C.F. Turner
November 30, 2005
P:\NIDDK\ICDB\Output_CTMemos\Analysis_Integrity_Nov30rev_First 4pagesonly.wpd

Integrity Check for ICDB Baseline File

As a partial check of the integrity of the ICDB analysis datasets archived in the NIDDK data repository, a set of tabulations was performed to verify that published results from the ICDB study can be reproduced using the archived analysis datasets. Selected publications were identified and selected analyses were performed to duplicate published results for the complete baseline data, preliminary baseline data, and longitudinal data. The results of this integrity check are described in the following sections.

Complete Baseline Data. An article by Propert et al. [4] published in the Journal of Urology (JoU) in 2000 reports results for "637 [ICDB] participants who met eligibility criteria (p. 1435)" over the entire study period from May 1993 through January 1997. As a partial check of the integrity of the ICDB analysis baseline dataset, a set of tabulations was performed to verify that results reported in Tables 2 and 3 of this article can be reproduced using the archived baseline dataset. Tables 2 and 3 from the Journal of Urology article are included in Attachment 1; STATA 8/SE code and output for our tabulations are included in Attachment 3. The full text of the JoU article can be found in Attachment 4.

Table 2 Tabulations. The published table breaks down the ICDB sample by: gender, race, age, marital status, employment, education, annual household income, symptom duration prior to study entry, and previous interstitial cystitis diagnosis. Our tabulation from the archived dataset (see our Table 1) produced counts that are identical to the published table with two exceptions.

1. Duration of symptoms prior to study entry was calculated as the integer difference between age at onset of urinary symptoms (*shx_1* recorded as an integer) and age at baseline admission (*age* recorded as a decimal number). In comparing the distribution of the resulting variable to the published tabulation, we noted that the published table listed overlapping intervals: <1; 1-**5**; **5-11; 11-16; 16** or greater. Our Table 2 displays our calculated duration of symptoms variable in single years. Based on this tabulation, it appears that the published table should have shown the categories: <1; 1-4; 5-10; 11-15; 16 or greater. Use of these categories would provide an exact match between published Ns and Ns tabulated from the archived data.

2. Our tabulated employment status variable has 391 employed persons (versus 390 in the published table) and 138 "not employed" persons (versus 139 in the published table). The study form for employment lists nine defined responses and each carries an explicit notation as to whether the category is "employed", "homemaker", or "not employed". A final "other" category appears to have generated four additional codes whose values (according to the FORMATS statement) were coded as: 10 = 'On leave, emp'; 11 = 'PT i/o home, emp'; 12 = 'IC, not emp'; 13 = 'Moved, not emp'; 14 = 'Between jobs'. The code 10 (on leave) was not assigned to any case; the other four new codes had one case each. Table 3 shows the cross-tabulation of the detailed employment codes by the 3-category indicator of employment status. We suspect that the 1-case deviation between the published table and the tabulation from the archived data arose from variations in assignment of one of the codes numbered 11 to 14.

Table 3 Tabulations. JoU Table 3 breaks down patients' overall[1] pain-urgency-frequency scores and their individual scores on each measure (pain, urgency, and frequency) into four categories: normal (absent), mild, moderate, and severe. Pain and urgency scores are reported for the last month and current

[1]Although we did not find an explicit statement in the article, we assumed that the ***overall*** pain-urgency-frequency scores of 0-9, were collapsed using the same rules used for individual pain and urgency scores as described in Table 1, i.e., 0 = normal or absent, 1-3 = mild, 4-6 = moderate, and 7-9 = severe.

24 hours period; frequency of voiding is taken from a 24-hour log and is reported for both a 24 hour period and for nighttime. Our tabulations from the archived data matched exactly the data reported in JoU Table 3; these results are shown in Table 4 of this memo and in Attachment 3.

Preliminary Baseline Data. Four ICDB publications appeared in a supplement of the journal ***Urology*** in 1997 (Kirkemo et al., 1997 [1]; Simon et al., 1997 [5]; Nigro et al., 1997 [3]; Messing, 1997 [2]). Each of these articles used ICDB sample accrued through December 31, 1995; for our analysis we selected the report of Simon et al. [5]. We initially had trouble matching the sample counts. Table 5 illustrates the results we obtained for Simon et al. (1997) which did not select sample by gender or by any optional procedures employed (e.g., cytoscopy). We used five alternative date variables from the baseline file in our attempt to replicate their definition of "[A]ll **424** study participants successfully enrolled in the ICDB Study prior to December 31, 1995 were selected for an interim analysis. . ." Our results are shown in Table 5. No date variable we employed gave a count of study participants for the period 1993 to 1995 that was less than 432.

Study investigators indicated that the 1997 reports used a baseline dataset that excluded 10 patients who had completed baseline interviews and who were included in the NIDDK repository baseline data file.[2] When these 10 cases were removed from the baseline NIDDK dataset and analysis was restricted to cases whose baseline interviews occurred before January 1, 1996, we obtained a sample size of 424. As Table 6 shows, the tabulated characteristics of these 424 respondents provide an almost perfect match to those published for the overall sample in Table 4 of Simon et al. (1997).

Longitudinal Data. Propert et al.[4] report longitudinal analysis of change in reported severity of urinary symptoms over 48 months of followup. We conducted exploratory analyses using archive data of the reporting of pain during the past month which was assessed in the symptoms questionnaire and recorded in the longitudinal analysis file as *purg_1*. We followed Propert et al.'s (2000, p. 1436) strategy:

> To evaluate longitudinal changes for the 6 primary outcomes (table 1) mean values of each outcome grouped into approximate 3-month intervals were plotted against the time of followup. Due to the categorical nature of the outcomes, the mean provided a better visual representation of changes with time than the median. For each outcome, patients were categorized according to the baseline value for that outcome (absent to mild, moderate, or severe) and separate lines were plotted for each group.

Our analysis focused on 1 of the 6 outcomes: Pain as reported on symptom questionnaire; and we used the 3-category variable *purg1c3b* to define the three baseline symptom groups (absent to mild pain, moderate, and severe pain at baseline). It was not readily apparent how the 3-month intervals should be constructed, so we tried three alternatives:

Method 1: Intervals of: exactly zero, then 1.50 to 4.49 assigned value 3; 4.50 to 7.49 assigned value 6; 7.0 to 10.49 assigned value 9; etc.

Method 2: Intervals of: exactly zero, then 0.01 to 2.99 assigned value 3; 3.00 to 5.99 assigned value

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[2] Eight subjects (210008, 220007, 220030, 310020, 310056, 310084, 410049, 520047) were excluded because they took longer than 14.5 weeks to complete baseline interview; two other subjects were excluded for other reasons (420068 had "CYST < UROD"; and 520020 had "UROD < SYMPTS, UROD < QUL, UROD < PRIOR"; source: Colleen Brensinger and Kathleen Propert, e-mail of November 8, 2005). One other case (510018) was excluded because urodynamics were performed before baseline inclusion eligibility criteria had been checked; this case does not appear in the NIDDK baseline dataset.

6; 6.00 to 8.99 assigned value 9; etc. (Note that assigned values in this series could be spatially displaced by -1.5 units to better represent their source value; however, the published series appears to have inflection points at exactly 3, 6, 9, ... months.)

Method 3: Time was truncated to an integer, and intervals 0 to 2 were assigned value 0; 3 to 5 were assigned value of 3; 6 to 8 were assigned value of 6; etc.

For all three methods, 17 records for which *timeseen* values were negative were treated as missing data, and cases with assigned values greater than 48 months were calculated but not included in our plotted figures. Our initial analyses replicated the published findings that: (1) followup periods ranged up to 52 months and (2) of 637 subjects 109 were lost to followup and 123 withdrew from the study.[3] For all subsequent analyses, we excluded the 232 cases that withdrew or were lost to followup.

Figure 1 in Attachment 2 presents Propert et al.'s published plot of trends over 48 months for reporting of pain in the past month. Figure 2 in Attachment 2 presents the same plot calculated from NIDDK archive data using Method 1.[4] While these two plots are not identical they appear to be quite similar. Given uncertainties in the definition of time periods and small sample sizes for some of the points represented in these plots,[5] we find this similarity reassuring.

References

[1] Kirkemo A, Peabody M, Diokno AC, Afanasyev A, Nyberg LM Jr, Landis JR, Cook YL, Simon LJ. Associations among urodynamic findings and symptoms in women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. **Urology.** 1997 May;49(5A Suppl):76-80.

[2] Messing E, Pauk D, Schaeffer A, Nieweglowski M, Nyberg LM Jr, Landis JR, Cook YL, Simon LJ. Associations among cystoscopic findings and symptoms and physical examination findings in women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. **Urology.** 1997 May;49(5A Suppl):81-5.

[3] Nigro DA, Wein AJ, Foy M, Parsons CL, Williams M, Nyberg LM Jr, Landis JR, Cook YL, Simon LJ. Associations among cystoscopic and urodynamic findings for women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. **Urology.** 1997 May;49(5A Suppl):86-92.

[4] Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JR and the ICDB Study Group. A prospective study of interstitial cystitis: results of longitudinal followup of the interstitial cystitis data base cohort. **Journal of Urology**. 2000 May;163(5):1434-9.

[5] Simon LJ, Landis JR, Erickson DR, Nyberg LM. The Interstitial Cystitis Data Base Study: concepts and preliminary baseline descriptive statistics. **Urology.** 1997 May;49(5A Suppl):64-75.

[3]Tabulation of *fup_stat* (followup status) for 637 initial interviews (i.e., *timeseen* == 0.00).

[4]Attachment 5 presents results for Methods 2 and 3.

[5]While the archive plots delete cases that withdrew from the study or were lost to followup, the sample represented at each series time point is not identical and the sample sizes fluctuate substantially (see STATA output). So, for example, the number of 1-month pain measurements for cases with moderate symptoms at baseline was 208 in Month 0 and 24 in Month 48.

TABLE 1. Comparison of charateristic of subjects reported by Propert et al. (2000) and results of tabulation from baseline data in NIDDK repository.

	Published Tabulation	Tabulation of Archived Data
Sex		
Male	56	56
Female	581	581
Race (b)		
White	592	592
Black	29	29
Other	14	14
Unknown	2	2
Age		
18-34	176	176
35-44	164	164
45-54	146	146
55+	151	151
Marital Status (c)		
Partnered	449	449
Alone	188	188
Employment (d)		
Employed	390	391
Homemaker	108	108
Not Employed	139	138
Education		
HS or less	272	272
College	248	248
Advanced	117	117
Annual household income		
Less than $30,000	182	182
More than $30,000	454	454
Not available	1	1
Symptom duration before study entry (yrs.)		
<1	15	15
1-4 (a)	210	210
5-10 (a)	168	168
11-15 (a)	73	73
16 or greater	171	171
Previous interstitial cystitis diagnosis by MD		
Yes	432	432
No	205	205

(a) The published categories overlap (<1; 1-**5; 5**-11; 11-**16; 16** or greater) and appear to be a typographical error. Based on our analysis of the archived data (see text), we suspect that the non-overlapping categories shown in this table represent the tabulation done for publication.

(b) Other includes persons coded as aleut, asian, multi-racial, and other. Unknown includes one person coded as "no answer" and one person coded as "unknown".

(c) "Partnered" includes persons coded as "married" and those coded as "living with a partner".

(d) In our tabulation from the archived data, one person coded as "between jobs" was classified as "not employed" when the 13 employment codes used in the data collection were collapsed into the three categories shown. If this person were re-categorized as "employed", the archived tabulation would exactly match the published table.

Table 2. Symptom duration prior to study entry. (Caculated to match Propert et al., 2000)

Single Years	N	Totals	Interval
0	15	15	**< 1**
1	49		
2	68		
3	50		
4	43	210	**1-4**
5	43		
6	31		
7	25		
8	28		
9	16		
10	25	168	**5-10**
11	14		
12	18		
13	15		
14	13		
15	13	73	**11-15**
16	7		
17	164	171	**16+**

TABLE 3. Cross-tabulation of detailed employment codes by 3-category employment status variable.

	Collapsed Codes			
Detailed Codes (a)	**Employed**	**Homemaker**	**Not Employed**	**TOTAL**
FT,emp	255	0	0	255
PT, emp	104	0	0	104
Home FT,emp	15	0	0	15
Home PT,emp	16	0	0	16
Homemaker	0	108	0	108
Laid off NE	0	0	11	11
Disabled NE	0	0	47	47
Retired NE	0	0	65	65
Student NE	0	0	12	12
PT i/o home,Emp	1	0	0	1
IC,NE	0	0	1	1
Moved,NE	0	0	1	1
Between jobs	0	0	1	1
ARCHIVE TOTAL	391	108	138	637
PUBLISHED	390	108	139	637

(a) Code labels are from SAS formats files but NE has been substituted "not emp".

TABLE 4. Comparison of published symptom outcomes and tabulation from archive data.

Outcome Measures	Tabulation	N Patients	SYMPTOM SEVERITY			
			Absent or Normal	Mild	Moderate	Severe
Pain-Urgency-Frequency Score	Published	637	0	44	283	310
	Archive	637	0	44	283	310
Pain - Last Month	Published	637	30	121	304	182
	Archive	637	30	121	304	182
Pain - Current 24hr.	Published	620	60	194	236	130
	Archive	620	60	194	236	130
Urgency - Last Month	Published	637	5	86	282	264
	Archive	637	5	86	282	264
Urgency - Current 24hr.	Published	621	15	144	276	186
	Archive	621	15	144	276	186
Frequency - 24hrs.	Published	628	45	152	176	255
	Archive	628	45	152	176	255
Frequency - Nocturnal	Published	628	148	159	218	103
	Archive	628	148	159	218	103

Note. Published source Propert et al. (2000, Table 3).

TABLE 5. Number of patients enrolled in ICDB study through December 31,1995 from published reports and tabulations using alternative date indicators in archived baseline file.

SAMPLE SIZE USING	1993-1995	1996-1997
Published Tabulation (a)	424	NA
Tabulation using archived variables:		
Inclusion date (incldate)	443	194
Screening sIgnboff Date (scrdate)	434	203
Visit date from "purg form" (v_date)	443	194
Date of symptoms form at baseline (sympdate)	442	195
Date voiding logs turned in (voiddate)	432	205

TABLE 6. Comparison of charateristic of subjects reported by Simon et al. (1997) and results of tabulation from baseline data in NIDDK repository (a).

CHARACTERISTICS	Published Tabulation	Tabulation of Archived Data
Age (Mean at Baseline)	**44.3**	**44.3**
Age (Mean, First Symptoms)	**32.2**	**32.2**
Sex		
Male	36	36
Female	388	388
Race (b)		
White	386	386
Black	24	24
Other	14	14
Latino/Hispanic (e)		
Yes, Hispanic	21	21
No, Non-Hispanic	402	402
Missing	1	1
Marital Status (c)		
Partnered	290	290
Alone	134	134
Education		
HS or less	186	186
College	161	162
Advanced	77	76
Employment (d)		
Employed	262	263
Homemaker	72	71
Not Employed	90	90
Job change due to symptoms (e)		
Yes, job change	46	46
No	270	270
Missing	108	108
Annual household income		
Less than $30,000	132	132
More than $30,000	292	292
Not available		

(a) Tabulation from NIDDK repository dataset eliminated all cases cases whose baseline interviews occurred before January 1, 1996 plus 10 additional cases explicitly dropped by investigators (210008, 220007, 220030, 310020, 310056, 310084, 410049, 520047, 420068, 520020); see text of memo.

(b) In tabulation from archive data, "Other" included persons coded as aleut, asian, multi-racial, other, plus unknown and no answer.

(c) "Partnered" includes persons coded as "married" and those coded as "living with a partner"; all others are coded as not partnered.

(d) Tabulation from archive data classified codes 1-4 as employed (FT emp, PT, emp, Home FT emp, Home PT emp); code 5 were homemakers, and codes 6-9 were Not Employed (Laid off; Diabled; Retired; Student).

ATTACHMENT 1

Journal of Urology
Tables 2 and 3

from

Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JR and the ICDB Study Group. A prospective study of interstitial cystitis: results of longitudinal followup of the interstitial cystitis data base cohort. .**J of Urology**. 2000 May;163(5):1434-9.

TABLE 2. *Baseline demographic characteristics of 637 patients*

Characteristic	No. Pts. (%)
Sex:	
F	581 (91.2)
M	56 (8.8)
Race:	
White	592 (93.2)
Black	29 (4.5)
Other	14 (2.2)
Unknown	2
Age:	
18–34	176 (27.6)
35–44	164 (25.7)
45–54	146 (22.9)
55+	151 (23.7)
Marital status:	
Partnered	449 (70.5)
Alone	188 (29.5)
Employment:	
Employed	390 (61.2)
Homemaker	108 (17.0)
Not employed	139 (21.8)
Education:	
High school or less	272 (42.7)
College	248 (38.9)
Advanced	117 (18.4)
Annual household income ($):	
Less than 30,000	182 (28.6)
30,000 or Greater	454 (71.4)
Not available	1
Symptom duration before study entry (yrs.):*	
Less than 1	15 (2.4)
1–5	210 (33.0)
5–11	168 (26.4)
11–16	73 (11.5)
16 or Greater	171 (26.8)
Previous interstitial cystitis diagnosis by physician:	
Yes	432 (67.8)
No	205 (32.2)

* Median 7.7 years (range 0 to 62).

Table 2. Baseline demographic characteristics of 637 patients* Median 7.7 years (range 0 to 62).

Table 3

TABLE 3. *Distribution of primary symptom outcomes at baseline in 637 patients*

Outcome	No. Pts.	No. Symptom Severity (%)			
		Absent	Mild	Moderate	Severe
Pain-urgency-frequency score	637	Not applicable	44 (6.9)	283 (44.4)	310 (48.7)
Pain:					
Last mo.	637	30 (4.7)	121 (19.0)	304 (47.7)	182 (28.6)
Current	620	60 (9.7)	194 (31.3)	236 (38.1)	130 (21.0)
Urgency:					
Last mo.	637	5 (0.8)	86 (13.5)	282 (44.3)	264 (41.4)
Current	621	15 (2.4)	144 (23.2)	276 (44.4)	186 (30.0)
Frequency:					
24-Hr.*	628	45 (7.2)	152 (24.2)	176 (28.0)	255 (40.6)
Nighttime†	628	148 (23.6)	159 (25.3)	218 (34.7)	103 (16.4)

* Day 1 voiding log median 13 voids per 24 hours (range 2 to 59).
† Median 2 voids nightly (range 0 to 18).

Table 3. Distribution of primary symptom outcomes at baseline in 637 patients* Day 1 voiding log median 13 voids per 24 hours (range 2 to 59).† Median 2 voids nightly (range 0 to 18).
From: PROPERT: J Urol, Volume 163(5).May 2000.1434-1439

ATTACHMENT 2

Longitudinal Analysis of 1-Month Pain Symptoms over 48 Months of Study by Baseline Pain Report

1. Figure 2a from Propert et al., 2000

2. Figure using values calculated from NIDDK archive dataset

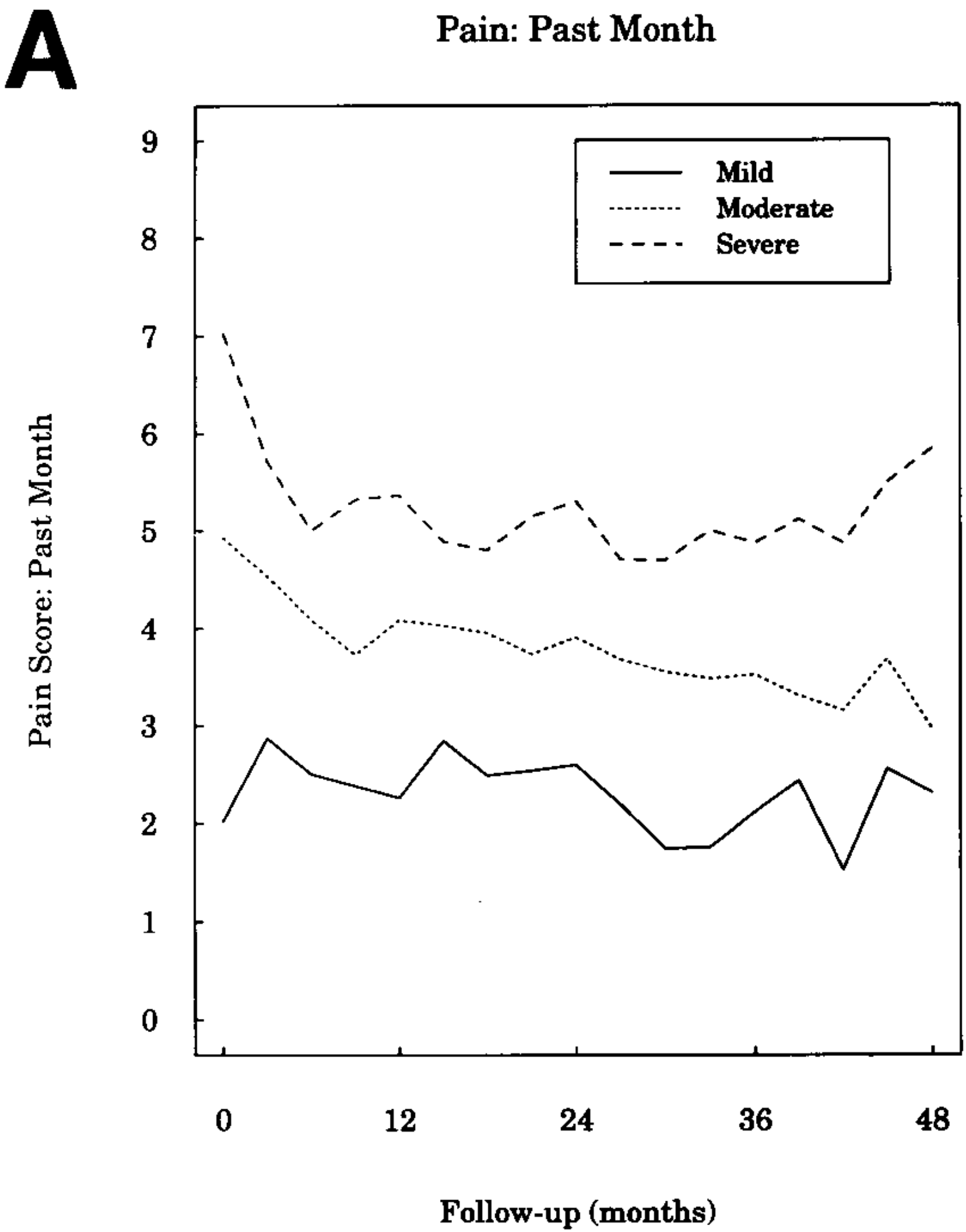
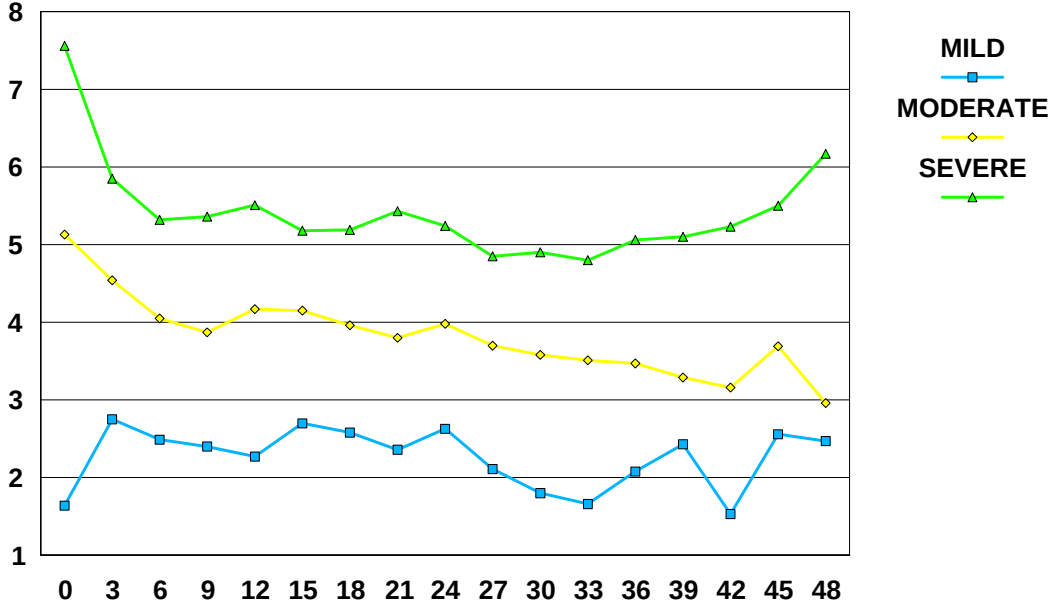

A
Pain: Past Month
Mild
Moderate
Severe
Pain Score: Past Month
9
8
7
6
5
4
3
2
1
0
0
12
24
36
48
Follow-up (months)

FIGURE 2: ICDB Archive Data, Method 1

Monthly Pain for 3 Baseline Pain Groupings



ATTACHMENT 3

STATA 8/SE Code and Output for
Tabulations from ICDB Baseline Dataset in NIDDK Repository

```
      log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\1.smcl
  log type:  smcl
 opened on:  31 Oct 2005, 16:33:28

. do "C:\DOCUME~1\cft\LOCALS~1\Temp\STD03000000.tmp"

. use"P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\baseline.dta", clear


.
. generate symp_age = int(age - shx_1)

. replace symp_age =0 if symp_age<1
(0 real changes made)

. replace symp_age = 4 if ((symp_age >=1) & (symp_age <=4))
(167 real changes made)

. replace symp_age = 10 if ((symp_age >=5) & (symp_age <=10))
(143 real changes made)

. replace symp_age = 15 if ((symp_age >=11) & (symp_age <=15))
(60 real changes made)

. replace symp_age = 17 if (symp_age >=16)
(162 real changes made)

. label define symp_age 0"< 1yr" 4"1-4yrs" 10"5-10yrs" 15"11-15 yrs" 17"16+
yrs"

. label values symp_age symp_age

. tab symp_age, missing

   symp_age |      Freq.     Percent        Cum.
------------+-----------------------------------
      < 1yr |         15        2.35        2.35
     1-4yrs |        210       32.97       35.32
    5-10yrs |        168       26.37       61.70
  11-15 yrs |         73       11.46       73.16
    16+ yrs |        171       26.84      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. generate ageYRS=int(age)

. generate ageC=int(age)

. replace ageC = 18 if ageC<=34
(176 real changes made)

. replace ageC = 44 if (ageC>34) & (ageC<=44)
(149 real changes made)

. replace ageC = 54 if (ageC>44) & (ageC<=54)
(134 real changes made)

. replace ageC = 55 if (ageC>54)
(142 real changes made)
```

```
. label define ages 18"18-34" 44"35-44" 54"45-54" 55"55+"

. label values ageC ages

. tab ageYRS ageC, missing
```

ageYRS	ageC 18-34	35-44	45-54	55+	Total
19	3	0	0	0	3
20	6	0	0	0	6
21	2	0	0	0	2
22	4	0	0	0	4
23	8	0	0	0	8
24	9	0	0	0	9
25	15	0	0	0	15
26	15	0	0	0	15
27	11	0	0	0	11
28	12	0	0	0	12
29	13	0	0	0	13
30	17	0	0	0	17
31	16	0	0	0	16
32	17	0	0	0	17
33	14	0	0	0	14
34	14	0	0	0	14
35	0	14	0	0	14
36	0	24	0	0	24
37	0	15	0	0	15
38	0	12	0	0	12
39	0	16	0	0	16
40	0	19	0	0	19
41	0	18	0	0	18
42	0	18	0	0	18
43	0	13	0	0	13
44	0	15	0	0	15
45	0	0	21	0	21
46	0	0	10	0	10
47	0	0	17	0	17
48	0	0	17	0	17
49	0	0	15	0	15
50	0	0	9	0	9
51	0	0	16	0	16
52	0	0	20	0	20
53	0	0	9	0	9
54	0	0	12	0	12
55	0	0	0	9	9
56	0	0	0	12	12
57	0	0	0	7	7
58	0	0	0	6	6
59	0	0	0	7	7
60	0	0	0	5	5
61	0	0	0	6	6
62	0	0	0	11	11
63	0	0	0	4	4
64	0	0	0	3	3
65	0	0	0	11	11
66	0	0	0	8	8
67	0	0	0	7	7
68	0	0	0	11	11
69	0	0	0	9	9
70	0	0	0	5	5
71	0	0	0	3	3
72	0	0	0	7	7
73	0	0	0	8	8

```
        74 |         0          0          0          1 |         1
        75 |         0          0          0          1 |         1
        76 |         0          0          0          2 |         2
        77 |         0          0          0          4 |         4
        79 |         0          0          0          1 |         1
        81 |         0          0          0          1 |         1
        82 |         0          0          0          2 |         2
-----------+--------------------------------------------+----------
     Total |       176        164        146        151 |       637
```

```
. tab ageC, missing

       ageC |      Freq.     Percent        Cum.
------------+-----------------------------------
      18-34 |        176       27.63       27.63
      35-44 |        164       25.75       53.38
      45-54 |        146       22.92       76.30
        55+ |        151       23.70      100.00
------------+-----------------------------------
      Total |        637      100.00
```

```
.
. label define race1 1"aleut" 2"asian" 3"black" 4"caucasian" 5"multi-racial"
6"other" 7"no answer" 8"unknown"

. label values race race1

. generate raceC = race

. replace raceC = 1 if race==4
(592 real changes made)

. replace raceC = 2 if race==3
(29 real changes made)

. replace raceC = 3 if (race<3)|(race==5)| (race==6)
(14 real changes made)

. replace raceC = 4 if (race>6)
(2 real changes made)

. label define race2 1"White" 2"Black" 3"Other" 4"Unknown"

. label values raceC race2

. tab race raceC, missing

             |                    raceC
        race |     White      Black      Other    Unknown |     Total
-------------+--------------------------------------------+----------
       aleut |         0          0          2          0 |         2
       asian |         0          0          7          0 |         7
       black |         0         29          0          0 |        29
   caucasian |       592          0          0          0 |       592
multi-racial |         0          0          3          0 |         3
       other |         0          0          2          0 |         2
   no answer |         0          0          0          1 |         1
     unknown |         0          0          0          1 |         1
-------------+--------------------------------------------+----------
       Total |       592         29         14          2 |       637
```

```
. tab raceC, missing

      raceC |      Freq.     Percent        Cum.
------------+-----------------------------------
      White |        592       92.94       92.94
      Black |         29        4.55       97.49
      Other |         14        2.20       99.69
    Unknown |          2        0.31      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. label define edustat1 1"< HS" 2"some HS" 3"HS grad(or GED)" 4"college"
5"grad school"

. label values ed_level edustat1

.
. generate educ2 = ed_level

. replace educ2 = 1 if ed_level<4
(261 real changes made)

. replace educ2 = 2 if ed_level==4
(248 real changes made)

. replace educ2 = 3 if ed_level==5
(117 real changes made)

. label define educstat2 1"HS or less" 2"College" 3"Advanced"

. label values educ2 educstat2

. tab ed_level educ2, missing

       level of |              educ2
      education | HS or les    College   Advanced |     Total
----------------+---------------------------------+----------
          < HS |        11          0          0 |        11
       some HS |        29          0          0 |        29
HS grad(or GED) |       232          0          0 |       232
        college |         0        248          0 |       248
    grad school |         0          0        117 |       117
----------------+---------------------------------+----------
          Total |       272        248        117 |       637


. tab educ2, missing

      educ2 |      Freq.     Percent        Cum.
------------+-----------------------------------
 HS or less |        272       42.70       42.70
    College |        248       38.93       81.63
   Advanced |        117       18.37      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. label define sex 1"male" 2"female"

. label values sex sex
```

```
. tab sex, missing

        sex |      Freq.     Percent        Cum.
------------+-----------------------------------
       male |         56        8.79        8.79
     female |        581       91.21      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. label define income 1"<$30K" 2">$30K"

. label values income income

. tab income, missing

  household |
     income |      Freq.     Percent        Cum.
------------+-----------------------------------
      <$30K |        182       28.57       28.57
      >$30K |        454       71.27       99.84
          . |          1        0.16      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. label define marstat1 1"married" 2"liv w/partnr" 3"sep" 4"div" 5"widow"
6"nvr marr"

. label values mar_st marstat1
. generate marst2 = mar_st
. replace marst2 = 1 if (mar_st<3)
(33 real changes made)

. replace marst2 = 2 if (mar_st>2)
(188 real changes made)

. label define marstat2 1"Partnered" 2"Alone"
. label values marst2 marstat2

. tab mar_st marst2, missing

     marital |        marst2
      status | Partnered      Alone |     Total
-------------+----------------------+----------
     married |       416          0 |       416
liv w/partnr |        33          0 |        33
         sep |         0         14 |        14
         div |         0         64 |        64
       widow |         0         19 |        19
    nvr marr |         0         91 |        91
-------------+----------------------+----------
       Total |       449        188 |       637


. tab marst2, missing
     marst2 |      Freq.     Percent        Cum.
------------+-----------------------------------
  Partnered |        449       70.49       70.49
      Alone |        188       29.51      100.00
------------+-----------------------------------
      Total |        637      100.00
```

```
. label define emp_cd 1"FT,emp" 2"PT, emp" 3"Home FT,emp" 4"Home PT,emp"
5"Homemaker" 6"Laid off NE" 7"Disabled NE" 8"Retire
> d NE" 9"Student NE" 10"On leave,emp" 11"PT i/o home,Emp" 12"IC,NE"
13"Moved,NE" 14"Between jobs"

. label values emp_st emp_cd

. generate employ2 = 3

. replace  employ2 = 1 if (emp_st <5) | (emp_st ==11)|(emp_st == 10)
(391 real changes made)

. replace  employ2 = 2 if (emp_st == 5)
(108 real changes made)


. label define employ2 1"Employed" 2"Homemaker" 3"Not Employed"

. label values employ2 employ2

. tab emp_st employ2, missing

     employment |             employ2
         status |  Employed  Homemaker  Not Emplo |     Total
----------------+---------------------------------+----------
         FT,emp |       255          0          0 |       255
        PT, emp |       104          0          0 |       104
    Home FT,emp |        15          0          0 |        15
    Home PT,emp |        16          0          0 |        16
      Homemaker |         0        108          0 |       108
    Laid off NE |         0          0         11 |        11
    Disabled NE |         0          0         47 |        47
     Retired NE |         0          0         65 |        65
     Student NE |         0          0         12 |        12
PT i/o home,Emp |         1          0          0 |         1
          IC,NE |         0          0          1 |         1
       Moved,NE |         0          0          1 |         1
   Between jobs |         0          0          1 |         1
----------------+---------------------------------+----------
          Total |       391        108        138 |       637


. tab employ2, missing

     employ2 |      Freq.     Percent        Cum.
-------------+-----------------------------------
    Employed |        391       61.38       61.38
   Homemaker |        108       16.95       78.34
Not Employed |        138       21.66      100.00
-------------+-----------------------------------
       Total |        637      100.00

.
. label define yn01 1"yes" 0"no"
. label values shx_2 yn01
```

```
. tab shx_2, missing

 previously |
  diagnosed |
   with ic? |      Freq.     Percent        Cum.
------------+-----------------------------------
         no |        205       32.18       32.18
        yes |        432       67.82      100.00
------------+-----------------------------------
      Total |        637      100.00

.
.
end of do-file

. exit, clear
```

```
      log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\3.smcl
  log type:  smcl
 opened on:   1 Nov 2005, 16:19:20

. do "C:\DOCUME~1\cft\LOCALS~1\Temp\STD03000000.tmp"

. use "P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\baseline.dta",
clear

.
. label define nmms -1"missing" 0"normal" 1"Mild" 2"Moderate" 3"Severe"

. generate t_score_4pt = -1

. replace t_score_4pt = 1 if (t_score > 0) & (t_score <=3)
(44 real changes made)

. replace t_score_4pt = 2 if (t_score >= 4) & (t_score <=6)
(283 real changes made)

. replace t_score_4pt = 3 if (t_score >=7) & (t_score <=9)
(310 real changes made)

. label values t_score_4pt nmms

. label values p_score nmms

. label values vpurg1b4 nmms

. label values u_score nmms

. label values vpurg2b4 nmms

. tab  t_score t_score_4pt, missing

     total |
     score |           t_score_4pt
     (puf) |      Mild   Moderate     Severe |     Total
-----------+---------------------------------+----------
         1 |         1          0          0 |         1
         2 |         9          0          0 |         9
         3 |        34          0          0 |        34
         4 |         0         57          0 |        57
         5 |         0         91          0 |        91
         6 |         0        135          0 |       135
         7 |         0          0        110 |       110
         8 |         0          0        112 |       112
         9 |         0          0         88 |        88
-----------+---------------------------------+----------
     Total |        44        283        310 |       637


. tab1 t_score_4pt p_score vpurg1b4 u_score vpurg2b4, missing
```

```
-> tabulation of t_score_4pt

t_score_4pt |      Freq.     Percent        Cum.
------------+-----------------------------------
       Mild |         44        6.91        6.91
   Moderate |        283       44.43       51.33
     Severe |        310       48.67      100.00
------------+-----------------------------------
      Total |        637      100.00

-> tabulation of p_score

   baseline |
 pain score |      Freq.     Percent        Cum.
------------+-----------------------------------
     normal |         30        4.71        4.71
       Mild |        121       19.00       23.70
   Moderate |        304       47.72       71.43
     Severe |        182       28.57      100.00
------------+-----------------------------------
      Total |        637      100.00

-> tabulation of vpurg1b4

 day 1 pain |
 score from |
       void |
log--baseli |
         ne |      Freq.     Percent        Cum.
------------+-----------------------------------
     normal |         60        9.42        9.42
       Mild |        194       30.46       39.87
   Moderate |        236       37.05       76.92
     Severe |        130       20.41       97.33
          . |         17        2.67      100.00
------------+-----------------------------------
      Total |        637      100.00

-> tabulation of u_score

   baseline |
    urinary |
    urgency |
      score |      Freq.     Percent        Cum.
------------+-----------------------------------
     normal |          5        0.78        0.78
       Mild |         86       13.50       14.29
   Moderate |        282       44.27       58.56
     Severe |        264       41.44      100.00
------------+-----------------------------------
      Total |        637      100.00
```

```
-> tabulation of vpurg2b4

      day 1 |
    urgency |
 score void |
log--baseli |
         ne |      Freq.     Percent        Cum.
------------+-----------------------------------
     normal |         15        2.35        2.35
       Mild |        144       22.61       24.96
   Moderate |        276       43.33       68.29
     Severe |        186       29.20       97.49
          . |         16        2.51      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. generate freq24B_4pt = -1

. replace freq24B_4pt = 0 if vf_24b < 7
(45 real changes made)

. replace freq24B_4pt = 1 if (vf_24b > 6) & (vf_24b < 11)
(152 real changes made)

. replace freq24B_4pt = 2 if (vf_24b > 10) & (vf_24b < 15)
(176 real changes made)

. replace freq24B_4pt = 3 if (vf_24b >= 15)& (vf_24b < 100)
(255 real changes made)

. label values freq24B_4pt nmms

. label variable freq24B_4pt "Baseline 24h freq voiding, 4-pt"

. tab vf_24b freq24B_4pt, missing
```

day 1 # voids/24hr . day--baseline	Baseline 24h freq voiding, 4-pt					
	missing	normal	Mild	Moderate	Severe	Total
2	0	2	0	0	0	2
4	0	6	0	0	0	6
5	0	15	0	0	0	15
6	0	22	0	0	0	22
7	0	0	35	0	0	35
8	0	0	35	0	0	35
9	0	0	45	0	0	45
10	0	0	37	0	0	37
11	0	0	0	51	0	51
12	0	0	0	50	0	50
13	0	0	0	41	0	41
14	0	0	0	34	0	34
15	0	0	0	0	28	28
16	0	0	0	0	33	33
17	0	0	0	0	31	31
18	0	0	0	0	29	29
19	0	0	0	0	19	19
20	0	0	0	0	15	15
21	0	0	0	0	10	10
22	0	0	0	0	9	9
23	0	0	0	0	14	14
24	0	0	0	0	9	9
25	0	0	0	0	6	6
26	0	0	0	0	10	10
27	0	0	0	0	5	5
28	0	0	0	0	7	7
29	0	0	0	0	7	7
30	0	0	0	0	5	5
31	0	0	0	0	2	2
32	0	0	0	0	5	5
34	0	0	0	0	2	2
35	0	0	0	0	1	1
36	0	0	0	0	1	1
38	0	0	0	0	1	1
39	0	0	0	0	1	1
40	0	0	0	0	1	1
44	0	0	0	0	2	2
47	0	0	0	0	1	1
59	0	0	0	0	1	1
.	9	0	0	0	0	9
Total	9	45	152	176	255	637

```
. tab freq24B_4pt, missing

   Baseline |
   24h freq |
   voiding, |
       4-pt |      Freq.     Percent        Cum.
------------+-----------------------------------
    missing |          9        1.41        1.41
     normal |         45        7.06        8.48
       Mild |        152       23.86       32.34
   Moderate |        176       27.63       59.97
     Severe |        255       40.03      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. generate freqNocB_4pt = -1

. replace freqNocB_4pt = 0 if vf_noctb ==0
(148 real changes made)

. replace freqNocB_4pt = 1 if vf_noctb ==1
(159 real changes made)

. replace freqNocB_4pt = 2 if (vf_noctb == 2) | (vf_noctb == 3)
(218 real changes made)

. replace freqNocB_4pt = 3 if (vf_noctb > 3)& (vf_noctb < 100)
(103 real changes made)

. label values freqNocB_4pt nmms

. label variable freqNocB_4pt "Baseline nocturnal freq voiding, 4-pt"

. tab vf_noctb freqNocB_4pt, missing

   day 1 # |
 nocturnal |
voids--bas |         Baseline nocturnal freq voiding, 4-pt
     eline |   missing     normal       Mild   Moderate     Severe |     Total
-----------+-------------------------------------------------------+----------
         0 |         0        148          0          0          0 |       148
         1 |         0          0        159          0          0 |       159
         2 |         0          0          0        130          0 |       130
         3 |         0          0          0         88          0 |        88
         4 |         0          0          0          0         35 |        35
         5 |         0          0          0          0         22 |        22
         6 |         0          0          0          0         21 |        21
         7 |         0          0          0          0          8 |         8
         8 |         0          0          0          0          3 |         3
        10 |         0          0          0          0          4 |         4
        11 |         0          0          0          0          1 |         1
        12 |         0          0          0          0          4 |         4
        14 |         0          0          0          0          2 |         2
        15 |         0          0          0          0          1 |         1
        17 |         0          0          0          0          1 |         1
        18 |         0          0          0          0          1 |         1
         . |         9          0          0          0          0 |         9
-----------+-------------------------------------------------------+----------
     Total |         9        148        159        218        103 |       637


. tab freqNocB_4pt, missing
```

```
   Baseline |
  nocturnal |
       freq |
   voiding, |
       4-pt |      Freq.     Percent        Cum.
------------+-----------------------------------
    missing |          9        1.41        1.41
     normal |        148       23.23       24.65
       Mild |        159       24.96       49.61
   Moderate |        218       34.22       83.83
     Severe |        103       16.17      100.00
------------+-----------------------------------
      Total |        637      100.00

.
end of do-file

. log off
       log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\3.smcl
  log type:  smcl
 paused on:   1 Nov 2005, 16:19:54
```

ICDB ANALYSIS 3

```
      log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\11_2_2005a.smcl
  log type:  smcl
 opened on:   2 Nov 2005, 11:15:10

. use "P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\baseline.dta", clear

. generate IYear = year(incldate)

. tab IYear

      IYear |      Freq.     Percent        Cum.
------------+-----------------------------------
       1993 |        111       17.43       17.43
       1994 |        175       27.47       44.90
       1995 |        157       24.65       69.54
       1996 |        192       30.14       99.69
       1997 |          2        0.31      100.00
------------+-----------------------------------
      Total |        637      100.00

. generate I1995 = 0

. replace I1995 = 1 if IYear <= 1995
(443 real changes made)

. label var I1995 "Inclusion date pre-1996 ?"

. label define X1995 0"1996+" 1"<=1995"

. label values I1995 X1995

. tab I1995

  Inclusion |
       date |
 pre-1996 ? |      Freq.     Percent        Cum.
------------+-----------------------------------
      1996+ |        194       30.46       30.46
     <=1995 |        443       69.54      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. generate ScrYear = year(scrdate)

. tab ScrYear

    ScrYear |      Freq.     Percent        Cum.
------------+-----------------------------------
       1993 |         99       15.54       15.54
       1994 |        180       28.26       43.80
       1995 |        155       24.33       68.13
       1996 |        197       30.93       99.06
       1997 |          6        0.94      100.00
------------+-----------------------------------
      Total |        637      100.00

. generate Scr1995 = 0

. replace Scr1995 = 1 if ScrYear <= 1995
(434 real changes made)
```

```
. label var Scr1995 "Screening signoff date pre-1996 ?"

. label values Scr1995 X1995

. tab Scr1995

  Screening |
    signoff |
       date |
 pre-1996 ? |      Freq.     Percent        Cum.
------------+-----------------------------------
      1996+ |        203       31.87       31.87
     <=1995 |        434       68.13      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. generate VYear = year(v_date)

. tab VYear

      VYear |      Freq.     Percent        Cum.
------------+-----------------------------------
       1993 |        111       17.43       17.43
       1994 |        175       27.47       44.90
       1995 |        157       24.65       69.54
       1996 |        192       30.14       99.69
       1997 |          2        0.31      100.00
------------+-----------------------------------
      Total |        637      100.00

. generate V1995 = 0

. replace V1995 = 1 if VYear <= 1995
(443 real changes made)

. label var V1995 "Visit date purg form, pre-1996 ?"

. label values V1995 X1995

. tab V1995

 Visit date |
 purg form, |
 pre-1996 ? |      Freq.     Percent        Cum.
------------+-----------------------------------
      1996+ |        194       30.46       30.46
     <=1995 |        443       69.54      100.00
------------+-----------------------------------
      Total |        637      100.00

.
. generate SymYear = year(sympdate)

. tab SymYear

    SymYear |      Freq.     Percent        Cum.
------------+-----------------------------------
       1993 |        109       17.11       17.11
       1994 |        175       27.47       44.58
       1995 |        158       24.80       69.39
       1996 |        193       30.30       99.69
       1997 |          2        0.31      100.00
------------+-----------------------------------
```

```
      Total |        637      100.00

. generate Sym1995 = 0

. replace Sym1995 = 1 if SymYear <= 1995
(442 real changes made)

. label var Sym1995 "Date of sympts form at baseline"

. label values Sym1995 X1995

. tab Sym1995

    Date of |
sympts form |
at baseline |      Freq.     Percent        Cum.
------------+-----------------------------------
      1996+ |        195       30.61       30.61
     <=1995 |        442       69.39      100.00
------------+-----------------------------------
      Total |        637      100.00

.

. generate VoidYear = year(voiddate)
(8 missing values generated)

. tab VoidYear

   VoidYear |      Freq.     Percent        Cum.
------------+-----------------------------------
       1993 |        103       16.38       16.38
       1994 |        171       27.19       43.56
       1995 |        158       25.12       68.68
       1996 |        191       30.37       99.05
       1997 |          6        0.95      100.00
------------+-----------------------------------
      Total |        629      100.00

. generate Void1995 = 0

. replace Void1995 = 1 if VoidYear <= 1995
(432 real changes made)

. label var Void1995 "Date voiding logs turned in at baseline"

. label values Void1995 X1995

. tab Void1995

       Date |
    voiding |
logs turned |
      in at |
   baseline |      Freq.     Percent        Cum.
------------+-----------------------------------
      1996+ |        205       32.18       32.18
     <=1995 |        432       67.82      100.00
------------+-----------------------------------
      Total |        637      100.00

.
.
end of do-file
```

ICDB ANALYSIS 4:
Fix Ns for Preliminary Analysis; Match to Simon et al. (1997)

```
      log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\Simon_11_11_2005a.log
  log type:  text
 opened on:  15 Nov 2005, 08:57:07

. use "P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\baseline.dta", clear

. *
. * Drop 11 cases specified by Propert / Brensinger
. *  NOTE that 1 case (510018) is not included in baseline database
.
. generate dropit = 0

. replace dropit=1 if subj == 210008
(1 real change made)

. replace dropit=1 if subj == 220007
(1 real change made)

. replace dropit=1 if subj == 220030
(1 real change made)

. replace dropit=1 if subj == 310020
(1 real change made)

. replace dropit=1 if subj == 310056
(1 real change made)

. replace dropit=1 if subj == 310084
(1 real change made)

. replace dropit=1 if subj == 410049
(1 real change made)

. replace dropit=1 if subj == 520047
(1 real change made)

. replace dropit=1 if subj == 420068
(1 real change made)

. replace dropit=1 if subj == 510018
(0 real changes made)

. replace dropit=1 if subj == 520020
(1 real change made)

. sort dropit

.
. generate ScrYear = year(scrdate)

. tab ScrYear

    ScrYear |      Freq.     Percent        Cum.
------------+-----------------------------------
       1993 |         99       15.54       15.54
       1994 |        180       28.26       43.80
       1995 |        155       24.33       68.13
       1996 |        197       30.93       99.06
       1997 |          6        0.94      100.00
------------+-----------------------------------
      Total |        637      100.00

. generate Scr1995 = 0

. replace Scr1995 = 1 if ScrYear <= 1995
(434 real changes made)
```

```
. label var Scr1995 "Screening signoff date pre-1996 ?"

. label values Scr1995 X1995

. tab Scr1995 dropit

 Screening |
   signoff |
      date |         dropit
pre-1996 ? |         0          1 |     Total
-----------+----------------------+----------
         0 |       203          0 |       203
         1 |       424         10 |       434
-----------+----------------------+----------
     Total |       627         10 |       637


. drop if dropit == 1 | ScrYear > 1995
(213 observations deleted)

.
. generate ageYRS=int(age)

. * generate ageC=int(age)
. * replace ageC = 18 if ageC<=34
. * replace ageC = 44 if (ageC>34) & (ageC<=44)
. * replace ageC = 54 if (ageC>44) & (ageC<=54)
. * replace ageC = 55 if (ageC>54)
. * label define ages 18"18-34" 44"35-44" 54"45-54" 55"55+"
. * label values ageC ages
. * tab ageYRS ageC, missing
. * tab ageC, missing
.
. summarize age

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
         age |       424      44.313    13.72838   19.27173   82.32991

. summarize shx_1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
       shx_1 |       424    32.15094    14.49842          3         73

.
. label define sex 1"male" 2"female"

. label values sex sex

. tab sex, missing

        sex |      Freq.     Percent        Cum.
------------+-----------------------------------
       male |         36        8.49        8.49
     female |        388       91.51      100.00
------------+-----------------------------------
      Total |        424      100.00

.
. label define race1 1"aleut" 2"asian" 3"black" 4"caucasian" 5"multi-racial"
6"other" 7"no answer" 8"
> unknown"

. label values race race1

. generate raceC = race

. replace raceC = 1 if race==4
(386 real changes made)
```

```
. replace raceC = 2 if race==3
(24 real changes made)

. replace raceC = 3 if (race<3)|(race>4)
(14 real changes made)

. label define race2 1"White" 2"Black" 3"Other+Unknown"

. label values raceC race2

. tab race raceC, missing

           |                raceC
      race |     White     Black  Other+Unk |     Total
-----------+---------------------------------+----------
     aleut |         0         0         2 |         2
     asian |         0         0         5 |         5
     black |         0        24         0 |        24
  caucasian |       386         0         0 |       386
multi-racial |         0         0         3 |         3
     other |         0         0         2 |         2
  no answer |         0         0         1 |         1
   unknown |         0         0         1 |         1
-----------+---------------------------------+----------
     Total |       386        24        14 |       424


. tab raceC, missing

      raceC |      Freq.     Percent        Cum.
------------+-----------------------------------
      White |        386       91.04       91.04
      Black |         24        5.66       96.70
Other+Unknown |         14        3.30      100.00
------------+-----------------------------------
      Total |        424      100.00

. tab ethnic, missing

    origin |
 (latino or |
  hispanic) |      Freq.     Percent        Cum.
------------+-----------------------------------
          0 |        402       94.81       94.81
          1 |         21        4.95       99.76
          . |          1        0.24      100.00
------------+-----------------------------------
      Total |        424      100.00

.
. label define marstat1 1"married" 2"liv w/partnr" 3"sep" 4"div" 5"widow"
6"nvr marr"

. label values mar_st marstat1

. generate marst2 = mar_st

. replace marst2 = 1 if (mar_st<3)
(20 real changes made)

. replace marst2 = 2 if (mar_st>2)
(134 real changes made)

. label define marstat2 1"Partnered" 2"Alone"

. label values marst2 marstat2
```

```
. tab mar_st marst2, missing

     marital |        marst2
      status | Partnered      Alone |     Total
-------------+----------------------+----------
     married |       270          0 |       270
liv w/partnr |        20          0 |        20
         sep |         0          8 |         8
         div |         0         43 |        43
       widow |         0         12 |        12
    nvr marr |         0         71 |        71
-------------+----------------------+----------
       Total |       290        134 |       424


. tab marst2, missing

     marst2 |      Freq.     Percent        Cum.
------------+-----------------------------------
  Partnered |        290       68.40       68.40
      Alone |        134       31.60      100.00
------------+-----------------------------------
      Total |        424      100.00

.
. label define edustat1 1"< HS" 2"some HS" 3"HS grad(or GED)" 4"college"
5"grad school"

. label values ed_level edustat1

. generate educ2 = ed_level

. replace educ2 = 1 if ed_level<4
(177 real changes made)

. replace educ2 = 2 if ed_level==4
(162 real changes made)

. replace educ2 = 3 if ed_level==5
(76 real changes made)

. label define educstat2 1"HS or less" 2"College" 3"Advanced"

. label values educ2 educstat2

. tab ed_level educ2, missing

      level of |               educ2
     education | HS or les    College   Advanced |     Total
---------------+---------------------------------+----------
           < HS |         9          0          0 |         9
        some HS |        17          0          0 |        17
HS grad(or GED) |       160          0          0 |       160
        college |         0        162          0 |       162
    grad school |         0          0         76 |        76
----------------+---------------------------------+----------
          Total |       186        162         76 |       424


. tab educ2, missing

      educ2 |      Freq.     Percent        Cum.
------------+-----------------------------------
 HS or less |        186       43.87       43.87
    College |        162       38.21       82.08
   Advanced |         76       17.92      100.00
------------+-----------------------------------
      Total |        424      100.00

.
. label define emp_cd 1"FT,emp" 2"PT, emp" 3"Home FT,emp" 4"Home PT,emp"
```

```
5"Homemaker" 6"Laid off NE"
> 7"Disabled NE" 8"Retired NE" 9"Student NE" 10"On leave,emp" 11"PT i/o
home,Emp" 12"IC,NE" 13"Moved,
> NE" 14"Between jobs"

. label values emp_st emp_cd

. generate employ2 = 3

. replace  employ2 = 1 if (emp_st <5) | (emp_st ==11)|(emp_st == 10)
(263 real changes made)

. replace  employ2 = 2 if (emp_st == 5)
(71 real changes made)

. label define employ2 1"Employed" 2"Homemaker" 3"Not Employed"

. label values employ2 employ2

. tab emp_st employ2, missing

     employment |             employ2
         status |  Employed  Homemaker  Not Emplo |     Total
----------------+---------------------------------+----------
         FT,emp |       176          0          0 |       176
        PT, emp |        69          0          0 |        69
    Home FT,emp |         8          0          0 |         8
    Home PT,emp |        10          0          0 |        10
      Homemaker |         0         71          0 |        71
    Laid off NE |         0          0         10 |        10
    Disabled NE |         0          0         33 |        33
     Retired NE |         0          0         38 |        38
     Student NE |         0          0          9 |         9
----------------+---------------------------------+----------
          Total |       263         71         90 |       424


. tab employ2, missing

     employ2 |      Freq.     Percent        Cum.
-------------+-----------------------------------
    Employed |        263       62.03       62.03
   Homemaker |         71       16.75       78.77
Not Employed |         90       21.23      100.00
-------------+-----------------------------------
       Total |        424      100.00

. tab job_chng, missing

    urinary |
 symptoms - |
 job change |      Freq.     Percent        Cum.
------------+-----------------------------------
          0 |        270       63.68       63.68
          1 |         46       10.85       74.53
          . |        108       25.47      100.00
------------+-----------------------------------
      Total |        424      100.00

.
. label define income 1"<$30K" 2">$30K"

. label values income income
```

```
. tab income, missing

  household |
     income |      Freq.     Percent        Cum.
------------+-----------------------------------
      <$30K |        132       31.13       31.13
      >$30K |        292       68.87      100.00
------------+-----------------------------------
      Total |        424      100.00

.
end of do-file

. log close
       log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\Simon_11_11_2005a.log
  log type:  text
 closed on:  15 Nov 2005, 08:57:20
```

ICDB ANALYSIS 5: Longitudinal File

```
      log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\longitudianl.txt
  log type:  text
 opened on:  16 Nov 2005, 15:09:43

.
. generate time_integer = int(timeseen)

. tab time_integer

time_intege |
          r |      Freq.     Percent        Cum.
------------+-----------------------------------
         -2 |          1        0.01        0.01
         -1 |         16        0.15        0.16
          0 |      1,546       14.51       14.67
          1 |        658        6.17       20.84
          2 |        536        5.03       25.87
          3 |        602        5.65       31.52
          4 |        332        3.12       34.64
          5 |        314        2.95       37.58
          6 |        434        4.07       41.66
          7 |        270        2.53       44.19
          8 |        268        2.52       46.71
          9 |        386        3.62       50.33
         10 |        228        2.14       52.47
         11 |        327        3.07       55.54
         12 |        341        3.20       58.74
         13 |        216        2.03       60.76
         14 |        263        2.47       63.23
         15 |        260        2.44       65.67
         16 |        148        1.39       67.06
         17 |        202        1.90       68.96
         18 |        272        2.55       71.51
         19 |        123        1.15       72.66
         20 |        188        1.76       74.43
         21 |        224        2.10       76.53
         22 |        126        1.18       77.71
         23 |        186        1.75       79.46
         24 |        241        2.26       81.72
         25 |        120        1.13       82.85
         26 |        139        1.30       84.15
         27 |        185        1.74       85.89
         28 |         76        0.71       86.60
         29 |        113        1.06       87.66
         30 |        153        1.44       89.10
         31 |         68        0.64       89.73
         32 |        117        1.10       90.83
         33 |        118        1.11       91.94
         34 |         76        0.71       92.65
         35 |        119        1.12       93.77
         36 |        128        1.20       94.97
         37 |         57        0.53       95.50
         38 |         89        0.84       96.34
         39 |         70        0.66       97.00
         40 |         28        0.26       97.26
         41 |         56        0.53       97.79
         42 |         42        0.39       98.18
         43 |         20        0.19       98.37
         44 |         26        0.24       98.61
         45 |         13        0.12       98.73
         46 |         18        0.17       98.90
         47 |         60        0.56       99.47
         48 |         40        0.38       99.84
```

```
         49 |          7        0.07       99.91
         50 |          8        0.08       99.98
         52 |          2        0.02      100.00
------------+-----------------------------------
      Total |     10,656      100.00

.
. label define status 1"active" 2"lost to folloup" 3"withdrawn"

. label values fup_stat status

. tab fup_stat if timeseen==0.00

      follow-up |
         status |      Freq.     Percent        Cum.
----------------+-----------------------------------
         active |        405       63.58       63.58
lost to folloup |        109       17.11       80.69
      withdrawn |        123       19.31      100.00
----------------+-----------------------------------
          Total |        637      100.00

. * pause
. *tab max_fup fup_stat if timeseen==0.00, missing
. *tab max_fup fup_stat
. tab subj fup_stat if subj <= 110100

           |         follow-up status
      subj |    active  lost to f  withdrawn |     Total
-----------+---------------------------------+----------
    110027 |         0         27          0 |        27
    110029 |         0         32          0 |        32
    110039 |         0         27          0 |        27
    110040 |        25          0          0 |        25
    110045 |         0         28          0 |        28
    110049 |        28          0          0 |        28
    110051 |         0         20          0 |        20
    110052 |         0         27          0 |        27
    110053 |        23          0          0 |        23
    110055 |         0         21          0 |        21
    110057 |        26          0          0 |        26
    110058 |         0          0         24 |        24
    110059 |         0         22          0 |        22
    110060 |         0          9          0 |         9
    110062 |        25          0          0 |        25
    110065 |         0          6          0 |         6
    110066 |         0          0         12 |        12
    110067 |         0         15          0 |        15
    110068 |         0          6          0 |         6
    110069 |         0          8          0 |         8
    110070 |         0         19          0 |        19
    110074 |         0          0          5 |         5
    110075 |         0          0         17 |        17
    110076 |         0          0          6 |         6
    110077 |         0         21          0 |        21
    110078 |        26          0          0 |        26
    110080 |         0         25          0 |        25
    110081 |        14          0          0 |        14
    110082 |        27          0          0 |        27
    110083 |         0          0          5 |         5
    110084 |         0          0          6 |         6
    110085 |         0          0          2 |         2
    110086 |        24          0          0 |        24
    110087 |        21          0          0 |        21
    110088 |         0          0          5 |         5
    110091 |        19          0          0 |        19
    110092 |         0         18          0 |        18
```

```
    110093 |         0         11          0 |        11
    110094 |        17          0          0 |        17
    110095 |        16          0          0 |        16
    110096 |         0          7          0 |         7
    110097 |         0          0         15 |        15
    110099 |         0          0         12 |        12
    110100 |        18          0          0 |        18
-----------+---------------------------------+----------
     Total |       309        349        109 |       767


. keep if fup_stat ==1
(2475 observations deleted)

. * pause
.
. generate time1 = .
(8181 missing values generated)

. label var time1 "Months: 0, 1.5 to 4.499,  4.5 to 7.499, 7.5 to 10.499 ... "

. replace time1 = .  if timeseen < 0
(0 real changes made)

. replace time1 = 0  if timeseen == 0.00
(405 real changes made)

. replace time1 = .   if timeseen   > 0 & timeseen < 1.5
(0 real changes made)

.
. replace time1 = 3 if timeseen   >=  1.5 & timeseen < 4.5
(1070 real changes made)

. replace time1 = 6 if timeseen   >= 4.5 & timeseen < 7.5
(773 real changes made)

. replace time1 = 9 if timeseen   >= 7.5 & timeseen < 10.5
(653 real changes made)

. replace time1 = 12 if timeseen >= 10.5 & timeseen < 13.5
(721 real changes made)

.
. replace time1 = 15 if timeseen >= 13.5 & timeseen < 16.5
(562 real changes made)

. replace time1 = 18 if timeseen >= 16.5 & timeseen < 19.5
(482 real changes made)

. replace time1 = 21 if timeseen >= 19.5 & timeseen < 22.5
(442 real changes made)

. replace time1 = 24 if timeseen >= 22.5 & timeseen < 25.5
(480 real changes made)

.
. replace time1 = 27 if timeseen >=  25.5 & timeseen < 28.5
(354 real changes made)

. replace time1 = 30 if timeseen >=  28.5 & timeseen < 31.5
(301 real changes made)

. replace time1 = 33 if timeseen >=  31.5 & timeseen < 34.5
(267 real changes made)

. replace time1 = 36 if timeseen >=  34.5 & timeseen < 37.5
```

```
(308 real changes made)

.
. replace time1 = 39 if timeseen >=  37.5 & timeseen < 40.5
(180 real changes made)

. replace time1 = 42 if timeseen >=  40.5 & timeseen < 43.5
(112 real changes made)

. replace time1 = 45 if timeseen >=  43.5 & timeseen < 46.5
(59 real changes made)

. replace time1 = 48 if timeseen >=  46.5 & timeseen < 49.5
(114 real changes made)

.
. replace time1 = 51 if timeseen >=  49.5 & timeseen < 52.5
(12 real changes made)

. replace time1 = 54 if timeseen >=  52.5 & timeseen < 55.5
(0 real changes made)

. replace time1 = 57 if timeseen >=  55.5 & timeseen < 58.5
(0 real changes made)

. replace time1 = 60 if timeseen >=  58.5 & timeseen < 61.5
(0 real changes made)

.
. tabulate time1 time_integer
```

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499 ...	time_integer							
	0	1	2	3	4	5	6	Total
0	405	0	0	0	0	0	0	405
3	0	159	360	424	127	0	0	1,070
6	0	0	0	0	94	223	338	773
9	0	0	0	0	0	0	0	653
12	0	0	0	0	0	0	0	721
15	0	0	0	0	0	0	0	562
18	0	0	0	0	0	0	0	482
21	0	0	0	0	0	0	0	442
24	0	0	0	0	0	0	0	480
27	0	0	0	0	0	0	0	354
30	0	0	0	0	0	0	0	301
33	0	0	0	0	0	0	0	267
36	0	0	0	0	0	0	0	308
39	0	0	0	0	0	0	0	180
42	0	0	0	0	0	0	0	112
45	0	0	0	0	0	0	0	59
48	0	0	0	0	0	0	0	114
51	0	0	0	0	0	0	0	12
Total	405	159	360	424	221	223	338	7,295

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499 ...	time_integer							
	7	8	9	10	11	12	13	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,070
6	118	0	0	0	0	0	0	773
9	67	200	290	96	0	0	0	653
12	0	0	0	66	268	287	100	721
15	0	0	0	0	0	0	66	562
18	0	0	0	0	0	0	0	482

21	0	0	0	0	0	0	0	442
24	0	0	0	0	0	0	0	480
27	0	0	0	0	0	0	0	354
30	0	0	0	0	0	0	0	301
33	0	0	0	0	0	0	0	267
36	0	0	0	0	0	0	0	308
39	0	0	0	0	0	0	0	180
42	0	0	0	0	0	0	0	112
45	0	0	0	0	0	0	0	59
48	0	0	0	0	0	0	0	114
51	0	0	0	0	0	0	0	12
Total	185	200	290	162	268	287	166	7,295

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499, ...

	time_integer							
	14	15	16	17	18	19	20	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,070
6	0	0	0	0	0	0	0	773
9	0	0	0	0	0	0	0	653
12	0	0	0	0	0	0	0	721
15	212	214	70	0	0	0	0	562
18	0	0	35	162	230	55	0	482
21	0	0	0	0	0	39	145	442
24	0	0	0	0	0	0	0	480
27	0	0	0	0	0	0	0	354
30	0	0	0	0	0	0	0	301
33	0	0	0	0	0	0	0	267
36	0	0	0	0	0	0	0	308
39	0	0	0	0	0	0	0	180
42	0	0	0	0	0	0	0	112
45	0	0	0	0	0	0	0	59
48	0	0	0	0	0	0	0	114
51	0	0	0	0	0	0	0	12
Total	212	214	105	162	230	94	145	7,295

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499, ...

	time_integer							
	21	22	23	24	25	26	27	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,070
6	0	0	0	0	0	0	0	773
9	0	0	0	0	0	0	0	653
12	0	0	0	0	0	0	0	721
15	0	0	0	0	0	0	0	562
18	0	0	0	0	0	0	0	482
21	189	69	0	0	0	0	0	442
24	0	34	161	220	65	0	0	480
27	0	0	0	0	40	121	154	354
30	0	0	0	0	0	0	0	301
33	0	0	0	0	0	0	0	267
36	0	0	0	0	0	0	0	308
39	0	0	0	0	0	0	0	180
42	0	0	0	0	0	0	0	112
45	0	0	0	0	0	0	0	59
48	0	0	0	0	0	0	0	114
51	0	0	0	0	0	0	0	12
Total	189	103	161	220	105	121	154	7,295

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499, ...

	time_integer							
	28	29	30	31	32	33	34	Total

0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,070
6	0	0	0	0	0	0	0	773
9	0	0	0	0	0	0	0	653
12	0	0	0	0	0	0	0	721
15	0	0	0	0	0	0	0	562
18	0	0	0	0	0	0	0	482
21	0	0	0	0	0	0	0	442
24	0	0	0	0	0	0	0	480
27	39	0	0	0	0	0	0	354
30	29	103	131	38	0	0	0	301
33	0	0	0	17	109	102	39	267
36	0	0	0	0	0	0	30	308
39	0	0	0	0	0	0	0	180
42	0	0	0	0	0	0	0	112
45	0	0	0	0	0	0	0	59
48	0	0	0	0	0	0	0	114
51	0	0	0	0	0	0	0	12
Total	68	103	131	55	109	102	69	7,295

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499 | time_integer

...	35	36	37	38	39	40	41	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,070
6	0	0	0	0	0	0	0	773
9	0	0	0	0	0	0	0	653
12	0	0	0	0	0	0	0	721
15	0	0	0	0	0	0	0	562
18	0	0	0	0	0	0	0	482
21	0	0	0	0	0	0	0	442
24	0	0	0	0	0	0	0	480
27	0	0	0	0	0	0	0	354
30	0	0	0	0	0	0	0	301
33	0	0	0	0	0	0	0	267
36	114	124	40	0	0	0	0	308
39	0	0	15	85	66	14	0	180
42	0	0	0	0	0	12	53	112
45	0	0	0	0	0	0	0	59
48	0	0	0	0	0	0	0	114
51	0	0	0	0	0	0	0	12
Total	114	124	55	85	66	26	53	7,295

Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499 | time_integer

...	42	43	44	45	46	47	48	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,070
6	0	0	0	0	0	0	0	773
9	0	0	0	0	0	0	0	653
12	0	0	0	0	0	0	0	721
15	0	0	0	0	0	0	0	562
18	0	0	0	0	0	0	0	482
21	0	0	0	0	0	0	0	442
24	0	0	0	0	0	0	0	480
27	0	0	0	0	0	0	0	354
30	0	0	0	0	0	0	0	301
33	0	0	0	0	0	0	0	267
36	0	0	0	0	0	0	0	308
39	0	0	0	0	0	0	0	180
42	40	7	0	0	0	0	0	112
45	0	11	26	13	9	0	0	59
48	0	0	0	0	9	60	40	114
51	0	0	0	0	0	0	0	12
Total	40	18	26	13	18	60	40	7,295

Months: 0, |

```
    1.5 to |
    4.499, |
    4.5 to |
7.499, 7.5 |
 to 10.499 |           time_integer
      ...  |        49         50         52 |     Total
-----------+---------------------------------+----------
         0 |         0          0          0 |       405
         3 |         0          0          0 |     1,070
         6 |         0          0          0 |       773
         9 |         0          0          0 |       653
        12 |         0          0          0 |       721
        15 |         0          0          0 |       562
        18 |         0          0          0 |       482
        21 |         0          0          0 |       442
        24 |         0          0          0 |       480
        27 |         0          0          0 |       354
        30 |         0          0          0 |       301
        33 |         0          0          0 |       267
        36 |         0          0          0 |       308
        39 |         0          0          0 |       180
        42 |         0          0          0 |       112
        45 |         0          0          0 |        59
        48 |         5          0          0 |       114
        51 |         2          8          2 |        12
-----------+---------------------------------+----------
     Total |         7          8          2 |     7,295
```

```
. tab purg1c3b

   baseline |
 pain score |
-- 3 levels |      Freq.     Percent        Cum.
------------+-----------------------------------
          1 |      2,259       27.61       27.61
          2 |      4,093       50.03       77.64
          3 |      1,829       22.36      100.00
------------+-----------------------------------
      Total |      8,181      100.00
```

```
. generate Paintime1 = (100*purg1c3b) + time1
(886 missing values generated)

. tab Paintime1 time1, missing

           |          Months: 0, 1.5 to 4.499,  4.5 to 7.499, 7.5 to 10.499 ...
 Paintime1 |         0          3          6          9         12         15         18 |     Total
-----------+-------------------------------------------------------------------------------+----------
       100 |       107          0          0          0          0          0          0 |       107
       103 |         0        282          0          0          0          0          0 |       282
       106 |         0          0        197          0          0          0          0 |       197
       109 |         0          0          0        178          0          0          0 |       178
       112 |         0          0          0          0        190          0          0 |       190
       115 |         0          0          0          0          0        157          0 |       157
       118 |         0          0          0          0          0          0        137 |       137
       121 |         0          0          0          0          0          0          0 |       132
       124 |         0          0          0          0          0          0          0 |       133
       127 |         0          0          0          0          0          0          0 |       104
       130 |         0          0          0          0          0          0          0 |        97
       133 |         0          0          0          0          0          0          0 |        76
       136 |         0          0          0          0          0          0          0 |        96
       139 |         0          0          0          0          0          0          0 |        60
       142 |         0          0          0          0          0          0          0 |        35
       145 |         0          0          0          0          0          0          0 |        15
       148 |         0          0          0          0          0          0          0 |        31
       151 |         0          0          0          0          0          0          0 |         1
       200 |       208          0          0          0          0          0          0 |       208
       203 |         0        546          0          0          0          0          0 |       546
       206 |         0          0        399          0          0          0          0 |       399
       209 |         0          0          0        322          0          0          0 |       322
       212 |         0          0          0          0        372          0          0 |       372
       215 |         0          0          0          0          0        270          0 |       270
       218 |         0          0          0          0          0          0        242 |       242
       221 |         0          0          0          0          0          0          0 |       220
       224 |         0          0          0          0          0          0          0 |       234
       227 |         0          0          0          0          0          0          0 |       182
       230 |         0          0          0          0          0          0          0 |       149
       233 |         0          0          0          0          0          0          0 |       137
       236 |         0          0          0          0          0          0          0 |       143
```

239	0	0	0	0	0	0	0	85
242	0	0	0	0	0	0	0	49
245	0	0	0	0	0	0	0	32
248	0	0	0	0	0	0	0	47
251	0	0	0	0	0	0	0	9
300	90	0	0	0	0	0	0	90
303	0	242	0	0	0	0	0	242
306	0	0	177	0	0	0	0	177
309	0	0	0	153	0	0	0	153
312	0	0	0	0	159	0	0	159
315	0	0	0	0	0	135	0	135
318	0	0	0	0	0	0	103	103
321	0	0	0	0	0	0	0	90
324	0	0	0	0	0	0	0	113
327	0	0	0	0	0	0	0	68
330	0	0	0	0	0	0	0	55
333	0	0	0	0	0	0	0	54
336	0	0	0	0	0	0	0	69
339	0	0	0	0	0	0	0	35
342	0	0	0	0	0	0	0	28
345	0	0	0	0	0	0	0	12
348	0	0	0	0	0	0	0	36
351	0	0	0	0	0	0	0	2
.	0	0	0	0	0	0	0	886
Total	405	1,070	773	653	721	562	482	8,181

	Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499 ...							
Paintime1	21	24	27	30	33	36	39	Total
100	0	0	0	0	0	0	0	107
103	0	0	0	0	0	0	0	282
106	0	0	0	0	0	0	0	197
109	0	0	0	0	0	0	0	178
112	0	0	0	0	0	0	0	190
115	0	0	0	0	0	0	0	157
118	0	0	0	0	0	0	0	137
121	132	0	0	0	0	0	0	132
124	0	133	0	0	0	0	0	133
127	0	0	104	0	0	0	0	104
130	0	0	0	97	0	0	0	97
133	0	0	0	0	76	0	0	76
136	0	0	0	0	0	96	0	96
139	0	0	0	0	0	0	60	60
142	0	0	0	0	0	0	0	35
145	0	0	0	0	0	0	0	15
148	0	0	0	0	0	0	0	31
151	0	0	0	0	0	0	0	1
200	0	0	0	0	0	0	0	208
203	0	0	0	0	0	0	0	546
206	0	0	0	0	0	0	0	399
209	0	0	0	0	0	0	0	322
212	0	0	0	0	0	0	0	372
215	0	0	0	0	0	0	0	270
218	0	0	0	0	0	0	0	242
221	220	0	0	0	0	0	0	220
224	0	234	0	0	0	0	0	234
227	0	0	182	0	0	0	0	182
230	0	0	0	149	0	0	0	149
233	0	0	0	0	137	0	0	137
236	0	0	0	0	0	143	0	143
239	0	0	0	0	0	0	85	85
242	0	0	0	0	0	0	0	49
245	0	0	0	0	0	0	0	32
248	0	0	0	0	0	0	0	47
251	0	0	0	0	0	0	0	9
300	0	0	0	0	0	0	0	90
303	0	0	0	0	0	0	0	242
306	0	0	0	0	0	0	0	177
309	0	0	0	0	0	0	0	153
312	0	0	0	0	0	0	0	159
315	0	0	0	0	0	0	0	135
318	0	0	0	0	0	0	0	103
321	90	0	0	0	0	0	0	90
324	0	113	0	0	0	0	0	113
327	0	0	68	0	0	0	0	68
330	0	0	0	55	0	0	0	55
333	0	0	0	0	54	0	0	54
336	0	0	0	0	0	69	0	69
339	0	0	0	0	0	0	35	35
342	0	0	0	0	0	0	0	28
345	0	0	0	0	0	0	0	12

348	0	0	0	0	0	0	0	36
351	0	0	0	0	0	0	0	2
.	0	0	0	0	0	0	0	886
Total	442	480	354	301	267	308	180	8,181

Paintime1	Months: 0, 1.5 to 4.499, 4.5 to 7.499, 7.5 to 10.499 ... 42	45	48	51	.	Total
100	0	0	0	0	0	107
103	0	0	0	0	0	282
106	0	0	0	0	0	197
109	0	0	0	0	0	178
112	0	0	0	0	0	190
115	0	0	0	0	0	157
118	0	0	0	0	0	137
121	0	0	0	0	0	132
124	0	0	0	0	0	133
127	0	0	0	0	0	104
130	0	0	0	0	0	97
133	0	0	0	0	0	76
136	0	0	0	0	0	96
139	0	0	0	0	0	60
142	35	0	0	0	0	35
145	0	15	0	0	0	15
148	0	0	31	0	0	31
151	0	0	0	1	0	1
200	0	0	0	0	0	208
203	0	0	0	0	0	546
206	0	0	0	0	0	399
209	0	0	0	0	0	322
212	0	0	0	0	0	372
215	0	0	0	0	0	270
218	0	0	0	0	0	242
221	0	0	0	0	0	220
224	0	0	0	0	0	234
227	0	0	0	0	0	182
230	0	0	0	0	0	149
233	0	0	0	0	0	137
236	0	0	0	0	0	143
239	0	0	0	0	0	85
242	49	0	0	0	0	49
245	0	32	0	0	0	32
248	0	0	47	0	0	47
251	0	0	0	9	0	9
300	0	0	0	0	0	90
303	0	0	0	0	0	242
306	0	0	0	0	0	177
309	0	0	0	0	0	153
312	0	0	0	0	0	159
315	0	0	0	0	0	135
318	0	0	0	0	0	103
321	0	0	0	0	0	90
324	0	0	0	0	0	113
327	0	0	0	0	0	68
330	0	0	0	0	0	55
333	0	0	0	0	0	54
336	0	0	0	0	0	69
339	0	0	0	0	0	35
342	28	0	0	0	0	28
345	0	12	0	0	0	12
348	0	0	36	0	0	36
351	0	0	0	2	0	2
.	0	0	0	0	886	886
Total	112	59	114	12	886	8,181

```
. tab Paintime1 purg1c3b, missing
```

Paintime1	baseline pain score -- 3 levels 1	2	3	Total
100	107	0	0	107
103	282	0	0	282
106	197	0	0	197
109	178	0	0	178
112	190	0	0	190

```
        115 |       157          0          0 |       157
        118 |       137          0          0 |       137
        121 |       132          0          0 |       132
        124 |       133          0          0 |       133
        127 |       104          0          0 |       104
        130 |        97          0          0 |        97
        133 |        76          0          0 |        76
        136 |        96          0          0 |        96
        139 |        60          0          0 |        60
        142 |        35          0          0 |        35
        145 |        15          0          0 |        15
        148 |        31          0          0 |        31
        151 |         1          0          0 |         1
        200 |         0        208          0 |       208
        203 |         0        546          0 |       546
        206 |         0        399          0 |       399
        209 |         0        322          0 |       322
        212 |         0        372          0 |       372
        215 |         0        270          0 |       270
        218 |         0        242          0 |       242
        221 |         0        220          0 |       220
        224 |         0        234          0 |       234
        227 |         0        182          0 |       182
        230 |         0        149          0 |       149
        233 |         0        137          0 |       137
        236 |         0        143          0 |       143
        239 |         0         85          0 |        85
        242 |         0         49          0 |        49
        245 |         0         32          0 |        32
        248 |         0         47          0 |        47
        251 |         0          9          0 |         9
        300 |         0          0         90 |        90
        303 |         0          0        242 |       242
        306 |         0          0        177 |       177
        309 |         0          0        153 |       153
        312 |         0          0        159 |       159
        315 |         0          0        135 |       135
        318 |         0          0        103 |       103
        321 |         0          0         90 |        90
        324 |         0          0        113 |       113
        327 |         0          0         68 |        68
        330 |         0          0         55 |        55
        333 |         0          0         54 |        54
        336 |         0          0         69 |        69
        339 |         0          0         35 |        35
        342 |         0          0         28 |        28
        345 |         0          0         12 |        12
        348 |         0          0         36 |        36
        351 |         0          0          2 |         2
          . |       231        447        208 |       886
----------+---------------------------------+----------
      Total |     2,259      4,093      1,829 |     8,181
```

```
. sort Paintime1

. *by Paintime1: summarize purg_1
. oneway purg_1 Paintime1, tabulate

           |  Summary of pain score over last 4
           |                weeks
  Paintime1 |        Mean   Std. Dev.       Freq.
------------+------------------------------------
        100 |    1.635514   1.0585904         107
        103 |        2.75   2.1394715         140
        106 |        2.49   2.1296132         100
```

109	2.3956044	1.9881824	91
112	2.2727273	2.137222	99
115	2.7037037	2.4054337	81
118	2.5820896	2.3429407	67
121	2.3636364	2.0277791	66
124	2.625	2.3128351	64
127	2.1111111	1.7338654	54
130	1.7959184	1.7075762	49
133	1.6578947	1.7441224	38
136	2.0816327	1.9667733	49
139	2.4333333	2.635086	30
142	1.5294118	1.3746657	17
145	2.5555556	3.0459445	9
148	2.4666667	2.3563491	15
151	0	0	1
200	5.125	.79475941	208
203	4.5378788	2.121429	264
206	4.0502513	2.1526323	199
209	3.867052	2.2307864	173
212	4.1736842	2.0769183	190
215	4.1527778	2.0765741	144
218	3.9586777	2.3783632	121
221	3.8034188	2.0977793	117
224	3.9827586	2.2840953	116
227	3.7021277	2.3363872	94
230	3.5810811	2.013698	74
233	3.5070423	2.3106786	71
236	3.4714286	2.3450313	70
239	3.2888889	2.1492305	45
242	3.16	2.0141168	25
245	3.6875	2.120338	16
248	2.9583333	2.2161299	24
251	3	2	5
300	7.5555556	.75119547	90
303	5.8547009	2.1745588	117
306	5.3181818	2.6675808	88
309	5.3636364	2.3221422	77
312	5.5121951	2.4355591	82
315	5.1780822	2.3531449	73
318	5.1875	2.7879395	48
321	5.4285714	2.7386128	49
324	5.2372881	2.160292	59
327	4.8529412	2.9246326	34
330	4.8965517	2.8074496	29
333	4.8	2.6444477	30
336	5.0588235	2.5577118	34
339	5.0952381	2.4063408	21
342	5.2307692	2.0475126	13
345	5.5	2.0736441	6
348	6.1666667	2.1760731	18
351	0	0	1
Total	3.9284982	2.4699709	3902

Analysis of Variance

Source	SS	df	MS	F	Prob > F
Between groups	6325.69828	53	119.352798	26.28	0.0000
Within groups	17473.3527	3848	4.54089208		
Total	23799.051	3901	6.10075647		

Bartlett's test for equal variances: chi2(51) = 490.2570 Prob>chi2 = 0.000

```
note: Bartlett's test performed on cells with positive variance:
      2 single-observation cells not used

. * pause
.
. generate time2 = .
(8181 missing values generated)

. label var time2 "Months:  0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ..."

. replace time2 = .  if timeseen < 0
(0 real changes made)

. replace time2 = 0 if timeseen == 0
(405 real changes made)

.
. replace time2 = 3 if timeseen   > 0 & timeseen < 3
(1221 real changes made)

. replace time2 = 6 if timeseen   >= 3 & timeseen < 6
(868 real changes made)

. replace time2 = 9 if timeseen   >= 6 & timeseen < 9
(723 real changes made)

. replace time2 = 12 if timeseen >= 9 & timeseen < 12
(720 real changes made)

.
. replace time2 = 15 if timeseen >= 12 & timeseen < 15
(665 real changes made)

. replace time2 = 18 if timeseen >= 15 & timeseen < 18
(481 real changes made)

. replace time2 = 21 if timeseen >= 18 & timeseen < 21
(469 real changes made)

. replace time2 = 24 if timeseen >= 21 & timeseen < 24
(453 real changes made)

.
. replace time2 = 27 if timeseen >=  24 & timeseen < 27
(446 real changes made)

. replace time2 = 30 if timeseen >=  27 & timeseen < 30
(325 real changes made)

. replace time2 = 33 if timeseen >=  30 & timeseen < 33
(295 real changes made)

. replace time2 = 36 if timeseen >=  33 & timeseen < 36
(285 real changes made)

.
. replace time2 = 39 if timeseen >=  36 & timeseen < 39
(264 real changes made)

. replace time2 = 42 if timeseen >=  39 & timeseen < 42
(145 real changes made)

. replace time2 = 45 if timeseen >=  42 & timeseen < 45
(84 real changes made)

. replace time2 = 48 if timeseen >=  45 & timeseen < 48
(91 real changes made)
```

```
. 
. replace time2 = 51 if timeseen >=  48 & timeseen < 51
(55 real changes made)

. replace time2 = 54 if timeseen >=  51 & timeseen < 54
(2 real changes made)

. replace time2 = 57 if timeseen >=  54 & timeseen < 57
(0 real changes made)

. replace time2 = 60 if timeseen >=  57 & timeseen < 60
(0 real changes made)

. 
. tabulate time2 time_integer
```

Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...	time_integer							
	0	1	2	3	4	5	6	Total
0	405	0	0	0	0	0	0	405
3	415	446	360	0	0	0	0	1,221
6	0	0	0	424	221	223	0	868
9	0	0	0	0	0	0	338	723
12	0	0	0	0	0	0	0	720
15	0	0	0	0	0	0	0	665
18	0	0	0	0	0	0	0	481
21	0	0	0	0	0	0	0	469
24	0	0	0	0	0	0	0	453
27	0	0	0	0	0	0	0	446
30	0	0	0	0	0	0	0	325
33	0	0	0	0	0	0	0	295
36	0	0	0	0	0	0	0	285
39	0	0	0	0	0	0	0	264
42	0	0	0	0	0	0	0	145
45	0	0	0	0	0	0	0	84
48	0	0	0	0	0	0	0	91
51	0	0	0	0	0	0	0	55
54	0	0	0	0	0	0	0	2
Total	820	446	360	424	221	223	338	7,997

Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...	time_integer							
	7	8	9	10	11	12	13	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,221
6	0	0	0	0	0	0	0	868
9	185	200	0	0	0	0	0	723
12	0	0	290	162	268	0	0	720
15	0	0	0	0	0	287	166	665
18	0	0	0	0	0	0	0	481
21	0	0	0	0	0	0	0	469
24	0	0	0	0	0	0	0	453
27	0	0	0	0	0	0	0	446
30	0	0	0	0	0	0	0	325
33	0	0	0	0	0	0	0	295
36	0	0	0	0	0	0	0	285
39	0	0	0	0	0	0	0	264
42	0	0	0	0	0	0	0	145
45	0	0	0	0	0	0	0	84
48	0	0	0	0	0	0	0	91
51	0	0	0	0	0	0	0	55
54	0	0	0	0	0	0	0	2
Total	185	200	290	162	268	287	166	7,997

Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...	time_integer							
	14	15	16	17	18	19	20	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,221
6	0	0	0	0	0	0	0	868
9	0	0	0	0	0	0	0	723
12	0	0	0	0	0	0	0	720
15	212	0	0	0	0	0	0	665

18	0	214	105	162	0	0	0	481
21	0	0	0	0	230	94	145	469
24	0	0	0	0	0	0	0	453
27	0	0	0	0	0	0	0	446
30	0	0	0	0	0	0	0	325
33	0	0	0	0	0	0	0	295
36	0	0	0	0	0	0	0	285
39	0	0	0	0	0	0	0	264
42	0	0	0	0	0	0	0	145
45	0	0	0	0	0	0	0	84
48	0	0	0	0	0	0	0	91
51	0	0	0	0	0	0	0	55
54	0	0	0	0	0	0	0	2
Total	212	214	105	162	230	94	145	7,997

Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...	time_integer							
	21	22	23	24	25	26	27	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,221
6	0	0	0	0	0	0	0	868
9	0	0	0	0	0	0	0	723
12	0	0	0	0	0	0	0	720
15	0	0	0	0	0	0	0	665
18	0	0	0	0	0	0	0	481
21	0	0	0	0	0	0	0	469
24	189	103	161	0	0	0	0	453
27	0	0	0	220	105	121	0	446
30	0	0	0	0	0	0	154	325
33	0	0	0	0	0	0	0	295
36	0	0	0	0	0	0	0	285
39	0	0	0	0	0	0	0	264
42	0	0	0	0	0	0	0	145
45	0	0	0	0	0	0	0	84
48	0	0	0	0	0	0	0	91
51	0	0	0	0	0	0	0	55
54	0	0	0	0	0	0	0	2
Total	189	103	161	220	105	121	154	7,997

Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...	time_integer							
	28	29	30	31	32	33	34	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,221
6	0	0	0	0	0	0	0	868
9	0	0	0	0	0	0	0	723
12	0	0	0	0	0	0	0	720
15	0	0	0	0	0	0	0	665
18	0	0	0	0	0	0	0	481
21	0	0	0	0	0	0	0	469
24	0	0	0	0	0	0	0	453
27	0	0	0	0	0	0	0	446
30	68	103	0	0	0	0	0	325
33	0	0	131	55	109	0	0	295
36	0	0	0	0	0	102	69	285
39	0	0	0	0	0	0	0	264
42	0	0	0	0	0	0	0	145
45	0	0	0	0	0	0	0	84
48	0	0	0	0	0	0	0	91
51	0	0	0	0	0	0	0	55
54	0	0	0	0	0	0	0	2
Total	68	103	131	55	109	102	69	7,997

Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...	time_integer							
	35	36	37	38	39	40	41	Total
0	0	0	0	0	0	0	0	405
3	0	0	0	0	0	0	0	1,221
6	0	0	0	0	0	0	0	868
9	0	0	0	0	0	0	0	723
12	0	0	0	0	0	0	0	720
15	0	0	0	0	0	0	0	665
18	0	0	0	0	0	0	0	481
21	0	0	0	0	0	0	0	469
24	0	0	0	0	0	0	0	453
27	0	0	0	0	0	0	0	446
30	0	0	0	0	0	0	0	325
33	0	0	0	0	0	0	0	295

```
       36 |      114          0          0          0          0          0          0 |       285
       39 |        0        124         55         85          0          0          0 |       264
       42 |        0          0          0          0         66         26         53 |       145
       45 |        0          0          0          0          0          0          0 |        84
       48 |        0          0          0          0          0          0          0 |        91
       51 |        0          0          0          0          0          0          0 |        55
       54 |        0          0          0          0          0          0          0 |         2
----------+-----------------------------------------------------------------------------+----------
    Total |      114        124         55         85         66         26         53 |     7,997
```

```
  Months: |
0, .01 to |
2.99, 3.00 |
  to 5.99, |
   6.00 to |                                time_integer
  8.99 ... |       42         43         44         45         46         47         48 |     Total
-----------+-----------------------------------------------------------------------------+----------
         0 |        0          0          0          0          0          0          0 |       405
         3 |        0          0          0          0          0          0          0 |     1,221
         6 |        0          0          0          0          0          0          0 |       868
         9 |        0          0          0          0          0          0          0 |       723
        12 |        0          0          0          0          0          0          0 |       720
        15 |        0          0          0          0          0          0          0 |       665
        18 |        0          0          0          0          0          0          0 |       481
        21 |        0          0          0          0          0          0          0 |       469
        24 |        0          0          0          0          0          0          0 |       453
        27 |        0          0          0          0          0          0          0 |       446
        30 |        0          0          0          0          0          0          0 |       325
        33 |        0          0          0          0          0          0          0 |       295
        36 |        0          0          0          0          0          0          0 |       285
        39 |        0          0          0          0          0          0          0 |       264
        42 |        0          0          0          0          0          0          0 |       145
        45 |       40         18         26          0          0          0          0 |        84
        48 |        0          0          0         13         18         60          0 |        91
        51 |        0          0          0          0          0          0         40 |        55
        54 |        0          0          0          0          0          0          0 |         2
-----------+-----------------------------------------------------------------------------+----------
    Total |       40         18         26         13         18         60         40 |     7,997
```

```
  Months: |
0, .01 to |
2.99, 3.00 |
  to 5.99, |
   6.00 to |            time_integer
  8.99 ... |       49         50         52 |     Total
-----------+---------------------------------+----------
         0 |        0          0          0 |       405
         3 |        0          0          0 |     1,221
         6 |        0          0          0 |       868
         9 |        0          0          0 |       723
        12 |        0          0          0 |       720
        15 |        0          0          0 |       665
        18 |        0          0          0 |       481
        21 |        0          0          0 |       469
        24 |        0          0          0 |       453
        27 |        0          0          0 |       446
        30 |        0          0          0 |       325
        33 |        0          0          0 |       295
        36 |        0          0          0 |       285
        39 |        0          0          0 |       264
        42 |        0          0          0 |       145
        45 |        0          0          0 |        84
        48 |        0          0          0 |        91
        51 |        7          8          0 |        55
        54 |        0          0          2 |         2
-----------+---------------------------------+----------
     Total |        7          8          2 |     7,997
```

```
.
. tab purg1c3b

  baseline |
pain score |
-- 3 levels |      Freq.     Percent        Cum.
------------+-----------------------------------
          1 |      2,259       27.61       27.61
```

```
          2 |      4,093       50.03       77.64
          3 |      1,829       22.36      100.00
------------+-----------------------------------
      Total |      8,181      100.00
```

```
. generate Paintime2 = (100*purg1c3b) + time2
(184 missing values generated)
```

```
. tab Paintime2 time2, missing
```

	Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...						
Paintime2	0	3	6	9	12	15	18	Total
100	107	0	0	0	0	0	0	107
103	0	316	0	0	0	0	0	316
106	0	0	232	0	0	0	0	232
109	0	0	0	190	0	0	0	190
112	0	0	0	0	199	0	0	199
115	0	0	0	0	0	170	0	170
118	0	0	0	0	0	0	136	136
121	0	0	0	0	0	0	0	143
124	0	0	0	0	0	0	0	131
127	0	0	0	0	0	0	0	128
130	0	0	0	0	0	0	0	97
133	0	0	0	0	0	0	0	83
136	0	0	0	0	0	0	0	89
139	0	0	0	0	0	0	0	79
142	0	0	0	0	0	0	0	44
145	0	0	0	0	0	0	0	24
148	0	0	0	0	0	0	0	24
151	0	0	0	0	0	0	0	16
200	208	0	0	0	0	0	0	208
203	0	621	0	0	0	0	0	621
206	0	0	442	0	0	0	0	442
209	0	0	0	372	0	0	0	372
212	0	0	0	0	358	0	0	358
215	0	0	0	0	0	328	0	328
218	0	0	0	0	0	0	240	240
221	0	0	0	0	0	0	0	230
224	0	0	0	0	0	0	0	216
227	0	0	0	0	0	0	0	223
230	0	0	0	0	0	0	0	168
233	0	0	0	0	0	0	0	146
236	0	0	0	0	0	0	0	143
239	0	0	0	0	0	0	0	127
242	0	0	0	0	0	0	0	69
245	0	0	0	0	0	0	0	39
248	0	0	0	0	0	0	0	38
251	0	0	0	0	0	0	0	27
254	0	0	0	0	0	0	0	2
300	90	0	0	0	0	0	0	90
303	0	284	0	0	0	0	0	284
306	0	0	194	0	0	0	0	194
309	0	0	0	161	0	0	0	161
312	0	0	0	0	163	0	0	163
315	0	0	0	0	0	167	0	167
318	0	0	0	0	0	0	105	105
321	0	0	0	0	0	0	0	96
324	0	0	0	0	0	0	0	106
327	0	0	0	0	0	0	0	95
330	0	0	0	0	0	0	0	60
333	0	0	0	0	0	0	0	66
336	0	0	0	0	0	0	0	53
339	0	0	0	0	0	0	0	58
342	0	0	0	0	0	0	0	32
345	0	0	0	0	0	0	0	21
348	0	0	0	0	0	0	0	29
351	0	0	0	0	0	0	0	12
.	0	0	0	0	0	0	0	184
Total	405	1,221	868	723	720	665	481	8,181

	Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...						
Paintime2	21	24	27	30	33	36	39	Total
100	0	0	0	0	0	0	0	107
103	0	0	0	0	0	0	0	316
106	0	0	0	0	0	0	0	232
109	0	0	0	0	0	0	0	190
112	0	0	0	0	0	0	0	199
115	0	0	0	0	0	0	0	170
118	0	0	0	0	0	0	0	136
121	143	0	0	0	0	0	0	143
124	0	131	0	0	0	0	0	131
127	0	0	128	0	0	0	0	128
130	0	0	0	97	0	0	0	97
133	0	0	0	0	83	0	0	83
136	0	0	0	0	0	89	0	89
139	0	0	0	0	0	0	79	79
142	0	0	0	0	0	0	0	44
145	0	0	0	0	0	0	0	24

148	0	0	0	0	0	0	0	24
151	0	0	0	0	0	0	0	16
200	0	0	0	0	0	0	0	208
203	0	0	0	0	0	0	0	621
206	0	0	0	0	0	0	0	442
209	0	0	0	0	0	0	0	372
212	0	0	0	0	0	0	0	358
215	0	0	0	0	0	0	0	328
218	0	0	0	0	0	0	0	240
221	230	0	0	0	0	0	0	230
224	0	216	0	0	0	0	0	216
227	0	0	223	0	0	0	0	223
230	0	0	0	168	0	0	0	168
233	0	0	0	0	146	0	0	146
236	0	0	0	0	0	143	0	143
239	0	0	0	0	0	0	127	127
242	0	0	0	0	0	0	0	69
245	0	0	0	0	0	0	0	39
248	0	0	0	0	0	0	0	38
251	0	0	0	0	0	0	0	27
254	0	0	0	0	0	0	0	2
300	0	0	0	0	0	0	0	90
303	0	0	0	0	0	0	0	284
306	0	0	0	0	0	0	0	194
309	0	0	0	0	0	0	0	161
312	0	0	0	0	0	0	0	163
315	0	0	0	0	0	0	0	167
318	0	0	0	0	0	0	0	105
321	96	0	0	0	0	0	0	96
324	0	106	0	0	0	0	0	106
327	0	0	95	0	0	0	0	95
330	0	0	0	60	0	0	0	60
333	0	0	0	0	66	0	0	66
336	0	0	0	0	0	53	0	53
339	0	0	0	0	0	0	58	58
342	0	0	0	0	0	0	0	32
345	0	0	0	0	0	0	0	21
348	0	0	0	0	0	0	0	29
351	0	0	0	0	0	0	0	12
.	0	0	0	0	0	0	0	184
Total	469	453	446	325	295	285	264	8,181

	Months: 0, .01 to 2.99, 3.00 to 5.99, 6.00 to 8.99 ...						
Paintime2	42	45	48	51	54	.	Total
100	0	0	0	0	0	0	107
103	0	0	0	0	0	0	316
106	0	0	0	0	0	0	232
109	0	0	0	0	0	0	190
112	0	0	0	0	0	0	199
115	0	0	0	0	0	0	170
118	0	0	0	0	0	0	136
121	0	0	0	0	0	0	143
124	0	0	0	0	0	0	131
127	0	0	0	0	0	0	128
130	0	0	0	0	0	0	97
133	0	0	0	0	0	0	83
136	0	0	0	0	0	0	89
139	0	0	0	0	0	0	79
142	44	0	0	0	0	0	44
145	0	24	0	0	0	0	24
148	0	0	24	0	0	0	24
151	0	0	0	16	0	0	16
200	0	0	0	0	0	0	208
203	0	0	0	0	0	0	621
206	0	0	0	0	0	0	442
209	0	0	0	0	0	0	372
212	0	0	0	0	0	0	358
215	0	0	0	0	0	0	328
218	0	0	0	0	0	0	240
221	0	0	0	0	0	0	230
224	0	0	0	0	0	0	216
227	0	0	0	0	0	0	223
230	0	0	0	0	0	0	168
233	0	0	0	0	0	0	146
236	0	0	0	0	0	0	143
239	0	0	0	0	0	0	127
242	69	0	0	0	0	0	69
245	0	39	0	0	0	0	39
248	0	0	38	0	0	0	38
251	0	0	0	27	0	0	27
254	0	0	0	0	2	0	2
300	0	0	0	0	0	0	90
303	0	0	0	0	0	0	284
306	0	0	0	0	0	0	194
309	0	0	0	0	0	0	161
312	0	0	0	0	0	0	163
315	0	0	0	0	0	0	167
318	0	0	0	0	0	0	105
321	0	0	0	0	0	0	96
324	0	0	0	0	0	0	106
327	0	0	0	0	0	0	95
330	0	0	0	0	0	0	60
333	0	0	0	0	0	0	66

336	0	0	0	0	0	0	53
339	0	0	0	0	0	0	58
342	32	0	0	0	0	0	32
345	0	21	0	0	0	0	21
348	0	0	29	0	0	0	29
351	0	0	0	12	0	0	12
.	0	0	0	0	0	184	184
Total	145	84	91	55	2	184	8,181

```
. tab Paintime2 purg1c3b, missing
```

Paintime2	baseline pain score -- 3 levels 1	2	3	Total
100	107	0	0	107
103	316	0	0	316
106	232	0	0	232
109	190	0	0	190
112	199	0	0	199
115	170	0	0	170
118	136	0	0	136
121	143	0	0	143
124	131	0	0	131
127	128	0	0	128
130	97	0	0	97
133	83	0	0	83
136	89	0	0	89
139	79	0	0	79
142	44	0	0	44
145	24	0	0	24
148	24	0	0	24
151	16	0	0	16
200	0	208	0	208
203	0	621	0	621
206	0	442	0	442
209	0	372	0	372
212	0	358	0	358
215	0	328	0	328
218	0	240	0	240
221	0	230	0	230
224	0	216	0	216
227	0	223	0	223
230	0	168	0	168
233	0	146	0	146
236	0	143	0	143
239	0	127	0	127
242	0	69	0	69
245	0	39	0	39
248	0	38	0	38
251	0	27	0	27
254	0	2	0	2
300	0	0	90	90
303	0	0	284	284
306	0	0	194	194
309	0	0	161	161
312	0	0	163	163
315	0	0	167	167
318	0	0	105	105
321	0	0	96	96
324	0	0	106	106
327	0	0	95	95
330	0	0	60	60
333	0	0	66	66
336	0	0	53	53
339	0	0	58	58
342	0	0	32	32
345	0	0	21	21
348	0	0	29	29

```
       351 |         0          0         12 |        12
         . |        51         96         37 |       184
-----------+---------------------------------+----------
     Total |     2,259      4,093      1,829 |     8,181


. sort Paintime2

. *by Paintime2: summarize purg_1
. oneway purg_1 Paintime2, tabulate

           |  Summary of pain score over last 4
           |                weeks
  Paintime2 |        Mean   Std. Dev.       Freq.
------------+------------------------------------
        100 |    1.635514   1.0585904         107
        103 |        2.93    2.266377         100
        106 |   2.3813559   1.9738439         118
        109 |    2.592233   2.1757888         103
        112 |   2.3434343   2.0660601          99
        115 |   2.5581395   2.2886145          86
        118 |   2.5135135   2.2098363          74
        121 |   2.4647887   2.2604107          71
        124 |         2.5   2.0778499          64
        127 |     2.40625   2.2090632          64
        130 |         1.9   1.7172593          50
        133 |   1.6585366   1.6372195          41
        136 |   1.8837209   1.8924575          43
        139 |   2.7142857   2.5015675          42
        142 |   1.2857143   1.4880476          21
        145 |         2.5   1.9903614          14
        148 |   2.1666667   2.7906771          12
        151 |   2.1111111   2.1473498           9
        200 |       5.125   .79475941         208
        203 |       4.715   2.0431956         200
        206 |   4.3333333   2.1609356         225
        209 |   3.7883598   2.0776603         189
        212 |    3.973262   2.2056456         187
        215 |   4.2742857   1.9635095         175
        218 |   3.9596774   2.2100995         124
        221 |   3.8559322   2.3288434         118
        224 |   3.7522936   2.1651959         109
        227 |    3.973913   2.3300511         115
        230 |      3.7125   2.1060116          80
        233 |   3.7228916   2.2213666          83
        236 |   3.4029851   2.3998718          67
        239 |   3.3768116   2.2102798          69
        242 |   3.1714286   2.0791078          35
        245 |   3.4090909   2.0391196          22
        248 |        3.05   2.3946212          20
        251 |   3.0714286   2.0555473          14
        254 |          5           0           1
        300 |   7.5555556   .75119547          90
        303 |   5.8444444   2.0274028          90
        306 |   5.5979381   2.4051152          97
        309 |   5.3896104   2.5810842          77
        312 |   5.4819277   2.3235877          83
        315 |   5.4615385   2.4689525          91
        318 |   4.9433962   2.3730465          53
        321 |         5.3    2.719919          50
        324 |   5.3018868   2.6427325          53
        327 |         5.2   2.3386722          50
        330 |     4.90625   2.6683253          32
        333 |   4.9714286   2.8541581          35
        336 |   4.8148148     2.61706          27
        339 |   4.9677419   2.7262168          31
        342 |   5.1666667   1.9174125          18
```

```
        345 |   5.3333333    2.348436          12
        348 |         6.5   1.6984156          14
        351 |   4.4285714   3.1547394           7
------------+------------------------------------
      Total |   3.9447039   2.4622298        4069

                      Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      6566.92692     54   121.609758     26.98     0.0000
 Within groups      18095.6314   4014   4.50812941
------------------------------------------------------------------------
    Total           24662.5584   4068    6.0625758

Bartlett's test for equal variances:  chi2(53) = 487.0457  Prob>chi2 = 0.000

note: Bartlett's test performed on cells with positive variance:
      1 single-observation cells not used

. * pause

.-------------------------------------------------------------------------------

       log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\longitudianl_add.txt
  log type:  text
 opened on:  18 Nov 2005, 14:30:25

.
. generate time_integer = int(timeseen)

. tab time_integer

time_intege |
          r |      Freq.     Percent        Cum.
------------+-----------------------------------
         -2 |          1        0.01        0.01
         -1 |         16        0.15        0.16
          0 |      1,546       14.51       14.67
          1 |        658        6.17       20.84
          2 |        536        5.03       25.87
          3 |        602        5.65       31.52
          4 |        332        3.12       34.64
          5 |        314        2.95       37.58
          6 |        434        4.07       41.66
          7 |        270        2.53       44.19
          8 |        268        2.52       46.71
          9 |        386        3.62       50.33
         10 |        228        2.14       52.47
         11 |        327        3.07       55.54
         12 |        341        3.20       58.74
         13 |        216        2.03       60.76
         14 |        263        2.47       63.23
         15 |        260        2.44       65.67
         16 |        148        1.39       67.06
         17 |        202        1.90       68.96
         18 |        272        2.55       71.51
         19 |        123        1.15       72.66
         20 |        188        1.76       74.43
         21 |        224        2.10       76.53
         22 |        126        1.18       77.71
         23 |        186        1.75       79.46
         24 |        241        2.26       81.72
         25 |        120        1.13       82.85
         26 |        139        1.30       84.15
         27 |        185        1.74       85.89
         28 |         76        0.71       86.60
         29 |        113        1.06       87.66
```

```
         30 |        153        1.44       89.10
         31 |         68        0.64       89.73
         32 |        117        1.10       90.83
         33 |        118        1.11       91.94
         34 |         76        0.71       92.65
         35 |        119        1.12       93.77
         36 |        128        1.20       94.97
         37 |         57        0.53       95.50
         38 |         89        0.84       96.34
         39 |         70        0.66       97.00
         40 |         28        0.26       97.26
         41 |         56        0.53       97.79
         42 |         42        0.39       98.18
         43 |         20        0.19       98.37
         44 |         26        0.24       98.61
         45 |         13        0.12       98.73
         46 |         18        0.17       98.90
         47 |         60        0.56       99.47
         48 |         40        0.38       99.84
         49 |          7        0.07       99.91
         50 |          8        0.08       99.98
         52 |          2        0.02      100.00
------------+-----------------------------------
      Total |     10,656      100.00

.
. label define status 1"active" 2"lost to folloup" 3"withdrawn"

. label values fup_stat status

. tab fup_stat if timeseen==0.00

      follow-up |
         status |      Freq.     Percent        Cum.
----------------+-----------------------------------
         active |        405       63.58       63.58
lost to folloup |        109       17.11       80.69
      withdrawn |        123       19.31      100.00
----------------+-----------------------------------
          Total |        637      100.00

. * pause
. *tab max_fup fup_stat if timeseen==0.00, missing
. *tab max_fup fup_stat
. tab subj fup_stat if subj <= 110100

           |         follow-up status
      subj |    active  lost to f  withdrawn |     Total
-----------+---------------------------------+----------
    110027 |         0         27          0 |        27
    110029 |         0         32          0 |        32
    110039 |         0         27          0 |        27
    110040 |        25          0          0 |        25
    110045 |         0         28          0 |        28
    110049 |        28          0          0 |        28
    110051 |         0         20          0 |        20
    110052 |         0         27          0 |        27
    110053 |        23          0          0 |        23
    110055 |         0         21          0 |        21
    110057 |        26          0          0 |        26
    110058 |         0          0         24 |        24
    110059 |         0         22          0 |        22
    110060 |         0          9          0 |         9
    110062 |        25          0          0 |        25
    110065 |         0          6          0 |         6
    110066 |         0          0         12 |        12
```

```
    110067 |         0         15          0 |        15
    110068 |         0          6          0 |         6
    110069 |         0          8          0 |         8
    110070 |         0         19          0 |        19
    110074 |         0          0          5 |         5
    110075 |         0          0         17 |        17
    110076 |         0          0          6 |         6
    110077 |         0         21          0 |        21
    110078 |        26          0          0 |        26
    110080 |         0         25          0 |        25
    110081 |        14          0          0 |        14
    110082 |        27          0          0 |        27
    110083 |         0          0          5 |         5
    110084 |         0          0          6 |         6
    110085 |         0          0          2 |         2
    110086 |        24          0          0 |        24
    110087 |        21          0          0 |        21
    110088 |         0          0          5 |         5
    110091 |        19          0          0 |        19
    110092 |         0         18          0 |        18
    110093 |         0         11          0 |        11
    110094 |        17          0          0 |        17
    110095 |        16          0          0 |        16
    110096 |         0          7          0 |         7
    110097 |         0          0         15 |        15
    110099 |         0          0         12 |        12
    110100 |        18          0          0 |        18
-----------+---------------------------------+----------
     Total |       309        349        109 |       767


. keep if fup_stat ==1
(2475 observations deleted)

. * pause
.
. generate time3 = .
(8181 missing values generated)

. label var time3 "Integer Months:  0-2, 3-5, 6-8 ... "

. replace time3 = .  if time_integer< 0
(0 real changes made)

.
. replace time3 = 0 if time_integer  >= 0 & time_integer< 3
(1796 real changes made)

.
. replace time3 = 3 if time_integer  >= 3 & time_integer< 6
(868 real changes made)

. replace time3 = 6 if time_integer  >= 6 & time_integer< 9
(723 real changes made)

. replace time3 = 9 if time_integer>= 9 & time_integer< 12
(720 real changes made)

. replace time3 = 12 if time_integer>= 12 & time_integer< 15
(665 real changes made)

.
. replace time3 = 15 if time_integer>= 15 & time_integer< 18
(481 real changes made)

. replace time3 = 18 if time_integer>= 18 & time_integer< 21
(469 real changes made)
```

```
. replace time3 = 21 if time_integer>= 21 & time_integer< 24
(453 real changes made)

. replace time3 = 24 if time_integer>=  24 & time_integer< 27
(446 real changes made)

.
. replace time3 = 27 if time_integer>=  27 & time_integer< 30
(325 real changes made)

. replace time3 = 30 if time_integer>=  30 & time_integer< 33
(295 real changes made)

. replace time3 = 33 if time_integer>=  33 & time_integer< 36
(285 real changes made)

. replace time3 = 36 if time_integer>=  36 & time_integer< 39
(264 real changes made)

.
. replace time3 = 39 if time_integer>=  39 & time_integer< 42
(145 real changes made)

. replace time3 = 42 if time_integer>=  42 & time_integer< 45
(84 real changes made)

. replace time3 = 45 if time_integer>=  45 & time_integer< 48
(91 real changes made)

. replace time3 = 48 if time_integer>=  48 & time_integer< 51
(55 real changes made)

.
. replace time3 = 51 if time_integer>=  51 & time_integer< 54
(2 real changes made)

. replace time3 = 54 if time_integer>=  54 & time_integer< 57
(0 real changes made)

. replace time3 = 57 if time_integer>=  57 & time_integer< 60
(0 real changes made)

.
. tabulate time3 time_integer
```

Integer Months: 0-2, 3-5, 6-8 ...	time_integer							Total
	0	1	2	3	4	5	6	
0	990	446	360	0	0	0	0	1,796
3	0	0	0	424	221	223	0	868
6	0	0	0	0	0	0	338	723
9	0	0	0	0	0	0	0	720
12	0	0	0	0	0	0	0	665
15	0	0	0	0	0	0	0	481
18	0	0	0	0	0	0	0	469
21	0	0	0	0	0	0	0	453
24	0	0	0	0	0	0	0	446
27	0	0	0	0	0	0	0	325
30	0	0	0	0	0	0	0	295
33	0	0	0	0	0	0	0	285
36	0	0	0	0	0	0	0	264
39	0	0	0	0	0	0	0	145
42	0	0	0	0	0	0	0	84
45	0	0	0	0	0	0	0	91
48	0	0	0	0	0	0	0	55
51	0	0	0	0	0	0	0	2
Total	990	446	360	424	221	223	338	8,167

```
   Integer |
```

Months: 0-2, 3-5, 6-8 ...	time_integer							Total
	7	8	9	10	11	12	13	
0	0	0	0	0	0	0	0	1,796
3	0	0	0	0	0	0	0	868
6	185	200	0	0	0	0	0	723
9	0	0	290	162	268	0	0	720
12	0	0	0	0	0	287	166	665
15	0	0	0	0	0	0	0	481
18	0	0	0	0	0	0	0	469
21	0	0	0	0	0	0	0	453
24	0	0	0	0	0	0	0	446
27	0	0	0	0	0	0	0	325
30	0	0	0	0	0	0	0	295
33	0	0	0	0	0	0	0	285
36	0	0	0	0	0	0	0	264
39	0	0	0	0	0	0	0	145
42	0	0	0	0	0	0	0	84
45	0	0	0	0	0	0	0	91
48	0	0	0	0	0	0	0	55
51	0	0	0	0	0	0	0	2
Total	185	200	290	162	268	287	166	8,167

Integer Months: 0-2, 3-5, 6-8 ...	time_integer							Total
	14	15	16	17	18	19	20	
0	0	0	0	0	0	0	0	1,796
3	0	0	0	0	0	0	0	868
6	0	0	0	0	0	0	0	723
9	0	0	0	0	0	0	0	720
12	212	0	0	0	0	0	0	665
15	0	214	105	162	0	0	0	481
18	0	0	0	0	230	94	145	469
21	0	0	0	0	0	0	0	453
24	0	0	0	0	0	0	0	446
27	0	0	0	0	0	0	0	325
30	0	0	0	0	0	0	0	295
33	0	0	0	0	0	0	0	285
36	0	0	0	0	0	0	0	264
39	0	0	0	0	0	0	0	145
42	0	0	0	0	0	0	0	84
45	0	0	0	0	0	0	0	91
48	0	0	0	0	0	0	0	55
51	0	0	0	0	0	0	0	2
Total	212	214	105	162	230	94	145	8,167

Integer Months: 0-2, 3-5, 6-8 ...	time_integer							Total
	21	22	23	24	25	26	27	
0	0	0	0	0	0	0	0	1,796
3	0	0	0	0	0	0	0	868
6	0	0	0	0	0	0	0	723
9	0	0	0	0	0	0	0	720
12	0	0	0	0	0	0	0	665
15	0	0	0	0	0	0	0	481
18	0	0	0	0	0	0	0	469
21	189	103	161	0	0	0	0	453
24	0	0	0	220	105	121	0	446
27	0	0	0	0	0	0	154	325
30	0	0	0	0	0	0	0	295
33	0	0	0	0	0	0	0	285
36	0	0	0	0	0	0	0	264
39	0	0	0	0	0	0	0	145
42	0	0	0	0	0	0	0	84
45	0	0	0	0	0	0	0	91
48	0	0	0	0	0	0	0	55
51	0	0	0	0	0	0	0	2
Total	189	103	161	220	105	121	154	8,167

Integer Months: 0-2, 3-5,	time_integer

6-8 ...	28	29	30	31	32	33	34	Total
0	0	0	0	0	0	0	0	1,796
3	0	0	0	0	0	0	0	868
6	0	0	0	0	0	0	0	723
9	0	0	0	0	0	0	0	720
12	0	0	0	0	0	0	0	665
15	0	0	0	0	0	0	0	481
18	0	0	0	0	0	0	0	469
21	0	0	0	0	0	0	0	453
24	0	0	0	0	0	0	0	446
27	68	103	0	0	0	0	0	325
30	0	0	131	55	109	0	0	295
33	0	0	0	0	0	102	69	285
36	0	0	0	0	0	0	0	264
39	0	0	0	0	0	0	0	145
42	0	0	0	0	0	0	0	84
45	0	0	0	0	0	0	0	91
48	0	0	0	0	0	0	0	55
51	0	0	0	0	0	0	0	2
Total	68	103	131	55	109	102	69	8,167

Integer Months: 0-2, 3-5, 6-8 ...	time_integer 35	36	37	38	39	40	41	Total
0	0	0	0	0	0	0	0	1,796
3	0	0	0	0	0	0	0	868
6	0	0	0	0	0	0	0	723
9	0	0	0	0	0	0	0	720
12	0	0	0	0	0	0	0	665
15	0	0	0	0	0	0	0	481
18	0	0	0	0	0	0	0	469
21	0	0	0	0	0	0	0	453
24	0	0	0	0	0	0	0	446
27	0	0	0	0	0	0	0	325
30	0	0	0	0	0	0	0	295
33	114	0	0	0	0	0	0	285
36	0	124	55	85	0	0	0	264
39	0	0	0	0	66	26	53	145
42	0	0	0	0	0	0	0	84
45	0	0	0	0	0	0	0	91
48	0	0	0	0	0	0	0	55
51	0	0	0	0	0	0	0	2
Total	114	124	55	85	66	26	53	8,167

Integer Months: 0-2, 3-5, 6-8 ...	time_integer 42	43	44	45	46	47	48	Total
0	0	0	0	0	0	0	0	1,796
3	0	0	0	0	0	0	0	868
6	0	0	0	0	0	0	0	723
9	0	0	0	0	0	0	0	720
12	0	0	0	0	0	0	0	665
15	0	0	0	0	0	0	0	481
18	0	0	0	0	0	0	0	469
21	0	0	0	0	0	0	0	453
24	0	0	0	0	0	0	0	446
27	0	0	0	0	0	0	0	325
30	0	0	0	0	0	0	0	295
33	0	0	0	0	0	0	0	285
36	0	0	0	0	0	0	0	264
39	0	0	0	0	0	0	0	145
42	40	18	26	0	0	0	0	84
45	0	0	0	13	18	60	0	91
48	0	0	0	0	0	0	40	55
51	0	0	0	0	0	0	0	2
Total	40	18	26	13	18	60	40	8,167

Integer Months: 0-2, 3-5, 6-8 ...	time_integer 49	50	52	Total

```
        0 |         0          0          0 |     1,796
        3 |         0          0          0 |       868
        6 |         0          0          0 |       723
        9 |         0          0          0 |       720
       12 |         0          0          0 |       665
       15 |         0          0          0 |       481
       18 |         0          0          0 |       469
       21 |         0          0          0 |       453
       24 |         0          0          0 |       446
       27 |         0          0          0 |       325
       30 |         0          0          0 |       295
       33 |         0          0          0 |       285
       36 |         0          0          0 |       264
       39 |         0          0          0 |       145
       42 |         0          0          0 |        84
       45 |         0          0          0 |        91
       48 |         7          8          0 |        55
       51 |         0          0          2 |         2
----------+---------------------------------+----------
    Total |         7          8          2 |     8,167


.
. tab purg1c3b

   baseline |
 pain score |
-- 3 levels |      Freq.     Percent        Cum.
------------+-----------------------------------
          1 |      2,259       27.61       27.61
          2 |      4,093       50.03       77.64
          3 |      1,829       22.36      100.00
------------+-----------------------------------
      Total |      8,181      100.00

. generate Paintime3 = (100*purg1c3b) + time3
(14 missing values generated)

. label var Paintime3 "Integer Months:  0-2, 3-5, 6-8 ... "

. tab Paintime3 time3, missing

   Integer |
   Months: |
 0-2, 3-5, |                      Integer Months:  0-2, 3-5, 6-8 ...
  6-8 ...  |         0          3          6          9         12         15         18 |     Total
-----------+-------------------------------------------------------------------------------+----------
       100 |       471          0          0          0          0          0          0 |       471
       103 |         0        232          0          0          0          0          0 |       232
       106 |         0          0        190          0          0          0          0 |       190
       109 |         0          0          0        199          0          0          0 |       199
       112 |         0          0          0          0        170          0          0 |       170
       115 |         0          0          0          0          0        136          0 |       136
       118 |         0          0          0          0          0          0        143 |       143
       121 |         0          0          0          0          0          0          0 |       131
       124 |         0          0          0          0          0          0          0 |       128
       127 |         0          0          0          0          0          0          0 |        97
       130 |         0          0          0          0          0          0          0 |        83
       133 |         0          0          0          0          0          0          0 |        89
       136 |         0          0          0          0          0          0          0 |        79
       139 |         0          0          0          0          0          0          0 |        44
       142 |         0          0          0          0          0          0          0 |        24
       145 |         0          0          0          0          0          0          0 |        24
       148 |         0          0          0          0          0          0          0 |        16
       200 |       916          0          0          0          0          0          0 |       916
       203 |         0        442          0          0          0          0          0 |       442
       206 |         0          0        372          0          0          0          0 |       372
       209 |         0          0          0        358          0          0          0 |       358
       212 |         0          0          0          0        328          0          0 |       328
       215 |         0          0          0          0          0        240          0 |       240
       218 |         0          0          0          0          0          0        230 |       230
       221 |         0          0          0          0          0          0          0 |       216
       224 |         0          0          0          0          0          0          0 |       223
       227 |         0          0          0          0          0          0          0 |       168
       230 |         0          0          0          0          0          0          0 |       146
       233 |         0          0          0          0          0          0          0 |       143
       236 |         0          0          0          0          0          0          0 |       127
       239 |         0          0          0          0          0          0          0 |        69
       242 |         0          0          0          0          0          0          0 |        39
```

245	0	0	0	0	0	0	0	38
248	0	0	0	0	0	0	0	27
251	0	0	0	0	0	0	0	2
300	409	0	0	0	0	0	0	409
303	0	194	0	0	0	0	0	194
306	0	0	161	0	0	0	0	161
309	0	0	0	163	0	0	0	163
312	0	0	0	0	167	0	0	167
315	0	0	0	0	0	105	0	105
318	0	0	0	0	0	0	96	96
321	0	0	0	0	0	0	0	106
324	0	0	0	0	0	0	0	95
327	0	0	0	0	0	0	0	60
330	0	0	0	0	0	0	0	66
333	0	0	0	0	0	0	0	53
336	0	0	0	0	0	0	0	58
339	0	0	0	0	0	0	0	32
342	0	0	0	0	0	0	0	21
345	0	0	0	0	0	0	0	29
348	0	0	0	0	0	0	0	12
.	0	0	0	0	0	0	0	14
Total	1,796	868	723	720	665	481	469	8,181

Integer Months: 0-2, 3-5, 6-8 ...	Integer Months: 0-2, 3-5, 6-8 ...							
	21	24	27	30	33	36	39	Total
100	0	0	0	0	0	0	0	471
103	0	0	0	0	0	0	0	232
106	0	0	0	0	0	0	0	190
109	0	0	0	0	0	0	0	199
112	0	0	0	0	0	0	0	170
115	0	0	0	0	0	0	0	136
118	0	0	0	0	0	0	0	143
121	131	0	0	0	0	0	0	131
124	0	128	0	0	0	0	0	128
127	0	0	97	0	0	0	0	97
130	0	0	0	83	0	0	0	83
133	0	0	0	0	89	0	0	89
136	0	0	0	0	0	79	0	79
139	0	0	0	0	0	0	44	44
142	0	0	0	0	0	0	0	24
145	0	0	0	0	0	0	0	24
148	0	0	0	0	0	0	0	16
200	0	0	0	0	0	0	0	916
203	0	0	0	0	0	0	0	442
206	0	0	0	0	0	0	0	372
209	0	0	0	0	0	0	0	358
212	0	0	0	0	0	0	0	328
215	0	0	0	0	0	0	0	240
218	0	0	0	0	0	0	0	230
221	216	0	0	0	0	0	0	216
224	0	223	0	0	0	0	0	223
227	0	0	168	0	0	0	0	168
230	0	0	0	146	0	0	0	146
233	0	0	0	0	143	0	0	143
236	0	0	0	0	0	127	0	127
239	0	0	0	0	0	0	69	69
242	0	0	0	0	0	0	0	39
245	0	0	0	0	0	0	0	38
248	0	0	0	0	0	0	0	27
251	0	0	0	0	0	0	0	2
300	0	0	0	0	0	0	0	409
303	0	0	0	0	0	0	0	194
306	0	0	0	0	0	0	0	161
309	0	0	0	0	0	0	0	163
312	0	0	0	0	0	0	0	167
315	0	0	0	0	0	0	0	105
318	0	0	0	0	0	0	0	96
321	106	0	0	0	0	0	0	106
324	0	95	0	0	0	0	0	95
327	0	0	60	0	0	0	0	60
330	0	0	0	66	0	0	0	66
333	0	0	0	0	53	0	0	53
336	0	0	0	0	0	58	0	58
339	0	0	0	0	0	0	32	32
342	0	0	0	0	0	0	0	21
345	0	0	0	0	0	0	0	29
348	0	0	0	0	0	0	0	12
.	0	0	0	0	0	0	0	14

Total	453	446	325	295	285	264	145	8,181

Integer Months: 0-2, 3-5, 6-8 ...	Integer Months: 0-2, 3-5, 6-8 ...					
	42	45	48	51	.	Total
100	0	0	0	0	0	471
103	0	0	0	0	0	232
106	0	0	0	0	0	190
109	0	0	0	0	0	199
112	0	0	0	0	0	170
115	0	0	0	0	0	136
118	0	0	0	0	0	143
121	0	0	0	0	0	131
124	0	0	0	0	0	128
127	0	0	0	0	0	97
130	0	0	0	0	0	83
133	0	0	0	0	0	89
136	0	0	0	0	0	79
139	0	0	0	0	0	44
142	24	0	0	0	0	24
145	0	24	0	0	0	24
148	0	0	16	0	0	16
200	0	0	0	0	0	916
203	0	0	0	0	0	442
206	0	0	0	0	0	372
209	0	0	0	0	0	358
212	0	0	0	0	0	328
215	0	0	0	0	0	240
218	0	0	0	0	0	230
221	0	0	0	0	0	216
224	0	0	0	0	0	223
227	0	0	0	0	0	168
230	0	0	0	0	0	146
233	0	0	0	0	0	143
236	0	0	0	0	0	127
239	0	0	0	0	0	69
242	39	0	0	0	0	39
245	0	38	0	0	0	38
248	0	0	27	0	0	27
251	0	0	0	2	0	2
300	0	0	0	0	0	409
303	0	0	0	0	0	194
306	0	0	0	0	0	161
309	0	0	0	0	0	163
312	0	0	0	0	0	167
315	0	0	0	0	0	105
318	0	0	0	0	0	96
321	0	0	0	0	0	106
324	0	0	0	0	0	95
327	0	0	0	0	0	60
330	0	0	0	0	0	66
333	0	0	0	0	0	53
336	0	0	0	0	0	58
339	0	0	0	0	0	32
342	21	0	0	0	0	21
345	0	29	0	0	0	29
348	0	0	12	0	0	12
.	0	0	0	0	14	14
Total	84	91	55	2	14	8,181

```
. tab Paintime3 purg1c3b, missing
```

Integer Months: 0-2, 3-5, 6-8 ...	baseline pain score -- 3 levels			
	1	2	3	Total
100	471	0	0	471
103	232	0	0	232
106	190	0	0	190
109	199	0	0	199
112	170	0	0	170
115	136	0	0	136

```
       118 |       143          0          0 |       143
       121 |       131          0          0 |       131
       124 |       128          0          0 |       128
       127 |        97          0          0 |        97
       130 |        83          0          0 |        83
       133 |        89          0          0 |        89
       136 |        79          0          0 |        79
       139 |        44          0          0 |        44
       142 |        24          0          0 |        24
       145 |        24          0          0 |        24
       148 |        16          0          0 |        16
       200 |         0        916          0 |       916
       203 |         0        442          0 |       442
       206 |         0        372          0 |       372
       209 |         0        358          0 |       358
       212 |         0        328          0 |       328
       215 |         0        240          0 |       240
       218 |         0        230          0 |       230
       221 |         0        216          0 |       216
       224 |         0        223          0 |       223
       227 |         0        168          0 |       168
       230 |         0        146          0 |       146
       233 |         0        143          0 |       143
       236 |         0        127          0 |       127
       239 |         0         69          0 |        69
       242 |         0         39          0 |        39
       245 |         0         38          0 |        38
       248 |         0         27          0 |        27
       251 |         0          2          0 |         2
       300 |         0          0        409 |       409
       303 |         0          0        194 |       194
       306 |         0          0        161 |       161
       309 |         0          0        163 |       163
       312 |         0          0        167 |       167
       315 |         0          0        105 |       105
       318 |         0          0         96 |        96
       321 |         0          0        106 |       106
       324 |         0          0         95 |        95
       327 |         0          0         60 |        60
       330 |         0          0         66 |        66
       333 |         0          0         53 |        53
       336 |         0          0         58 |        58
       339 |         0          0         32 |        32
       342 |         0          0         21 |        21
       345 |         0          0         29 |        29
       348 |         0          0         12 |        12
         . |         3          9          2 |        14
-----------+---------------------------------+----------
     Total |     2,259      4,093      1,829 |     8,181
```

```
. sort Paintime3

. *by Paintime3: summarize purg_1
. oneway purg_1 Paintime3, tabulate
```

Integer Months: 0-2, 3-5, 6-8 ...	Summary of pain score over last 4 weeks		
	Mean	Std. Dev.	Freq.
100	2.2608696	1.8616115	207
103	2.3813559	1.9738439	118
106	2.592233	2.1757888	103
109	2.3434343	2.0660601	99
112	2.5581395	2.2886145	86
115	2.5135135	2.2098363	74

```
        118 |   2.4647887   2.2604107          71
        121 |         2.5   2.0778499          64
        124 |     2.40625   2.2090632          64
        127 |         1.9   1.7172593          50
        130 |   1.6585366   1.6372195          41
        133 |   1.8837209   1.8924575          43
        136 |   2.7142857   2.5015675          42
        139 |   1.2857143   1.4880476          21
        142 |         2.5   1.9903614          14
        145 |   2.1666667   2.7906771          12
        148 |   2.1111111   2.1473498           9
        200 |   4.9240196   1.5506554         408
        203 |   4.3333333   2.1609356         225
        206 |   3.7883598   2.0776603         189
        209 |    3.973262   2.2056456         187
        212 |   4.2742857   1.9635095         175
        215 |   3.9596774   2.2100995         124
        218 |   3.8559322   2.3288434         118
        221 |   3.7522936   2.1651959         109
        224 |    3.973913   2.3300511         115
        227 |      3.7125   2.1060116          80
        230 |   3.7228916   2.2213666          83
        233 |   3.4029851   2.3998718          67
        236 |   3.3768116   2.2102798          69
        239 |   3.1714286   2.0791078          35
        242 |   3.4090909   2.0391196          22
        245 |        3.05   2.3946212          20
        248 |   3.0714286   2.0555473          14
        251 |           5           0           1
        300 |         6.7   1.7493814         180
        303 |   5.5979381   2.4051152          97
        306 |   5.3896104   2.5810842          77
        309 |   5.4819277   2.3235877          83
        312 |   5.4615385   2.4689525          91
        315 |   4.9433962   2.3730465          53
        318 |         5.3    2.719919          50
        321 |   5.3018868   2.6427325          53
        324 |         5.2   2.3386722          50
        327 |     4.90625   2.6683253          32
        330 |   4.9714286   2.8541581          35
        333 |   4.8148148     2.61706          27
        336 |   4.9677419   2.7262168          31
        339 |   5.1666667   1.9174125          18
        342 |   5.3333333    2.348436          12
        345 |         6.5   1.6984156          14
        348 |   4.4285714   3.1547394           7
------------+--------------------------------------
      Total |   3.9447039   2.4622298        4069

                        Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      6331.41376     51   124.145368     27.20     0.0000
 Within groups      18331.1446   4017   4.56339174
------------------------------------------------------------------------
    Total           24662.5584   4068    6.0625758

Bartlett's test for equal variances:  chi2(50) = 168.4627  Prob>chi2 = 0.000

note: Bartlett's test performed on cells with positive variance:
      1 single-observation cells not used

.
.
end of do-file

. log close
```

```
      log:  P:\NIDDK\ICDB\ICDB_CD\SAS derived_data\longitudianl_add.txt
 log type:  text
closed on:  18 Nov 2005, 14:30:55
```

ATTACHMENT 4

Full Text of Article

Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JR and the ICDB Study Group. A prospective study of interstitial cystitis: results of longitudinal followup of the interstitial cystitis data base cohort. **J of Urology**. 2000 May;163(5):1434-9.

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A PROSPECTIVE STUDY OF INTERSTITIAL CYSTITIS: RESULTS OF LONGITUDINAL FOLLOWUP OF THE INTERSTITIAL CYSTITIS DATA BASE COHORT

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ABSTRACT

Purpose: We present baseline characteristics and longitudinal profiles of symptoms in the Interstitial Cystitis Data Base study, a prospective cohort study of patients with interstitial cystitis.

Materials and Methods: A total of 637 eligible patients were entered into the study and followed for symptoms of pain, urgency and urinary frequency. Median followup was 31 months.

Results: More than 90% of patients were white women with a median age of 43 years. Using the overall pain-urgency-frequency score 7% of participants presented with mild, 44% with moderate and 49% with severe symptoms. Severe urgency in 41% of cases and severe 24-hour frequency in 41% were more common than severe pain in 29%. Of the patients 51% reported nighttime frequency of 2 or more voids. Median duration of interstitial cystitis symptoms was 8 years and 68% of participants were previously diagnosed with the condition. The 36% of patients who withdrew from study or were lost to followup were more likely to have had more severe symptoms at baseline. Patterns of change with time suggest initial symptom improvement due to regression to the mean, and an intervention effect associated with the increased followup and care of cohort participants. Although all symptoms fluctuated, there was no evidence of significant long-term change in overall disease severity.

Conclusions: Our observations support the clinical observation that interstitial cystitis is a chronic disease and no current treatments have a significant impact on symptoms with time. These results provide a foundation for the design and performance of future clinical trials in interstitial cystitis using these end points in a similar patient population.

KEY WORDS: bladder; cystitis, interstitial; cohort study; pain; urination disorders

Interstitial cystitis is a disease of unknown etiology characterized by bladder pain and irritative voiding symptoms without evidence of overt infection. The true prevalence of interstitial cystitis in the United States is unknown but estimates range from 37[1] to 52 to 67/100,000[2] individuals. Although interstitial cystitis was described more than 80 years ago,[3] to our knowledge its natural history and epidemiology have never been completely characterized. Several factors have limited progress in the understanding of interstitial cystitis, including the lack of objective diagnostic criteria, unpredictable symptom fluctuation, and the variability of symptoms, objective findings and treatment outcomes. Furthermore, although a feline model has been used in some studies,[4–7] no ideal animal model mimics the evaluation of symptoms in humans, limiting our understanding of pathophysiology.

To understand better the natural history of interstitial cystitis in 1993 the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) established the Interstitial Cystitis Data Base (ICDB) study, the initial multicenter prospective cohort study of interstitial cystitis. The goals of this prospective study were to assess the demographic and clinical characteristics of patients with interstitial cystitis, examine treatment patterns and evaluate the treated natural history of the disease. We report baseline characteristics of the ICDB cohort overall as well as patterns of patient self-reported pain, urinary urgency and frequency with time.

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MATERIALS AND METHODS

Inclusion and exclusion criteria defining the eligible patient population have been previously described in detail.[8,9] Briefly, entry criteria were based on the diagnosis of interstitial cystitis, similar to the NIDDK research criteria developed in 1987 to 1988.[10–12] All patients had symptoms of urinary urgency, frequency and/or pelvic pain at least 6 months in duration before study entry. However, unlike the NIDDK criteria the ICDB did not require baseline cystoscopy to confirm glomerulations or Hunner's ulcer. These broader inclusion criteria allowed the enrollment of patients who did not meet the strict NIDDK criteria but would be considered to have interstitial cystitis by experienced clinicians.[12] Because no treatment intervention was specified by the protocol, patients were treated according to usual clinical practice. Each participant was evaluated at study entry, and 1 and approximately every 3 months thereafter for up to 4 years. The time corresponding to each subsequent contact was based on the difference between the actual date of contact and the date of the initial clinic visit.

Institutional review board approval at each clinic site was obtained before study initiation. Participating sites and investigators were previously reported in 1997 by Simon et al.[8] Participants were recruited primarily from the available patient pool of each principal investigator. This population was supplemented by referrals from other physicians and self-referral of individuals who responded to endorsements and publicity of the Interstitial Cystitis Association. All patients provided written informed consent before study participation.

Symptom related outcomes were assessed at baseline and at each followup. Using a symptom questionnaire patients were asked to rate pain and urinary urgency during the last 4 weeks on a Likert scale of 0 to 9, with 9 representing the worst symptoms. In addition, a 3-day voiding log was maintained to determine urinary frequency. Pain and urgency were also evaluated at that time on the same 0 to 9 Likert scale. For simplicity we used only voiding log day 1 outcomes for this report since little precision is gained by using information obtained during a 3-day period.[13]

We present 6 outcomes, including 2 in each primary domain of pain, urgency and frequency. Table 1 lists the source and type of measurement of each outcome. For some analyses each outcome was grouped into 3 or 4 categories representing absent, mild, moderate or severe symptoms (table 1). In addition, a pain-urgency-frequency summary score consisting of mild, moderate and severe categories was used at baseline to evaluate study entry criteria and categorize patients based on overall severity.[9]

Mean, median, range and proportions were used to summarize demographic and outcome variables. Wilcoxon rank sum and Fisher's exact tests were done to compare measurements among groups. Kaplan-Meier curves and log rank tests were performed to compare followup distributions among groups.

TABLE 2. *Baseline demographic characteristics of 637 patients*

Characteristic	No. Pts. (%)
Sex:	
F	581 (91.2)
M	56 (8.8)
Race:	
White	592 (93.2)
Black	29 (4.5)
Other	14 (2.2)
Unknown	2
Age:	
18–34	176 (27.6)
35–44	164 (25.7)
45–54	146 (22.9)
55+	151 (23.7)
Marital status:	
Partnered	449 (70.5)
Alone	188 (29.5)
Employment:	
Employed	390 (61.2)
Homemaker	108 (17.0)
Not employed	139 (21.8)
Education:	
High school or less	272 (42.7)
College	248 (38.9)
Advanced	117 (18.4)
Annual household income ($):	
Less than 30,000	182 (28.6)
30,000 or Greater	454 (71.4)
Not available	1
Symptom duration before study entry (yrs.):*	
Less than 1	15 (2.4)
1–5	210 (33.0)
5–11	168 (26.4)
11–16	73 (11.5)
16 or Greater	171 (26.8)
Previous interstitial cystitis diagnosis by physician:	
Yes	432 (67.8)
No	205 (32.2)

* Median 7.7 years (range 0 to 62).

RESULTS

Patient enrollment began in May 1993 and continued through January 1997. Patient followup was terminated in November 1997. Our report comprises 637 participants who met eligibility criteria. Table 2 lists essential demographic and other baseline characteristics. Of the participants 91% were female and 93% were white. Median patient age was 43 years (range 19 to 82). Females were younger than males with a median age of 42 versus 53 years ($p = 0.0001$). Median symptom duration was 8 years (range 0 to 62), although this measure is probably subject to some recall bias. However, only 68% of patients reported being previously diagnosed with interstitial cystitis formally by a physician.

Median urine volume at the first sensation to void was 67 cc (range 4 to 468). Of 634 patients 221 (35%) had a volume of less than 50 cc. Median maximum bladder capacity was 200 cc (range 13 to 900). Of 633 patients 71 (11%) had a maximum bladder capacity of less than 100 cc, indicating small functional capacity. Involuntary bladder contractions were observed in 93 of the 633 participants (15%). During the initial few study months cystoscopy and hydrodistention were performed in 228 of all 637 patients (36%), while 211 of 228 (93%) also underwent simultaneous bladder biopsy.[14, 15] In addition to cystoscopy and hydrodistention, more than 100 other treatments were reported at baseline.[16] Of the 581 females at baseline 18% were receiving no treatment at study entry, 34% were receiving 1, 20% 2 and 28% 3 or more combined treatments. A maximum of 26 (5%) females were receiving a certain treatment or treatment combination at baseline. Since the number of patients reporting any unique or combined therapy was small and treatment was done at the discretion of the treating physician, it was not possible to evaluate the effects of treatment on symptoms even in the period immediately after study entry.

Table 3 shows the distribution at baseline of the pain-urgency-frequency score and each of the 6 primary outcomes grouped into the 3 or 4 severity categories. According to the overall pain-urgency-frequency severity score 7% of patients presented with mild, 44% with moderate and 49% with severe symptoms. However, the distribution of symptoms in patients differed among the 4 primary outcome domains.

Approximately 48% and 29% of participants reported moderate and severe pain, respectively, in the month before study entry. Urgency, which was more common than pain, was rated during the last month as severe by 41% of patients. Current pain and urgency from the voiding log were graded at less severe levels than when assessed during the last

TABLE 1. *Definitions and grouping criteria of primary symptom outcomes*

Outcome	Source	Scale	Group Scores			
			Normal	Mild	Moderate	Severe
Pain and urgency:						
Last mo.	Symptom questionnaire	0–9	0	1–3	4–6	7–9
Current	Voiding log day 1	0–9	0	1–3	4–6	7–9
Frequency:						
24-Hr.	Voiding log day 1	Count	0–6	7–10	11–14	15 or Greater
Nighttime	Voiding log day 1	Count	0	1	2–3	4 or Greater

TABLE 3. *Distribution of primary symptom outcomes at baseline in 637 patients*

Outcome	No. Pts.	No. Symptom Severity (%)			
		Absent	Mild	Moderate	Severe
Pain-urgency-frequency score	637	Not applicable	44 (6.9)	283 (44.4)	310 (48.7)
Pain:					
Last mo.	637	30 (4.7)	121 (19.0)	304 (47.7)	182 (28.6)
Current	620	60 (9.7)	194 (31.3)	236 (38.1)	130 (21.0)
Urgency:					
Last mo.	637	5 (0.8)	86 (13.5)	282 (44.3)	264 (41.4)
Current	621	15 (2.4)	144 (23.2)	276 (44.4)	186 (30.0)
Frequency:					
24-Hr.*	628	45 (7.2)	152 (24.2)	176 (28.0)	255 (40.6)
Nighttime†	628	148 (23.6)	159 (25.3)	218 (34.7)	103 (16.4)

* Day 1 voiding log median 13 voids per 24 hours (range 2 to 59).
† Median 2 voids nightly (range 0 to 18).

month. Urinary frequency was common with 41% of participants reporting at least 15 voids in 24 hours. Some degree of nocturia, defined as more than 1 episode of nighttime voiding, was noticed by 51% of patients, while 16% reported severe nocturia of at least 4 voids nightly. To evaluate the degree of agreement among frequency measures the patient self-report of urinary frequency at baseline included in the pain-urgency-frequency score was compared with voiding frequency as reported on day 1 of the baseline voiding log. Of 628 patients 36 (6%) over and only 4 (0.6%) under reported frequency.

The components of the pain-urgency-frequency score were used to evaluate the primary symptomatology that qualified patients for the study. A total of 35 patients (6%) entered the study with mild symptoms only. Of the remainder 66 (10%) entered with moderate to severe symptoms in only 1, 177 (28%) with moderate to severe symptoms in 2 and 359 (56%) with moderate to severe symptoms in all 3 domains.

Median followup was 31 months (range 1 to 52) (fig. 1). For patients who withdrew from study immediately after baseline followup was considered to be 1 month. Of the 637 participants 109 (17%) were lost to followup and 123 (19%) withdrew during the study course. Reasons for withdrawal varied but 73 patients indicated that they were no longer interested in participating. Of the patients with severe symptoms at baseline 42% were lost to followup or withdrew from study versus 33% with moderate and 16% with mild symptoms (log rank test $p < 0.001$).

To evaluate longitudinal changes for the 6 primary outcomes (table 1) mean values of each outcome grouped into approximate 3-month intervals were plotted against the time of followup. Due to the categorical nature of the outcomes the mean provides a better visual representation of changes with time than the median. For each outcome patients were categorized according to the baseline value for that outcome (absent to mild, moderate or severe) and separate lines were plotted for each group. Figures 2 to 4 show the results.

Changes observed with time were consistent across all 6 symptom outcomes. For patients in the moderate or severe category at baseline there was an average improvement of 1 to 2 points on the pain and urgency scales in the initial 6 months. Frequency similarly decreased an average of 1 to 3 voids per 24 hours and approximately 1 void nightly in these cases. In contrast, those who entered the study with mild symptoms did not have significant changes during the initial 6-month period and even appeared to worsen slightly on the

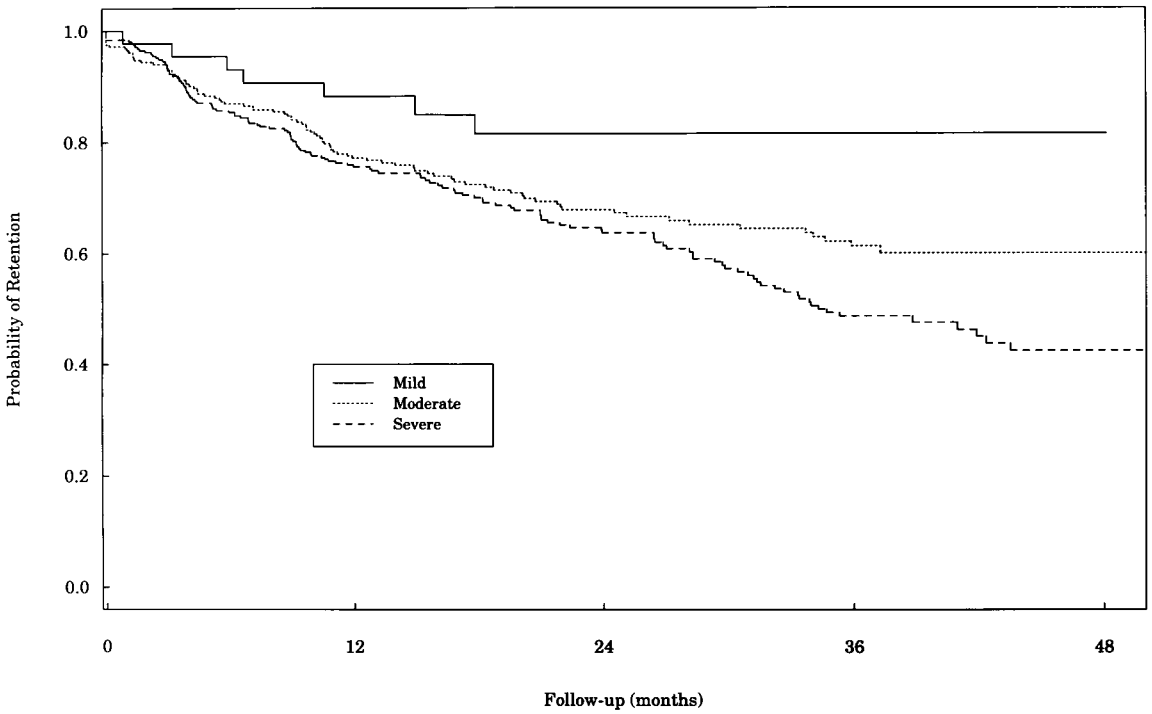

FIG. 1. Time to study withdrawal by baseline pain-urgency-frequency score (Kaplan-Meier curve log rank $p < 0.001$). Patients not withdrawn from study or lost to followup were considered censored observations.

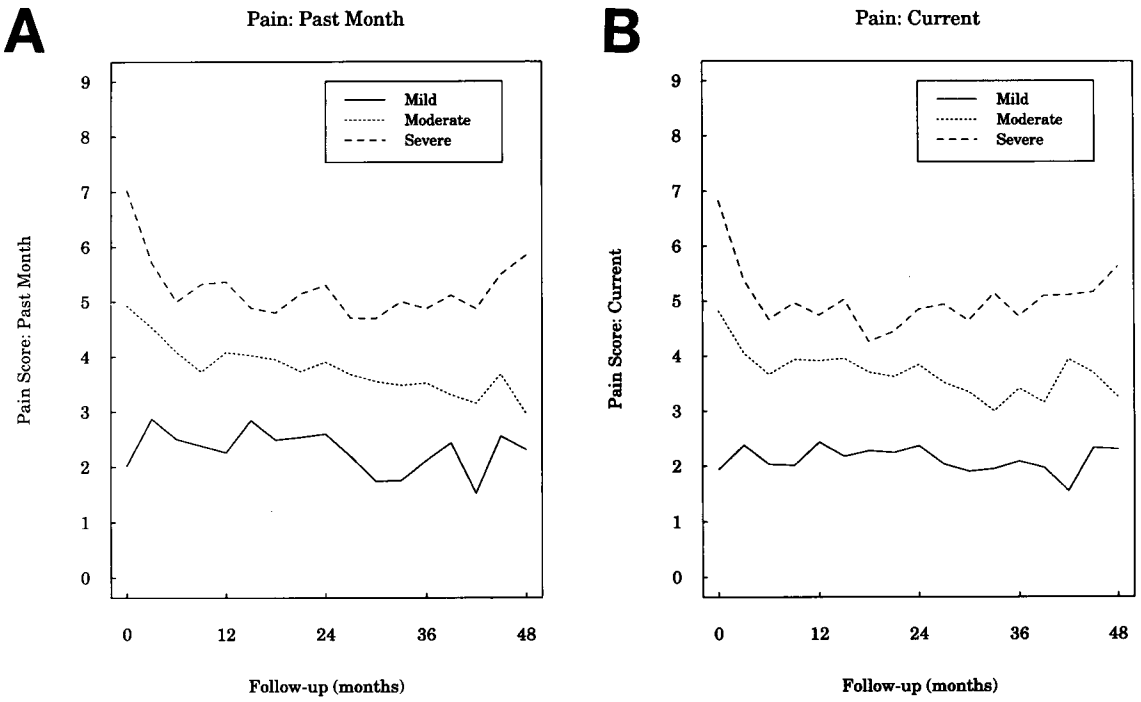

FIG. 2. Pain score on 0 to 9 Likert scale with time by baseline pain score. Mean pain scores were grouped into 3-month intervals for each baseline pain group. *A*, pain during last month from symptom questionnaire. *B*, current pain measured from voiding log.

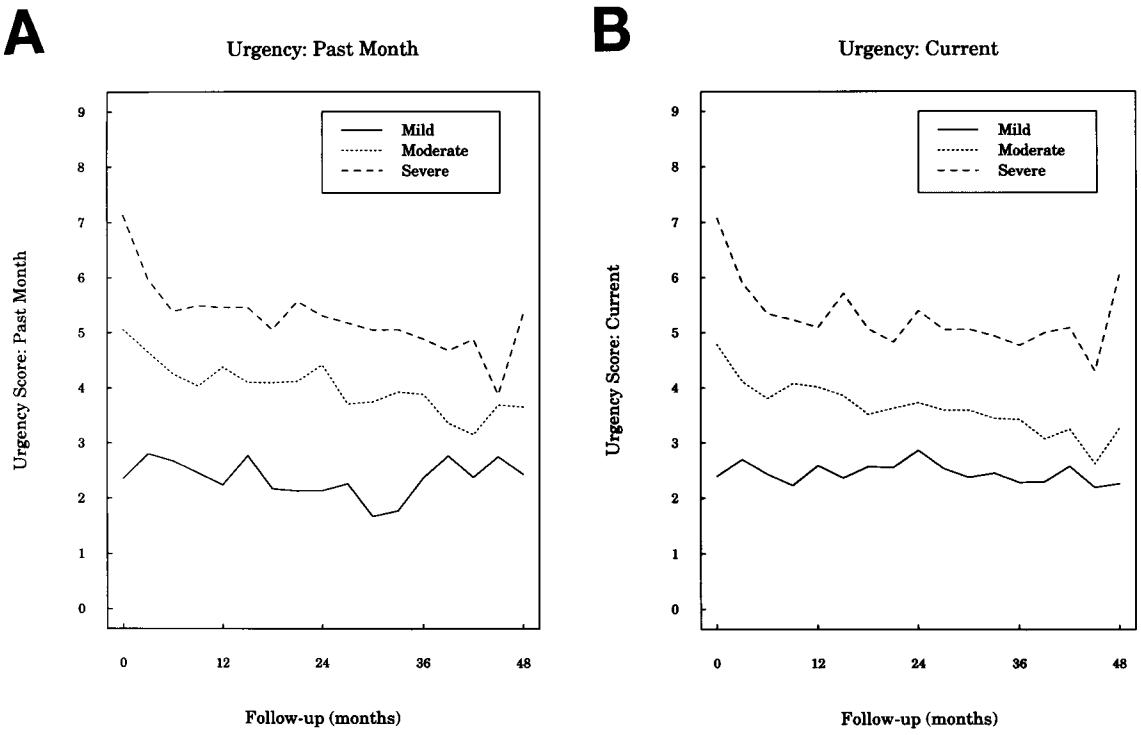

FIG. 3. Urgency scores on 0 to 9 Likert scale with time by baseline urgency score. Mean urgency scores were grouped into 3-month intervals for each baseline urgency group. *A*, urgency during last month from symptom questionnaire. *B*, current urgency measured from voiding log.

pain and urgency scales. These observed changes are likely due to combined regression to the mean and intervention effects. Also, although some plots suggest overall improvement during the 4-year period, the slope of the changes after 6 months is negligibly different from 0, indicating no long-term trend in symptoms for as long as 4 years. Notably any long-term trends apparent in the values are confounded by the effect of patient withdrawal. For example, since those with a higher symptom score at baseline were more likely to withdraw from the study, those with less severe symptoms are overrepresented in later mean values, suggesting overall improvement.

Average changes and fluctuations were generally modest. Changes in pain and urgency were represented by 1 to 1.5 points on the 0 to 9 Likert scale. Average frequency tended to fluctuate by only 1 or 2 voids in a 24-hour period and gener-

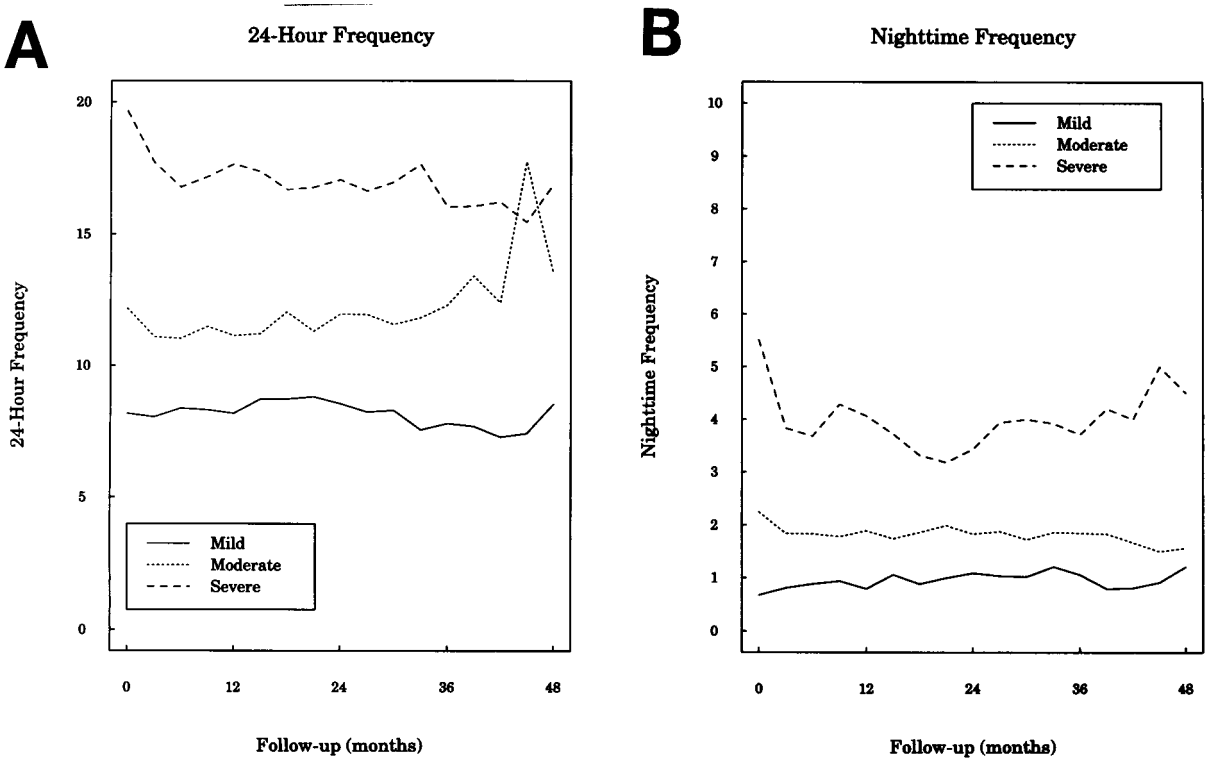

FIG. 4. Mean urinary frequency with time measured from voiding log and grouped into 3-month intervals by baseline value. *A*, 24-hour. *B*, nighttime.

ally less than 1 voiding episode nightly. However, fluctuations with time were also observed in individuals, of whom many had the familiar pattern of remission and flare characteristic of interstitial cystitis. Table 4 shows the categories of change from 6 to 12 months for the 6 outcomes. For example, a change of 1 category represents a change from mild to moderate or moderate to severe. This 6-month period was chosen to represent a time after initial symptom changes had presumably stabilized but during which loss to followup was minimal. However, these results are restricted to the subset of participants who did not withdraw from study before 12 months and should be interpreted accordingly. Table 4 shows that 60% to 70% of patients remained in a given symptom category during the 6-month period, 15% to 20% improved and 15% to 20% worsened. These observations were remarkably consistent in the 6 outcomes studied.

DISCUSSION

The majority of patients in the ICDB study were white middle-aged women. Median duration of interstitial cystitis symptoms was 8 years. The higher incidence of interstitial cystitis in women is consistent with the report of Jones et al.[17] The preponderance of white patients in the ICDB probably reflects the patterns of referral at the participating clinical sites, while the prevalence of interstitial cystitis in other racial subgroups is mostly unknown.[18] Curhan et al recently reported a prevalence of up to 67/100,000 individuals, indicating the potential importance of interstitial cystitis as a public health problem,[2] especially in women. Most patients described multiple types of symptoms, including pain, urgency and frequency, while approximately 70% to 80% noticed moderate to severe urgency or frequency. The frequency and severity of these symptoms may have an important impact on overall quality of life.[19]

Despite the high prevalence and clinical importance of interstitial cystitis to our knowledge few epidemiological or other studies have contributed to understanding the natural history of the disease. The ICDB is the largest prospective study of patients with symptoms consistent with interstitial cystitis. Although the natural history of the disease in the ICDB indicates a great deal of variability within and among patients, little long-term change in interstitial cystitis symptoms was observed even during a period as long as 4 years. Although this result is consistent with clinical observations, it also reflects the chronic and debilitating nature of interstitial cystitis as well as the lack of efficacy of currently available treatment.

The difficulties inherent in identifying and retaining patients for intensive followup for a long period in a cohort study are illustrated by the study withdrawal rate of 36%.

TABLE 4. *Change in symptom categories from 6 to 12 months of followup*

	No. Categories	No. Pain (%)		No. Urgency (%)		No. Frequency (%)	
		Last Mo.	Current	Last Mo.	Current	24-Hr.	Nighttime
No. pts.		394	357	395	357	363	363
No change	0	236 (60)	225 (63)	227 (57)	202 (57)	261 (72)	241 (66)
Improved	1*	65 (16)	50 (14)	75 (19)	71 (20)	42 (12)	53 (15)
	2	9 (2)	3 (1)	12 (3)	6 (2)	11 (3)	5 (1)
Worse	1†	77 (20)	73 (20)	69 (17)	71 (20)	42 (12)	64 (18)
	2	7 (2)	6 (2)	12 (3)	7 (2)	7 (2)	0

* Moderate to mild or severe to moderate.
† Mild to moderate or moderate to severe.

This rate is not atypical for a series of this duration in which no specific treatment approach was offered. It is interesting but not surprising that patients who withdrew from study or were lost to followup were much more likely to have severe symptoms. There are a number of explanations for this phenomenon but it is likely that they lost interest in participating because symptoms failed to improve, especially in those for whom travel was particularly difficult due to symptoms. However, the effect of these withdrawals on evaluation with time in this and other similar studies must be carefully evaluated since differential study withdrawal may lead to serious biases when assessing symptom outcome.

This study clearly illustrates problems with reporting case series of diseases characterized primarily by symptoms, that is regression to the mean and the intervention effect. Regression to the mean is a statistical phenomenon in which subjects selected based on particularly high or low values tend to move toward the population mean when tested further. The effect of this phenomenon for assessing urological outcome was recently described for the peak urinary flow rate[20,21] and symptom indexes.[21] Regression to the mean may be particularly problematic in a study of disorders such as interstitial cystitis in which the diagnosis depends completely on symptoms, so that the patient population studied is necessarily restricted to those with at least minimal symptoms. This problem is clearly illustrated by the pain and urgency outcomes. The moderate and severe subgroups appeared to improve during the initial 6-month period, whereas participants who began with mild symptoms in these domains appeared to worsen (figs. 2 and 3). Although this observation is a factor in the initial changes observed in the ICDB cohort, it is also likely that a true intervention effect is present. The intervention effect is a well-known phenomenon, especially in symptomatic disease, that may be evident in 30% to 50% of cases. This effect is a real consequence of the increased followup of and attention given to patients. It may partially include the numerous medical and nonmedical interventions provided at baseline and throughout the study as part of the continuing standard of clinical care for interstitial cystitis. Each effect underscores the need for placebo or another appropriate control in clinical trials, especially when patient selection is based on symptom severity.

CONCLUSIONS

We present the initial analysis of baseline characteristics and longitudinal profiles of symptoms in the ICDB study. More than 90% of the 637 participants were white females, reflecting the prevalence of interstitial cystitis in the general population. Approximately 50% of patients presented with an overall symptom profile classified as severe. Severe urgency and frequency, including nocturia, were more common than severe pain. Although there was initial improvement in symptoms partially due to regression to the mean and the intervention effect, there was no evidence of a long-term change in average symptom severity. Our findings support the status of interstitial cystitis as a chronic disease and the current lack of effective treatments in the majority of patients. These results may be used for designing and performing future clinical trials in interstitial cystitis.

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ATTACHMENT 5

Longitudinal Analysis of 1-Month Pain Symptoms using Methods 2 and 3 to Calculate Time

FIGURE 3: ICDB Archive Data, Method 2

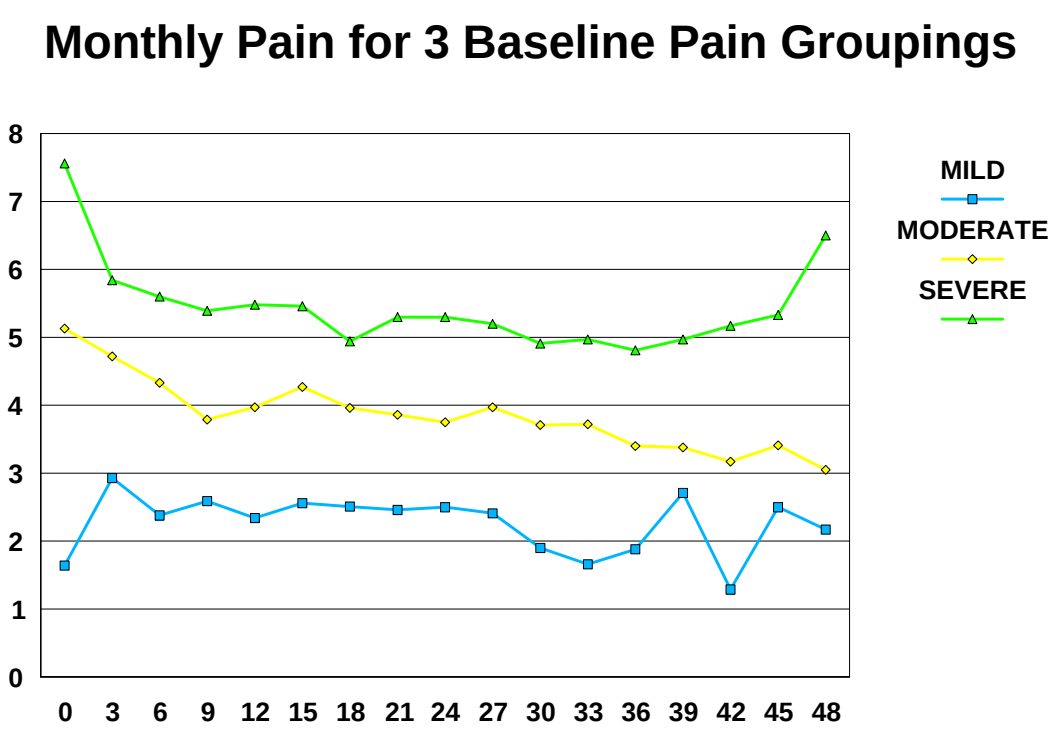

FIGURE 4: ICDB Archive Data, Method 3