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LabAnimal

Translational science: a survey of US biomedical researchers' perspectives and practices

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This national survey aimed to identify how biomedical researchers using vertebrate animals viewed issues of significance for translational science, including oversight and public engagement, and to analyze how researcher characteristics and animal model choice correlate with those views. Responses from 1,187 researchers showed awareness of, and concerns about, problems of translation, reproducibility and rigor. Surveyed scientists were nevertheless optimistic about the value of animal studies, were favorable about research oversight and reported openness with non-scientists in discussing their animal work. Differences in survey responses among researchers also point to diverse perspectives within the animal research community on these matters. Most significant was variability associated with the primary type of animal that surveyed scientists used in their work. Other significant divergence in opinion appeared on the basis of professional role factors, including the type of degree held, workplace setting, type of funding, experience on an institutional animal care and use committee and personal demographic characteristics of age and gender.

A focus on rigor and reproducibility, alongside concerns about high attrition rates in drug development, have become commonplace in translational research[1–5]. Proffered explanations for high attrition rates are diverse, with some studies raising concern about animal models for specific human health conditions[6–11] and others focusing on study design and rigor[12–15]. Similarly, there are multiple potential contributors to problems of reproducibility from variability in animal models or housing environments[16,17] to a lack of detail in published studies[18,19]. Standards for the care and use of laboratory animals, including environmental requirements for different animal species and reduction in the numbers of animals used to conduct the science, are implemented through research oversight[20,21]. Critical commentary on animal use in science has nevertheless remained focused on gaps in translation to human health[22–24], and public support for animal research is generally mixed[25,26]. Translational scientists thus face intersecting demands in their work, including management of rigor, reproducibility and attrition rates; oversight standards; and consideration of whether or how to engage the public about their work. The purpose of this national survey was to identify how biomedical researchers using vertebrate animals view these issues of significance for translational science including oversight and public engagement and to analyze how researcher characteristics and animal model choice correlate with those views.

Results

Demographics. A total of 4,910 biomedical researchers using vertebrate animals were sent a survey invitation, and one-quarter participated, with a completion rate of 96% (or 1,187 respondents). Participant demographic characteristics are provided in Table 1. Most respondents were men (64%) and were white (79%). Respondents' median age was 52, and over half had more than 20 years of experience with animal research. PhD (doctor of philosophy) was the most held degree (83%). Two-thirds of respondents worked at public academic institutions, and most had recent funding from the National Institutes of Health (NIH) (72%). Most researchers (68%) reported primarily using mice, although respondents used a diverse range of animal species as their primary model. Descriptive statistics for attitudinal variables are presented in Table 2.

Animal model choice. Respondents reported selecting their primary animal model species on the basis of scientific value (89%), practical constraints (70%), past experience (55%), funder expectations (29%) and other institutional expectations (4.7%). Respondents could select multiple responses, and greater granularity of response categories is presented in Table 2. The proportion of researchers who endorsed the proffered reasons for selecting an animal model differed by animal species. These differences across animal species were statistically significant for scientific value ($P = 0.005$), practical constraints ($P \leq 0.001$), past experience ($P \leq 0.001$) and funder expectations ($P \leq 0.001$) (Table 3). Specifically, 100% of non-human primate (NHP) researchers compared with 86% of mouse researchers reported that they selected their animal model for its scientific value, whereas 79% of mouse researchers compared with 14% of NHP researchers selected their animal model because of practical constraints. In addition, past experience was most often a driver of animal model selection for non-mouse rodent researchers (67%) and non-mammal/other vertebrate researchers (68%) compared to researchers studying other animals. Finally, funder expectations were most often selected by mouse researchers (34%) compared to researchers studying other animals.

The results of the logit analysis identifying factors associated with selection of different primary animal model species, compared to the selection of mice, are provided in Table 4 and Fig. 1. Respondents with institutional animal care and use committee (IACUC) experience were more likely to use NHPs (odds ratio (OR): 2.00; 95% confidence interval (CI): 1.06–3.78) or non-mammal/other animals (OR: 1.95; 95% CI: 1.08–3.52) than those without such experience. MD (doctor of medicine) researchers were less likely than PhD

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Table 1 | Respondent characteristics

Category	Subcategory	Frequency	Median (IQR) or probability (%)	Category (cont.)	Subcategory	Frequency	Probability (%)
Age (n = 1,134)	–	NA	52 (44–61)	Institution type (n = 1,185)	Public academic	784	66
Years of experience with animal research (n = 1,186)	1–5 years	46	3.9		Private academic	351	30
	6–10 years	112	9.4		Non-academic public[a]	7	0.6
	11–20 years	374	32		Industry/non-academic private	43	3.6
	>20 years	654	55	NIH-funded PI in the past 5 years (n = 1,184)	–	852	72
Race[a] (n = 1,175)	White	930	79	IACUC experience (n = 1, 187)	–	366	31
	Asian	216	18	Species of primary vertebrate animal model (n = 1,187)	Mice	809	68
	Black or African American	30	2.6		*Non-mouse rodents*		
	American Indian[b] or Alaska Native	11	0.9		Rats	182	15
	Native Hawaiian or other Pacific Islander	6	0.5		Other rodents	11	0.9
Ethnicity (n = 1,177)	Hispanic[a]	56	4.8		Non-human primates	51	4.3
Gender (n = 1,181)	Men	764	64		*Other mammals*		
	Women	413	35		Pigs	26	2.2
	Gender fluid[a]	4	0.3		Cattle, sheep, other livestock	15	1.3
Degree (n = 1,184)	PhD only	980	83		Cats	10	0.8
	MD or equivalent only	47	4.0		Dogs	8	0.7
	DVM or equivalent only	14	1.2		Rabbits	7	0.6
	Dual degree				Ferrets/weasels	2	0.2
	MD and PhD	99	8.4		*Non-mammals and all other*		
	DVM and PhD	37	3.1		Fish	38	3.2
	MD and DVM	2	0.2		*Birds*[b]	13	1.1
	None of the above[a]	7	0.6		Amphibians	8	0.7
					Reptiles	3	0.3
					Other, write-in[c]	4	0.3

The total number of completed surveys was 1,187; in each category, the number of surveys including a response in that category is indicated in parentheses. Percentages are of those who selected a response in each category. Italicized categories were not visible to survey respondents. cont., continued; DVM, doctor of veterinary medicine; IACUC, institutional animal care and use committee; IQR, interquartile range; MD, doctor of medicine; NA, not applicable; PhD, doctor of philosophy; PI, principal investigator. [a]Category or variable excluded from subsequent regression analyses because of small cell sizes. [b]Self-reported as American Indian. [c]'Birds' was not provided as an option in the survey, but it represented the largest number of write-in responses. Write-in responses not fitting any provided option were sea mammals and bears.

researchers to use rodents other than mice (OR: 0.26; 95% CI: 0.08–0.87), and all MD researchers in the sample primarily used rodents. In contrast, DVM (doctor of veterinary medicine) researchers were more likely than PhD researchers to use NHPs (OR: 10.78; 95% CI: 1.83–63.58) or other non-rodent mammals (OR: 22.03; 95% CI: 4.76–101.89). Researchers with dual degrees were less likely than PhD-only researchers to use rodents other than mice (OR: 0.43; 95% CI: 0.23–0.83) or non-mammal/other animals (OR: 0.23; 95% CI: 0.05–0.97). Finally, respondents working in private academic institutions compared with public academic institutions were less likely to use mammals other than rodents and NHPs (OR: 0.29; 95% CI: 0.13–0.62). Researchers not recently funded by the NIH were more likely than those receiving such funding to use mammals other than rodents and NHPs (OR: 2.16; 95% CI: 1.22–3.83) or non-mammal/other animals (OR: 4.62; 95% CI: 2.66–8.03).

Translation, rigor and reproducibility. The results of the ordered logit and logit analysis identifying factors associated with attitudes about the translation, rigor and reproducibility of animal research are provided in Table 5 and Figs. 2 and 3. Most respondents reported that animal studies predict safety of potential therapeutics in humans to a moderate (68%) or great (22%) extent (Table 2). Older respondents were more likely to report that animal studies accurately predict human safety (OR: 1.03; 95% CI: 1.01–1.04). Those with an MD (OR: 0.37; 95% CI: 0.19–0.72) were less likely than those with a PhD to report that animal studies predict safety.

Table 2 | Descriptive statistics

Category	Subcategory	Frequency	Median (IQR) or probability (%)	Category (cont.)	Subcategory	Frequency	Median (IQR) or probability (%)
Animal research oversight ensures animal welfare (1–5) (n = 1,184)	–	NA	5 (4–5)	Main issue with poor rates of drug success (n = 1,174)[b]	Problems with animal models	570	49
Animal research oversight protects institutions (1–5) (n = 1,182)	–	NA	5 (4–5)		Problems with study design	439	37
Animal research oversight improves study design (1–5) (n = 1,184)	–	NA	4 (3–4)		Some other problem	165	14
Investigators should be given more latitude for minor changes (1–5) (n = 1,175)	–	NA	4 (2–5)	View of reproducibility 'crisis'[b]	Exaggerated problem	204	17
Current standards for housing and caretaking are sufficient (n = 1,185)	–	1,155	97		Unsure how important	873	9.1
Ever a viable alternative to using live animals in field (n = 1,186)	–	274	23		Important problem	108	74
Emphasis on reduction leads to too few animals used (n = 1,186)	Rarely	261	22	Biggest contributors to reproducibility problem in animal research (select up to three)[b] (n = 1185)	*Scientific shortcomings*		
	Sometimes	680	57		Lack of rigor in design of studies	772	65
	Often	245	21		Insufficient details on methods in published reports	731	62
Main reasons for selecting primary animal (select all that apply) (n = 1187)	*Practical constraints*				*Variation*		
	Ease of procuring animals	468	39		Variability in animals used	615	52
	Cost of maintaining animals	490	41		Differences across animal housing/husbandry environments	515	43
	Availability of housing space	344	29		Differences in personnel	239	20
	Availability of reagents/ research tools	643	54		*Ethics*		
	Past experience				Falsification of published results	143	12
	Familiarity from past experience	649	55		Commercial interests biasing the design or analysis of studies	104	8.8
	Scientific value				Other[a]	136	11
	Non-translational scientific value	610	51	Comfort discussing use of animals with non-scientists (1–4) (n = 1,183)	–	NA	3 (3–4)
	How well the animal models human disease	822	69	Open with non-scientists about animal species used (n = 1,183)	Prefer not to tell	91	7.7
	Translational potential for treatments	663	56		Selective in telling	341	29
	Funder expectations				Very open	751	63
	Grant agency's or reviewer's expectations	350	29	How often have you been personally criticized by non-scientists? (n = 1,186)	Never	343	29
	Institutional expectations[a]				Rarely	560	47
	Institutional promotion of specific species use	31	2.6		Sometimes	253	21
	Institutional avoidance of specific species use	25	2.1		Often/always	30	2.5
	Other[a]	109	9.2	How transparent should scientists be about limitations of animal research? (n = 1,182)	Be very transparent	798	68
Extent to which animal studies are accurate predictors of safety for therapeutics (n = 1,180)[b]	Small	117	9.9		Be prepared to discuss but not bring it up	375	32
	Moderate	805	68		Not talk about it because of negative impact on public support[a]	9	0.8
	Great	258	22	–	–	–	–

Continued

Table 2 | Descriptive statistics (continued)

Category	Subcategory	Frequency	Median (IQR) or probability (%)	Category (cont.)	Subcategory	Frequency	Median (IQR) or probability (%)
View on high attrition in translating animal research to drug development (n = 1,181)	Not a problem, normal part of the drug development process	358	30	–	–	–	–
	Unsure what to think	89	7.5	–	–	–	–
	Important problem	734	62	–	–	–	–

The total number of completed surveys was 1,187; in each category, the number of surveys including a response in that category is indicated in parentheses. Percentages are of those who selected a response in each category. Italicized categories were not visible to survey respondents. [a]Category or variable excluded from subsequent regression analyses because of small cell sizes. [b]Data previously published in ref. [50].

Table 3 | Reasons for selecting primary animal model species

	Mice (%)	Non-mouse rodents (%)	Non-human primates (%)	Other mammals (%)	Non-mammal / other (%)	P value (χ^2)
Practical constraints	79	65	14	15	68	<0.001
Past experience	54	67	27	37	68	<0.001
Scientific value	86	93	100	91	89	0.005
Funder expectations	34	21	24	26	12	<0.001
Institutional expectations	4.0	4.2	2.0	4.4	6.1	0.86

However, researchers using NHPs were more likely than those primarily using mice to report that animal studies accurately predict safety (OR: 3.42; 95% CI: 1.84–6.33).

Most respondents reported that high attrition (low success) rates in translating animal research to human drug development is an important problem (62%) (Table 2). Older respondents were less likely to indicate that it is a problem (OR: 0.98; 95% CI: 0.97–0.99), and those who primarily study mammals other than rodents or NHPs were more likely to indicate that it is an important problem than those who primarily study mice (OR: 2.52; 95% CI: 1.20–5.33).

Respondents were somewhat divided between viewing problems with animal models (49%) and problems with study design (37%) as driving low translational success (Table 2). MD respondents were more likely to indicate that animal models were the main issue compared to those with PhDs (OR: 2.32; 95% CI: 1.09–4.94). Respondents who had not recently received NIH funding were also more likely to report that animal models were the main issue compared to those who had received NIH funding (OR: 1.64; 95% CI: 1.20–2.26). Compared to those primarily using mice, researchers using mammals other than rodents or NHPs (OR: 2.12; 95% CI: 1.13–3.99) and those using NHPs (OR: 2.70; 95% CI: 1.32–5.54) were much more likely to report that animal models drove low rates of success in drug development.

Nearly three quarters of respondents (74%) indicated that the reproducibility 'crisis' is an important problem (Table 2). Those who primarily study mammals other than rodents or NHPs were more likely to report that reproducibility is an important problem compared to those who primarily study mice (OR: 3.09; 95% CI: 1.08–8.85). When asked to select up to three of the biggest contributors to reproducibility problems in animal research, respondents most often selected lapses in scientific rigor, including lack of rigor in study design (65%) and insufficient details on methods in published reports (62%). Many respondents also selected variation rationales, including variability in animals used (52%), environmental and husbandry variation (43%) and personnel differences (20%). Fewer respondents selected research integrity or ethics problems including falsification (12%) or conflict of interest (8.8%) (Table 2). Older researchers were less likely to think that ethics contributed to the problems of reproducibility (OR: 0.98; 95% CI: 0.97–1.00), and compared to men, women were less likely to think that ethics contributed (OR: 0.59; 95% CI: 0.41–0.84). Those with dual degrees were more likely than those with PhDs to report that ethics contributed to reproducibility problems (OR: 2.18; 95% CI: 1.41–3.36), and those who use non-mammal/other animals were more likely than those who use mice to report that ethics contributed (OR: 1.96; 95% CI: 1.05–3.64). Those who use NHPs were less likely than those who use mice to report rigor problems as contributing (OR: 0.41; 95% CI: 0.20–0.83). Women were more likely than men to report that variation contributes to reproducibility problems (OR: 1.56; 95% CI: 1.12–2.17). Those who primarily study non-mouse rodents were less likely than those who primarily study mice to report that variation contributes to reproducibility problems (OR: 0.64; 95% CI: 0.43–0.94).

Oversight, reduction and replacement. Respondents reported a high degree of confidence that the animal research oversight system ensures animal welfare (median score of 5 on a scale of 1–5), protects institutions (median score of 5) and improves study design (median score of 4) (Table 2). The results of the ordered logit analysis identifying factors associated with the animal research oversight system are provided in Table 6 and Fig. 4. Compared to those without IACUC experience, those with such experience were more likely to agree that the oversight system ensures animal welfare (OR: 1.58; 95% CI: 1.16–2.14), and those who worked at private academic institutions were also more likely than those at public academic institutions to agree (OR: 1.36; 95% CI: 1.01–1.82). By contrast, those who had not received NIH funding as a principal investigator in the past 5 years were less likely than those who had done so to agree that the oversight system ensures animal welfare (OR: 0.70; 95% CI: 0.53–0.94). Similarly, when asked whether the oversight

Table 4 | Factors associated with selecting a non-mouse primary animal model

	Primary animal model (relative risk (95% CI); *P* value)			
	Non-mouse rodents	**NHPs**	**Other mammals**	**Non-mammal/other animal**
Ever served on an IACUC	1.31 (0.91–1.90); 0.148	2.00* (1.06–3.78); 0.032	1.46 (0.81–2.61); 0.205	1.95* (1.08–3.52); 0.027
Age (continuous)	1.01 (0.99–1.03); 0.103	1.03 (0.99–1.06); 0.094	1.02 (0.99–1.04); 0.189	1.01 (0.98–1.03); 0.717
Gender (reference = man)				
Woman	1.38 (0.97–1.95); 0.074	1.65 (0.87–3.12); 0.123	0.89 (0.48–1.62); 0.691	1.36 (0.78–2.39); 0.278
Degree (reference = PhD)				
MD or equivalent[a]	0.26* (0.08–0.87); 0.029	–	–	–
DVM or equivalent[b]	–	10.78** (1.83–63.58); 0.009	22.03*** (4.76–101.89); <0.001	1.68 (0.16–17.72); 0.668
Dual degree	0.43* (0.23–0.83); 0.012	1.82 (0.86–3.86); 0.117	1.16 (0.54–2.50); 0.699	0.23* (0.05–0.97); 0.045
Institution (reference = public academic)				
Private academic	0.75 (0.51–1.09); 0.125	1.57 (0.85–2.89); 0.151	0.29** (0.13–0.62); 0.002	0.51 (0.26–1.00); 0.051
Industry/non-academic private[c]	0.56 (0.21–1.51); 0.253	0.58 (0.07–4.82); 0.616	0.34 (0.07–1.63); 0.176	–
NIH funded PI in the past 5 years (reference = yes)				
No	1.42 (0.97–2.08); 0.071	0.95 (0.45–2.01); 0.896	2.16** (1.22–3.83); 0.009	4.62*** (2.66–8.03); <0.001
Constant	0.11*** (0.05–0.28); <0.001	0.01*** (0.0–0.05); <0.001	0.03*** (0.01–0.13); 0.001	0.037*** (0.01–0.15); <0.001

The model type was multinomial logit; $n = 1{,}127$. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. [a]No MD researchers studied primates, mammals other than rodents or primates or non-mammals. [b]No DVM researchers studied non-mouse rodents. [c]No researchers in non-academic private institutions studied non-mammals.

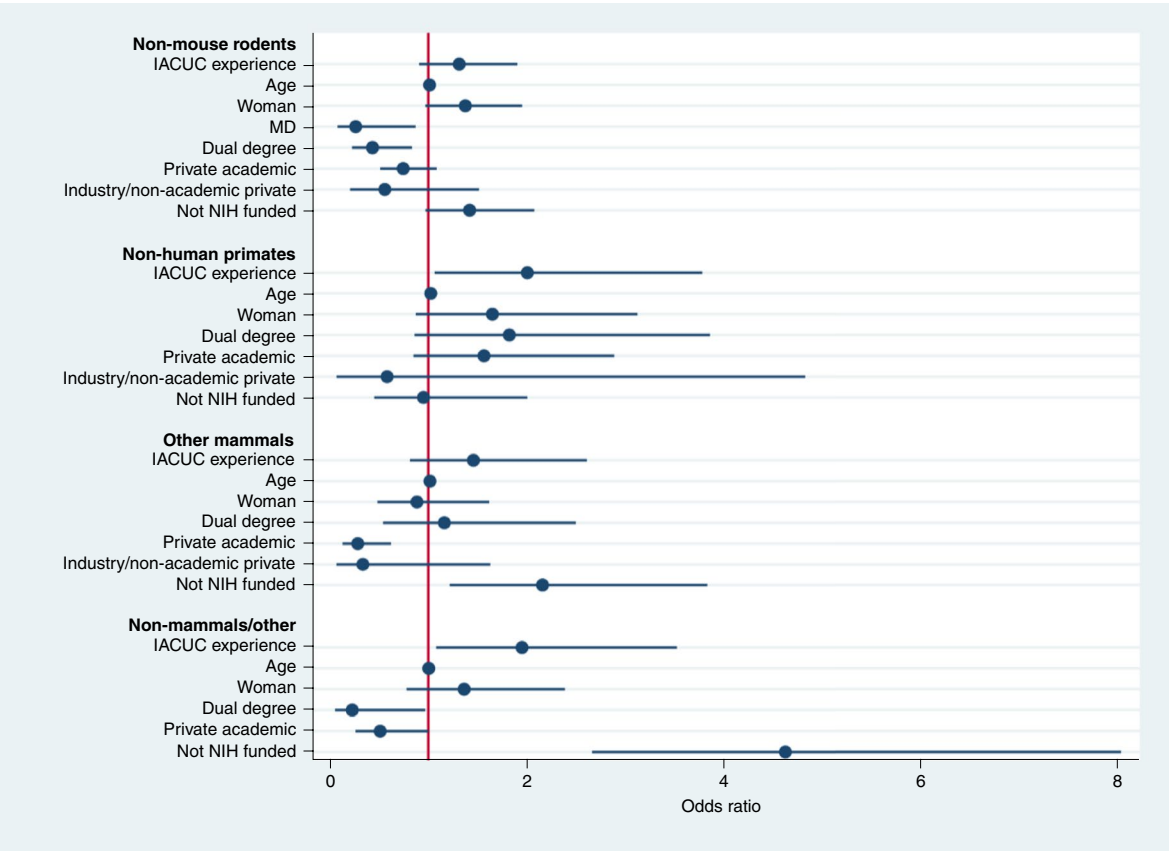

Fig. 1 | IACUC experience, academic degree, institution type and NIH funding are associated with primarily using non-mouse animal models. Multinomial logistic regression (mlogit), odds ratios with 95% confidence intervals ($n = 1{,}107$). Odds ratios >1 indicate greater odds of primarily using a given animal type as compared to primarily using mice. Results are not displayed for variables with perfect prediction or extremely large error bars because of small cell sizes (that is, no MD researchers studied non-rodents, no researchers at industry/non-academic institutions studied non-mammals/other animals and error bars for DVM researchers were very large because of small cell sizes). Refer to Table 4 for additional details, *P* values and results from categories not displayed in the figure.

Table 5 | Factors associated with views about translation, rigor and reproducibility

	Category (odds ratio (95% CI); *P* value)						
	Extent animal studies accurately predict safety for humans	**View on high drug attrition rates**	**Main issue driving attrition**	**View on the reproducibility 'crisis' in animal research**	**Biggest contributor to problems with reproducibility in animal research**		
Observations (*n*)	1,101	1,021	948	994[a]	1,107	1,068[b]	1,107
Model type	Ologit	Logit	Logit	Logit	Logit	Logit	Logit
Independent variables	Great versus moderate versus small extent	Important problem versus not a problem (excluded 'unsure')	Animal models versus study design (excluded 'other')	Important problem versus exaggerated (excluded 'unsure')	Selected one or more ethics reasons	Selected one or more scientific rigor reasons	Selected one or more variation reasons
Ever served on an IACUC	1.20 (0.90–1.60); 0.213	1.03 (0.76–1.40); 0.854	0.85 (0.63–1.15); 0.292	0.81 (0.56–1.15); 0.238	1.21 (0.85–1.71); 0.290	1.51 (0.97–2.33); 0.066	1.10 (0.79–1.54); 0.562
Age (continuous)	1.03*** (1.01–1.04); <0.001	0.98** (0.97–0.99); 0.003	1.00 (0.99–1.01); 0.753	0.99 (0.97–1.00); 0.136	0.98* (0.97–1.00); 0.038	0.99 (0.97–1.01); 0.246	1.00 (0.98–1.01); 0.444
Gender (reference = man)							
Woman	0.80 (0.61–1.06); 0.121	1.16 (0.87–1.56); 0.311	0.98 (0.74–1.30); 0.903	1.42 (0.98–2.05); 0.063	0.59** (0.41–0.84); 0.003	1.07 (0.72–1.60); 0.723	1.56** (1.12–2.17); 0.008
Degree (reference = PhD)							
MD or equivalent	0.37** (0.19–0.72); 0.004	1.45 (0.72–2.93); 0.296	2.32* (1.09–4.94); 0.028	1.80 (0.68–4.75); 0.234	1.19 (0.53–2.66); 0.671	1.58 (0.55–4.57); 0.397	1.21 (0.54–2.68); 0.642
DVM or equivalent	0.61 (0.19 –1.95); 0.406	4.11 (0.49–34.32); 0.192	0.68 (0.17–2.68); 0.581	–	0.50 (0.06–4.13); 0.522	1.60 (0.19–13.55); 0.665	0.37 (0.11–1.24); 0.107
Dual degree	1.15 (0.77–1.71); 0.503	1.35 (0.87–2.10); 0.180	0.84 (0.56–1.26); 0.395	0.98 (0.60–1.59); 0.918	2.18*** (1.41–3.36); <0.001	1.33 (0.73–2.42); 0.359	0.89 (0.56–1.39); 0.595
Institution (reference = public academic)							
Private academic	1.17 (0.88–1.55); 0.283	0.75 (0.56 –1.01); 0.058	0.83 (0.62 –1.11); 0.203	0.99 (0.70–1.41); 0.953	0.74 (0.52–1.06); 0.099	0.96 (0.65–1.42); 0.827	1.03 (0.74–1.42); 0.863
Industry/non-academic private	1.42 (0.69 –2.92); 0.339	2.34 (0.94–5.81); 0.068	1.22 (0.57–2.62); 0.601	1.84 (0.62–5.48); 0.272	1.15 (0.51–2.57); 0.737	–	0.68 (0.32–1.45); 0.321
NIH funded PI in the past 5 years (reference = yes)							
No	0.74 (0.55–1.00); 0.050	0.97 (0.70–1.33); 0.83	1.64** (1.20–2.26); 0.002	1.01 (0.68–1.49); 0.982	1.06 (0.74–1.52); 0.747	0.91 (0.59–1.38); 0.645	0.96 (0.68–1.35); 0.815
Primary animal model (reference = mice)							
Non-mouse rodents	1.12 (0.79–1.59); 0.531	0.96 (0.67–1.39); 0.846	0.96 (0.66–1.39); 0.819	0.98 (0.63–1.53); 0.920	1.46 (0.97–2.20); 0.072	1.23 (0.72–2.09); 0.444	0.64* (0.43–0.94); 0.022
NHPs	3.42*** (1.85–6.33); <0.001	2.14 (1.00–4.59); 0.050	2.70** (1.32–5.54); 0.007	0.82 (0.39–1.74); 0.609	0.82 (0.35–1.92); 0.651	0.41* (0.20–0.83); 0.013	0.63 (0.32–1.20); 0.155
Other mammals	1.28 (0.73–2.26); 0.385	2.52* (1.20–5.33); 0.015	2.12* (1.13–3.99); 0.020	3.09* (1.08–8.85); 0.035	0.65 (0.29–1.42); 0.280	1.32 (0.54–3.24); 0.542	1.36 (0.67–2.77); 0.397
Non-mammal/ other animal	0.85 (0.47–1.53); 0.589	1.02 (0.55–1.90); 0.940	1.00 (0.55–1.83); 0.993	1.55 (0.66–3.61); 0.311	1.96* (1.05–3.64); 0.035	1.70 (0.65–4.42); 0.279	0.79 (0.41–1.51); 0.471
Cut 1/constant	0.39** (0.20–0.77); 0.006	5.37*** (2.61–11.05); <0.001	1.33 (0.66–2.69); 0.432	7.39*** (3.06–17.80); <0.001	0.53 (0.23–1.20); 0.126	9.95*** (3.79–26.14); <0.001	4.78*** (2.20–10.38); <0.001
Cut 2	14.53*** (7.23–29.19); <0.001	–	–	–	–	–	–

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. [a]All DVM holders viewed reproducibility as an important problem, so 12 observations were dropped from the model. [b]All researchers in private non-academic institutions selected scientific reasons, so 39 observations were dropped from the model.

system protects institutions, those who had not recently received NIH funding were less likely to agree than those who had received such funding (OR: 0.77; 95% CI: 0.59–1.00), and women were less likely than men to agree (OR: 0.76; 95% CI: 0.59–0.97). Regarding study design, older researchers were more likely to agree that the oversight system improves study design (OR: 1.02; 95% CI: 1.01–1.03), and those who primarily use mammals other than rodents or NHPs (OR: 0.60; 95% CI: 0.37–0.97) and those using non-mammal/other animals (OR: 0.55; 95% CI: 0.34–0.88) were less likely than those using mice to agree.

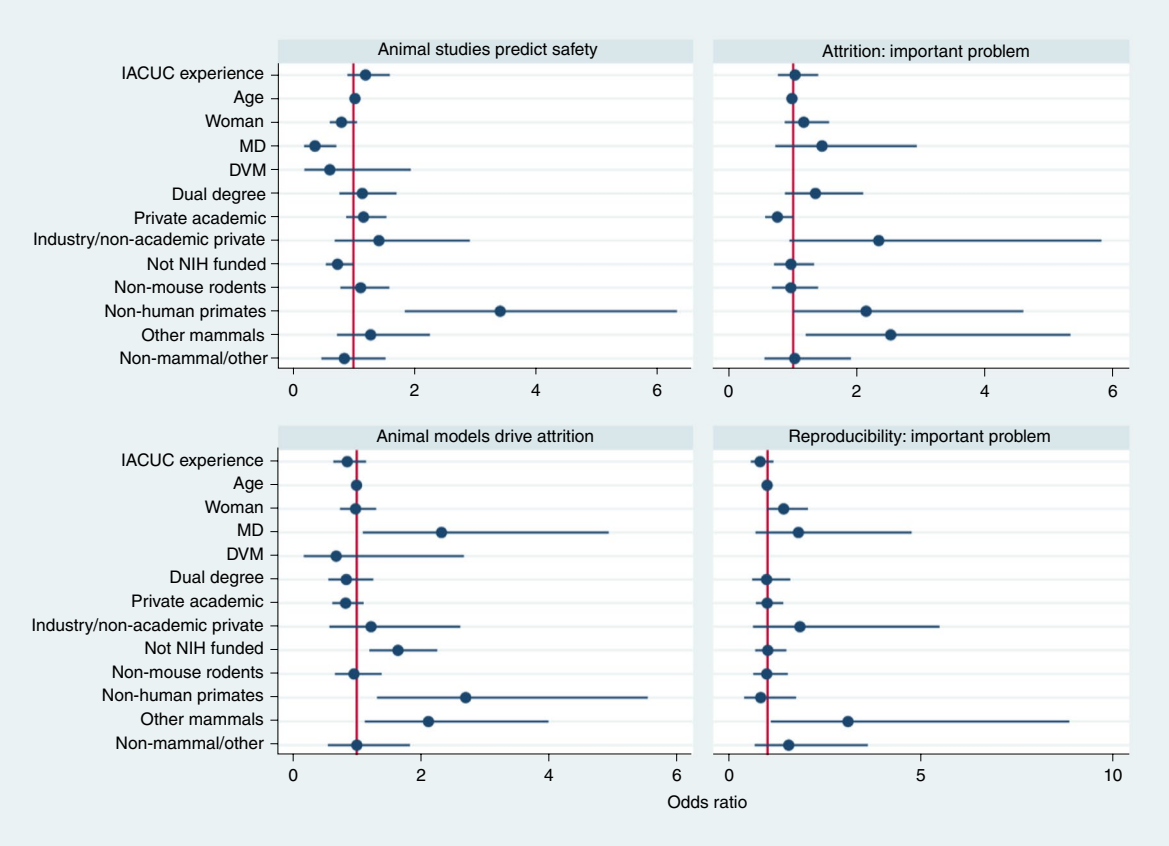

Fig. 2 | Age, academic degree, NIH funding and primary animal model species are associated with views on translation, rigor and reproducibility. Logit or ologit regressions, odds ratios with 95% confidence intervals. Older age or using NHPs is associated with reporting that animal studies of potential therapies predict human safety to a greater extent, whereas holding an MD is associated with reporting that safety is predicted to a lesser extent (ologit, $n = 1{,}101$). Younger age or use of mammals other than rodents and NHPs is associated with the view that drug attrition is an important problem (logit, $n = 1{,}021$; DVM results not displayed because of small cell size). Holding an MD, not being an NIH-funded principal investigator (PI) or using NHPs or other non-rodent mammals is associated with the view that animal models (rather than study design) are the main issue driving drug attrition rates (logit, $n = 948$). Using mammals other than rodents and NHPs is associated with perceiving that the reproducibility 'crisis' is an important problem (logit, $n = 994$; DVM results not displayed because all DVM researchers reported that reproducibility is an important problem). Refer to Table 5 for additional details. *P* values and results from categories not displayed in the figure.

Most respondents indicated that investigators should be given more latitude to make minor protocol changes without IACUC approval (median score of 4 on a scale of 1–5) (Table 2). Those with IACUC experience were less likely to agree that researchers should be given such latitude (OR: 0.67; 95% CI: 0.52–0.86). Similarly, women were less likely than men (OR: 0.77; 95% CI: 0.61–0.97) to agree with such latitude, and those who had not recently received NIH funding were less likely to agree than those who had received NIH funding (OR: 0.61; 95% CI: 0.47–0.78). Respondents using NHPs were less likely than those using mice to agree that researchers should be given more latitude (OR: 0.53; 95% CI: 0.29–0.94). Finally, DVM respondents were less likely than PhD respondents to agree that researchers should be given additional latitude for protocol revision (OR: 0.34; 95% CI: 0.13–0.89).

On the issue of animal replacement, a minority of respondents believe that there will ever be viable alternatives to using live animals in their area of research (23%) (Table 2). Older respondents were less likely to believe that there would ever be viable alternatives (OR: 0.98; 95% CI: 0.97–1.00), and those with dual degrees were also less likely than those with PhDs to think that there would ever be such alternatives (OR: 0.53; 95% CI: 0.31–0.90). Compared to those who primarily use mice, researchers using mammals other than rodents or NHPs were more likely to think alternatives would become available (OR: 1.85; 95% CI: 1.03–3.31), as were those who had not recently received NIH funding (OR: 1.64; 95% CI: 1.19–2.26). Finally, most respondents perceive that an emphasis on reducing the number of animals used in research sometimes (57%) or often (21%) leads to studies in which too few animals are used to achieve robust scientific results (Table 2).

Public engagement. Respondents indicated that they were somewhat comfortable discussing their use of animals with non-scientists (median score of 3 on a scale of 1–4), and most (63%) reported being very open with non-scientists about their primary animal model species. Only 2.5% of researchers reported frequent personal criticism from non-scientists for their animal use, with 21% reporting sometimes being criticized. Most respondents reported either rarely (47%) or never (29%) being criticized. Most (68%) also indicated that scientists should be transparent about the limitations of animal research (Table 2). The results of the ordered logit analysis identifying factors associated with researcher attitudes about public engagement are provided in Table 7 and Fig. 5. Older respondents indicated a greater degree of comfort talking with non-scientists about their animal use (OR: 1.03; 95% CI: 1.02–1.04), and women reported being less comfortable than men (OR: 0.70; 95% CI: 0.55–0.89). Researchers primarily using cats or dogs reported less

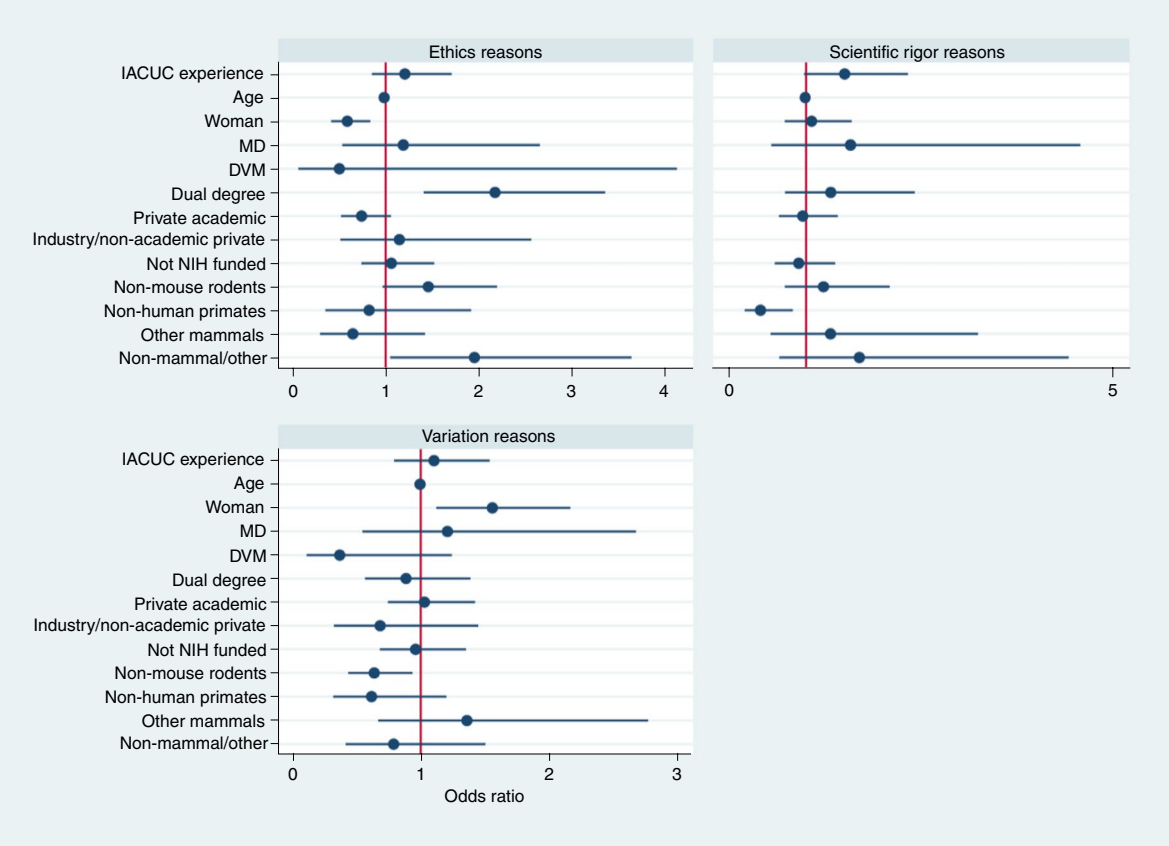

Fig. 3 | Age, gender, academic degree and primary animal model species are associated with endorsement of various factors contributing to reproducibility problems. Logit regressions, odds ratios with 95% confidence intervals. Younger age, being a man, holding a dual degree or using non-mammals is associated with endorsing one or more ethics reasons for reproducibility problems ($n = 1{,}107$). Using NHPs is associated with lower endorsement of scientific rigor reasons ($n = 1{,}068$; all researchers in private non-academic institutions selected scientific rigor reasons; results not displayed for DVM researchers because of small cell size). Being a woman is associated with endorsing one or more variation reasons, whereas using non-mouse rodents is associated with less endorsement of these reasons ($n = 1{,}107$). Refer to Table 5 for additional details. *P* values and results from categories not displayed in the figure.

comfort talking with non-scientists about their work than researchers using animals other than cats, dogs or NHPs (OR: 0.39; 95% CI: 0.15–0.97). Older respondents, again, reported more openness with non-scientists about the particular species of animal used in their work (OR: 1.03; 95% CI: 1.01–1.04), whereas researchers using cats or dogs (OR: 0.21; 95% CI: 0.08–0.50) or NHPs (OR: 0.40; 95% CI: 0.23–0.68) reported less openness about the species of animal used in their work compared to those using other species. Regarding criticism from non-scientists, respondents who had served on an IACUC were more likely to report criticism by non-scientists for conducting research on animals compared to those who had not served (OR: 1.57; 95% CI: 1.22–2.02). Those using cats or dogs (OR: 3.02; 95% CI: 1.08–8.40) or NHPs (OR: 3.52; 95% CI: 2.02–6.13) were much more likely to report criticism by non-scientists as compared to those using other animals. Finally, older respondents were more likely to report that scientists should be transparent about the limitations of animal research (OR: 1.02; 95% CI: 1.00–1.03), and researchers working in industry and other non-academic institutions were more likely to support such transparency than those working at public academic institutions (OR: 2.34; 95% CI: 1.00–5.48).

Discussion

Overall findings. Data from this national survey support themes about translation, reproducibility and rigor that are probably familiar to biomedical scientists using vertebrate animals. Specifically, researchers were well aware of, and concerned about, problems in each of these areas of their science, yet they nevertheless perceived animal studies as valuable—indeed the large majority (77%) did not believe that there will ever be a viable replacement for the use of live animals in their research. Similarly, regarding research oversight, surveyed scientists were optimistic about its value in protecting animal welfare, with almost all agreeing that current welfare standards are sufficient. Despite these clear messages, differences in survey responses among researchers also point to diverse perspectives within the animal research community that defy a simple narrative. Most significant is the variability associated with the primary type of animal that surveyed scientists use in their work. Specifically, both researcher demographic characteristics and reasons driving primary animal selection varied by the type of animal used, and the type of animal primarily used heralded differences in perspective on most other issues queried. Other significant divergence in opinion appeared on the basis of professional role factors, including type(s) of degree held, workplace setting, type(s) of funding, experience on an IACUC and personal demographic characteristics of age and gender. Overall, these results identify a need to better understand and address not only general matters of translational science concern for the animal research community, but also perspectives of individuals with diverse experiences within the field. In the remainder of this discussion, key findings and their potential implications for the animal research community are addressed.

Table 6 | Factors associated with animal research oversight

	Category (odds ratio (95% CI); *P* value)				
	Animal research oversight system ensures animal welfare	**Animal research oversight system protects institutions**	**Animal research oversight system improves study design**	**Investigators should be given more latitude to make minor protocol changes**	**Believe there will ever be viable alternatives to using live animals in area of research**
Observations (*n*)	1,104	1,103	1,105	1,096	1,106
Model type	Ologit	Ologit	Ologit	Ologit	Logit
Response	Strongly disagree to strongly agree (1–5)	Strongly disagree to strongly agree (1–5)	Strongly disagree to strongly agree (1–5)	Strongly disagree to strongly agree (1–5)	Yes versus No
Ever served on an IACUC	1.58** (1.16–2.14); 0.004	0.99 (0.76–1.28); 0.908	1.13 (0.88–1.45); 0.332	0.67** (0.52–0.86); 0.002	0.85 (0.64–1.25); 0.513
Age (continuous)	1.01 (1.00–1.02); 0.134	1.00 (0.99–1.01); 0.664	1.02*** (1.01–1.03); <0.001	1.01 (1.00–1.02); 0.122	0.98* (0.97–1.00); 0.023
Gender (reference = man)					
Woman	0.88 (0.67–1.15); 0.346	0.76* (0.59–0.97); 0.028	1.00 (0.79–1.26); 0.989	0.77* (0.61–0.97); 0.029	0.99 (0.73–1.34); 0.946
Degree (reference = PhD)					
MD or equivalent	0.66 (0.33–1.19); 0.151	1.03 (0.56–1.92); 0.918	0.78 (0.45–1.34); 0.369	0.87 (0.50–1.52); 0.629	1.53 (0.77–3.03); 0.222
DVM or equivalent	0.45 (0.15–1.34); 0.15	0.55 (0.21–1.44); 0.221	1.62 (0.61–4.33); 0.334	0.34* (0.13–0.89); 0.029	0.37 (0.08–1.82); 0.222
Dual degree	0.99 (0.66–1.48); 0.945	1.04 (0.72–1.50); 0.832	1.01 (0.71–1.42); 0.975	1.16 (0.82–1.65); 0.398	0.53* (0.31–0.90); 0.019
Institution (reference = public academic)					
Private academic	1.36* (1.01–1.82); 0.04	0.97 (0.75–1.25); 0.821	1.15 (0.91–1.47); 0.242	0.94 (0.74–1.20); 0.613	1.04 (0.75–1.43); 0.815
Industry/non-academic private	1.17 (0.58–2.35); 0.665	0.99 (0.53–1.85); 0.966	1.00 (0.54–1.81); 0.971	0.68 (0.38–1.20); 0.179	1.19 (0.57–2.49); 0.636
NIH-funded PI in the past 5 years (reference = yes)					
No	0.70* (0.53–0.94); 0.016	0.77* (0.59–1.00); 0.049	1.00 (0.78–1.28); 0.983	0.61*** (0.47–0.78); <0.001	1.64** (1.19–2.26); 0.003
Primary animal model (reference = mice)					
Non-mouse rodents	0.76 (0.54–1.09); 0.134	0.76 (0.56–1.04); 0.090	0.93 (0.68–1.25); 0.614	1.04 (0.77–1.40); 0.796	0.86 (0.57–1.29); 0.455
Non-human primates	0.91 (0.46–1.79); 0.777	0.89 (0.50–1.61); 0.707	0.91 (0.52–1.59); 0.731	0.53* (0.29–0.94); 0.030	0.58 (0.24–1.40); 0.223
Other mammals	0.74 (0.43–1.28); 0.285	0.90 (0.55–1.50); 0.695	0.60* (0.37–0.97); 0.038	0.72 (0.44–1.19); 0.204	1.85* (1.03–3.31); 0.038
Non-mammal/other animal	0.68 (0.40–1.16); 0.155	1.29 (0.77–2.15); 0.334	0.55* (0.34–0.88); 0.013	0.93 (0.59–1.47); 0.756	0.71 (0.36–1.40); 0.324
Cut 1/constant	0.03*** (0.01–0.06); <0.001	0.02*** (0.01–0.03); <0.001	0.13*** (0.07–0.24); <0.001	0.09*** (0.05–0.16); <0.001	0.64 (0.30–1.37); 0.254
Cut 2	0.06*** (0.03–0.11); <0.001	0.04*** (0.02–0.07); <0.001	0.74 (0.42–1.30); 0.295	0.33*** (0.18–0.58); <0.001	–
Cut 3	0.09*** (0.05–0.19); <0.001	0.14*** (0.08–0.26); <0.001	2.25** (1.27–3.96); 0.005	0.55* (0.31–0.98); 0.043	–
Cut 4	0.72 (0.37–1.42); 0.346	0.62 (0.34–1.13); 0.116	13.28*** (7.39–23.87); <0.001	1.99* (1.12–3.54); 0.02	–

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

Primary animal model species. The reasons scientists selected particular animals as a primary species to use in their work differed in important ways. Mouse researchers were those who most commonly selected practical constraints (79%), such as the ease of procuring animals, cost, vivarium space or the availability of research tools as informing their species choice. These researchers were also the group most likely to select funder expectations (34%) as important for their animal model choice. By contrast, only 14% of NHP researchers and 15% of researchers using mammals other than rodents or NHPs selected practical constraints as driving

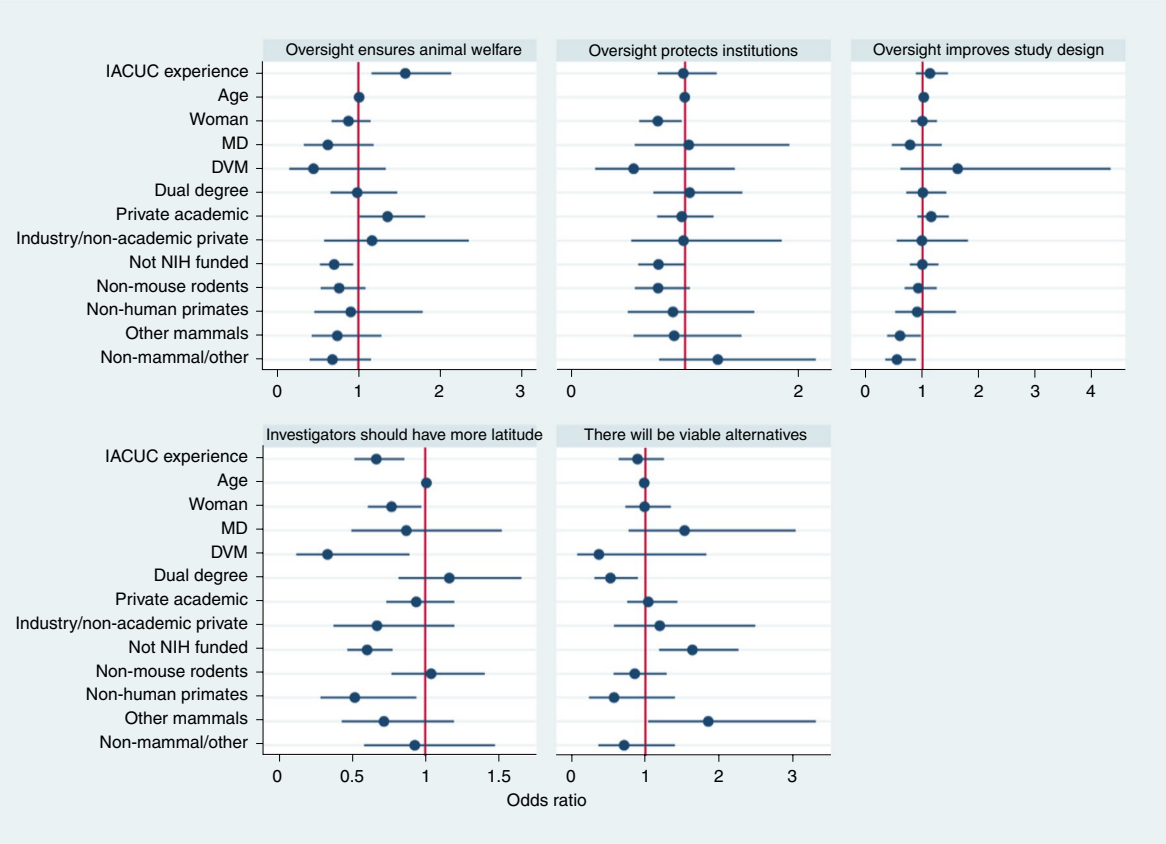

Fig. 4 | IACUC experience, age, gender, academic degree, institution type, NIH funding and primary animal model species are associated with views on animal research oversight. Logit or ologit regressions, odds ratios with 95% confidence intervals. IACUC service, being at a private academic institution (as compared to a public academic institution) or being an NIH-funded PI is associated with greater confidence that animal research oversight ensures animal welfare (ologit, $n = 1{,}104$). Being a man or being an NIH-funded PI is associated with greater confidence that animal research oversight protects institutions (ologit, $n = 1{,}103$). Older age is associated with greater confidence that animal research oversight improves study design, whereas using non-mammals or mammals other than rodents or NHPs is associated with less confidence (ologit, $n = 1{,}105$). Having IACUC experience, being a woman, holding a DVM, not being an NIH-funded PI or using NHPs is associated with less agreement that investigators should be given additional latitude to make minor protocol changes (ologit, $n = 1{,}096$). Younger age, not holding a dual degree, not being an NIH-funded PI or using mammals other than rodents and NHPs is associated with the view that there will be viable alternatives to the use of live animals in their field (logit, $n = 1106$). Refer to Table 6 for additional details and *P* values.

their animal model choice. These results imply that there are fewer barriers to the use of mice in research, whereas the use of NHPs and mammals other than rodents typically already involves overcoming practical hurdles[27,28]. Consistent with this interpretation is our finding that, although reasons pertaining to scientific value (e.g., how well the animal models the disease, advances scientific understanding or extrapolates to medical applications) were the most frequently selected reasons for animal model choice overall, these were least often selected by mouse researchers (86%), whereas 100% of NHP researchers selected at least one scientific value reason as underwriting their choice of primary animal. Because NHP use is heavily scrutinized[29,30], these researchers may feel a particular burden to justify their animal choice on a scientific basis. Overall, researchers using non-rodent vertebrate animals may appreciate additional support to overcome practical hurdles in their science. In addition, there is an apparent need to promote the clear articulation of scientific rationales for the selection and use of mice in research to avoid them as a default choice of vertebrate animal model[31,32].

Translation, reproducibility and rigor. The survey findings regarding translation, reproducibility and rigor similarly indicate patterns of substantially diverse opinion depending both on the primary type of animal that researchers use and their professional and demographic profiles. Although most indicated that animal studies predicted safety in humans to at least a moderate extent (90%), researchers using NHPs (and those using mammals other than rodents) were more confident than those using mice that animal safety data could be extrapolated to humans. However, researchers with an MD degree were less likely than PhD researchers to report that animal studies predicted safety in humans, even when controlling for the animal model used. These findings probably reflect researchers' individual circumstances and experiences. For example, NHP researchers may have selected these animals precisely because of a perception of their better translation to humans[33,34]. Compared to PhD scientists, MD researchers, given their human-focused medical training, may be more acutely aware of the limitations in moving from rodent models into humans[6,11,35]. This interpretation is borne out by the finding that MD respondents were also more likely than PhD researchers to think that low success rates in drug development are due to problems with animal models. Interestingly, researchers using NHPs (and those using other non-rodent mammals) were also more likely than mouse researchers to indicate that drug attrition rates are due to problems with animal models and that these high rates are an important problem. These researchers may place the onus for poor

Table 7 | Factors associated with public engagement

	Category (odds ratio (95% CI); *P* value)			
	Comfort discussing animal use with non-scientists	**Openness in identifying animal species used with non-scientists**	**Faced personal criticism about use of animals**	**Transparency regarding limitations of animal research**
Observations	1,103	1,105	1,106	1,095
Model type	Ologit	Ologit	Ologit	Logit
Response	More comfortable versus less comfortable (1–4)	Open versus prefer not to tell (1–3)	Higher frequency (never, rarely, sometimes, often/always)	Should be transparent versus should be prepared to discuss
Ever served on an IACUC	1.18 (0.92–1.53); 0.195	0.93 (0.70–1.23); 0.591	1.57*** (1.22–2.02); 0.001	0.90 (0.67–1.21); 0.500
Age (continuous)	1.03*** (1.02–1.04); <0.001	1.03*** (1.01–1.04); <0.001	0.99 (0.98–1.00); 0.232	1.02* (1.00–1.03); 0.013
Gender (reference = man)				
Woman	0.70** (0.55–0.89); 0.004	0.89 (0.68–1.15); 0.371	1.24 (0.98–1.58); 0.075	0.98 (0.74–1.28); 0.855
Degree (reference = PhD)				
MD or equivalent	0.96 (0.54–1.70); 0.855	0.78 (0.41–1.49); 0.458	1.06 (0.60–1.85); 0.852	1.68 (0.79–3.57); 0.177
DVM or equivalent	1.09 (0.37–3.23); 0.879	0.68 (0.22–2.08); 0.499	0.90 (0.32–2.56); 0.850	0.53 (0.16–1.70); 0.285
Dual degree	1.29 (0.91–1.83); 0.158	1.07 (0.72–1.58); 0.734	1.06 (0.75–1.49); 0.760	0.83 (0.55–1.23); 0.344
Institution (reference = public academic)				
Private academic	1.19 (0.93–1.52); 0.176	1.13 (0.86–1.48); 0.389	0.82 (0.64–1.05); 0.111	0.97 (0.73–1.28); 0.810
Industry/non-academic private	0.76 (0.41–1.40); 0.376	0.74 (0.38–1.44); 0.371	1.06 (0.56–2.01); 0.852	2.34* (1.00–5. 48); 0.050
NIH-funded PI in the past 5 years (reference = yes)				
No	0.97 (0.75–1.25); 0.811	1.00 (0.75–1.33); 0.972	1.08 (0.84–1.40); 0.551	0.98 (0.72–1.31); 0.868
Primary animal model (reference = all others)				
Cat or dog	0.36* (0.15–0.97); 0.044	0.21*** (0.08–0.50); 0.001	3.02* (1.08–8.40); 0.035	0.64 (0.23–1.77); 0.388
NHP	0.840 (0.49–1.44); 0.531	0.40*** (0.23–0.68); 0.001	3.52*** (2.02–6.13); <0.001	1.96 (0.95–4.04); 0.068
Cut 1/constant	0.122*** (0.06–0.24); <0.001	0.26*** (0.13–0.52); <0.001	0.360*** (0.20–0.66); 0.001	0.94 (0.47–1.86); 0.856
Cut 2	1.05 (0.58–1.91); 0.873	1.88 (0.95–3.70); 0.068	2.93*** (1.60–5.37); <0.001	–
Cut 3	6.83*** (3.72–12.53); <0.001	–	39.22*** (19.36–79.43); <0.001	–

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

translation on the use of rodent models in particular. Overall, these findings, as well as the split over whether drug attrition rates are generally due to problems with study design or animal models, show a lack of consensus within the animal research community regarding what solutions might best improve drug development. Because most researchers queried (62%) also viewed this issue as an important problem, more investigation into finding appropriate solutions is warranted.

Even more than drug attrition rates, researchers agreed that lack of reproducibility of preclinical animal studies is an important problem (74%). As to factors driving failures of reproducibility, however, no set of issues fully dominated. Although scientific shortcomings (i.e., lack of rigor in the design of studies or detail in their reporting) were most often cited, variation between studies because of differences in environments, personnel or the animals themselves were also commonly selected factors. As with the other findings, there was significant diversity among researchers in the selection of these factors based on the animal model that they primarily used. Relevant to respondents' divergent views are different perspectives in the scientific literature regarding how to manage variability in animal research. Some researchers argue that studies should be designed in ways that account for variability and thus have greater potential for generalizability[36,37], whereas others focus on doing more to control both animal models and environments[17,38,39]. Although it cannot be gleaned from the present study how this debate influenced respondents' perceptions, a better understanding of the contributing roles of scientific rigor and variability in reproducibility is needed.

Ethical issues including the falsification of results or study bias due to conflicts of interest were least commonly selected as contributors to reproducibility problems, even though they have been cited as concerns in the literature[1,40]. The contribution of ethical issues was perceived differently depending on the type of animal that scientists primarily used, as well as by age, gender and degree type. Of particular interest, women were both less likely than men to select ethical issues as contributing to reproducibility problems and more likely than men to select variability factors as main

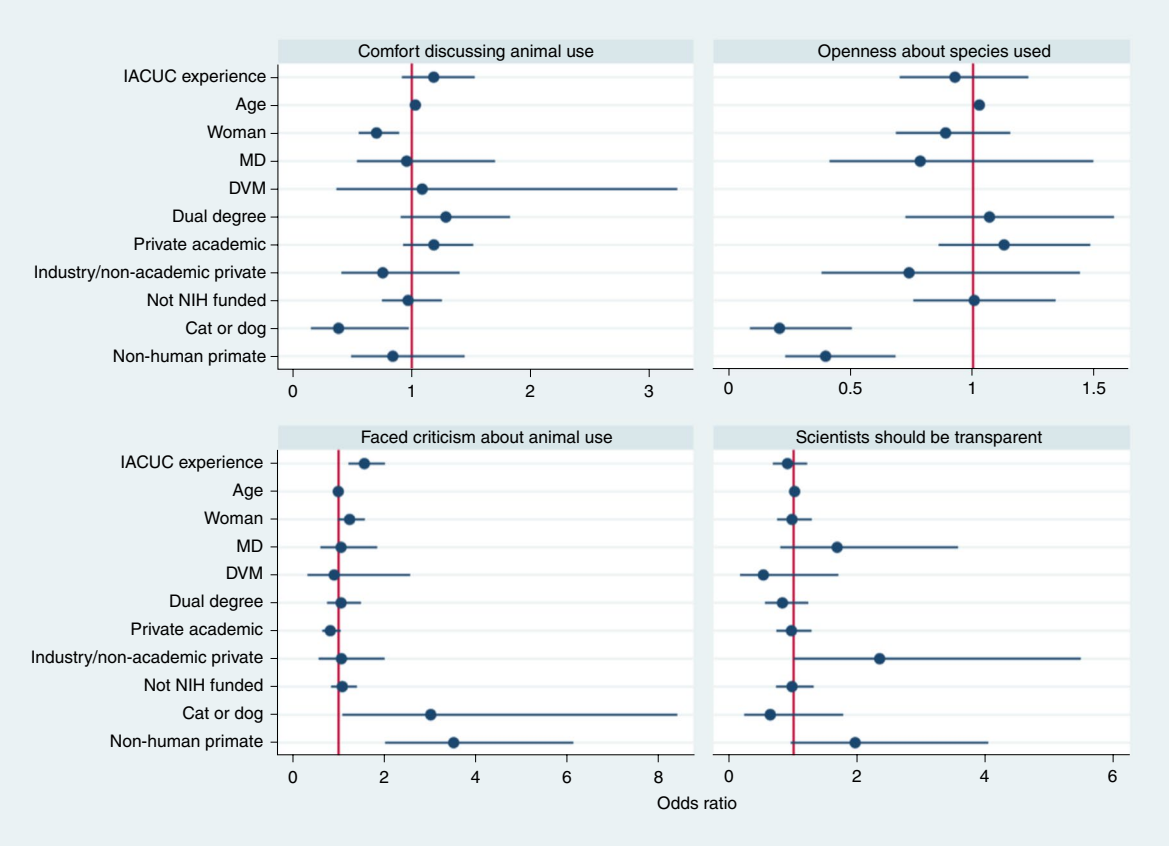

Fig. 5 | IACUC experience, age, gender, institution type and primary animal model species are associated with public engagement practices and experience. Logit or ologit regressions, odds ratios with 95% confidence intervals. Older age is associated with greater reported comfort discussing animal use with non-scientists, whereas being a woman or using cats or dogs is associated with less comfort (ologit, $n = 1{,}103$). Older age is associated with greater openness with non-scientists in identifying their used animal species, whereas using cats or dogs or NHPs is associated with preferring not to disclose this information (ologit, $n = 1{,}105$). IACUC experience or using cats or dogs or NHPs is associated with reporting more frequent personal criticism about the use of animals (ologit, $n = 1{,}006$). Older age or being at an industry/non-academic private institution is associated with the view that researchers should be transparent about the limitations of animal research (logit, $n = 1{,}095$). Refer to Table 7 for additional details and *P* values.

contributors. The finding regarding the contribution of ethical issues to reproducibility problems is consistent with some evidence that women are less likely than men to have personally engaged in falsification or bias[41].

Oversight. The system of research oversight tries to balance the appropriate role of the IACUC, given the volume of research that most boards oversee on one hand and concern within the animal research community of the already heavy 'burden' of oversight compliance on the other[42,43]. Consistent with the theme of oversight burden, most respondents at least somewhat agreed with granting researchers more latitude in making minor protocol changes. However, multiple subgroups of researchers were less sanguine about this proposal. Among these were individuals with IACUC experience and veterinarians, who may better understand the reasons why even minor protocol changes must be reviewed to protect animal welfare. Similarly, NHP researchers may view strong oversight as underwriting their justification for studying these animals and therefore resist any weakening of this system. Overall, given the discrepancy between IACUC and non-IACUC researchers' views, IACUCs may need to do more to explain why additional protocol latitude is inconsistent with oversight goals.

Other oversight issues holding less resonance with respondents were reduction and replacement, two of the three Rs widely considered the foundation of the humane use of animals in science[21]. Despite the oversight requirement to consider replacing the use of live animals[20], the survey results show that a strong majority of researchers believe there will never be a replacement for the use of live animals in their work. At the practical level, this may mean that oversight requests—for example, literature searches for alternatives—may be met with cynicism or low effort if researchers hold a background belief in the necessity of live vertebrate animals for their work. Such opinions, whether well justified or not, may be self-fulfilling because funding to investigate alternatives to live animal studies is generally a low priority despite some important advances already made in organoids or other alternatives[44]. Similar to the results regarding replacement, 78% of surveyed researchers indicated that reducing the numbers of animals used in research can at least sometimes lead to faulty science. This apparent tension over the 3 R goal of reducing animal numbers is consistent with an observation that improved rigor within animal research could result from better statistics consultation to help researchers appropriately power their studies[14]. In sum, although biomedical researchers generally agreed that oversight goals are met in terms of animal welfare, additional work is needed if replacement and reduction goals are to succeed as more than regulatory hurdles.

Public engagement. Regarding public engagement, the survey results reveal somewhat more openness among animal researchers than rhetoric about the divisiveness of the topic might imply[45,46]. Most researchers indicated that they are at least somewhat comfortable talking with nonscientists about their animal use, are open

about the species of animals that they use and are rarely or never personally criticized for their use of animals. Nevertheless, working with a sensitive species of animal, such as cats and dogs, was associated with being less comfortable talking about animal use. Moreover, these same researchers, along with NHP researchers, reported being less open about the species that they work with and more likely to have been personally criticized. These results serve as an important reminder that perceived barriers to public transparency about animal research may vary depending on how much social controversy is associated with the research. At the same time, researchers' general willingness to engage the public about their use of animals is consistent with recent efforts to increase transparency within biomedical science[47,48]. The result that researchers supported transparency even about the shortcomings of animal use shows the potential for such engagement to move beyond simplistic reiteration of the benefits of animal research for human health[49].

Limitations. This study has some important limitations. There is no national database to draw from to ensure that this study represents the general demographic profile of biomedical researchers using vertebrate animals in the United States. Specifically, it is unclear whether the underrepresentation of women and some racial and ethnic minorities is reflective of broader realities in animal research or constitutes a limitation of this study. Although searches of additional historically black colleges and universities were conducted to increase sampling pool diversity, low numbers of respondents in some racial and ethnic groups, as well as individuals identifying as gender fluid, meant regression analyses for these categories could not be conducted. In addition, because the identification of researchers meeting study criteria was web based, older, more-established researchers and those in public academic institutions were probably overrepresented. Excepting for non-academic public institutions, the association of respondent views with type of workplace institution and age was analyzed, and these results may be extrapolated to the broader population and tested if a relevant national database becomes available. A second limitation of this study is that information about respondents' research field was not collected, and so the analyses do not reflect field-based differences. A third limitation is that respondents were not asked about their personal use of non-animal and other alternative research methods, and such information may help contextualize perspectives on alternatives to the use of live animals in research.

Conclusion. Attrition rates in drug development, among other factors, have spurred growing awareness of the need for better reproducibility and rigor in preclinical research using animals. Translation of biomedical interventions from bench to bedside is further complicated by how different animal species best model human diseases and disorders, as well as the need to protect animals during the research process. The purpose of this national survey was to query the opinions of biomedical researchers using vertebrate animals on these topics and their perspectives on public engagement over their use of animals. The resulting data show that while scientists have predictable views about the significance of animal studies and the strength of welfare protections, there are important and nuanced differences in researcher perspectives depending on the animals that they use and demographic and experiential factors. These findings indicate that the animal research community must not be painted as monolithic in its perspectives on important questions having to do with scientific practices, oversight or public engagement. Furthermore, although scientists are concerned about apparent shortcomings in translation, reproducibility and rigor in their work, they do not necessarily agree on what is driving these problems when they occur. This indicates that there is no general consensus on the most effective solutions to these problems. Because the value of using vertebrate animals in biomedical research often depends on success in advancing human health, finding such solutions should be a priority.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41684-021-00890-0.

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Methods

Survey instrument. A 45-item survey was developed to query scientists' perceptions of translational science issues, research oversight and animal welfare, sex as a biological variable (SABV) policies and practices and societal views of animal research (see Supplementary Information for the instrument). In addition, the survey collected data about scientists' research experience and demographic information. The survey was developed by authors R.L.W. and J.A.F. on the basis of the goals of the overall research project and preliminary results from prior qualitative interviews with biomedical researchers using vertebrate animals. After developing a first draft of the survey, it was refined in consultation with an independent expert in survey methodology. The survey was then piloted with five laboratory animal researchers to solicit feedback on the questions and to establish face validity. After this stage of development, the survey was streamlined to re-order several questions and to cut several others to shorten the overall length of the instrument. With the use of Qualtrics, the survey was administered online in late March 2020 and was available to respondents over a 6-week period. The Biomedical Institutional Review Board at the University of North Carolina at Chapel Hill deemed the study to be exempt from oversight.

Study participants and recruitment. No pre-existing list of biomedical researchers who use vertebrate animals in their studies was available to draw from for use in this survey. To obtain broad national representation from biomedical researchers using vertebrate animals, a database was generated of potential respondents who work in academia and public or private research institutions in the United States. Organizations included: (1) academic institutions from US News and World Report's 2019 top 100 colleges and universities that were also 2018 Carnegie R1 doctoral research institutions, (2) the 10 top-ranked historically black colleges and universities that were not already included, (3) the top 20 highest-earning pharmaceutical companies and (4) other private institutions that are well-known hubs of biomedical animal research. For each institution, web searches were conducted to identify relevant researchers (see Supplementary Information for institutions and academic departments). For academic institutions, departments most likely to have faculty involved in biomedical research using vertebrate animals were prioritized. All biomedical researchers with a PhD, MD, DVM or other equivalent degree who, on the basis of their research profile and publications, conducted research with live vertebrate animals and who had a publicly available email address were included in the database. The final database included 4,910 eligible researchers.

To recruit participants, an email was sent with information about the study to the entire database with a request to complete the survey. To prevent multiple entries from single individuals and/or unsolicited responses, Qualtrics generated a single-use unique survey link for each potential respondent. Solicited respondents were asked to affirm that their research involved the use of vertebrate animals as part of the electronic consent to participate as well as through two other survey questions (see the survey instrument in Supplementary Information). To improve the response, follow-up emails were sent 1 week and 1 month after the initial request, but only to those individuals who had not completed the survey or opted out of receiving emails. Qualtrics provided confidentiality to respondents by blinding details of which potential participants completed the survey. Participation was incentivized by allowing respondents the opportunity to enter a drawing to win one of 20 $100 Visa gift cards.

Statistical analysis. All analysis was completed by using Stata (v16.1). Only respondents who completed the survey were included in the analysis. If respondents reached the end of the survey and selected responses to questions on each page, then the survey was considered complete. Descriptive statistics were generated for all variables with potential implications for attitudes and beliefs related to animal research oversight, public engagement and the translational value of animal research. Regression analysis was used to identify demographic and attitudinal factors associated with each outcome of interest. Relationships were modeled by using logistic regression for binary outcome variables, ordinal logit (ologit) for ordered or Likert-type outcome variables and multinomial logit for categorical outcome variables. We tested whether ordinal models met the parallel lines assumption by using gologit2 with autofit, and there were no differences in coefficients across levels; thus, we used ologit for all ordinal models. For regression models, a one-unit change in an independent variable is associated with a percentage change in the conditional probability of the outcome of interest. Respondents who selected options that were very rare (such as degree other than PhD, MD or DVM) were excluded from regression analyses that used the variable in question; the excluded response options are shown in Tables 1 and 2. Observations with missing data on any variable were dropped from that specific model but not from the dataset. Scientists' views on SABV are reported separately[50]. Some data on scientists' perceptions of translational science issues were also used to analyze their views on SABV, as indicated in Table 2.

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

Processed survey data reported on in this article and information about the related analyses are deposited in UNC Libraries Digital Repository at https://cdr.lib.unc.edu/concern/data_sets/k643bb08t?locale=en. Data have been redacted to protect participant privacy. Researchers requiring access to removed data may contact R.L.W. at the provided email address.

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Author contributions

J.A.F. and R.L.W. designed the survey. All authors contributed to the analysis plans and interpretation of the findings, and K.W.S. conducted the statistical analysis. All authors contributed to the writing and revising of the work for intellectual content, with R.L.W. taking the lead in drafting. All authors gave final approval of the submitted version and agreed to be accountable for all aspects of the work.

Competing interests

The authors declare no competing interests.

Additional information

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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Qualtrics
Data analysis	STATA version 16.1

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

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Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	Quantitative cross-sectional survey of scientists' perceptions of translational science issues, research oversight and animal welfare, sex as a biological variable policies and practices, and societal views of animal research
Research sample	The sample includes biomedical researchers who use vertebrate animals in their studies. To obtain broad national representation from established biomedical researchers using vertebrate animals, a database was generated of potential respondents who work in academia and public or private research institutions in the United States. See below for more details.
Sampling strategy	A database was generated of potential respondents who work in academia and public or private research institutions in the United States. Organizations included: (1) academic institutions from US News and World Report's 2019 top 100 colleges and universities that were also 2018 Carnegie R1 doctoral research institutions; (2) the 10 top-ranked historically black colleges and universities that were not already included; (3) the top 20 highest-earning pharmaceutical companies; and (4) other private institutions that are well-known hubs of biomedical animal research. For each institution, web-searches were conducted to identify relevant researchers. For academic institutions, departments most likely to have faculty involved in animal research were prioritized, such as biomedical engineering, genetics, neuroscience, pathology, and psychiatry (See Supplemental Materials for a full listing of institutions and departments). All biomedical researchers with a PhD, MD, DVM, or other equivalent degree who, based on their research profile and publications, conducted research with live vertebrate animals and who had a publicly available email address were included in the database. The final database included 4910 eligible biomedical researchers.
Data collection	Data were collected online using Qualtrics. Qualtrics provided confidentiality to respondents by blinding details of which potential participants completed the survey.
Timing	The survey was administered online in late March 2020 and was available to respondents over a 6-week period
Data exclusions	We included only complete surveys in the analysis. Complete surveys were those in which respondents reached the end of the survey and selected responses to questions on each page. Observations with missing data on any variable included in a model were dropped from that specific model, not from the dataset.
Non-participation	4910 biomedical researchers using vertebrate animals were sent a survey invitation, and 1234 (25.13%) participated, with a completion rate of 96.19% or 1187 respondents.
Randomization	n/a

Reporting for specific materials, systems and methods

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Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	Most respondents were men (64.36%), and the majority of respondents were White (79.15%). Respondents' median age was 52, and most had more than 20 years of experience with animal research (55.14%). PhD (82.77%) was the most commonly held

degree. Two-thirds of respondents (66.16%) worked at public academic institutions, and most had recent funding from NIH (71.96%). Most researchers (68.16%) reported primarily using mice, though respondents used a diverse range of animal species.

Recruitment

To recruit participants, an email was sent with information about the study to the entire database with a request to complete the survey. To prevent multiple entries from single individuals and/or unsolicited responses, Qualtrics generated a single-use, unique survey link for each potential respondent. To improve the response, follow-up emails were sent one week and one month after the initial request, but only to those individuals who had not completed the survey or opted out of receiving emails. Qualtrics provided confidentiality to respondents by blinding details of which potential participants completed the survey. Participation was incentivized by allowing respondents the opportunity to enter a drawing to win one of 20 $100 Visa gift cards.

Ethics oversight

The Biomedical Institutional Review Board at the University of North Carolina at Chapel Hill deemed the study to be exempt from oversight.

Note that full information on the approval of the study protocol must also be provided in the manuscript.