sup> <sup>33</sup> <sup>38-42</sup> where the proportion of CPG authors with personal payments ranged from 66.0% in obstetrics and gynecology<sup>42</sup> to 96.3% in otolaryngology.

In contrast, research from other developed countries, such as the United States, reports lower proportions of CPG authors with financial COIs. For instance, 67% of authors for the DSM-5 mood disorders section disclosed financial COIs with the healthcare industry.<sup>9</sup> Additionally, a study by Cosgrove et al. found that only 18% of major depressive disorder CPG authors across eight countries had financial COIs with pharmaceutical companies.<sup>4 10</sup> In Canada, half of the authors of the CPG for depressive disorder developed by the Canadian Network for Mood and Anxiety Treatments reported financial COIs with the healthcare industry.<sup>43</sup> Other specialties in the United States also showed lower percentages, with 53% of gastroenterology CPG authors<sup>44</sup> and 59.3% of urology CPG authors receiving personal and/or research payments.<sup>45</sup> Moreover, Mooghali et al. reported that 73.7% of physician CPG authors in the United States received personal and/or research payments from healthcare companies.<sup>46</sup> The higher proportion of CPG authors receiving payments in Japan can be attributed to the fact that most professional medical societies in Japan have implemented less transparent COI policies. This is in line with our previous studies reporting on the matter.<sup>18 20</sup> Furthermore, this investigation revealed that a select group of CPG authors, including 

the chairperson, received substantial personal payments from pharmaceutical companies. Only authors involved in writing the CPGs were mandated to declare their financial COIs, while other contributors did not publicly disclose any financial COIs with these companies. These results indicate that authors of Japanese CPGs for bipolar disorder and major depressive disorder clearly violate international COI policies on CPG development in several respects. The U.S. National Academy of Medicine's 2011 report and the Guidelines International Network advocate for a majority of CPG authors to be free from financial COIs.<sup>12</sup> These policies also stipulate that the chairperson of CPG development should not hold any COIs.<sup>12</sup> The Guideline Panel Review Working Group's criteria for red flags, as published in the British Medical Journal in 2013, indicate that financial COIs held by a CPG chairperson and multiple authors are significant concerns for the trustworthiness of the CPGs.<sup>47</sup> The prevalence of COIs 

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exceeding 93% in this study is not a marginal discrepancy but a significant deviation
from these standards, casting doubt on the objectivity and reliability of the guidelines.

302 Moreover, the study revealed that substantial payments were made by pharmaceutical 303 companies marketing new antidepressants and sleep aids in Japan. For example, 304 Sumitomo Pharma, the top payer, produces lurasidone (brand name: Latuda), which was 305 approved for bipolar disorder and schizophrenia in 2020, and has been co-marketing 306 venlafaxine hydrochloride (brand name: Effexor) with Pfizer Japan since 2018. MSD, 307 another major payer, produces suvorexant (brand name: Belsomra), the world's first 308 orexin receptor antagonist used for insomnia. Otsuka Pharmaceutical is known as one of 309 the major manufacturers of atypical antipsychotics, such as aripiprazole (brand name: 310 Abilify) and brexpiprazole (brand name: Rexulti), which are the most widely prescribed atypical antipsychotics in Japan.<sup>48</sup> Despite these financial ties between CPG authors and 311 312 pharmaceutical companies manufacturing relevant drugs, the Japanese Society of Mood Disorders actively endorses adherence to these CPGs.<sup>49 50</sup> Given that the CPGs for 313 bipolar disorder and major depressive disorder include pharmacotherapy 314 recommendations that include medications from these companies, it is imperative that 315 316 the close financial ties between CPG authors and the pharmaceutical industry be 317 addressed. We strongly recommend the Japanese Society of Mood Disorders to enforce 318 more transparent and stringent COI management strategies in the CPG development 319 process for bipolar disorder and major depressive disorder to ensure the integrity and 320 credibility of these guidelines.

## 322 Limitations

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323 This study is subject to several limitations. Primarily, the study focus on CPGs for bipolar disorder and major depressive disorder in Japan would limit the generalizability 324 325 of our findings to other medical fields or countries. Additionally, the payment data were 326 derived from a secondary source, the Medical Governance Research Institute's database, 327 which contains payment information from member companies of the Japan 328 Pharmaceutical Manufacturers Association for the period 2016-2020.<sup>27 51</sup> Absent legal 329 mandates for precise payment disclosures in Japan, the potential for inaccuracies or underreporting in the database cannot be discounted. Furthermore, the voluntary nature 330 331 of these disclosures means that financial interactions between CPG authors and nondisclosing pharmaceutical entities may remain undetected. Nevertheless, given that the 332 member companies account for 80% of the market share for drugs and medical products 333 334 in Japan,<sup>52</sup> the impact of financial relationships between the CPG authors and uncovered companies would be minimized. 335

18 336 19 337 Conclusions

50 338 More than 93% of the authors of the Treatment Guidelines for Bipolar Disorder and 51 Major Depressive Disorder developed by the Japanese Society of Mood Disorders 339 52 340 received personal payments for the reimbursement of their lecturing, consulting, and 53 341 writing activities from the pharmaceutical companies manufacturing related drugs. The 54 total amounts of personal payments to the CPG authors were more than \$4.0 million 55 342 56 343 over the five years. Nevertheless, the financial COIs were only declared by the limited 57 344 group of CPG authors. Further transparent and rigorous COI management strategies 58 must be warranted in the Japanese Society of Mood Disorders. 345 59

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347 Author contribution:

A.M. contributed to data collection, resource, software, formal analysis, visualization, supervision, and study administration. All authors (A.M., H.K., and Y.S.) contributed to study conceptualization, methodology, writing the original draft, and reviewing the draft.

# **Conflicts of interest:**

The authors declare that there were no conflicts of interest for this study.

# 66 Funding sources:

The authors declare that there were no funding sources for this study.

# 359 IRB Statement

As this study was a retrospective analysis of publicly available data and met the definition of non-human subjects research, no institutional board review and approval were required in accordance with the Japanese Ministry of Health, Labor, and Welfare's Ethical Guidelines for Medical and Health Research Involving Human Subjects. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

# **Declaration of generative AI in scientific writing**

During the preparation of this work, the authors used ChatGPT version 4.0 solely for the purpose of identifying and correcting grammatical and spelling errors, and we did not use it for the creation of any intellectual parts of the manuscript. After using this tool, the authors carefully reviewed and edited the content as needed and take full responsibility for the content of the publication.

# **Data availability statement:**

All data used in this study is available from Yen For Docs database run by Medical Governance Research Institute (<u>https://yenfordocs.jp/</u>) and each pharmaceutical companies belonging to the Japan Pharmaceutical Manufacturers Association. Due to privacy protection, payment data of individual CPG authors will be available from the corresponding author upon reasonable request.

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# **References**

Schunemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: Principles for
 Disclosure of Interests and Management of Conflicts in Guidelines. *Ann Intern Med*

### BMJ Open

2		
3		
4		
5	303	2015:162(7):548 52 doi: 10.7226/M14.1885 [published Opling First: 2015/10/06]
6	301	2015,105(7).546-55. doi: 10.7520/W14-1665 [published Ollinic First. 2015/10/00]
7	205	2. Institute of Medicine. Chinical Fractice Outdennes we Can Trust. Washington, DC. The National
8	393	Academies Press 2011.
9	390 207	3. Koenr B. Professor files complaint of scientific misconduct over allegation of gnostwriting. <i>BMJ</i>
10	397	2011;343:d4458. doi: 10.1136/bmj.d4458 [published Online First: 20110/13]
11	398	4. Cosgrove L, Shaughnessy AF, Peters SM, et al. Conflicts of Interest and the Presence of
10	399	Methodologists on Guideline Development Panels: A Cross-Sectional Study of Clinical Practice
12	400	Guidelines for Major Depressive Disorder. <i>Psychother Psychosom</i> 2017;86(3):168-70. doi:
13	401	10.1159/000458727 [published Online First: 20170511]
14	402	5. Cosgrove L, Krimsky S, Vijayaraghavan M, Schneider L. Financial ties between DSM-IV panel
15	403	members and the pharmaceutical industry. <i>Psychother Psychosom</i> 2006;75(3):154-60. doi:
16	404	10.1159/000091772 [published Online First: 2006/04/26]
17	405	6. Cosgrove L, Bursztajn HJ, Krimsky S. Developing unbiased diagnostic and treatment guidelines in
18	406	psychiatry. <i>N Engl J Med</i> 2009;360(19):2035-6. doi: 10.1056/NEJMc0810237
19	407	7. Cosgrove L, Bursztajn HJ, Krimsky S, et al. Conflicts of interest and disclosure in the American
20	408	Psychiatric Association's Clinical Practice Guidelines. <i>Psychother Psychosom</i> 2009;78(4):228-
21	409	32. doi: 10.1159/000214444 [published Online First: 20090428]
22	410	8. Nejstgaard CH, Bero L, Hrobjartsson A, et al. Association between conflicts of interest and favourable
23	411	recommendations in clinical guidelines, advisory committee reports, opinion pieces, and
24	412	narrative reviews: systematic review. BMJ 2020;371:m4234. doi: 10.1136/bmj.m4234
25	413	[published Online First: 20201209]
26	414	9. Cosgrove L, Krimsky S. A comparison of DSM-IV and DSM-5 panel members' financial associations
20	415	with industry: a pernicious problem persists. PLoS Med 2012;9(3):e1001190. doi:
27	416	10.1371/journal.pmed.1001190 [published Online First: 20120313]
20	417	10. Cosgrove L, Krimsky S, Wheeler EE, et al. Conflict of Interest Policies and Industry Relationships of
29	418	Guideline Development Group Members: A Cross-Sectional Study of Clinical Practice
30	419	Guidelines for Depression. Account Res 2017;24(2):99-115. doi:
31	420	10.1080/08989621.2016.1251319 [published Online First: 20161024]
32	421	11. Davis LC, Diianni AT, Drumheller SR, et al. Undisclosed financial conflicts of interest in DSM-5-
33	422	TR: cross sectional analysis. BMJ 2024;384:e076902. doi: 10.1136/bmj-2023-076902 [published
34	423	Online First: 20240110]
35	424	12. Murayama A, Ozaki A, Saito H, et al. Pharmaceutical company payments to dermatology Clinical
36	425	Practice Guideline authors in Japan. PLoS One 2020;15(10):e0239610. doi:
37	426	10.1371/journal.pone.0239610 [published Online First: 20201013]
38	427	13. Kida F, Murayama A, Saito H, et al. Pharmaceutical company payments to authors of the Japanese
39	428	Clinical Practice Guidelines for Hepatitis C treatment. Liver Int 2021;41(3):464-69. doi:
40	429	10.1111/liv.14761 [published Online First: 20201223]
41	430	14. Harada K, Ozaki A, Saito H, et al. Financial payments made by pharmaceutical companies to the
42	431	authors of Japanese hematology clinical practice guidelines between 2016 and 2017. Health
43	432	<i>Policy</i> 2021;125(3):320-26. doi: 10.1016/j.healthpol.2020.12.005 [published Online First:
44	433	20201217]
45	434	15. Hashimoto T, Murayama A, Mamada H, et al. Evaluation of financial conflicts of interest and drug
45	435	statements in the coronavirus disease 2019 clinical practice guideline in Japan. Clin Microbiol
40	436	Infect 2022;28(3):460-62. doi: 10.1016/j.cmi.2021.11.019 [published Online First: 20211124]
47	437	16. Kamamoto S, Murayama A, Kusumi E, et al. Evaluation of financial relationships between Japanese
48	438	certified pediatric hematologist/oncologists and pharmaceutical companies: a cross-sectional
49	439	analysis of personal payments from pharmaceutical companies between 2016 and 2019. <i>Pediatr</i>
50	440	<i>Blood Cancer</i> 2022:69(10):e29891. doi: 10.1002/pbc.29891 [published Online First: 20220810]
51	441	17. Murayama A, Kida F, Ozaki A, et al. Financial and Intellectual Conflicts of Interest Among Japanese
52	442	Clinical Practice Guidelines Authors for Allergic Rhinitis Otolaryngol Head Neck Surg
53	443	2022:166(5):869-76 doi: 10.1177/01945998211034724 [multished Online First: 20210817]
54	444	18 Murayama A Yamada K Yoshida M et al Evaluation of Conflicts of Interest among Participants of
55	445	the Jananese Nephrology Clinical Practice Guideline Clin I Am Soc Nonhrol 2022:17(6):810-26
56	446	doi: 10 2215/CIN 14661121 [nublished Online First: 2022/05/28]
57	447	19 Mamada H. Muravama A. Kamamoto S. et al. Evaluation of Financial and Nonfinancial Conflicts of
58	448	Interest and Quality of Evidence Underlying Psoriatic Arthritis Clinical Practice Guidelines:
59	110	increation and Quanty of Evidence Ondertying I solitatic Artiffus Chinear Flactice Outdellies.
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Analysis of Personal Payments From Pharmaceutical Companies and Authors' Self-Citation Rate

in Japan and the United States. Arthritis Care Res (Hoboken) 2023;75(6):1278-86. doi:

Murayama A, Kamamoto S, Murata N, et al. Evaluation of financial conflicts of interest and quality of evidence in Japanese gastroenterology clinical practice guidelines. J Gastroenterol Hepatol

Murayama A. Financial Conflicts of Interest Among the Authors of the Clinical Practice Guidelines for Rheumatoid Arthritis in Japan. *Cureus* 2023;15(10):e46650. doi: 10.7759/cureus.46650

Yamamoto K, Murayama A, Ozaki A, et al. Financial conflicts of interest between pharmaceutical

Japanese Society of Mood Disorders. Treatment Guideline I: Bipolar Disorder Online: Japanese Society of Mood Disorders; 2020 [updated June 16, 2020. 4th edition:[Available from: https://www.secretariat.ne.jp/jsmd/iinkai/katsudou/data/guideline\_sokyoku2020.pdf accessed

Japanese Society of Mood Disorders. Treatment Guideline II: Major Depressive Disorder Online:

https://www.secretariat.ne.jp/jsmd/iinkai/katsudou/data/20190724-02.pdf accessed October 20

Ozaki A, Saito H, Senoo Y, et al. Overview and transparency of non-research payments to healthcare organizations and healthcare professionals from pharmaceutical companies in Japan: Analysis of payment data in 2016. *Health Policy* 2020;124(7):727-35. doi: 10.1016/j.healthpol.2020.03.011

Murayama A, Kamamoto S, Saito H, et al. Characteristics and Distribution of Scholarship Donations From Pharmaceutical Companies to Japanese Healthcare Institutions in 2017: A Cross-sectional Analysis. *International Journal of Health Policy and Management* 2023;12(1) doi: ARTN 7621

 Murayama A, Kamamoto S, Saito H, et al. Pharmaceutical Payments to Japanese Board-Certified Infectious Disease Specialists: A Four-Year Retrospective Analysis of Payments from 92 Pharmaceutical Companies between 2016 and 2019. *Int J Environ Res Public Health* 2022;19(12):7417. doi: 10.3390/ijerph19127417 [published Online First: 20220616]
 Medical Governance Research Institute. Yen For Docs [Online database]. 2023 [updated December

Murayama A, Kamamoto S, Saito H, Ozaki A. Pharmaceutical payments to Japanese board-certified dermatologists: a 4-year retrospective analysis of personal payments from pharmaceutical companies between 2016 and 2019. *Sci Rep* 2023;13(1):7425. doi: 10.1038/s41598-023-34705-8

payments to Japanese board-certified gastroenterologists between 2016 and 2019. *BMJ Open* 2023;13(4):e068237. doi: 10.1136/bmjopen-2022-068237 [published Online First: 20230418] Murayama A, Senoo Y. Cross-sectional analysis of financial relationships between board certified allergists and the pharmaceutical industry in Japan. *BMC Med Ethics* 2024;25(1):22. doi:

23, 2023. Available from: https://yenfordocs.jp/ accessed March 6, 2024 2024.

Murayama A, Kamamoto S, Kawashima M, et al. Cross-sectional analysis of pharmaceutical

Murayama A, Shin N, Higuchi K, et al. Financial conflicts of interest between infectious diseases clinical practice guideline authors and the pharmaceutical industry in Japan. *Infect Dis (Lond)* 

2024:1-5. doi: 10.1080/23744235.2024.2309351 [published Online First: 20240201] Murayama A, Saito H, Kamamoto S, et al. Evaluation of non-research payments from pharmaceutical companies to urologists in Japan between 2016 and 2019. *Int Urogynecol J* 2023;34(6):1285-92.

Kusumi E, Murayama A, Kamamoto S, et al. Pharmaceutical payments to Japanese certified

hematologists: a retrospective analysis of personal payments from pharmaceutical companies between 2016 and 2019. *Blood Cancer J* 2022;12(4):54. doi: 10.1038/s41408-022-00656-y

10.1186/s12910-024-01014-2 [published Online First: 20240220]

doi: 10.1007/s00192-023-05463-y [published Online First: 20230201]

Japanese Society of Mood Disorders; 2019 [2nd edition: Available from:

companies and the authors of urology clinical practice guidelines in Japan. *Int Urogynecol J* 2021;32(2):443-51. doi: 10.1007/s00192-020-04547-3 [published Online First: 20201105] Ministry of Health, Labour and Welfare. Patient Survey: Ministry of Health, Labour, and Welfare; 2020 [Available from: https://www.mhlw.go.jp/toukei/saikin/hw/kanja/20/index.html accessed

2023;38(4):565-73. doi: 10.1111/jgh.16089 [published Online First: 20221229]

10.1002/acr.25032 [published Online First: 20230114]

[published Online First: 20231007]

[published Online First: 20200426]

[published Online First: 20230508]

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5	505	
6	505	[published Online First: 20220407]
7	506	36. Murayama A, Hoshi M, Saito H, et al. Nature and Trends in Personal Payments Made to the
, 8	507	Respiratory Physicians by Pharmaceutical Companies in Japan between 2016 and 2019.
0	508	<i>Respiration</i> 2022;101(12):1088-98. doi: 10.1159/000526576 [published Online First: 20221109]
9	509	37. Numata S, Nakataki M, Hasegawa N, et al. Improvements in the degree of understanding the
10	510	treatment guidelines for schizophrenia and major depressive disorder in a nationwide
11	511	dissemination and implementation study. <i>Neuropsychopharmacol Rep</i> 2021;41(2):199-206. doi:
12	512	10.1002/npr2.12173 [published Online First: 20210311]
13	513	38. Murayama A, Kamamoto S, Shigeta H, et al. Undisclosed financial conflicts of interest with
14	514	pharmaceutical companies among the authors of the Esophageal Cancer Practice Guidelines
15	515	2017 by the Japan Esophageal Society. Dis Esophagus 2022;35(10) doi: 10.1093/dote/doac056
16	516	39. Murayama A, Mamada H, Shigeta H, et al. Financial Relationships Between Pharmaceutical
17	517	Companies and Rheumatologists in Japan Between 2016 and 2019. J Clin Rheumatol
18	518	2023;29(3):118-25. doi: 10.1097/RHU.0000000000001922 [published Online First: 20221207]
19	519	40. Kamamoto S. Ozaki A. Murayama A. Assessment of Financial Relationships Between
20	520	Otorhinolaryngologists and Pharmaceutical Companies in Japan Between 2016 and 2019.
20	521	<i>Cureus</i> 2023:15(8):e43633 doi: 10.7759/cureus 43633 [nublished Online First: 20230817]
21	522	41 Muravama A Aizawa M Byreddy KR et al Conflicts of Interest Among Cardiology Clinical
22	523	Practice Guideline Authors in Japan J Am Heart Assoc 2024:13(8):e034506 doi:
23	524	10 1161/jaha 124 034506 [nublished Online First: 20240412]
24	525	42 Muravama A Miyazawa K Kamamoto S et al Financial conflicts of interest in Japanese obstetrics
25	526	and gynaecology clinical practice guidelines. <i>Clinical and Translational Discovery</i>
26	527	2024:4(1):e273 doi: 10.1002/otd2.273
27	528	43 Elder K Turner KA Cosgrave L et al Reporting of financial conflicts of interest by Canadian
28	520	clinical practice guideline producers: a descriptive study. CMAL2020:102(23):E617-E25. doi:
29	530	10 1502/cmpi 101727 [published Online First: 2020/06/17]
30	531	AA Combe TP. Scott I. Jorski A. et al. Evaluation of Industry Palationshing Among Authors of Clinical
31	532	44. Comos TK, Scott J, JOISKI A, et al. Evaluation of industry Ketationships Aniong Authors of Chinear Dractice Guidelines in Castroenterology 14M4 Intern Med 2018:178(12):1711-12. doi:
32	532	10 1001/iomainternmed 2018 4720 [muhlished Online First: 2018/11/02]
33	533	10.1001/jamainternined.2016.4/30 [published Online First. 2016/11/02]
34	525	45. Calliste A, Bowels A, Wayan C, et al. Financial Connects of Interest Among Autors of Ofology
35	555	Clinical Practice Guidelines. Eur Orol 2018,74(3):348-54. doi: 10.1010/j.eururo.2018.04.025
36	330 527	[published Online First: 20180507]
27	557	40. Moognall M, Glick L, Ramachandran R, Ross JS. Financial conflicts of interest among US physician
20	530	authors of 2020 clinical practice guidelines: a cross-sectional study. <i>BMJ Open</i>
20	559 540	2023;13(1):e009115. doi: 10.1136/omjopen-2022-069115 [published Online First: 20230123]
39	540	47. Lenzer J, Horiman JR, Furberg CD, et al. Ensuring the integrity of clinical practice guidelines: a tool
40	541	for protecting patients. BMJ 2013;34/:15535. doi: 10.1136/bmj.15535 [published Online First:
41	54Z	20130917]
42	543	48. Jiho. Yakuji Handbook 2021: Jiho 2021:522.
43	544	49. Takaesu Y, Watanabe K, Numata S, et al. Improvement of psychiatrists' clinical knowledge of the
44	545	treatment guidelines for schizophrenia and major depressive disorders using the 'Effectiveness of
45	546	Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)' project: A
46	547	nationwide dissemination, education, and evaluation study. <i>Psychiatry Clin Neurosci</i>
47	548	2019;73(10):642-48. doi: 10.1111/pcn.12911 [published Online First: 20190822]
48	549	50. Kodaka F, Ohi K, Yasuda Y, et al. Relationships Between Adherence to Guideline Recommendations
49	550	for Pharmacological Therapy Among Clinicians and Psychotic Symptoms in Patients With
50	551	Schizophrenia. Int J Neuropsychopharmacol 2023;26(8):557-65. doi: 10.1093/ijnp/pyad037
51	552	51. Ozieranski P, Saito H, Rickard E, et al. International comparison of pharmaceutical industry payment
57	553	disclosures in the UK and Japan: implications for self-regulation, public regulation, and
5Z E2	554	transparency. Global Health 2023;19(1):14. doi: 10.1186/s12992-022-00902-9 [published
23	555	Online First: 20230303]
54	556	52. Japan Pharmaceutical Manufacturers Association. Data Book 2023 2023 [Available from:
55	557	https://www.jpma.or.jp/news_room/issue/databook/en/rfcmr00000000an3-
56	558	att/DATABOOK2023_en.pdf accessed August 9 2023.
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<ul><li>561 Table 1. Summary of pe</li><li>562 2020</li><li>563</li></ul>	rsonal payments	from pharmaceut	ical companies to	o psychiatry clini	cal practing guid	eline authors from	2016 to
Variables	2016	2017	2018	2019	2029 Enseigne relat	Four-year total amounts from 2016 to 2019	Five-year total amounts from 2016 to 2020
Total amount of payments, \$	959.289	872.245	769.649	743.295	697. <b>979</b> 0	3.344.478	4.041.648
Mean payments per author	21 318	19 383	17 103	16 518	15 49 2 4	74 322 (93 767)	89 814 (111 760)
(standard deviation). \$	(27.281)	(24.380)	(24,797)	(21.363)			
Median payments per author	11.992 (1.877 -	10.678 (2.309 -	5.452 (1.251 -	4.506 (834 -	2.701 (12)	44.688 (9.325 -	51.403 (9.982 -
(interguartile range). \$	24.498)	25.058)	22.591)	26.830)	22.968	93.393)	111.567)
Maximum payment amounts, \$	120,927	100,635	114,153	107,553	94,362	411,745	506,108
Authors receiving personal	,		,	,		,	,
payments (N=45), n (%)			1				
Any payments	39 (86.7)	41 (91.1)	36 (80.0)	37 (82.2)	34 (75.6)	42 (93.3)	42 (93.3)
>\$10,000	24 (53.3)	23 (51.1)	20 (44.4)	22 (48.9)	19 (42.2)	32 (71.1)	33 (73.3)
>\$50,000	6 (13.3)	5 (11.1)	4 (8.9)	2 (4.4)	3 (627)	21 (46.7)	23 (51.1)
>\$100,000	1 (2.2)	1 (2.2)	1 (2.2)	1 (2.2)	0 (5) 5	10 (22.2)	15 (33.3)
>\$250,000	0 (0)	0 (0)	0 (0)	0 (0)		2 (4.4)	3 (6.7)
564 Japanese yen (¥) were co 565	onverted to US do	llars (\$) using the	e 2020 average m	onthly exchange	rate of ¥ <b>1</b> 06. similar technologies.	er \$1.	13
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Table 2. Payment a	mounts by top 1	0 companies.				396 on uding	
Variables			Pavment am	nounts (%). \$		for 21	Major products
	2016	2017	2018	2019	2020	Dunge 202. Egseign Uses rela	bipolar and r depressive dis (generic na
Total amounts of payments	959,289 (100)	872,245 (100)	769,649 (100)	743,295 (100)	697,170 (100)	4,0 <b>4 8</b>	(generic in
Top 10 companies making the largest payment amounts		Or,				nloaded t Superieu ext and c	
Sumitomo Pharma	180,436 (18.8)	105,531 (12.1)	127,847 (16.6)	106,975 (14.4)	174,243 (25.0)	ABES) . ABES) . Ba mining, Al training, and similar technologies	Effexor (venla co-promotion Pfizer Japa Erispan (fludia Excegran (zonis Halomonth (hal- decanoate Mystan (clobs Noritren (nortri Landosen (clona Latuda (luras) Lonasen Ta (blonanser Lullan (perosp Sediel (tandos)
Eisai	45,779 (4.8)	78,418 (9.0)	52,244 (6.8)	80,026 (10.8)	151,856 (21.8)	408,3 <b>2</b> 3 (10. <b>19</b>	Dayvigo (lembo Spriropitan spi
MSD	122,880 (12.8)	83,528 (9.6)	79,420 (10.3)	57,679 (7.8)	14,020 (2.0)	357,526 <b>2</b> 8.8) Bibli	Belsomra (suvo Remeron (mirta Reslin (trazo

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						udi 396	Tetramide (mianserin)
Otsuka						354 638 78 8)	Abilify (aripiprazole)
Pharmaceutical	64 794 (6 8)	73 028 (8 4)	64 161 (8 3)	86 679 (11 7)	65 976 (9 5)		Rexulti (brexpiprazole)
Takeda	01,771 (0.0)	75,020 (0.1)	01,101 (0.5)			337 970 £8 3)	Depas (etizolam)
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Pfizer Japan	78,269 (8.2)	(12.3)	65,996 (8.6)	46,086 (6.2)	14,247 (2.0)	311, <b>5</b> 71 <b>7</b> .7)	mirtrzapin)
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Mitsubishi	50 501 (6 1)	47.005 (5.4)	(1,05)	50 114 (0.0)	25 700 (2 7)		(levomepromazine)
Tanabe Pharma	58,501 (6.1)	47,295 (5.4)	61,056 (7.9)	59,114 (8.0)	25,789 (3.7)	201,500 <b>8</b> 0.2)	Rize (clotiazepam)
						5 a ies	Strattera (atomoxetine)
						· t A	Zyprexa (olanzapine)
Eli Lilly Jonan	56 227 (5 0)	60,800 (7,0)	50.221(7.7)	26.214 (4.0)	28 120 (5 5)		Zyprexa Zydis
Eli Liliy Japan Majiji Sajka	30,337 (3.9)	00,899 (7.0)	39,231 (7.7)	50,514 (4.9)	36,130 (3.3)	230,910 (0.2)	(otalizapilie)
Pharma	75 608 (7 9)	53 110 (6 1)	57 841 (7 5)	27 228 (3 7)	24 235 (3 5)	238 023 <b>55</b> 0)	(fluvovamine)
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Page 17 of 21				I	3MJ Open		bmjopei d by cop	
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4 5 6 7							196 on 21 Jur Er uding for use	Reflex (mirtazapine) Sycrest (asenapine) Aripiprazole (generic aripiprazole)
8 9 10 11 12	Mochida Pharmaceutical	35,768 (3.7)	29,405 (3.4)	31,597 (4.1)	41,378 (5.6)	17,209 (2.5)	srelated to 2024. D 155,0000 155,0000 155,0000 155,0000 155,0000 155,0000 155,0000 155,0000 155,0000 155,0000 155,0000 155,00000 155,0000000000	Lexapro (escitalopram) Tecipul (setiptiline) Zolpidem (generic zolpidem)
13       568         14       15         16       17         18       19         20       21         21       22         23       24         25       26         27       28         29       30         31       32         33       34         35       36         37       38         39       40         41       42							vnloaded from http://bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique t Superieur (ABES) . text and data mining, Al training, and similar technologies.	
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# Table 3. Payments by author categories in the bipolar disorder and major depressive disorder clinical practice guidelines

Variables	Guideline disease category				
	Bipolar disorder	Major depressive disorder			
Number of all authors, N	33	42			
Role of guideline authors, n (%)					
Writing authors <sup>a</sup>	4 (12.1)	14 (33.3)			
Supporting authors <sup>b</sup>	5 (15.2)	12 (28.6)			
Guideline development committee authors <sup>c</sup>	24 (72.7)	16 (38.1)			
Payments by author roles					
Total payment amounts, \$					
Writing authors <sup>a</sup>	532,717	1,659,595			
Supporting authors <sup>b</sup>	12,140	930,986			
Guideline development committee authors <sup>c</sup>	2,548,718	1,448,508			
Number of authors receiving payments by author roles, n (%)					
Writing authors <sup>a</sup>	4 (100)	14 (100)			
Supporting authors <sup>b</sup>	4 (80.0)	10 (83.3)			
Guideline development committee authors <sup>c</sup>	22 (91.7)	16 (100)			
Median payment amounts per author, \$	2.				
Writing authors <sup>a</sup>	135,867 (78,553 – 187,806)	87,610 (16,945 – 111,567)			
Supporting authors <sup>b</sup>	1,788 (715 – 1,845)	60,120 (1,573 – 142,732)			
Guideline development committee authors <sup>c</sup>	34,569 (11,588 – 184,068)	34,569 (14,331 – 149,624)			

<sup>572</sup> <sup>a</sup> Writing authors directly contributed to the creation of guidelines.

<sup>573</sup> <sup>b</sup> Supporting authors could have contributed to identifying relevant evidence and <sup>574</sup> performing literature reviews.

<sup>c</sup> Guideline development committee authors were not directly involved in the creation of the guidelines, but critically reviewed the contents and recommendations of the initial guideline draft and revised them if necessary.

Variables	Bipolar disorder (N=4)	Major depressive disorder (N=14)
Number of authors self-reporting		
conflicts of interest by category		
Speaking compensation	4 (100)	11 (78.6)
Scholarship donation	3 (75.0)	6 (42.9)
Consulting payments	0 (0)	4 (28.6)
Collaborative research funds	1 (25.0)	2 (14.3)
Advisory board	2 (50.0)	1 (7.1)
Contracted research funds	1 (25.0)	0 (0)
Any category	4 (100)	12 (85.7)
Industry-reported payments to		
authors		
Number of writing authors		
receiving payments from 2016		
to 2020 by payment category,		
n (%)		
Lecturing payments	4 (100)	14 (100)
Consulting payments	4 (100)	12 (85.7)
Writing payments	4 (100)	9 (64.3)
Any payment category	4 (100)	14 (100)
Total payment amounts to		
writing authors from 2016 to		
2020, \$		
Lecturing payments	399,929	1,073,071
Consulting payments	101,805	430,660
Writing payments	30,983	155,864

d by copyright, including fo bmjopen-2024-08639<mark>6</mark> STROBE Statement-checklist of items that should be included in reports of observational studies **9** Page **Relevant text from** Item No. Recommendation N NO. manuscript June 2024. Downloaded Enseignement Superie Uses related to text and (a) Indicate the study's design with a commonly used term in the title or the abstract Title and abstract 1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found Introduction Explain the scientific background and rationale for the investigation being reported Background/rationale 2 State specific objectives, including any prespecified hypotheses 3 Objectives Methods ur (A data Present key elements of study design early in the paper Study design 4 t http://bmjopen.bmj.com/ on BES). ㎡ning, 邓 training, and simil 5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, Setting follow-up, and data collection (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of All training, and similar technologies: Participants 6 participants. Describe methods of follow-up Case-control study-Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants June 11, 2025 (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case at Age Variables 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable nce For each variable of interest, give sources of data and details of methods of assessment Data sources/ 8\* 4 (measurement). Describe comparability of assessment methods if there is more than one group Bib measurement 9 Describe any efforts to address potential sources of bias n/a 👼 Bias raphique Explain how the study size was arrived at 3 Study size 10 Continued on next page del For peer review only - http://bmjopen.bmj.com/site/about/quidelines.xhtml

**BMJ Open** 

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	24-08639 ht, Thclue
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	б ог
methods		(b) Describe any methods used to examine subgroups and interactions	10 21
		(c) Explain how missing data were addressed	
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	sstre 2
		Case-control study-If applicable, explain how matching of cases and controls was addressed	elate
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	- Down
		(e) Describe any sensitivity analyses	extunition
Results			and d
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	ar (Antala)
		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	, <u>→</u> /a <u>∃</u>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	open.b
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg. average and total amount)	and of
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category or summary measures of exposure	ilar Ju
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and if applicable confounder-adjusted estimates and their precision	111, :
ivium results	10	(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	10 gi
		included	s. at /
		(b) Report category boundaries when continuous variables were categorized	5-6 <b>9</b>
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	n/a ce
		period	Bit
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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			clud
Key results	18	Summarise key results with reference to study objectives	ing on
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	för 21
		both direction and magnitude of any potential bias	use En
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	s fei
		analyses, results from similar studies, and other relevant evidence	Jate
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other informat	ion		o tex
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	
-		original study on which the present article is based	nd d
			ata
*Give information	on sep	arately for cases and controls in case-control studies and, if applicable, for exposed and unexposed group	$\mathbf{p}_{\mathbf{r}}$ in $\mathbf{c}_{\mathbf{r}}$ and cross-sectional studies.
<b>Note:</b> An Explar	nation	and Elaboration article discusses each checklist item and gives methodological background and publishe	ed examples of transparent reporting The STROBE
Note: An Explan	nation	and Elaboration article discusses each checklist item and gives methodological background and publishe	ed examples of transparent reporting. The STROBE
checklist is best	used i	n conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosme	edicine .ora/, Annals of Internal Medicine at
http://www.anna	ls.org	/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at v	www.jetroge-statement.org.
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### Cross-sectional analysis of pharmaceutical industry payments to authors of clinical practice guidelines for bipolar disorder and major depressive disorder in Japan

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-086396.R2
Article Type:	Original research
Date Submitted by the Author:	31-May-2024
Complete List of Authors:	Murayama, Anju; Tohoku University School of Medicine; Icahn School of Medicine at Mount Sinai, Department of Population Health Science and Policy Kugo, Hinari; Tohoku University School of Medicine Senoo, Yuki; Higashi Totsuka Kinen Byoin
<b>Primary Subject Heading</b> :	Ethics
Secondary Subject Heading:	Evidence based practice, Ethics, Health policy, Mental health
Keywords:	MEDICAL ETHICS, ETHICS (see Medical Ethics), Depression & mood disorders < PSYCHIATRY, PSYCHIATRY, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT





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Title: Cross-sectional analysis of pharmaceutical industry payments to authors of clinical practice guidelines for bipolar disorder and major depressive disorder in Japan Authors: Anju Murayama<sup>1,2\*</sup>; Hinari Kugo<sup>1</sup>; Yuki Senoo, MD<sup>3</sup> **Affiliations:** <sup>1</sup>Tohoku University School of Medicine, Sendai, Miyagi, Japan <sup>2</sup> Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York City, NY, USA <sup>3</sup> Higashi Totsuka Memorial Hospital, Yokohama, Kanagawa, Japan \* Corresponding authors Correspondence Anju Murayama Tohoku University School of Medicine, 2-1 Seiryo-machi, Aoba ward, Sendai City, Miyagi, 980-0872, Japan Telephone: +81-22-717-8006 Email address: anju.murayama.s8@dc.tohoku.ac.jp 24 19 25 20 **Keywords:** Conflicts of interest, pharmaceutical companies, clinical practice guideline, health policy, evidence-based medicine, ethics, depression, bipolar disorder elezoni 

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#### <sup>3</sup> 24 Abstract <sup>4</sup> 25 Objective

# <sup>4</sup> 25 **Objective**

Clinical practice guidelines (CPGs) are essential for standardizing patient care based on evidence based medicine. However, the presence of financial conflicts of interest (COIs) among CPG authors
 can undermine their credibility. This study aimed to examine the extent and size of COIs among
 authors of psychiatry CPGs in Japan.

## 31 Methods

This cross-sectional analysis of disclosed payments from pharmaceutical companies assesses the prevalence and magnitude of personal payments for lecturing, consulting, and writing to CPGs for bipolar disorder and major depressive disorder in Japan between 2016 and 2020.

## **Results**

This study found that 93.3% of authors received payments over a five-year period, with total payments exceeding \$4 million. The median payment per author was \$51,403 (interquartile range: \$9,982 – \$111,567), with a notable concentration of payments among a small number of authors, including the CPG chairperson. Despite these extensive financial relationships, only a fraction of authors disclosed their COIs in the CPGs. These large amounts of personal payments were made by pharmaceutical companies manufacturing new antidepressants and sleeping aids listed in the CPGs. 

## 44 Conclusions

This study found that more than 93% of authors of Japanese major depressive disorder and bipolar
disorder CPGs received considerable amounts of personal payments from the pharmaceutical
industry. The findings highlight deviations from international COI management standards and
suggest a need for more stringent COI policies for psychiatry CPGs in Japan.

## Strengths and limitations

- 51 This study utilized a publicly accessible database containing all payments to physicians for 52 lecturing, consulting, and writing disclosed by over 70 pharmaceutical companies in Japan.
  - All authors of the clinical guidelines for major depressive disorder and bipolar disorder published by the Japanese Society of Mood Disorders were included in this study.
  - The study was unable to encompass other types of payments to the guideline authors such as research, royalties, licensing fees, ownership interests, and other miscellaneous fees.
  - There might be payments to the guideline authors that are under-disclosed and/or undisclosed by the pharmaceutical companies.

# <sup>3</sup> 60 Introduction

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Clinical practice guidelines (CPGs) have been increasingly used as a tool to endorse evidence-based 61 5 medicine for healthcare professionals in their clinical practice.<sup>12</sup> CPGs aim to summarize the best 62 6 available evidence and often include recommendations for specific diagnosis and treatment of 63 7 specific diseases. Nevertheless, the integrity and recommendations of CPGs are frequently 64 8 9 65 compromised by conflicts of interest (COIs) between the guideline authors and the pharmaceutical 10 66 industry, spanning various medical specialties. In the field of psychiatry, there is documentation of 11 ghostwriting by pharmaceutical industry<sup>3</sup> and widespread financial COIs between CPG authors and 67 12 pharmaceutical companies.<sup>4-7</sup> Furthermore, studies showed that financial COIs are associated with a 68 13 69 propensity for CPGs to make recommendations favorable to the healthcare industry in general.<sup>48</sup> 14 This underscores the necessity for rigorous management of financial COIs among CPG authors, 70 15 particularly in psychiatry.<sup>6910</sup> A recent study demonstrated that 60% of panel members of the 71 16 17 72 Diagnostic and Statistical Manual of Mental Disorders (DSM-5), fifth edition, text revision published 18 73 by the American Psychiatry Association in 2022 received payments from the pharmaceutical 19 74 industry.<sup>11</sup> As the DSM-5 is widely used as a standard for psychiatric disorders' definitions and 20 symptom criteria, influencing treatment selection and approval of new drugs worldwide,<sup>11</sup> the 75 21 76 widespread financial COIs among the DSM-5 panel members are concerning. However, financial 22 COIs among psychiatry experts are not unique to international criteria and CPGs: they may also be 77 23 78 problematic among authors of regional or national CPGs, as these guidelines include specific 24 25 79 treatment recommendations that can influence the clinical practice of clinicians in each country or 26 80 region. 27 81

28 82 To enhance the transparency of financial relationships between healthcare professionals and 29 pharmaceutical companies, members of the Japan Pharmaceutical Manufacturers Association have 83 30 84 voluntarily disclosed their financial interactions with healthcare professionals and organizations.<sup>12</sup> 31 32 85 Subsequent research using this disclosed information has revealed that the vast majority of CPG 33 86 authors in Japan received personal payments during the CPG development across various medical 34 87 specialties.<sup>12-22</sup> However, these financial relationships between pharmaceutical companies and 35 88 Japanese CPG authors in psychiatry remain largely unexplored. Considering the patterns observed in 36 89 previous studies, we hypothesized that financial COIs are widespread among psychiatry CPG authors 37 90 in Japan. 38

## 40 92 Methods

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41 93 Study setting and participants

42 94 This cross-sectional analysis evaluated the extent and prevalence of financial interactions between 43 95 pharmaceutical companies and authors of CPGs for major depressive disorder and bipolar disorder in 44 Japan. Mood disorders, including bipolar disorder and major depressive disorder, are the most 96 45 97 prevalent mental disorders in Japan. According to surveys conducted by the Japanese Ministry of 46 47 98 Health, Labor, and Welfare, the number of patients with mood disorders has steadily increased over 48 99 the past two decades, from 0.4 million in 1999 to 1.7 million in 2020.<sup>23</sup> The Japanese Society of 49<sub>100</sub> Mood Disorders is responsible for the development of the sole CPGs for these conditions, namely <sup>50</sup>101 Treatment Guideline I: Bipolar Disorder<sup>24</sup> and Treatment Guideline II: Major Depressive Disorder.<sup>25</sup> 51 52<sup>102</sup> At the time of this study, the most recent versions were published in June 2020 and July 2019, **53**103 respectively. 54104

## 55105 Data collection

The Japan Pharmaceutical Manufacturers Association, representing over 70 major pharmaceutical
 companies, mandates the disclosure of payments for lectures, consultancy, and writing to healthcare
 professionals, listing the recipients' names on company websites since 2013.<sup>26-28</sup> Despite annual

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109 updates and removal of previous years' data by these companies, the Medical Governance Research 110 Institute has independently collected and disclosed this payment data on its public online database

5 111 from 2016 to 2020, detailing individual physician and company names.<sup>29</sup> 6

7 112 8 113 Information about payments to CPG authors was extracted as follows. First, a list of the names of all 9 114 CPG authors was created and saved as a CSV file. We then searched for their names in the payments 10115 database and extracted speaking, consulting, and writing payments to physicians whose names 11 11 12 11 13 117 matched the CPG authors' names from the database using Python programming code. After extracting the relevant payment information, a manual review was performed to identify and remove 14118 any payments made to physicians whose names were similar to those of the CPG authors but who were actually different individuals, as we previously noted.<sup>30-33</sup> Finally, we randomly selected five 15119 16120 CPG authors (representing 11.1% of all authors) and manually searched the authors' names in the 17121 payments database to ensure that the payment data extracted using Python were accurate and <sup>18</sup>122 complete.

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20<sup>123</sup> 21<sup>124</sup> As the pharmaceutical companies have not individually disclosed other categories of non-research 22125 payments such as travel and accommodation fees, food and beverage fees, royalties and licensing fees, and ownership interests, this study incorporated all personal payments for lectures, consultancy, 23126 24127 and writing from pharmaceutical companies to the CPG authors from 2016 to 2020, following the

25128 approach of prior studies.<sup>30 34-36</sup>

# 26<sub>129</sub> 27<sub>130</sub> 28<sub>121</sub> Data analysis

- 28 29<sup>131</sup> The study calculated the proportion of CPG authors receiving personal payments and assessed per-
- 30132 author payment amounts, including median, interquartile range, mean, and standard deviation.
- 31133 We performed a sensitivity analysis examining personal payments to the CPG authors from 2016 to 32134 2019, to evaluate financial relationships between the CPG authors and pharmaceutical companies
- 33135 before the CPG publication.
- <sup>34</sup>136 35 Additionally, we also calculated the proportion of authors receiving payments, total payment 35 36<sup>137</sup> amounts, and median payment amounts by the roles of CPG authors.
- 37<sup>138</sup> Payments were converted from Japanese yen to US dollars using the 2020 average monthly exchange
- 38139 rate of 106.8 yen per \$1. Data extraction and analyses were executed using Python 3.9.12 (Python
- **39**140 Software Foundation, Beaverton, OR, USA), Microsoft Excel, version 16.0 (Microsoft Corp.,
- 40141 Redmond, WA, USA), and Stata version 17.0 (StataCorp, College Station, TX, USA). 41142

# Ethical clearance

42 143 43 144 44 144 As a retrospective analysis of publicly available data, this study was classified as non-human

- **4 4 4 5 1 1 4 5** subjects research and did not require institutional review board approval in accordance with the **46**146 Japanese Ministry of Health, Labor, and Welfare's Ethical Guidelines for Medical and Health
- 47147 Research Involving Human Subjects. This study was reported according to the Strengthening the
- 48148 Reporting of Observational Studies in Epidemiology (STROBE) guidelines.
- **49**149
- 50 51 51 Patient and public involvement
- 51 52<sup>151</sup> No patients were involved in the preparation of this manuscript or the research project. **53**152

#### 54153 Results

55154 The study included 33 authors for the bipolar disorder CPG and 42 for the major depressive disorder 56155 CPG. Of these authors, 30 individual physicians contributed to both CPGs. Consequently, a total of <sup>57</sup>156 45 unique CPG authors were analyzed in this study.

3 158 Of all 45 authors, 42 (93.3%) received personal payments for lectures, consulting, and writing from 4 159 pharmaceutical companies between 2016 and 2020 (Table 1). The total amount of personal payments 5 160 received by the 55 pharmaceutical companies over the course of the study period was \$4,041,648. 6 The median payment per author was 51,403 (IQR: 9,982 - 111,567), and the mean payment was 161 7 8 162 \$89,814 (SD: \$111,760), indicating a skewed distribution where a few authors received 9 163 disproportionately high payments. Notably, 15 authors (33.3%) received in excess of \$100,000 over 10164 the five-year period. The majority of payments, constituting 65.8% (\$2.7 million) of the total, were <sup>11</sup>165 12 for lecturing fees, with consulting and writing compensations accounting for 25.8% (\$1.0 million) 12 13<sup>166</sup> and 8.3% (\$337,255) in total, respectively. All two chairs of each CPG development committee 14<sup>167</sup> received personal payments from pharmaceutical companies totaling \$506,108 (the highest total) for 15168 the chair of the bipolar disorder CPG development committee and \$97,288 for the chair of the major 16169 depressive disorder CPG development committee over the five-year period. 17170

<sup>18</sup>171 Annual analysis revealed a decline in total payments to CPG authors from \$959,289 in 2016 to 19<sub>172</sub> 20<sub>173</sub> 21<sup>173</sup> \$697,170 in 2020 (Table 1). Correspondingly, the median annual payment per author decreased from \$11,992 (IQR: \$1,877 - \$24,498) in 2016 to \$2,702 (IQR: \$120 - \$22,968) in 2020. The proportion <sup>21</sup> 22<sup>174</sup> of authors receiving payments also fell from 91.1% in 2017 to 75.6% in 2020, yet a majority still 23175 received at least one personal payment annually. The sensitivity analysis of payments to the CPG 24176 authors from 2016 to 2019 showed that 42 (93.2%) authors received at least one payment from 25177 pharmaceutical companies. The total amounts of personal payments were \$3,344,478 for the four-26<sub>178</sub> 27<sub>179</sub> 28<sub>180</sub> 29<sup>180</sup> year period. Median amounts of four-year payments were \$44,688 (IQR: \$9,325 - \$93,393) per author.

Payments from the top 5 and 10 pharmaceutical companies constituted 53.3% (\$2.2 million) and
83.1% (\$3.4 million) of the total payments from 2016 to 2020, respectively (Table 2). Sumitomo
Pharma made the largest total amounts of personal payments amounting to \$695,031 (17.2%),
followed by Eisai (10.1%, \$408,323), MSD (8.8%, \$357,526), Otsuka Pharmaceutical (8.8%,
\$354,638), and Takeda Pharmaceutical (8.3%, \$337,370). Among these companies, MSD, Pfizer
Japan, and Meiji Seika notably reduced their personal payments from 2016 to 2020, whereas Eisai
increased its payments from \$45,779 in 2016 to \$151,856 in 2020.

The two CPGs included three categories of author roles: writing authors, who were primarily responsible for developing the CPGs and making recommendations; supporting authors, who may have contributed to the CPG development in a limited capacity, such as identifying relevant evidence, performing literature reviews, and making recommendations for specific situations; and guideline development committee authors, who did not directly contribute to the creation of CPGs and recommendations but critically reviewed the initial CPG drafts and revised the drafts and recommendations. The CPGs explicitly indicated that all of these authors were involved in the formulation of recommendations.

<sup>48</sup>197 Of three categories of author roles, all writing authors for both CPGs received personal payments
<sup>49</sup>198 from pharmaceutical companies between 2016 and 2020 (Table 3), while lower proportion of
<sup>50</sup>199 supporting authors received payments than those for writing authors and guideline development
<sup>51</sup>200 committee authors in both CPGs. Median payment amounts were the highest for writing authors
<sup>53</sup>201 (\$135,867 (IQR: \$78,553 - \$187,806) for the bipolar disorder CPG and \$87,610 (IQR: \$16,945 - \$111,567) for the major depressive disorder CPG).

<sup>56</sup>204 Disclosure of financial COIs in the CPGs was self-reported only by writing authors. There were no
 <sup>57</sup>205 COI declaration statements for other types of authors. All authors (100%, 4 out of 4) of the bipolar
 <sup>58</sup>206 disorder CPG and 85.7% (12 out of 14) of the major depressive disorder CPG authors declared

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3 207 financial COIs with pharmaceutical companies. Table 4 presents the types of financial COIs self-4 208 reported by the CPG authors within each respective guideline. Among the six categories extracted

5 209 from the disclosure statements in the CPGs, compensation for lecturing was the most frequently 6

210 declared (100% for the bipolar disorder CPG authors and 78.6% for the major depressive disorder 7

8 211 CPG authors). This was followed by scholarship donations and participation in pharmaceutical

9 212 company advisory boards. Although there were discrepancies in the number of writing authors 10213

- receiving payments between industry-sponsored payment data and authors' self-declared COI statements by payment/declaration category (Table 4), the lack of a specified declaration period
- 11213 12213 12214 12215 13215 14216 15217 precluded the assessment of the accuracy of each CPG author's self-reported COI statements against
- the payment data reported by the pharmaceutical companies.

#### 16218 Discussion

17219 This cross-sectional analysis of publicly disclosed payment data from pharmaceutical companies 18220 19221 20221 21222 22223 provides a detailed examination of the extent and fraction of financial COIs among authors of the Japanese Society of Mood Disorders' Treatment Guideline I: Bipolar Disorder<sup>24</sup> and Treatment Guideline II: Major Depressive Disorder.<sup>25</sup> These CPGs are considered by physicians the authoritative and trustworthy sources for the treatment of bipolar disorder and major depressive 23224 disorder in Japan.<sup>37</sup> To the best of our knowledge, this is the first in-depth study to analyze the 24225 financial relationships between psychiatry CPG authors and pharmaceutical companies in Japan 25226 using pharmaceutical industry-disclosed data. The findings reveal that a large majority (93.3%) of 26227 27228 28228 29229 30230 CPG authors received personal payments for lecturing, consulting, and writing, with a total sum of \$4.0 million between 2016 and 2020. The median payment per author was \$51,403, with a minority, including the CPG chairperson, receiving substantial sums. Nearly all authors involved in writing the CPGs self-reported financial COIs with pharmaceutical companies. Notably, the bulk of personal 31231 payments to CPG authors came from companies that manufacture antidepressants and sleeping pills 32232 in Japan. However, other CPG authors did not publicly disclose their financial COIs with these **33**233 companies. When compared to previous studies and international COI policies for CPG authors, 34234 35235 36235 37236 38237 these findings raise concerns for physicians, patients, policymakers, and other stakeholders within and beyond Japan.

The study highlights that over 93% of the authors of CPGs for bipolar disorder and major depressive 39238 disorder had financial relationships with pharmaceutical industry. Given the publication dates of the 40239 CPGs between 2019 and 2020, these financial relationships likely occurred during the development 41240 42241 43242 44242 45243 of the CPGs. This high percentage of authors receiving personal payments aligns with findings from other specialties within Japan,<sup>12-15 17-22 31 33 38-42</sup> where the proportion of CPG authors with personal payments ranged from 66.0% in obstetrics and gynecology<sup>42</sup> to 96.3% in otolaryngology.

**46**244 In contrast, research from other developed countries, such as the United States, reports lower 47245 proportions of CPG authors with financial COIs. For instance, 67% of authors for the DSM-5 mood 48246 disorders section disclosed financial COIs with the healthcare industry.<sup>9</sup> Additionally, a study by 49247 50248 51248 52249 53250 Cosgrove et al. found that only 18% of major depressive disorder CPG authors across eight countries had financial COIs with pharmaceutical companies.<sup>410</sup> In Canada, half of the authors of the CPG for depressive disorder developed by the Canadian Network for Mood and Anxiety Treatments reported financial COIs with the healthcare industry.<sup>43</sup> Other specialties in the United States also showed 54251 lower percentages, with 53% of gastroenterology CPG authors<sup>44</sup> and 59.3% of urology CPG authors 55252 receiving personal and/or research payments.<sup>45</sup> Moreover, Mooghali et al. reported that 73.7% of 56253 physician CPG authors in the United States received personal and/or research payments from 57<sub>254</sub> healthcare companies.<sup>46</sup> The higher proportion of CPG authors receiving payments in Japan can be 58<sup>254</sup> 59<sup>255</sup> attributed to the fact that most professional medical societies in Japan have implemented less

2 3 256 transparent COI policies. This is in line with our previous studies reporting on the matter.<sup>18 20</sup> 4 257 5 Furthermore, this investigation revealed that a select group of CPG authors, including the 258 6 259 chairperson, received substantial personal payments from pharmaceutical companies. Only authors 7 8 260 involved in writing the CPGs were mandated to declare their financial COIs, while other contributors 9 261 did not publicly disclose any financial COIs with these companies. These results indicate that authors 10262 of Japanese CPGs for bipolar disorder and major depressive disorder clearly violate international 11263 12264 13264 14265 15266 COI policies on CPG development in several respects. The U.S. National Academy of Medicine's 2011 report and the Guidelines International Network advocate for a majority of CPG authors to be free from financial COIs.<sup>12</sup> These policies also stipulate that the chairperson of CPG development should not hold any COIs.<sup>12</sup> The Guideline Panel Review Working Group's criteria for red flags, as 16267 published in the British Medical Journal in 2013, indicate that financial COIs held by a CPG 17268 chairperson and multiple authors are significant concerns for the trustworthiness of the CPGs.<sup>47</sup> The 18269 prevalence of COIs exceeding 93% in this study is not a marginal discrepancy but a significant 19270 20271 21271 22272 deviation from these standards, casting doubt on the objectivity and reliability of the guidelines. Moreover, the study revealed that substantial payments were made by pharmaceutical companies 23273 marketing new antidepressants and sleep aids in Japan. For example, Sumitomo Pharma, the top **24**274 paver, produces lurasidone (brand name: Latuda), which was approved for bipolar disorder and 25275 schizophrenia in 2020, and has been co-marketing venlafaxine hydrochloride (brand name: Effexor) 26273 26276 27277 28277 29278 30279 with Pfizer Japan since 2018. MSD, another major payer, produces suvorexant (brand name: Belsomra), the world's first orexin receptor antagonist used for insomnia. Otsuka Pharmaceutical is known as one of the major manufacturers of atypical antipsychotics, such as aripiprazole (brand name: Abilify) and brexpiprazole (brand name: Rexulti), which are the most widely prescribed 31280 atypical antipsychotics in Japan.<sup>48</sup> Despite these financial ties between CPG authors and 32281 pharmaceutical companies manufacturing relevant drugs, the Japanese Society of Mood Disorders actively endorses adherence to these CPGs.<sup>49 50</sup> Given that the CPGs for bipolar disorder and major 33282 34283 35284 36284 37285 38286 depressive disorder include pharmacotherapy recommendations that include medications from these companies, it is imperative that the close financial ties between CPG authors and the pharmaceutical industry be addressed. We strongly recommend the Japanese Society of Mood Disorders to enforce more transparent and stringent COI management strategies in the CPG development process for 39287 bipolar disorder and major depressive disorder to ensure the integrity and credibility of these 40288 guidelines. 41289

## Limitations

42<sub>290</sub> 43<sub>291</sub> 44<sup>291</sup> 45<sup>292</sup> This study is subject to several limitations. Primarily, the study focus on CPGs for bipolar disorder and major depressive disorder in Japan would limit the generalizability of our findings to other 46293 medical fields or countries. Additionally, the payment data were derived from a secondary source, 47294 the Medical Governance Research Institute's database, which contains payment information from 48295 member companies of the Japan Pharmaceutical Manufacturers Association for the period 2016-49<sub>296</sub> 2020.<sup>27 51</sup> Absent legal mandates for precise payment disclosures in Japan, the potential for 50297 51297 52298 53299 inaccuracies or underreporting in the database cannot be discounted. Furthermore, the voluntary nature of these disclosures means that financial interactions between CPG authors and non-disclosing pharmaceutical entities may remain undetected. Nevertheless, given that the member companies 54300 account for 80% of the market share for drugs and medical products in Japan,<sup>52</sup> the impact of 55301 financial relationships between the CPG authors and uncovered companies would be minimized. 56302

57303 **Conclusions** 

58<sup>303</sup> 59<sup>304</sup> More than 93% of the authors of the Treatment Guidelines for Bipolar Disorder and Major

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## Author contribution:

<sup>11</sup>312 12313 13<sup>214</sup> A.M. contributed to data collection, resource, software, formal analysis, visualization, supervision, 14<sup>314</sup> and study administration. All authors (A.M., H.K., and Y.S.) contributed to study conceptualization, 15315 methodology, writing the original draft, and reviewing the draft.

Depressive Disorder developed by the Japanese Society of Mood Disorders received personal

payments for the reimbursement of their lecturing, consulting, and writing activities from the

were only declared by the limited group of CPG authors. Further transparent and rigorous COI

management strategies must be warranted in the Japanese Society of Mood Disorders.

pharmaceutical companies manufacturing related drugs. The total amounts of personal payments to

the CPG authors were more than \$4.0 million over the five years. Nevertheless, the financial COIs

#### 16316 17317 **Conflicts of interest:**

18318 The authors declare that there were no conflicts of interest for this study. 19<sub>319</sub>

## **Funding sources:**

20 21 21 22 320 22 321 The authors declare that there were no funding sources for this study. 23322

#### 24323 **IRB Statement**

25324 As this study was a retrospective analysis of publicly available data and met the definition of non-26325 27326 28326 29327 30328 human subjects research, no institutional board review and approval were required in accordance with the Japanese Ministry of Health, Labor, and Welfare's Ethical Guidelines for Medical and Health Research Involving Human Subjects. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

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#### 32330 Declaration of generative AI in scientific writing

33331 During the preparation of this work, the authors used ChatGPT version 4.0 solely for the purpose of 34<sub>332</sub> 35<sub>333</sub> 36<sup>333</sup> 37<sup>334</sup> identifying and correcting grammatical and spelling errors, and we did not use it for the creation of any intellectual parts of the manuscript. After using this tool, the authors carefully reviewed and edited the content as needed and take full responsibility for the content of the publication.

#### 38335 **39**336 Data availability statement:

40337 All data used in this study is available from Yen For Docs database run by Medical Governance 41338 Research Institute (https://yenfordocs.jp/) and each pharmaceutical companies belonging to the Japan 42<sub>339</sub> 43<sub>340</sub> 45<sup>341</sup> Pharmaceutical Manufacturers Association. Due to privacy protection, payment data of individual CPG authors will be available from the corresponding author upon reasonable request.

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47343 We appreciate Ms. Megumi Aizawa, MSE, for her dedicated support of this research, including 48344 development of programming codes for data collection. She was not compensated for her **49**345 contributions. During the preparation of this work, the authors used ChatGPT version 4.0 solely for 50<sub>346</sub> 51<sup>346</sup> 52<sup>347</sup> the purpose of identifying and correcting grammatical and spelling errors, and we did not use it for the creation of any intellectual parts of the manuscript. After using this tool, the authors carefully 53348 reviewed and edited the content as needed and take full responsibility for the content of the 54349 publication. 55350

#### 56351 References

57352 1. Schunemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: Principles for Disclosure of 58353 Interests and Management of Conflicts in Guidelines. Ann Intern Med 2015;163(7):548-53. doi: 10.7326/M14-

2 3 354 1885 [published Online First: 2015/10/06] 4 355 2. Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press 356 5 2011 6 357 3. Roehr B. Professor files complaint of scientific misconduct over allegation of ghostwriting. BMJ 2011;343:d4458. doi: 7 358 10.1136/bmj.d4458 [published Online First: 20110713] 359 8 4. Cosgrove L, Shaughnessy AF, Peters SM, et al. Conflicts of Interest and the Presence of Methodologists on Guideline 9 360 Development Panels: A Cross-Sectional Study of Clinical Practice Guidelines for Major Depressive Disorder. 10361 Psychother Psychosom 2017;86(3):168-70. doi: 10.1159/000458727 [published Online First: 20170511] 11362 5. Cosgrove L, Krimsky S, Vijayaraghavan M, Schneider L. Financial ties between DSM-IV panel members and the 12363 pharmaceutical industry. Psychother Psychosom 2006;75(3):154-60. doi: 10.1159/000091772 [published Online 13364 First: 2006/04/26] 14<sup>365</sup> 6. Cosgrove L, Bursztajn HJ, Krimsky S. Developing unbiased diagnostic and treatment guidelines in psychiatry. N Engl 15 366 16 367 17 368 17 369 18 369 19 370 19 371 20 372 21 373 J Med 2009;360(19):2035-6. doi: 10.1056/NEJMc0810237 7. Cosgrove L. Bursztain HJ, Krimsky S, et al. Conflicts of interest and disclosure in the American Psychiatric Association's Clinical Practice Guidelines. Psychother Psychosom 2009;78(4):228-32. doi: 10.1159/000214444 [published Online First: 20090428] 8. Nejstgaard CH, Bero L, Hrobjartsson A, et al. Association between conflicts of interest and favourable recommendations in clinical guidelines, advisory committee reports, opinion pieces, and narrative reviews: systematic review. BMJ 2020;371:m4234. doi: 10.1136/bmj.m4234 [published Online First: 20201209] 9. Cosgrove L, Krimsky S. A comparison of DSM-IV and DSM-5 panel members' financial associations with industry: a 22<sub>374</sub> pernicious problem persists. PLoS Med 2012;9(3):e1001190. doi: 10.1371/journal.pmed.1001190 [published 23<sub>375</sub> Online First: 20120313] **24**376 10. Cosgrove L, Krimsky S, Wheeler EE, et al. Conflict of Interest Policies and Industry Relationships of Guideline 25377 Development Group Members: A Cross-Sectional Study of Clinical Practice Guidelines for Depression. Account 26378 Res 2017;24(2):99-115. doi: 10.1080/08989621.2016.1251319 [published Online First: 20161024] 27379 11. Davis LC, Diianni AT, Drumheller SR, et al. Undisclosed financial conflicts of interest in DSM-5-TR: cross sectional 28380 analysis. BMJ 2024;384:e076902. doi: 10.1136/bmj-2023-076902 [published Online First: 20240110] 29381 12. Murayama A, Ozaki A, Saito H, et al. Pharmaceutical company payments to dermatology Clinical Practice Guideline 30382 authors in Japan. PLoS One 2020;15(10):e0239610. doi: 10.1371/journal.pone.0239610 [published Online First: 31383 20201013] 32384 13. Kida F, Murayama A, Saito H, et al. Pharmaceutical company payments to authors of the Japanese Clinical Practice 33385 Guidelines for Hepatitis C treatment. Liver Int 2021;41(3):464-69. doi: 10.1111/liv.14761 [published Online 34386 First: 20201223] 35387 14. Harada K, Ozaki A, Saito H, et al. Financial payments made by pharmaceutical companies to the authors of Japanese 36388 hematology clinical practice guidelines between 2016 and 2017. Health Policy 2021;125(3):320-26. doi: 36388 37389 38390 39391 40392 41393 41394 42395 43396 44397 10.1016/j.healthpol.2020.12.005 [published Online First: 20201217] 15. Hashimoto T, Murayama A, Mamada H, et al. Evaluation of financial conflicts of interest and drug statements in the coronavirus disease 2019 clinical practice guideline in Japan. Clin Microbiol Infect 2022;28(3):460-62. doi: 10.1016/j.cmi.2021.11.019 [published Online First: 20211124] 16. Kamamoto S, Murayama A, Kusumi E, et al. Evaluation of financial relationships between Japanese certified pediatric hematologist/oncologists and pharmaceutical companies: a cross-sectional analysis of personal payments from pharmaceutical companies between 2016 and 2019. Pediatr Blood Cancer 2022;69(10):e29891. 44397 doi: 10.1002/pbc.29891 [published Online First: 20220810] 17. Murayama A, Kida F, Ozaki A, et al. Financial and Intellectual Conflicts of Interest Among Japanese Clinical 45398 Practice Guidelines Authors for Allergic Rhinitis. Otolaryngol Head Neck Surg 2022;166(5):869-76. doi: 46399 10.1177/01945998211034724 [published Online First: 20210817] 47400 18. Murayama A, Yamada K, Yoshida M, et al. Evaluation of Conflicts of Interest among Participants of the Japanese 48401 Nephrology Clinical Practice Guideline. Clin J Am Soc Nephrol 2022;17(6):819-26. doi: 49402 10.2215/CJN.14661121 [published Online First: 2022/05/28] 50403 19. Mamada H, Murayama A, Kamamoto S, et al. Evaluation of Financial and Nonfinancial Conflicts of Interest and 51404 Quality of Evidence Underlying Psoriatic Arthritis Clinical Practice Guidelines: Analysis of Personal Payments 52405 From Pharmaceutical Companies and Authors' Self-Citation Rate in Japan and the United States. Arthritis Care 53406 *Res (Hoboken)* 2023;75(6):1278-86. doi: 10.1002/acr.25032 [published Online First: 20230114] 54407 20. Murayama A, Kamamoto S, Murata N, et al. Evaluation of financial conflicts of interest and quality of evidence in Japanese gastroenterology clinical practice guidelines. J Gastroenterol Hepatol 2023;38(4):565-73. doi: 55408 56409 10.1111/jgh.16089 [published Online First: 20221229] 57410 21. Murayama A. Financial Conflicts of Interest Among the Authors of the Clinical Practice Guidelines for Rheumatoid 58411 Arthritis in Japan. Cureus 2023;15(10):e46650. doi: 10.7759/cureus.46650 [published Online First: 20231007] **59**412 22. Yamamoto K, Murayama A, Ozaki A, et al. Financial conflicts of interest between pharmaceutical companies and the 60 9

1	
2	
3 413	authors of urology clinical practice guidelines in Japan. Int Urogynecol J 2021;32(2):443-51. doi:
4 414 5 415	10.100//s00192-020-0454/-3 [published Online First: 20201105]
6 416	from: https://www.mblw.go.ip/toukei/saikin/hw/kania/20/index.html.accessed May 2 2024
7 417	24 Japanese Society of Mood Disorders. Treatment Guideline I: Bipolar Disorder Online: Japanese Society of Mood
8 418	Disorders; 2020 [updated June 16, 2020. 4th edition: [Available from:
<b>9</b> 419	https://www.secretariat.ne.jp/jsmd/iinkai/katsudou/data/guideline_sokyoku2020.pdf accessed October 20 2023.
10420	25. Japanese Society of Mood Disorders. Treatment Guideline II: Major Depressive Disorder Online: Japanese Society of
11421	Mood Disorders; 2019 [2nd edition: [Available from:
12422	https://www.secretariat.ne.jp/jsmd/iinkai/katsudou/data/20190724-02.pdf accessed October 20 2023.
13423	26. Ozaki A, Saito H, Senoo Y, et al. Overview and transparency of non-research payments to healthcare organizations
$14^{424}$	Health Policy 2020:124(7):727.35 doi: 10.1016/j.bealthpol.2020.03.011 [published Online First: 20200426]
$15^{-12.5}$	27 Muravama A. Kamamoto S. Saito H. et al. Characteristics and Distribution of Scholarship Donations From
16 427	Pharmaceutical Companies to Japanese Healthcare Institutions in 2017: A Cross-sectional Analysis.
428	International Journal of Health Policy and Management 2023;12(1) doi: ARTN 7621
10429	10.34172/ijhpm.2023.7621
20430	28. Murayama A, Kamamoto S, Saito H, et al. Pharmaceutical Payments to Japanese Board-Certified Infectious Disease
21 431	Specialists: A Four-Year Retrospective Analysis of Payments from 92 Pharmaceutical Companies between 2016
22 4 3 2	and 2019. Int J Environ Res Public Health 2022;19(12):7417. doi: $10.3390/1$ jerph19127417 [published Online
433 $23_{131}$	First: 20220616] 20. Medical Coversance Research Institute Van For Dees [Online database] 2022 [undated December 22, 2022
24435	Available from: https://venfordocs.in/ accessed March 6, 2024 2024
25436	30. Murayama A. Kamamoto S. Saito H. Ozaki A. Pharmaceutical payments to Japanese board-certified dermatologists:
26437	a 4-year retrospective analysis of personal payments from pharmaceutical companies between 2016 and 2019.
27438	Sci Rep 2023;13(1):7425. doi: 10.1038/s41598-023-34705-8 [published Online First: 20230508]
28439	31. Murayama A, Kamamoto S, Kawashima M, et al. Cross-sectional analysis of pharmaceutical payments to Japanese
29440	board-certified gastroenterologists between 2016 and 2019. BMJ Open 2023;13(4):e068237. doi:
30441	10.1136/bmjopen-2022-068237 [published Online First: 20230418]
31442 22/1/3	32. Murayama A, Senoo Y. Cross-sectional analysis of financial relationships between board certified allergists and the pharmaceutical industry in Japan. <i>BMC Mad Ethics</i> 2024;25(1):22. doi: 10.1186/s12010.024.01014.2
32443	[nublished Online First: 20240220]
34445	33. Murayama A. Shin N. Higuchi K. et al. Financial conflicts of interest between infectious diseases clinical practice
35446	guideline authors and the pharmaceutical industry in Japan. <i>Infect Dis (Lond)</i> 2024:1-5. doi:
36447	10.1080/23744235.2024.2309351 [published Online First: 20240201]
37448	34. Murayama A, Saito H, Kamamoto S, et al. Evaluation of non-research payments from pharmaceutical companies to
38449	urologists in Japan between 2016 and 2019. Int Urogynecol J 2023;34(6):1285-92. doi: 10.1007/s00192-023-
$39^{450}_{451}$	05463-y [published Online First: 20230201]
$40^{431}_{452}$	35. Kusumi E, Murayama A, Kamamoto S, et al. Pharmaceutical payments to Japanese certified nematologists: a retrospective analysis of personal payments from pharmaceutical companies between 2016 and 2019. <i>Blood</i>
$41_{453}^{+52}$	Cancer 12022:12(4):54 doi: 10.1038/s41408-022-00656-v [published Online First: 20220407]
42454	36. Murayama A. Hoshi M. Saito H. et al. Nature and Trends in Personal Payments Made to the Respiratory Physicians
<sup>43</sup> 455	by Pharmaceutical Companies in Japan between 2016 and 2019. <i>Respiration</i> 2022;101(12):1088-98. doi:
<sup>44</sup> 456	10.1159/000526576 [published Online First: 20221109]
<sup>45</sup> 457	37. Numata S, Nakataki M, Hasegawa N, et al. Improvements in the degree of understanding the treatment guidelines for
40458	schizophrenia and major depressive disorder in a nationwide dissemination and implementation study.
48460	Neuropsychopharmacol Rep 2021;41(2):199-206. doi: 10.1002/npr2.12173 [published Online First: 20210311]
49461	38. Murayama A, Kamamoto S, Shigeta H, et al. Undisclosed financial conflicts of interest with pharmaceutical
50462	Society Dis Esophagus 2022:35(10) doi: 10.1093/dote/doac056
51463	39 Murayama A Mamada H Shigeta H et al Financial Relationships Between Pharmaceutical Companies and
52464	Rheumatologists in Japan Between 2016 and 2019. J Clin Rheumatol 2023;29(3):118-25. doi:
<b>53</b> 465	10.1097/RHU.000000000001922 [published Online First: 20221207]
54466	40. Kamamoto S, Ozaki A, Murayama A. Assessment of Financial Relationships Between Otorhinolaryngologists and
55467	Pharmaceutical Companies in Japan Between 2016 and 2019. Cureus 2023;15(8):e43633. doi:
56468	10.7759/cureus.43633 [published Online First: 20230817]
5/409 50/70	41. IVIII ayama A, Alzawa IVI, Byreduy KK, et al. Conflicts of Interest Among Cardiology Clinical Practice Guideline Authors in Japan I Am Haart Assoc 2024:12(9):e024506 doi: 10.1161/jaba.124.024506 [published Online
50 <sup>±10</sup>	First: 20240412]
60	
50	10

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

- Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies
- 472 42. Murayama A, Miyazawa K, Kamamoto S, et al. Financial conflicts of interest in Japanese obstetrics and gynaecology 4 473 clinical practice guidelines. Clinical and Translational Discovery 2024;4(1):e273. doi: 10.1002/ctd2.273
- 5 474 43. Elder K, Turner KA, Cosgrove L, et al. Reporting of financial conflicts of interest by Canadian clinical practice 6 475 guideline producers: a descriptive study. CMAJ 2020;192(23):E617-E25. doi: 10.1503/cmaj.191737 [published 7 476 Online First: 2020/06/17]
- 8 477 44. Combs TR, Scott J, Jorski A, et al. Evaluation of Industry Relationships Among Authors of Clinical Practice 9 478 Guidelines in Gastroenterology. JAMA Intern Med 2018;178(12):1711-12. doi: 10479 10.1001/jamainternmed.2018.4730 [published Online First: 2018/11/02]
- 11480 45. Carlisle A, Bowers A, Wayant C, et al. Financial Conflicts of Interest Among Authors of Urology Clinical Practice 12481 Guidelines. Eur Urol 2018;74(3):348-54. doi: 10.1016/j.eururo.2018.04.023 [published Online First: 20180507]
- 13482 46. Mooghali M, Glick L, Ramachandran R, Ross JS. Financial conflicts of interest among US physician authors of 2020 14<sup>483</sup> clinical practice guidelines: a cross-sectional study. BMJ Open 2023;13(1):e069115. doi: 10.1136/bmjopen-2022-069115 [published Online First: 20230123]
  - 47. Lenzer J, Hoffman JR, Furberg CD, et al. Ensuring the integrity of clinical practice guidelines: a tool for protecting patients. BMJ 2013;347:f5535. doi: 10.1136/bmj.f5535 [published Online First: 20130917]
  - 48. Jiho. Yakuji Handbook 2021: Jiho 2021:522.

1 2 3

32502

- 15 484 16 485 17 486 17 486 18 487 18 487 19 489 20 490 21 491 49. Takaesu Y, Watanabe K, Numata S, et al. Improvement of psychiatrists' clinical knowledge of the treatment guidelines for schizophrenia and major depressive disorders using the 'Effectiveness of Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)' project: A nationwide dissemination, education, and evaluation study. Psychiatry Clin Neurosci 2019;73(10):642-48. doi: 10.1111/pcn.12911 22492 [published Online First: 20190822]
- 23<sub>493</sub> 50. Kodaka F, Ohi K, Yasuda Y, et al. Relationships Between Adherence to Guideline Recommendations for **24**494 Pharmacological Therapy Among Clinicians and Psychotic Symptoms in Patients With Schizophrenia. Int J 25495 Neuropsychopharmacol 2023;26(8):557-65. doi: 10.1093/ijnp/pyad037 26496
- 51. Ozieranski P, Saito H, Rickard E, et al. International comparison of pharmaceutical industry payment disclosures in 27497 the UK and Japan: implications for self-regulation, public regulation, and transparency. Global Health 28498 2023;19(1):14. doi: 10.1186/s12992-022-00902-9 [published Online First: 20230303]

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29499 52. Japan Pharmaceutical Manufacturers Association. Data Book 2023 2023 [Available from: 30500 https://www.jpma.or.jp/news room/issue/databook/en/rfcmr00000000an3-att/DATABOOK2023 en.pdf 31501 accessed August 9 2023.

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Table 1. Summary of personal p	ayments from ph	armaceutical cor	npanies to psychi	atry clinical prac	ight, in Colorado tice guiderine au	uthors from 2016 to	o 2020
Variables	2016	2017	2018	2019	2020 on 21 2020 or 21 En	Four-year total amounts from 2016 to 2019	Five-year f amounts fi 2016 to 20
Total amount of payments. \$	959.289	872.245	769.649	743.295	697.1 <b>702</b> .1	3.344.478	4.041.64
Mean payments per author	21.318	19.383	17.103	16.518	15.4935 N	74.322 (93.767)	89.814 (111
(standard deviation). \$	(27.281)	(24.380)	(24,797)	(21.363)		(,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	0,011(111
Median payments per author	11.992 (1.877	10.678 (2.309	5.452 (1.251 -	4.506 (834 -	2,701 ( 24 %	44.688 (9.325 -	51.403 (9.9
(interguartile range). \$	- 24,498)	-25.058	22.591)	26.830)	22.968	93.393)	111.567
Maximum payment amounts. \$	120.927	100.635	114.153	107.553	94.3 <b>6</b> 200 d	411.745	506.108
Authors receiving personal payments (N=45), n (%)			, , , , , , , , , , , , , , , , , , , ,		ed fron ieur (A id data		
Any payments	39 (86.7)	41 (91.1)	36 (80.0)	37 (82.2)	34 (75)	42 (93.3)	42 (93.3
>\$10,000	24 (53.3)	23 (51.1)	20 (44.4)	22 (48.9)	19 (42395	32 (71.1)	33 (73.3
>\$50,000	6 (13.3)	5 (11.1)	4 (8.9)	2 (4.4)	3 (6.7)	21 (46.7)	23 (51.1
>\$100,000	1 (2.2)	1 (2.2)	1 (2.2)	1 (2.2)	0 (0 1	10 (22.2)	15 (33.3
>\$250,000	0 (0)	0 (0)	0 (0)	0 (0)	0 (0 🖣 . 💆	2 (4.4)	3 (6.7)
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Table 2. Payment amounts	by top	10 companies.
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able 2. Payment amo	ounts by top 10	companies.					, inclu	-08639
Variables			Payment am	nounts (%), \$			ling	Aajor products used for bipolar and major
	2016	2017	2018	2019	2020	Overall	fo	depressive disorders (generic name)
Fotal amounts of	959,289	872,245	769,649	743,295	697,170	4,041,648	. use	
Top 10 companies naking the largest payment amounts	(100)		(100)			(100)	seigneme s related t	e 2024. Dc
Sumitomo Pharma	180,436 (18.8)	105,531 (12.1)	127,847 (16.6)	106,975 (14.4)	174,243 (25.0)	695,031 (17.2)	ht-Superieur (ABES) . to text and data mining, AI training, and	<ul> <li>Resor (venlafaxine, co-promotion with Pfize Japan)</li> <li>Erispan (fludiazepam)</li> <li>Excegran (zonisamide)</li> <li>Halomonth (haloperidol decanoate)</li> <li>Mystan (clobazam)</li> <li>Noritren (nortriptyline)</li> <li>Landosen (clonazepam)</li> <li>Latuda (lurasidone)</li> <li>Lonasen Tapes (blonanserin)</li> <li>Lullan (perospirone)</li> <li>Sediel (tandospirone)</li> <li>Serenace (haloperidol)</li> </ul>
Eisai	45,779 (4.8)	78,418 (9.0)	52,244 (6.8)	80,026 (10.8)	151,856 (21.8)	408,323 (10.1)	simili	Dayvigo (lemborexant) Spriropitan spiperone)
MSD	122,880 (12.8)	83,528 (9.6)	79,420 (10.3)	57,679 (7.8)	14,020 (2.0)	357,526 (8.8)	ar technolog	Belsomra (suvorexant) Remeron (mirtazapine) Reslin (trazodone) Tetramide (mianserin)
Otsuka Pharmaceutical	64 794 (6 8)	73 028 (8 4)	64 161 (8 3)	86 679 (11 7)	65 976 (9 5)	354,638 (8.8)	ies.	Abilify (aripiprazole) Resulti (brevniprazole)
Takeda Pharmaceutical	69,017 (7.2)	78,990 (9.1)	45,019 (5.8)	71,206 (9.6)	73,138 (10.5)	337,370 (8.3)		Depas (etizolam) Eurodin (estazolam) Trintellix (vortioxetine)
Pfizer Japan	78,269 (8.2)	106,973	65,996 (8.6)	46,086 (6.2)	14,247 (2.0)	311,571 (7.7)		<b>bi</b> Amoxan (amoxapine)
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		(12.3)					24-086396 on 21 Jun En nt, including for use	Desyrel (trazodone) Effexor (venlafaxin) Halcion (triazolam) Jzoloft (sertraline) Wypax (lorazepam) Mirtrzapin (generic mirtrzapin)	
Mitsubishi Tanabe Pharma	58,501 (6.1)	47,295 (5.4)	61,056 (7.9)	59,114 (8.0)	25,789 (3.7)	251,755 (6.2)	e 2024. Downli seignement Si s related to tex	Clofekton (clocapramine hydrochloride) Contomin (chlorpromazine) Levotomin (levomepromazine) Rize (clotiazepam)	_
Eli Lilly Japan	56,337 (5.9)	60,899 (7.0)	59,231 (7.7)	36,314 (4.9)	38,130 (5.5)	250,910 (6.2)	oaded fro uperieur ( (t and dat	Zyprexa (olanzapine) Zyprexa Zydis (olanzapine) Depromel (fluvoxamine)	_
Meiji Seika Pharma	75,608 (7.9)	53,110 (6.1)	57,841 (7.5)	27,228 (3.7)	24,235 (3.5)	238,023 (5.9)	m http://bm ABES) . a mining, A	Reflex (mirtazapine) Sycrest (asenapine) Aripiprazole (generic aripiprazole)	
Mochida Pharmaceutical	35,768 (3.7)	29,405 (3.4)	31,597 (4.1)	41,378 (5.6)	17,209 (2.5)	155,356 (3.8)	Jopen.b	Tecipul (setiptiline) Zolpidem (generic zolpidem)	
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	5 of 19 Mitsubishi Tanabe Pharma Eli Lilly Japan Meiji Seika Pharma Mochida Pharmaceutical	5 of 19 Mitsubishi Tanabe Pharma 58,501 (6.1) Eli Lilly Japan 56,337 (5.9) Meiji Seika Pharma 75,608 (7.9) Mochida Pharmaceutical 35,768 (3.7)	S of 19       (12.3)         Mitsubishi Tanabe       58,501 (6.1)       47,295 (5.4)         Eli Lilly Japan       56,337 (5.9)       60,899 (7.0)         Meiji Seika       75,608 (7.9)       53,110 (6.1)         Mochida       35,768 (3.7)       29,405 (3.4)	5 of 19 (12.3) (12.3) Mitsubishi Tanabe Pharma 58,501 (6.1) 47,295 (5.4) 61,056 (7.9) Eli Lilly Japan 56,337 (5.9) 60,899 (7.0) 59,231 (7.7) Meiji Seika Pharma 75,608 (7.9) 53,110 (6.1) 57,841 (7.5) Mochida 35,768 (3.7) 29,405 (3.4) 31,597 (4.1)	5 of 19 (12.3) (12.3) Mitsubishi Tanabe Pharma 58,501 (6.1) 47,295 (5.4) 61,056 (7.9) 59,114 (8.0) Eli Lilly Japan 56,337 (5.9) 60,899 (7.0) 59,231 (7.7) 36,314 (4.9) Meiji Seika Pharma 75,608 (7.9) 53,110 (6.1) 57,841 (7.5) 27,228 (3.7) Mochida Pharmaccutical 35,768 (3.7) 29,405 (3.4) 31,597 (4.1) 41,378 (5.6)	5 of 19 BM Open (12.3) (12.3	Sof 19     BMJ Open	S of 19     BMJ Open     Py opping       Image: 200 more provided from the provid	BMJ Open     BMJ Open     Open     Open     Open     Desyrel (trazodone) Effector (vnlaktisni)       Misubishi Tanabe Pharma     1

Table 3. Payments by author categories in the bip practice guidelines	oolar disorder and major depressive disorder clinical
Variables	Guideline disease category

Variables	Guideline dis	ease category
	Bipolar disorder	Major depressive disorder
Number of all authors, N	33	42
Role of guideline authors, n (%)		
Writing authors <sup>a</sup>	4 (12.1)	14 (33.3)
Supporting authors <sup>b</sup>	5 (15.2)	12 (28.6)
Guideline development committee authors <sup>c</sup>	24 (72.7)	16 (38.1)
Payments by author roles		
Total payment amounts, \$		
Writing authors <sup>a</sup>	532,717	1,659,595
Supporting authors <sup>b</sup>	12,140	930,986
Guideline development committee authors <sup>c</sup>	2,548,718	1,448,508
Number of authors receiving payments by		
author roles, n (%)		
Writing authors <sup>a</sup>	4 (100)	14 (100)
Supporting authors <sup>b</sup>	4 (80.0)	10 (83.3)
Guideline development committee authors <sup>c</sup>	22 (91.7)	16 (100)
Median payment amounts per author, \$		
Writing authors <sup>a</sup>	135,867 (78,553 - 187,806)	87,610 (16,945 - 111,567)
Supporting authors <sup>b</sup>	1,788 (715 – 1,845)	60,120 (1,573 - 142,732)
Guideline development committee authors <sup>c</sup>	<b>34,569 (11,588 – 184,068)</b>	$34,5\overline{69}(14,331 - 149,624)$

<sup>a</sup> Writing authors directly contributed to the creation of guidelines.

<sup>b</sup> Supporting authors could have contributed to identifying relevant evidence and performing literature reviews. <sup>c</sup> Guideline development committee authors were not directly involved in the creation of the guidelines, but critically reviewed the contents and recommendations of the initial guideline draft and revised them if necessary.

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Variables	Bipolar disorder (N=4)	Major depressive disorder (N=14)
Number of authors self-reporting conflicts of interest by category		
Speaking compensation	4 (100)	11 (78.6)
Scholarship donation	3 (75.0)	6 (42.9)
Consulting payments	0 (0)	4 (28.6)
Collaborative research funds	1 (25.0)	2 (14.3)
Advisory board	2 (50.0)	1 (7.1)
Contracted research funds	1 (25.0)	0 (0)
Any category	4 (100)	12 (85.7)
Industry-reported payments to authors		
Number of writing authors receiving		
payments from 2016 to 2020 by		
payment category, n (%)		
Lecturing payments	4 (100)	14 (100)
Consulting payments	4 (100)	12 (85.7)
Writing payments	4 (100)	9 (64.3)
Any payment category	4 (100)	14 (100)
Total payment amounts to writing		
authors from 2016 to 2020, \$		
Lecturing payments	399,929	1,073,071
Consulting payments	101,805	430,660
Writing payments	30,983	155,864

Legends: Proportion of authors reporting conflicts of interest were number of authors reporting conflicts of interest to the total number of writing authors.

d by copyright, including fo bmjopen-2024-08639<mark>6</mark> STROBE Statement-checklist of items that should be included in reports of observational studies **9** Page **Relevant text from** Item No. Recommendation N NO. manuscript June 2024. Downloaded Enseignement Superie Uses related to text and (a) Indicate the study's design with a commonly used term in the title or the abstract Title and abstract 1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found Introduction Explain the scientific background and rationale for the investigation being reported Background/rationale 2 State specific objectives, including any prespecified hypotheses 3 Objectives Methods ur (A data Present key elements of study design early in the paper Study design 4 t http://bmjopen.bmj.com/ on BES). ㎡ning, 邓 training, and simil 5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, Setting follow-up, and data collection (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of All training, and similar technologies: Participants 6 participants. Describe methods of follow-up Case-control study-Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants June 11, 2025 (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case at Age Variables 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable nce For each variable of interest, give sources of data and details of methods of assessment Data sources/ 8\* 4 (measurement). Describe comparability of assessment methods if there is more than one group Bib measurement 9 Describe any efforts to address potential sources of bias n/a 👼 Bias raphique Explain how the study size was arrived at 3 Study size 10 Continued on next page del For peer review only - http://bmjopen.bmj.com/site/about/quidelines.xhtml

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	024-08639 9ht, Thclu
Statistical	12	( <i>a</i> ) Describe all statistical methods, including those used to control for confounding	
methods		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	estre 2
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	igne elat
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling	ed f
		strategy	o te
		( <u>e</u> ) Describe any sensitivity analyses	
Results		6	and ded
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	daft
<b>I</b>		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	<u>y</u> a/a ∃
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	
I I I I I I I I I I I I I I I I I I I		exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) <i>Cohort study</i> —Summarise follow-up time (eg. average and total amount)	and on
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	sim or
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	ilar Ju
		Cross-sectional study—Report numbers of outcome events or summary measures	en ne en la companya de
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	11, 2
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	logi
		included	es.
		(b) Report category boundaries when continuous variables were categorized	<u>→</u> 5-6 <b>'@</b>
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	n/a Ce
		period	Bit
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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		00 00 00
Discussion			udi	39 <del>6</del>
Key results	18	Summarise key results with reference to study objectives		0 
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	о°° г	21 J
		both direction and magnitude of any potential bias	ISes	un e
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	felg	20
		analyses, results from similar studies, and other relevant evidence	nem	24
Generalisability	21	Discuss the generalisability (external validity) of the study results		
Other informati	on	<u> </u>	text	3
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	an	a de
		original study on which the present article is based	d er	۵ ۲
Give informatio	1		=	0
Note: An Explan checklist is best u http://www.annal	ation ised i ls.org	and Elaboration article discusses each checklist item and gives methodological background and published n conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosme /, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at w	ng, Ann, dicination www.g, and similar technologies.	on June 11, 2025 at A