

The use of fluoxetine by veterinarians in dogs and cats: a preliminary survey

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ABSTRACT

Objective: To describe the prescribing habits of a sample of small animal veterinarians pertaining to use of fluoxetine in dogs and cats.

Design: Exploratory descriptive survey using a questionnaire, available on paper and through email, distributed to small animal veterinarians by convenience sampling.

Participants: Veterinarians practicing small animal medicine in North America contacted by email and at local veterinary meetings.

Results: Of 127 initial respondents, 106 prescribed fluoxetine for dogs and/or cats. The majority (91 per cent) indicated the drug be given once every 24 hours. Respondents used one or more formulations of fluoxetine. Of those who prescribed fluoxetine for both dogs and cats (57 per cent), 80 per cent used a generic form. A third prescribed fluoxetine only for dogs (31 per cent) and 72 per cent of these prescribed the US Food and Drug Administration approved product that was available at that time. The primary use of fluoxetine was related to behaviour problems. Overall for dogs, uses of fluoxetine were organised into five major categories by the investigators: Anxieties, Aggression, Compulsive Disorders, Phobias/Fear and Other, Anxieties being the most common. Of those who prescribed fluoxetine, 12 per cent did so only for cats and the majority of these prescribed generic (58 per cent) and or compounded (42 per cent) forms. Overall for cats, uses of fluoxetine were organised into six major categories: Elimination behaviours, Anxieties, Aggression, Dermatologic/Grooming, Compulsive Disorders and Other, Elimination behaviours being most common.

Conclusions: This study indicates that practitioners prescribed fluoxetine in generic, proprietary and compounded formulations for a variety of behaviour problems of dogs and cats. The broad use by the respondents suggests how important psychotropic drugs are in veterinary medicine. Research, information and continuing education regarding such drugs and animal behaviour should be made available to the general practitioner.

INTRODUCTION

Use of pharmacological interventions for treating behavioural disorders in dogs and cats in veterinary practice is recommended

by behaviour specialists (Hart and others 2006, Horwitz and Neilson 2007, Horwitz and Mills 2009, Landsberg and others 2013, Overall 2013). Psychopharmacological treatments in veterinary medicine are believed to be most helpful in conjunction with behaviour modification (Marder 1991). With numerous non-approved behaviour modifying drugs available and few approved by government agencies in the USA or Europe, it would be beneficial to assess the prescribing practices amongst small animal veterinarians.

Fluoxetine hydrochloride, a selective serotonin reuptake inhibitor, is one of the commonly used drugs in small animal behavioural medicine. The US Food and Drug Administration (FDA) first approved fluoxetine under the brand name Prozac (Eli Lilly) in 1987 for treatment of depression in people. However, its use soon expanded to other non-approved and approved diagnoses in people. Fluoxetine was soon adopted by veterinarians for use in clinical small animal medicine (Rapoport and others 1992). Even before its labelled use, fluoxetine was widely prescribed in veterinary medicine for several behaviour problems (Dodman and Shuster 1994, Dodman and others 1996, Pryor and others 2001, Hart and others 2005). The effectiveness of the drug, eventual availability of generic formulations and affordability likely contributed to the use of fluoxetine in small animal medicine. In January of 2007, the FDA approved Reconcile (fluoxetine made by Elanco) for use in dogs for separation anxiety in conjunction with behavioural modification.

In human medicine, surveys of prescribing practices regarding fluoxetine demonstrate widespread acceptance and use for non-approved diagnoses (Mandos and others 1990, Levin and DeVane 1993). However, similar studies pertaining to dosage schedules and off-label use have not been undertaken in veterinary medicine. Most behaviour textbooks recommend once a day dosing

without specifying AM or PM. There is a need for more research and understanding of the use of fluoxetine and other behaviour modifying drugs in veterinary medicine. The objective of this study was to describe the prescribing habits of a sample of small animal veterinarians for fluoxetine use in dogs and cats. This study is an initial step in investigating the use of psychopharmacological drugs in veterinary behaviour medicine.

MATERIALS AND METHODS

Questionnaire

A cross-sectional study was used to describe the use of fluoxetine in dogs and cats. A one-page single-sided questionnaire (see online supplemental file 1) containing eight questions pertaining to: frequency and timing of dosage, the form of fluoxetine prescribed (Compounded, Generic form (not compounded), Prozac, Reconcile or Other), indications for prescribing fluoxetine in dogs and cats, and demographic questions of year of graduation and veterinary school of the prescribing veterinarian, was distributed through email or local veterinary meetings. Three demographic questions, and the question 'For what do you prescribe fluoxetine/Prozac/Reconcile?' in dogs and cats, were open-ended. Respondents who agreed to participate further in the study were sent follow-up emails requesting more specific information on the form(s) of fluoxetine used and instructions regarding administration.

Survey population

Email invitations to participate in the study were sent to Western University of Health Sciences small animal clinical faculty, preceptors and alumni, local area hospitals and professional contacts of the investigators. The questionnaire was also distributed at local veterinary meetings. Participants were encouraged to share the questionnaire with as many contacts as possible. The

questionnaire stated that all of the information provided would be treated as confidential and all data would be pooled and reported in aggregate. No additional verbal or ancillary materials/instructions were given to the participants. The only inclusion criterion was that participants practice small animal medicine (exclusive, predominant or mixed, at least at a part-time level). There were no exclusion criteria and all completed or partially completed surveys were included in analysis. The participants could return the survey by fax, email or by hand. All data were collected from June through December, 2013. The study protocol was reviewed and approved by the Western University of Health Sciences Institutional Review Board.

Statistical analysis

Data from the survey responses were tabulated and descriptive statistics were used to summarise survey results (SAS 9.2, SAS Institute, Cary, North Carolina, USA). The behavioural indications specified by veterinarians for prescribing fluoxetine in dogs and cats were organised into major categories by the investigators. Chi-squared tests or Fisher's exact tests (where $n < 5$) were used to compare responses between veterinarians who graduated before or during/after 2007, the year Reconcile was approved by FDA for separation anxiety in dogs. $P < 0.05$ was considered statistically significant.

RESULTS

One hundred and twenty-seven questionnaires were returned (Fig 1). The respondents were practicing small animal veterinarians in the USA and Canada (representing 21 veterinary schools in the USA and 9 foreign veterinary schools), ranging from <1 to 45 years postgraduation. The majority of respondents ($n=106$, 83 per cent), prescribed fluoxetine to dogs and/or cats, and prescribed it once every 24 hours ($n=96$, 91 per

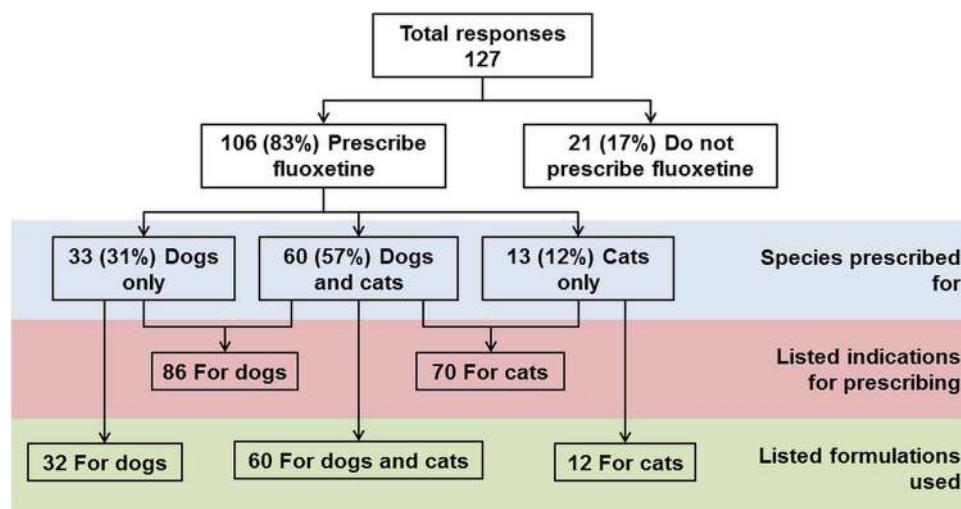


FIG 1: Flow chart showing number of responses to survey questionnaire related to prescribing habits of fluoxetine for dogs and cats

cent). Of those prescribing the drug once every 24 hours, 61 per cent ($n=57$) did not specify either AM or PM dosing and 36 per cent ($n=34$) specified AM dosing (Fig 2). The following reasons were reported for choosing AM dosing: the behavioural signs occur during day ($n=8$), convenience ($n=3$), increased activity during the day ($n=2$) and 'habit' ($n=1$). One respondent reported choosing PM dosing so the drug levels would be at peak in the morning for getting the patient through the day.

Veterinarians used one or more formulations of fluoxetine, that is, compounded, generic (not compounded), Prozac and Reconcile. Practitioners who prescribed fluoxetine both for dogs and cats ($n=60$), largely used a generic form ($n=48$, 80 per cent). Practitioners who used fluoxetine for dogs but not for cats ($n=33$), generally prescribed Reconcile ($n=23$, 72 per cent). Practitioners who prescribed fluoxetine only for cats but not for dogs ($n=13$), used a generic ($n=7$, 58 per cent), or a compounded ($n=5$, 42 per cent) form (Fig 3).

Veterinarians who used only one form of fluoxetine ($n=57$) and responded to the follow-up email ($n=20$, 35 per cent) reported following reason/s for choice: cost ($n=8$, 40 per cent), availability ($n=4$, 20 per cent), preference for the FDA approved drug ($n=4$, 20 per cent), ease of administration and dosing ($n=4$, 20 per cent), personal experience with good response to specific form ($n=3$, 15 per cent), convenience ($n=2$, 10 per cent) and familiarity with the specific product ($n=1$, 5 per cent). Veterinarians who used more than one form of fluoxetine ($n=47$), and responded to the follow-up email ($n=15$, 32 per cent), reported following reason/s to decide which formulation to use for a case: availability ($n=9$, 60 per cent), ease of administration and dosing ($n=6$, 40 per cent), cost ($n=3$, 20 per cent), species

($n=3$, 20 per cent), preference for veterinary approved drug ($n=2$, 13 per cent) and owner request ($n=2$, 13 per cent).

Fluoxetine was prescribed for dogs for a wide variety of behaviours. The 32 indications listed by the veterinarians for dogs were organised into five major diagnostic categories: Anxieties, Aggression, Compulsive Disorders, Phobias/Fear and Other. Behaviour problems related to Anxieties were the most common reasons for prescribing fluoxetine in dogs ($n=103$), followed by Aggression ($n=23$), Other ($n=21$), Compulsive Disorders ($n=15$) and Phobias/Fear ($n=8$). The most common indications in the Other category were 'behavioural issues/problems', chronic lick granuloma, destructive behaviour, hyperactivity, allergy and excessive barking (Table 1).

Fluoxetine was also prescribed for a wide variety of behaviours in cats. The 22 indications for cats were organised into 6 major diagnostic categories: Elimination behaviours, Anxieties, Aggression, Dermatologic/Grooming behaviours, Compulsive Disorders and Other. Elimination behaviours were the most common reason for prescribing fluoxetine in cats ($n=65$), followed by Anxieties ($n=28$), Aggression ($n=17$), Other ($n=10$), Dermatological/Grooming behaviours ($n=9$) and Compulsive Disorders ($n=7$). The most common indications in the Other category were 'behavioural issues/problems', pica and tail chasing (Table 2).

Responses were compared among respondents who graduated before 2007 ($n=69$) and those who graduated in/after 2007 ($n=35$). No significant differences among the two groups of graduates were found regarding the following prescribing habits: whether the drug was prescribed in dogs or cats or both ($P=0.4$), frequency of dosage ($P=0.7$), schedule of dosing ($P=0.5$) and formulations used ($P=0.4$) (Table 3a-d). Results

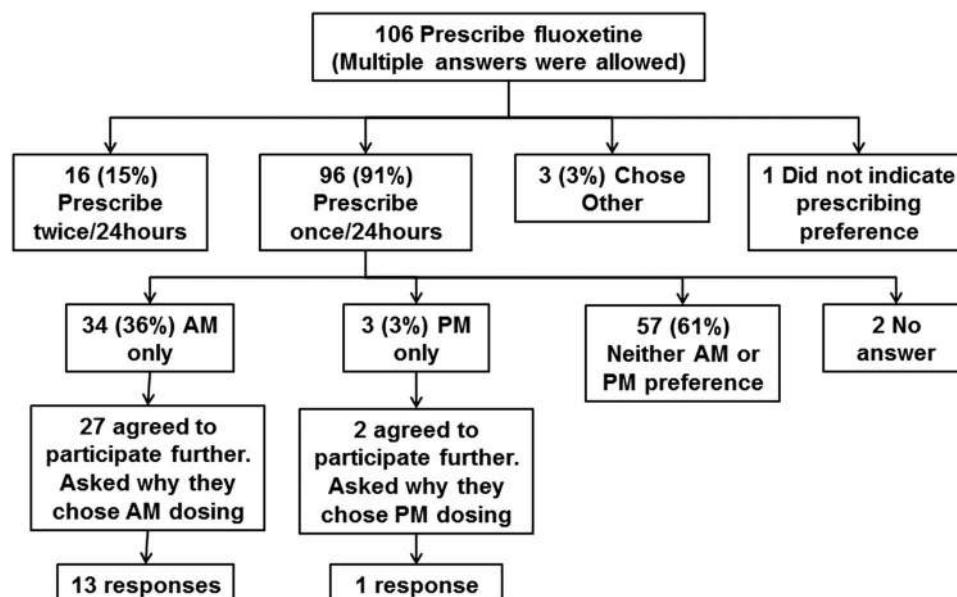


FIG 2: Flow chart showing number of responses to survey questionnaire related to dosing schedule for dogs and cats

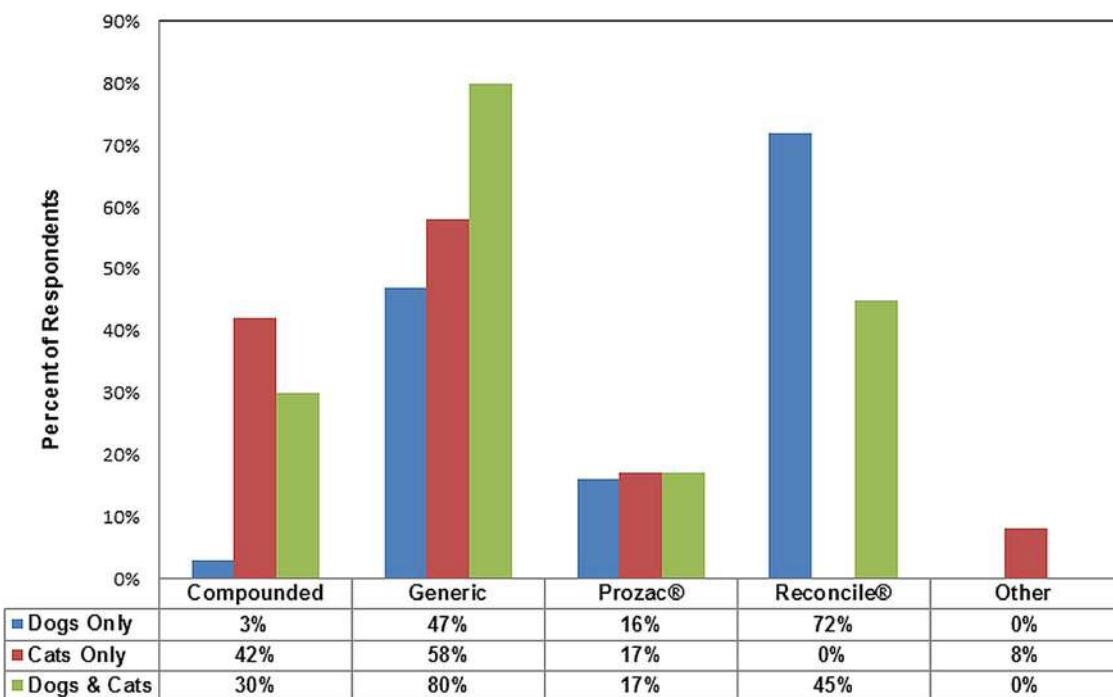


FIG 3: Percentage of veterinarians using specific formulations of fluoxetine for dogs only (blue bars, N=32), cats only (red bars, N=12), and dogs and cats (green bars, N=60). More than one formulation may have been chosen. For example for *Dogs Only*, 23 respondents indicated use of Reconcile [(23/32)×100=72%]

were not compared between specialists and general practitioners due to small sample size of the former (three behaviourists, three internal medicine specialists, three board certified practitioners, one surgeon, and one theriogenologist).

DISCUSSION

Results of the present survey indicate that fluoxetine is prescribed by small animal veterinarians for a variety of behavioural disorders in dogs and cats. Generic formulation is the most commonly prescribed form of the drug and the majority of the responding veterinarians prescribe fluoxetine to be administered once a day. This dosage schedule is found in the literature for several conditions in dogs and cats (Dodman and Shuster 1994, Overall 2001, Simpson and Papich 2003). For dogs, this is in accordance with directions for administration of the veterinary approved drug Reconcile for separation anxiety (Simpson and others 2007). The majority of those who prescribed fluoxetine once every 24 hours did not indicate AM or PM administration. Although no study has been done on the efficacy of AM versus PM dosing of fluoxetine in companion animals, a study in people did not show any significant difference in efficacy of morning versus evening dosing (Usher and others 1991).

Respondents reported using one or more forms of fluoxetine. At the time of the present study (June–December 2013), several formulations of fluoxetine were available for use in veterinary medicine (generic fluoxetine, Reconcile, Prozac, compounded formulations). The

manufacturing of Reconcile was discontinued in the USA in the August of 2013. The authors do not know how many respondents had Reconcile in stock at the time of the survey. The present survey found that generic formulations were the most commonly prescribed form of fluoxetine in both dogs and cats. The respondents who prescribed fluoxetine only for dogs generally used Reconcile. This may indicate that some practitioners were more comfortable using FDA-approved drugs. Those who prescribed fluoxetine only for cats generally used a generic form or compounded form. There was and is no FDA-approved form of fluoxetine available for cats. Some veterinarians used compounded formulations of fluoxetine, especially for cats. However, the sources (whether it came from generic, trade or bulk drug) of compounded fluoxetine were not reported. A limitation of the study was not inquiring what formulation, whether oral tablet/capsule/liquid or transdermal gel, was used. It should be noted that for most of the veterinary compounded drugs, species-specific efficacy and pharmacokinetics have not been determined and that compounding may also interfere with stability of the drug, decreasing absorption, potency and therefore efficacy (Davidson 2003, Papich 2005). One published study in cats has reported that bioavailability after transdermal administration is significantly lower than after oral administration of a single dose of fluoxetine (Ciribassi and others 2003).

Thirty-two behaviours in dogs and 22 in cats were listed by the responding veterinarians for prescribing fluoxetine. Separation anxiety was the most common reason for prescribing fluoxetine in dogs, likely due to

TABLE 1: Major categories and behaviours for which fluoxetine is prescribed for dogs by 86 small animal veterinarians

Major categories*	Canine behaviour specified by respondents	Per cent	n
Anxieties	Separation anxiety	74	64
	Anxiety (unspecified)	42	36
	Situational anxiety	2	2
Aggression	Adjusting to new homes/anxiety	1	1
	Aggression (unspecified)	15	13
	Fear aggression	3	3
	Companion aggression	1	1
	Territorial aggression	1	1
	Aggression towards resident dogs	1	1
	Aggression towards resident people	1	1
	Dominance aggression	1	1
	Dominance aggression towards dogs	1	1
	Dominance aggression towards people	1	1
Compulsive disorders	OCD	17	15
Phobias/fear	Phobias – noise	3	3
	Phobias	2	2
	Phobias – thunderstorm	2	2
	Fears (unspecified)	1	1
Others (behaviours listed independently of above categories)	Behavioural issues/problems	3	3
	Chronic lick granuloma	2	2
	Destructive behaviour	2	2
	Hyperactivity	2	2
	Allergy	2	2
	Excessive barking	2	2
	Impulsive control	1	1
	Inappropriate urination	1	1
	Reactive behaviour	1	1
	Self-inflicted wounds	1	1
	Inappropriate chewing of objects	1	1
	Excessive licking	1	1
	Licking objects	1	1
	Repetitive motions	1	1

*Behaviours listed by respondents organised into major categories by investigators

FDA approval of Reconcile for use in treatment of separation anxiety in dogs and the robust article published by Simpson and others (2007). In cats, inappropriate elimination was the most common reason for prescribing fluoxetine. This is likely the consequence of numerous continuing education presentations mentioning use of fluoxetine and published studies reporting effect of fluoxetine on cat elimination behaviours (urine spraying (Pryor and others 2001, Mills and others 2011), urine marking (Hart and others 2005)). Some of the other behavioural diagnoses for which respondents prescribed fluoxetine, are supported by published studies (Dodman and others 1996, Wynchank and Berk 1998, Landsberg and others 2008, Ibáñez and Anzola 2009, Irimajiri and others 2009, Pekmezci and others 2009, Yalcin 2010, Pineda and others 2014). Additional studies are still needed to explore how practitioners diagnose separation anxiety, ‘inappropriate urination’ or any kind of behaviour problems of companion animals, how they decide what dosages or drugs to use and when to administer them, and how they evaluate outcome of their therapeutic interventions. Some studies report greater efficacy

of fluoxetine when used in conjunction with behaviour modification, in comparison with a combination of placebo and behaviour modification (Simpson and others 2007, Ibáñez and Anzola 2009). It should be noted that fluoxetine is not as effective without behaviour modification (Landsberg and others 2008), and as reported in the Freedom of Information summary (US Food and Drug Administration 2007) for Reconcile.

Reconcile was approved by the FDA for separation anxiety in dogs in 2007. There were no significant differences among the respondents graduating before and in/after 2007 regarding the prescribing habits. This may be indicative of self-directed learning and/or the value of mandatory continuing education requirements and commercial marketing by pharmaceutical companies. Responses were received from 11 specialists but due to small number, the results were not compared with the other respondents. The 11 specialists belonged to five different specialties (behaviourists, internists, surgeon, theriogenologist and board certified veterinary practitioners).

The major limitation of this study was the use of convenience sampling which decreases the generalisability

TABLE 2: Major categories and behaviours for which fluoxetine is prescribed for cats by 70 small animal veterinarians

Major categories*	Feline behaviour specified by respondents	Per cent	n
Elimination behaviours	Inappropriate elimination (unspecified)	34	24
	Inappropriate urination	26	18
	Marking	13	9
	Spraying	9	6
	Idiopathic cystitis	6	4
	FUS/FLUTD	6	4
Anxieties	Anxieties	29	20
	Separation anxiety	7	5
	Stress	4	3
Aggression	Aggression towards other cats	11	8
	Aggression (unspecified)	10	7
	Aggression towards people	1	1
	Redirected aggression	1	1
Dermatological/grooming	Excessive grooming/fur barbering	11	8
	Neurodermatitis	1	1
Compulsive disorders	OCD	10	7
Others (behaviours listed independently of above categories)	Behavioural issues/problems	4	3
	Pica	3	2
	Tail chasing	3	2
	Fear (unspecified)	1	1
	Allergies	1	1
	Hyperactive cat	1	1

*Behaviours listed by respondents organised into major categories by investigators

of the results. Some practitioners declined to fill out the questionnaire because they did not prescribe fluoxetine and it would have been useful to include these responses. This could lead to an overestimation of the practitioners who used fluoxetine. An additional limitation was the small sample size.

Overall this study shows that fluoxetine was prescribed for dogs and cats for a wide variety of behavioural disorders. The generic form was the most commonly prescribed formulation, with once a day dosing as the most

preferred. Widespread off-label use of fluoxetine for behavioural disorders highlights the need for research, academic education and continuing education of veterinarians regarding animal behaviour and psychopharmacology. This initial study was not designed to investigate the side effects of fluoxetine, behavioural modification techniques or the dosages being used. However, this study is an initial step in understanding the use of psychopharmacological drugs in veterinary behaviour medicine and provides a baseline for future studies.

TABLE 3: Comparisons between responding veterinarians who graduated before and in/after 2007

		<2006		≥2007		P value*
		Per cent	n	Per cent	N	
a	Prescribe fluoxetine for dogs and cats	61	42	49	17	0.4
	Prescribe fluoxetine only for dogs	28	19	40	14	
	Prescribe fluoxetine only for cats	12	8	11	4	
b†	Prescribe once every 24 hours	91	62	91	32	0.7
	Prescribe twice every 24 hours	15	10	14	5	
	Other	4	3	0	0	
c	AM	39	25	33	11	0.5
	PM	5	3	0	0	
	Neither AM or PM	56	36	67	22	
d†	Compounded	27	18	14	5	0.4
	Generic	67	45	71	25	
	Prozac	13	9	23	8	
	Reconcile	48	32	46	16	
	Other	1	1	0	0	

*Chi-squared test, and Fisher's exact test (where n<5)

†Multiple answers may have been chosen

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Contributors All authors made substantial contributions to the design of the work, interpretation of the data and manuscript preparation.

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Competing interests None declared.

Ethics approval Western University of Health Sciences Institutional Review Board.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement This study is part of a broader research project and there are unpublished results which may be published in the future.

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