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Prescribing of Psychiatric Medication to Bereaved Parents Following Perinatal/Neonatal Death: An Observational Study

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Perinatal/Neonatal Death and Psychiatric Medication Jeffrey R. Lacasse etal.,

Prescribing of Psychiatric Medication to Bereaved Parents Following Perinatal/Neonatal Death: An Observational Study

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Abstract

To examine psychiatric prescribing in response to perinatal/neonatal death, we analyzed data from a cross-sectional survey of 235 bereaved parents participating in an on-line support community. Of the 88 respondents prescribed medication, antidepressants were most common (n = 70, 79.5%) followed by benzodiazepines/sleep aids (n = 18, 20.5%). Many prescriptions were written shortly after the death (32.2% within 48 hours, 43.7% within a week, and 74.7% within a month). Obstetrician/gynecologists wrote most prescriptions given shortly after loss. Most respondents prescribed antidepressants took them long-term. This sample is select, but these data raise disturbing questions about prescribing practices for grieving parents.

KEYWORDS: Stillbirth, bereavement, antidepressive agents, benzodiazepines,

evidence-based medicine

Both stillbirth and perinatal/neonatal death are important global health issues (e.g., Froen, et al., 2011) that can cause both acute and enduring psychological distress in the bereaved. Experiencing a stillbirth puts women at increased risk of post-traumatic

stress disorder (PTSD), depression, and anxiety (Boyle, Vance, Najman, & Thearle, 1996). A cohort study found that 29% of women met criteria for PTSD in pregnancy subsequent to stillbirth (Turton, Evans, & Hughes, 2009). Other studies have found an association between child death and anxiety, depression, psychiatric hospitalization, and completed suicide (e.g., Qin & Mortenson, 2011).

Faced with a patient in acute bereavement and with awareness of the potential for long-term psychological sequelae, clinicians have several options for meaningful intervention. Psychosocial care on the part of clinicians clearly has an important role, ideally including patient-centered psychosocial care (Cacciatore, 2010). Physicians can refer bereaved parents to support groups and/or to non-medical helping professionals for evidence-based psychotherapy (e.g., Shear, Frank, Houch, & Reynolds, 2005). However, there is a paucity of well-replicated interventional research for traumatic bereavement, raising the question of whether any of the currently available psychosocial interventions can be said to be evidence-based.

Psychiatric medications are another potential intervention, and physicians sometimes prescribe sedatives such as benzodiazepines (BZs) for bereavement. A survey of obstetricians found that roughly half believed that BZs could be a useful to bereaved parents who recently lost an infant (Gold, Schwenk, & Johnson, 2008; see also Cook, Biyanova, & Marshall, 2007). Only one randomized controlled trial (RCT) of BZs for acute bereavement has taken place (Warner, Metcalfe, & King, 2001). This small trial found no positive impact of BZs on either grief severity or sleep, and patients randomized

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to diazepam reported more sleep problems. In a survey of the RCT participants, some opined that BZs could be helpful, but the majority also agreed that the prescription of BZ can "delay coming to terms with loss" (Warner et al., 2001, p. 40). None of the participants developed BZ dependence, likely due to the close monitoring within the RCT. However, the potential for short-term BZ use to lead to dependence remains a concern within real-world clinical practice (van Hulter, Teeuw, Bakker, & Leufkens, 2003). Data suggesting that BZs are not helpful in the recently traumatized should also be considered (Gelpin, Bonnie, Peri, Brandes, & Shalev, 1996).

Antidepressant (AD) medications are also an option for the treatment of bereavement. There are several studies for both bereavement-related depression and complicated grief. The limitations of the evidence for antidepressants have been noted (Bui, Nadal-Viens, & Simon, 2012). The trials are small, not randomized, and/or demonstrate a statistically significant impact on symptoms of clinical depression, but no clinically important impact on grief severity or duration. Several open-label trials find a positive impact for ADs (Bui et al., 2012). However, psychopharmacological trials are easily confounded by the placebo effect (Kirsch, 2010) and confirmatory bias; without double-blind, randomized controlled trials, it is not possible to isolate the clinical impact of ADs from the potential presence of rater bias or expectancy effects (e.g., Gaudiano & Herbert, 2005) and especially problematic to assert that ADs are superior to other forms of clinical intervention, such as evidence-based psychotherapy.

In short, at present, there exists no rigorous evidence to support the prescription of ADs in bereavement. Yet, it is common for ADs to be prescribed off-label for conditions which do not have supporting RCT evidence (e.g., McManus, Mant, Mitchell, Britt, & Dudley, 2003). Given the serenic-like effects of ADs (Glenmullen, 2000), they are likely to be prescribed to the bereaved. The positive effects must be carefully balanced with other issues, such as the overestimation of AD efficacy (Kirsch, 2010; Turner, Matthews, Linaradatos, Tell, & Rosenthal, 2008), the medicalization of grief (Moules, 1998), and the risk of adverse effects, including discontinuation syndrome (Gentile, 2011; Haddad, 2001).

Distinct from the use of BZs, a prescription for an AD can be viewed as implicitly assuming that the patient is being treated for a long-term problem, and that short-term relief is not the goal. Selective serotonin reuptake inhibitors (SSRIs), the most-prescribed class of ADs, are generally not considered to provide a short-term benefit, often taking 14-30 days to take full effect (Nirenberg et a., 2009). They are therefore inappropriate for short-term use. Treatment guidelines suggest that depressed patients complete \geq 4-6 months of treatment (e.g., American Psychiatric Association, 2000). Patients are more likely to discontinue ADs early when the prescriber is a non-psychiatrist and/or the diagnosis is not depression or anxiety (Pomerantz et al., 2004).

In terms of both evidence-based medicine and evidence-based psychosocial intervention, the interrelated issues of acute bereavement, psychiatric diagnosis (Horowitz & Wakefield, 2007) and timing of prescription are important to consider. If a

bereaved parent meets DSM-IV-TR criteria (American Psychiatric Association, 2000b) for major depression, then prescription of an SSRI could conceivably be supported by citing the RCT evidence. A recent Cochrane review finds a median Number-Needed-to-Treat (NNT) of 7 for SSRIs prescribed for depression versus inactive placebo in primary care (Arroll et al., 2009). However, diagnosing a recently bereaved person with a mental disorder is controversial (e.g., Thieleman & Cacciatore, in press).

The DSM-IV-TR defined definition of Major Depression (MDD) requires clinically significant symptoms sustained for at least two weeks, at eight weeks post-loss. The DSM-IV-TR authorizes the application of the depression diagnosis before eight weeks when a client is experiencing "marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, or psychomotor agitation" (APA, 2000b, p. 356), but provides no guidance regarding a minimum amount of time required for such symptoms. This leads to obvious questions regarding the reliability and validity of such diagnoses in the recently bereaved – what one clinician may deem MDD, another may consider a normal grief reaction. Importantly, the benefits of ADs are unclear when prescribed to patients with an uncertain psychiatric diagnosis, or for contradicted indications such as "dysphoric complaints or demoralization" (Fava, 2003, p. 129).

The dilemma is similar when treating a bereaved person who shows signs of psychological trauma. SSRIs are used in PTSD (Asnis, Kohn, Henderson, & Brown, 2004), the diagnosis of which requires more than one month of symptoms following the trauma (American Psychiatric Association, 2000b). The time period before diagnosis is

allowed reflects the fact that many traumatized individuals have acute reactions but do not go on develop PTSD (Yehuda, Mcfarlane, & Shalev, 1998). Similarly, the diagnosis of complicated grief proposed for DSM-5 (Shear, et al., 2011) requires that the bereaved individual be at no less than six months post-loss and have experienced significant impairment for the last month.

Thus, the practice of prescribing ADs to bereaved individuals shortly after a loss is questionable. This is particularly true given that the intense clinical distress manifested immediately after a loss is often a poor predictor of long-term functioning (Neimeyer & Currie, 2009). Arguably, a conservative approach to prescribing, which would maximize benefit and minimize risk, would be to reserve ADs until it was clear that the patient met full criteria for MDD, PTSD, or, perhaps complicated grief as proposed for DSM-5. At present, though, there is a paucity of empirical data regarding psychiatric prescribing in response to perinatal/neonatal death, when diagnosis and prognosis are uncertain but patients are in significant clinical distress.

The objective of this study was to describe patterns of psychiatric medication prescribing among parents who had experienced the perinatal/neonatal death of a child. Specifically, we examined the: (1) rate at which psychiatric medications were prescribed to deal with loss, and the types of medication used; (2) time lapse between loss and prescription across different prescriber specialties; (3) demographic and clinical variables associated with the prescription of medication; and (4) persistence of treatment.

METHOD

Participants

This study analyzes data from a cross-sectional on-line survey of bereaved parents participating in an on-line support community from 2009-2010. The survey methodology and description of the full sample are reported at length elsewhere (Cacciatore, Lacasse, Lietz & McPherson, in-press). The survey had a response rate of 51.75% (N = 503). There were 273 respondents who experienced perinatal/neonatal death at > 20 weeks gestation or lost their child \leq 28 days after birth since calendar year 2000. Six did not answer the question on psychiatric medication, and, as we sought to assess prescription patterns in response to loss, we censored any cases taking psychiatric medication at the time of loss (n = 32), leaving 235 cases for analysis.

The majority of respondents were women (n = 227, 99.6%), had education beyond high school (n = 206, 87.7%), were Caucasian/White (n = 195, 82.3%) and had experienced an unexpected perinatal/neonatal death (n = 123, 52.3%), most frequently, a stillbirth (n = 168, 71.5%). Only a small proportion (n = 21, 8.7%) had been diagnosed with a mental disorder at the time of their loss. Of the 235 respondents, 88 (37.4%) had been prescribed psychiatric medication at some point in response to their loss.

Measures

Demographic And Clinical Variables

Each respondent completed a demographic questionnaire (age, race/ethnicity, education) as well as questions regarding the circumstances of the death of their child. We asked whether the child death had been a stillbirth, whether the death was expected, and at what

point in the pregnancy/neonatal period it took place. We also asked "In the months before the loss, were you diagnosed with any mental health condition?", followed by a list of common mental health conditions. Respondents were also asked about their participation in professional counseling and support groups.

Self-Report Of Psychiatric Prescribing History

Respondents were asked, "Have you ever been prescribed psychiatric medications to deal with your loss?"; those who answered affirmatively were piped to a series of detailed questions, including a list of prescribed medications, the specialty of the clinician who initially prescribed them, and the time delay between loss and prescription. Respondents were then asked if they were still on medications and asked to list them; if they were no longer on medication, we asked the date of discontinuation.

We classified prescriptions into the following discreet categories: No psychiatric prescription in response to loss; BZ /sleep aid only; antidepressant monotherapy only; or combination treatment. Combination treatment referred to the combination of two ADs or an AD plus an additional medication. Trazadone was classified as a sleep aid in all cases except for one, in which other available data suggested that it was prescribed for depression.

Procedure

Pilot testing of survey questions among stakeholders helped refine the survey. Ethical approval was obtained from the Institutional Review Board of Arizona State

University, and the research committee of the participating nonprofit organization. A database of active forum participants from 2009-2010 was provided by the participating nonprofit, and participants were emailed an invitation to participate in the study by accessing an on-line Qualtrics survey. The survey instrument was lengthy and contained many instruments which are reported elsewhere, such as measures of mental health functioning (see Cacciatore, et al., in-press). To encourage participation, we followed up the initial request with an email reminder, a video message from the collaborating non-profit, and finally, a solicitation offering a \$20 gift card as incentive for participation. A cover letter informed participants that the study was voluntary and that data would only be reported in aggregate, anonymous form. The subgroup data analyses reported here focus on the prescribing of psychiatric medications and have not been reported elsewhere.

RESULTS

Frequency And Type Of Medication

Of the 88 bereaved parents who received medication, 20.5% (n = 18) received a prescription for BZ or sleep aid monotherapy, 39.8% (n = 35) received AD monotherapy, and 39.8% (n = 35) received treatment with a combination of psychiatric drugs. Combination treatment primarily consisted of AD + BZ and/or sleep aids (n = 23, 26.1%). Four participants (4.5%) received a medication combination including an antipsychotic; two had a mental health diagnosis in the months preceding the loss. The most popularly prescribed antidepressants were sertraline, fluoxetine, and escitalopram,

while the most popular benzodiazepines were lorazepam and alprazolam, and zolpidem was the most frequently prescribed sleep aid.

Medications By Prescriber Specialty And Time-Since-Loss

Prescriptions were cross-tabulated by time-to-prescription and specialty of the prescriber (see table 1). Medication was frequently prescribed shortly after the loss; 32.2% (n = 28) were written within 48 hours, 43.7% (n = 38) within a week, and 74.7% (n = 65) within a month. Obstetricians/gynecologists wrote the majority of prescriptions written less than a month after loss (n = 46, 70.8%). Of the prescriptions written by OB/GYNs, 78.3% (n = 36) were for AD or combination therapy. Of those 36 bereaved parents receiving AD or combination treatment from their OB/GYN, nine reported that they were diagnosed with a mental disorder at the time of loss.

Demographic And Clinical Variables Associated With Prescribing

We performed a series of exploratory logistic regressions performed using one block and forced entry, examining variables that might increase the odds of receiving a prescription for ADs. The odds ratio for a mental health diagnosis at the time of loss was 3.66 (95% CI 1.04, 12.84, p = .043). All other variables examined (e.g., number of professional counseling sessions, support groups attended, stillbirth or not) did not reach statistical significance (Odds Ratios <1.04, p > .05 for all).

Persistence Of Treatment With Psychiatric Medication

Life table analysis was used to determine the median time-to-discontinuation for each category of medication (See figure 1). For this analysis, we collapsed the categories of antidepressant monotherapy and combination treatment. As respondents sometimes reported moderate changes in medication regimen across time (e.g., changing from fluoxetine monotherapy to fluoxetine + zolpidem), this allowed us to quantify the persistence of treatment while retaining most data for analysis. Respondents who made more notable medication switches are discussed below. We included all respondents prescribed psychiatric medication < 6 months after loss for which we had usable data on stop and start dates (n = 75). We constrained the life table analysis to 730 days (two years).

For AD/combination treatment, discontinuation rates were similar for both those prescribed within a week of loss (median = 539 days) and those > 1 week < 1 month (median = 523 days). Approximately half of respondents in both groups had discontinued treatment within one year. The subsample of those prescribed AD/combination treatment > 1 month after loss (n = 12) discontinued treatment much earlier, at a median of 294 days, with only three such respondents (25%) continuing for the entire two-year period. For those prescribed BZs or sleep aid monotherapy within four weeks of loss (n = 14), the median time to discontinuation was 60 days; from day 300 forward, only one respondent continued the original BZ prescription.

Medication Status At Time Of Survey

Consistent with the life table analysis presented above, many respondents had discontinued their original medication, but some notable medication switches did occur (see table 2). The general trend otherwise was toward simplification of medication regimens; only 11 respondents were on multiple medications at the time of the survey (see table 2). All respondents originally placed on antipsychotics reported that they had been discontinued. Of the 18 respondents originally prescribed BZ/sleep aid therapy, 15 (83.3%) were off all medication; one remained on a benzodiazepine, and two had been switched to antidepressant monotherapy

DISCUSSION

In this cross-sectional survey of bereaved parents who suffered the perinatal/neonatal death of a child, we find that 37.4% (n = 88) of the total sample (n = 235) have been prescribed medication to help deal with their loss. Most respondents who received medication were prescribed antidepressant (AD) medication (n = 70, 79.5%) either as monotherapy or in combination with other medications. Most AD prescriptions were written < 4 weeks post-loss (n = 65, 73.9%), with OB/GYNs responsible for the largest proportion of AD prescriptions (n = 39, 44.8%). Many were written by OB/GYNs in the first week (n = 24, 27.6%), before these bereaved parents could have qualified for a diagnosis of PTSD or MDD, a questionable practice.

However, we begin by cautioning against a rush to judgment toward the prescribers within our sample. We do not have data on the patient-clinician interactions, and

bereaved parents may have requested medication. In general, contemporary mental health treatment is focused on use of medication (Kirk, Gomory & Cohen, 2013). Both prescribers and patients in this sample have been subject to promotional efforts from pharmaceutical companies (i.e., Gomory, Wong, Cohen, & Lacasse, 2011) which may have shaped how they see mental distress and the role of psychiatric medication. Many prescribers undoubtedly do reach for the prescription pad too quickly, and the over-use of AD drugs in medicine is well-documented (e.g., Glenmullen, 2000). However, the rate of prescription found in this study- 29.8% receiving ADs in some form, and 7.7% receiving BZ or sleep aid monotherapy- should be seen in the context of contemporary psychiatric prescribing rates in other settings. In general practice, pseudopatients who reported depressive adjustment disorder symptoms were prescribed antidepressants 10% of the time when they did not directly request medication, and 39% of the time when they made a general request (Kravitz et al., 2005). As respondents had contact with prescribers who are no doubt familiar with ADs, it seems only fair to note that 62.6% of this sample (on average, ~ 3 years post-loss) were never prescribed medication to deal with their loss. Given the tragic nature of perinatal/neonatal death and the understandable inclination to do something to help, the prescribing practices observed here could be interpreted as reflecting therapeutic restraint.

That said, our primary finding is that many respondents received AD prescriptions shortly after loss from their OB/GYNs. OB/GYNs wrote such prescriptions for 15 patients (17.2%) within *48 hours* of the death of a child, and for 24 patients (27.6%) within a week. There were only two other such prescriptions reported in the first week;

one by a psychiatrist, the other by a primary care physician to a respondent previously diagnosed with multiple mental disorders. OB/GYNs thus prescribed 84.6% (n = 11) of all AD monotherapy and 100% (n = 13) of all combination therapy prescribed within seven days. One week of clinical symptoms is not sufficient for a DSM-IV-TR diagnosis of MDD or PTSD, and thus 60% (n = 24) of AD prescriptions written by OB/GYNs were for patients who could not have met diagnostic criteria for PTSD or MDD. We know of no method through which a prescriber could reliably ascertain, so quickly, whether a recently bereaved parent would develop a sustained clinical problem best treated through ADs. Yehuda et al. (1998) examined clinical symptoms in response to trauma longitudinally. They found similar reactions for all patients at two days posttrauma, which separated a bit at day ten, with clear separation between no disorder, PTSD, depression and anxiety at six months. Such data suggests that prescribers simply cannot know the prognosis of acute bereavement. Indeed, awareness of such data may be one reason why the overall rate of prescribing was low. However, when ADs are prescribed shortly after loss, the purpose is essentially prophylaxis, which has been characterized as an overuse of AD medication (Conti, Bush and Cutler, 2011; Leo & Lacasse, 2010). Assuming that ADs can only have positive effects in this context would seemingly be naïve, especially given emerging data on the complicated risk-benefit calculus regarding use of psychiatric medication (Whitaker, 2010).

AD prescriptions often resulted in long-term treatment. Most strikingly, roughly half of those prescribed AD medication within a week of losing their child were still taking them two years later. Although BZs have a reputation for causing dependence, there is

increasing recognition of an AD discontinuation syndrome that is of clinical concern (see Healy, 2004). If avoiding long-term treatment with psychiatric medication is seen as preferable, the small subsample prescribed BZ/sleep aid therapy fared best. Almost all discontinued treatment rapidly and only one respondent took BZs long-term.

The use of SSRIs in women of childbearing age is also noteworthy, especially when prescribed without first exhausting psychosocial treatment options. SSRI use in pregnancy is associated with a long list of obstetrical problems, such as miscarriage, preterm birth and low birth weight (Urato, 2011, p. 190). The odds ratio for congenital heart defects among women exposed to SSRIs in the first trimester of pregnancy is 2.01 (95% CI, 1.53, 2.72) which suggests that ADs should be used conservatively among fertile women (Jiminez-Solem et al., 2012).

Our data are retrospective, observational data reached through a cross-sectional selfreport. We did not have access to clinical documentation, respondents could have made errors in their recollection of past events. There were no data collected on clinical interactions, and we did not ask bereaved parents if they requested medication. We surveyed participants in an on-line support community, a group that may differ from the larger population of bereaved parents. While the on-line support group was not oriented around the use of medication, selection bias remains a concern, and these findings should be replicated in other samples. Finally, these data were collected under the DSM-IV-TR, and the impending DSM-5 removes the bereavement exclusion (Thieleman & Cacciatore, 2013). However, our results have a similar interpretation under DSM-5, which requires

two weeks of symptoms to diagnosis MDD, and also cautions the clinician to consider context (bereavement) before diagnosing MDD.

Most respondents did not receive psychiatric medication, and among those that did, it seems likely that it was thought of as an early intervention strategy. While early intervention may have appeal to prescribers, the potential for unintended consequences should be considered. To draw a parallel from the psychological literature, immediate debriefing after trauma has been a frequently used intervention. The idea that immediate intervention could prevent PTSD seems commonsensical. However, careful analysis of intervention data showed that those receiving debriefing fared no better, and possibly worse, than those receiving no treatment at all. Some hypothesized that debriefing interferes with natural coping mechanisms (McNally, Bryant, & Ehlers, 2003). Treatment guidelines now recommend against universal use of debriefing (Forbes et al., 2010). While the use of ADs in bereavement differs because of the lack of RCT data to settle the question, the debriefing example should give us pause. We do not know that AD treatment shortly after child death is helpful, and it could be harmful (Whitaker, 2010).

CONCLUSION

A recent editorial in *The Lancet* stated, "Medicalising grief, so that treatment is legitimized routinely with antidepressants, for example, is not only dangerously simplistic, but also flawed. The evidence base for treating recently bereaved people with standard antidepressant regimens is absent" (p. 589). Thus, our findings should be disturbing. If intervention is needed in bereavement, there are many options beyond the

use of psychopharmacology (e.g., Cacciatore & Flint, 2012). Improving psychiatric practice in traumatic bereavement – especially among OB/GYNs who may reach for the prescription pad too quickly- has the potential to significantly improve care, and perhaps outcomes, for bereaved parents. We are concerned that current practices have the potential to cause harm, and hope the field can move toward a more evidence-based use of psychiatric medication.

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Table 1 Time Delay Until	Prescription by Medical	Specialty $(N = 87)$

Medication	Specialty	0-2	3-7	1-4	1-2	2-3	3-6	>6	Total
		davs	davs	week	months	month	month	month	
BZ monotherapy ^a	OB/GYN	9	1	0	0	0	0	0	10
	PC	2	0	1	0	0	0	1	4
	Psych	0	0	2 ⁽²⁾	0	0	0	1	3
Antidepressant	OB/GYN	6 ⁽²⁾	5 ⁽¹⁾	5	0	1	0	0	17
	PC	1 ⁽¹⁾	0	3 ⁽²⁾	2	0	2	4 ⁽¹⁾	12
	Psych	1	0	2 ⁽¹⁾	0	0	0	1	4
	Other ^b	0	0	0	0	1	0	1	2
Combination	OB/GYN	9 ⁽²⁾	4	7	1	1	0	0	22
	PC	0	0	2	1	1	0	2	6
	Psych	0	0	5	2 ⁽²⁾	0	0	0	7
Total		28	10	27	6	4	2	10	87

Note: Numbers in superscript (e.g.,⁽¹⁾) represent the number of cases in each cell that were diagnosed with anxiety, depression, PTSD, or multiple diagnoses at the time of loss. BZ = benzodiazepine; OB/GYN = obstetrician/gynecologist; PC = Primary care; Psych =psychiatrist. Numbers of prescriptions in **boldface** were written < 4 weeks post-loss. One case had missing data.

^a Represents 12 prescriptions for benzodiazepines, two for zolpidem, two for "other sedative," and one for trazadone

^bRepresents one cardiologist and one neurologist

Medi	cation status at survey	Initial prescription							
		BZ/Slee p monotherapy		Antidepressant monotherapy		Combination therapy		Total	
		п	%	п	%	п	%	п	%
No m	nedication to deal with loss	15	17.0	19	21.6	22	25.0	56	63.6
BZ n	nonotherapy	1	1.1	0		0		1	1.1
Sleep	aid monotherapy	0		0		0		0	
AD n	nonotherapy	2	2.2	13	14.8	8	9.0	23	26.1
Com	bination therapy	0		3	3.5	3	3.5	6	6.8
	2 antidepressants			2	2.4				
	AD + BZ					1	1.2		
	AD + sleep aid					1	1.2		
	AD + psychostimulant			1	1.2				
Total		18	20.5	38	43.2	35	39.8	86	97.8

Table 2 Medication Status at Time of Survey by Initial Prescription Pattern

Note: Two cases had missing data on these variables, thus these frequencies do not sum to 100%.

Figure 1. Life table analysis plotting persistence of initial treatment with psychiatric medication prescribed in response to perinatal/neonatal death, within 6 months of loss, by prescription pattern, from day 1-730. To aid in visual interpretation, the trajectories have been smoothed by presenting them in straight line rather than stepped format. For BZ/sleep aid <1 month, n = 14; for AD/combination treatment in first week, n = 27; for AD/combination treatment >1 week < 1 month, n = 22; for AD/combination treatment >1 month, n = 12.

