

UCSF

UC San Francisco Electronic Theses and Dissertations

Title

Mucositis pain induced by radiation therapy

Permalink

<https://escholarship.org/uc/item/4n40q9b8>

Author

Wong, Piera,

Publication Date

2003

Peer reviewed|Thesis/dissertation

Running Head: MUCOSITIS PAIN INDUCED BY RADIATION THERAPY

**Mucositis Pain Induced by Radiation Therapy:
The Self-Care Behaviors of Patients with Head and Neck Cancer**

Piera C. Wong, RN, MS

Marylin J. Dodd, RN, PhD, FAAN

Christine Miaskowski, RN, PhD, FAAN

Steven M. Paul, PhD

Gayle H. Shiba, RN, DNSc

Noreen Facione, RN, PhD

University of California, San Francisco

School of Nursing

May 2002

Abstract

Purpose/Objectives: To determine (a) the pattern, severity, and time course of mucositis pain induced by radiation therapy (RT) in patients with head and neck cancer; (b) self-care behaviors (SCBs) used by patients to manage mucositis pain; and (c) the effectiveness of these behaviors in relieving such pain.

Design: Prospective and descriptive with repeated measures.

Setting: A radiation oncology department within a large university medical center.

Sample: Forty-nine patients with head and/or neck cancer.

Methods: The MacDibbs Mouth Assessment Tool was used to measure the severity of oral mucositis. A Self-Care Diary was used weekly by the patients to record their SCBs and the effectiveness of these behaviors.

Main Research Variables: Severity of RT-induced mucositis, mucositis pain, SCBs, and the effectiveness of SCBs.

Findings: All participating patients developed pain due to mucositis induced by RT therapy. The mean pain-intensity score with swallowing was significantly higher than that without swallowing. At the follow-up visit, scores were higher with swallowing than when not swallowing; however, pain was still significantly higher than reported at baseline.

Conclusions: The most effective SCBs were mouth rinsing and taking oral analgesics for pain control when not swallowing; more severe pain with swallowing was not managed well throughout the study.

Implications for Nursing Practice: Mucositis pain is a significant clinical problem for patients with head and neck cancer undergoing RT. Such pain is not adequately

controlled. It is therefore recommended that future studies focus on the search for more effective strategies in the management of mucositis pain.

Key Words: mucositis pain, mucositis pain induced by radiation therapy, self-care behaviors, head and neck cancer patients

Background

Cancer of the head and neck includes disease of the oral cavity, pharynx, paranasal sinuses, nasal cavity, salivary glands, thyroid gland, and larynx. An estimated 28,900 new cases involving cancer of the oral cavity and pharynx will be diagnosed within the United States in 2002, and an estimated 7,400 people will die from these cancers in (Jemal, Thomas, Murray, & Thun, 2002).

Sixty percent of patients with head and neck cancers (HNCs) receive standard radiation therapy (RT) and over 90% receive a combination of chemotherapy and RT. RT-induced mucositis is an acute inflammation of the oral mucosa effecting free nerve endings and causing pain as early as 7 days after the initiation of RT. An oral ulcer is often induced by RT and manifests as an erosion of the oral mucosa during the first few weeks of therapy. These painful ulcerative erosions primarily effect the nonkeratinized tissues such as the soft palate, the pharynx, the floor of the mouth, and the lateral borders of the tongue (Sutherland & Browman, 2001).

Mucositis pain can be exacerbated by superinfection of the ulcerated mucosa (Whitmyer, Waskowski, & Iffland, 1997). Ulcerations and mucosal infections can cause edema and inflammation, which in turn, cause pain. During the fifth week of RT (i.e., when patients have received approximately 5000 to 6000 cGy), severe pain and discomfort frequently occur. Mucositis pain is likely to improve within 2 to 4 weeks following the completion of RT and 2 months is usually required to reach the final phase of healing (Cooper, 1994). Assessment of oral pain is critical in distinguishing mucositis pain from that of another etiology (Ashby, 1993).

Review of Related Literature

Weissman, Janjan, and Byhardt (1989) conducted one of the first studies to characterize the temporal development and intensity of pain associated with RT-induced mucositis. One hundred percent of the patients with HNC ($n = 21$) developed mucositis pain during the second or third week of RT. Severe pain occurred during the fifth week of therapy, despite the use of analgesics on 37% of the treatment days.

In a retrospective study of 40 patients with HNC (Chua, Reddy, Lee, & Patt, 1999) that focused primarily on pain and loss of function, 52% of the patients reported severe pain that lasted for 6 months or more following the completion of treatment. Chua and colleagues concluded that pain in HNC patients following surgery and/or RT was severe and chronic and was multifactorial in nature. Pain was difficult to treat and did not respond well to this various combinations of opioid analgesics.

Sutherland and Browman (2001) conducted a meta-analysis on the various agents used for prevention of oral mucositis pain. Approximately 15% of the HNC patients studied were hospitalized for inadequate pain control due to severe RT-induced mucositis. These researchers concluded that the narrow-spectrum antibacterials were advantageous to prevent oral mucositis pain, and the most notable limitation of all of the reviewed studies was their small sample sizes.

In a qualitative study of the side effects of RT, Wells (1998) found that, in patients with HNC ($n = 12$), most symptoms peaked between the third and final week of RT and continued for 1 month following the completion of therapy. Patients provided vivid descriptions of these symptoms, such as “a sore throat which made it ‘murder’ to swallow and also disturbed sleeping, eating and breathing” (p. 844). The actual pain intensity ratings were not provided in this article.

Epstein, Robertson, Emerton, Phillips, and Stevenson-Moore (2001) investigated oral complications and quality of life in 20 patients with HNC prior to RT, as well as at 1 month and 6 months following RT using a general quality of life survey. Pain of unknown etiology was present in 60% of the patients prior to RT. At 1 month posttreatment, oral pain was reported by 75% of the patients. The most severe oral pain was present at the end of RT which correlated with the severity of mucositis. Pain was above pretreatment levels at the 6-month follow up.

Only three studies were found that evaluated the intensity of oral mucositis pain during the course of RT (Epstein et al., 2001; Weissman et al., 1989; Wells, 1998). Only 53 patients were evaluated and the evaluations points were limited to the beginning, midpoint, and end of RT. No studies have conducted detailed evaluations on the onset, pattern, severity, and duration of RT-induced mucositis pain. In addition, the types and effectiveness of self-care behaviors (SCBs) used by patients with mucositis pain has not been reported. Therefore, the purposes of this study were to determine (a) the pattern, severity, and time course of RT-induced mucositis pain in patients with HNC; (b) the SCBs used by patients to manage mucositis pain; and (c) the effectiveness of patient SCBs in relieving such pain.

Methodology

Study Design, Sample, and Setting

This study used a prospective, longitudinal design to describe RT-related mucositis, mucositis pain, and the SCBs used by patients with HNC. Data were collected throughout the course of RT (i.e., from the initiation to the completion of RT and at the 1-

month follow-up visit). Patients were recruited in a RT department in a large university medical center in San Francisco, California.

Forty-nine HNC patients met the following inclusion criteria: (a) were over the age of 18 with HNC, (b) were scheduled for RT to all or part of the oral cavity or oropharynx, (c) were able to read, write, and understand English, (d) were able to understand and complete the informed-consent form, (e) were willing to participate in the study, and (f) had no previous RT to the head and/or neck region.

Instrumentation

The Patient Demographic Questionnaire was used to collect baseline data such as age, gender, living situation, marital status, educational level, ethnicity, and employment status. The Disease and Treatment Questionnaire was used to obtain data on specific clinical variables (e.g., height and pretreatment weight). Only one investigator (G. Shiba) collected all the data on the number of RT treatments administered, the cumulative RT doses, and weights. Medical records were reviewed to obtain disease and treatment information.

The MacDibbs Mouth Assessment Tool is a 15-item instrument used to assess RT-induced mucositis. It includes nine subjective and five objective items measuring the severity of oral mucositis. The nine subjective items focus on oral symptoms and are scored on a 4-point rating scale by the patient with “0” indicating *no problems*, and “3” indicating *severe problems*. Pain was one of the subjective items and patients were asked to rate their pain with and without swallowing using the 4-point scale. The total MacDibbs Symptom Score (MSS) is determined by adding the scores for each item, with the total score ranging from 0 to 27. The five objective items provide information on the

number of ulcers in the oral cavity; the size of the largest ulcer in millimeters; as well as the presence or absence of vesicles, reddened areas, or white patches.

The oral cavity of the study participants was assessed at the initiation of RT and three times per week once they reported symptoms of mucositis during evaluation with the MacDibbs Mouth Assessment Tool. If no mucositis was indicated, assessment was repeated weekly for the first 2 weeks of RT, then three times per week until completion of RT, and again at the 1-month follow-up visit. In a pilot study of 10 adult HNC outpatients receiving RT, the MacDibbs Mouth Assessment Tool was instrumental in determining the development and presence of RT-related mucositis, as well as in detecting changes in mucositis over time. Content validity was established through a panel of experts in dentistry, nursing, and radiation oncology. Interrater reliability was excellent (96% interrater agreement) for all items except for the largest ulcer in which measurements varied by as much as 2 mm between raters when disagreements occurred.

The Self-Care Diary implemented in this study is a modification of an earlier version developed by Nail, Jones, Greene, Schipper, and Jensen (1991), which included the most common side effects of RT such as mucositis, mucositis pain, xerostomia, taste changes, weight loss, fatigue, and loss of appetite. Participating patients completed the diary weekly and were asked to rate the severity of each side effect experienced on a 5-point numeric rating scale (e.g., the mucositis pain item presented descriptive anchors of 0 = *not painful* to 4 = *extremely painful*). The patients indicated any SCBs they used, as well as the effectiveness of each behavior. The list of SCBs for mucositis pain from which the patients could choose are provided in Table 1. The effectiveness of each behavior was rated using by a 5-point numeric scale with descriptive anchors of "0"

indicating *no relief* and “4” indicating *complete relief*. To ensure content validity, a list of side effects and SCBs relevant to HNC and RT were obtained from the literature. Content validity was established through a review by four patients with HNC receiving RT and three radiation oncology nurses.

Procedures and Data Analysis

The Committee on Human Research at the University of California, San Francisco, approved this study. Informed consent was obtained from all patients who also completed the demographic questionnaire and the Self-Care Diary. Only one investigator administered the MacDibbs Mouth Assessment Tool in the RT department of the study site. The patients completed the Self-Care Diary on a weekly basis. The oral cavities of the participants were assessed three times per week once they reported symptoms suggestive of oral mucositis during evaluation with the MacDibbs Mouth Assessment Tool. If no mucositis was present, assessment continued on a weekly basis for the first 2 weeks of RT, then three times a week beginning with the third week of RT. The Disease and Treatment Questionnaire was completed by the researcher weekly and at the follow-up visit. The medical-record review was conducted at baseline, at the completion of RT, and at the follow-up visit.

Means, standard deviations, and ranges were determined for continuous variables such as age, education, cumulative dose of RT, and number of RT treatments.

Frequencies and percentages were calculated on nominal variables such as marital status, living arrangements, cancer site, stage of disease, fraction dose, and hospitalizations. To fulfill the primary purpose of the study, the onset, severity, and duration of RT-induced mucositis pain were determined from data collected using the MacDibbs Mouth

Assessment Tool. Means and standard deviations were calculated for pain severity and the patterns and duration of RT-induced oral mucositis pain were determined subsequently. The time course of mucositis pain was determined from data collected using the Self-Care Diary, a one-way ANOVA repeated measure was performed. To fulfill the second purpose of the study, the week with the highest SCBs performed by the patients to decrease RT-induced mucositis pain was described. The third purpose of the study was addressed by examining the means and standard deviations for the effectiveness of each SCB individually during the time of their RT.

Results

Demographic Characteristics

As shown in Table 2, the majority of patients were male (78%) and Caucasian (60%) with an average age of 56.1 years ($SD = 14.0$) and a minimum of 2 years of college education. Most of the patients were single (60%), and the majority had a positive history of smoking (74%) and alcohol use (80%). As shown in Table 3, cancer of the tongue was the most common diagnosis in this sample. The total cumulative dose of RT for patients with treatment schedules of once per day averaged 6639 cGy ($SD = 782.96$) over approximately 34 treatments. Patients who received hyperfractionated RT were administered a cumulative dose of 7607 cGy ($SD = 383.18$) over 58 treatments.

Mucositis Induced by Radiation Therapy

Prevalence. At the initiation of RT, only one patient had a break in the lining of the oral mucosa. Patients who received RT twice per day developed mucositis 3 days sooner than those who received daily treatment. The mean MSS was 11.71

($SD = 3.94$, range 6 to 21) 15 days after the start of RT for the patients treated once per day ($SD = 5.92$), and 12.31 ($SD = 4.90$, range 8 to 23) 12 days after the start of RT for patients treated twice a day. All patients developed one or more oral ulcers by 14.5 days after the start of RT ($SD = 5.79$). The mean dose of cumulative RT once ulcers developed, was 2130 cGy ($SD = 614.43$). Forty-six of the 49 patients (94%) had mucositis at the completion of their RT. Three of the 49 patients (6%) who entered the study failed to complete the prescribed course of RT. At the 1-month follow-up visit, 59% of the participants had mucositis, and the mean MSS score for these patients was 13.78 ($SD = 3.92$).

Pain intensity. As shown in Figure 1 from data obtained from the Self-Care Diary, the intensity of mucositis pain increased significantly during the course of RT ($F [7,343] = 10.9, p < .001$), (using a one-way ANOVA repeated measure). The mean pain intensity scores ranged from 0.45 ($SD = .98$) at baseline to 2.11 ($SD = 1.60$) at the completion of RT (0 = *not very severe*, 4 = *extremely severe*). The average pain intensity score peaked at the completion of RT. The mean pain intensity score at the 1-month follow-up visit was 1.23 ($SD = 1.34$).

Pain intensity with and without swallowing was obtained from the MacDibbs Mouth Assessment Tool. The throat was the most common site of pain throughout RT, followed by the mouth and tongue regions. All patients reported pain with swallowing during the course of RT, and 96% reported pain when not swallowing. As illustrated in Figure 2, no differences were found between pain intensity scores with and without swallowing at baseline and Week 2. However, matched-pair t-tests indicated that from Week 3 to the 1-month follow up, patients reported significantly higher pain intensity



scores with swallowing compared to those without swallowing. These scores peaked at the end of Week 7 with a mean pain score of 2.40 ($SD = .71$) with swallowing and 1.36 ($SD = .75$) without swallowing, equating to moderate to severe pain with swallowing and mild to moderate pain when not swallowing (0 = *not painful*, 3 = *extremely painful*).

Self-care Behaviors. As the severity of mucositis pain increased throughout the course of RT, the percentage of patients engaging in SCBs also increased. More than 80% of the participating patients engaged in some form of SCB throughout the course of RT. Of the eight SCBs used by the patients, 49% of the participants rinsed their mouths more frequently and the same percentage used pain medication to help alleviate mucositis pain. Table 1 presents a list of the SCBs and the percentage of patients using them at the completion of RT that had the highest level of self-care activity.

The effectiveness of patient SCBs was determined by summing the relief scores of those SCBs tried, divided by the total number of behaviors performed with an effectiveness score of “0” (i.e., *not effective*) to “4” (i.e., *completely effective*) (see Figure 3). The mean effectiveness of the SCB scores for mouth pain during RT ranged from 2.14 ($SD = .78$) in Week 2 to 2.44 ($SD = .70$) in Week 7. The most effective behaviors were frequent mouth rinsing and the use of pain medication. The medication most frequently used by patients throughout the course of RT was acetaminophen with codeine. See Table 4 for a listing of pain medications used by patients throughout the course of RT and at the 1-month follow up.

Discussion and Conclusions

This study is the first to document the prevalence and pattern of RT-induced mucositis pain in patients with HNC. It is also the first research to target and document

the types and effectiveness of SCBs used by patients for mucositis pain. RT-induced mucositis occurs in 100% of HNC patients. Consistent with previous reports (Weissman, et al., 1989; Wells, 1998) the onset of mucositis occurred during the second week of RT and occurred three days sooner in patients receiving hyperfractionated RT. The finding not reported in previous literature was the significant difference in pain levels with and without swallowing. One patient described pain with swallowing as “razor blades cutting up your insides.” The pain was so intense that patients “avoided swallowing at all cost.” Study participants also commented on their feeling that the pain would be forever present. The duration of the RT-related mucositis pain was longer than these patients expected with no sign of improvement upon RT completion. At the follow-up visit, pain scores from all measures were lower. However, the patients still experienced higher levels of pain than those reported at baseline.

An important contribution that this study makes is that more frequent oral assessments of mucositis pain were obtained. Therefore, the pattern of pain intensity scores is more precise than previous studies. These data permit us to determine the peak or worst scores that these patients experienced.

The strength of this study is that two instruments were used to obtain the reported pain-intensity scores and both tools yielded similar results. Although pain is a subjective symptom for which the patients provided the ratings, one instrument was used by the participants to record their own pain ratings (i.e., via the Self-Care Diary), and the other instrument required the investigator to ask the patients to rate their pain (i.e., via the MacDibbs Mouth Assessment Tool). This may be a superior strategy to previous studies that used only a single instrument.

A critical factor to this research was that the pain experienced by the sample was not managed by any systemic or topical analgesics. The most frequently used SCBs were the use of pain medication (58% of the patients used acetaminophen with codeine during the study period) and frequent mouth rinsing, which were rated only moderately effective in controlling pain. Twenty percent of the patients required unscheduled hospitalizations and emergency-room visits for treatment-related problems, especially for pain management. This remains a major clinical problem for these patients.

Limitations and Implications

The findings of this current study are likely to be generalized to similar hospitals with RT departments that perform daily or twice-daily RT. The three patients who dropped from the study before completing the course of treatment, due to their inability to cope with the side effects or their deteriorating physical condition, were not evaluated for their symptoms. Six patients out of the 46 who still received RT were hospitalized for treatment-related complications and were unable to complete the study instruments. Consequently, the results of this study may be affected by the missing and/or incomplete data. Additionally, a methodological limitation existed in the measurement of mucositis-related pain. Patients often reported experiencing the *worst pain possible* (i.e., the maximum score), then at the subsequent visit would rate their pain as *even worse than before*. However, on a numeric rating scale, patients are unable to report beyond the maximum score even if their pain had increased.

Pain is one of the side effects for which patients most actively and continuously implement SCBs. Because mucositis pain is frequently the major cause of decreased oral

intake and dehydration, effective pain management is of utmost importance. Future research should provide frequent nutritional assessments on this at-risk group of patients.

In today's managed-care environment, patients are more commonly evaluated and treated in outpatient settings. Therefore, the importance of patient knowledge and self-care skills cannot be overstated. Both patients and their families must learn to manage RT-related symptoms and side effects. It is within the realm of nursing responsibility to provide the information and skills enabling patients to participate in their care as outpatients. If patient symptoms/side effects can be identified early, they can be treated more effectively through self-care at a far lower cost.

This study successfully achieved an important mission in outpatient care. It provides valuable information to the field of radiation oncology and outpatient nursing care for patients with HNC at specific time points within their course of RT. Nurses can now anticipate the potential needs of these patients and provide relevant and timely information to enhance and optimize patient self-care. The findings reveal that mucositis-related pain is the dominant side effect of RT. Future research with larger study samples should focus exclusively on seeking effective treatment for mucositis-related pain prior to and throughout the course of RT, as well as post-RT. Unless pain is controlled by effective pain-management strategies, the health status of these cancer patients will continue to deteriorate throughout the course of RT. Emergency-room visits will increase along with unforeseen hospitalizations, which will, in turn, further burden the health-care system by driving up related costs.

References

- Ashby, M. A. (1993). The role of radiotherapy in management of cancer-related pain. In E. Arbit (Ed.), *Management of cancer-related pain* (pp. 121–141). Mount Kisco, NY: Futura.
- Chua, K. S. G., Reddy, S. K., Lee, M., & Patt, R. B. (1999). Pain and loss of function in head and neck cancer survivors. *Journal of Pain and Symptom Management, 18*, 193–202.
- Cooper, J. S. (1994). Carcinomas of the oral cavity and oropharynx. In J. Cox (Ed.), *Moss' radiation oncology: Rationale, technique, results* (7th ed., pp. 169–213). St. Louis, MO: Mosby.
- Epstein, J. B., Robertson, M., Emerton, S., Phillips, N., & Stevenson-Moore, P. (2001, May). Quality of life and oral function in patients treated with radiation therapy for head and neck cancer. *Head and Neck, 23*, 389–398.
- Jemal, A., Thomas, A., Murray, T., & Thun, M. (2002). Cancer statistics, 2002. *A Cancer Journal for Clinicians, 52*(1), 23–47.
- Nail, L. M., Jones, L. S., Greene, D., Schipper, D. L., & Jensen, R. (1991). Use and perceived efficacy of self-care activities in patients receiving chemotherapy. *Oncology Nursing Forum, 18*(5), 883–887.
- Sutherland, S. E., & Browman, G. P. (2001). Prophylaxis of oral mucositis in irradiated head-and-neck cancer patients: A proposed classification scheme of interventions and meta-analysis of randomized controlled trials. *International Journal of Radiation Oncology, Biology and Physics, 49*(4), 917–930.

- Weissman, D., Janjan, N., & Byhardt, R. W. (1989). Assessment of pain during head and neck irradiation. *Journal of Pain and Symptom Management*, 4(2), 90–95.
- Wells, M. (1998). The hidden experience of radiotherapy to the head and neck: A qualitative study of patients after completion of treatment. *Journal of Advanced Nursing*, 28(4), 840–848.
- Whitmyer C. C., Waskowski J. C., & Iffland, H. A. (1997). Radiotherapy and oral sequelae: Preventive and management protocols. *Journal of Dental Hygiene*, 71(1), 23–29.

Table 1

*Patient Self-Care Behaviors for Mucositis Pain Following Completion of Radiation**Therapy*

Self-care behavior	Percentage
Take pain medications	49
Rinse mouth more often	49
Use medicated mouthwash	43
Put medicine on sores	27
Wear dentures less	14
Keep busy	6
Change diet	2
Other	2

Table 2

Sample Demographics

Variable	<i>n</i>	Mean	<i>SD</i>	Percentage
Age (Years)	49	56.1	14.0	
Education (years)	47	13.8	3.7	
Karnofsky (baseline)	49	88.7	10.4	
Gender				
Female	11			22
Male	38			78
Married/Partnered				
Yes	19			40
No	29			60
Lives alone				
Yes	18			37
No	31			63
Ethnicity				
Caucasian	29			60
Asian	8			16
African-American	6			12
Other	6			12

(table continues)

Variable	<i>n</i>	Mean	<i>SD</i>	Percentage
Employment status				
Retired	18			37
Full/Part time	13			27
Disability	11			22
Other	7			14
Smoking history				
Yes	36			73
No	13			27
Alcohol history				
Yes	39			80
No	10			20

Table 3

Disease and Treatment Characteristics

Characteristics	<i>n</i>	Percentage
Diagnosis		
Tongue	12	25
Nasopharynx	9	18
Tonsil	7	14
Pharynx	5	10
Other	16	33
Treatment schedule		
Once per day	42	86
Twice per day	7	14
Treatment status		
Current chemotherapy	10	20
Prescribed course of radiation therapy completed	46	94
Unscheduled breaks in treatment longer than 3 days	13	27
Unscheduled hospitalization during the course of radiation therapy	14	28
Emergency-room visit with no subsequent hospitalization	10	20

Table 4

Pain Medications Prescribed to Study Participants Throughout the Course of Radiation Therapy and at the 1-Month Follow Up

Medication	Percentage of Participants
Acetaminophen with codeine	58
Hydrocodone	42
Ibuprofen	42
Acetaminophen	30
Morphine liquid	28
Oxycodone with acetaminophen	26
Codeine	22
Acetylsalicylic acid	20
Oxycodone	18
Morphine tablets	16
Amitriptyline hydrochloride	12
Morphine injection	10
Naproxen sodium	8
Fluoxetine hydrochloride	6
Methadone	6
Dilantin	4
Carbamazepine	2

(table continues)

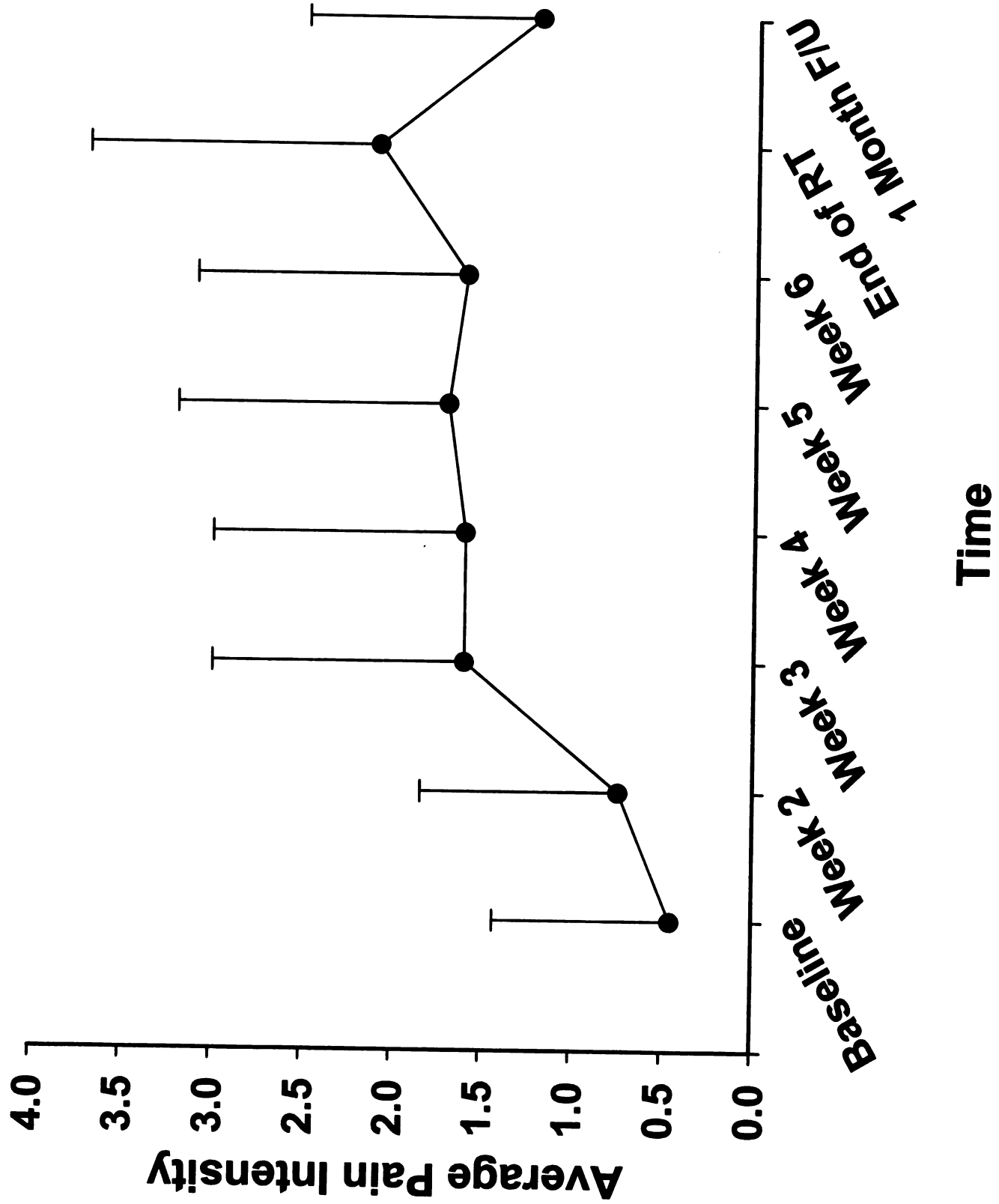
Medication	Percentage of Participants
Dilaudid	2
Propoxyphene	2
Propoxyphene with acetaminophen	2
Oxycodone with aspirin	2
Hydrocodone with acetaminophen	2

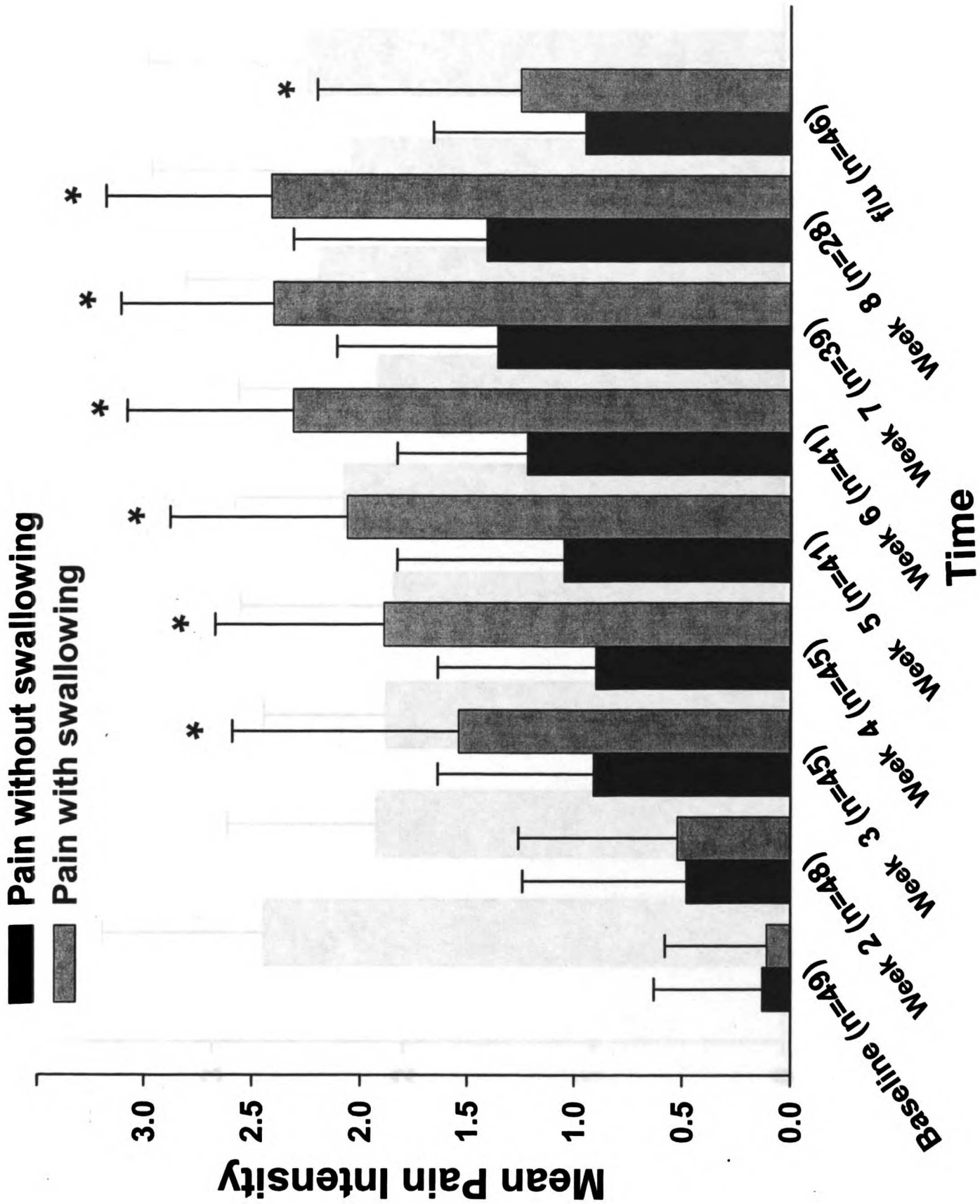
Figure Captions

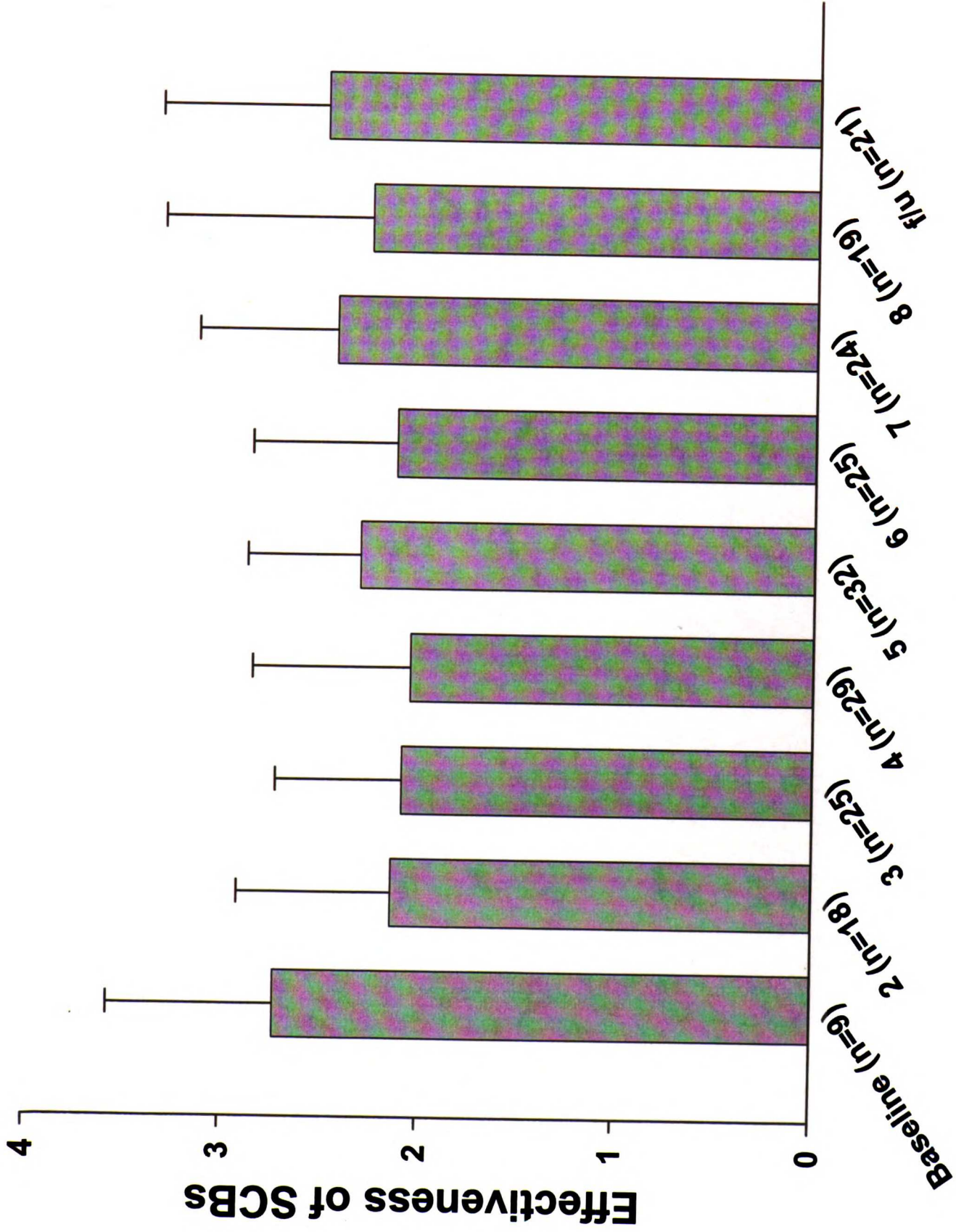
Figure 1. Self-Care Diary of average pain intensity over time ($N = 49$). RT = radiation therapy; F/U = follow up.

Figure 2. Average weekly pain ratings using the MacDibbs Mouth Assessment Tool with patients swallowing and not swallowing. Significant differences were found from Week 3 to follow up ($p = .001$). F/U = follow up.

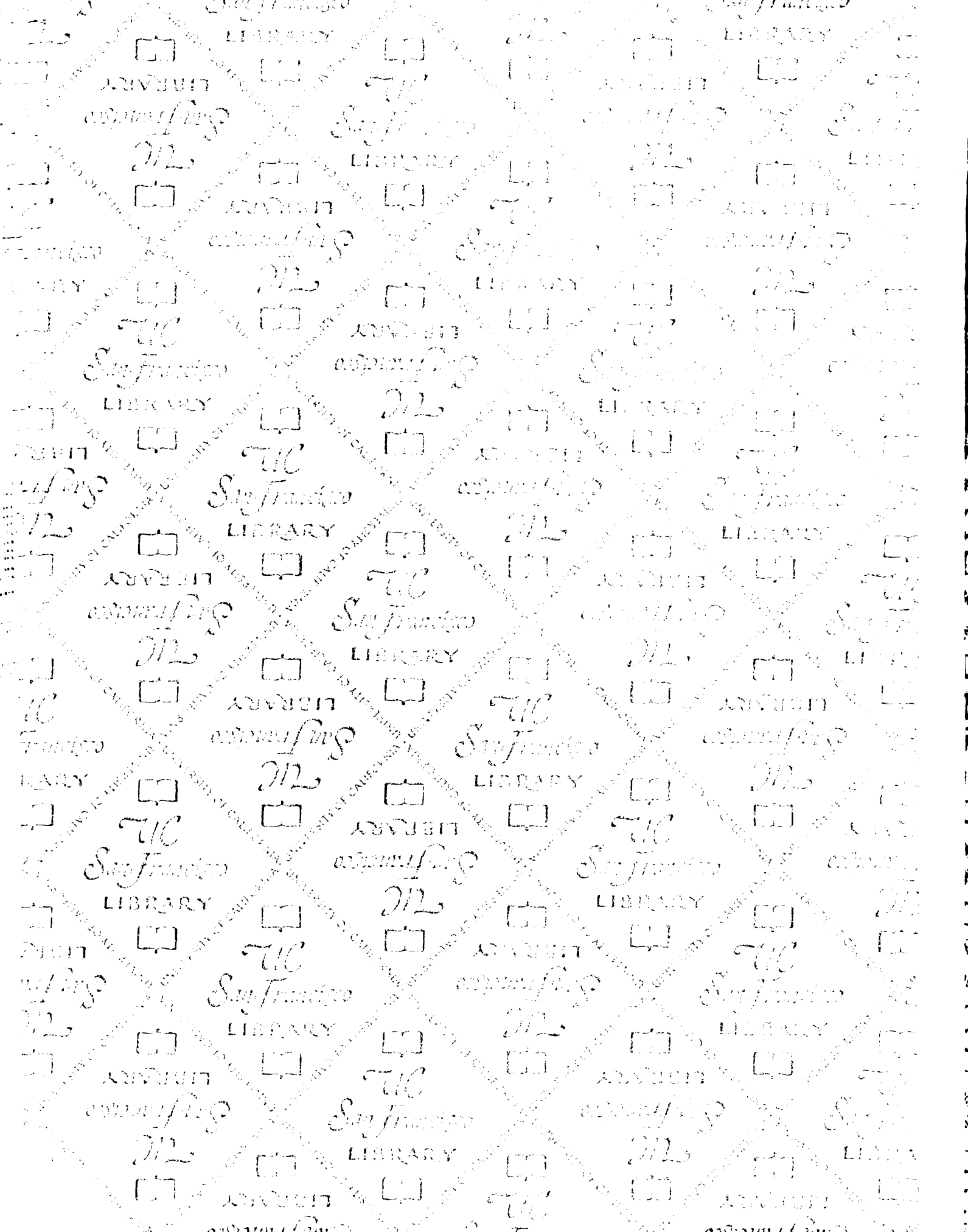
Figure 3. Average weekly self-care effectiveness ratings using the Self-Care Diary ($n = 49$). SCBs = self-care behaviors; F/U = follow up.







Time



For reference

Not to be taken
from the room.

7277794



3 1378 00727 7794

LIBRARY

