Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Final Report

Submitted to:

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Contract No. GS10F0114L/Order No. 263-FQ-511584 ■ March 31, 2006

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Consulting Services & Research

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1. Introduction

Under a contract awarded in January 2005 by the National Cancer Institute (NCI) and the National Institutes of Health (NIH) Clinical Center, CSR, Incorporated conducted a feasibility study entitled "Evaluation of Patient Recruitment Strategies." This report describes the study findings, our recommendations regarding data elements that should be collected to guide and evaluate the effectiveness of patient recruitment strategies, and our recommendations for future studies, both retrospective and prospective. In Section 2, we provide background on clinical research at the NIH Clinical Center and on the programs to be evaluated and a review of the literature. Section 3 presents the methods, Section 4 presents our findings, and Section 5 discusses and recommends changes and additions to the existing Patient Recruitment and Public Liaison (PRPL) and Clinical Studies Support Center (CSSC) databases, and suggests further research studies to be undertaken. References and appendices are provided at the end of the report.

2. Background

NIH is one of the world's foremost medical and research centers. It provides a Federal focus for conducting and supporting medical research or that leads the way toward important discoveries that improve people's health and save lives. Clinical trials are a critical link in this chain of discovery.

2.1 Clinical Research at the NIH Clinical Center

Since its inception, NIH has recognized the importance of clinical research. When the Warren G. Magnuson Clinical Center opened in 1953, it was one of the few—if not only—places that had the staff, infrastructure, and resources to conduct cutting-edge clinical trials. Although the landscape of clinical research has changed considerably during the intervening years, NIH remains deeply committed to excellence and innovation in clinical research as evidenced by the opening of the new hospital, the Mark O. Hatfield Clinical Research Center, in September 2004. This new hospital, completely dedicated to clinical research, provides a unique opportunity for scientists, clinicians, and patients to study and conquer both chronic and acute disease in the 21st century. Fifteen NIH Institutes have active clinical protocols at the Clinical Center, with approximately 1,000 protocols being conducted across Institutes. Nearly 90 percent of these protocols are actively recruiting participants at any given time. While clinical researchers in the intramural program have special advantages, such as the new hospital, they also face special barriers. Unlike researchers in other medical settings, NIH clinicians do not provide regular routine care to a patient population from which they can draw clinical trial participants. They must recruit their clinical trial participants from external sources, such as referrals from other physicians and from the community.

2.2 Background of the Programs

As detailed in the statement of work for this contract, in 1996 the Clinical Center's Medical Executive Committee identified patient recruitment as a major impediment to the completion of clinical trials at the Clinical Center. This led to the formation of centralized recruiting offices including the Patient Recruitment and Public Liaison (PRPL) Office at the Clinical Center and the Clinical Studies Support Center (CSSC) in the Center for Cancer Research (CCR) at the National Cancer Institute (NCI).

These two programs have been in operation for approximately 7 years and operate on a request for service basis. They conduct recruitment campaigns for protocols within the NIH intramural program. PRPL provides services to investigators across institutes while CSSC recruits patients to NCI studies.

PRPL and CSSC services include recruitment planning and implementation, toll-free telephone information and referral service (call center) including information and referral for active Clinical Center studies, telephone prescreening, and database searches (from the PRPL application). PRPL also assists in recruiting, registering, and compensating healthy volunteers for study participation.

CSSC and PRPL conduct both protocol-specific and program-specific recruitment strategies. Program-specific efforts might recruit for several protocols addressing the same broad disease category (e.g., breast cancer, rheumatoid arthritis). Recruitment for a particular study may consist of the implementation of one or more strategies. These strategies may be implemented simultaneously or sequentially, based on the request of the investigator and the available budget. The programs operate separate call centers where staff respond to protocol inquiries and refer prospective patients to studies. Each program collects its own data about patient recruitment strategies and outcomes for different protocols or clusters of protocols.

While their goals are the same and there are many similarities between CSSC and PRPL, there are also

major differences. PRPL performs a number of services for intramural investigators at all of the Institutes and Centers at NIH, including development of recruitment materials, recruitment plans, provision of lists of patients and/or healthy volunteers to researchers, preliminary phone screening for studies, and compensation for healthy volunteers. They also conduct an annual advertising campaign (print, radio, and Internet) for selected diseases. The major steps to the development of a PRPL recruitment plan include:

- Perform a needs assessment.
  - Interview the Principal Investigator (P.I.).
  - Review the protocol.
- Inform the Institute communications officer of the recruitment request.
- Obtain market research about the audience and disease to determine the best strategies and audiences and disease demographics. [Note: The market research about the disease and who is affected by it is conducted for PRPL, upon request, by the NIH library. PRPL staff base the strategies on what they know about how different audiences obtain their health information, past experience, and budget.]
- Determine timelines and target evaluation dates.
- Research placement of information and costs for strategies.
- Develop materials.
- Present the plan to the P.I.
- Forward the materials to the IRB for approval.
- Implement the plan.
- Evaluate the plan.
- Present the evaluation information to the research team.

CSSC provides services to intramural investigators at NCI. For individual protocols, the major steps in the development of a recruitment plan are similar to those of PRPL and include:

- Meet with the Principal Investigator and research team to learn about the study.
- Identify the target populations.
- Identify target advocacy groups and physicians from CSSC resources.
- Create a study promotion plan including recruiting strategies to be used.
- Present the plan to the research team for concurrence.
- Implement recruiting strategies.
- Track referrals.

It should be noted that the focus of CSSC recruiting strategies has evolved considerably from 1998 to 2003. In the early years, CSSC efforts were aimed at recruiting participants for individual protocols. Given the large number of NCI protocols active at any one time, referring physicians noted that it was difficult to remember the specifics of any particular protocol. CSSC also received feedback that physicians would refer more patients if they were certain that CSSC had a study for a particular patient. Therefore, CSSC began to aggregate all of the protocols studying a given type of cancer (breast, prostate, etc.) into a program and transitioned to recruiting for programs instead of individual protocols. For example, they aggregated all of the breast cancer protocols into the breast cancer program and developed recruiting strategies that applied to protocols across the program. CSSC develops standard scripts for referring callers for each program and then works with individual P.I.s to develop additional questions specific to their protocols. In recent years, the focus has changed further to reflect an emphasis on promoting CSSC services. The message to physicians then became—"CSSC knows the study protocols so you don't have to. Just refer patients to us and we will find the right protocol." While evolving over the years, CSSC recruitment activities continued to function within the key strategy of indirect recruitment of patients, working with physicians to refer patients rather than patients to self-refer.

2.3 Project Rationale

This project is proposed because clinical trials are a crucial component in the research, development, and evaluation of disease treatment strategies. However,

clinicians and researchers historically have experienced problems in recruiting adequate numbers of participants to clinical trials. In fact, patient recruitment is one of the most significant bottlenecks in treatment development. The costs of failed or delayed trials are significant in terms of waste of financial resources and in terms of loss of participants' time and discouragement of primary care professionals from cooperating with further research. Recruitment and retention of patients for clinical research at the Clinical Center has become more difficult (Gallin and Varmus, 1998). Recruitment to Clinical Center trials faces additional challenges because, unlike major medical centers that rely on their own patients, affiliated physician networks, or faculty, the Clinical Center must recruit patients directly from external sources. In the past, community physicians referred most patients. However, some long-time senior investigators at NIH speculate that the advent of managed care and the increased number of clinical trials being conducted by major medical centers and pharmaceutical companies result in the need to initiate other strategies to recruit patients.

In addition to the efforts of PRPL and CSSC, patient recruitment continues to be carried out in a decentralized fashion by research nurses and principal investigators across institutes. For example, in FY 03, PRPL was responsible for enrolling 1,679 (16 percent) patients and 709 (7 percent) healthy volunteers. The remaining 7,878 (77 percent) were enrolled independently of PRPL. Each entity operates in relative isolation, and to date, little is known about methods used to capture data on strategies, cost, and return on investment of patient recruitment efforts.

This fact, coupled with the paucity of information in the literature, makes it difficult to predict outcomes or determine the most successful recruitment practices for different studies conducted across the NIH intramural program.

Though a difficult undertaking, this project marks the first known effort to collect, compare, and contrast recruitment strategies and results across protocols. The project will capture and compare recruitment data, initially from two offices and subsequently from other investigators across the intramural program.

2.4 Purpose of the Evaluation

This is a multiphase, multiyear project beginning with Phase I feasibility study of existing patient recruitment methods and strategies employed by PRPL and CSSC. The results of the multiphase evaluation will be the identification of successful/best recruitment strategies, in terms of the number of contacts, referrals and enrollments, by type of protocol. This information will serve as the baseline for the development of a prospective study and of methods to collect improved recruitment outcome metrics. Evaluation results will provide:

- Evidence-based guidance for NIH investigators to direct future recruitment efforts.
- Development of a systematic, trans-NIH approach to data collection and evaluation of recruitment efforts.
- Application of the rigors of the scientific method to a process that, even with the best market research and application of marketing and public relations principles, is costly and time-consuming when conducted in isolation on a trial-and-error basis.
- Publications that will assist any investigator with patient recruitment efforts.

2.5 Timeliness of the Evaluation

Now more than ever, NIH intramural investigators are sensitized to the need to improve recruitment to studies conducted at the Clinical Center. Despite the successes of centralized recruitment offices and an increase in patient recruitment activities, many studies are slow to accrue patients. The recent opening of the NIH Clinical Research Center emphasizes the need to approach the problem of under-recruitment in a systematic evidence-based way.

As the government's premier research facility, the NIH Clinical Center provides a superb, unique environment for clinical research, particularly early

phase clinical trials. In order to advance the NIH mission, the new Clinical Research Center must be used to its full capacity. Therefore it is imperative to increase awareness of the intramural program and the studies available to the public.

Many NIH investigators are frustrated because they are uncertain how to spend the limited budgets that they have to recruit patients. Others continue to implement outmoded or ineffective strategies. Some are confused because strategies that worked well for a colleague's protocol produced few patients for their study. On the other hand, those strategies that have proven effective are not widely known or communicated.

One of the major themes of Dr. Zerhouni's NIH Roadmap initiative is Re-engineering the Clinical Research Enterprise, in which he stresses the need to build better integrated networks with academic medical centers and community-based physicians who care for sufficiently large groups of patients who may be willing and available to participate in medical research.

In this context a project such as the one described here is timely and essential for NIH to fulfill its mission.

2.6 Review of the Literature

Two reviews of the literature were performed with NCI funds prior to award of this contract. The first, dated January 5, 2004, is entitled "Enhancing Recruitment to Early Phase Cancer Clinical Trials: Literature Review." The draft of the second report, dated February 2, 2004, was entitled "Enhancing Recruitment to Early Phase Clinical Trials: Literature Review II."

In order to provide context and a frame of reference for the current review of the literature, sections of the text from these two earlier reviews have been included. The executive summary from the first review is included in its entirety. Since a final version of the second review was never prepared, no executive summary exists. Therefore a portion of the introduction and the section on review strategy are reproduced here.

2.6.1 *Executive Summary: Enhancing Recruitment to Early Phase Cancer Clinical Trials: Literature Review (WESTAT, January 5, 2004)*

[Please note: the italicized text is taken directly from the report.]

Clinical trials are critical to the development and evaluation of disease treatment strategies. Recruiting enough patients to complete individual trials in a scientifically sound and timely manner is, however, problematic, and an estimated 78 percent of all clinical studies fail to enroll the required number of patients on time (Getz. 2000). For phase I and II cancer clinical trials, recruiting is a particular challenge, as researchers strive to accrue cancer patients into trials that are designed to answer scientific questions and improve treatment overall, but are not designed specifically to try to make the participants well.

Patient accrual is affected by factors related both to people (i.e., patients, principal investigators, research nurses, referring physicians) and to activities (e.g., protocol design, recruiting outreach, patient screening, informed consent, medical procedures). Within each are elements that can facilitate recruiting and those that can hinder it. This review strives to describe the roles of these factors, as they are explained in the literature, and outlines proposed strategies to improve recruitment and accrual of patients to early phase cancer trials.

The literature suggests a strong disconnect between physicians' and patients' expectations of therapeutic benefit of early phase trials. Numerous flaws in the informed consent process (e.g. patients' lack of full comprehension of the consent forms) are seen as a possible reason for such disconnect. A new wave of studies, however, suggests that the complexity of the decision-making context for terminally ill patients might result in possible change in values, making a risk-benefit ratio more acceptable to cancer patients than to anyone else. Among the factors that may motivate cancer patients' participation in phase I and II trials are harboring hope of therapeutic benefit, having a desire to help future cancer patients by advancing the science of treatment, holding positive expectations about the experience

of participating, and refusing to "give up." On the other hand, lack of awareness of clinical trials among cancer patients may be a major hindrance to recruiting. Also, concerns about such issues as quality of life and feeling like a "guinea pig," and practical matters related to money, work, and family can reduce the likelihood that a potential participant will agree to join an early phase cancer trial. Physicians, particularly oncologists, play a major role in patient accrual, and their lack of sufficient information about available cancer clinical trials might pose a serious barrier to recruiting. Additionally, ethical concerns about the scientific—that is, nonmedical—goals of phase I and II trials and other ethical imperatives related to human experimentation might also hinder physicians' referrals. Still more factors mentioned in the literature but not yet thoroughly explored, include the role of protocol design and the effectiveness of various recruiting methods for cancer clinical trials.

Difficulties in clinical trials patient recruitment in general, and early phase cancer trials recruitment in particular, are a significant barrier to treatment development, and the literature about this problem and what can be done to improve recruiting overall is characterized by significant gaps and limitations. Although all of the studies described in this review help to illuminate the issues, most of them relied upon research techniques that make generalizations to a larger population imprudent. Also there is a particular paucity of studies that focus on phase I and II clinical trials. More scientific, hypothesis-driven analyses are needed to help inform and improve patient recruitment planning and activities.

2.6.2 *Introduction and Review Strategy from Enhancing Recruitment to Early Phase Clinical Trials: Literature Review II, Draft (WESTAT, February 2, 2004)*

[Please note: the italicized text is taken directly from the report.]

2.6.2.1 *An Excerpt from the Introduction*

The prolonged or inefficient recruitment can have negative economic and scientific consequences, resulting in wasted resources, in discouragement of participants, patients and research teams, but most importantly in delayed development of new treatment strategies (Spilker & Cramer, 1992). Therefore a better understanding of the factors that contribute to successful recruitment and barriers that prevent potential participants from enrolling in clinical trials is necessary in order to improve patient participation in clinical research. The related need to improve efficiency of NIH early phase clinical trials recruitment guided this analysis. This paper reviews broadly issues concerning patient and healthy volunteer participation in clinical trials for chronic and terminal diseases, and provides insight into some barriers to recruitment as well as successful strategies. This review is focused on trials for conditions studied by NIAID, NINDS, NHLBI, and NIMH and carried out at the National Institutes of Health Warren Grant Magnuson Clinical Center.

2.6.2.2 *Review Strategy*

The review strategy was to focus on peer-reviewed and NCI-focused materials concerning recruitment for phase I and phase II clinical trials, focusing exclusively on early phase clinical trials for chronic and terminal diseases studied by NIAID, NINDS, NHLBI, NIMH. However, due to the scarcity of literature on this specific subject, the search was expanded to include randomized clinical trials and clinical trials in general, as well as the broader issues related to accrual of participants in clinical research. Following Lovato et al., (1996), recruitment was defined as "the initial and subsequent contact(s) of human subjects, including population selection and planning, that lead(s) to the first clinic screening visit" (p.330). The retrieved articles were searched for information that could be extrapolated to the early phase clinical trials. The strategy encompassed searching computerized databases (MEDLINE, PUBMED), Internet sites (www.nih.gov CenterWatch.com) and reference lists from retrieved articles. The search keywords included phase I clinical trials, phase II clinical trials, clinical trials recruitment, clinical trials and volunteers and recruitment, early phase recruitment, recruitment phase I, recruitment phase 11, chronic terminal, chronic terminal debate, asthma recruitment, multiple sclerosis recruitment,

diabetes recruitment, lupus recruitment, clinical trials and media coverage. Additionally, several books and reports were used.

The collected articles pertained primarily to a limited number of conditions that were found to be more thoroughly researched (e.g. depression, cardiovascular diseases, diabetes, HIV), while no literature was located on many other illnesses. The search yielded a large proportion of studies published by international authors and based on non-US populations. These articles were excluded from this review, except for when their content was deemed by the review team to be pertinent to general, non-country and -health system specific issues in patient recruitment. A limited number of U.S.-based studies reported on their recruitment experiences, including successful methods and strategies and patient yields from various recruitment strategies. Most information that was available, however, came from large randomized studies, in many cases conducted in multicenter settings. The amount of available information on recruitment to early phase clinical trials proved to be extremely scarce. Only a couple of articles systematically compared cost effectiveness of different recruitment methods; no literature on this subject pertaining specifically to phase I or II treatment trials was located. This review suggests that, while very limited, a growing body of literature exists on recruitment methodology in general. An urgent need, however, exists for exploration of barriers and motivators, as well as best practices for recruitment to early phase clinical trials.

2.6.3 CSR Review of the Literature

Briefly, the reviews mentioned in sections 2.6.1 and 2.6.2 disclosed that little systematic research has been published on the effectiveness of various methods of recruitment to clinical trials in general, and to early-phase trials in particular. In most instances when such information is provided, it is anecdotal rather than systematic, and/or pertains to Phase III clinical trials. Also, although such analysis is not available for the early-phase trials, a review of general randomized trials reports (Gross et al., 2002) suggested that investigators rarely documented how many people were identified as eligible for enrollment and the number of potential participants that needed to be screened to identify one enrollee.

Furthermore, a study of methods utilized in patient recruitment to randomized controlled trials (Foy et al., 2003) found that the recruitment methods used by the investigators were not evidence-based, and that organizational characteristics, such as previous research experience or patient eligibility criteria, could be more influential in trial recruitment than the use of specific interventions. No similar analysis has been conducted for the Phase I or II clinical trials, and these gaps in the literature clearly suggest that further research is necessary to discern the effectiveness of various recruitment methods for the early-phase clinical trials. Likewise, these literature reviews uncovered nothing directly related to recruiting patients to specific types of trials at the NIH Clinical Center.

2.6.3.1 *Literature Search Strategy*

One of the requirements of this Phase I feasibility study was to update the literature reviews. In order to locate relevant articles that have appeared since the earlier literature reviews were performed, the following databases were searched: PubMed; the EBSCO databases PsycINFO, SocINDEX, and Academic Search Elite; Science Direct; and Google and Google Scholar. The search strategy included the terms “patient” and “recruitment” and “clinical trials.” An alternate search that also included the term “strategies” was performed as well. In addition, the PubMed search was limited to “human.” Originally, all searches were limited to the years 2000 through 2005; however, early in 2006 additional papers became available and were also evaluated.

When a particularly relevant article was found, “related articles” also were called up. Searches also were performed on the authors of such articles. References cited in some of these articles also were checked for inclusion (this search usually was run in the Single Citation Matcher of PubMed). All abstracts were read and all irrelevant articles excluded. Also excluded were items that were referenced in the two previously mentioned reviews of the literature as well as the proposal that CSR

submitted in response to the solicitation for this contract.

2.6.3.2 *Search Results—General Characteristics of the Literature Retrieved*

This search strategy yielded a total of 218 papers, 10 of which had been cited previously in one of the two literature reviews mentioned above. The numbers of relevant citations by year are displayed in Exhibit 2-1.

Exhibit 2-1. Literature Review Summary Statistics

Year	Number of papers	Number cited in the two literature reviews performed for NCI	New total
2000	17	3	14
2001	24	3	21
2002	33	1	32
2003	50	3	47
2004	47	0	47
2005	45	0	45
2006	2	0	2
Total	218	10	208

An additional pertinent reference was located—a news release, which lead to a report posted on the Internet, raising the total number of unduplicated references to 209. In the report *Enhancing Recruitment to Early Phase Cancer Clinical Trials: Literature Review*, the authors limited their search to literature published in English but did not otherwise restrict the citations by country of origin. In the second report *Enhancing Recruitment to Early Phase Clinical Trials: Literature Review II*, the authors excluded international authors and papers based on populations outside the United States except where their content was deemed by the review team to be pertinent to general, non-country and non-health system specific issues in patient recruitment.

Our search included studies that were conducted in a number of countries and reported in the papers identified in our search, and this information is displayed in Exhibit 2-2.

Exhibit 2-2. Distribution of Search Results by Country of Origin

Country	Number of papers
Australia/New Zealand	7
Canada	13
Europe	10
United Kingdom	30
United States	149

Review of the abstracts and, if indicated, the complete text of the article, revealed that all papers dealt with some aspect of recruiting patients to clinical research studies; however, few dealt with the specific focus of this project—which recruitment strategies are most effective for recruiting specific types of patients with specific diseases into specific types of clinical trials.

The majority of the papers dealt with barriers to recruitment rather than recruitment strategies. The recent literature varies on the issue of under-representation of minority populations in clinical trials and barriers to recruitment. Oddone et al. (2004) summarized the experience of the VA Cooperative Studies Program in enrolling white, black, and Hispanic patients over the period from 1975 to 2000. They found that 83 trials, involving 71,463 patients, reported information on race/ethnicity. They found that in trials that targeted diseases that affect minority populations to a greater degree than white populations (diabetes, hypertension, and end stage renal disease), 11 of the 14 trials enrolled more minority patients than expected. Trials that included an invasive arm enrolled fewer minority participants than expected. This finding suggests that in trials that involve invasive therapies, it may be necessary to adopt special recruitment strategies to reach minority populations. Research has yet to be done to determine what special recruitment strategies might be effective. In a very recent article, Wendler and colleagues (2006) performed a comprehensive literature search to identify all published health research studies that report consent rates by race or

ethnicity. They report very small differences in the willingness of minorities, most of whom were African Americans and Hispanics in the United States, to participate in health research compared to non-Hispanic whites. In assessing these findings, it is necessary to appreciate the fact that several of the largest studies were interview surveys and other non-intervention studies. For the 10 clinical intervention studies, overall there were no differences in willingness to participate by race/ethnicity; however, there was significant lack of homogeneity among the studies. The authors suggest that race/ethnic minority groups in the United State are as likely as non-minority individuals to participate in health research but that they are underrepresented among invited participants. The authors conclude that increased attention should be paid to offering participation to more minority individuals. The issue of effective recruitment strategies was not addressed in this paper. Other papers dealt with prevention studies, multi-site trials (often large phase III clinical trials), or studies in settings very dissimilar to the NIH Clinical Center (community, neonatal intensive care unit, hospice, etc.). A few papers reported on measurement of intention to participate in clinical trials rather than actual participation.

2.6.3.3 *Search Results—Findings Directly Related to Patient Recruitment Strategies*

The content of the 15 papers most directly related to the topic of patient recruitment is summarized below. The five papers discussed in the Evidence Report detailed below are not summarized again.

One of the most directly relevant resources is *Evidence Report/Technology Assessment Number 122: Knowledge and Access to Information on Recruitment of Underrepresented Populations to Cancer Clinical Trials*, a report prepared by investigators at the Johns Hopkins University Evidence-based Center for the Agency for Healthcare Research and Quality (AHRQ) (Ford et al. 2005). For our purposes, this report has several limitations. First, it deals exclusively with cancer clinical trials while our interests are broader. Second, it focuses exclusively on underrepresented populations rather than the population as a whole. Third, it deals with prevention trials as well as treatment trials. Finally, the topic of recruitment strategies is one of several topics addressed. Since this report is based on a comprehensive and very recent review of the literature, it contains valuable information pertaining to recruitment strategies and validates the thoroughness of our own search strategy.

Recent studies of patients enrolled in cancer treatment trials sponsored by the NCI have demonstrated that several populations are underrepresented in terms of their participation in cancer treatment trials. Therefore at the request of NCI, AHRQ commissioned a systematic review of the existing evidence on the recruitment of underrepresented populations into cancer clinical trials. Six key questions were considered by the report published in June 2005:

Question 3. Which recruitment strategies (e.g. media appeals, incentives, etc.) have been shown to be efficacious and/or effective in increasing participation of underrepresented populations in cancer treatment trials? [Note: Question 3 is analogous to the focus of the literature review that CSR conducted for this project.]

Question 4. Which recruitment strategies have been shown to be efficacious and/or effective in increasing participation of underrepresented populations in cancer prevention trials?

The authors of the report had a comprehensive search strategy that yielded 4,436 citations, 1,089 of which were eligible for abstract review. Of those, 218 were eligible for article review. Only 67 of the articles were eligible for inclusion after article review. Only five of the 67 articles dealt with the key questions articulated, above. None of these articles was cited in the *Enhancing Recruitment to Early Phase Cancer Clinical Trials: Literature Review* performed by WESTAT. The articles accompanied by very brief summaries are as follows:

Brewster WR, Anton-Culver H, Ziogas A, et al. Recruitment strategies for cervical cancer prevention study. Gynecol Oncol 2002;85(2): 250–4.

Differences in recruitment into cancer prevention clinical trials between a clinic registry method and a media campaign targeting Latina women are examined. The odds of presenting to the clinic and of recruitment were nearly three times more successful via the media campaign than via the clinic registry.

Ford M, Havstad S, Davis SD. A randomized trial of recruitment methods for older African-American Men in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Clinical Trials. 2004:1:343–51.

Recruitment differences among African Americans randomized into either a control group or three increasingly intensive intervention arms were examined. The most intensive church-based, face-to-face recruitment intervention arm produced significantly higher recruitment compared to the other two intervention arms or the control group.

Moinpour CM, Atkinson JO, Thomas SM, et al. Minority recruitment in the prostate cancer prevention trial. Ann Epidemiol 2000;10(8 Suppl):S85–1.

The results of a randomized trial in increasing participation of minorities were reported. Minority recruitment strategies were designed and implemented in five pilot sites. The overall impact was minimal and it is unclear if, and at which sites the interventions were fully implemented.

Paskett ED, Cooper MR, Stark N, et al. Clinical trial enrollment of rural patients with cancer. Cancer Pract. 2002;10(1):28–5.

The effect of an intervention program aimed at physicians and the community to increase the number of rural patients with breast cancer or colorectal cancer enrolled in clinical trials was examined. The rates of enrollment into clinical treatment trials did not improve significantly in the intervention communities.

Linnan LA, Emmons KM, Klar N, et al. Challenges to improving the impact of worksite cancer prevention programs: comparing reach, enrollment, and attrition using active versus passive recruitment strategies. Ann Behav Med. 2002;24(2):157–6.

The differences between passive and active recruitment into a home-based cancer prevention randomized trial among employees were examined. While lower enrollment and higher attrition were observed in the passive recruitment arm, the passive recruitment method enrolled a more diverse group of participants than did the active recruitment arm.

The authors of the report concluded that there is only scant evidence to support specific interventions to improve recruitment of underrepresented minorities into cancer clinical trials (AHRQ 2005). Since only a couple of these articles dealt with studies akin to those being conducted at the Clinical Center, even less evidence is available on our specific focus.

The report also addressed the issue of barriers to and promoters of participation of underrepresented populations in cancer prevention and treatment trials. Their search yielded 45 eligible studies that identified 118 distinct barriers to accrual to cancer clinical trials. Many more barriers to opportunity were reported than to awareness or acceptance. Of the 59 distinct promoters of recruitment, most were promoters of opportunity to participate. Nine studies provided data on how provider attitudes/perceptions were barriers to and promoters of accrual to cancer clinical trials. The findings on providers were mixed. Four studies reported provider attitudes to be a barrier to enrollment while another study found it to be a promoter. Likewise, two studies of provider communication style or method of presentation were barriers to patient enrollment while another study found it to be a promoter of enrollment.

One study (Buchbinder et al. 2004) which examined hypothetical versus actual willingness to participate in an HIV vaccine trial reported that only 20 percent of those stating hypothetical willingness actually enrolled in this vaccine trial. These findings supported our decision to exclude studies examining only hypothetical willingness to participate in clinical trials. Very few of the papers uncovered in

our search are directly related to patient recruitment strategies in a single site equivalent to the NIH Clinical Center, but each has elements of interest. Arean and colleagues (2003) reviewed problems associated with recruiting older minority individuals into mental health services studies. They concluded that although their data were observational, the results suggested that consumer-centered recruiting strategies such as utilizing experienced recruiters yield greater overall recruitment and retention than do traditional research methods. They recommended that rigorous research on the best methods of recruiting and retaining older minorities be performed.

Cambron and colleagues (2004) investigated accrual rates and recruitment processes among three midwestern sites during a pilot study of manual therapy for chronic pelvic pain. Overall they found that direct mail and radio advertisements were the most effective recruitment methods but recruitment success varied by site.

Cooley et al (2003) examined recruitment and retention in a multi-site, multi-state prospective cross-sectional study focused on quality of life among women with lung cancer. Although this is a multi-site study, it was included because the effectiveness of various recruitment strategies was examined. Passive recruitment strategies included letters from the tumor registry, letters from physicians, posters/pamphlets, radio public service announcements and newspaper advertisements. Active recruitment strategies included direct telephone follow-up to letters sent and attending community support groups. Although the research design was consistent and all the procedures standardized, recruitment methods varied among the sites due to differences in IRB approval and state cancer registry regulations. The authors did not examine individual recruitment strategies; rather, they compared active to passive strategies. They concluded that passive recruitment strategies had a higher recruitment efficacy and a lower attrition rate but cautioned that the results were merely suggestive since the active and passive strategies were not randomized. They did conclude that passive recruitment strategies were successful in recruiting women with lung cancer.

Unsom et al. (2004) examined strategies for recruiting woman age 65 and older into an osteoporosis clinical trial. They reported that media and mass mailings were effective when the target population was large and knowledgeable about the disease and treatments being investigated. An interpersonal approach was found to be more effective than a media-based approach when the target population was small, unaware of its personal risk of disease and unfamiliar with research and the research center.

Hughs and colleagues (2004) recently reviewed the literature on the topic of minority recruitment in hereditary breast cancer research. Their search yielded 15 articles on breast cancer susceptibility and genetic testing. As part of the review, they tabulated the types of recruitment strategies reported in each paper. The authors concluded that it was not possible to determine which methods were most and least effective for recruiting ethnic and racial minority because response rates were not reported consistently. They recommended that future cancer genetics research studies should incorporate an evaluation component into the recruitment methods used. Shuhatovich et al (2005) analyzed the effectiveness of recruitment strategies utilized in recruiting women into a trial of optical spectroscopy for the diagnosis of cervical neoplasia. They reported that newspaper reportorial coverage and advertising, followed by family and friends and television news coverage, were the most effective recruitment methods. Baigis, Francis, and Hoffman (2003) compared clinic center site-visit recruitment to community-based recruitment strategies (presentations at local groups, mail/phone canvasses of caregivers, neighborhood network promotion, public site postings and print media notices) in recruiting participants for a community-based intervention study of HIV-infected individuals. The percentage of screened candidates who were subsequently enrolled was 13.5% for clinic recruitment strategies compared with 21% for community-based recruitment strategies.

2.6.3.4 *CSR Literature Review Summary*

Our detailed search strategy yielded very little new literature directly related to evaluating the effectiveness of various recruitment strategies. The

findings from several comprehensive literature reviews on related topics validate our search methodology and confirm the dearth of relevant literature. Given the importance of patient recruitment to the success of clinical research, we are pleased to note that some investigators evaluate the effectiveness of various recruitment strategies. However, this emerging literature is focusing on the research settings, types of studies, and recruitment strategies are not directly comparable to those of the NIH Clinical Center. Therefore, later phases of this project should seek to establish a high quality database and conduct prospective studies to ascertain effective recruitment strategies. Findings from these studies will position NIH to make significant contributions to the field.

3. Methods

In this section, we describe the methods used to conduct the feasibility study. We present the evaluation goals, conceptual framework, and research questions; and describe the data sources and data management and analysis techniques used.

3.1 Goals of the Evaluation

The goals of the multiphase Evaluation of Patient Recruitment Strategies (EPRS) are to gather and combine retrospective data from both PRPL and CSSC (and possibly other programs in the future) in order to:

- Evaluate the effectiveness of recruitment strategies across protocols and Institutes;
- Design a prospective study based on initial findings; and
- Develop methods to gather recruitment data in a standardized manner.

Initially, the target population for this first phase of the proposed evaluation was to be Phase I and Phase II clinical trials. When it was discovered that 27 percent of the PRPL protocols were natural history studies, the co-project officers decided to include these studies as well.

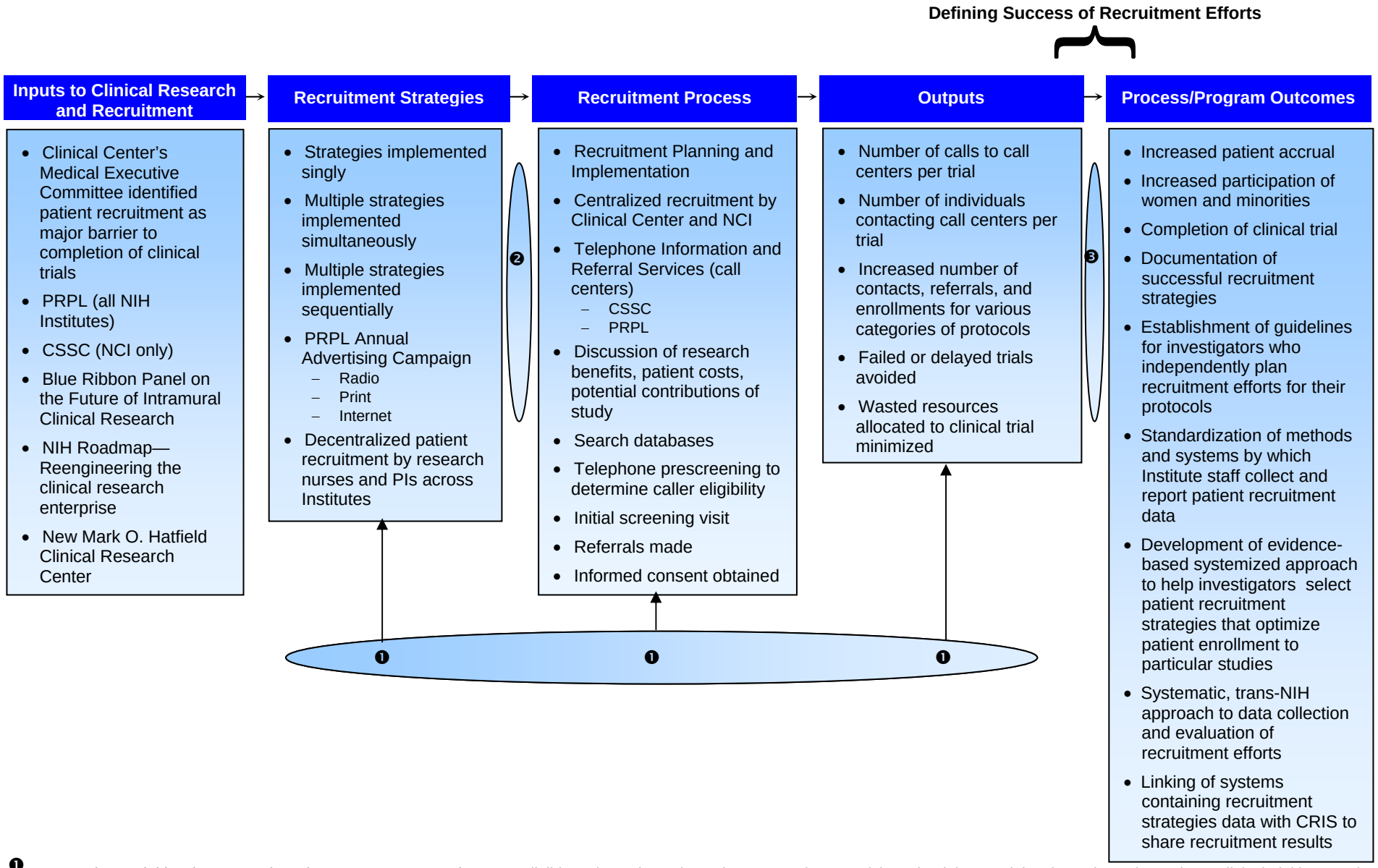
3.2 Conceptual Framework

CSR developed a broad conceptual framework for the feasibility study (see Exhibit 3–1). This framework depicts the interrelationships among the programs' inputs, recruitment strategies and processes, outputs, and anticipated outcomes. This model incorporates the overall goals of the PRPL and CSSC; the environment in which the programs operate; the interrelationships of various project goals and program functions; the intended short-term and long-term outcomes of the programs; and environmental/contextual variables. Although CSR was not able to address in its evaluation all the components included in the conceptual framework, the framework helps provide a context for the study.

3.3 Research Questions

CSR developed research questions to guide the design and implementation of the Phase I feasibility study. These questions flow from the conceptual framework presented in Exhibit 3-1, but are more focused and specific, and address elements that could be measured within the time and budgetary boundaries of the evaluation. Research questions were modified after preliminary review of available data. A primary research question focused on the effect of different recruitment strategies on protocol accrual. In addition, a key goal of the study was to assess the feasibility of evaluating recruitment strategy impact on protocol accrual. Therefore, we focused especially on process questions related to type of data available and feasibility of different analyses. Exhibit 3–2 lists the final research questions used to guide the evaluation, as well as corresponding measures and data sources.

Exhibit 3-1. Preliminary Conceptual Framework



❶ *Intervening Variables that Pose Obstacles to Treatment Development:* Eligible patients do not have the opportunity to participate in trial; potential patients do not know that a clinical trial is an option; many physicians are not aware of clinical trials available to their patients; patients refuse to participate in clinical trials.

❷ *Contextual Variables that Affect Recruitment:* Clinical Center must recruit patients directly from external sources (as opposed to major medical centers that can rely on their patients, affiliated physician networks, or faculty); advent of managed care may inhibit community physicians from directly referring their own patients to trial; increased number of clinical trials being conducted by major medical centers and pharmaceutical companies.

❸ *Contextual Variables that Affect Patient Accrual:* People factors (e.g., patients, PIs, research nurses, referring physicians), protocol factors (e.g., protocol design, recruiting outreach, patient screening, medical procedures required for screening and continued participation in trial).

Exhibit 3-2. Research Questions and Analysis Variables Matrix

Research Questions	Measures	Data Sources
1. What recruitment strategies result in the greatest number of contacts, referrals, and admissions of various categories of protocols? a. What recruitment strategies are used simultaneously?	• Specific recruitment strategies • Timing of implementation of recruitment strategies (simultaneous, sequential) • Patients referred per protocol	• PRPL and CSSC databases • PRPL and CSSC Project Managers • Project Advisory Group
2. What data (contacts, referrals, enrollments, and recruiting strategies per study) are available from PRPL and CSSC? a. What data elements are common to both databases? b. How can a crosswalk be structured to maximize use of data that are different in the two databases? c. What tracking supports continued updating of protocol information and monitoring of accrual? d. For critical variables, what incomplete or missing data can be gleaned from other sources?	• Individual data elements in PRPL and CSSC databases	• PRPL and CSSC databases • PRPL and CSSC Project Managers and staff
3. How do we define success for recruitment efforts? Should the definition of "success" be "all or none," categorical, or continuous?	• Number of calls to call center per trial • Number of individuals contacting call center per trial (one individual may call more than once) • Number accrued	• PRPL and CSSC databases • PRPL and CSSC Project Managers • Project Advisory Group
4. How can data be categorized for analysis by patient characteristics? a. What categorization scheme allows for a significant number of patients to be included in each category? b. What information is collected on the educational attainment of participants?	• Gender • Age • Race/ethnicity • Education/literacy • Geographic location • Other	• PRPL and CSSC databases • PRPL and CSSC Project Managers • Project Advisory Group
5. How can data be categorized for analysis by disease characteristics?	• Type of disease • Time course of disease • Prevalence • Other	• PRPL and CSSC databases • PRPL and CSSC Project Managers • Project Advisory Group
6. How can data be categorized for analysis by study (protocol) characteristics?	• Phase • Invasiveness of treatment • Frequency/duration of visits required • Other	• PRPL and CSSC databases • PRPL and CSSC Project Managers • Project Advisory Group

3.4 Project Advisory Group

Early in the course of the project, the co-project officers convened a Project Advisory Group comprised of individuals representing various NIH Institutes (usually nominated by the Institute Clinical Director) to advise them about project processes and outcomes as well as serve as a liaison to their Institute and encourage participation in subsequent phases of the project (e.g., data collection). A roster of the Project Advisory Group members and alternates can be found in Appendix A.

The Project Advisory Group met twice during the study. The first meeting was held on July 18, 2005. Participants in the meeting included:

- **Advisory Group members and alternates**—Ms. Kelli Carrington, Ms. Marjorie Gillespie, Dr. Stephen Kaler, Dr. Claude Kasten-Sportes, Dr. Dee Koziol, Dr. Janine Smith, Ms. Susanna Sung, and Ms. Terri Wakefield
- **NIH Co-project Officers**—Ms. Dottie Cirelli (Clinical Center) and Ms. Tracy Thompson (NCI)
- **CSR staff**—Dr. Sherrie Aitken, Dr. Mary Dufour, Dr. Gabriella Newes-Adeyi, Mr. Chiung Ming Chen, Mr. Sanjeev Rana, and Ms. Tara Filmyer

At the meeting, the Project Officers for the evaluation study, Ms. Thompson and Ms. Cirelli, provided background information on the project and the Advisory Group's expected role in the project. CSR staff presented the basic research questions and the data sources available to answer the questions (the PRPL and CSSC patient data, CSSC and PRPL recruitment strategy data, and protocol data from ClinicalTrials.gov).

The Project Advisory Group was charged with helping to answer two major questions:

1. How do we define "success" for recruitment efforts?
2. How can data be characterized for analysis—e.g., by disease, by protocol characteristics, by patient characteristics?

Main points from the discussion at this Advisory Group meeting as well as from followup correspondence are included in the Findings section (Section 4) as well as the Discussion and Recommendations section (Section 5).

The second Project Advisory Group meeting was held on March 17, 2006. Participants in the meeting included:

- **Advisory Group members and alternates—** Ms. Kelli Carrington, Ms. Marjorie Gillespie, Dr. Stephen Kaler, Dr. Claude Kasten-Sportes, Dr. Janine Smith, and Ms. Terri Wakefield
- **NIH Co-project Officer—**Ms. Dottie Cirelli (Clinical Center)
- **CSR staff—**Dr. Mary Dufour, Dr. Gabriella Newes-Adeyi, Mr. Sanjeev Rana, and Mr. Chiung Ming Chen.

Ms. Dottie Cirelli and Dr. Mary Dufour opened the meeting by briefly summarizing the purposes of the project. The Project Advisory Group was then given two charges:

- To review and comment on the draft final report for the projects and, more importantly,
- To make recommendations regarding next steps in this multiphase study.

Ms. Cirelli added that she would like the Advisory Group to discuss what kinds of future studies would be most feasible and useful. Specifically, she asked the Advisory Group to discuss:

- Whether to continue the task of examining which recruitment strategies are effective for which kinds of clinical trial protocols; and
- Since the currently available data are problematic, how can data be collected in a standardized fashion across Institutes and Centers (ICs) recruiting patients for clinical trials.

Dr. Dufour presented an overview of the methods and findings of the feasibility study and then opened the floor for discussion. The main points from the discussion as well as feedback following the

meeting are included in the Discussion and Recommendations section (Section 5).

3.5 Data Sources

As described earlier, data for the evaluation were drawn from CSSC and PRPL. There were two separate data sources from both CSSC and PRPL: (1) database data and (2) recruitment strategies data. The term "database data" refers to the raw call log and other data collected by PRPL and CSSC between 1998 and 2003. "Recruitment strategies data" refers to the different strategies used by CSSC and PRPL to recruit participants into clinical studies. At the request of the Project Officers, CSR limited its analyses to data from 1998–2003. The earlier date corresponds to the year both recruitment centers initiated activities. CSSC launched major revisions to its recruitment database system in 2004. Therefore, 2003 was selected as the final year from which data were included. We further describe the data sources below.

3.5.1 *CSSC*

CSSC used a Web-based application to capture its recruitment efforts. The data were stored on an MS SQL back-end. A copy of this dataset was made available to CSR. Because a data dictionary detailing the definition of variables and of variable values was not initially available, CSR worked closely with CSSC and the contractor holding the database to create a study data dictionary. Due to the complexity of the dataset, this was a labor-intensive effort. The CSSC Project Officer identified 67 protocols for the analyses (see Appendix B). These 67 protocols were selected because both database data and recruitment strategies data exist for this subset of protocols.

A separate CSSC Excel spreadsheet listed recruitment strategies for each of the 67 protocols. A total of 17 different recruitment strategies were identified and tracked by CSSC (see Appendix C).

3.5.2 *PRPL*

PRPL collected information on persons who contacted the recruitment office via a stand-alone relational database. The PRPL Project Officer provided these data to CSR in the form of protocol-specific Excel spreadsheets. A total of 34 PRPL protocols having both database and recruitment strategy data were identified for the study (see Appendix D). As for the CSSC data, because no data dictionary was readily available for the PRPL data, CSR worked with the database administrator at PRPL to develop a dictionary for variables used in the analysis. CSR also received a PRPL User's Manual, PRPL Database – Patient Recruitment Public Liaison Office") from the database administrator at the PRPL office.

PRPL conducts periodic evaluations of its recruitment strategies for individual protocols. Results of these evaluations are summarized in Word documents. The Project Officer provided copies of the relevant recruitment strategy documents to CSR. Because of variations in the language used to describe recruitment efforts in each of the evaluation documents, CSR recoded the strategies into eight separate recruitment strategies (see Appendix E).

3.5.3 *ClinicalTrials.gov*

As mentioned above, one of the research questions to be answered was how could CSSC and PRPL data be categorized for analysis by study characteristics. Therefore, locating a source of study or protocol characteristics was necessary. In CSSC and PRPL, the information by which studies (also called protocols) are identified is the unique NIH protocol number. Both CSSC and PRPL have access to the individual study protocols in the form of extensive paper files; however, extracting data from these files would have been labor intensive and inefficient. Therefore, various electronic sources of the study protocols were explored. Both PRPL and CSSC have searchable electronic databases of clinical trials being conducted at NIH. The NIH Clinical Center website provides links to a database called "Search the Studies." The collection of studies being conducted at the NIH Clinical Center can be searched by entering a diagnosis, sign, symptom, or other key words or phrases. In addition, the site permits browsing by the Institute of the principal investigator. While it is possible to

locate protocols by searching on the NIH protocol number, only protocols for which patients are currently being recruited or actively being followed up will be identified. Identification of completed or terminated protocols would require utilization of a second data source. In addition, the content of the protocol descriptions was very concise and quite variable across studies. The CSSC portion of the NCI Web site also provides links by which to search NCI clinical trials at NIH. This database also can be searched by NIH protocol number; however, again, only protocols for which patients are actively being recruited are listed and the descriptions of the protocols are extremely telegraphic.

ClinicalTrials.gov, a service of NIH developed by the National Library of Medicine, provides regularly updated information about federally and privately supported clinical research in human volunteers, including studies conducted at the Clinical Center. In this database:

- Protocols can be located by searching on the NIH protocol number;
- Studies that are no longer recruiting, have been completed, or have been terminated can be located; and
- Protocol summaries are quite detailed and follow a consistent format.

In ClinicalTrials.gov, protocol information generally includes:

- Title of the study,
- Recruiting status,
- Sponsoring entity,
- Source of information recorded,
- ClinicalTrials.gov unique identifier,
- Purpose of the study,
- Condition (disease),
- Intervention (procedure, drug, etc., if applicable),
- Phase (if applicable),
- Study type (interventional or observational),
- Study design (treatment, safety/efficacy, natural history),
- Official title,
- Expected total enrollment,
- Study start date,
- Study completion date (if applicable),
- Eligibility:
  - Inclusion criteria,
  - Exclusion criteria,
- NIH Protocol number, and
- Date information last updated.

Given the features and data elements available in this database, ClinicalTrials.gov was selected as the source of information on the specific protocols.

3.6 Data Security and Quality Control

CSR instituted standard data management and quality control measures to ensure confidentiality of data and accuracy of data analysis.

3.6.1 *Data Security*

All project files were stored in a project folder on the local CSR network. The project folder had user-level permissions restricted to CSR personnel working on the project. Two CSR staff also gained NIH clearance to view the PRPL recruitment monitoring database application. They also were granted remote-terminal access to view selected portions of the PRPL tracking system, although no data were downloaded from this database. Data confidentiality forms were signed by CSR staff to view and report the CSSC data.

3.6.2 *Quality Control*

The quality of the data was assured through the use of the data dictionaries and a crosswalk of CSSC and PRPL data. Data dictionaries provide definitions for the different variables and their values for the study analyses. With the help of the data dictionaries, we were able to create a crosswalk between the CSSC and PRPL variables. A crosswalk enabled CSR to identify common variables in the two datasets. It also assisted in recoding data values between the two datasets into a common set.

3.7 Data Preparation

Data preparation involved several steps:

1. *Creation of separate folders*—Separate folders were created for the CSSC and PRPL files.
2. *Creation of a project database*—Descriptive information of the PRPL datasets and protocol information from ClinicalTrials.gov were tracked in a project database (for a screenshot, see Exhibit 3–3). Information regarding each PRPL e-mail/file also was stored in the project database (Exhibit 3–4).
3. *PRPL database*—A separate PRPL database was created to "tie-in" the multiple spreadsheets containing data from the PRPL office. The original PRPL data were separated into individual spreadsheets, with different formats, according to a specified medical condition. This database enabled CSR to reformat the various spreadsheets into a common format dataset.
4. *Documentation*—Steps were taken to ensure that there was appropriate documentation for each of the datasets. In cases where they were not available, they were created by CSR staff with input from the appropriate CSSC or PRPL office.
5. *Conversion*—All data files, from CSSC and PRPL, were converted into SPSS files as a final preparation toward data analyses.

3.7.1 *Data Extraction from CSSC*

The CSSC data consisted of 67 protocols stipulated by the CSSC office. Unlike the PRPL data, all CSSC data were available within a single SQL database. After identifying the required protocols and the necessary tables, the CSSC data were exported as a SPSS dataset for our analyses. After filtering for the 67 CSSC protocols and the study dates, there were 29,855 records available for analyses.

Exhibit 3-3. Screenshot of the Project Database

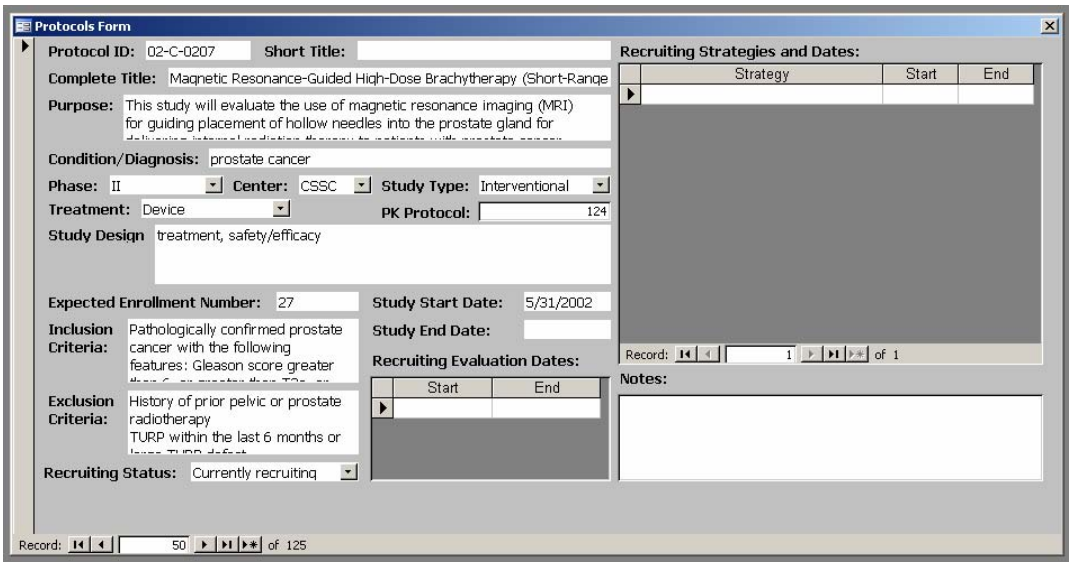
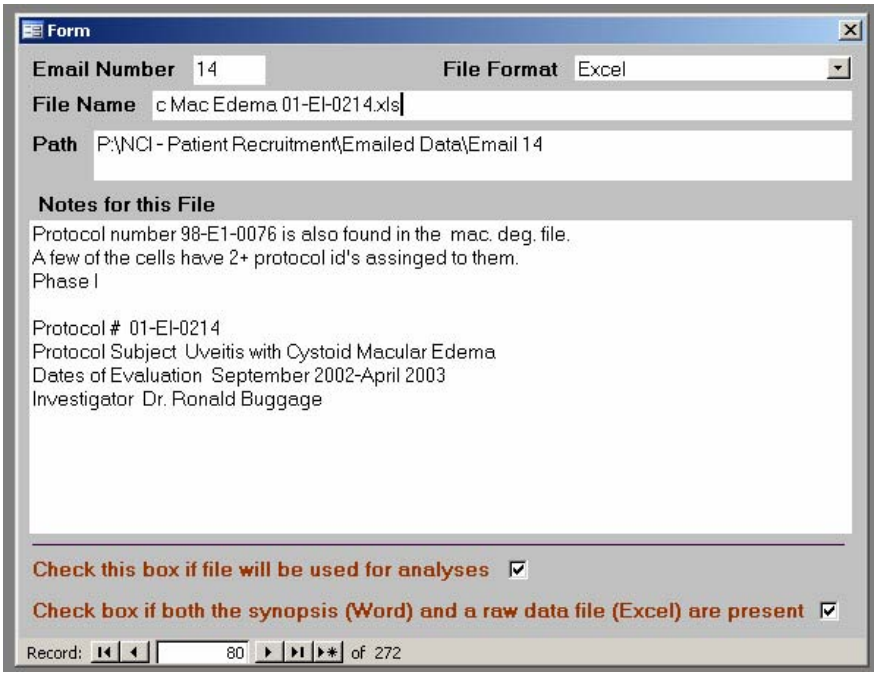


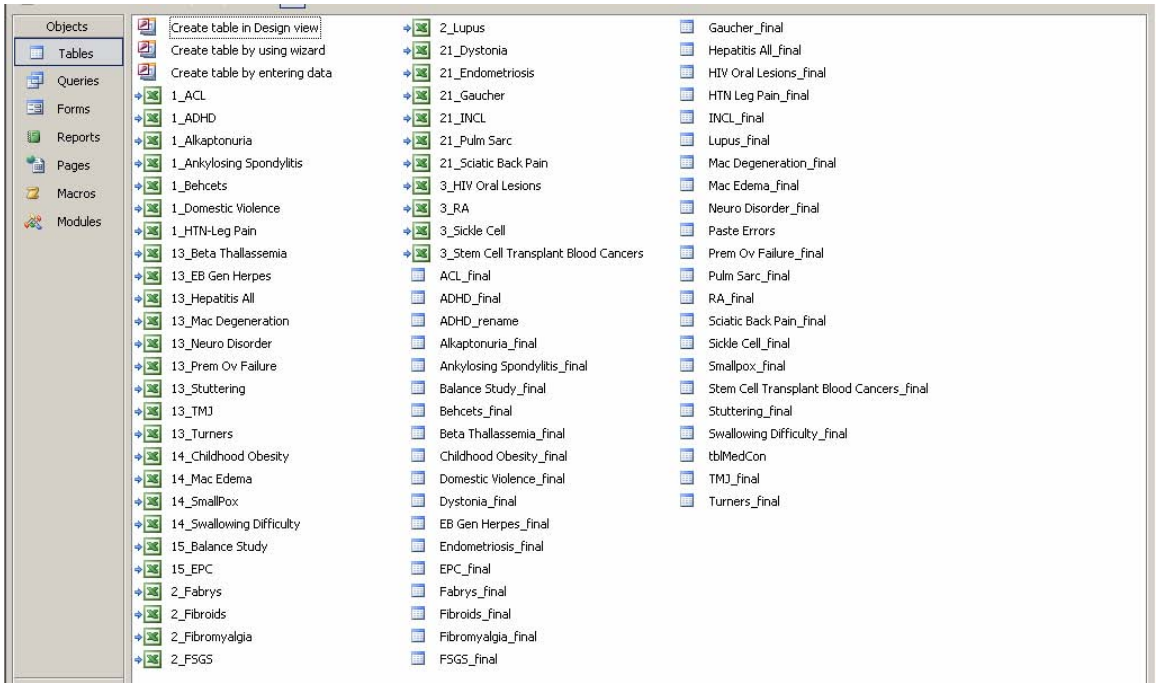
Exhibit 3-4. Screenshot of the Project Database



3.7.2 *Data Extraction from PRPL*

As explained above, a separate database was established for PRPL datasets. The PRPL datasets were organized by their medical condition type, such as Alkaptonuria, Dystonia, Endometriosis, etc. The 34 separate PRPL datasets selected for the study were converted into a uniform format in SPSS in preparation for analyses. A total of 1,833 records were available from the different medical conditions dataset for our analyses. A screenshot of the different datasets, according to their prescribed medical condition, is shown below (Exhibit 3–5).

Exhibit 3-5. Screenshot of the PRPL Database



3.7.3 *Data Extraction from ClinicalTrials.gov*

The following steps were utilized to extract protocol data from ClinicalTrials.gov:

1. The home page for ClinicalTrials.gov (http://www.clinicaltrials.gov./) was accessed.
2. The link to Focused Search was selected.
3. On the Focused Search page, the NIH protocol number was entered in the input box following "NCT or Study ID" and the search button selected.
4. This search strategy brought up the title of the protocol.
5. Clicking on the title of the protocol then yielded the full protocol summary.
6. The data items shown on the left side of Exhibit 3–3 (screenshot of page) were entered into the Protocol Information section of the Access Database created for the project.
   a. Drop-down menus were created for several items:
      i. Phase (I, II, III, not applicable, and other),
      ii. Center (PRPL or CSSC),
      iii. Study type (Interventional or Observational),
      iv. Treatment (one drug, multiple drugs, device, procedure, combination),
      v. Recruiting status (currently recruiting, no longer recruiting, completed).
   b. Short items were keyed in and long items (complete title, purpose, inclusion and exclusion criteria) were cut-and-pasted from the narrative on the protocol Web page.
7. For handy reference, a paper copy of each protocol also was made and the NIH protocol number affixed to the top of the first page (on the printout, the NIH protocol number is at the very end of the protocol summary).

3.8 Data Analysis

The analyses were carried out for CSSC and PRPL both together and separately to provide:

- Basic descriptive statistics using referrals as the outcome,
- Additional descriptive statistics stratified by
  – Patient age,

  - Patient sex,
  - Patient race/ethnicity,
  - Phase of trial,
  - Rare vs. common vs. both rare and common disease protocols,

- Overall analyses of protocols over time, and
- Best predictors of number of calls and/or patient accrual by protocol.

CSR used referral as the unit of analysis as opposed to patient because one patient could be referred to more than one protocol. Of the 1,831 patients referred to PRPL protocols, only 2 were referred to two protocols, making a total of 1,833 referrals. In contrast, of the 15,239 patients referred to CSSC protocols, 13 were referred to as many as 6 protocols, and more than 70 percent of patients were referred to more than one protocol, bringing the total number of referrals to 29,855.

We also looked at the type of recruitment strategies utilized for each protocol (e.g., PI presentations, PSAs, mailings, etc.) and the corresponding rates of referrals. For PRPL, as noted above, the recruitment strategies were examined qualitatively and then grouped into eight categories. The original CSSC recruitment strategies were recoded to match the categories used for PRPL as much as possible. The recodes are show in Exhibit 3–6.

The time periods covered by the data on type of recruitment strategies do not fully cover the time periods for which we have patient data. In addition, recruitment efforts by other entities (e.g., the protocol PI's own recruitment activities) were not documented in the PRPL or CSSC data. For these reasons, we were unable to draw definitive conclusions about the effects of specific strategies on referral numbers. We were able, however, to qualitatively examine the relationship between recruitment strategies and referrals. For PRPL data, we were also able to examine the relationship between strategies and initial contacts. For each protocol, we graphed the referrals (for PRPL and CSSC) and contacts (for PRPL only) by year and month and overlaid the recruitment strategies. This provided a visual display of possible relationships between strategy and outcome. We identified a sample of CSSC and PRPL protocols to describe in more detail as case studies. The graphs for all protocols are included in Appendixes F, G, and H. The case studies are presented in section 4.

Exhibit 3-6. CSSC Recruitment Strategies Recoding

CSSC Original Strategy	Recoded Strategy
Print Ad Placed	Advertisement
Advocacy Group Interactions	Community Relations
Matrix	Mailings/flyers
Fast Track Sent	Mailings/flyers
Doctor Fact Sheet	Mailings/flyers
Patient Fact Sheet	Mailings/flyers
Brochure	Mailings/flyers
Physician Letter	Mailings/flyers
Clinical Studies List FOCUS	Mailings/flyers
Clinical Research Update	Mailings/flyers
Web Links	Marketing/Web links
Web Site Developed	Marketing/Web links
Google (or other) promotion	Marketing/Web links
PI Presentations Arranged	Presentation
Newsletter Article	Press articles
News Release	Press articles
Print PSA	PSA

To complement the incomplete data on recruitment strategies, we examined the sources from which patients reported they found out about the PRPL and CSSC services. The 13 broad categories in the PRPL were previously recoded from more detailed accounts. The categories are book, community outreach, direct mail/letter, healthcare provider, Internet, magazine, newsletter, newspaper, physician, professional journal, radio, TV, and word of mouth. Patients who first contacted PRPL by e-mail but who did not report how they found out about the office were coded as having found out about PRPL through the Internet . As shown in Exhibit 3–7, for CSSC, similar categories were constructed from the original sources of referral. Whereas book and direct mailer/letter are unique to PRPL, CIS, NIH main office/PRPL, and support group are unique to CSSC. It should be noted that

Exhibit 3-7. CSSC Information Source Recodes

CSSC Original Source	Recoded Source
Organizations	Community Outreach
Cancer Information Service (CIS)	Cancer Information Service (CIS)
NIH Main Office – PRPL	NIH Main Office – PRPL
Cancer TX Centers of America	Health care provider
NIH PI – Research Nurse	Health care provider
Internet	Internet
Magazine	Magazine
Clinical Research Update	Magazine
Cancer Bulletin	Magazine
Newsletter	Newspaper
Newspaper	Newspaper
STAR	Newspaper
Repeat Caller	Other
Not Sure	Other
CME Event	Other
Promotional Materials	Other
Phone Book	Other
Did Not Ask – NA	Other
PI Presentation	Other
Other	Other
Patient Referral Form	Other
Pharmaceutical company	Other
NY media blitz	Other
Contact Referral Form	Other
Merck	Other
Office of the Director	Other
HCP – Physician	Physician
Science – Medical Journal	Professional Journal
Medical Journal	Professional Journal
Radio	Radio
Advocacy	Support Group
Support Group	Support Group
TV	TV
PBS	TV
Friend – Relative	Word of mouth
Pat Klevins	Word of mouth
Patient	Word of mouth

PRPL also heavily utilizes support groups and NIH offices. But in PRPL's categorization scheme, both are subsumed under community outreach.

3.8.1 *CSSC*

Data on referrals were available for the 67 CSSC protocols included in the study. Three primary tables and one lookup table were identified in the CSSC database for analysis purposes:

- NCI_tblParticipants—This table consisted of information on the participants in the studies.
- NCI_tblPersonalInfo—This table contained contact information, including name and address, for the patients as well as anyone who contacted CSSC on the patient's behalf (e.g., family member, physician). A filter was applied to select only patient records.
- NCI_tblProtocolInfo—This table contained information regarding the caller's relationship to the study protocol, including the protocol sent to, and the protocol enrolled in.
- NCI_tlkpProtocols—This was a lookup table with 462 records. It identified the protocol numbers with internal IDs that were used in the database.

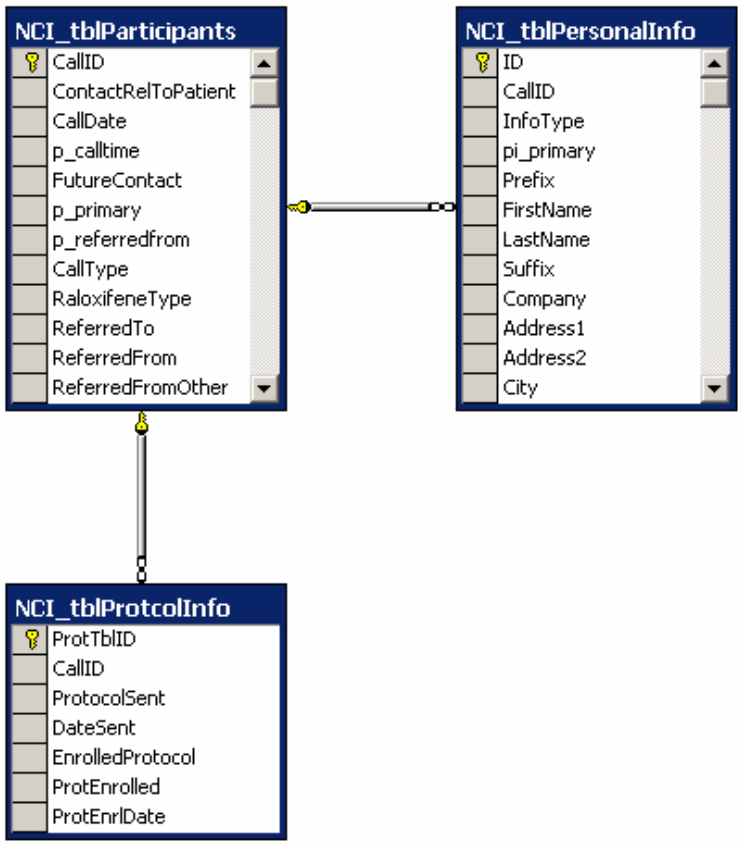
The relationships among the three primary tables are shown below in Exhibit 3–8.

From the three primary tables, after filtering for the 67 CSSC protocols and the study dates, there were 29,855 records available for analyses.

3.8.2 *PRPL*

The first step in analyzing the PRPL data was to finalize the available number of protocols. In data provided to CSR, patient and recruitment strategy data were not available for every protocol. CSR therefore identified an initial set of 39 protocols

Exhibit 3-8. Relationship Between Three CSSC Primary Tables



with both patient information and recruitment strategy data. Excluding two training protocols (85-N-0195 and 95-H-0047), two screening protocols (00-HG-0058 and 91-CH-0127), and one Phase III protocol (00-DK-0186), as recommended by the Advisory Group and the Project Officers, we identified 34 protocols that had at least one contact for analysis, including one protocol (00-D-0037) that had no referrals.

4. Findings

In this section, we present findings from the feasibility study, discussing findings related to each of the research questions separately.

4.1 Identification of Key Variables

As noted above under Methods, CSR conducted preliminary exploratory analysis of the PRPL and CSSC data to determine variables of interest in each dataset and key variables common to both datasets. Basic patient demographic characteristics were recorded in each dataset, although some key variables were missing (e.g., sex was not recorded in the CSSC data). Both datasets contained information about how the patient or patient representative first found out about the recruitment center. PRPL collected data on patient or patient representative contact to the recruitment center, referral to a protocol, and protocol admission. CSSC recorded patient referral and protocol admission. Exhibit 4–1 presents a crosswalk of major unique and common data elements for the PRPL and CSSC datasets, with their definitions.

4.2 Definition of Success in Recruiting

Early in the feasibility study, CSR sought to answer the fundamental question of how to define success in recruiting, as the decision had significant implications for the selection of outcome variables and the kinds of analyses we would conduct. Three

Exhibit 4-1. Crosswalk of PRPL and CSSC Analyses of Variables

PRPL Variable	Variable Definition	CSSC Variable
Age	Age in years	TrtAge
CallDate	Date and time of call	CallDate
CFirstName	First name of caller	FirstName
CLastName	Last name of caller	LastName
DOB	Date of birth	TrtDOB
FoundOutService	Source of information for caller (e.g., Internet, newsletter, etc.)	ReferredFrom
PatientId	Numeric ID for patient	CallD
PRace_code	Race	P_RaceID
Prrc_nih_protocol_id1	NIH protocol ID for protocol considered at first contact	
Prrc_nih_protocol_id2	NIH protocol ID for protocol referred to	ProtocolSent
Prrc_nih_protocol_id3	NIH protocol ID for protocol admitted to	EnrolledProtocol
PState	Patient's state abbreviation	State
QualifiedOrNo	Qualified or not for protocol	
Ref Date	Date of referral	
Ref Prot	NIH protocol ID of protocol referred to	ProtocolSent
Referred_date	Date of referral	DateSent
ScreeningDate	Date of screening	
Sex	Patient sex	Prefix
	Ethnicity of enrolled patient	P_EthnicityID
	Branch or office patient referred to	ReferredTo
	Caller relationship to patient	ContactRelToPatient/InfoType

data sources were used to decide on the definition—(1) discussions with the Project Advisory Group, (2) discussions with the CSSC and PRPL Project Managers, and (3) exploration of available data.

4.2.1 *Discussions with Project Advisory Group*

As described in the Methods section, at their first meeting, the Project Advisory Group was asked to provide expertise on how to define recruitment success and how to characterize the data for analysis. With regard to definitions of success, Advisory Group members felt strongly that the best measure of success was enrollment (admission) of participants in clinical studies. Many members believed one should still use a measure of getting the information out as a way to determine success. For example, the number of flyers sent out should still be measured.

A suggestion was made to select primary and secondary outcomes. For example, the number of participants enrolled would be primary and the number of calls and number of referrals would be secondary. It would not be appropriate to select the number of calls as a primary measure of success. Although a patient or patient representative may call the PRPL or CSSC office, study criteria beyond the control of either recruitment center may make the patient ineligible for referral to the study.

The Project Advisory Group members also were asked whether there was a consistent definition of "completed" and whether the completed group of protocols would be an informative category for analysis. Project Advisory Group members stated that "no longer recruiting" is not the same as "completed." They further explained that there is no single, consistent definition of "completed." "Completed" could mean that the study was closed because not enough people were enrolled. If a study principal investigator leaves NIH, the study may be terminated prematurely. Such a study would be labeled "completed" even though the work was not finished. Members further stated that the "expected total enrollment" numbers and "study end dates" were very unreliable and should not be used.

In assessing overall success of a program, the Advisory Group identified additional information as valuable:

- *Raw number of hits (for example, on a Google ad) as an indicator of the potential audience for a particular medium and a particular disease or condition.*
- *Number of totally irrelevant calls.*
- *Number of responses by "a friend" or "a family member."*
- *Number of patients actually coming to a screening visit.*
- *Whether patients were encouraged or discouraged from coming by their local physician.*
- *Patient coming to a visit but excluded.*
- *Patients enrolling but not completing the study.*

One Advisory Group member, a health educator, laid out an approach in which evaluation of a program is viewed as a continuum, assessing activities from planning to implementation to outcome. She felt that since a great deal of staff time goes into planning and implementation, evaluation of these stages is crucial in assessing the effective use of staff time and other resources. She then detailed her conceptualization of three levels of evaluation—Process, Impact, and Outcome.

According to this member, Process Evaluation can look at materials, services, and systems set up to notify the public about studies, such as brochures/ flyers (for readability, cultural relevance and sensitivity, and attractiveness) or presentations and presenters (Is the information relevant? Is it presented in an understandable and acceptable way to the audience?). In terms of services, are requests for information responded to in a timely manner? Is the staff easy to work with? In terms of systems, is it easy to order materials or schedule speakers? Success indicators could be the production and number of appropriate materials (brochures, PowerPoint presentation), number of requests for materials or presentations, number of materials distributed, or presentations made.

She further stated that Impact Evaluation can look at responses to promotion efforts, such as (1) number of calls to PRPL for study information and (2) number of physician referrals. (This can help investigators identify whether study factors are affecting recruitment; e.g., eligibility criteria may be affecting recruitment, not lack of interest in the study topic.) Success indicators could be numbers of calls for information and numbers of physician referrals.

The advisory group member concluded by stating that Outcome Evaluation can look at the number of patients recruited in the study and, to some extent, the number of patients retained in the study to its completion. Success indicators could be numbers of patients recruited and numbers retained.

4.2.2 *Discussions with CSSC and PRPL Project Managers*

CSR held several discussions with the CSSC and PRPL Project Managers to discuss the definition of success. The Project Managers explained that their offices have input into whether and how patients or patient representatives contact CSSC or PRPL, and whether patients are referred to a clinical trial protocol for consideration. CSSC and PRPL, however, do not have control over whether a patient is subsequently admitted into a protocol. Admission depends on whether the patient fits the specific study needs of the clinical trial. The decision to admit a participant to a study is made by the clinical trial PI and team, not by CSSC or PRPL. Although CSSC and PRPL record admissions data for patients they have referred, these data are not complete, as both recruiting offices must search external databases to capture the data. The Project Managers, therefore, recommended defining success as referral to a clinical trial protocol.

4.2.3 *Data Exploration*

CSR conducted exploratory analyses of the CSSC and PRPL data to assess the types of outcome variables available in the data set and to make a final decision on the definition of recruitment success for the study. As noted above, only the PRPL data contained data on number of contacts to this office. In addition, data on admissions were limited in both datasets, with 256 admissions in the PRPL data and 363 admissions in the CSSC data.

In light of the findings from discussions with the Project Advisory Group and the Project Officers, and the exploratory data analyses, CSR decided to treat referrals as the study outcome variable for recruitment success. CSR did examine the intermediate outcome of patient contacts for PRPL data when assessing potential associations between recruitment strategies and referrals from PRPL.

4.3 Categorization of Data

A variety of possible categories of patients, diseases, and protocols were suggested by the literature, the co-project officers, members of the Advisory Group, and CSR project staff.

4.3.1 *Consultation with Project Advisory Group*

During their first meeting, members of the Advisory Group discussed how to categorize the data and provided further insights in followup correspondence. They recommended comparing protocols studying common diseases compared with those studying rare diseases. Other suggestions for categories included:

1. *Public perception of a "life threatening condition" (for example, clinically significant congestive heart failure has a worse short-term overall survival outcome than many cancers, yet cancer is perceived as the life-threatening disease);*
2. *Other treatment options in the community versus no other options;*
3. *Newly diagnosed versus recurrent disease;*
4. *Possible scientific competition for the study*
   - *Within NIH or locally,*
   - *In general (e.g., perception that there are equally good alternative options in the community),*
   - *Number of FDA-approved Rx for same condition (if any),*
   - *Number of "standard of care" alternative Rx for the same condition;*

5. *Notoriety of the investigators:*
   - *Members of editorial boards for publications,*
   - *Cooperative group responsibilities,*
   - *Published review articles in their field,*
   - *Member of NIH Study section or other panel,*
   - *Number of peer reviewed publications;*
6. *Economic issues: "Standard of care" for disease treatment represents a major (or significant) source of income for potential referring physicians even if that "standard of care" is largely inadequate (e.g., a study of newly diagnosed metastatic breast cancer; even though the outcome with conventional treatment is almost invariably poor, these conventional treatments constitute a major source of patients for a practicing oncologist and they will not refer these patients for experimental treatment);*
7. *Existing pharmaceutical trial or other paid trial versus no such trial;*
8. *Existing treatments expensive or not covered by insurance versus treatments covered by insurance or not expensive;*
9. *Existing treatments have high risk of complications/adverse effects versus minimal risk/adverse affects;*
10. *Existing treatments difficult/require many visits;*
11. *Disease serious/life threatening versus not;*
12. *Treatment resistant versus treatment naïve/regular course of illness;*
13. *Treatment study versus evaluation study.*

4.3.2 Discussions with Project Officers

CSR discussed data categorization with the Project Officers during several telephone discussions and meetings. As stated in the study Statement of Work, the focus of the study was on early phase (i.e., Phases I and II) studies. Phase III and IV studies were excluded. In addition, after discussions with the Project Officers, it was decided to also omit screening and training studies. Because of the nature of these protocols, recruitment efforts are substantially different and are not easily comparable to efforts for early phase trials. The Project Officers also agreed with the Advisory Group members regarding comparing common-disease protocols with rare-disease protocols.

4.3.3 Data Exploration

Based on discussions with the Advisory Group and the Project Officers, CSR conducted preliminary analyses of the CSSC and PRPL data to determine how the data could be categorized. Although the primary types of studies included were Phase I and II trials, early exploration of the PRPL dataset revealed a number of natural history trials. Excluding these trials would reduce the available data substantially. The Project Officers, therefore, agreed to expand the scope of the study to include natural history studies, as well as Phase I and II trials.

Data also were available from the protocol descriptions to categorize protocols by whether they targeted rare or common diseases. CSR utilized the NIH Office of Rare Diseases definition of a rare disease (one having a prevalence of fewer than 200,000 affected individuals in the United States) for the study. Using the Rare Disease Terms section of the NIH Office of Rare Diseases Web site (http://rarediseases.info.nih.gov/asp/diseases/diseases.asp), each condition being studied in any of the protocols was searched on the list of more than 6,000 rare diseases and related conditions. Those listed were categorized as rare. The remaining conditions were categorized as common. Many protocols in this study cover more than one disease. Protocols in which all diseases fulfilled the definition for rare were designated as rare. Protocols having all common diseases were defined as common. Protocols studying both rare and common diseases were defined as "rare and common." Most of the protocols thus designated were those studying hematologic malignancies. Most lymphomas are designated as rare by the Office of Rare Diseases. Some leukemias are rare while others are common. Thus, a protocol studying lymphomas and leukemias will be designated "rare and common."

Although CSSC had a high proportion of missing cases for some demographic variables, enough data were available to conduct analyses by patient sex, racial and ethnic background, and age group. Based

on the discussions with the Advisory Group and the Project Officers, CSR identified the following categories as available for analysis.

1. Protocol categories:
   a. Type of trial (Phase I, Phase I and/or II, Phase II, natural history)
   b. Type of disease (rare, common, common and rare)
2. Categories of patients:
   a. Sex (i.e., male or female)
   b. Race/Ethnicity (i.e., Black, White, Hispanic, Asian, American Indian, or other
   c. Age (i.e., 0–9 years, 10–17, 18–29, 30–39, 40–49, 50–59, 60–69, 70–79, or 80+)

Exhibit 4–2 shows the number of CSSC and PRPL protocols by protocol characteristic. Distributions across patient characteristics are shown in Exhibit 4–5, discussed below.

Exhibit 4-2. Number of Protocols by Protocol Characteristic

Protocol Characteristic	Total	CSSC	PRPL
Total	101	67	34
Protocol Phase			
Phase I	29	26	3
Phase II	54	40	14
Phase I and/or II	1	1	0
Natural History	17	0	17
Type of Disease			
Rare and common	8	7	1
Rare	34	19	15
Common	59	41	18

4.4 Recruitment Strategies by Selected Categories

The ultimate goal of the study was to determine the feasibility of evaluating which types of recruitment strategies conducted by CSSC and PRPL had the most impact on recruitment. CSR, therefore, conducted analyses to answer this research question using data from CSSC and PRPL.

4.4.1 *Referrals by Category*

CSR first conducted descriptive analyses to examine the number of referrals to each protocol and the distribution of referrals by protocol, disease, and patient categories. Exhibits 4–3 and 4–4 list the individual protocols from PRPL and CSSC, respectively, included in the feasibility study, as well as their total number of referrals.

Exhibit 4-3. PRPL: Referrals by Protocol

Protocol		Number	Percent
Total		**1,833**	**(100)**
00-CH-0134	Childhood Obesity	191	(10.4)
00-CH-0141*	Alkaptonuria	17	(0.9)
00-CH-0219	Turner Syndrome	28	(1.5)
00-D-0037	Temperomandibular Joint Disorder (TMJ)	0	(0.0)
00-D-0066	Fibromyalgia	125	(6.8)
00-DK-0042	Focal Segmental Glomerulosclerosis (FSGS)	3	(0.2)
00-DK-0166	Beta Thalassemia	8	(0.4)
01-CC-0135	Swallowing Difficulty	20	(1.1)
01-CH-0086	Infantile Neuronal Ceroid Lipofuscinosis (INCL)	6	(0.3)
01-D-0076	Sciatic Back Pain	156	(8.5)
01-EI-0214	Macular Edema	6	(0.3)
01-H-0119	Epithelial Progenitor Cells (EPC)	64	(3.5)
01-H-0162	Stem Cell Transplant	39	(2.1)
01-N-0147	Dystonia	16	(0.9)
02-AR-0267	Lupus	7	(0.4)
02-AR-0272	Lupus	1	(0.1)
02-CH-0287	Fibroids	47	(2.6)
02-I-0316	Smallpox	143	(7.8)
03-AR-0130	Ankylosing Spondylitis	6	(0.3)
03-AR-0131	Ankylosing Spondylitis	12	(0.7)
03-AR-0133	Rheumatoid Arthritis (RA)	9	(0.5)
03-DK-0170	Sickle Cell Anemia	4	(0.2)
90-CC-0168	Anterior Cruciate Ligament (ACL)	17	(0.9)
90-CC-0168B	Stroke Balance Study	30	(1.6)
91-DK-0214	Hepatitis-All	60	(3.3)
91-N-0225	Gaucher	4	(0.2)
93-CH-0054	Turner Syndrome	2	(0.1)
93-N-0202	Dystonia	39	(2.1)
94-DK-0127	Focal Segmental Glomerulosclerosis (FSGS)	31	(1.7)
94-DK-0133	Focal Segmental Glomerulosclerosis (FSGS)	1	(0.1)
95-N-0121	Fabry's	18	(1.0)
96-N-0088	Stuttering	13	(0.7)
99-CH-0012	Endometriosis	533	(29.1)
99-H-0057	Pulmonary Sarcoidosis	177	(9.7)

* After 2003, this protocol number was changed to 00-HG-0141 when the Principal Investigator moved to the National Human Genome Research Institute (NHGRI).

Exhibit 4-4. CSSC: Referrals by Protocol

Protocol		Number	Percent
00-C-0044	Breast cancer, lung cancer, ovarian cancer	585	(2.0)
00-C-0069	Peritoneal cancer confined to the abdomen	319	(1.1)
00-C-0088	Primary lung cancer or cancers spread to the lung	803	(2.7)
00-C-0119	Breast cancer–metastatic	342	(1.1)

Protocol		Number	Percent
00-C-0121	Advanced solid tumor cancers	4,238	(14.2)
00-C-0128	Recurrent or metastatic squamous cell carcinoma of the head and neck	261	(0.9)
00-C-0133	Mantle cell lymphoma	31	(0.1)
00-C-0137	Prostate cancer–advanced	162	(0.5)
00-C-0149	Breast cancer	48	(0.2)
00-C-0154	Prostate cancer–confined to prostate	169	(0.6)
00-C-0173	Malignant gliomas and benign and malignant meningiomas	6	(0.0)
00-C-0206	Breast cancer–Stage IV	176	(0.6)
00-C-0218	Pancreatic cancer–advanced	100	(0.3)
00-C-0224	Cancer	1,116	(3.7)
01-C-0011	Malignant mesothelioma, ovarian cancer, pancreatic cancer, squamous cell ca head and neck and cervix	662	(2.2)
01-C-0021	B cell lymphoma	98	(0.3)
01-C-0049	Cutaneous T cell lymphoma	69	(0.2)
01-C-0067	HIV-associated Kaposi's sarcoma	21	(0.1)
01-C-0082	Solid tumors unresposive to standard therapy	548	(1.8)
01-C-0104	Squamous cell carcinoma head and neck	147	(0.5)
01-C-0173	Breast cancer–inflammatory or locally advanced	28	(0.1)
01-C-0213	Lymphomas	108	(0.4)
01-C-0256	Solid malignancies unresectable or metastatic	1,869	(6.3)
02-C-0006	HIV–pediatric	2	(0.0)
02-C-0083	Adult solid tumors or lymphomas	789	(2.6)
02-C-0149	Prostate cancer	172	(0.6)
02-C-0190	Ovarian, pelvic, or peritoneal cancer	149	(0.5)
02-C-0207	Prostate cancer	46	(0.2)
02-C-0215	Prostate cancer	34	(0.1)
02-C-0218	Prostate cancer	109	(0.4)
02-C-0229	Breast cancer, male breast cancer	200	(0.7)
03-C-0005	Breast cancer–stage II or III	4	(0.0)
03-C-0077	Lymphoma, leukemia	116	(0.4)
93-C-0133	Non-Hodgkin's lymphoma	104	(0.3)
94-C-0074	Lymphomatoid granulomatosis	11	(0.0)
94-C-0096	Adult solid tumors	257	(0.9)
95-C-0054	T cell large granular lymphocytic leukemia	69	(0.2)
95-C-0119	Osteosarcoma	8	(0.0)
95-C-0154	Cervial cancer and other cancers carrying HPV	418	(1.4)
96-C-0004	Breast cancer	7	(0.0)
96-C-0011	HIV-associated Kaposi's sarcoma	357	(1.2)
96-C-0064	Ovarian cancer	565	(1.9)
97-C-0024	Lymphomas and rare leukemias	10	(0.0)
97-C-0040	AIDS-related lymphoma	15	(0.1)
97-C-0068	Recurrent colorectal cancer	11	(0.0)
97-C-0141	Adult solid tumors	1,167	(3.9)

Protocol		Number	Percent
97-C-0178	Chronic lymphocytic leukemia	64	(0.2)
98-C-0040	Metastatic melanoma, renal cell carcinoma	686	(2.3)
98-C-0074	Childhood brain tumors	13	(0.0)
98-C-0078	Breast, colon, lung, ovarian, stomach cancer	1,596	(5.3)
98-C-0118	Leukoplakia	7	(0.0)
98-C-0123	Breast cancer	46	(0.2)
98-C-0139	Renal cell carcinoma	836	(2.8)
99-C-0014	CD22+ lymphomas and leukemias	271	(0.9)
99-C-0025	Liver malignancies	1,265	(4.2)
99-C-0071	Breast, lung, pancreatic, stomach cancer	1,052	(3.5)
99-C-0093	Colorectal cancer of the liver	150	(0.5)
99-C-0102	Colon or rectal cancer–Stage IV	1,240	(4.2)
99-C-0117	Cancer of the colon, rectum, small bowel, or appendix	1,585	(5.3)
99-C-0121	Metastatic breast or ovarian cancer	610	(2.0)
99-C-0123	Liver cancer	623	(2.1)
99-C-0125	Osteosarcoma	7	(0.0)
99-C-0127	Leukemias and lymphomas	102	(0.3)
99-C-0129	Cancer of the esophagus or lung or pleural mesothelioma	1,403	(4.7)
99-C-0137	Adenocarcinoma of the ovary	421	(1.4)
99-C-0138	Adenocarcinoma of the breast or ovary	627	(2.1)
99-C-0143	Lymphomas, leukemias, multiple myeloma	725	(2.4)
Total		**29,855**	**(100)**

Exhibit 4–5 shows the distribution of referrals by protocol and patient characteristics for CSSC and PRPL protocols, and for all protocols together, using the categories presented above. CSSC and PRPL referred a total of 31,688 patients to one or more protocols during the years 1998–2003, including 29,855 patients referred through CSSC and 1,833 through PRPL.

As shown in Exhibit 4–5, close to two-thirds of CSSC referrals (62.3 percent) were to Phase I trials, whereas almost the same proportion (64.7 percent) of PRPL referrals were to Phase II trials. The majority of both CSSC (66.1 percent) and PRPL (79.7 percent) referrals were to protocols addressing common diseases. About a quarter (25.5 percent) of CSSC referrals were to protocols addressing both common and rare diseases, and almost one-fifth (18.2 percent) of cases in the PRPL dataset were referred to protocols targeting rare diseases. Although patient sex was not available for a third (34.3 percent) of CSSC cases, proxy variables showed that about a third of cases were female and another third were male. Among cases referred through the PRPL office, two-thirds were female and about a quarter were male (for the remainder of the cases, information on sex was missing). Over half (59.3 percent) of PRPL cases were non-Hispanic Whites. In addition, one-fifth of patients referred from PRPL were non-Hispanic Blacks. The large proportion (68.7 percent) of missing data on race and ethnicity in the CSSC dataset made it difficult to interpret the results. Available data suggested that non-Hispanic whites were the largest group of patients referred through CSSC data as well. Most patients referred through either CSSC or PRPL ranged from 18 to 59 years of age. Over 10 percent of referrals out of PRPL were pediatric cases. Exhibit 4–5 shows that the key states from which clinical trial cases were drawn between 1998 and 2003 were the nearby states of Maryland and Virginia. A large number of cases originating in New York State also were referred through CSSC.

Data were available from both CSSC and PRPL on how patients reported first learning about the

Exhibit 4-5. Referrals by Protocol and Patient Characteristics

Protocol and Patient Characteristics	CSSC		PRPL		Total	
	Number	Percent	Number	Percent	Number	Percent
Total	**29,855**	**(100)**	**1,833**	**(100)**	**31,688**	**(100)**
Protocol Phase						
Phase I	18,593	(62.3)	150	(8.18)	18,743	(59.0)
Phase I and/or II	6	(0.0)			6	(0)
Phase II	11,256	(37.7)	1,186	(64.70)	12,442	(39.0)
Natural history			497	(27.11)	497	(2.0)
Type of Disease						
Rare and Common	7,619	(25.5)	39	(2.13)	7,658	(24.0)
Common	19,720	(66.1)	1,461	(79.71)	21,181	(67.0)
Rare	2,516	(8.4)	333	(18.17)	2,849	(9.0)
Year of First Referral						
1998	420	(1.4)	8	(0.44)	428	(1.0)
1999	3,054	(10.2)	106	(5.78)	3,160	(10.0)
2000	6,424	(21.5)	157	(8.57)	6,581	(21.0)
2001	7,239	(24.2)	332	(18.11)	7,571	(24.0)
2002	7,643	(25.6)	551	(30.06)	8,194	(26.0)
2003	5,069	(17.0)	679	(37.04)	5,748	(18.0)
Missing	6	(0.0)	0	(0)	6	(0)
Patient Sex*						
Female	9,689	(32.5)	1223	(66.72)	10,912	(34.0)
Male	9,929	(33.3)	513	(27.99)	10,442	(33.0)
Missing	10,237	(34.3)	97	(5.29)	10,334	(33.0)
Patient Race/Ethnicity						
Black	578	(1.9)	401	(21.88)	979	(3.0)
White	8,208	(27.5)	1,086	(59.25)	9,294	(29.0)
Hispanic	98	(0.3)	78	(4.26)	176	(1.0)
Asian	336	(1.1)	42	(2.29)	378	(1.0)
American Indian	24	(0.1)	11	(0.60)	35	(0)
Other	99	(0.3)			99	(0)
Missing	20,512	(68.7)	215	(11.73)	20,727	(65.0)
Patient Age						
0–9	15	(0.1)	134	(7.31)	149	(0)
10–17	1	(0.0)	99	(5.40)	100	(0)
18–29	656	(2.2)	416	(22.70)	1,072	(3.0)
30–39	1,830	(6.1)	418	(22.80)	2,248	(7.0)
40–49	4,708	(15.8)	361	(19.69)	5,069	(16.0)
50–59	7,525	(25.2)	196	(10.69)	7,721	(24.0)
60–69	6,157	(20.6)	114	(6.22)	6,271	(20.0)
70–79	3,007	(10.1)	31	(1.69)	3,038	(10.0)
80+	473	(1.6)	3	(0.16)	476	(2.0)
Missing	5,483	(18.4)	61	(3.33)	5,544	(18.0)
Patient State of Residence*						
AK	22	(0.07)	1	(0.05)	23	(0.07)
AL	142	(0.48)	5	(0.27)	147	(0.46)

Protocol and Patient Characteristics	CSSC		PRPL		Total	
	Number	Percent	Number	Percent	Number	Percent
AR	71	(0.24)	2	(0.11)	73	(0.23)
AZ	228	(0.76)	12	(0.65)	240	(0.76)
CA	930	(3.12)	31	(1.69)	961	(3.03)
CO	228	(0.76)	11	(0.60)	239	(0.75)
CT	133	(0.45)	6	(0.33)	139	(0.44)
DC	159	(0.53)	169	(9.22)	328	(1.04)
DE	46	(0.15)	5	(0.27)	51	(0.16)
FL	887	(2.97)	44	(2.40)	931	(2.94)
GA	360	(1.21)	22	(1.20)	382	(1.21)
HI	49	(0.16)	1	(0.05)	50	(0.16)
IA	97	(0.32)	5	(0.27)	102	(0.32)
ID	53	(0.18)	3	(0.16)	56	(0.18)
IL	365	(1.22)	20	(1.09)	385	(1.21)
IN	126	(0.42)	14	(0.76)	140	(0.44)
KS	91	(0.30)	5	(0.27)	96	(0.30)
KY	124	(0.42)	7	(0.38)	131	(0.41)
LA	112	(0.38)	7	(0.38)	119	(0.38)
MA	160	(0.54)	4	(0.22)	164	(0.52)
MD	1,158	(3.88)	692	(37.75)	1,850	(5.84)
ME	59	(0.20)	2	(0.11)	61	(0.19)
MI	290	(0.97)	11	(0.60)	301	(0.95)
MN	176	(0.59)	7	(0.38)	183	(0.58)
MO	180	(0.60)	17	(0.93)	197	(0.62)
MS	70	(0.23)	4	(0.22)	74	(0.23)
MT	50	(0.17)	4	(0.22)	54	(0.17)
NC	323	(1.08)	26	(1.42)	349	(1.10)
ND	38	(0.13)	1	(0.05)	39	(0.12)
NE	44	(0.15)	2	(0.11)	46	(0.15)
NH	16	(0.05)	7	(0.38)	23	(0.07)
NJ	318	(1.07)	33	(1.80)	351	(1.11)
NM	90	(0.30)	5	(0.27)	95	(0.30)
NV	86	(0.29)	5	(0.27)	91	(0.29)
NY	1,024	(3.43)	46	(2.51)	1,070	(3.38)
OH	322	(1.08)	30	(1.64)	352	(1.11)
OK	158	(0.53)	9	(0.49)	167	(0.53)
OR	155	(0.52)	11	(0.60)	166	(0.52)
PA	438	(1.47)	51	(2.78)	489	(1.54)
PR	11	(0.04)	1	(0.05)	12	(0.04)
RI	38	(0.13)	3	(0.16)	41	(0.13)
SC	175	(0.59)	18	(0.98)	193	(0.61)
SD	36	(0.12)	2	(0.11)	38	(0.12)
TN	217	(0.73)	11	(0.60)	228	(0.72)
TX	409	(1.37)	22	(1.20)	431	(1.36)
UT	55	(0.18)	4	(0.22)	59	(0.19)
VA	867	(2.90)	308	(16.80)	1,175	(3.71)
VT	11	(0.04)	1	(0.05)	12	(0.04)

Protocol and Patient Characteristics	CSSC		PRPL		Total	
	Number	Percent	Number	Percent	Number	Percent
WA	207	(0.69)	17	(0.93)	224	(0.71)
WI	195	(0.65)	13	(0.71)	208	(0.66)
WV	158	(0.53)	18	(0.98)	176	(0.56)
WY	14	(0.05)	2	(0.11)	16	(0.05)
(Missing)	18,084	(60.57)	76	(4.15)	18,160	(57.31)
Patient Source of Information						
Cancer Information Services	8,167	(27.4)			8,167	(26.0)
NIH main office–PRPL	3,426	(11.5)			3,426	(11.0)
Internet	5,099	(17.1)	611	(33.33)	5,710	(18.0)
Physician	3,538	(11.9)	67	(3.66)	3,605	(11.0)
Other healthcare provider	1,438	(4.8)	12	(0.65)	1,450	(5.0)
Word of mouth	1,775	(5.9)	357	(19.48)	2,132	(7.0)
Community outreach	1,134	(3.8)	100	(5.46)	1,234	(4.0)
Direct mail/letter			15	(0.82)	15	(0)
Professional journal	36	(0.1)	2	(0.11)	38	(0)
Book			15	(0.82)	15	(0)
Magazine	163	(0.5)	55	(3.00)	218	(1.0)
Newspaper	365	(1.2)	423	(23.08)	788	(2.0)
Newsletter	10	(0.0)	70	(3.82)	80	(0)
Radio	8	(0.0)	58	(3.16)	66	(0)
TV	336	(1.1)	39	(2.13)	375	(1.0)
Other	4,307	(14.4)			4,307	(14.0)
Missing	53	(0.2)	9	(0.49)	62	(0)

*Because patient sex was not available in the CSSC dataset, the prefix (Mr., Mrs., Ms.) was used to identify sex.

**Missing cases for patient state include cases from Canada.

recruitment offices and clinical trial recruitment options. The Internet appears to have been an important source of information about clinical trial recruitment options for patients referred through CSSC (17.1 percent) or PRPL (33.3 percent). It is possible that the PRPL figure might be slightly inflated because, as noted earlier, patients who contacted PRPL via e-mail and who did not report how they learned about PRPL were automatically coded to Internet. Other important sources of information for CSSC patients were the Cancer Information Service (CIS), PRPL (i.e., patients who contacted PRPL first and were then referred to CSSC), and physicians or other health care providers. Notices in newspapers and word of mouth contact with knowledgeable friends, acquaintances, or family members were important sources of information about clinical trial recruitment for patients referred through PRPL.

The original Statement of Work for the feasibility study called for merging the CSSC and PRPL datasets to conduct aggregated analyses. After discussions with the Project Officers about the benefits and problems with this approach, CSR conducted both separate and merged analyses. As expected, because of the disproportionately large number of CSSC cases as compared to PRPL cases, the results for the merged dataset mirrored those from the CSSC data. In order to retain the uniqueness of the two datasets, CSR decided to continue with separate analyses for CSSC and PRPL data in looking at the effects of various types of recruitment efforts.

4.4.2 *Recruitment Strategies and Sources of Information—CSSC Data*

CSR examined the number of referrals made to each CSSC protocol according to the patient's reported source of information about CSSC (Appendix I).

CSR also examined the number and types of recruitment strategies used by CSSC for each protocol (Appendix J). It must be kept in mind that these strategies represent the minimum number and type of strategies conducted, as others may have been implemented before or after the time period captured by the CSSC strategy data. CSSC used from none to six different types of strategies for the protocols; and, because some strategies were used multiple times for one protocol, the total number of strategies ranged from none to nine.

Exhibit 4–6 presents the number of referrals accrued to protocols by protocol and patient characteristics and patient self-reported source of information about CSSC. Patients reported similar sources of information, whether they were referred to Phase I or Phase II trials. The small number of referrals to the one Phase I and/or II trial precludes drawing conclusions about source of information for these types of studies. Referral distributions across source of information were similar for protocols studying both rare and common diseases and those examining only common diseases. The most cited sources of information on clinical trial recruitment were CIS (24.2 and 29.8 percent for rare/common and common-only protocols, respectively), the Internet (18.8 and 16.2 percent), physicians (12.2 and 11.5 percent), and PRPL (11.3 and 11.2 percent). For patients referred to rare disease protocols, the Internet appeared to be the most important source of information (18.9 percent of referrals), closely followed by CIS (17.8 percent), PRPL (14.1 percent), and physicians (13 percent).

There were no differences between male and female patients in the reported source of information. CIS was the primary source of information for close to a third of both female (30.7 percent) and male (31.7 percent) patients. There were more evident differences across racial and ethnic groups. Among non-Hispanic Blacks, almost one-fifth (18.7 percent) reported having learned about CSSC from CIS. Other important sources of information for Blacks were non-physician healthcare providers (16.6 percent), newsletters (15.7 percent), the Internet (15.1 percent), and word of mouth (15.9 percent). Primary information sources for Hispanics were non-physician healthcare providers (19.4 percent) and word of mouth (18.4 percent), although CIS, PRPL, the Internet, physicians, and newsletters also were noted. Whites reported having obtained information primarily from CIS (22.6 percent), through word of mouth (21.8 percent), or from newsletters (14.2 percent) or the Internet (11.4 percent). Exhibit 4–6 shows that CIS remained the primary source of information across age groups, and increased in importance with increasing age. The proportion of patients reporting word of mouth as the source of information increased with younger age groups.

Exhibit 4–7 shows the distribution of protocols by type of recruitment strategy employed. Because CSSC used multiple types of strategies to recruit patients to each protocol, the recruitment strategies are not mutually exclusive. That is, the numbers of protocols in each strategy category may add up to more than the total number of protocols. CSSC distributed mailings and/or flyers about the clinical trial to healthcare providers or other outlets for 34 percent of Phase I trials. Press articles were used for 9 percent of Phase I protocols. Mailings and/or flyers were distributed for over half (51 percent) of the Phase II trials; and press articles (16 percent) and community relations (13 percent) also were important Phase II strategies. Mailings and/or flyers also were primary recruitment strategies for common-disease (54 percent) and rare-disease (25 percent) protocols. CSSC used press articles for 10 (15 percent) of the common-disease protocols, public service announcements for 7 (10 percent) and community relations also for 7 (10 percent) of these trials. For rare-disease protocols, press articles were used for 6 (9 percent) trials and community relations for 5 (7.5 percent).

4.4.3 *CSSC Case Studies*

For each CSSC protocol, CSR plotted recruitment strategies by individual referrals to determine potential associations between strategies and number of referrals. A complete set of figures showing monthly number of referrals and types of recruitment strategies by data can be found in Appendix F. Included here are the descriptions of a few “case studies” of protocols.

4.4.3.1 *Case Study 1: Protocol 02-C-0083 Adult Solid Tumors or Lymphomas*

Protocol 02-C-0083 is a Phase I study of multiple doses of a drug, which is a derivative of Thalidimide on patients with refractory metastatic cancer. Desired participants for this study were individuals with adult solid tumors or lymphomas which had not responded to previous therapy. This study began in 2002. As shown on the figure on page F-26 in Appendix F, in May of 2002, over 30 potential participants were referred to this protocol. In subsequent months, referrals increased, peaking at nearly 70 referrals in October. After that, monthly referrals dropped dramatically. In May of 2003, the recruitment strategy of mailings/flyers was implemented. The following month, the number of referrals increased to nearly 70 compared with 30 the previous month. Over the next several months, referrals continued to increase, reaching nearly 100 in September 2003. Since many mailings are directed toward physicians rather than patients themselves, it is difficult to know how much lag time is required before one would expect to see an effect on referrals directly related to the recruitment strategy. Nevertheless, it does appear that there is a temporal association between the implementation of the recruitment strategy and an increase in the number of patient referrals in subsequent months, possibly suggesting that, in this setting, mailings may be an effective strategy.

4.4.3.2 *Case Study 2: Protocol 96-C-0011 Ovarian Cancer*

Protocol 96-C-0011 is a Phase I study in which patients with recurrent, evaluable ovarian cancer will receive intravenous therapy with autologous peripheral blood lymphocytes that have been genetically modified to recognize an ovarian cancer associated antigen. The figure for this protocol can be found on page F-42. This study began in 1996. As mentioned earlier in this report, CSSC was not created until 1998 and thus did not begin recruiting research participants until then. Although numbers of referrals were relatively small (rarely more than 15 per month), CSSC referred generally increasing numbers beginning in August of 1998. The numbers of referrals were quite brisk from April through December of 2000. After that the numbers of referrals varied. CSSC made no referrals to this protocol from December 2001, through April 2002. A few referrals were made in May and June 2002. Following the utilization of press articles as a recruitment strategy in June 2002, referrals picked up in July followed by marked increases in September 2002. Again, it is purely speculation, but there does appear to be a temporal association between utilization of the press articles recruitment strategy and a temporary increase in patient referrals to this protocol.

4.4.3.3 *Case Study 3: Protocol 99-C-0123 Liver Cancer*

Protocol 99-C-0123 is a Phase II study testing whether the administration of a drug called melphalan directly into the liver (isolated hepatic perfusion) can shrink tumors in patients with inoperable cancer whose tumor is confined to the liver. The figure showing monthly referrals and recruitment strategies over time can be found on page F-62. CSSC began making referrals to this protocol in September 1999. Over the years referrals varied from month to month, with two peaks in numbers of referrals being noted—a prominent one on June, 2000 and a smaller one in February of 2001. After February 2001, the number of referrals dwindled. In September 2001, a recruitment effort of mailings/flyers was implemented with minimal impact noted. Additional mailings were conducted in October and November. Minimal change in the number of referrals was noted over the next several months, followed by a gradual upswing in referrals in March, April, and May and a subsequent decline. In August another mailing strategy was implemented. The following month a dramatic increase in referrals was observed. In this case study, the associations between the recruiting strategies and the number of referrals are less clear. Some of the mailings/flyers seem to be associated with little change in numbers of referrals, while others seem to be associated with increases in referrals. Perhaps differences in the recipients of the mailings might account for the differences in impact on referrals. It should be noted that a fifth mailing effort was performed for this protocol but the dates for this strategy were not recorded. Therefore, the

possible impact of this strategy cannot be ascertained.

4.4.3.4 *Case Study 4: Protocol 99-C-0071 Breast, Lung, Pancreatic, Stomach Cancer*

Protocol 99-C-0071 is a Phase II clinical trial of suppression of human antimouse antibody and human antitoxin response to immunotoxin LMB-1 by the investigational drug, Rituximab. Potential participants include patients with breast, lung, colon, pancreatic, stomach and other advanced carcinomas that express the B3 antigen. The figure showing monthly referrals and recruitment strategies can be found on page F-57. CSSC began making referrals to this protocol in May 1999. From May through August, CSSC implemented several recruitment strategies—first two mailings, followed by press articles, public service announcements, presentations and community relations. CSSC referrals for this protocol were highest in June and July of 1999—during the same timeframe as the recruitment strategies, and subsequently oscillated. For this protocol, there does seem to be an association between the multiple recruitment strategies and the number of referrals. It would be informative if it were possible to tease out the impact of the individual strategies from the impact of the combination of the multiple strategies.

4.4.3.5 *Case Study 5: Protocols 02-C-0207, 0215, 0218 Prostate Cancer*

Since CSSC gradually transitioned from protocol-specific recruiting to broader program-specific recruiting, included here is a "case study" examining the CSSC recruiting strategies and referrals to three Phase II prostate cancer protocols. Protocol 02-C-0207 is a study evaluating the use of magnetic resonance imaging (MRI) for guiding placement of hollow needles into the prostate gland for delivering internal radiation therapy to patients with prostate cancer. Prostate cancer is often treated with a combination of external beam radiation therapy and brachytherapy (internal radiation delivered close to the tumor). This study will determine whether MRI is more accurate in guiding needle placement than ultrasound, which is currently used for this purpose. Protocol 02-C-0215 is a study evaluating the safety and effectiveness of a drug called amifostine in reducing the bowel side effects of radiation treatment for prostate cancer. Protocol 02-C-0218 is a study comparing the effectiveness of an experimental vaccine alone or vaccine with the anti-cancer drug docetaxel in treating prostate cancer. All three protocols began in 2002. CSSC sent out mailings/flyers in May of 2003. Marketing and weblinks were also used as a recruiting strategy but the implementation date for this strategy is not recorded. As can be seen on page F-29 for protocol 02-C-0207, the peak number of referrals (9 referrals) from CSSC occurred in October of 2002, the first month that CSSC referred patients to the protocol. Referrals gradually decreased in subsequent months. In May, CSSC sent out mailings/flyers followed by a noticeable increase in referrals for July and August. As shown in the figure on page F-30, a similar picture is seen for protocol 02-C-0215. Peak CSSC referrals occurred during the first month of CSSC involvement and decreased thereafter. Following the mailing in May of 2003, a moderate increase in referrals was seen during July and August. The picture for protocol 02-C-0218, as seen on page F-31, is somewhat different. Again the highest spike in CSSC referrals occurs early in the trial; however the pattern of CSSC referrals in the 6 months prior to implementation of the mailings is very similar to that for the 6 months following the strategy. In other words, the mailings did not appear to have had the impact on referrals seen for the other two prostate cancer protocols. A significant increase in referrals was seen in December of 2003, which does not appear to be related to CSSC recruiting strategies. It is possible that the increase could be related to the implementation of the marketing and weblink strategies, but, since we do not know the date of those strategies, it is impossible to determine whether any such association exists.

Exhibit 4-6. CSSC: Referrals by Patient Self-Reported Source of Information and Type of Protocol

		Total	Cancer Information Services	NIH main office–PRPL	Internet	Physician	Healthcare provider	Word of mouth	Community outreach	Professional journal	Magazine	Newspaper	Newsletter	Radio	TV	Other	Missing
Phase		29,855	8,167	3,426	5,099	3,538	1,438	1,775	1,134	36	163	365	10	8	336	4,307	53
I	N	18,593	5,130	2,114	3,186	2,107	931	1,124	670	26	94	226	5	3	216	2,719	42
	%	(100)	(27.6)	(11.4)	(17.1)	(11.3)	(5.0)	(6.0)	(3.6)	(0.1)	(0.5)	(1.2)	(0)	(0)	(1.2)	(14.6)	(0.2)
I and/or II	N	6		2	1	1	1									1	
	%	(100)	(0)	(33.3)	(16.7)	(16.7)	(16.7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(16.7)	(0)
II	N	11,256	3,037	1,310	1,912	1,430	506	651	464	10	69	139	5	5	120	1,587	11
	%	(100)	(27.0)	(11.6)	(17.0)	(12.7)	(4.5)	(5.8)	(4.1)	(0.1)	(0.6)	(1.2)	(0)	(0)	(1.1)	(14.1)	(0.1)
Disease Type																	
Rare and Common	N	7,619	1,846	864	1,429	933	373	412	348	8	34	70	2	1	81	1,210	8
	%	(100)	(24.2)	(11.3)	(18.8)	(12.2)	(4.9)	(5.4)	(4.6)	(0.1)	(0.4)	(0.9)	(0)	(0)	(1.1)	(15.9)	(0.1)
Common	N	19,720	5,872	2,207	3,195	2,277	952	1,216	645	17	112	255	7	6	209	2,715	35
	%	(100)	(29.8)	(11.2)	(16.2)	(11.5)	(4.8)	(6.2)	(3.3)	(0.1)	(0.6)	(1.3)	(0)	(0)	(1.1)	(13.8)	(0.2)
Rare	N	2,516	449	355	475	328	113	147	141	11	17	40	1	1	46	382	10
	%	(100)	(17.8)	(14.1)	(18.9)	(13.0)	(4.5)	(5.8)	(5.6)	(0.4)	(0.7)	(1.6)	(0)	(0)	(1.8)	(15.2)	(0.4)
Sex																	
Female	N	9,689	2,976	470	1,159	573	1,165	1,508	8	33	104	393	1,193	1	84	0	22
	%	(100.0)	(30.7)	(4.9)	(12.0)	(5.9)	(12.0)	(15.6)	(0.1)	(0.3)	(1.1)	(4.1)	(12.3)	(0.0)	(0.9)	(0.0)	(0.2)
Male	N	9,929	3,146	442	1,262	551	1,150	1,420	16	34	112	453	1,248	5	69	1	20
	%	(100.0)	(31.7)	(4.5)	(12.7)	(5.5)	(11.6)	(14.3)	(0.2)	(0.3)	(1.1)	(4.6)	(12.6)	(0.1)	(0.7)	(0.0)	(0.2)
Unknown	N	19,691	4,972	972	2,241	1,200	2,242	3,645	20	129	247	681	3,039	3	261	9	30
	%	(100.0)	(25.3)	(4.9)	(11.4)	(6.1)	(11.4)	(18.5)	(0.1)	(0.7)	(1.3)	(3.5)	(15.4)	(0.0)	(1.3)	(0.0)	(0.2)
Race/Ethnicity																	
Black	N	578	108	19	87	41	96	92	0	0	20	15	91	0	9	0	0
	%	(100.0)	(18.7)	(3.3)	(15.1)	(7.1)	(16.6)	(15.9)	(0.0)	(0.0)	(3.5)	(2.6)	(15.7)	(0.0)	(1.6)	(0.0)	(0.0)
Hispanic	N	98	11	12	12	11	19	18	0	0	0	3	12	0	0	0	0
	%	(100.0)	(11.2)	(12.2)	(12.2)	(11.2)	(19.4)	(18.4)	(0.0)	(0.0)	(0.0)	(3.1)	(12.2)	(0.0)	(0.0)	(0.0)	(0.0)
White	N	8,208	1,853	371	785	557	933	1,789	9	100	166	316	1,162	3	154	10	0
	%	(100.0)	(22.6)	(4.5)	(9.6)	(6.8)	(11.4)	(21.8)	(0.1)	(1.2)	(2.0)	(3.8)	(14.2)	(0.0)	(1.9)	(0.1)	(0.0)
Other	N	459	113	13	31	17	29	144	0	5	8	21	77	0	1	0	0

		Total	Cancer Information Services	NIH main office–PRPL	Internet	Physician	Healthcare provider	Word of mouth	Community outreach	Professional journal	Magazine	Newspaper	Newsletter	Radio	TV	Other	Missing
	%	(100.0)	(24.6)	(2.8)	(6.8)	(3.7)	(6.3)	(31.4)	(0.0)	(1.1)	(1.7)	(4.6)	(16.8)	(0.0)	(0.2)	(0.0)	(0.0)
Missing	N	20,512	6,082	1,023	2,623	1,149	2,349	3,056	27	58	171	779	2,965	5	172	0	53
	%	(100.0)	(29.7)	(5.0)	(12.8)	(5.6)	(11.5)	(14.9)	(0.1)	(0.3)	(0.8)	(3.8)	(14.5)	(0.0)	(0.8)	(0.0)	(0.3)
Age Group																	
0–17	N	16	0	2	1	0	2	6	0	0	1	0	3	0	1	0	0
	%	(100.0)	(0.0)	(12.5)	(6.3)	(0.0)	(12.5)	(37.5)	(0.0)	(0.0)	(6.3)	(0.0)	(18.8)	(0.0)	(6.3)	(0.0)	(0.0)
18–39	N	2,486	628	95	315	133	310	561	3	9	15	91	297	0	29	0	0
	%	(100.0)	(25.3)	(3.8)	(12.7)	(5.3)	(12.5)	(22.6)	(0.1)	(0.4)	(0.6)	(3.7)	(11.9)	(0.0)	(1.2)	(0.0)	(0.0)
40–59	N	12,233	3,547	611	1,395	788	1,467	2,091	9	79	117	523	1,429	6	168	3	0
	%	(100.0)	(29.0)	(5.0)	(11.4)	(6.4)	(12.0)	(17.1)	(0.1)	(0.6)	(1.0)	(4.3)	(11.7)	(0.0)	(1.4)	(0.0)	(0.0)
60+	N	9,637	3,159	427	1,088	613	1,036	1,472	12	63	213	381	1,063	0	105	5	0
	%	(100.0)	(32.8)	(4.4)	(11.3)	(6.4)	(10.8)	(15.3)	(0.1)	(0.7)	(2.2)	(4.0)	(11.0)	(0.0)	(1.1)	(0.1)	(0.0)
(Missing)	N	5,483	833	303	739	241	611	969	12	12	19	139	1,515	2	33	2	53
	%	(100.0)	(15.2)	(5.5)	(13.5)	(4.4)	(11.1)	(17.7)	(0.2)	(0.2)	(0.3)	(2.5)	(27.6)	(0.0)	(0.6)	(0.0)	(1.0)

Exhibit 4-7. CSSC: Number of Protocols by Recruitment Strategy and Protocol Characteristics

Protocol Characteristic	Total		Mailing/Flyers		Advertisements		Presentation		Press Articles		Public Service Announcements		Marketing Web Links		Community Relations	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	67	(100)	58	(87)	2	(3)	12	(18)	17	(25)	7	(10)	6	(9)	12	(18)
Phase																
Phase I	26	(38.8)	23	(34.3)	2	(3.0)	4	(6.0)	6	(9.0)	4	(6.0)	1	(1.5)	3	(4.5)
Phase II	40	(59.7)	34	(50.7)	0	(0.0)	8	(11.9)	11	(16.4)	3	(4.5)	5	(7.5)	9	(13.4)
Phase I and/or II	1	(1.5)	1	(1.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Type of Disease																
Rare and common	7	(10.4)	5	(7.5)	0	(0.0)	1	(1.5)	1	(1.5)	0	(0.0)	1	(1.5)	0	(0.0)
Common	41	(61.2)	36	(53.7)	2	(3.0)	8	(11.9)	10	(14.9)	7	(10.4)	5	(7.5)	7	(10.4)
Rare	19	(28.4)	17	(25.4)	0	(0.0)	3	(4.5)	6	(9.0)	0	(0.0)	0	(0.0)	5	(7.5)

4.4.4 *Recruitment Strategies and Sources of Information—PRPL Data*

Analyses of the PRPL data paralleled those conducted for the CSSC data. Appendix K presents referrals made to each PRPL protocol by patient self-reported source of information about PRPL. Appendix L shows the number and type of recruitment strategies used for each protocol. PRPL used from one to five different types of strategies for each protocol. As reported for CSSC, PRPL often used the same type of strategy multiple times for each protocol. The total number of strategies used for individual protocols therefore ranged from one to seven.

Protocols are categorized by protocol and patient characteristics in Exhibit 4–8. This table shows that, across type of protocol and patient category, the Internet, newspapers, and word of mouth were primary sources of information for patients, with variations by which source was predominant. For example, newspapers (45 percent of referrals) were most often reported as the information source for patients referred to Phase I trials. The radio (15 percent), word of mouth (14 percent), and community outreach (13 percent) also were noted sources. On the other hand, for patients referred to Phase II trials, the Internet (35 percent) was the most cited source, followed by newspapers (23 percent) and word of mouth (18 percent). Patients referred to natural history studies reported learning about PRPL especially through the Internet (36 percent), word of mouth (24 percent), or newspapers (16 percent).

The Internet was the predominant source of information for female patients (34 percent), and newspapers were for male patients (31 percent). However, the Internet, newspapers, and word of mouth were the three main information sources for both male and female patients. The Internet was the primary source of information among non-Hispanic White patients (34 percent) and Hispanic patients (28 percent), whereas newspapers were the source most cited by non-Hispanic Blacks.

As shown in Exhibit 4–9, PRPL adopted a wide range of strategies for the different types of protocols. Advertisements were used for two-thirds (67 percent) of all Phase I protocols. In addition, community relations, mailings and/or flyers, Web marketing, and public service announcements were each used for a third of these trials. PRPL distributed mailings and/or flyers for over three-fourths (79 percent) of Phase II protocols, and used advertisements and/or public service announcements for over 70 percent of this group of studies. These two strategies also were the principal strategies for the natural history protocols.

For protocols addressing rare diseases, PRPL especially used public service announcements (81 percent of protocols), mailings and/or flyers (69 percent), and Web marketing (62 percent). For common-disease protocols, PRPL focused efforts using advertisements (71 percent of protocols) and mailings and/or flyers (71 percent).

4.4.5 *PRPL Case Studies*

CSR plotted recruitment strategies by individual contacts and referrals for each protocol to determine potential associations between strategies and number of contacts and referrals. A complete set of figures showing monthly numbers of contacts and types of recruitment strategies by date can be found in Appendix H. A comparable set of figures for monthly referrals can be found in Appendix G. Included here are a few "case studies" of individual protocols.

4.4.5.1 *Case Study 1: 00–CH–0134 Childhood Obesity*

This Phase II trial examined the effects of the diabetes drug Metformin on energy intake, energy expenditure, and body weight in overweight children ages 6-13 with insulin resistance. The study was initiated in May 2000. As shown on p. H-2 of Appendix H and p. G-2 of Appendix G, there were some notable spikes in contacts and referrals, respectively, in 2001 prior to PRPL-initiated recruitment activities. There were over 15 calls regarding this protocol and between 14 and 15 referrals to the protocol in February and March 2001. Calls and referrals dropped in the following

Exhibit 4-8. PRPL: Referrals by Patient Self-Reported Source of Information and Type of Protocol

Characteristic		Total	Book	Community Outreach	Direct Mail/Letter	Healthcare Provider	Internet	Magazine	Newsletter	Newspaper	Physician	Professional Journal	Radio	TV	Word of Mouth	Missing
Phase																
I	n	150	0	19	0	0	13	0	3	67	2	0	23	1	21	1
	%	(100)	(0.00)	(12.67)	(0.00)	(0.00)	(8.67)	(0.00)	(2.00)	(44.67)	(1.33)	(0.00)	(15.33)	(0.67)	(14.00)	(0.67)
II	n	1,186	9	51	13	6	421	47	32	276	41	1	33	36	215	5
	%	(100)	(0.76)	(4.30)	(1.10)	(0.51)	(35.50)	(3.96)	(2.70)	(23.27)	(3.46)	(0.08)	(2.78)	(3.04)	(18.13)	(0.42)
Natural history	n	497	6	30	2	6	177	8	35	80	24	1	2	2	121	3
	%	(100)	(1.21)	(6.04)	(0.40)	(1.21)	(35.61)	(1.61)	(7.04)	(16.10)	(4.83)	(0.20)	(0.40)	(0.40)	(24.35)	(0.60)
Disease Type																
Rare and common	n	39	0	2	0	0	11	1	0	9	0	0	0	0	16	0
	%	(100)	(0.00)	(5.13)	(0.00)	(0.00)	(28.21)	(2.56)	(0.00)	(23.08)	(0.00)	(0.00)	(0.00)	(0.00)	(41.03)	(0.00)
Rare	n	333	0	18	5	1	150	3	8	34	8	1	12	25	67	1
	%	(100)	(0.00)	(5.41)	(1.50)	(0.30)	(45.05)	(0.90)	(2.40)	(10.21)	(2.40)	(0.30)	(3.60)	(7.51)	(20.12)	(0.30)
Common	n	1,461	15	80	10	11	450	51	62	380	59	1	46	14	274	8
	%	(100)	(1.03)	(5.48)	(0.68)	(0.75)	(30.80)	(3.49)	(4.24)	(26.01)	(4.04)	(0.07)	(3.15)	(0.96)	(18.75)	(0.55)
Sex																
Male	n	513	1	31	4	6	125	20	21	158	18	0	26	8	92	3
	%	(100)	(0.19)	(6.04)	(0.78)	(1.17)	(24.37)	(3.90)	(4.09)	(30.80)	(3.51)	(0.00)	(5.07)	(1.56)	(17.93)	(0.58)
Female	n	1,223	14	68	11	6	419	35	43	259	47	2	30	25	259	5
	%	(100)	(1.14)	(5.56)	(0.90)	(0.49)	(34.26)	(2.86)	(3.52)	(21.18)	(3.84)	(0.16)	(2.45)	(2.04)	(21.18)	(0.41)
(Missing)	n	97	0	1	0	0	67	0	6	6	2	0	2	6	6	1
	%	(100)	(0.00)	(1.03)	(0.00)	(0.00)	(69.07)	(0.00)	(6.19)	(6.19)	(2.06)	(0.00)	(2.06)	(6.19)	(6.19)	(1.03)
Race/Ethnicity																
White	n	1,086	8	61	11	10	372	24	43	249	35	2	38	11	218	4
	%	(100)	(0.74)	(5.62)	(1.01)	(0.92)	(34.25)	(2.21)	(3.96)	(22.93)	(3.22)	(0.18)	(3.50)	(1.01)	(20.07)	(0.37)
Black	n	401	4	23	1	2	77	20	16	118	22	0	11	21	84	2
	%	(100)	(1.00)	(5.74)	(0.25)	(0.50)	(19.20)	(4.99)	(3.99)	(29.43)	(5.49)	(0.00)	(2.74)	(5.24)	(20.95)	(0.50)
Hispanic	n	78	0	7	2	0	22	5	1	15	1	0	5	1	19	0
	%	(100)	(0.00)	(8.97)	(2.56)	(0.00)	(28.21)	(6.41)	(1.28)	(19.23)	(1.28)	(0.00)	(6.41)	(1.28)	(24.36)	(0.00)
Other	n	53	0	3	0	0	9	1	6	17	4	0	2	1	10	0
	%	(100)	(0.00)	(5.66)	(0.00)	(0.00)	(16.98)	(1.89)	(11.32)	(32.08)	(7.55)	(0.00)	(3.77)	(1.89)	(18.87)	(0.00)

Characteristic		Total	Book	Community Outreach	Direct Mail/Letter	Healthcare Provider	Internet	Magazine	Newsletter	Newspaper	Physician	Professional Journal	Radio	TV	Word of Mouth	Missing
(Missing)	n	215	3	6	1	0	131	5	4	24	5	0	2	5	26	3
	%	(100)	(1.40)	(2.79)	(0.47)	(0.00)	(60.93)	(2.33)	(1.86)	(11.16)	(2.33)	(0.00)	(0.93)	(2.33)	(12.09)	(1.40)
Age Group																
0–17	n	233	1	13	1	4	34	41	11	50	22	1	2	2	47	4
	%	(100)	(0.43)	(5.58)	(0.43)	(1.72)	(14.59)	(17.60)	(4.72)	(21.46)	(9.44)	(0.43)	(0.86)	(0.86)	(20.17)	(1.72)
18–39	n	834	6	53	9	3	331	6	23	170	21	1	41	15	152	3
	%	(100)	(0.72)	(6.35)	(1.08)	(0.36)	(39.69)	(0.72)	(2.76)	(20.38)	(2.52)	(0.12)	(4.92)	(1.80)	(18.23)	(0.36)
40–59	n	557	7	26	3	3	171	6	28	141	21	0	12	21	116	2
	%	(100)	(1.26)	(4.67)	(0.54)	(0.54)	(30.70)	(1.08)	(5.03)	(25.31)	(3.77)	(0.00)	(2.15)	(3.77)	(20.83)	(0.36)
60+	n	148	1	8	2	2	22	2	7	60	3	0	3	1	37	0
	%	(100)	(0.68)	(5.41)	(1.35)	(1.35)	(14.86)	(1.35)	(4.73)	(40.54)	(2.03)	(0.00)	(2.03)	(0.68)	(25.00)	(0.00)
(Missing)	n	61	0	0	0	0	53	0	1	2	0	0	0	0	5	0
	%	(100)	(0.00)	(0.00)	(0.00)	(0.00)	(86.89)	(0.00)	(1.64)	(3.28)	(0.00)	(0.00)	(0.00)	(0.00)	(8.20)	(0.00)
Total	n	1,833	15	100	15	12	611	55	70	423	67	2	58	39	357	9
	%	(100)	(0.82)	(5.46)	(0.82)	(0.65)	(33.33)	(3.00)	(3.82)	(23.08)	(3.66)	(0.11)	(3.16)	(2.13)	(19.48)	(0.49)

Exhibit 4-9. PRPL: Number of Protocols by Recruitment Strategy and Protocol Characteristics

Protocol Characteristic	Total		Advertisements		Community Relations		Mailings/Flyers		Marketing/ Web Links		Presentations		Press Articles		PSA		Standard PRPL Outlets	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
All	34	(100)	20	(58.82)	9	(26.47)	24	(70.59)	16	(47.06)	6	(17.65)	1	(2.94)	22	(64.71)	9	(26.47)
Phase																		
Phase I	3	(100)	2	(66.67)	1	(33.33)	1	(33.33)	1	(33.33)	0	(0.00)	0	(0)	1	(33.33)	0	(0)
Phase II	14	(100)	10	(71.43)	3	(21.43)	11	(78.57)	8	(57.14)	3	(21.43)	0	(0)	10	(71.43)	5	(35.71)
Natural history	17	(100)	8	(47.06)	5	(29.41)	12	(70.59)	7	(41.18)	3	(17.65)	1	(5.88)	11	(64.71)	4	(23.53)
Disease Type																		
Rare and common	1	(100)	0		0		1	(100)	1	(100)	1	(100)	0	(0)	0	(0)	1	(100)
Common	18	(100)	12	(70.59)	6	(35.29)	12	(70.59)	5	(29.41)	2	(11.76)	0	(0)	9	(52.94)	4	(23.53)
Rare	15	(100)	8	(50.00)	3	(18.75)	11	(68.75)	10	(62.50)	3	(18.75)	1	(6.25)	13	(81.25)	4	(25.00)

months of 2001, with a more moderate peak in June. PRPL initiated strategies in February 2002 to recruit for this protocol, including drawing on community relations, distributing mailings and flyers, and placing advertisements. Whereas the number of contacts and referrals remained around 10 during most of 2002 and 2003, the spikes in the graphs do suggest a temporal association between PRPL recruitment activities implemented in February–March 2002 and January–April 2003 and contacts and referrals in April 2002 and April 2003.

4.4.5.2 *Case Study 2: 01–D–0076 Sciatic Back Pain*

Initiated in January 2001, this Phase II trial tested the effectiveness of Morphine and Nortriptyline and their combination in sciatica treatment for adults. As shown in the figures presented on pages H-9 and G-9, there were large increases in contacts from February to March–April 2003, and even larger from April to May of that year, with close to 35 calls coming in about this protocol during the month of May. The increase in referrals also was evident in May 2003. These spikes occurred before the implementation of PRPL strategies, however. From June through November 2003, PRPL used advertisements and other standard PRPL outlets to recruit patients to this protocol. There were important increases in contacts and in referrals in August 2003, approximately 2 months after the first set of advertisements was implemented by PRPL in conjunction with continuing implementation of other usual recruitment outlets. Because we do not have contact and referral data for after this time period, however, we cannot examine whether there were corresponding spikes in the months shortly after the second or third set of advertisements. It is therefore difficult to draw any conclusions about possible temporal relationships between PRPL recruitment strategies and contacts and referrals. Marked increases in contacts and referrals before the initiation of PRPL outreach may reflect recruitment activities conducted by the study team using PRPL materials.

4.4.5.3 *Case Study 3: 01–H–0119 Epithelial Progenitor Cells (EPC)*

This natural history protocol, initiated in March 2001, recruited men age 21 and older and postmenopausal women to study EPC and risk factors for coronary artery disease. When PRPL became involved in the study in December 2001, it sent out mailings and flyers regarding the protocol, and implemented community relations activities in February through April 2002. The patterns shown on pages H-12 and G-12 and the relatively small scale (with a range of 1 to 20 contacts and 1 to 15 referrals) make it difficult to draw conclusions about the relationship between PRPL outreach strategies and accruals to the protocol. The graphs do suggest, however, that PRPL strategies contributed to a sharp increase in contacts in April 2002. On the other hand, the large spike in referrals for November 2002 does not seem to be related to any PRPL recruitment efforts.

4.4.5.4 *Case Study 4: 02–CH–0287 Fibroids*

This Phase II study evaluated the selective progesterone receptor modulator CDB-2914 for treating uterine fibroids in pre-menopausal women. The protocol began in September 2002, and PRPL contributed to recruitment activities during 2003. The figures on pages H-17 and G-17 appear to show a fairly strong temporal relationship between PRPL activities and contacts and referrals. There was a substantial increase from one to over 25 contacts and from two to 13 referrals between January 2003, when PRPL conducted marketing activities for this study, and February 2003. Similarly, after advertisements were implemented in combination with public service announcements, there was an increase in contacts from 6 in May to over 35 in June, and from 4 to 12 referrals during the same months. Although the available data do not allow us to differentiate between the possible effects of advertisements versus PSAs, it appears that the combined effect of both these strategies contributed to increased recruitment among this target population for this protocol.

5. Discussion and Recommendations

It is well documented in the literature that patient recruitment is a serious bottleneck in the successful completion of clinical trials. During their first 7 years of existence, clearly PRPL and CSSC have made significant contributions to enhancing recruitment of participants into clinical studies at the NIH Clinical Center. Recruiting patients is a costly endeavor, and NIH intramural clinical investigators often have limited budgets for recruitment. Therefore, at this stage in the evolution of the programs, a feasibility study is well justified. The intent of this study was to conduct a systematic review of the existing patient recruitment data. If possible, this study would also determine which patient recruitment strategy or combination of strategies is most successful in recruiting particular categories of patients, diseases, and protocols.

5.1 Discussion

As disclosed in the findings, we were able to:

- Identify a number of key variables of interest in each data set as well as a more limited number of key variables common to both;
- Determine that the primary definition of "success" in recruiting patients into clinical trials would be referral to a study protocol;
- Develop several basic categories of patients, diseases, and protocols; and
- Examine the distribution of use of different recruitment strategies as well as the source of information reported by the patients across these categories.

Both the PRPL and CSSC databases are extensive and serve well the purposes for which they were designed. As is the case with many analytic studies of retrospective data collected for another purpose, the structure and composition of the existing patient recruitment data severely limited both the types of analyses that could be performed and the research questions that could be addressed by this feasibility study. Selection of key variables was restricted by the existing data. Examination of basic patient demographic characteristics was complicated by the fact that certain data either were not collected or were missing. CSSC, for example, did not record the sex of the potential research participants. We were able to ascertain the sex of two-thirds of the CSSC patients through the use of data in other fields. A review of the literature, the co-project officers, members of the Project Advisory Group, and CSR project staff members identified a wide variety of possible definitions of success in recruiting and possible categories of patients, diseases, and protocols. It was uniformly decided that the best definition of success in recruiting is enrollment of the patient in a clinical study. However, since neither PRPL nor CSSC has control over actual enrollment, it was decided that success should be defined as referral to a study.

Examination of different recruiting strategies across the categories of patients, diseases, and protocols offered tentative suggestions of differences; however, the existing data regarding implementation of recruitment strategies severely limited the analyses that could be performed. In order to demonstrate a strong association between utilization of a particular recruiting strategy or combination of strategies and referral to or enrollment in a specific protocol, one requires data regarding patient referral prior to, during, and after implementation of each strategy or combination of strategies. At present, for example, PRPL performs periodic evaluations looking at a given time frame, such as 6 months, following implementation of strategies. We were unable to ascertain the actual complete timeframe during which any given strategy was implemented. We had only information on certain "snapshots" of utilization of recruitment strategies. In addition, by their nature, retrospective studies may demonstrate associations but are unable to determine causality. Therefore, as planned in subsequent phases of this project, a prospective study should be able to demonstrate association and suggest causation as well.

Other information, which would strengthen the findings, includes a solid measure of desired total enrollment in a protocol. With this data it would be possible to utilize actual enrollment vs. desired enrollment as a measure of success in recruiting. In ClinicalTrials.gov, information is collected on "expected total enrollment;" however, the Project Advisory Group members agreed that these figures are meaningless and should not be used. A better measure of desired enrollment would be required.

Evaluating the effectiveness of various CSSC and PRPL recruitment strategies is a very challenging research endeavor for a number of additional reasons. Both CSSC and PRPL operate on a request for service basis. While approximately 1,000 protocols at the Clinical Center may be actively recruiting participants at any given time, CSSC and PRPL are only asked to assist in recruiting for a portion of these protocols. In addition, principal investigators, research nurses, and others associated with these same protocols may be engaging in various recruitment strategies in order to recruit participants, making it difficult to tease out the role of CSSC or PRPL relative to these other efforts or the actual impact of individual recruitment strategies. In order to obtain a more complete and accurate picture of the effectiveness of various recruitment strategies, these other recruiters must collect patient and recruiting strategy data comparable to that collected by CSSC and PRPL.

At their March 2006 meeting, the Project Advisory Group Members had a lengthy discussion of the difficulties in linking individual recruitment strategies for specific protocols to patient contacts and referrals. One mechanism for linking a recruitment strategy to individual contacts is using a unique telephone number. Ms. Cirelli reported that PRPL now has about 40 telephone numbers assigned to specific recruitment strategies. Because these telephone lines are very expensive, PRPL has to recycle them as much as possible. This creates problems with linking recruitment strategy to patient contact or referral.

Finally, there are many external factors that may have more impact on patient recruitment than any strategies implemented by PRPL or CSSC. Project Advisory Group members were quite vocal about these outside factors and offered their thoughts regarding the difficulties in recruiting patients to studies at NIH. We drew on their own words to offer the following observations:

1. *NIH is in fierce economic competition for treatment of patients who may have other (conventional) therapeutic options. Universities are just as anxious as private physicians to retain their patient population, and they have research alternatives to offer their patients, which allows them to enroll the patients and continue to get the revenues. For example, in spite of several "academic" presentations about our studies to local medical school staff and quite satisfactory scientific interaction with the physicians, we do not receive from them referrals for patients who have health insurance coverage. The very few referrals we do receive are indigent people with no healthcare coverage. Nowadays, many institutions and private offices not only offer great patient-oriented care but also have access to superb research programs. There is enormous economic pressure on private physicians and universities alike to maintain their revenues. A pure scientific rationale and, unfortunately, even a pure human compassionate rationale are now too often not enough to convince these potential referring centers to let go of revenue-generating patients.*
2. *NIH does not build a base of referring physicians around the Clinical Center arising from their fellowship training programs. For example, referrals to Johns Hopkins or other major regional universities come from former fellows they have trained, now in private practice in the area. These referring physicians are "faithful" to their institution of training.*
3. *The attention span and retention ability of potential referring physicians in the community is quite short due to the high pressure and pace of their practices. This is not a criticism; it is an observation. In the absence of sustained, specific, and nonintrusive interaction with NIH, they quickly get confused with the particulars of our studies, go back to their routine, and forget*

about us within days of a seemingly successful interaction.

4. *The NIH support structure is still not "customer oriented," and even the research teams dedicated to and practicing very good public relations with their referring physicians continue to pay the price of decades of ivory tower mentality. In spite of definite progress in some of these areas, all it takes is a couple of flip remarks from an inconsiderate clerk or the condescending comments from an arrogant, out-of-touch principal investigator to a referring party to rekindle the old image for months to years!*
5. *The general public, even right here in Bethesda, is, by and large, unaware that there is a hospital treating "real patients" (not mice!) at the Clinical Center. We all see many ads on TV or other media for a number of hospitals around the area, never one for the NIH Clinical Center.*

One member concluded that these "unscientific considerations probably outweigh most of the scientific ones in explaining poor referral patterns, and considering only the scientific factors would not uncover the real causes of the problem and, therefore, would be of no help in fixing it."

5.2 Recommendations

In this section, we describe several sets of recommendations developed in conjunction with the Co-Project Officers and Project Advisory Group members. The overarching long-term goal of the overall project is to develop an evidence-based systematized approach that will assist PRPL, CSSC, and individual investigators in selecting patient recruitment strategies that will result in optimal patient enrollment in particular studies. First, we provide general recommendations for an ideal patient recruitment database. Next, we offer recommendations regarding specific data elements that should be included or modified. Finally we suggest work that should be included in the remaining phases of this project.

5.2.1 *General Recommendations for Data to be Collected*

The following changes are proposed for both the CSSC and PRPL databases:

- Document the data management protocol so that data can be entered, managed, and analyzed faithfully. This includes having a data dictionary and other supporting documentation (e.g., user's manual) for both CSSC and PRPL databases.
- Implement error-checking and validation mechanisms for both databases, to ensure that data are collected systematically and consistently across all protocols.
- Use more closed-ended response categories in order to maximize the consistency of data entry over time and among different users.
- Use consistent data types, values, and formats for similar data types across all protocols (e.g., race and ethnicity).

Other suggestions include:

- Collect strategy data continuously rather than for a limited time period, such as 6 months.
- Collect more detailed strategy data to the extent that it is possible to differentiate cost, duration, and intensiveness of each strategy and to compare across all protocols.
- Include more protocols. The protocols available for the current study are few, yet very heterogeneous. Under the current circumstances, it is difficult to match a given protocol with a suitable control. The measured protocol characteristics such as phase and disease type are not likely to explain the differences. For example, among the PRPL protocols analyzed, only three were Phase I studies and only one protocol included both rare and common diseases. Therefore, what we learn about recruitment strategies utilized in these protocols is not likely to be generalizable to Phase I studies as a whole or to all protocols which include both rare and common diseases. The effects of phase and disease type are confounded by too many unmeasured variables.

5.2.2 *Specific Recommendations for Data to be Collected*

For CSSC:

- Capture information on the sex of the research participant. Currently, the only indicator of the sex of a participant is a prefix such as Mr. or Mrs., and this is not an adequate substitute because the caller is often a relative or healthcare provider, rather than the potential participant.
- Develop a mechanism to capture the contact protocols.
- Introduce a mechanism to capture admission data, in relation to protocols to which the client was referred.

For PRPL:

- Improve data editing attributable to:
  - Inconsistent data format. For example, dates were entered in a variety of formats and some dates had an unusual format such as 6/11/2002 10:04:14:78, which is not recognized by standard statistical packages, such as SPSS.
  - Duplicates. For example, among 57 duplicate patient records, patient ID="57895" appears twice for the protocol 99-CH-0012.
  - Missing values. For example, some patient data lack admission information. It is not clear if the patients were not admitted or the admission status was unknown. Some patients also had missing values on age even though the age could have been derived from the date of birth if it is available.
  - Data entry errors. For example, the referral protocols were recorded as "ID", "IL", "MI", "OR" for four cases from Turner's syndrome patient data. In these cases the state of residence was accidentally entered in the wrong field. If protocol identification numbers are selected from a drop-down list, this finding may indicate an inconsistency between data import and data export. If that is the case, a formalized data export/output protocol should be established.

Ms. Susanna Sung, one of the Project Advisory Group members, provided information on some procedures utilized by the NIMH patient recruitment team. Below is a summary of the process utilized by NIMH.

1. *The particular recruitment effort (Web, paid print/audio/video advertising/outreach, etc.) is initiated.*
2. *Calls come in to a centralized team.*
   a. *Caller contact information is logged in and the caller is called back.*
   b. *Caller's basic situation is assessed and studies described. At this point NIMH records the disposition of the call and caller:*
      i. *Caller obviously ineligible/rejected.*
      ii. *Interested in a study that NIMH does not have.*
      iii. *Referred directly to a particular intramural branch.*
      iv. *Referred to an extramural research program at NIMH.*
      v. *Information given; patient to follow up.*
      vi. *Unable to reach.*
      vii. *Screened.*
      viii. *Applicant declined participation.*
      ix. *Requested information only, and information provided.*
      x. *Requested information only, information provided, and referred to NIMH extramural program.*
3. *If the caller is screened, an in-depth psychosocial interview is conducted over the phone. Here NIMH indicates if:*
   a. *Patient appropriate to present to branch.*
   b. *Patient rejected by team.*
   c. *Patient declined.*
      The reason why a patient was rejected or declined is recorded.
   d. *If the caller is presented to the branch, the outcome of the meeting is recorded:*
      i. *Patient taken.*
      ii. *Rejected (and reason why).*
      iii. *Pending.*
   e. *If the patient is taken, the outcome of branch screening is recorded:*
      i. *Patient rejected after phone screening.*
      ii. *Patient declined after phone screening.*
      iii. *Screened the potential participant in person rather than by phone.*

iv. Screened in person and declined.
v. Admitted.

Again, if the patient was rejected or declined, the reason why is recorded.

CSSC and PRPL do not provide in-depth telephone interviewing, so much of paragraph 3 above is not applicable.

5.2.3 *Recommendations Regarding Future Work on This Project*

Project Advisory Group members, the Co-Project Officers, and CSR staff all feel strongly that ascertaining which recruitment strategy or combination of strategies is most successful in recruiting specific categories of patients, diseases, and protocols would be a genuine contribution to clinical research at NIH and to the medical literature. Therefore, based on what has been learned during this feasibility study, we recommend the following:

- Utilizing both the general and specific recommendations regarding data elements and database structure, redesign both the PRPL and CSSC databases and data collection systems to collect a common set of data items. The key data item categories to include are:
  - Patient demographics (including age, sex, race, ethnicity, education level, primary language(s) spoken)
  - Source of information about the recruitment center and/or specific protocol
  - Specific telephone number or Web site address used to contact the recruitment center—this would be most informative if each recruitment strategy were assigned a separate telephone number and/or Web site address to facilitate tracking of incoming inquiries to specific outreach efforts
  - Other recruitment strategies conducted separately by the study team
  - Date of first contact to the recruitment center
  - Date of referral to a protocol
  - Date of admission to a protocol
- Solicit the input of the Project Advisory Group in the redesign of the databases.
- Utilizing the Project Advisory Group as liaison, solicit the input of NIH intramural clinical researchers and their recruiting staff in the redesign of the databases with the understanding that, in the future, all individuals participating in patient recruiting for studies at the NIH Clinical Center would collect such data.
- Design this new database so that it is comparable with both the NIH Clinical Research Information System (CRIS) at the Clinical Center and the NIH Clinical Informatics and Management System (CIMS).
- After this new database has been operational for 2 years, repeat and, if possible, expand upon the analyses performed under the current project.
- Based on the results of the analyses performed in the 2-year followup described above, design and carry out a prospective study to test recruitment strategies that appear to be successful in recruiting for specific types of patients, diseases, and protocols.
- Consider cost. Recommendations to improve the quality of the data collected, as well as to redesign the databases are very important. Equally important, but beyond the scope of this report, is what these improvements would cost, in terms of staff and financial resources. Project Advisory Group members strongly advised that such costs must be considered. Recommended changes that involve minimal cost (e.g., can be implemented by existing personnel and in-house resources) should definitely be implemented. Those that would involve hiring additional personnel or require costly outsourcing should be carefully evaluated before implementation, especially in light of the importance of external factors and current NIH budgetary constraints. Therefore the Project Advisory Group recommended the following:
- Rather than conducting a major database redesign across NIH, conduct a prospective study on a carefully-chosen set of protocols. Selection criteria would include, for example, representation across rare versus common diseases and across NIH Institutes and Centers (ICs) that perform clinical studies, providing a

total of about 15 trials to follow. ICs would be asked to select a clinical trial to include in the study. All trials would have to conduct recruitment activities through PRPL or CSSC or all would have to agree to implement the same recruitment strategies. On the one hand, it would be desirable to design this study to measure the impact of a limited number of selected strategies with as few confounding variables as possible. On the other hand, such a study would have many limitations because of the small size and possible protocol heterogeneity. If protocol selection is limited for the sake of comparability, then the findings from the study can only be extrapolated to those same kinds of protocols. Such a study, while descriptive, would be useful for generating hypotheses to be tested in a larger group of protocols. Clearly careful attention must be given to study design. The following issues also should be considered in designing such a study:

- Distribution of diseases: Clinical trials would have to address distinct diseases, to avoid "bleeding" of patients across trials, i.e., secondary referral of a patient to a protocol similar to the base protocol and also included in the study.
- The mix of recruitment strategies for the prospective study: Although using a wide array of strategies may seem like an unnecessary expenditure, such a design would provide the needed data. Another option would be to apply a smaller set of strategies to a set of similar clinical trials, e.g., all Phase I trials.
- The impact of the Web on recruitment: A large proportion of patients now obtain their information from the Web. This has even affected the demographics of studies. For example, one Project Advisory Group member reported that patients in a current breast cancer trial are younger than the average age of breast cancer patients, because younger patients tend to have greater access to the Web and, therefore, to information about clinical trials.
- Timing of recruitment strategies: Ms. Cirelli pointed out that patient contacts to PRPL tend to come in waves, with a higher volume of contacts in September and June, and a lull from after Thanksgiving to January 1.
- Criteria for enrollment: These affect the number and type of patients accrued to a trial and would need to be factored into the selection of clinical trials for the next study.
- Take every effort to make the database created for this research project relational to relevant existing NIH databases for ease in tracking admissions to protocols.
- Other factors: Compensation for clinical trial patients or other benefits such as reimbursement for travel expenses could also impact the effectiveness of recruitment strategies.
- Revisit recruitment strategies used by pharmaceutical companies and the advertising agencies that often advise them.

- Insuring adequate sample sizes is critical to the design of future work. In this Phase I Feasibility Study, our ability to analyze data was severely limited by the plethora of variables, missing data, and consequent small sample sizes of comparable elements. It is impossible, at this point, to recommend specific numbers of protocols or participants; however, we strongly recommend that in future work on this project, consideration be given to effect sizes and that sample sizes be selected accordingly. One Advisory Group member cautioned that because of the large number of potential variables involved, and heterogeneity of protocols, 15 protocols may be too small a number to consider and that a much larger number of protocols may be necessary to achieve adequate sample sizes. Timely accrual of eligible protocols to study may itself be difficult to achieve. If it takes a long time to accrue sufficient numbers of protocols, the results of analyses may be uninterruptible or no longer valid. The feasibility of conducting further studies in a timely manner needs further consideration. Study design issues will be challenging, but additional studies are clearly warranted and would constitute a major contribution to the field.
- One advisory group member suggested creating a brief summary of the Discussion and Recommendations (Section 5) section of this report and circulating it to the NIH intramural community in order to raise awareness of this project, to develop a better understanding of why

followup may need to be done, and to increase the chances of getting buy in for follow on projects.

Advisory Group members were heavily engaged in this project. They feel strongly that ascertaining effective patient recruitment strategies is vital to the future success of clinical research at NIH. All members agree that additional research is needed and have volunteered to remain active in the project. In these tight budgetary times, the One Percent Evaluation Set-Aside, a critical funding mechanism by which NIH can evaluate program performance as well as improve program implementation and effectiveness, provides the ideal vehicle for supporting future research to answer these questions.

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Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix A: Advisory Group for the Patient Recruitment Project

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Appendix A: Advisory Group for the Patient Recruitment Project

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*In March 2006, Dr. Mittleman became Director of the Program Private Partnerships in the Office of Science Policy, NIH Office of the Director.

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix B: List of CSSC Protocols

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Appendix B: List of CSSC Protocols

Trial Type		Protocol	Medical Condition(s)	Study Title
Phase I	1	00-C-0044	Breast, lung, and ovarian cancer	A Clinical Trial of the P-Glycoprotein Antagonist, XR9576, in Combination with Vinorelbine in Patients with Cancer: Analysis of the Interaction Between XR9576 and Vinorelbine
Phase II	2	00-C-0069	Peritoneal cancer confined to the abdomen	Phase II Trial of Continuous Hyperthermic Peritoneal Perfusion (CHPP) with Cisplatin plus Early Postoperative Intraperitoneal Paclitaxel and 5-Fluorouracil for Peritoneal Carcinomatosis
Phase I	3	00-C-0088	Primary lung cancer or cancers that have spread to the lung	Phase I and Clinical Pharmacologic Study of Inhaled Doxorubicin in Adults with Advanced Solid Tumors Affecting the Lungs
Phase I	4	00-C-0119	Breast Cancer—metastatic	Allogeneic Breast Protocol I: T-cell Depleted Allogeneic Blood Stem Cell Transplantation Using an Immunoablative Conditioning Regimen in Metastatic Breast Cancer
Phase I	5	00-C-0121	Solid tumors—advanced	A Phase I Investigation of IL-12/Pulse IL-2 in Adults with Advanced Solid Tumors
Phase II	6	00-C-0128	Recurrent or metastatic squamous cell carcinoma of the head and neck	A Phase II Trial of Daily Bolus Flavopiridol for Five Consecutive Days in Patients with Recurrent/Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN)
Phase II	7	00-C-0133	Mantle cell lymphoma	Pilot Study of Idiotype Vaccine and EPOCH-Rituximab Chemotherapy in Untreated Mantle Cell Lymphoma
Phase II	8	00-C-0137	Prostate cancer—advanced	A Randomized Phase II Study of Either Immunotherapy with a Regimen of Recombinant Pox Viruses that Express PSA/B7.1 Plus Adjuvant GM-CSF and IL2 or Hormone Therapy with Nilutamide in Patients with Hormone Refractory Prostate Cancer and No Radiographic Evidence
Phase II	9	00-C-0149	Breast cancer	A Pilot Trial of Sequential Primary (Neoadjuvant) Combination Chemotherapy with Docetaxel/Capecitabine (TX) and Doxorubicin/Cyclophosphamide (AC) in Primary Breast Cancer with Evaluation of Chemotherapy Effects on Gene Expression
Phase II	10	00-C-0154	Prostate cancer—confined to the prostate	A Randomized Phase II Study of a PSA-based Vaccine in Patients with Localized Prostate Cancer Receiving Standard Radiotherapy
Phase I/II	11	00-C-0173	Malignant primary gliomas and benign and malignant meningiomas	A Phase I/II Trial of SU5416 in Patients with Recurrent High Grade Astrocytomas or Mixed Gliomas
Phase I	12	00-C-0206	Breast Cancer—stage IV	Phase I Study of Yttrium 90-labeled Monoclonal Antibody B3 with Autologous Stem Cell Support for Metastatic Breast Cancer
Phase II	13	00-C-0218	Pancreatic cancer—advanced	A Phase II Trial of Combined Intraperitoneal Gemcitabine, Intravenous Gemcitabine, Radiotherapy, and Surgery for Advanced Adenocarcinoma of the Pancreas

Trial Type		Protocol	Medical Condition(s)	Study Title
Phase I	14	00-C-0224	Cancer (for which there is no standard therapy capable of extending life expectancy)	A Phase I Clinical Trial of BMS-247550 (NSC 710428), an Epothilone B analog, in Patients with Refractory Neoplasms
Phase I	15	01-C-0011	Malignant mesothelioma, ovarian carcinoma, pancreatic cancer, squamous cell cancer of the lung, head and neck, and cervix	Phase I Study of SS1(dsFv)-PE38 (SS1P) Anti-Mesothelin Immunotoxin in Advanced Malignancies: Continuous Infusion x 10 days
Phase I	16	01-C-0021	B cell lymphoma	A Phase I Study of Therapy with Mono-dgA-RFB4 in Patients with Relapsed and Refractory CD22+ B-Cell Lymphoma
Phase II	17	01-C-0049	Cutaneous T cell lymphoma, peripheral T cell lymphoma	A Phase II Trial of Depsipeptide in Patients with Cutaneous T-Cell Lymphoma and Relapsed Peripheral T-Cell Lymphoma
Phase II	18	01-C-0067	HIV-Associated Kaposi's Sarcoma	A Phase II Study of Liposomal Doxorubicin and Interleukin-12 in AIDS-Associated Kaposi's Sarcoma Followed by Chronic Administration of Interleukin-12
Phase I	19	01-C-0082	Solid tumors that do not respond to standard therapy	A Phase I & Pharmacologic Trial of Sequential Irinotecan as a 24-hour IV Infusion, Leucovorin, & Fluorouracil as a 48-hour IV Infusion in Adult Cancer Patients
Phase I	20	01-C-0104	Squamous cell carcinoma of the head and neck (metastatic or recurrent)	A Phase I Study of Concomitant Therapy with Proteasome Inhibitor PS-341 and Radiation in Patients with Recurrent of Metastatic Squamous Cell Carcinoma of the Head and Neck
Phase II	21	01-C-0173	Breast cancer—inflammatory or locally advanced	A Pilot Study to Evaluate Angiogenesis after Treatment with Bevacizumab (Anti-VEGF Humanized Monoclonal Antibody) in Previously Untreated Patients with Stage IIIB or IV Inflammatory Breast Cancer
Phase I	22	01-C-0213	B cell lymphoma, lymphoma, chronic lymphocytic leukemia (CLL) (CD22+ lymphomas and leukemias)	Phase I Study of BL22, A Recombinant Immunotoxin for Chronic Lymphocytic Leukemia and CD22+ Lymphomas
Phase I	23	01-C-0256	Solid malignancy that is unresectable or metatatic	A Phase I Trial of 2-Methoxyestradiol (2ME2), (NSC-659853) an Angiogenesis Inhibitor, in Patients with Solid Tumors
Phase I	24	02-C-0006	HIV—pediatric	A Phase I Study of Tenofovir Disoproxil Fumarate (PMPA Prodrug), a Novel Nucleotide Analog Reverse Transcriptase Inhibitor, in Children with HIV Infection
Phase I	25	02-C-0083	Adult solid tumors or lymphomas that did not respond to previous therapy	A Multidose Phase I Study of Oral CC5013, a Thalidomide Derivative, in Patients with Refractory Metastatic Cancer
Phase I	26	02-C-0149	Prostate cancer	A Phase I Trial of High Dose Ketoconazole Plus Weekly Docetaxel in Metastatic Androgen Independent Prostate Cancer
Phase II	27	02-C-0190	Ovarian, pelvic, fallopian tube or primary peritoneal cancer	Phase II Clinical Trial with Proteomic Profiling of Imatinib Mesylate (Gleevec; STI571), a PDGFR and c-Kit Inhibitor, in Patients with Refractory or Relapsed Epithelial Ovarian Cancer, Fallopian Tube and Primary Peritoneal Cancer
Phase II	28	02-C-0207	Prostate cancer	A Phase II Study of MR-Guided High-Dose Rate Brachytherapy Boosts for Prostate Cancer

Trial Type		Protocol	Medical Condition(s)	Study Title
Phase II	29	02-C-0215	Prostate cancer	Amifostine as a Rectal Protector during External Beam Radiotherapy for Prostate Cancer: A Phase II Study
Phase II	30	02-C-0218	Prostate cancer	A Pilot Trial of Pox Vector PSA Vaccine with Concurrent Docetaxel versus Pox Vector PSA Vaccine Followed by Docetaxel in Metastatic Androgen Independent Prostate Cancer
Phase II	31	02-C-0229	Breast cancer—locally advanced or metastatic, male breast cancer	A Phase II Clinical Trial of BMS-247550 (NSC 710428), an Epothilone B Analog, in Patients with Breast Carcinoma
Phase II	32	03-C-0005	Breast cancer—stage II or III	A Pilot Study of Sequential Vaccinations with Recombinant Vaccinia-CEA (6D) - Tricom, and Recombinant Fowlpox-CEA (6D) - Tricom (B7.1/ICAM-1/LFA - 3) with Sargramostim (GM-CSF), in Conjunction with Standard Adjuvant Chemotherapy in High Risk Breast Cancer
Phase II	33	03-C-0077	Cancers of the blood and immune system	A Pilot Study of EPOCH-F/R Induction Chemotherapy and Reduced-Intensity, HLA-Matched, Related Allogeneic Hematopoietic Stem Cell Transplantation for Refractory or Relapsed Hematologic Malignancies, with Cyclosporine & Methotrexate for Graft-Versus-Host Di
Phase II	34	93-C-0133	Non-Hodgkin's Lymphoma—aggressive	Dose-Adjusted EPOCH Chemotherapy and Rituximab (CD20+) in Previously Untreated Aggressive Non-Hodgkin's Lymphoma
Phase II*	35	94-C-0074	Lymphomatoid granulomatosis	Treatment and Natural History Study of Lymphomatoid Granulomatosis (LYG)
Phase I	36	94-C-0096	Solid tumors—Adult	Adjuvant Vaccine Therapy with Tumor Specific Mutated Ras Peptides in Patients with Colon or Pancreatic Cancers
Phase I	37	95-C-0054	T-Cell Large Granular Lymphocytic Leukemia associated with granulocytopenia, thrombocytopenia, or anemia	Phase I Study of T-Cell Large Granular Lymphocytic Leukemia Using the Mik-Beta-1 Monoclonal Antibody Directed Toward the IL-2R-Beta Subunit
Phase I	38	95-C-0119	Osteosarcoma	A Phase I Study of OncoLAR (NSC 685403) with/without Tamoxifen in Patients with Osteosarcoma
Phase I	39	95-C-0154	Metastatic or locally advanced cervical cancer and other cancers carrying HPV	Vaccine Therapy and Detection of Immunologic Responses with Human Papillomavirus 16 E6 and E7 Peptides in Patients with Metastatic or Locally Advanced Cervical Cancer and Other Cancers Carrying the HPV
Phase II	40	96-C-0004	HIV-Associated Kaposi's Sarcoma	A Phase II Study of Oral Thalidomide for Patients with HIV Infection and Kaposi's Sarcoma
Phase I	41	96-C-0011	Ovarian cancers—advanced epithelial	Treatment of Patients with Advanced Epithelial Ovarian Cancer Using Peripheral Blood Lymphocytes Transduced with a Gene Encoding a Chimeric T-Cell Receptor Reactive with Folate Binding Protein
Phase I	42	96-C-0064	Hodgkin's disease, CLL, prolymphocytic leukemia, hairy cell leukemia, acute myeloid leukemia, non Hodgkin's lymphoma, T cell leukemia	Phase I Study of Anti-Tac(Fv)-PE38 (LMB-2), a Recombinant Single-Chain Immunotoxin for Treatment of Tac-Expressing Malignancies

Trial Type		Protocol	Medical Condition(s)	Study Title
Phase II	43	97-C-0024	Kaposi's Sarcoma with and without HIV infection	Phase II Protocol with Laboratory Correlates of 1-[(S)-3-hydroxy-2-(phosphomethoxy)propyl]cytosine dihydrate (Cidofovir) in Patient's with Kaposi's Sarcoma (KS)
Phase II	44	97-C-0040	AIDS-related lymphoma	EPOCH Chemotherapy Plus Rituximab for Previously Treated Patients with AIDS-Associated Lymphoma
Phase II	45	97-C-0068	Colorectal carcinoma—recurrent	Phase II Study of the Role of Anti-CEA Antibody Immunoscintigraphy and Positron Emission Tomography in the Localization of Recurrent Colorectal Carcinoma in Patients with Rising Serum CEA Levels in the Absence of Imageable Disease by Conventional Modalities
Phase II	46	97-C-0141	Solid tumors—adult	Vaccine Therapy with Tumor Specific Mutated Ras Peptides and IL-2 or GM-CSF for Adult Patients with Solid Tumors
Phase II*	47	97-C-0178	Chronic lymphocytic leukemia (CLL)	Fludarabine Treatment of Chronic Lymphocytic Leukemia: c-DNA Microarray Gene Expression Analysis, and Pre-Clinical Bone Marrow Transplant/Immunotherapy Studies
Phase II	48	98-C-0040	Metastatic Melanoma, renal cell carcinoma	A Phase II Protocol of FLT3 Ligand in Patients with Metastatic Melanoma and Renal Cancer
Phase II	49	98-C-0074	Ependymoma, glioma, medullulo blastoma (childhood brain tumors)	A Phase II Trial of Intravenous Cereport (RMP-7) and Carboplatin in Childhood Brain Tumors
Phase I	50	98-C-0078	Breast, colonic, lung, ovarian, stomach neoplasm (advanced carcinomas that express Lewis Y antigen)	Phase I Study of LMB-9, a Recombinant Disulfide Stabilized Immunotoxin for Advanced Carcinomas that Express Lewis-Y Antigen
Phase II	51	98-C-0118	Leukoplakia	A Randomized, Double-Blind, Placebo-Controlled, Phase IIB Trial of Ketorolac Mouth Rinse Evaluating the Effect of Cyclooxygenase Inhibition on Oropharyngeal Leukoplakia: Collaborative Study of the NCI, NIDCD and the NIDCR
Phase II	52	98-C-0123	Breast cancer (Premenopausal women at high risk for developing invasive breast cancer)	A Phase II Trial of Raloxifene in Pre-Menopausal Women at High Risk for Developing Invasive Breast Cancer
Phase II	53	98-C-0139	Renal cell carcinoma (adult)	Vaccine Therapy with Tumor-Specific Mutated VHL Peptides in Adult Cancer Patients with Renal Cell Carcinoma
Phase I	54	99-C-0014	B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), prolymphocytic leukemia, and hairy cell leukemia (CD22+ Lymphomas and leukemias)	Phase I Study of BL22, A Recombinant Immunotoxin for Treatment of CD22+ Leukemias and Lymphomas
Phase II	55	99-C-0025	Liver neoplasm—either primary or metastatic liver lesions not candidates for surgical resection	The Use of Radiofrequency Ablation to Treat Hepatic Neoplasms

Trial Type		Protocol	Medical Condition(s)	Study Title
Phase II	56	99-C-0071	Breast, colon, lung, pancreatic, stomach neoplasm (advanced carcinomas that express B3 antigen)	A Phase II Clinical Trial of Suppression of Human Antimouse Antibody and Human Antitoxin Response to Immunotoxin LMB-1 by Rituximab
Phase II	57	99-C-0093	Metastatic, unresectable colorectal cancer of the liver	A Phase II Study of Isolated Hepatic Perfusion (IHP) with Melphalan Followed by Postoperative Hepatic Arterial Chemotherapy Infusion for Metastatic Unresectable Colorectal Cancers of the Liver
Phase II	58	99-C-0102	Stage IV colon or rectal cancer, recurrent or metastatic colon or rectal cancer	A Phase II Trial of Oral Thalidomide as an Adjuvant Agent Following Metastasectomy in Patients with Recurrent Colorectal Cancer
Phase I	59	99-C-0117	Carcinoma of the colon, rectum, small bowel or appendix	A Pilot Study of Oxaliplatin in Combination with Capecitabine in Adult Cancer Patients
Phase II	60	99-C-0121	Metastatic breast or ovarian cancer	Study of Trastuzumab (Herceptin) and Paclitaxel in Patients with HER2 Overexpressing Metastatic Breast Cancer
Phase II	61	99-C-0123	Liver—inoperable cancer whose tumor is confined to the liver	A Phase II Study of Isolated Hepatic Perfusion (IHP) with Melphalan for Metastatic Unresectable Cancers of the Liver
Phase II	62	99-C-0125	Osteosarcoma (non-metastatic)	Osteosarcoma: Outcome of Therapy Based on Histologic Response. A Collaborative Effort of the POB/NCI, Texas Children's Hospital and University of Oklahoma
Phase I	63	99-C-0127	CLL, hairy cell leukemia, lymphoma, Waldenstrom's macroglobulinemia	Phase I and Pharmacokinetic Study of UCN-01 and Fludarabine in Relapsed or Refractory Low-Grade Lymphoid Malignancies
Phase I	64	99-C-0129	Esophageal cancer, lung cancer, pleural mesothelioma	Phase I Study of Decitabine Mediated Induction of Tumor Antigen and Tumor Suppressor Gene Expression in Patients with Cancers Involving the Lung, Esophagus, or Pleura
Phase II	65	99-C-0137	Adenocarinoma of the Ovary	Vaccine Therapy with Tumor-Specific p53 Peptides in Adult Patients with Low Burden Adenocarcinoma of the Ovary
Phase II	66	99-C-0138	Adenocarcinoma of the Breast or Ovary	Vaccine Therapy with Tumor-Specific p53 Peptides in Adult Patients with Adenocarcinoma of the Breast or ovary
Phase I	67	99-C-0143	CLL, Hodgkin's Disease, non Hodgkin's lymphoma, Multiple Myeloma, Acute Myelogenous Leukemia, Acute Lymphocytic Leukemia, Myelodysplastic Syndrome, Chronic Myelogenous Leukemia	Pilot Study of Donor Th2 Cells for the Prevention of Graft-Versus-Host Disease in the Setting of Non-Myeloablative, HLA-Matched Allogeneic Peripheral Blood Stem Cell Transplantation

*Trial also has a natural history component.

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix C: CSSC Recruitment Strategies

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Appendix C: CSSC Recruitment Strategies

	CSSC Original Strategy
1	Print Ad Placed
2	Advocacy Group Interactions
3	Matrix
4	Fast Track Sent
5	Doctor Fact Sheet
6	Patient Fact Sheet
7	Brochure
8	Physician Letter
9	Clinical Studies List FOCUS
10	Clinical Research Update
11	Web Links
12	Web Site Developed
13	Google (or other) promotion
14	PI Presentations Arranged
15	Newsletter Article
16	News Release
17	Print PSA

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix D: List of PRPL Protocols

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Appendix D: List of PRPL Protocols

Trial Type		Protocol	Medical Condition(s)	Study Title
Phase II	1	00-CH-0134	Childhood Obesity	Effects of Metformin on Energy Intake, Energy Expenditure, and Body Weight in Overweight Children with Insulin Resistance
Natural History	2	00-CH-0141*	Alkaptonuria	Clinical, Biochemical, and Molecular Investigations into Alkaptonuria
Natural History	3	00-CH-0219	Turner Syndrome	Turner Syndrome: Genotype and Phenotype
Phase II	4	00-D-0037	Temperomandibular Joint Disorder (TMJ)	The Role of Cytokines as Inflammatory Mediators in Painful Temporomandibular Joints
Natural History	5	00-D-0066	Fibromyalgia	Screening Protocol to Evaluate Patients for Approved Studies
Phase II	6	00-DK-0042	Focal Segmental Glomerulosclerosis (FSGS)	Pirfenidone in Focal Segmental Glomerulosclerosis Phase II Study
Phase II	7	00-DK-0166	Beta Thalassemia	A Pilot Study of 5-Azacytidine and Oral Sodium Phenylbutyrate in Severe Thalassemia Phase II Study of Azacitidine and Phenylbutyrate in Patients With Thalassemia Major 2 studies listed—1st completed 2nd terminated see which one we have
Natural History	8	01-CC-0135	Swallowing Difficulty	Effect of Task on Oral Pressure Dynamics During Swallowing
Phase II	9	01-CH-0086	Infantile Neuronal Ceroid Lipofuscinosis (INCL)	A Combination Therapy with Cystagon and N-Aetylcysteine for INCL Patients
Phase II	10	01-D-0076	Sciatic Back Pain	Morphine, Nortriptyline and Their Combination in Sciatica Treatment
Phase I	11	01-EI-0214	Macular Edema	Randomized Masked Study to Evaluate the Use of Vitamin E in the Treatment of Uveitis-Associated Macular Edema
Natural History	12	01-H-0119	Epithelial Progenitor Cells (EPC)	Endothelial Progenitor Cells and Risk Factors for Coronary Artery Disease
Phase II	13	01-H-0162	Stem Cell Transplant	Ex Vivo Selective Depletion of Alloreactive Donor T-Lymphocytes Utilizing RFT5-SMPT-dgA, a Specific Anti-Interleukin-2 Receptor Immunotoxin: Reducing GVHD Risk Associated with HLA-Matched Nonmyeloablative Peripheral Blood Stem Cell Transplantation
Phase II	14	01-N-0147	Dystonia	Trial of Amlodipine Combined with Botulinum Toxin Injections for Focal Dystonia
Natural History	15	02-AR-0267	Systemic Lupus Erythematosis (SLE)	Role of the Antibody Against NR2 Glutamate Receptor in Cognitive Dysfunction in Patients with Systemic Lupus Erythematosus
Phase I	16	02-AR-0272	Systemic Lupus Erythematosis (SLE)	A Phase I, Open-Labeled, Dose-Ascending Clinical Trial of Immunotherapy of MRA, A Humanized Anti-IL 6 Receptor Monoclonal Antibody, In Patients with Systemic Lupus Erythematosus
Phase II	17	02-CH-0287	Fibroids	Treatment of Leiomyomata with the Selective Progesterone Receptor Modulator CDB-2914
Phase I	18	02-I-0316	Small Pox	A Phase I/II Clinical Trial of Modified Vaccinia Virus Ankara (MVA) to Evaluate its Safety, Dosing Schedule, Immunogenicity and Protective Efficacy Against Dryvax Challenge in Vaccinia-Naive Individuals

Trial Type		Protocol	Medical Condition(s)	Study Title
Natural History	19	03-AR-0130	Ankylosing Spondylitis	Genetic Determinants of Ankylosing Spondylitis Severity – Cross Sectional Study
Natural History	20	03-AR-0131	Ankylosing Spondylitis	Genetic Determinants of Ankylosing Spondylitis Severity – Longitudinal Study
Natural History	21	03-AR-0133	Rheumatoid Arthritis (RA)	Clinically Important Changes in Rheumatoid Arthritis
Phase II	22	03-DK-0170	Sickle Cell Anemia	Nonmyeloablative Allogeneic Peripheral Blood Mobilized Hematopoietic Precursor Cell Transplantation For Severe Congenital Anemias Including Sickle Cell Anemia, Thalassemia, and Diamond Blackfan Anemia
Natural History	23	90-CC-0168	ACL Disorders	Anterior Cruciate Ligament (ACL)
Natural History	24	90-CC-0168B**	Leg Weakness	Stroke Balance Study
Natural History	25	91-DK-0214	Hepatitis-All	Evaluation of Patients with Liver Disease
Phase II	26	91-N-0225	Gaucher's Disease	Clinical and Biochemical Effects of Macrophage-Targeted Glucocerebrosidase on Neurological Involvement in Neuronopathic Gaucher's Disease
Phase II	27	93-CH-0054	Turner Syndrome	The Relative Effects of Androgen, Estrogen, and the Combination of Androgen and Estrogen on Growth Rate, GH Binding Protein, IGF-I, and Cognitive Function in Growth Hormone-Treated Girls with Turner Syndrome
Natural History	28	93-N-0202	Dystonia	Diagnosis and Natural History Protocol for Patients with Different Neurological Conditions
Natural History	29	94-DK-0127	Focal Segmental Glomerulosclerosis (FSGS)	Pathogenesis of Focal Segmental Glomerulosclerosis
Natural History	30	94-DK-0133	Focal Segmental Glomerulosclerosis (FSGS)	Genetic Markers for Focal Segmental Glomerulosclerosis
Natural History	31	95-N-0121	Fabry's Disease	The Natural History and Pathogenesis of Fabry Disease
Natural History	32	96-N-0088	Stuttering	Characteristics of Idiopathic Familial Speech Disorders
Phase II	33	99-CH-0012	Endometriosis	The Safety and Effectiveness of Surgery with or without Raloxifene (Evista™ (Trademark), Lilly) for the Treatment of Pelvic Pain Caused by Endometriosis
Phase II	34	99-H-0057	Pulmonary Sarcoidosis	Treatment of Pulmonary Sarcoidosis with Pentoxifylline

* After 2003, this protocol number was changed to 00-HG-0141 when the Principal Investigator moved to the National Human Genome Research Institute.

** Multiple related studies were conducted under protocol number 90-CC-0168.

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix E: PRPL Recruitment Strategies

CSR Incorporated
Consulting Services & Research

Appendix E: PRPL Recruitment Strategies

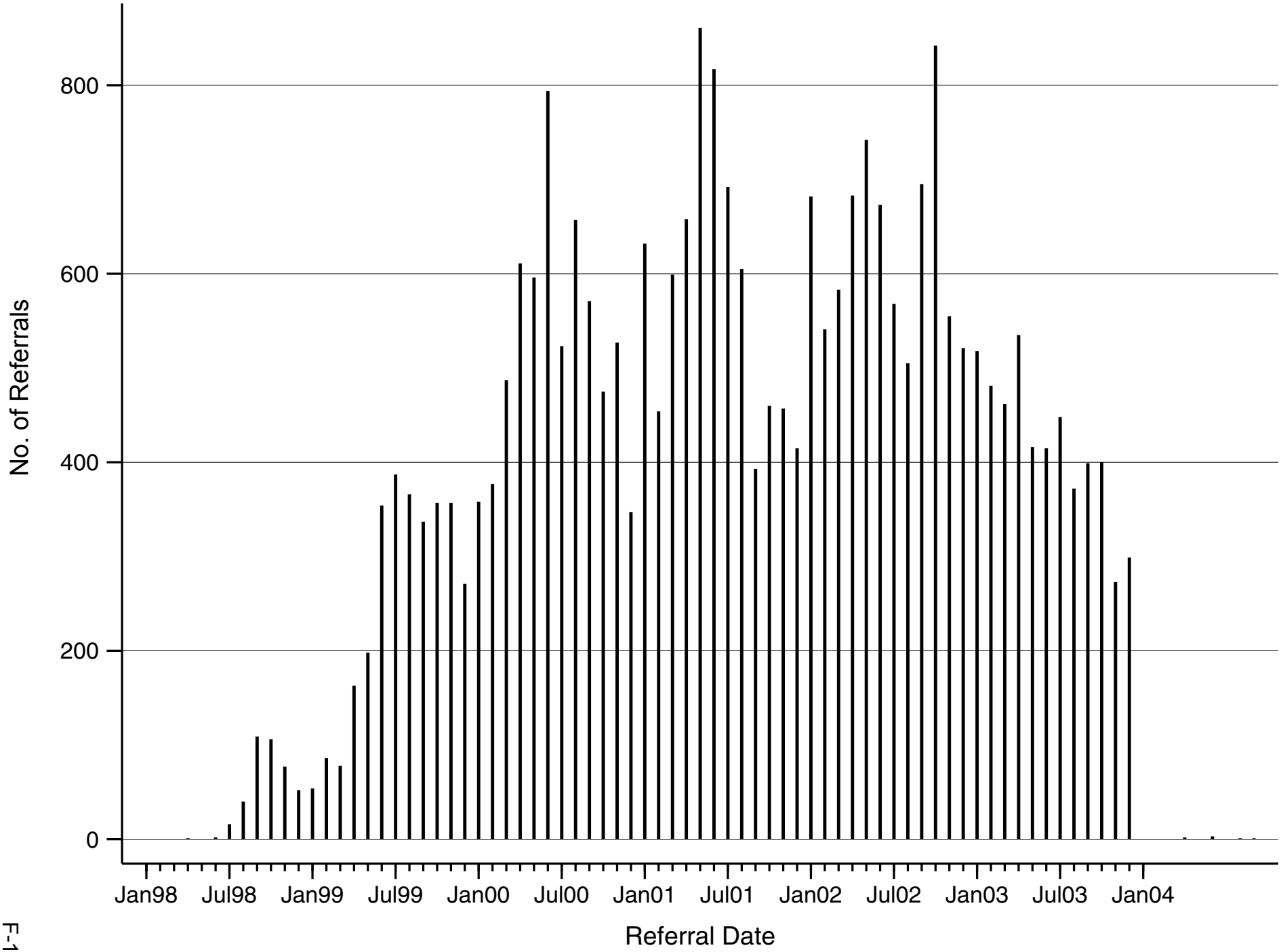
	Strategies
1	Advertisements
2	Community Relations
3	Mailings/Flyers
4	Marketing/Web Links
5	Presentations
6	Press Articles
7	PSA
8	Standard PRPL Outlets

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix F: CSSC Monthly Referrals

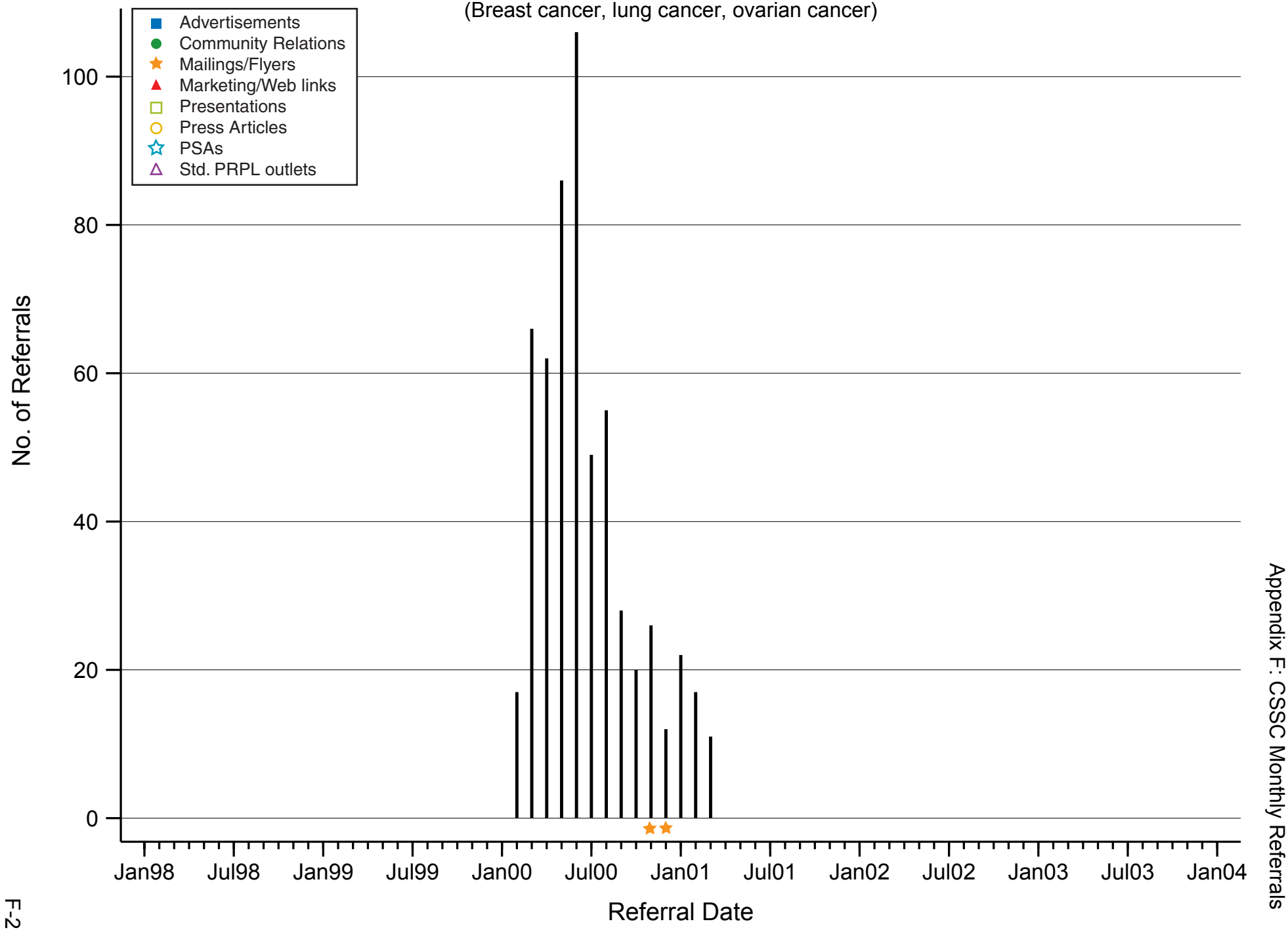
CSR Incorporated
Consulting Services & Research

Appendix F: CSSC Monthly Referrals—Distribution of 67 Protocols



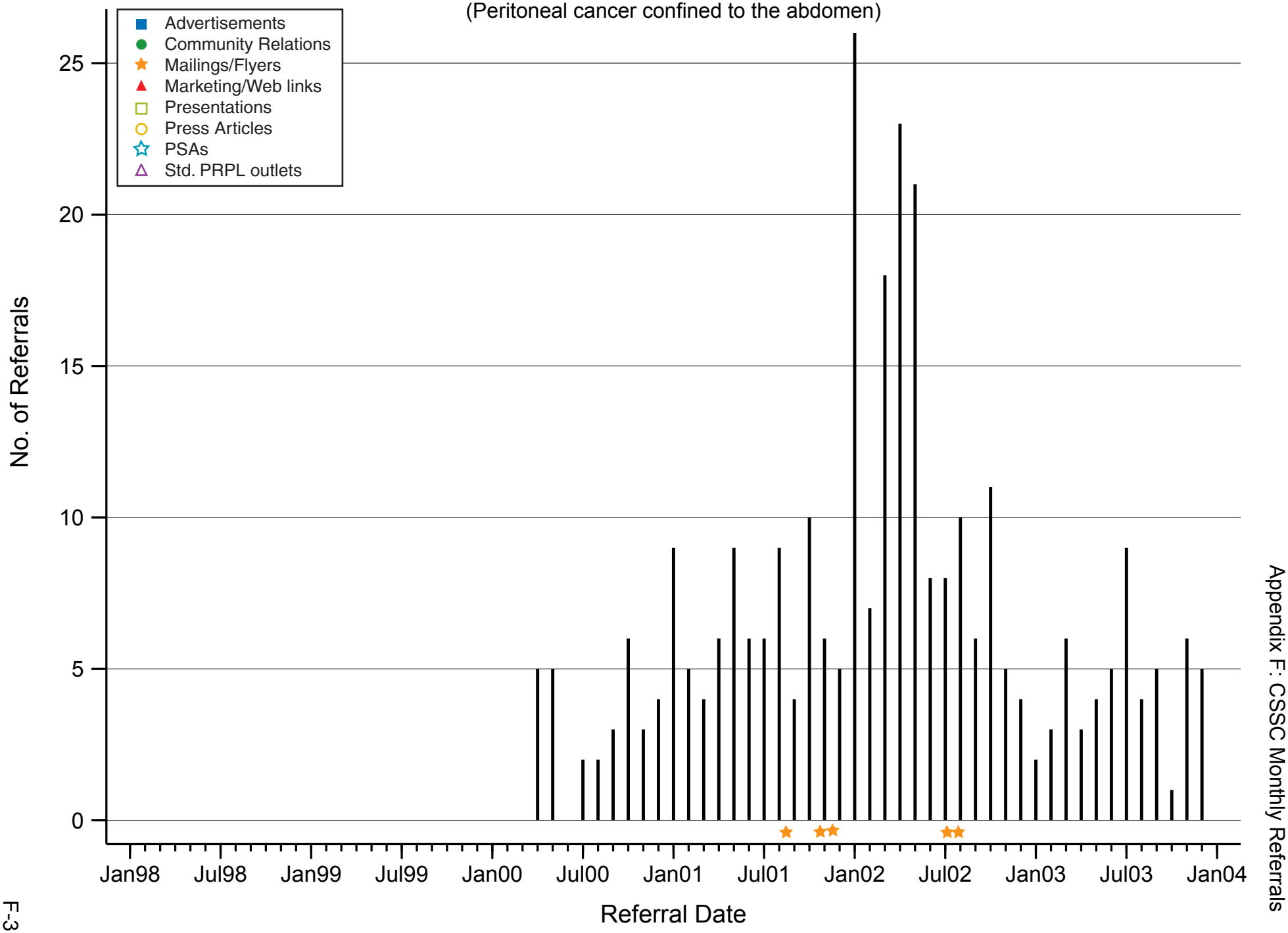
Monthly Referral Distribution of 00-C-0044

(Breast cancer, lung cancer, ovarian cancer)



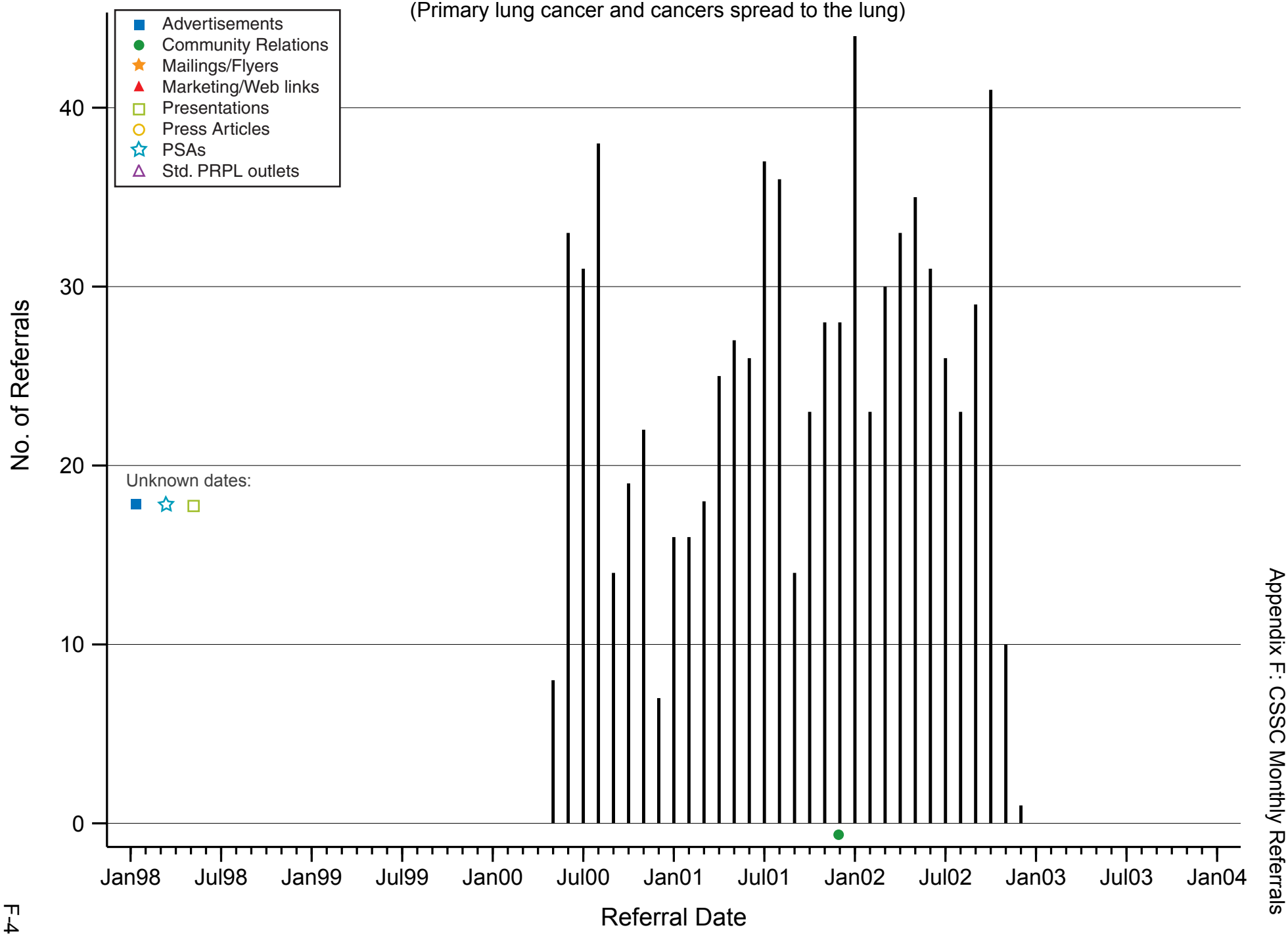
Monthly Referral Distribution of 00-C-0069

(Peritoneal cancer confined to the abdomen)



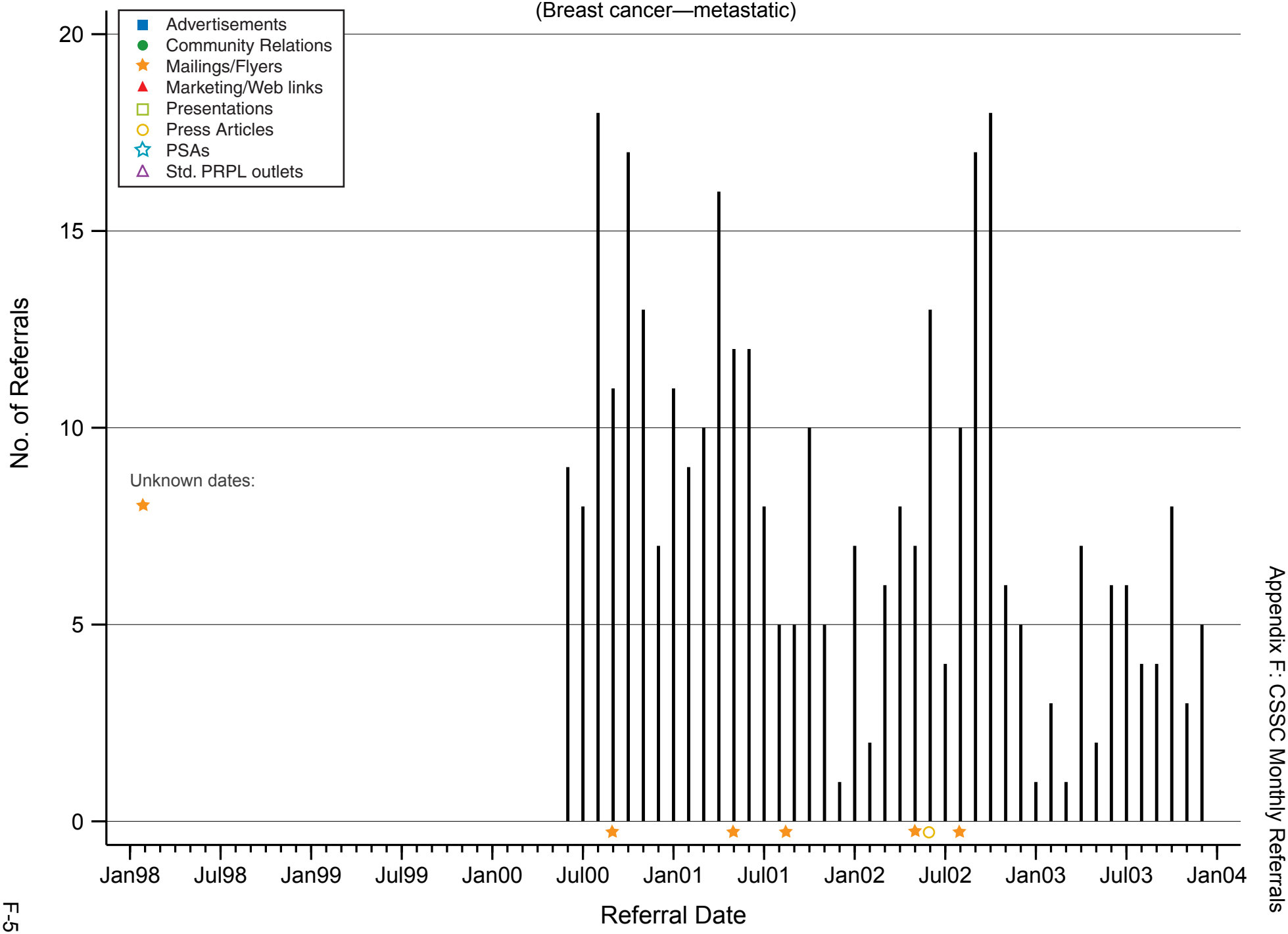
Monthly Referral Distribution of 00-C-0088

(Primary lung cancer and cancers spread to the lung)



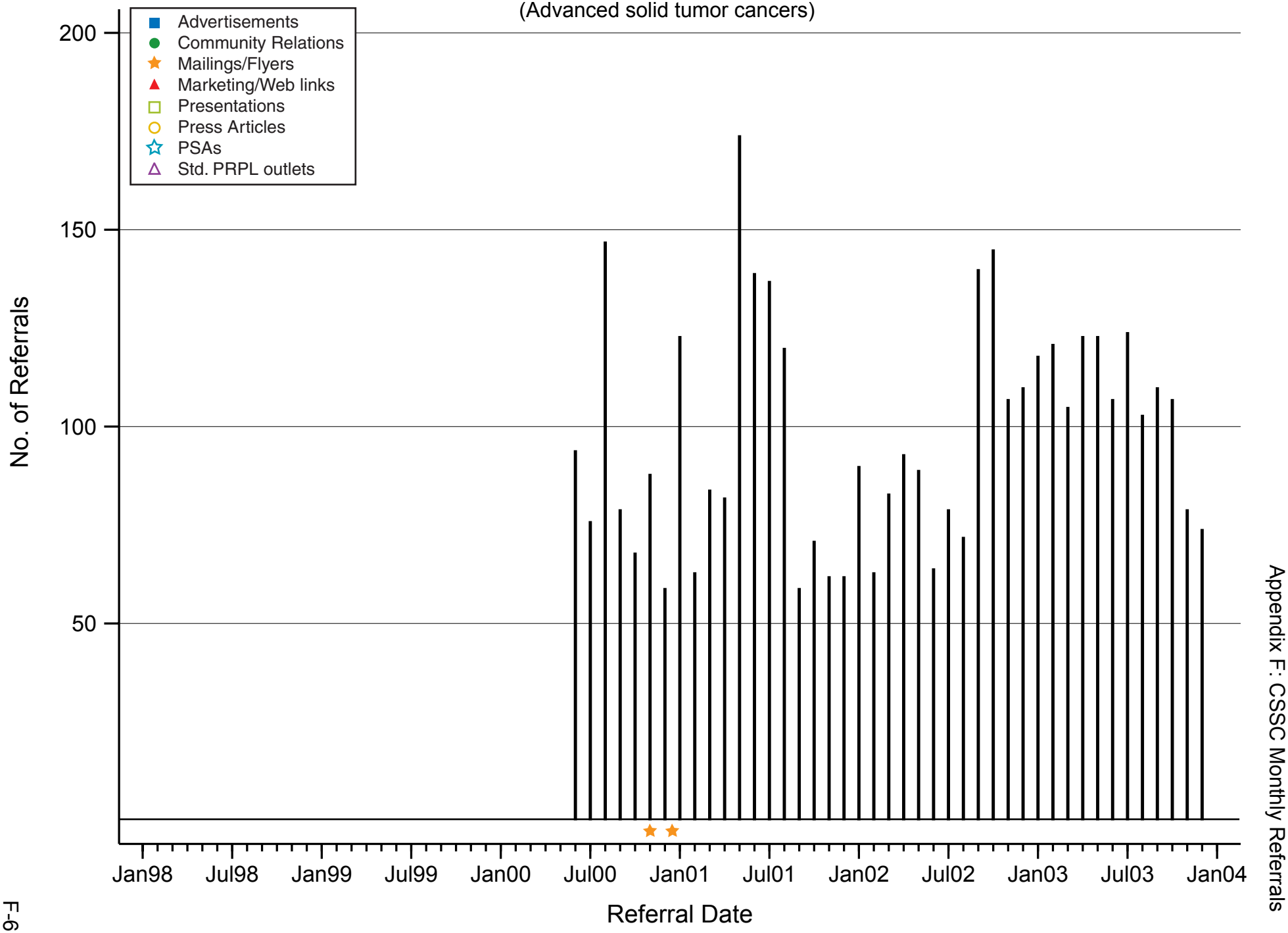
Monthly Referral Distribution of 00-C-0119

(Breast cancer—metastatic)



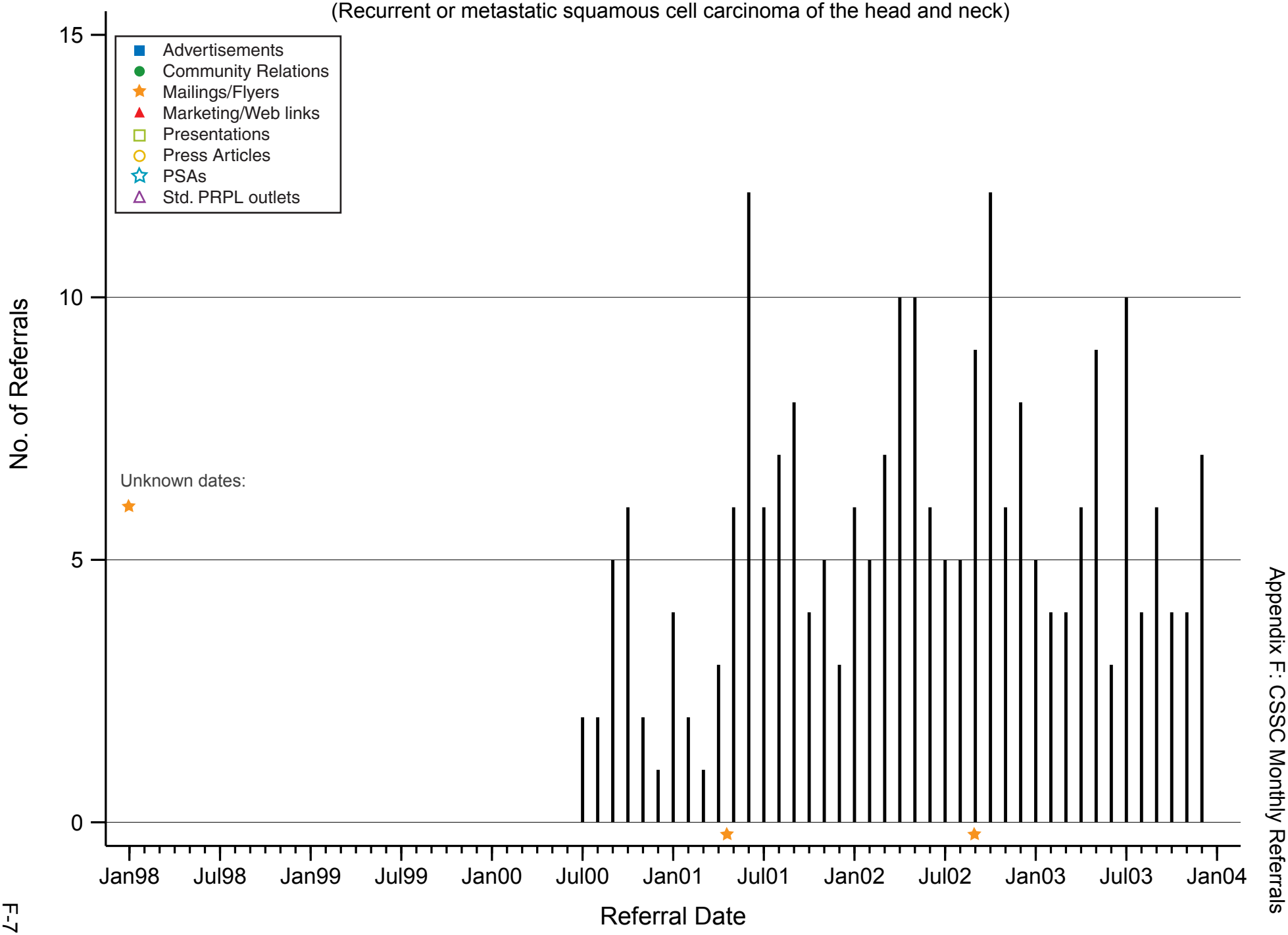
Monthly Referral Distribution of 00-C-0121

(Advanced solid tumor cancers)



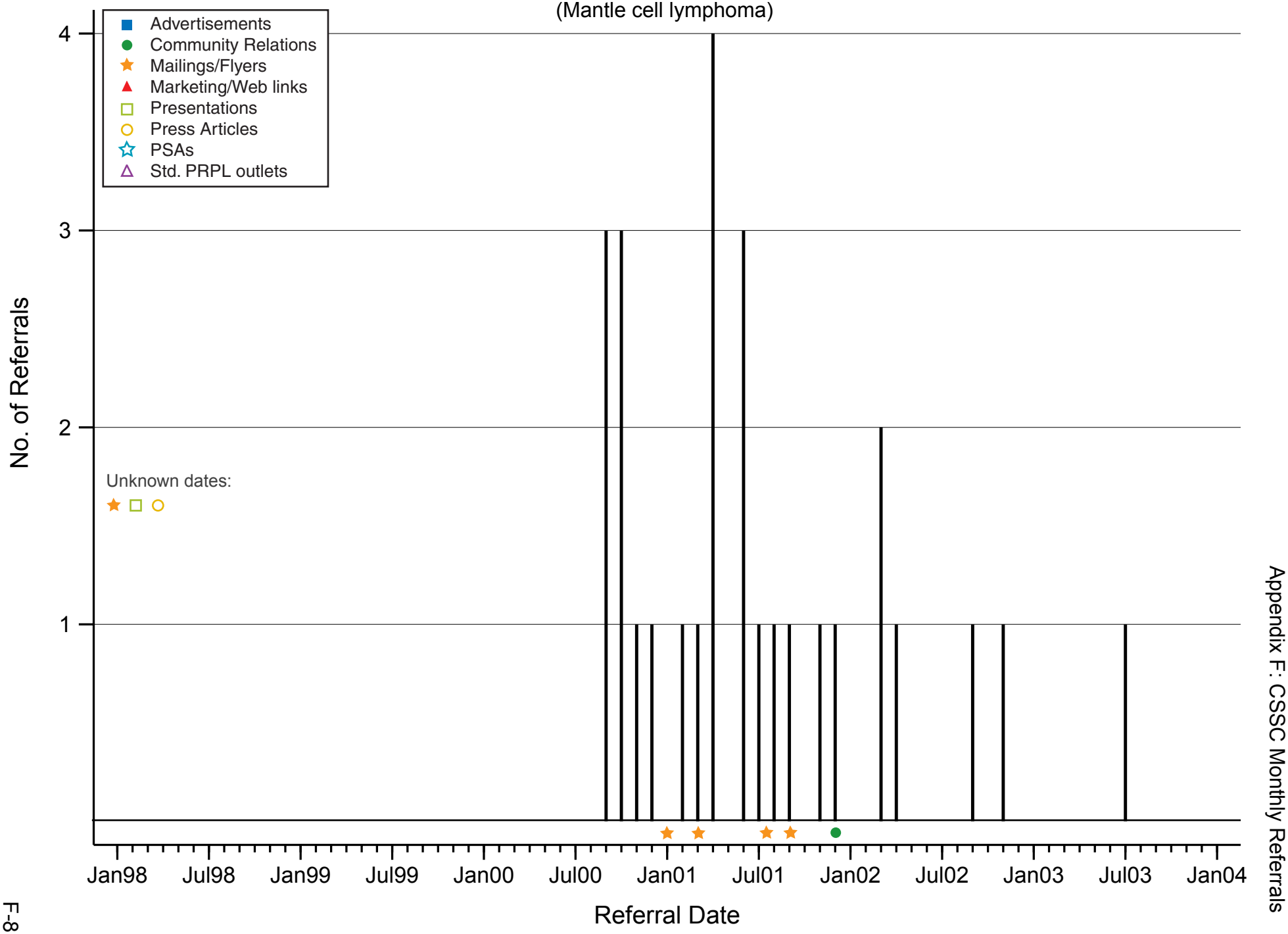
Monthly Referral Distribution of 00-C-0128

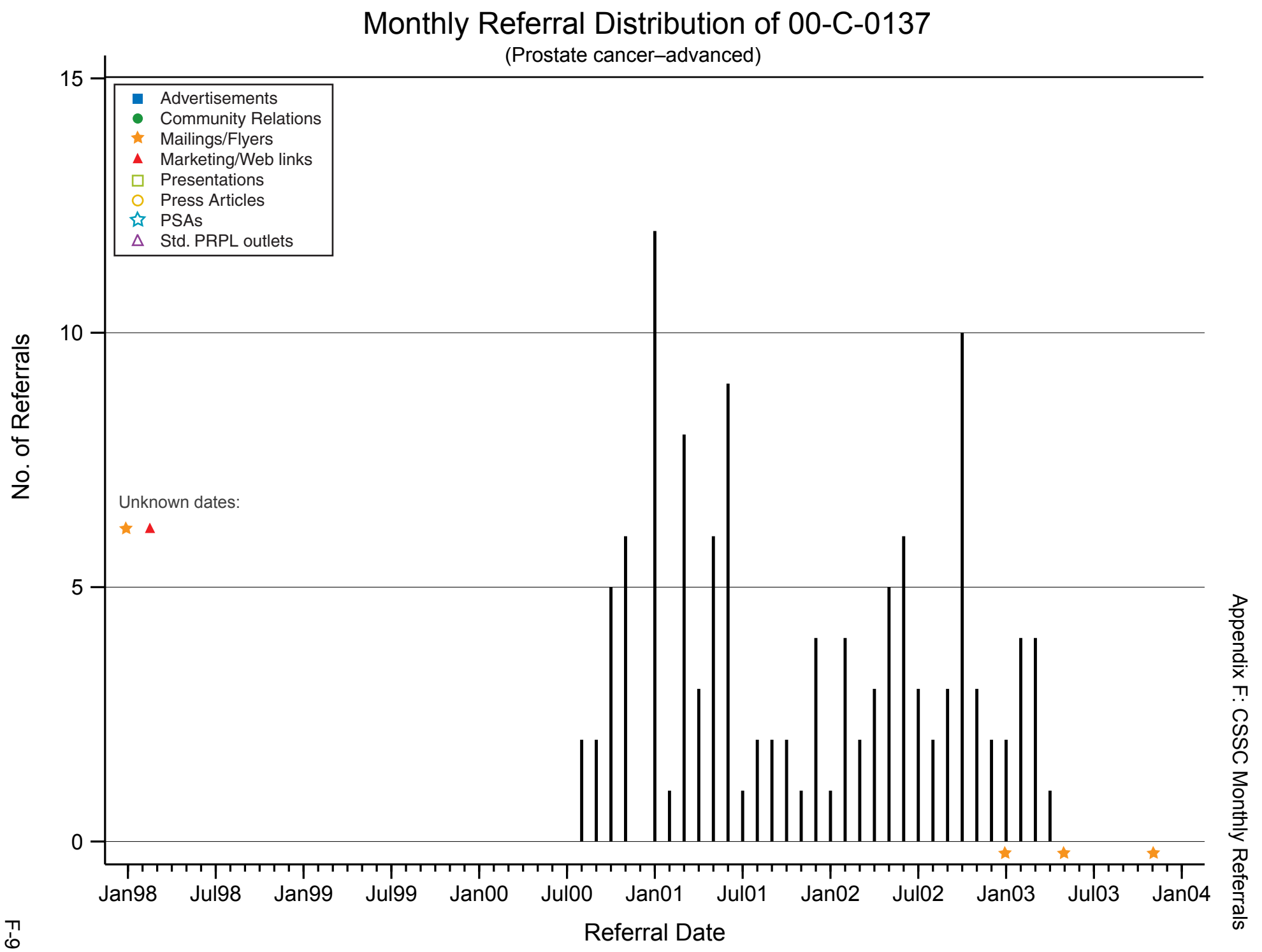
(Recurrent or metastatic squamous cell carcinoma of the head and neck)



Monthly Referral Distribution of 00-C-0133

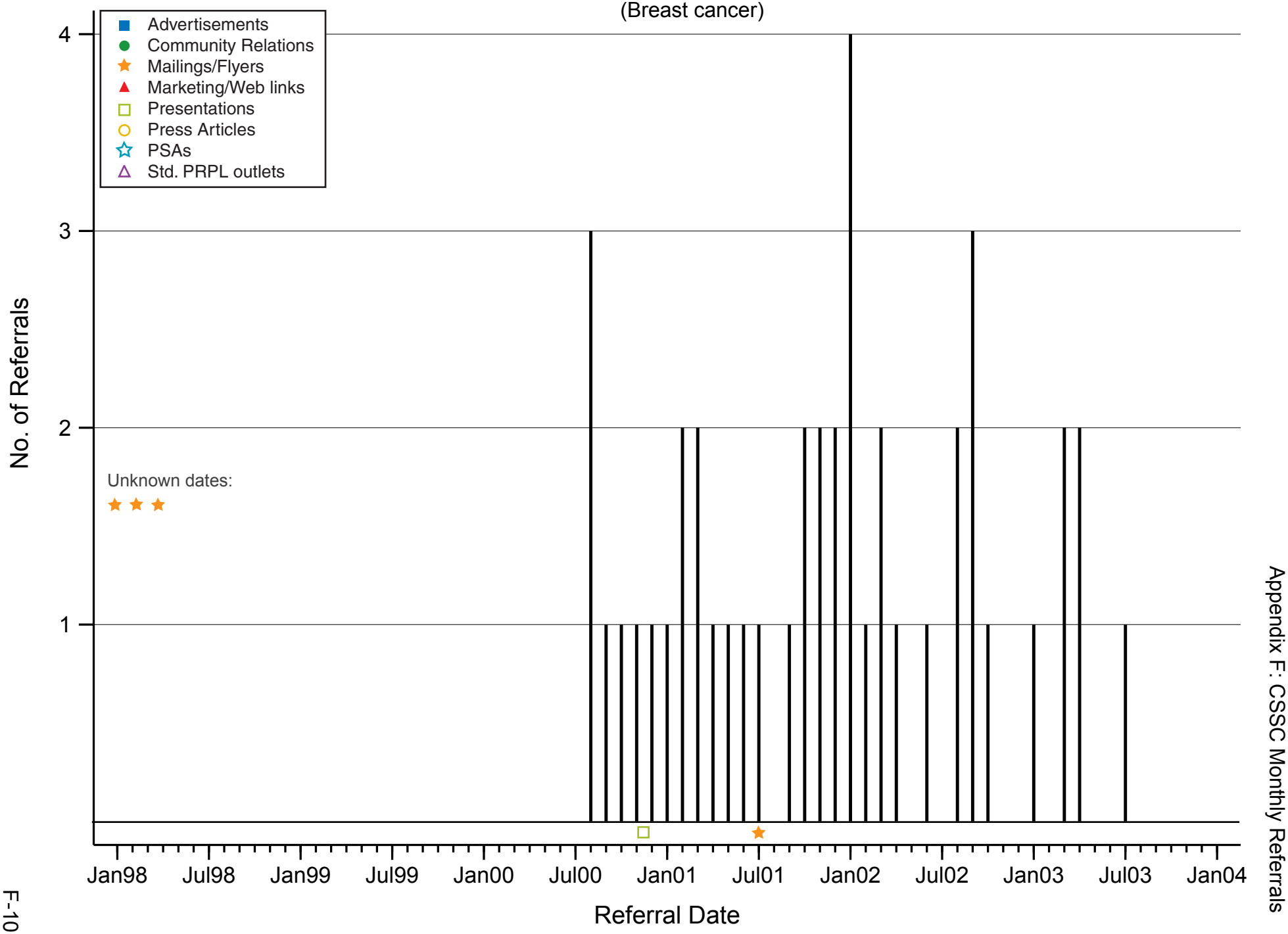
(Mantle cell lymphoma)




Monthly Referral Distribution of 00-C-0137
(Prostate cancer–advanced)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown dates:
No. of Referrals
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

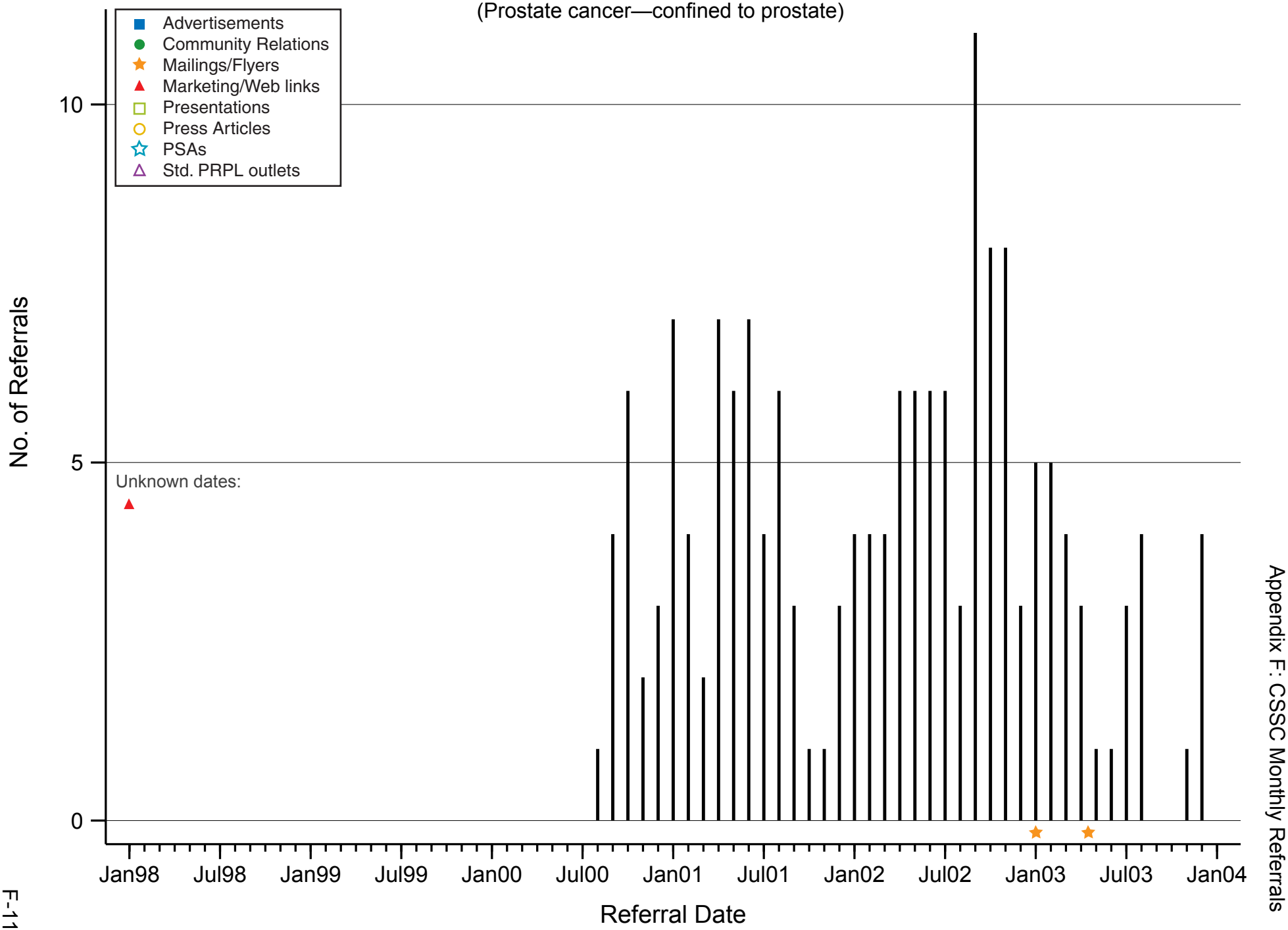
Monthly Referral Distribution of 00-C-0149

(Breast cancer)



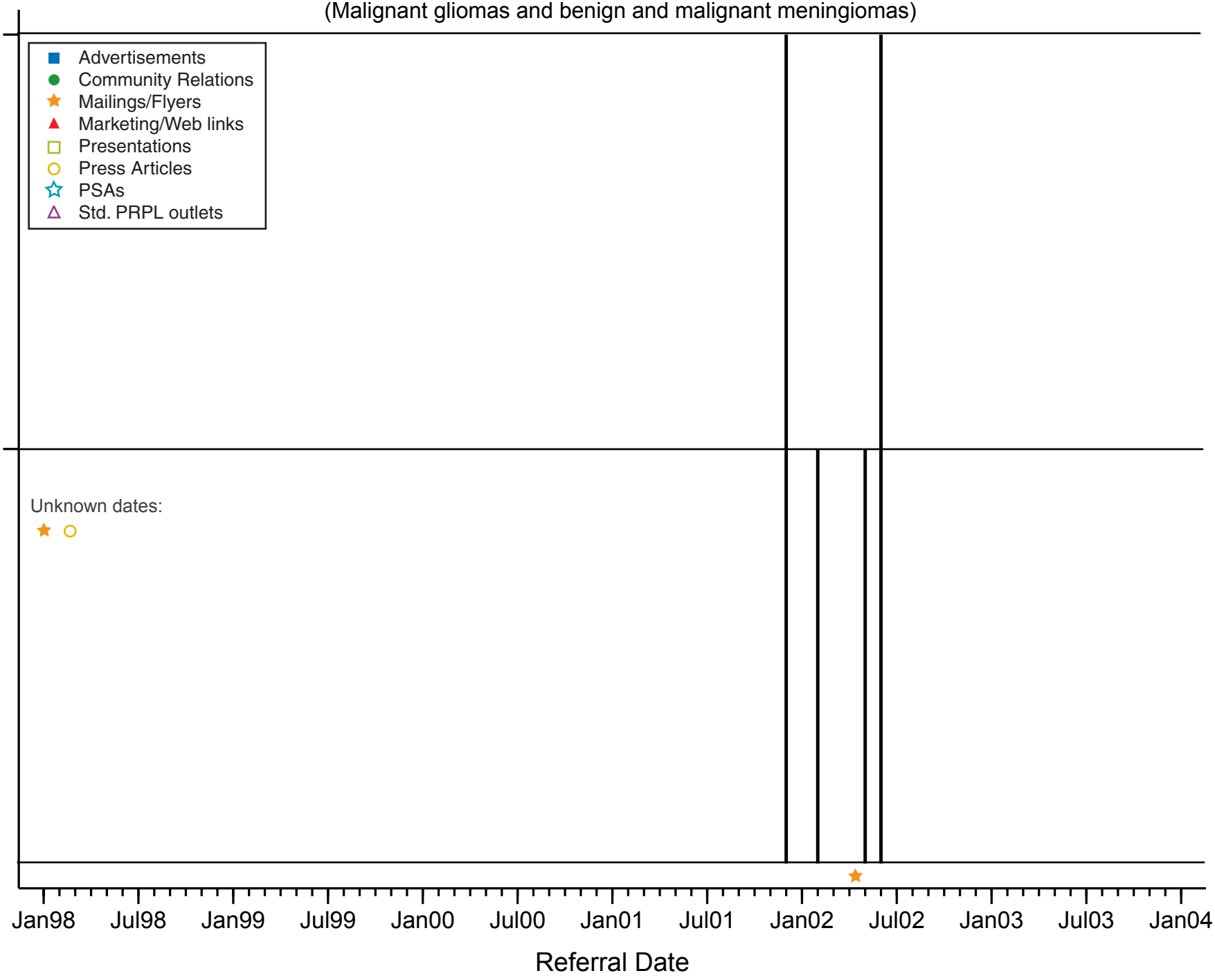
Monthly Referral Distribution of 00-C-0154

(Prostate cancer—confined to prostate)



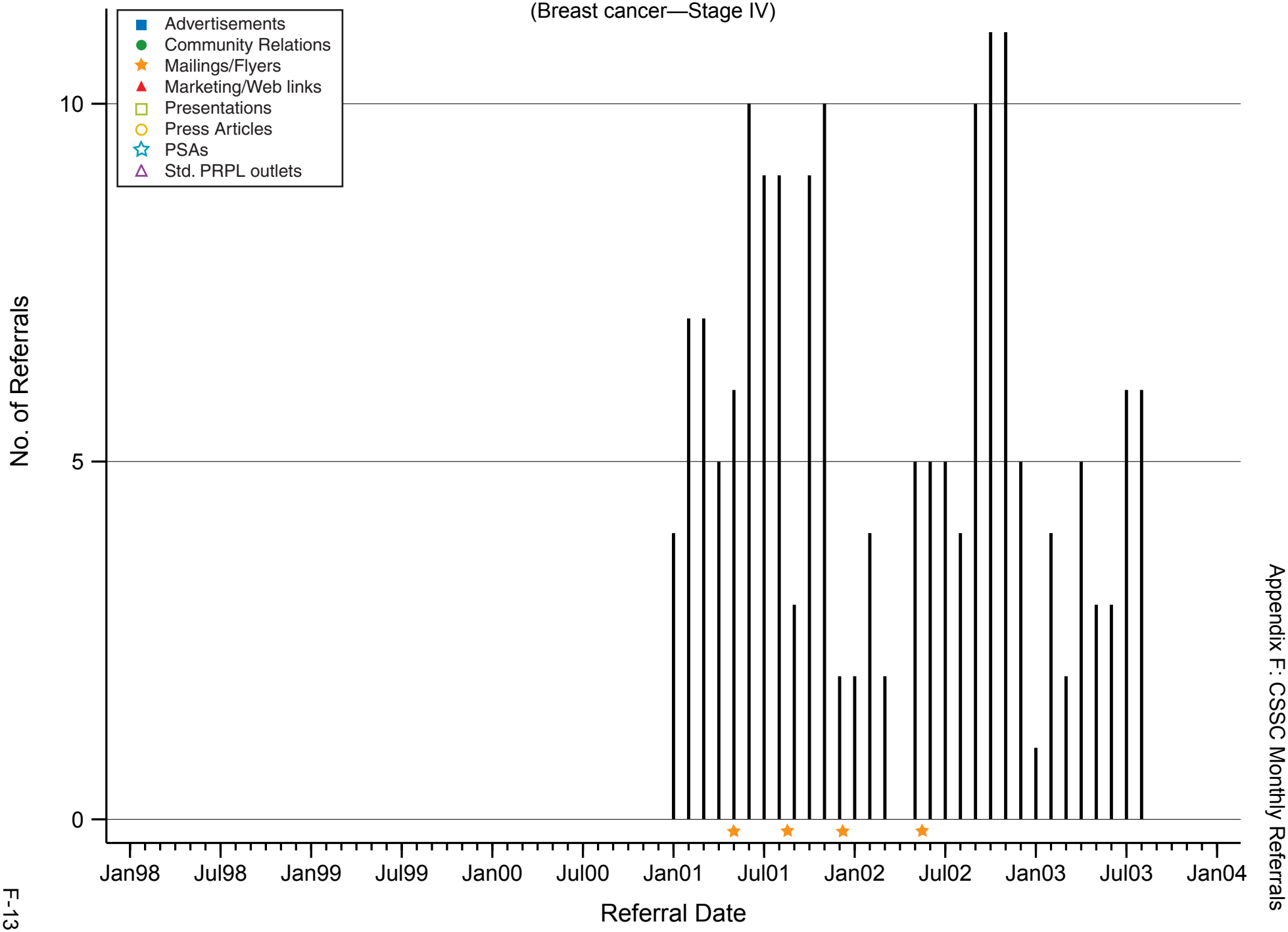
Monthly Referral Distribution of 00-C-173

(Malignant gliomas and benign and malignant meningiomas)



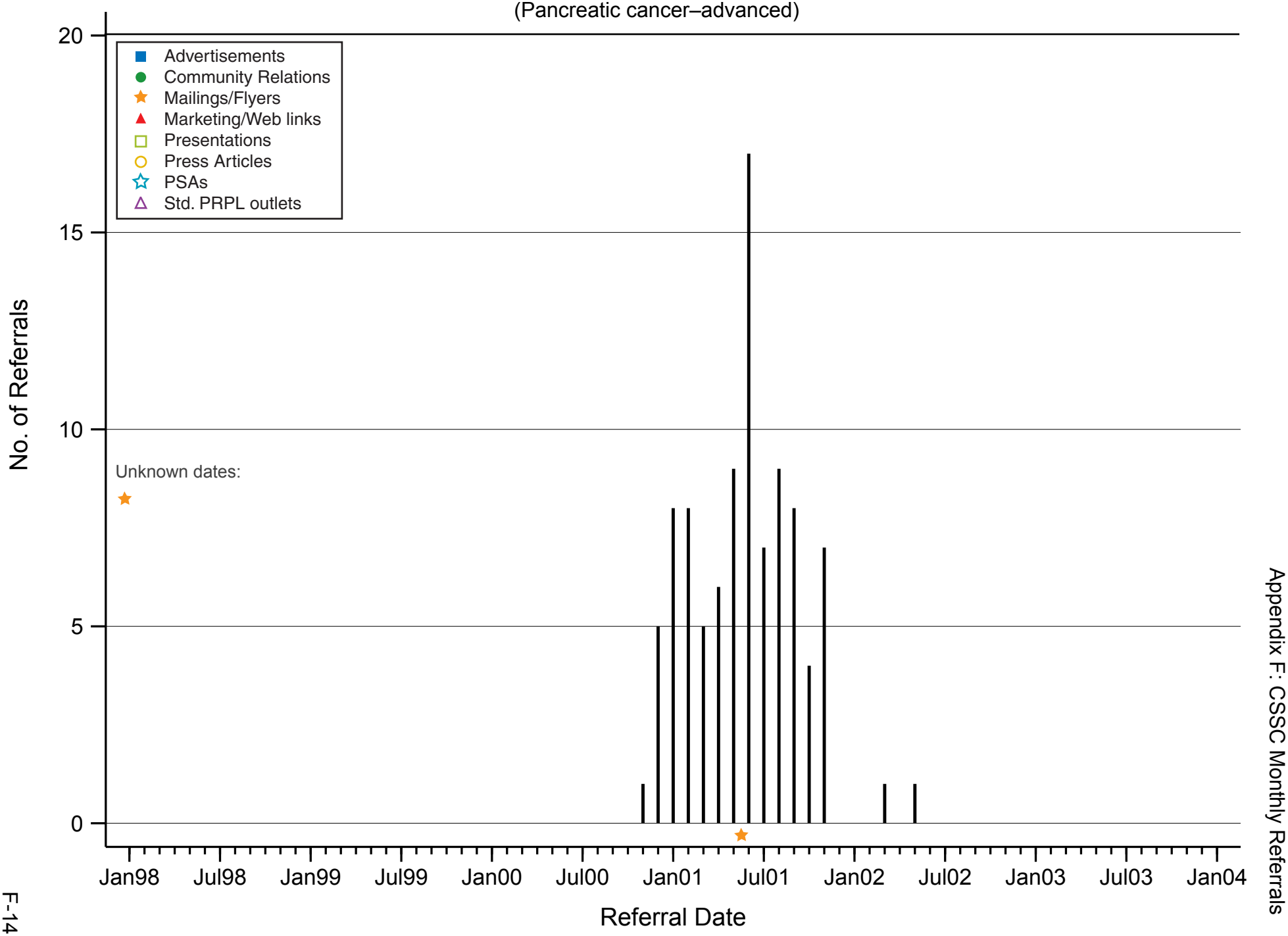
Monthly Referral Distribution of 00-C-0206

(Breast cancer—Stage IV)



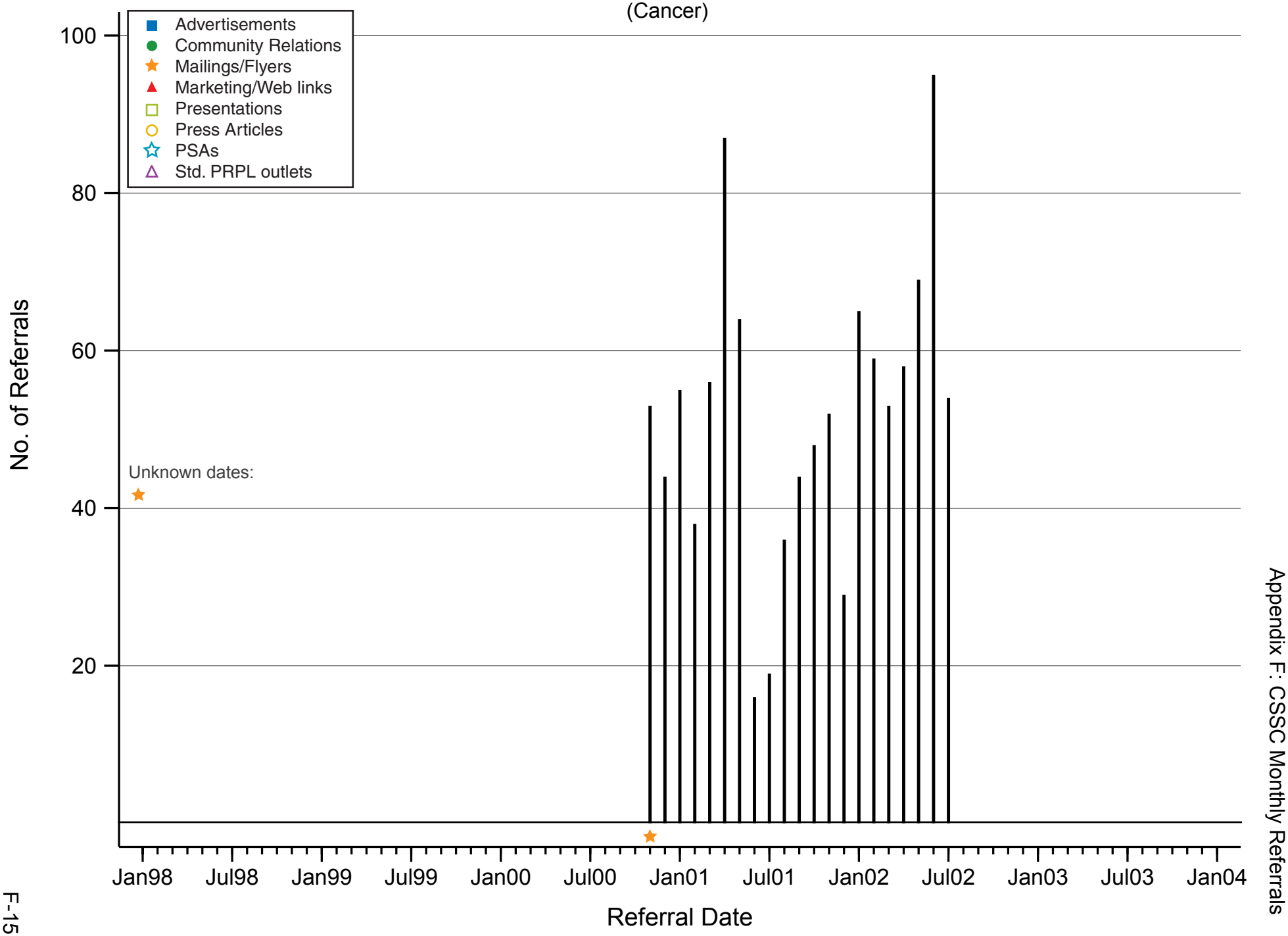
Monthly Referral Distribution of 00-C-0218

(Pancreatic cancer–advanced)



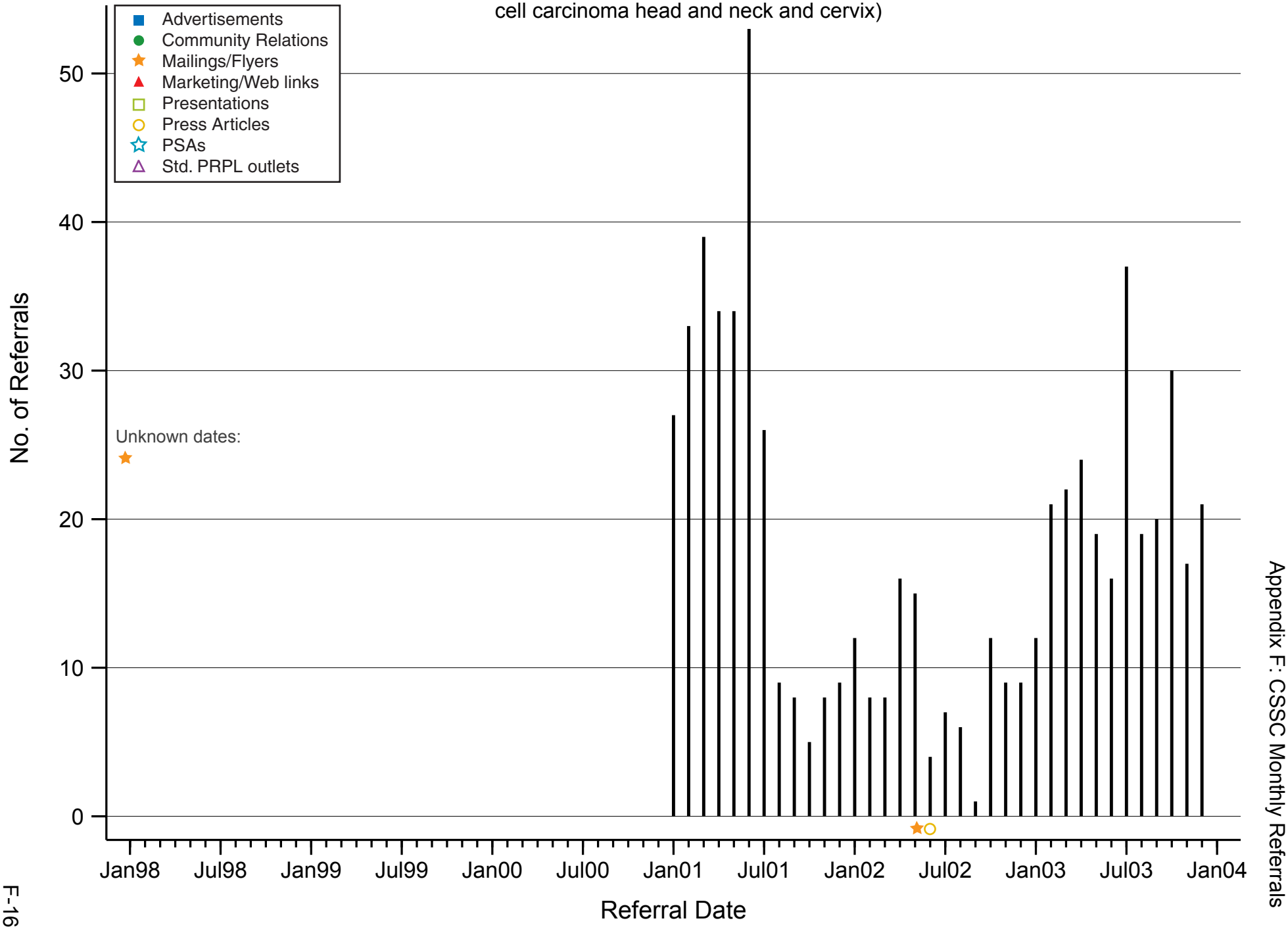
Monthly Referral Distribution of 00-C-0224

(Cancer)



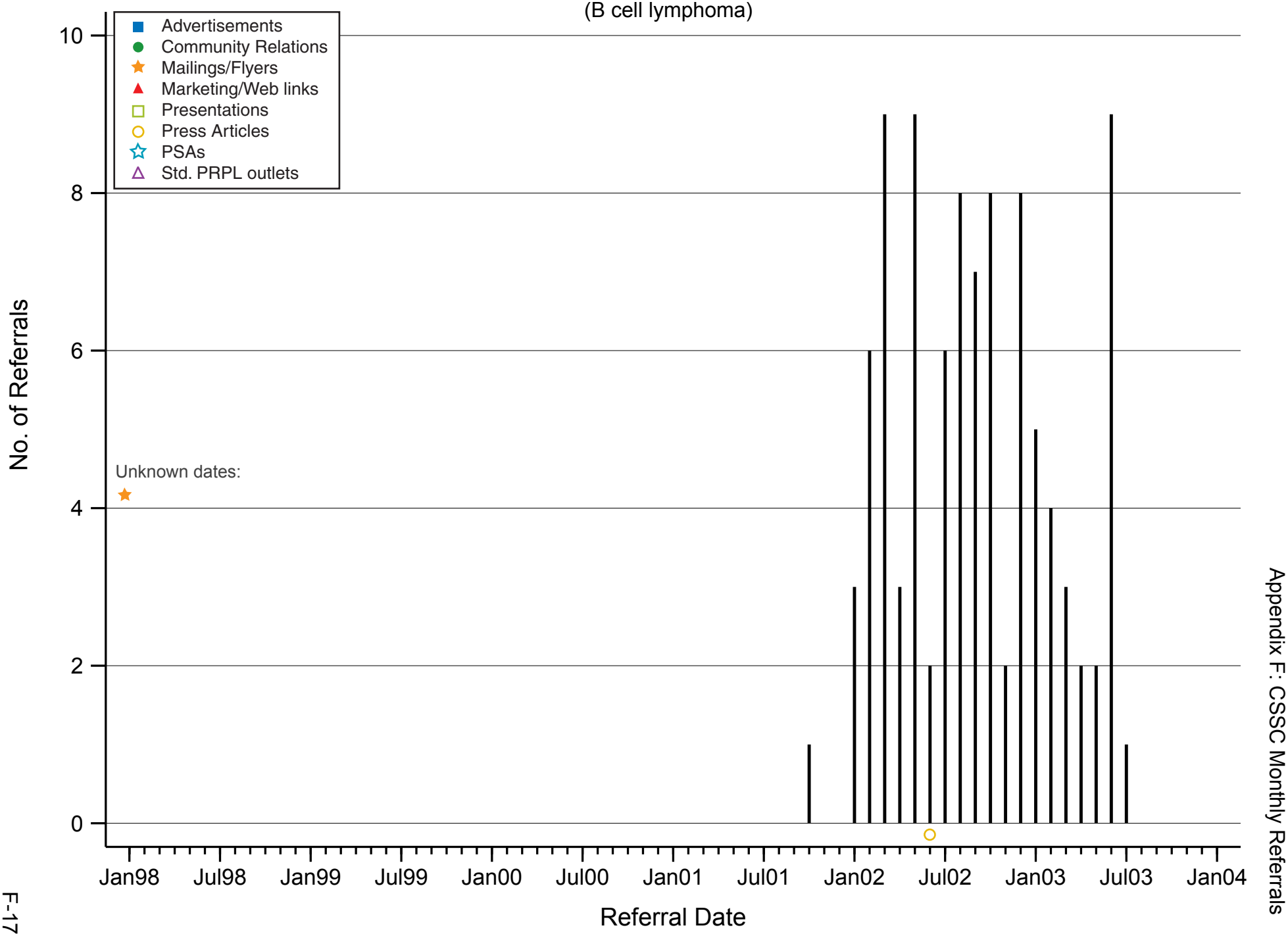
Monthly Referral Distribution of 01-C-0011

(Malignant mesothelioma, ovarian cancer, pancreatic cancer, squamous cell carcinoma head and neck and cervix)



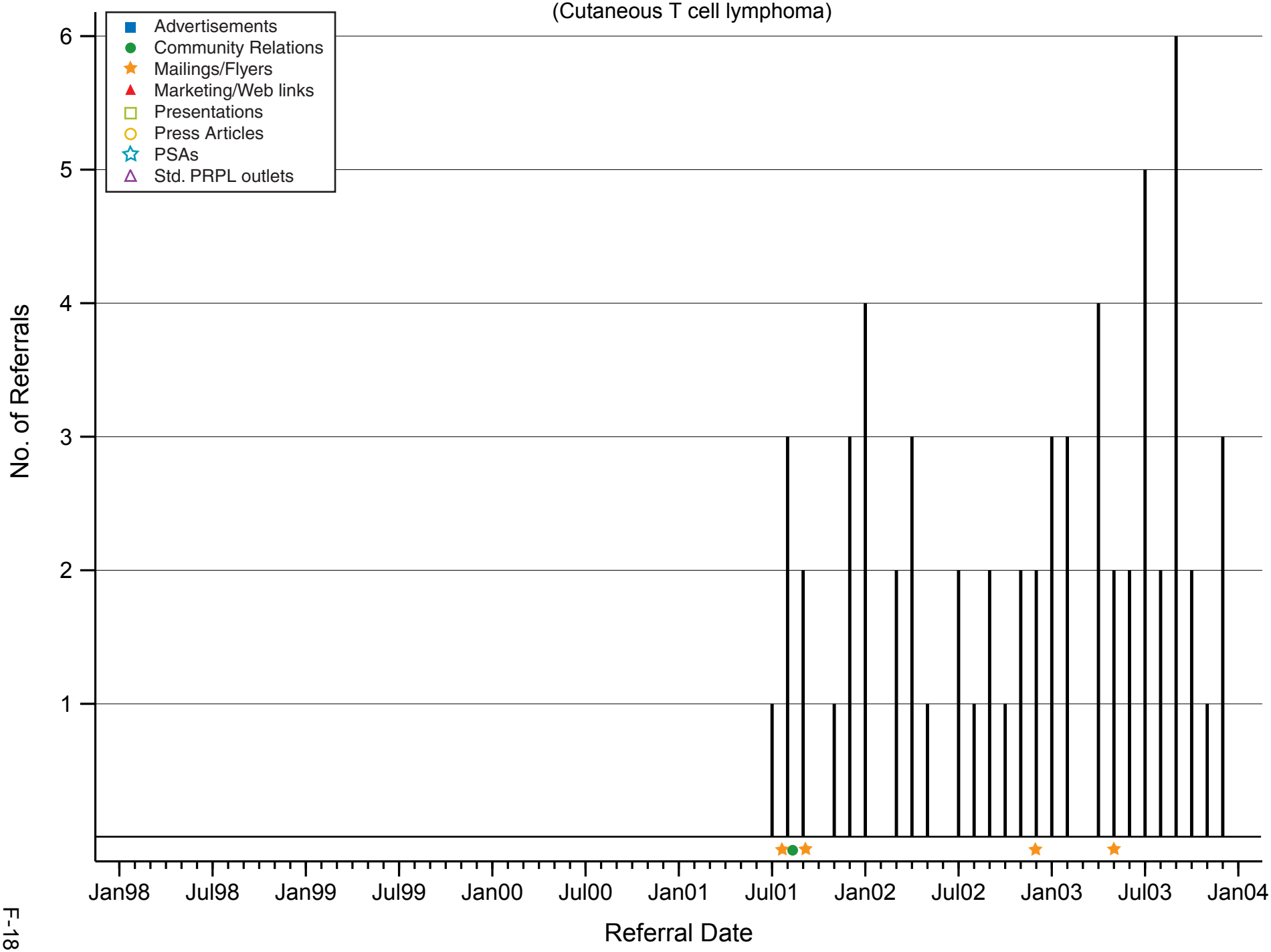
Monthly Referral Distribution of 01-C-0021

(B cell lymphoma)



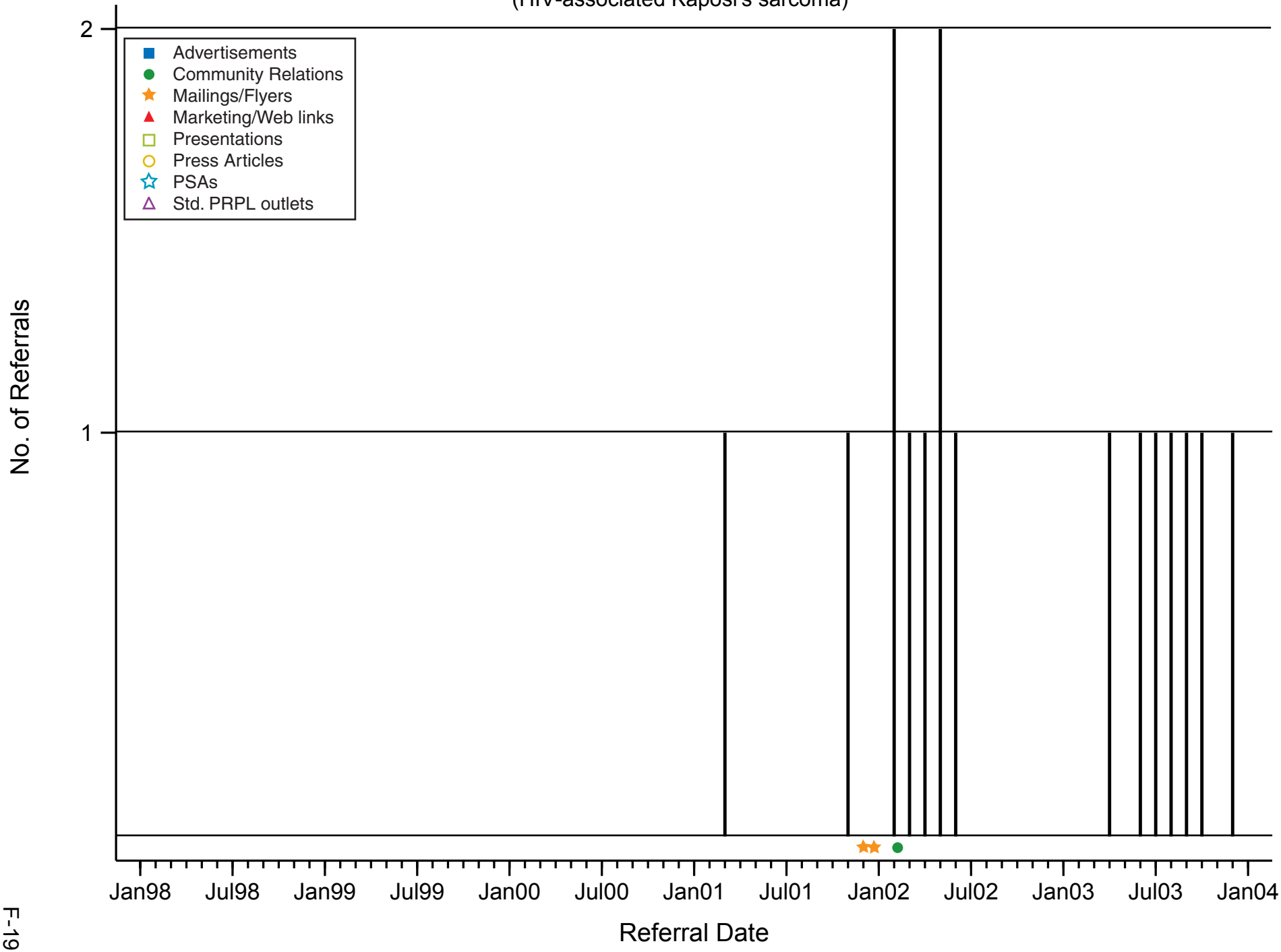
Monthly Referral Distribution of 01-C-0049

(Cutaneous T cell lymphoma)



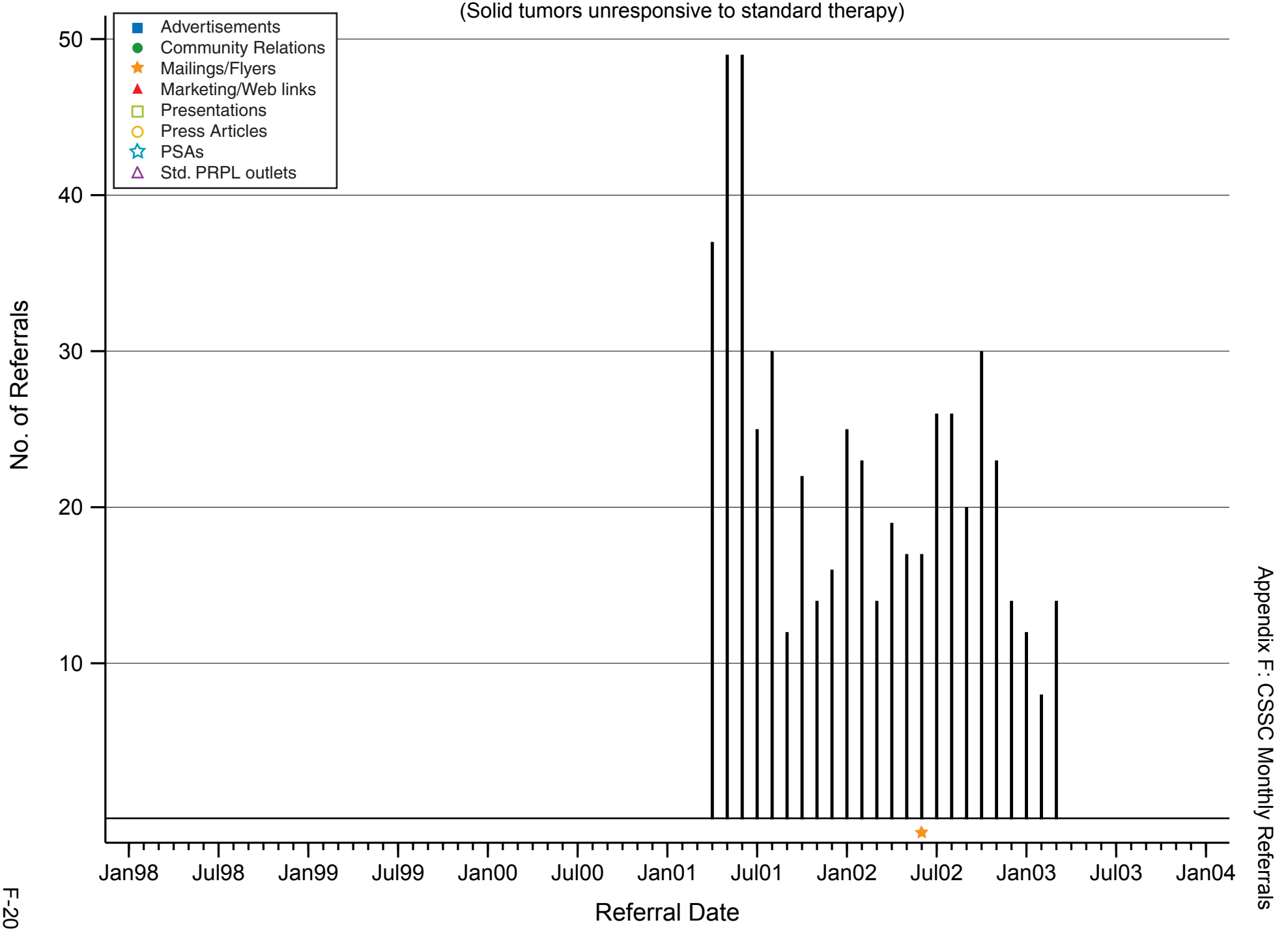
Monthly Referral Distribution of 01-C-0067

(HIV-associated Kaposi's sarcoma)



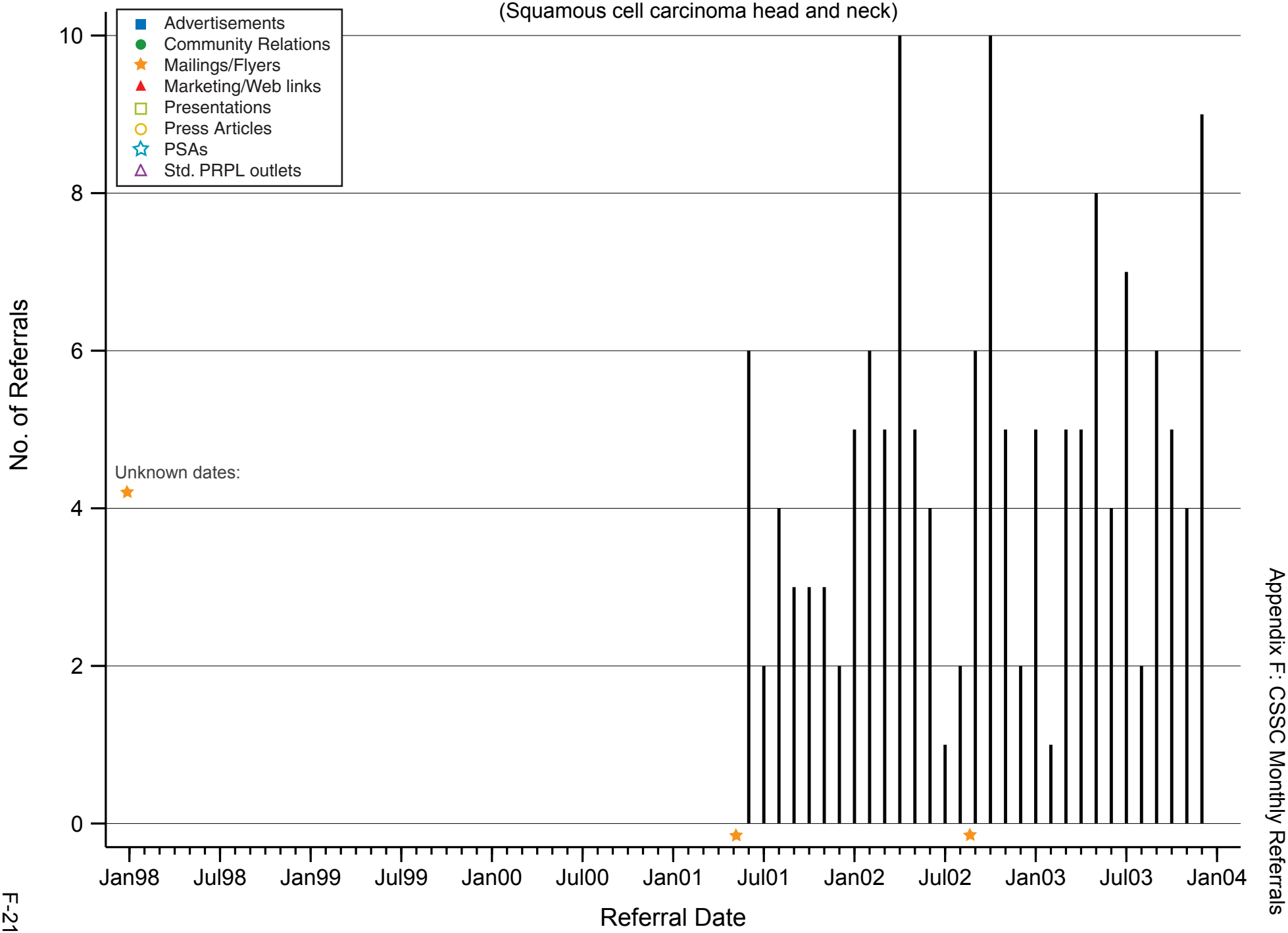
Monthly Referral Distribution of 01-C-0082

(Solid tumors unresponsive to standard therapy)



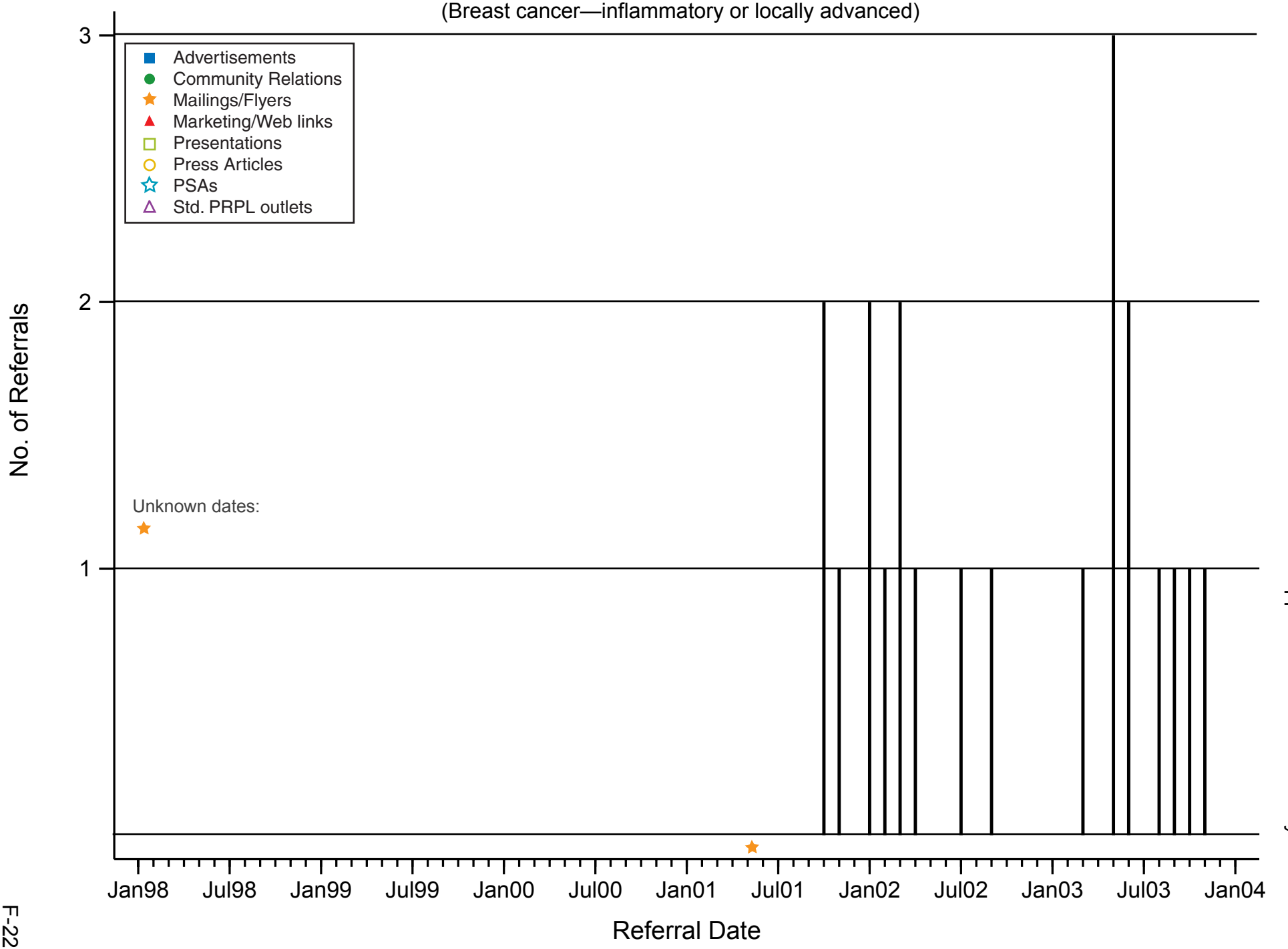
Monthly Referral Distribution of 01-C-0104

(Squamous cell carcinoma head and neck)



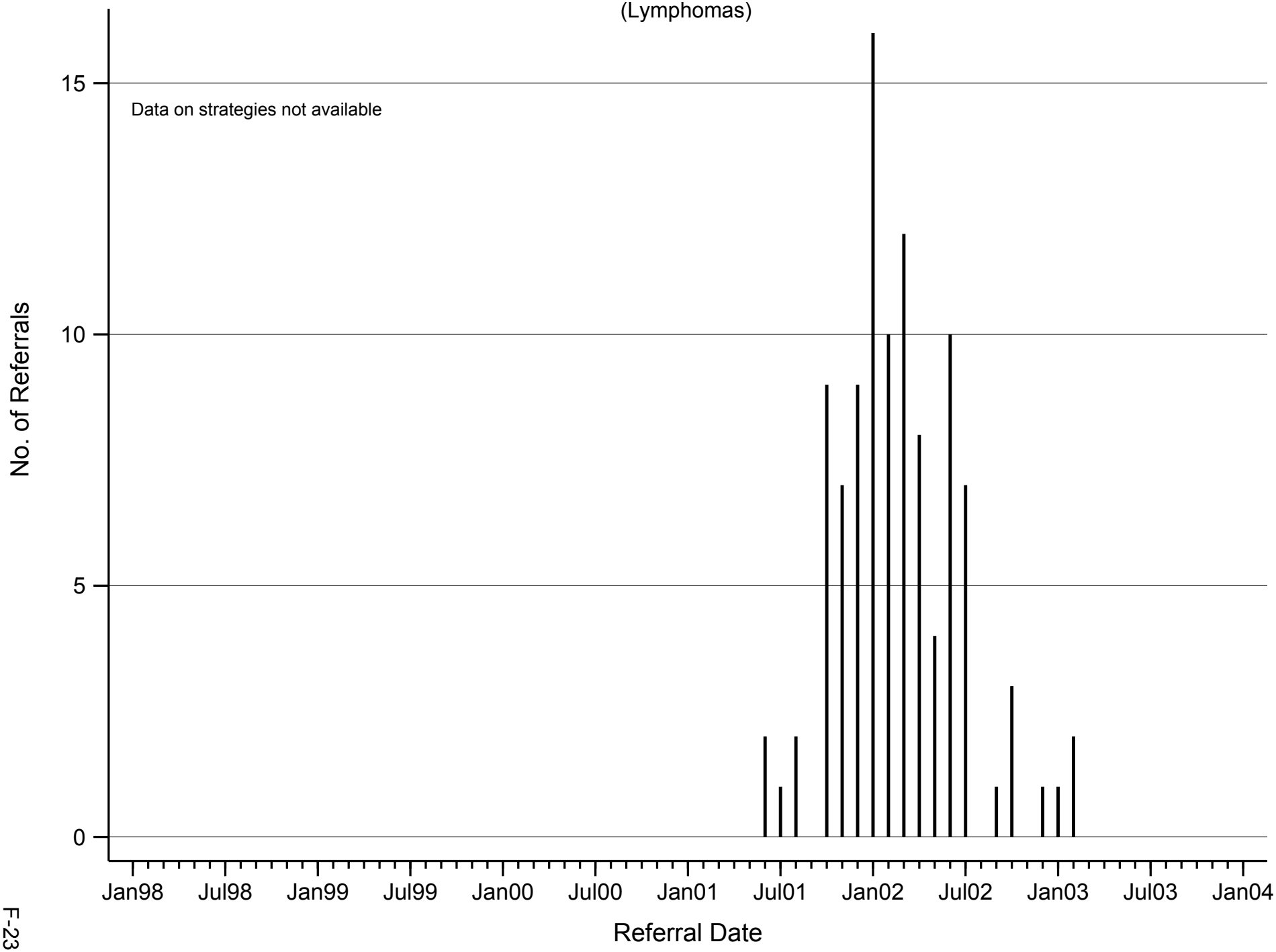
Monthly Referral Distribution of 01-C-0173

(Breast cancer—inflammatory or locally advanced)



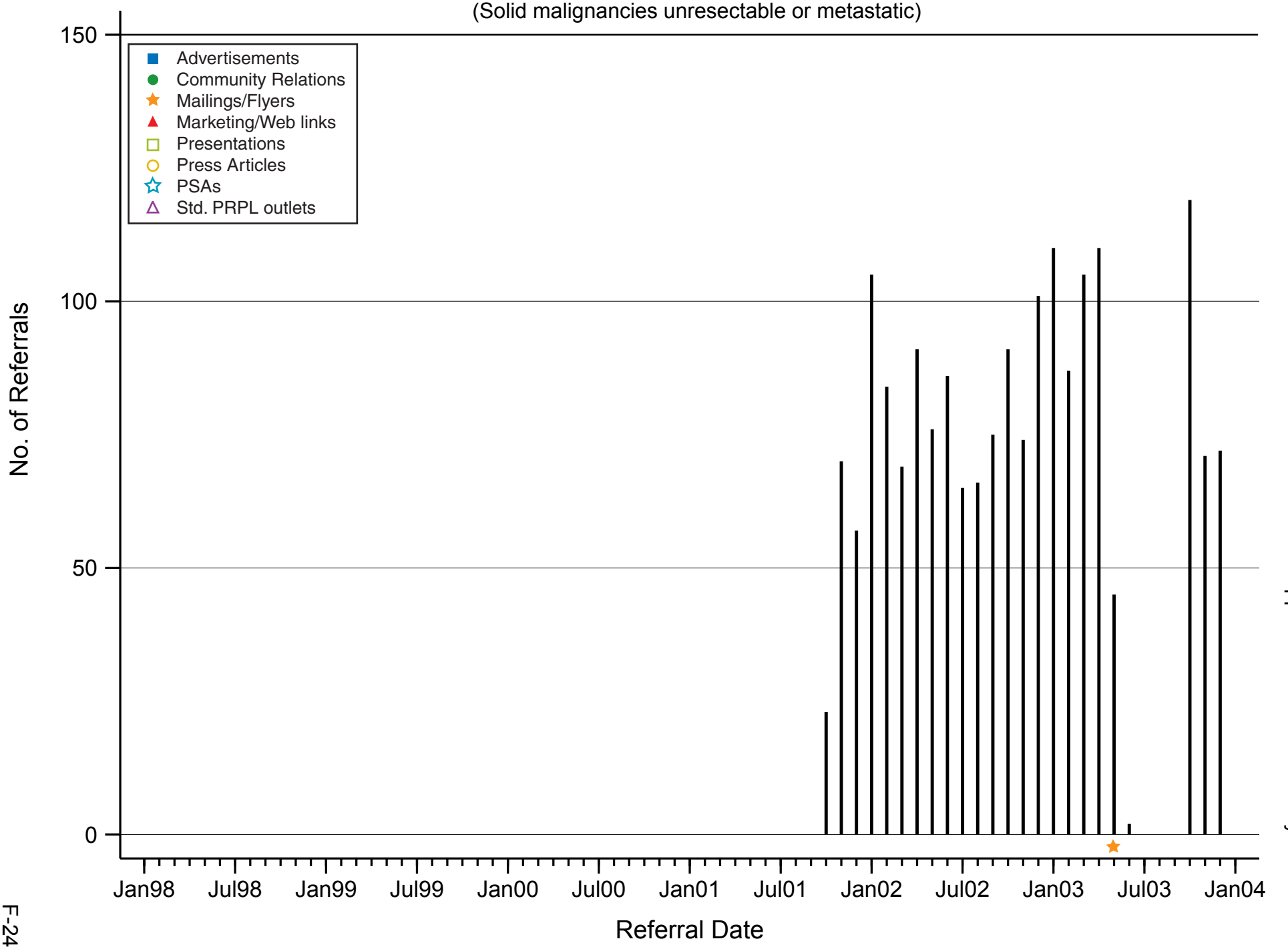
Monthly Referral Distribution of 01-C-0213

(Lymphomas)



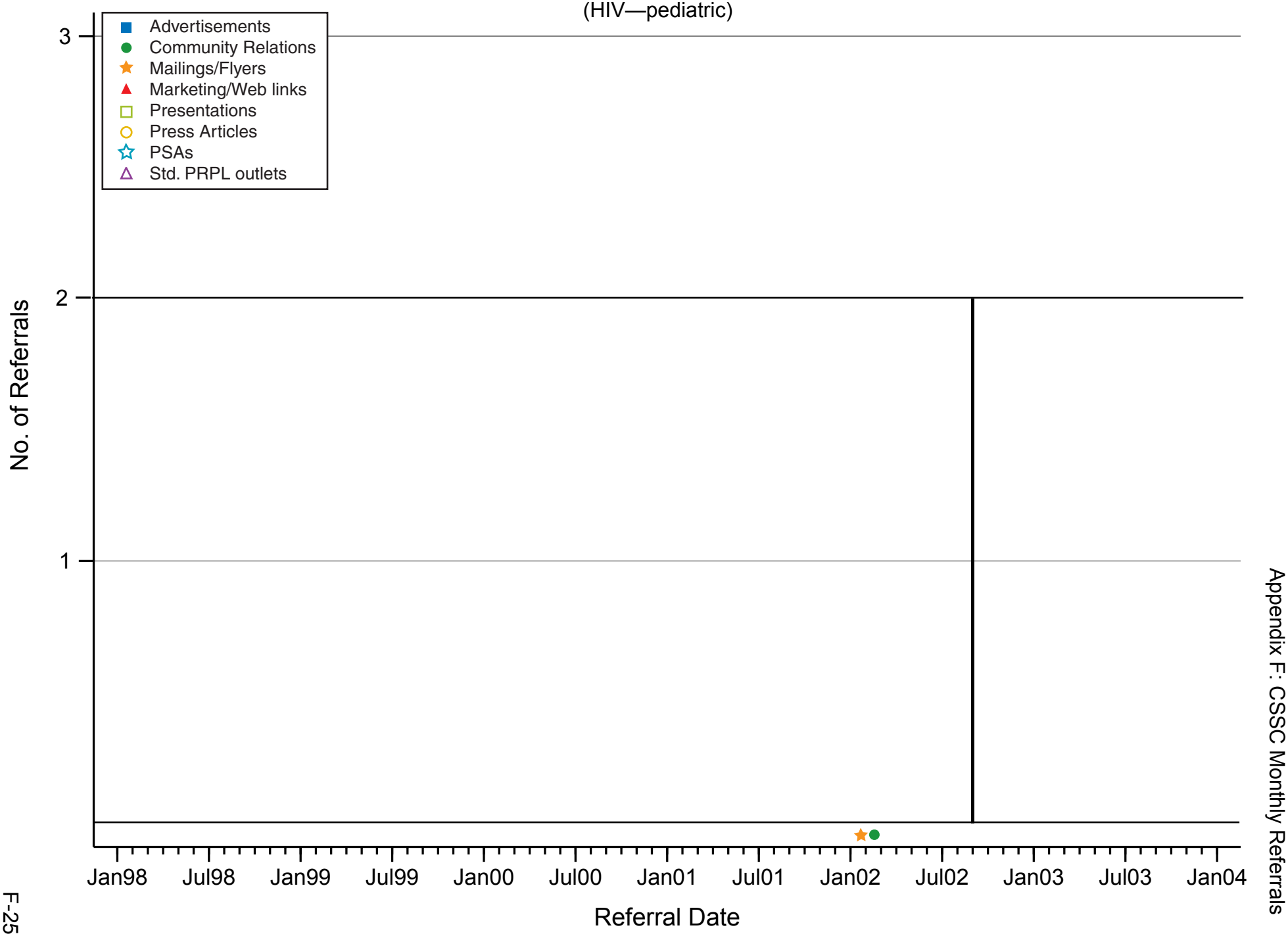
Monthly Referral Distribution of 01-C-0256

(Solid malignancies unresectable or metastatic)



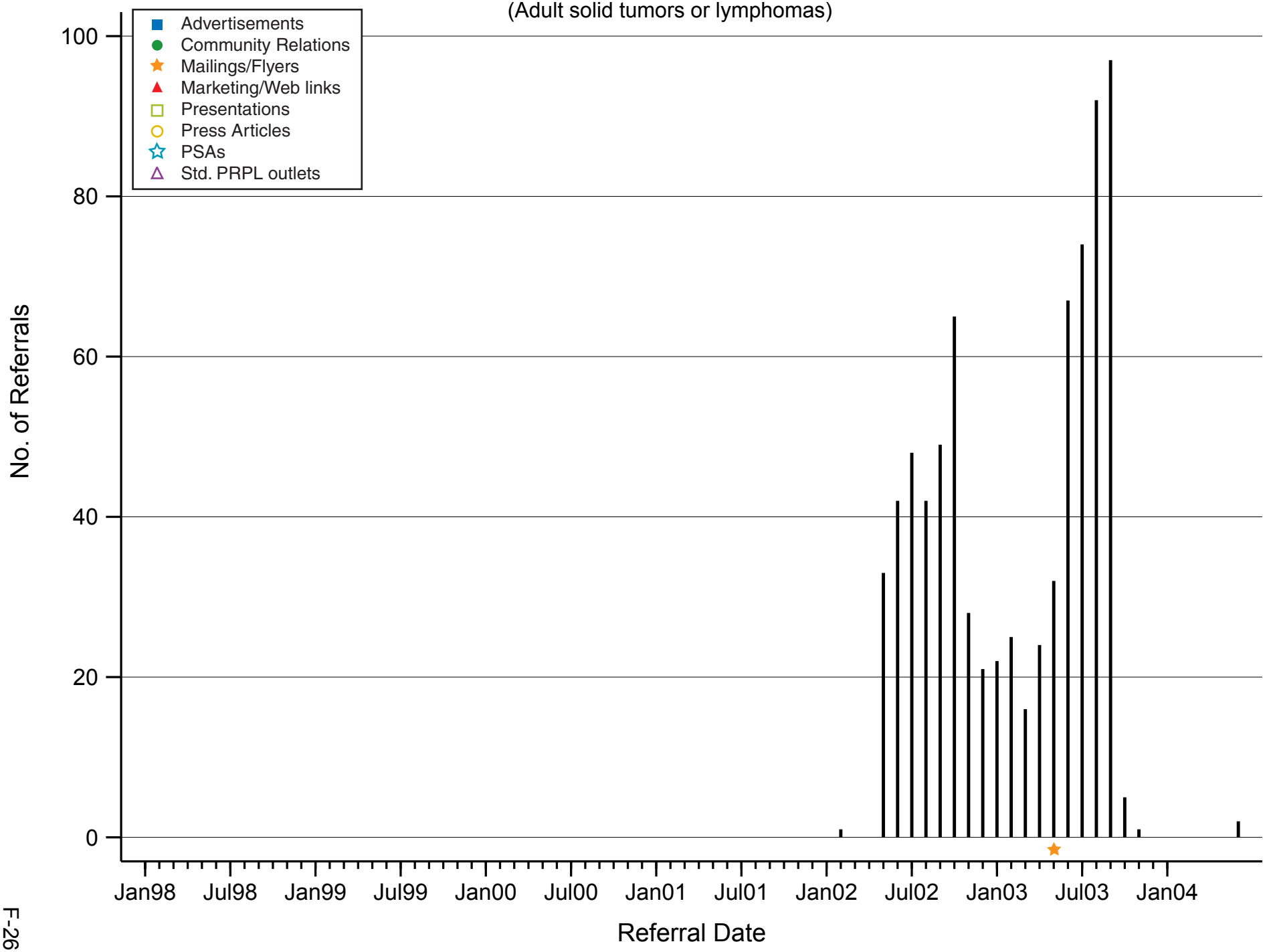
Monthly Referral Distribution of 02-C-0006

(HIV—pediatric)



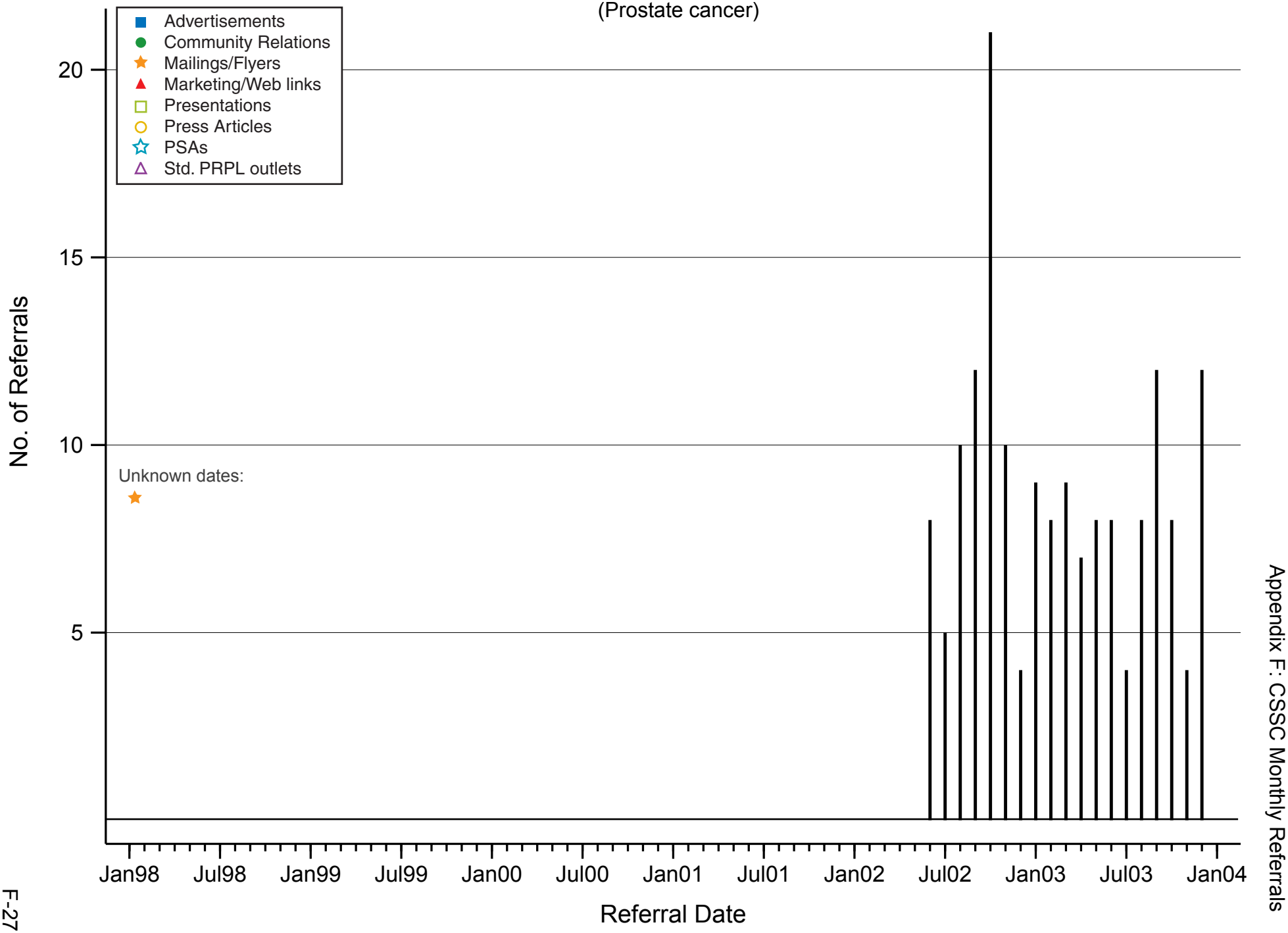
Monthly Referral Distribution of 02-C-0083

(Adult solid tumors or lymphomas)



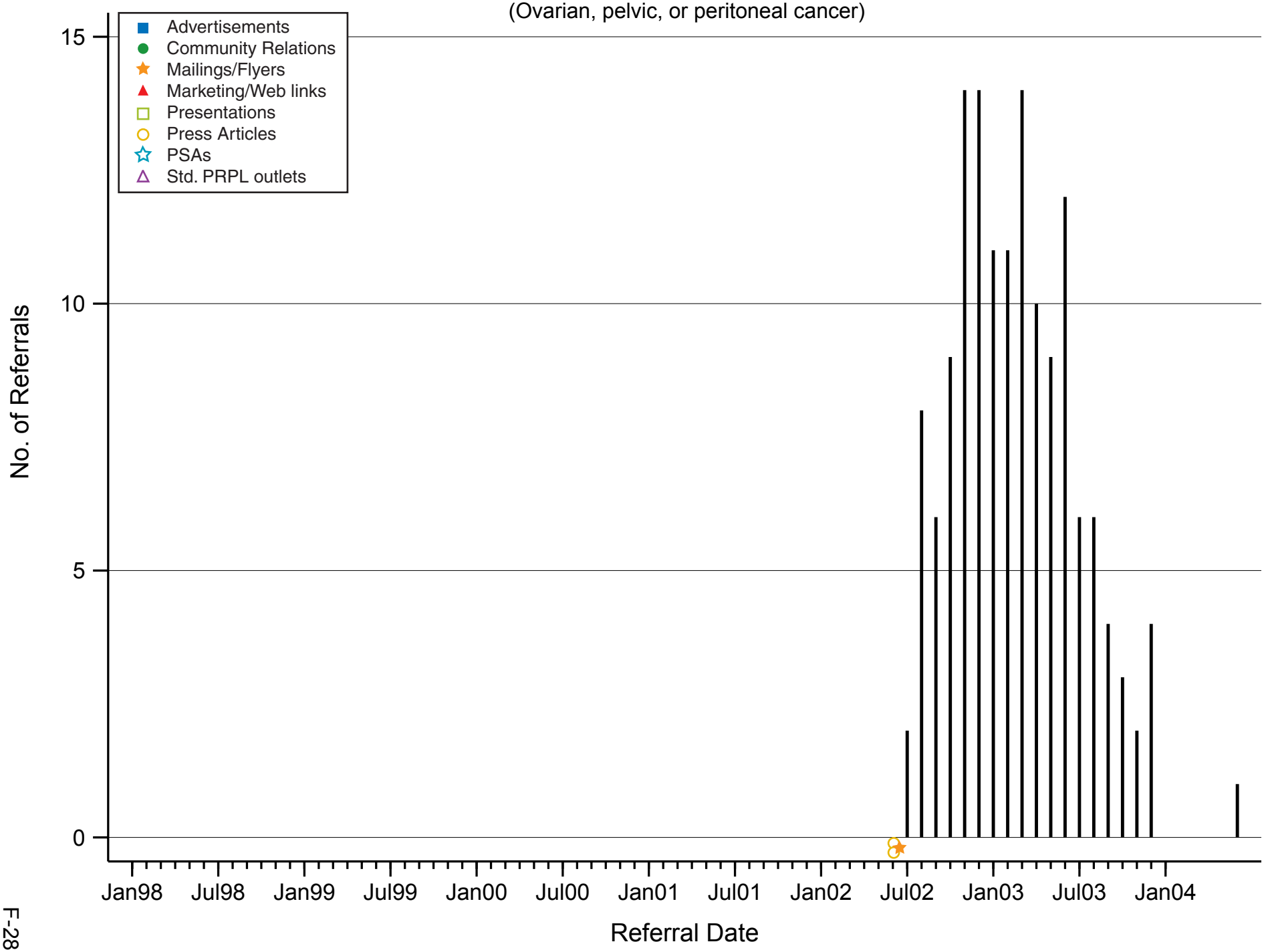
Monthly Referral Distribution of 02-C-0149

(Prostate cancer)



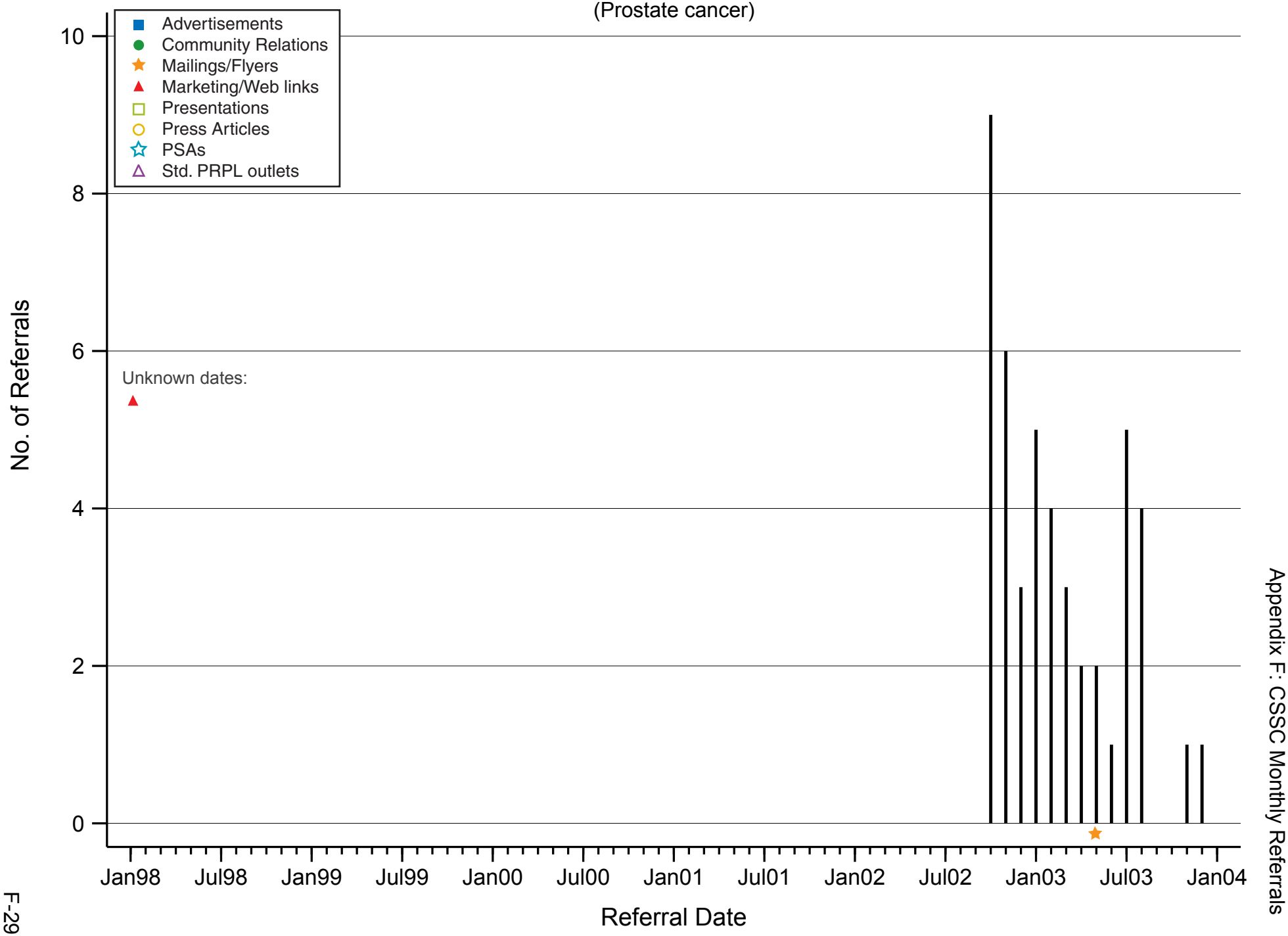
Monthly Referral Distribution of 02-C-0190

(Ovarian, pelvic, or peritoneal cancer)



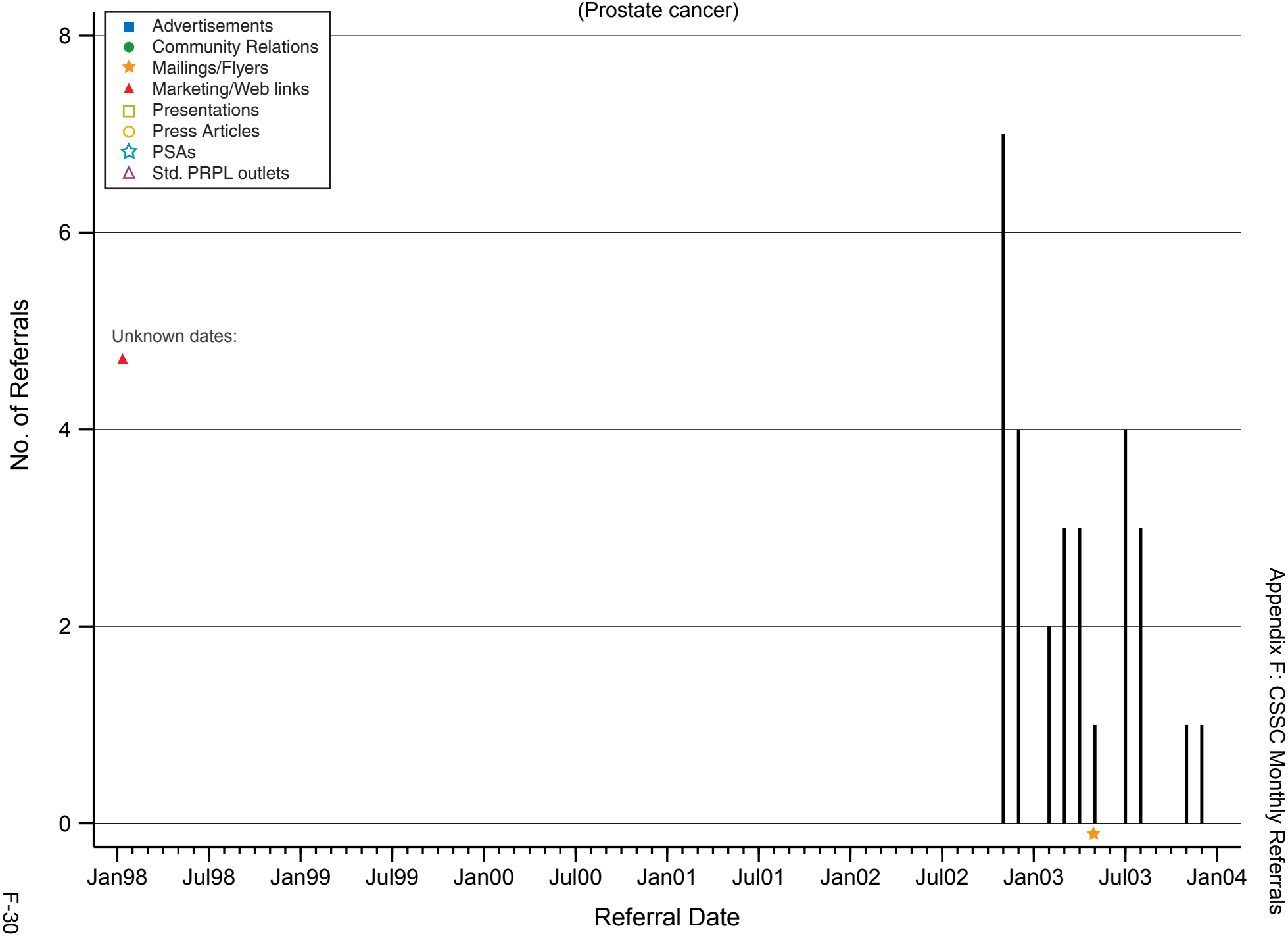
Monthly Referral Distribution of 02-C-0207

(Prostate cancer)



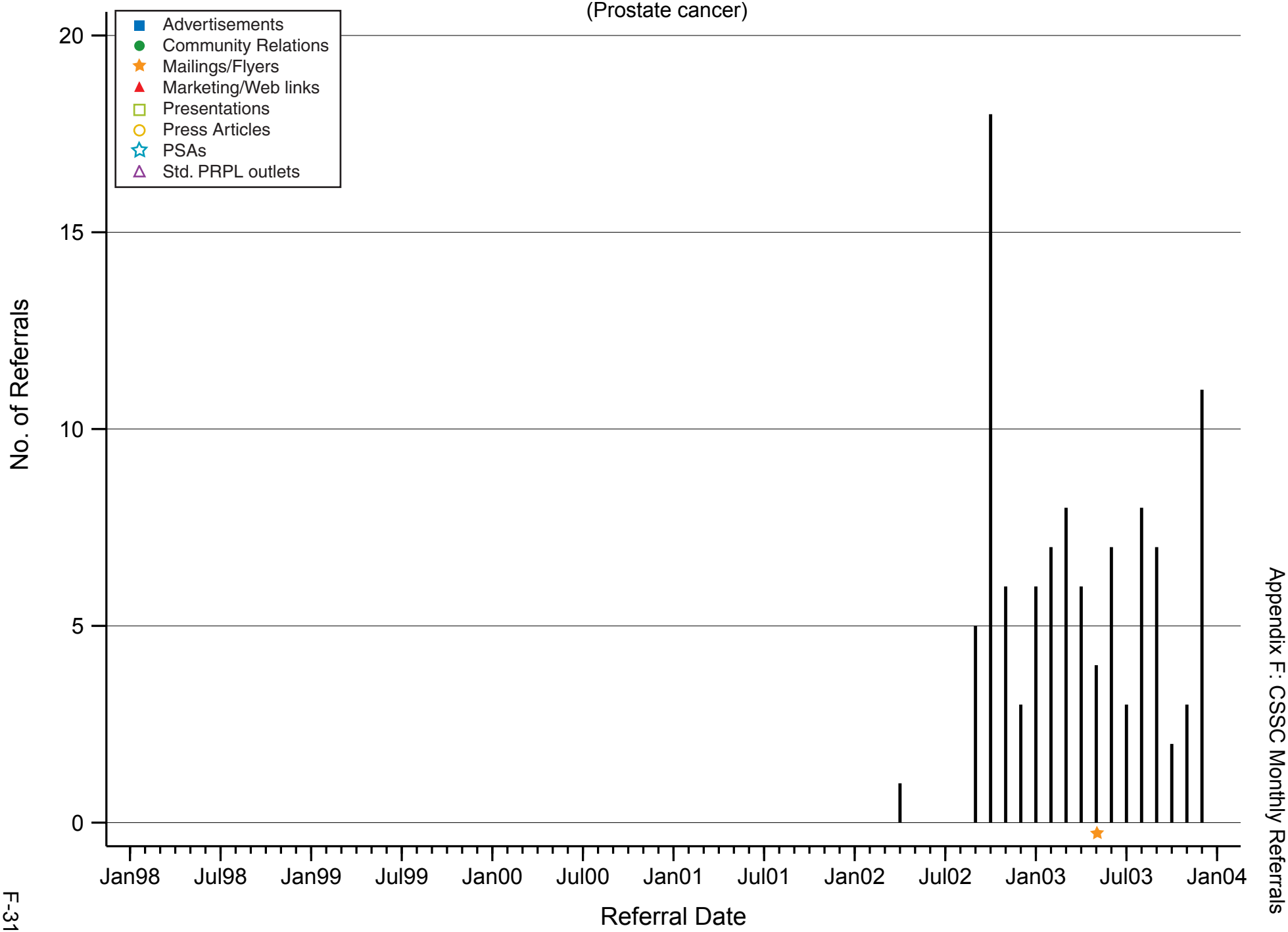
Monthly Referral Distribution of 02-C-0215

(Prostate cancer)



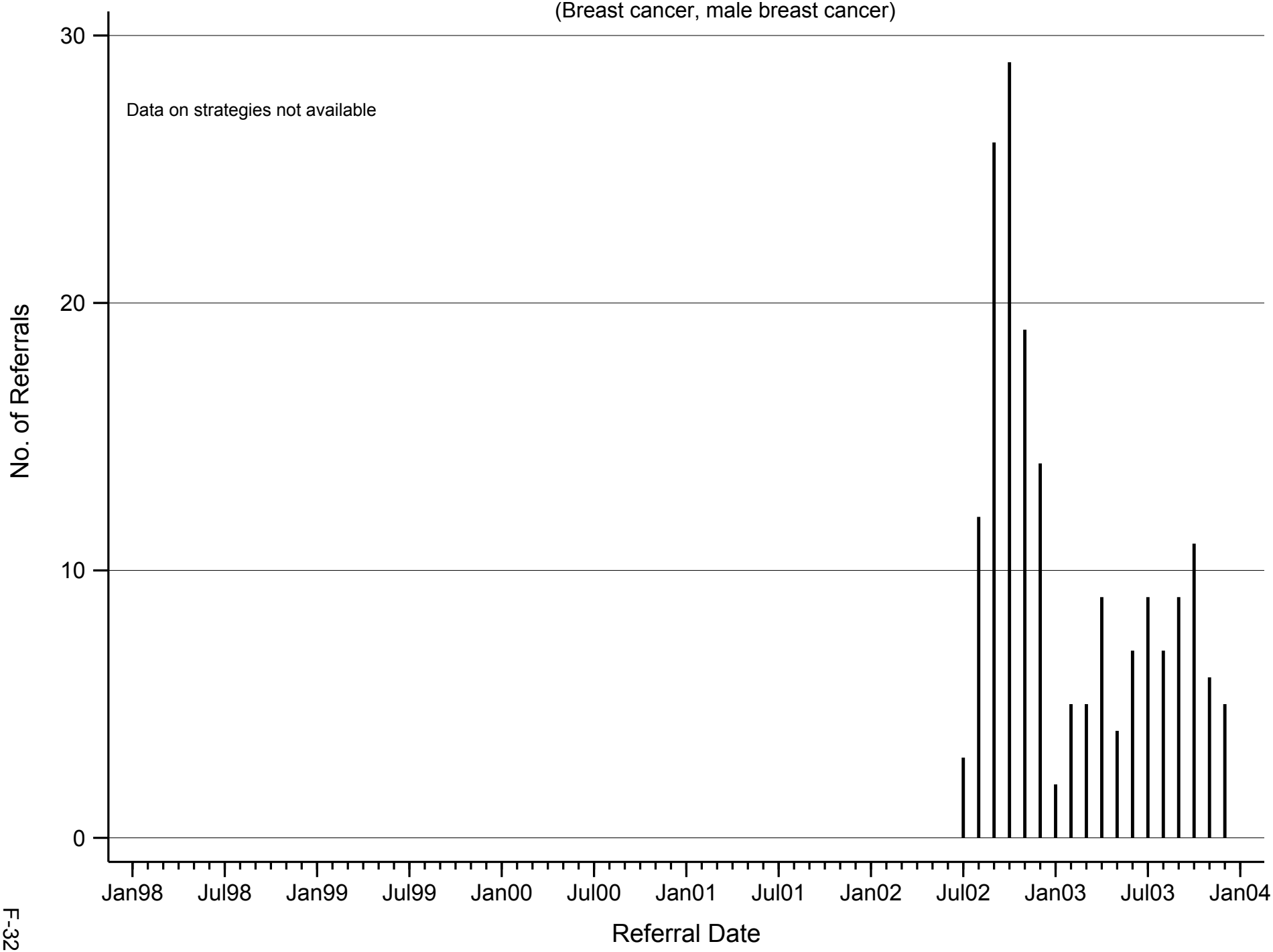
Monthly Referral Distribution of 02-C-0218

(Prostate cancer)



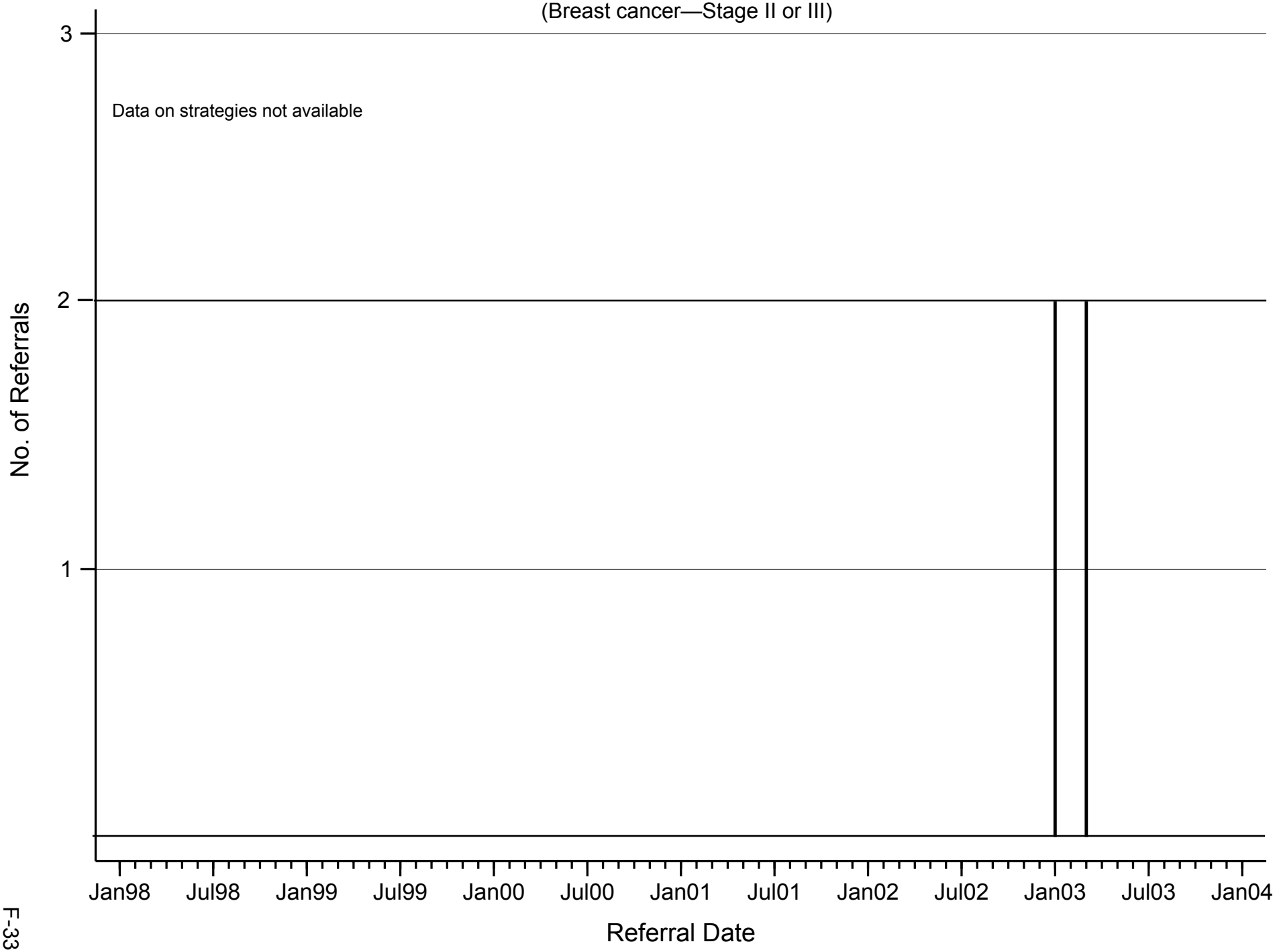
Monthly Referral Distribution of 02-C-0229

(Breast cancer, male breast cancer)



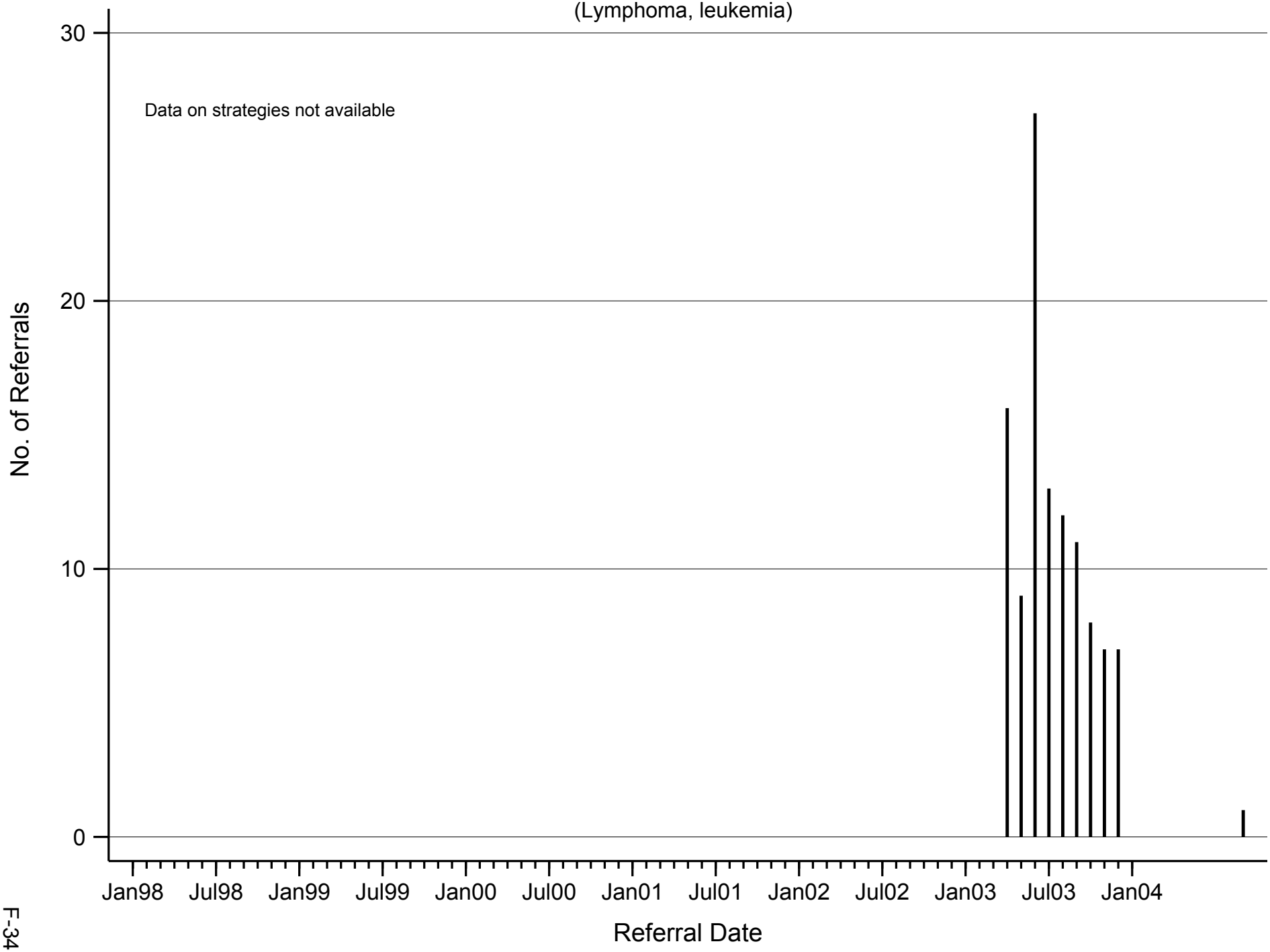
Monthly Referral Distribution of 03-C-0005

(Breast cancer—Stage II or III)



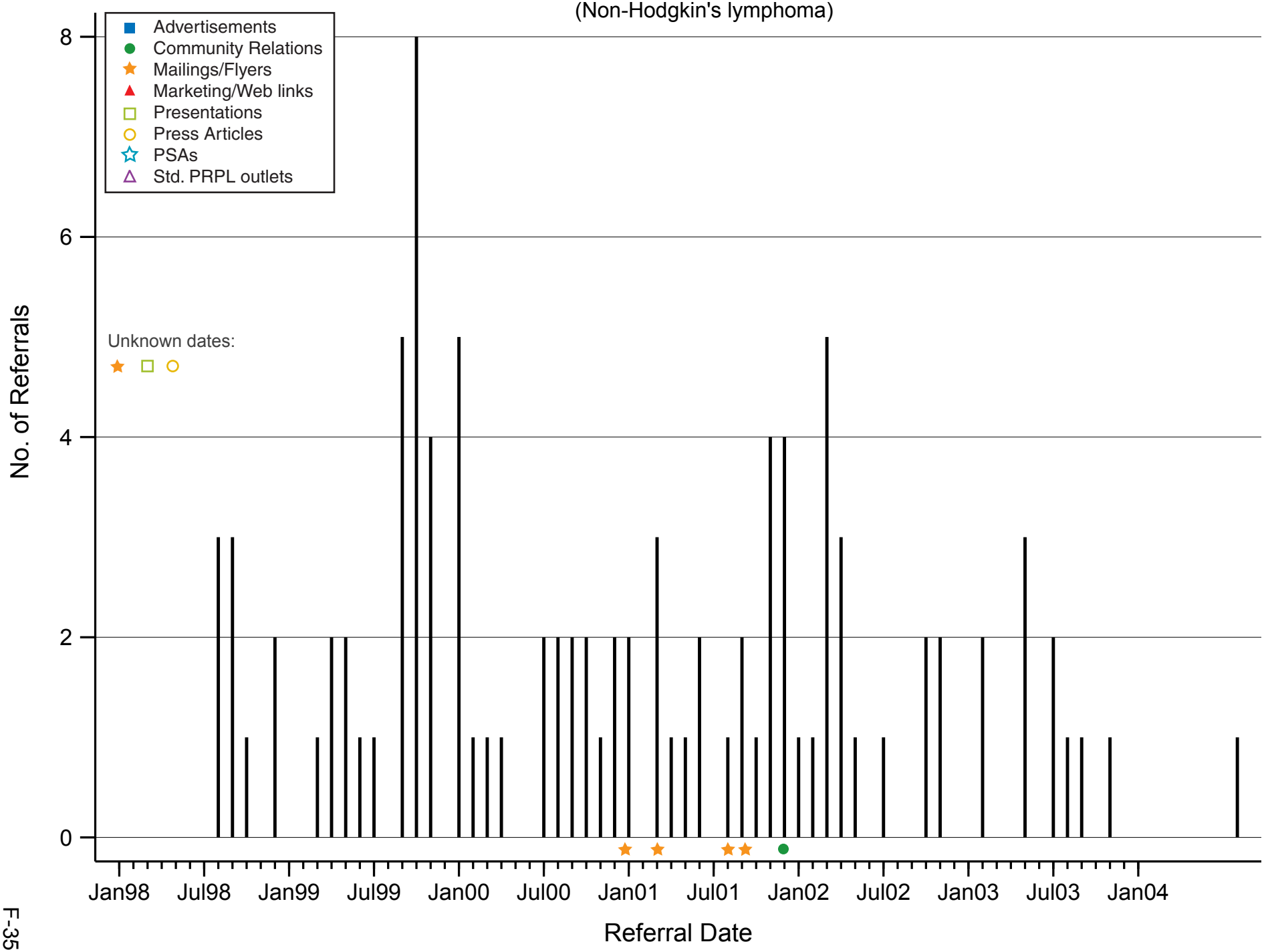
Monthly Referral Distribution of 03-C-0077

(Lymphoma, leukemia)



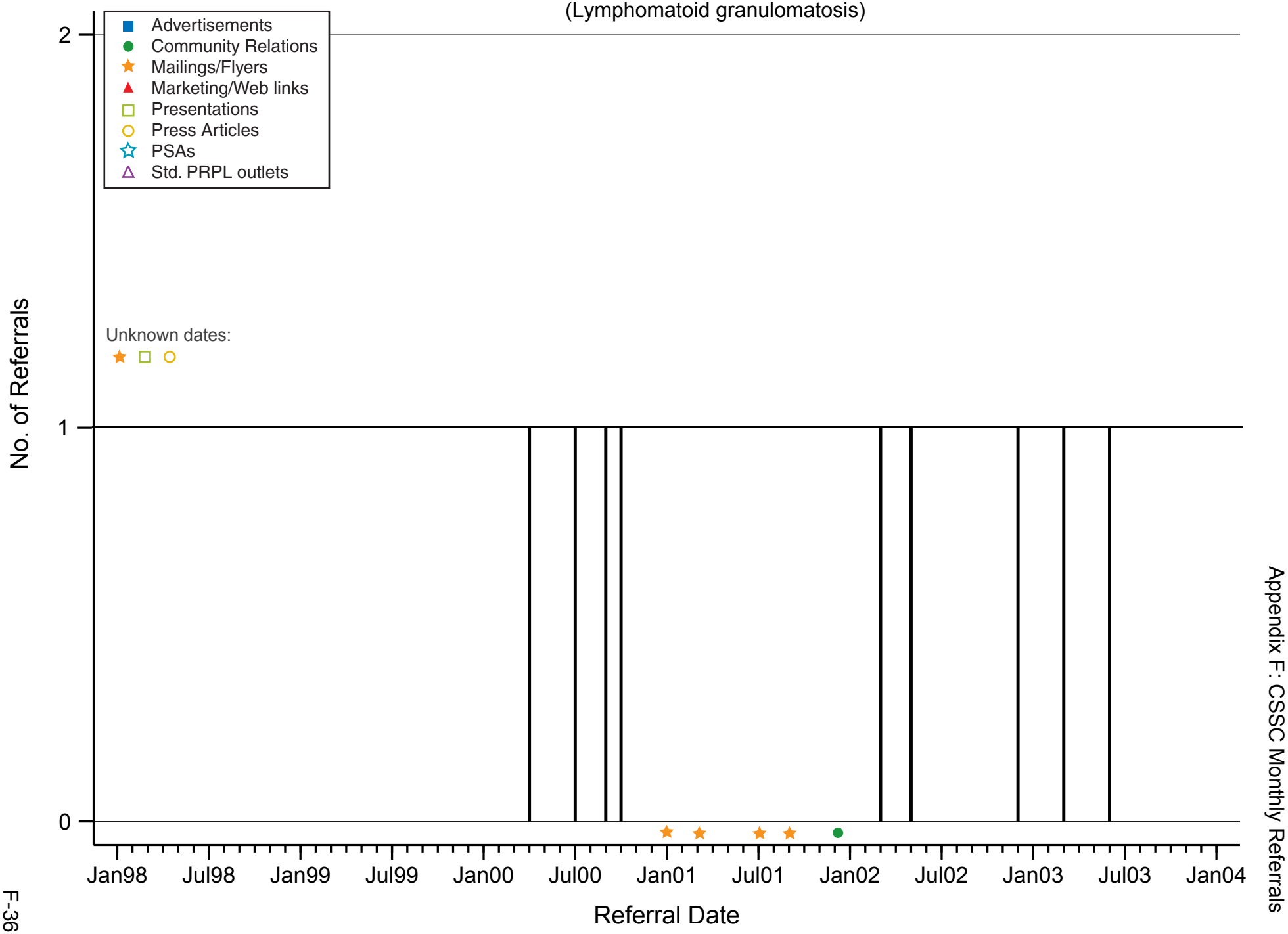
Monthly Referral Distribution of 93-C-0133

(Non-Hodgkin's lymphoma)



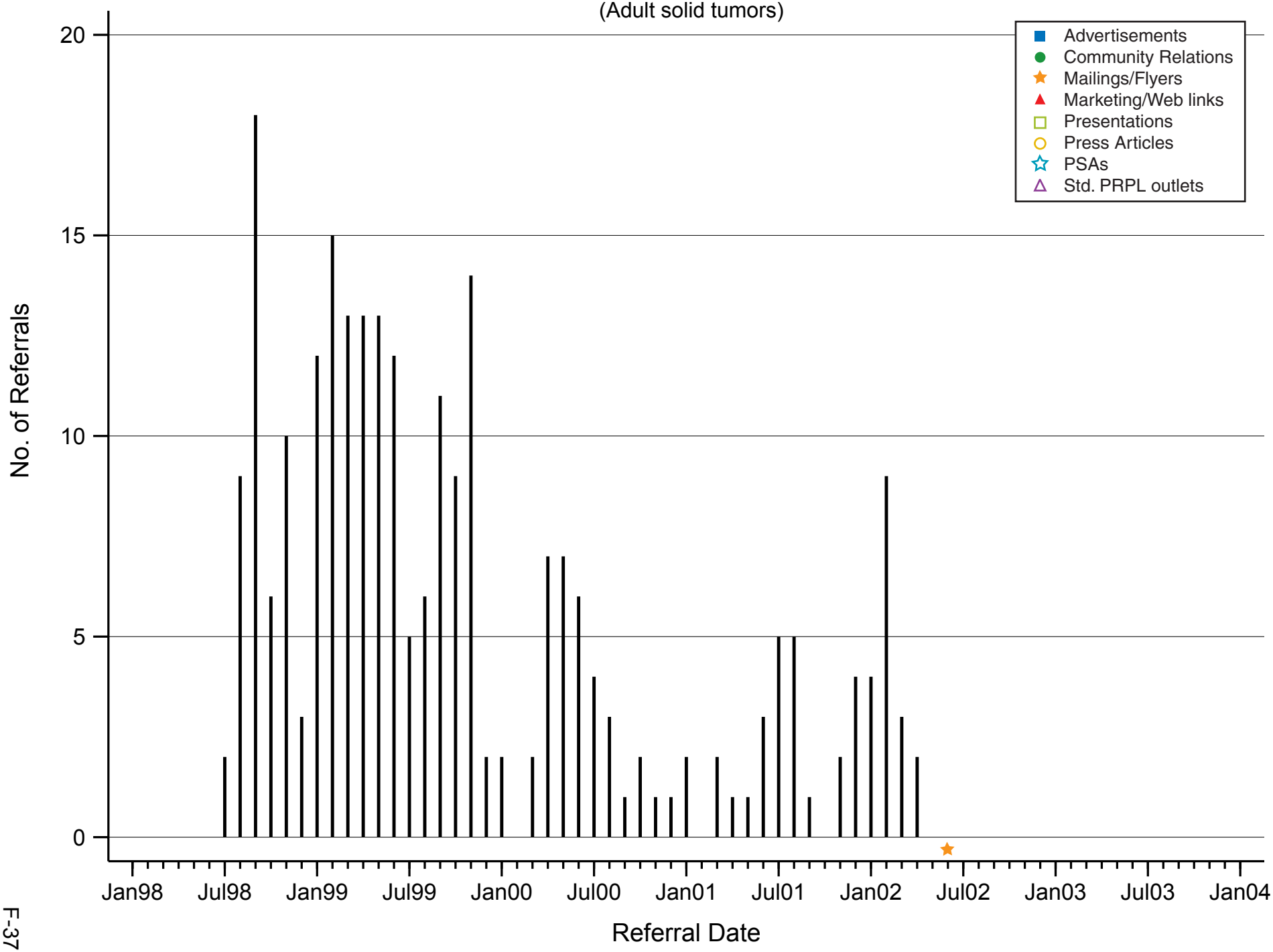
Monthly Referral Distribution of 94-C-0074

(Lymphomatoid granulomatosis)



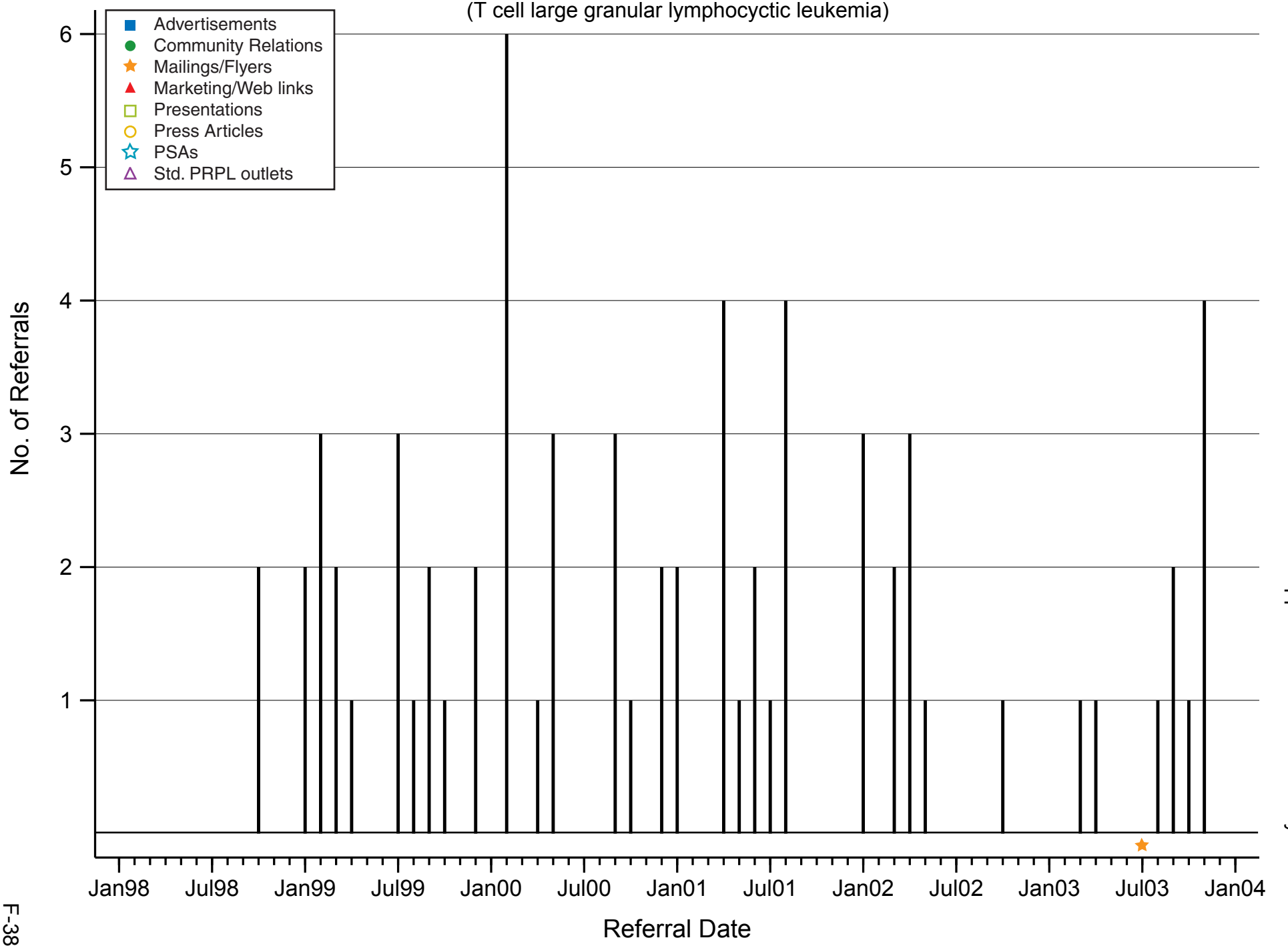
Monthly Referral Distribution of 94-C-0096

(Adult solid tumors)



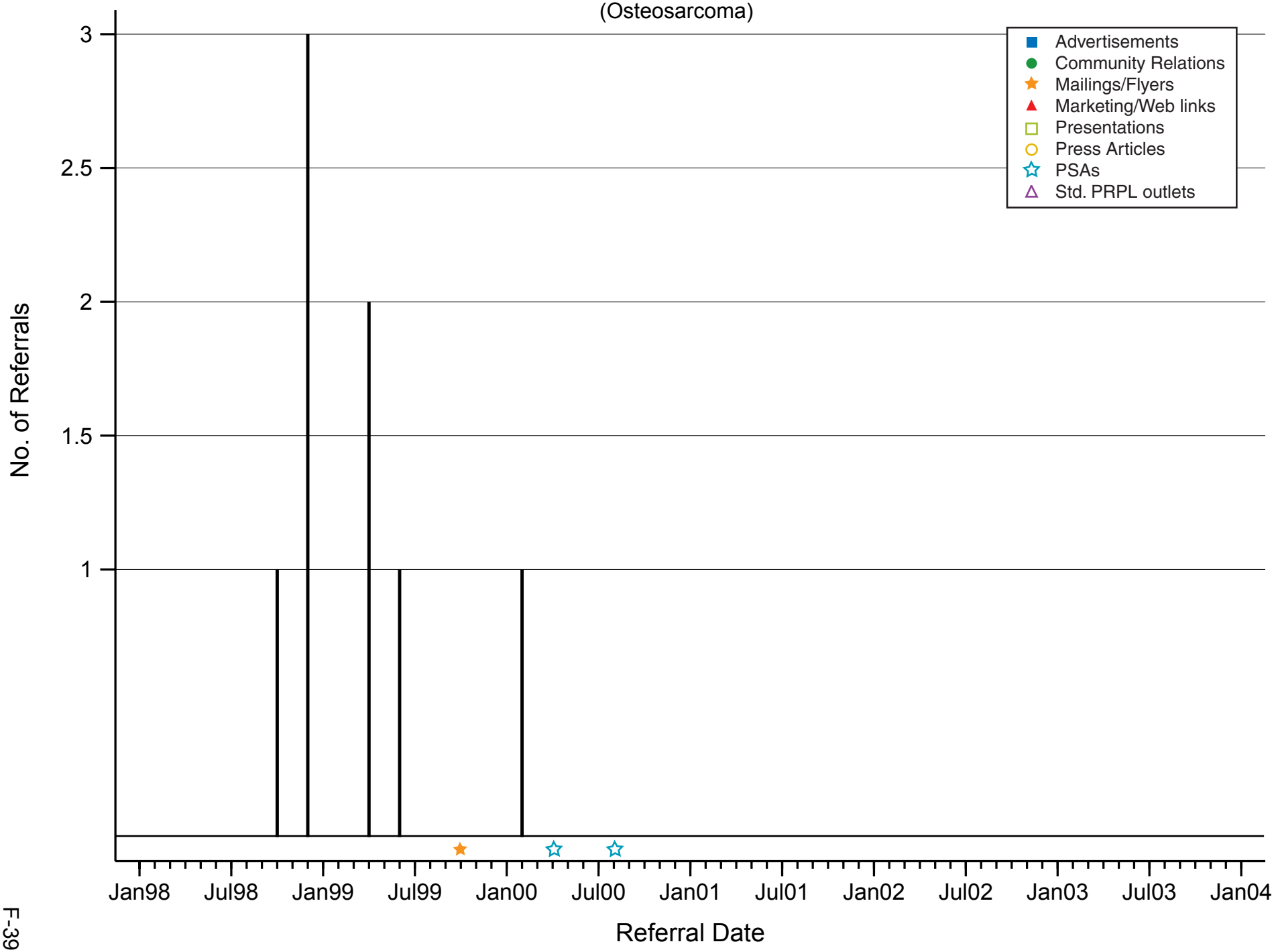
Monthly Referral Distribution of 95-C-0054

(T cell large granular lymphocytic leukemia)



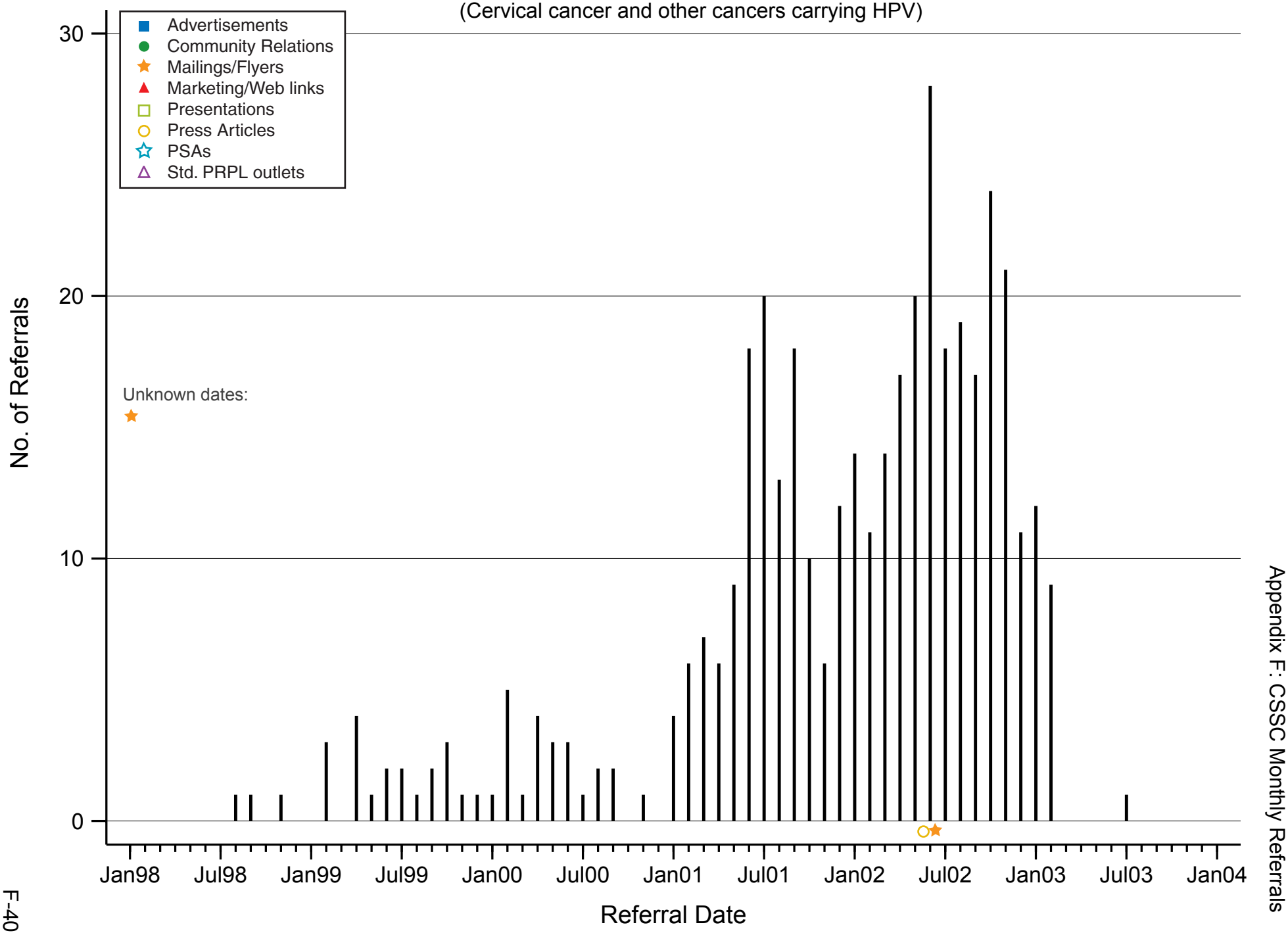
Monthly Referral Distribution of 95-C-0119

(Osteosarcoma)



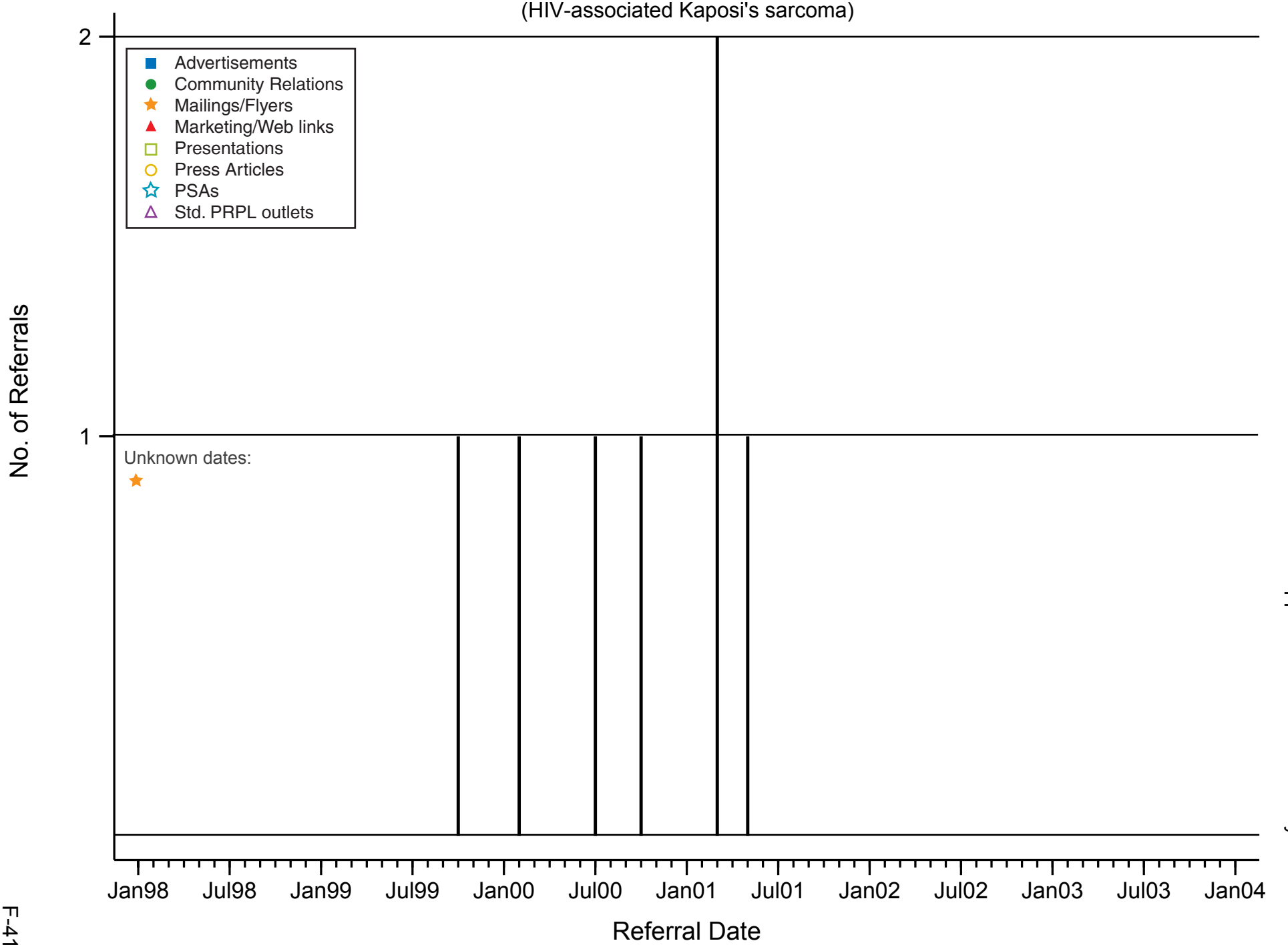
Monthly Referral Distribution of 95-C-0154

(Cervical cancer and other cancers carrying HPV)



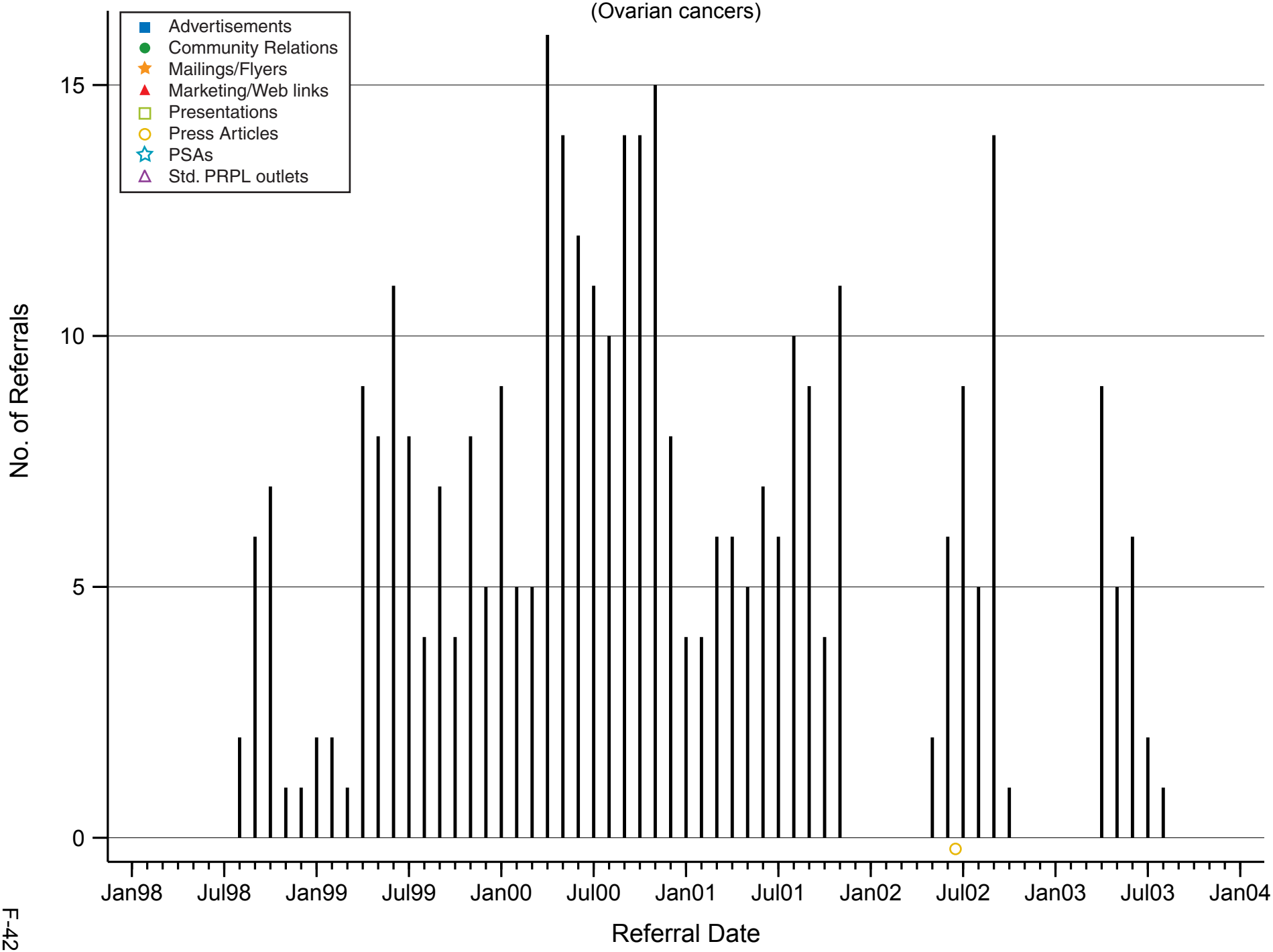
Monthly Referral Distribution of 96-C-0004

(HIV-associated Kaposi's sarcoma)



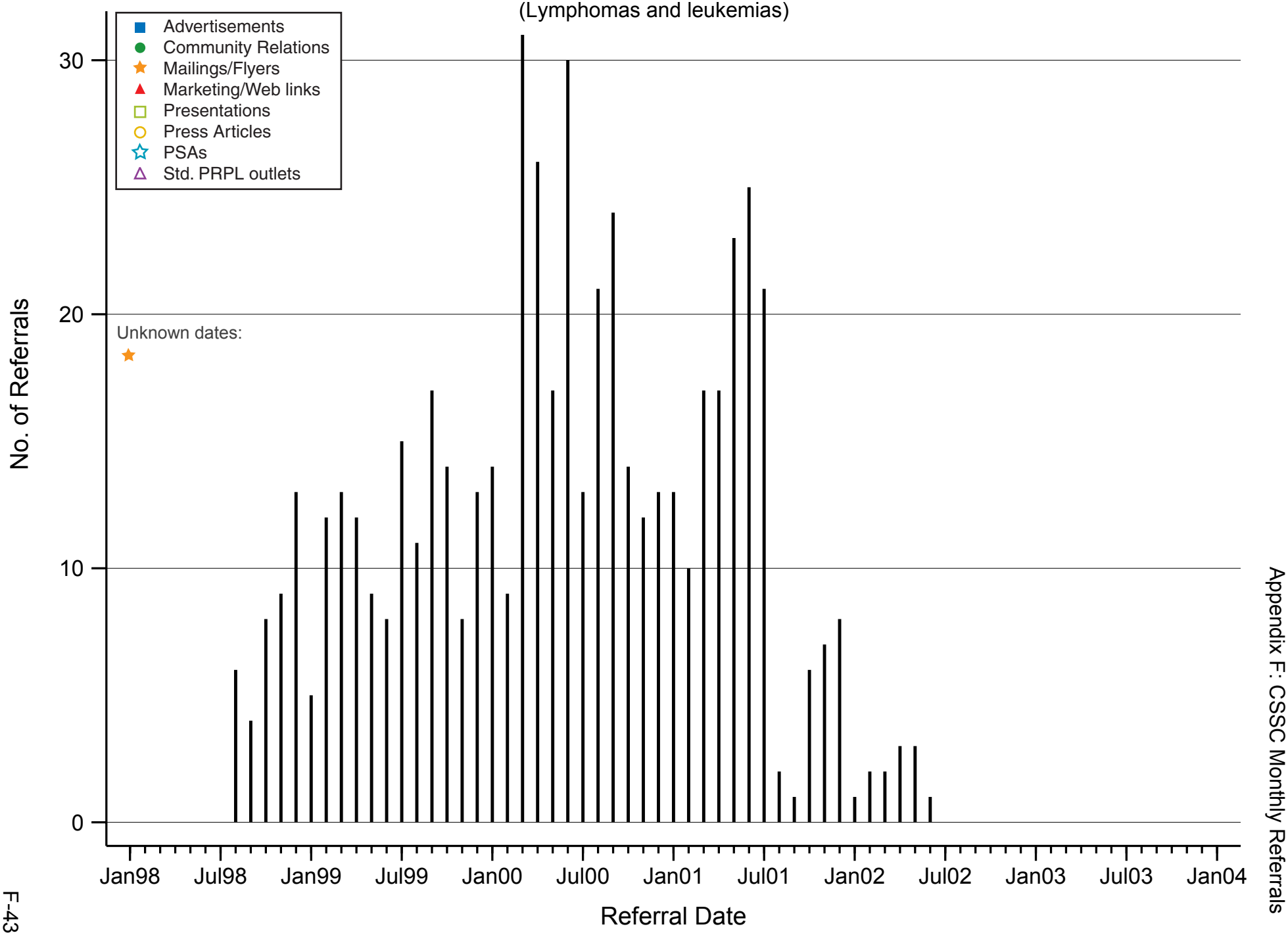
Monthly Referral Distribution of 96-C-0011

(Ovarian cancers)



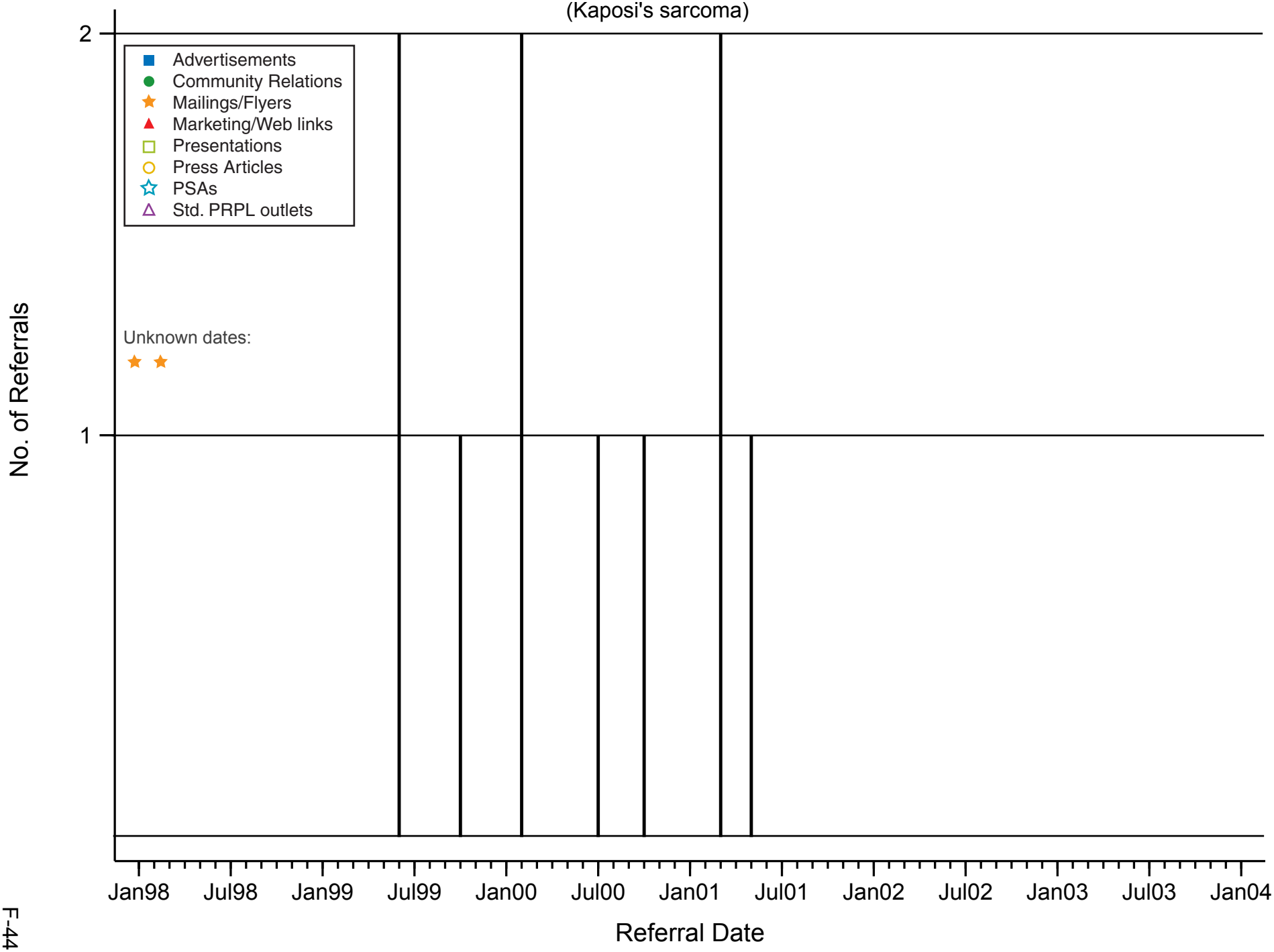
Monthly Referral Distribution of 96-C-0064

(Lymphomas and leukemias)



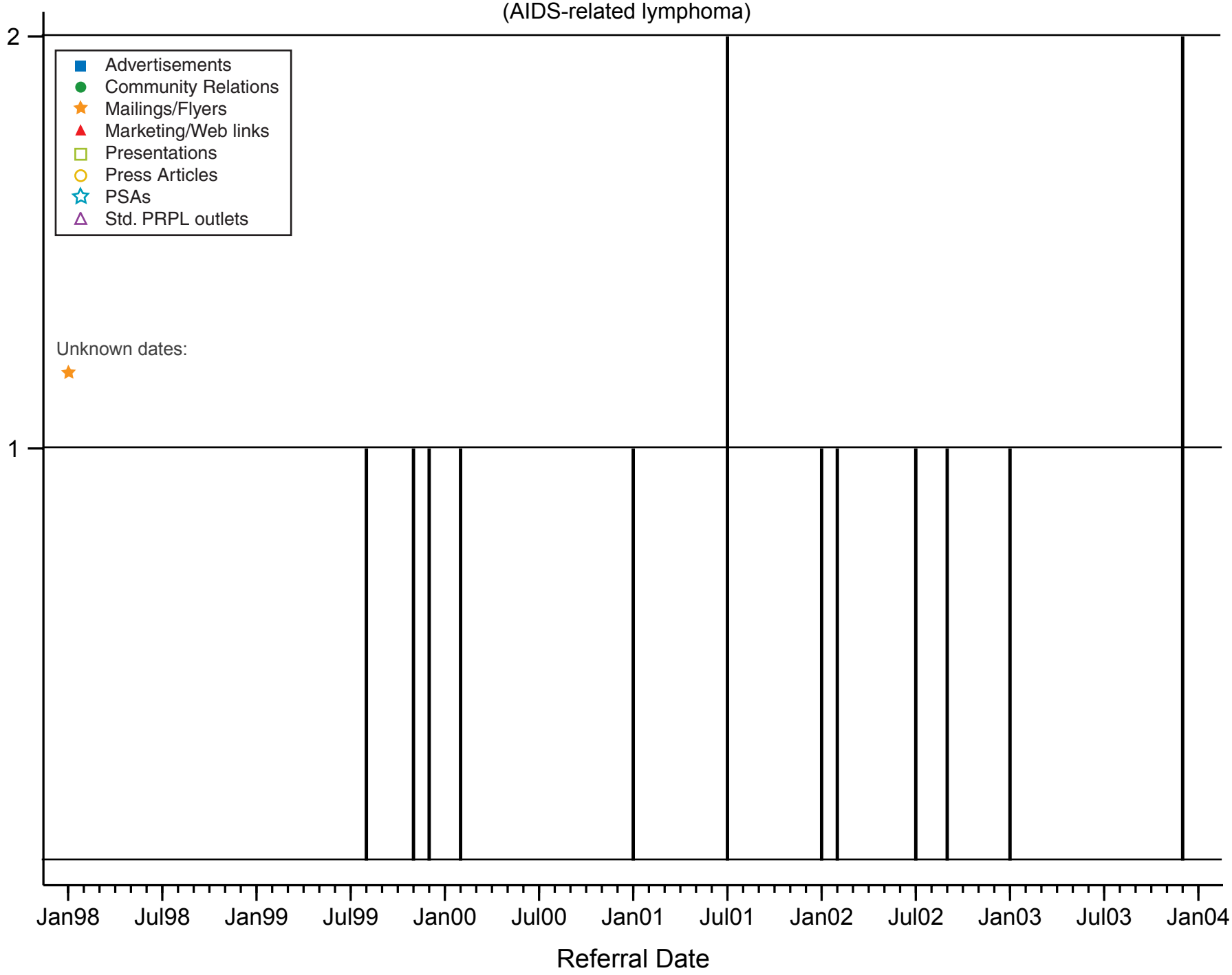
Monthly Referral Distribution of 97-C-0024

(Kaposi's sarcoma)



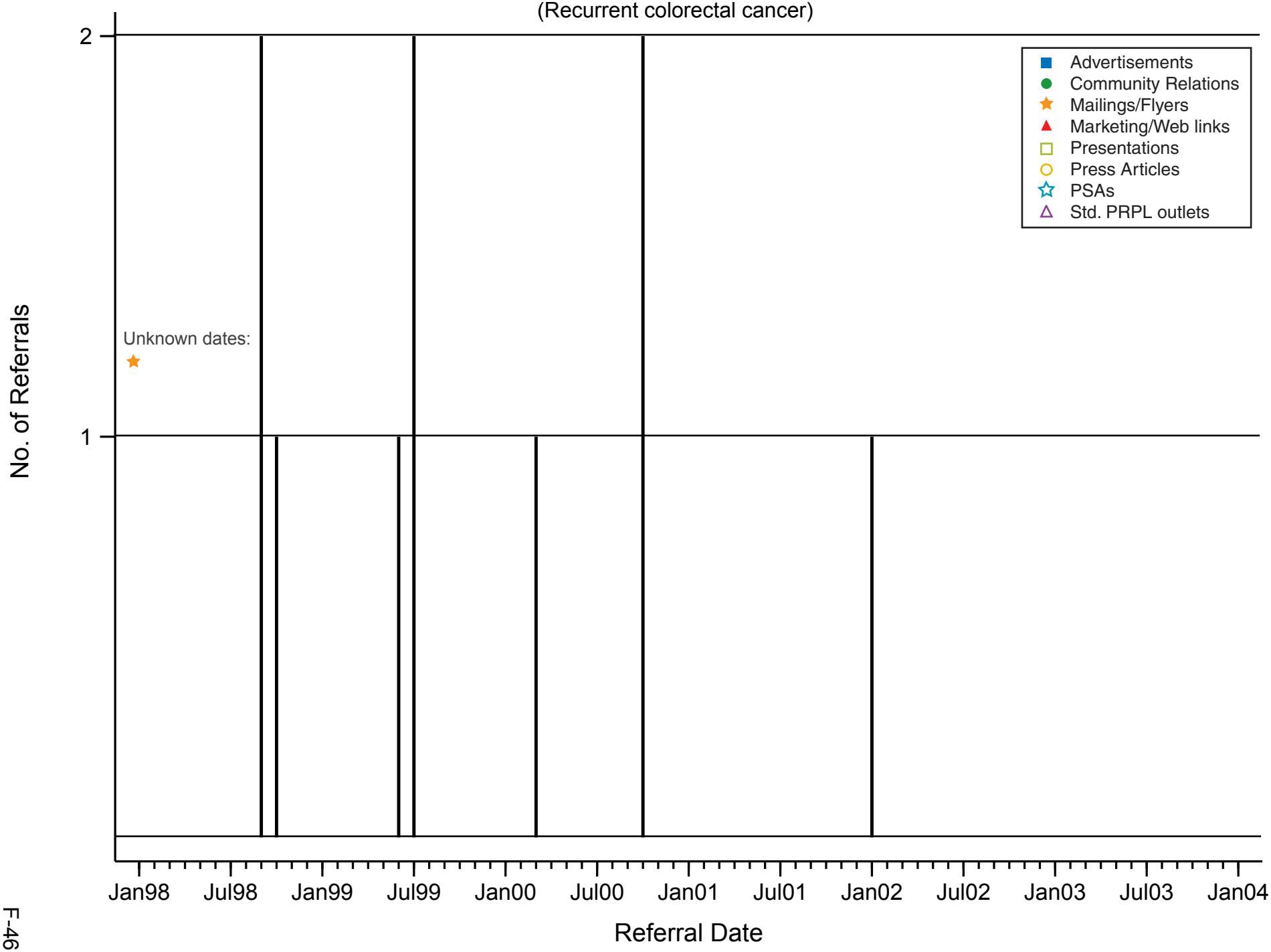
Monthly Referral Distribution of 97-C-0040

(AIDS-related lymphoma)



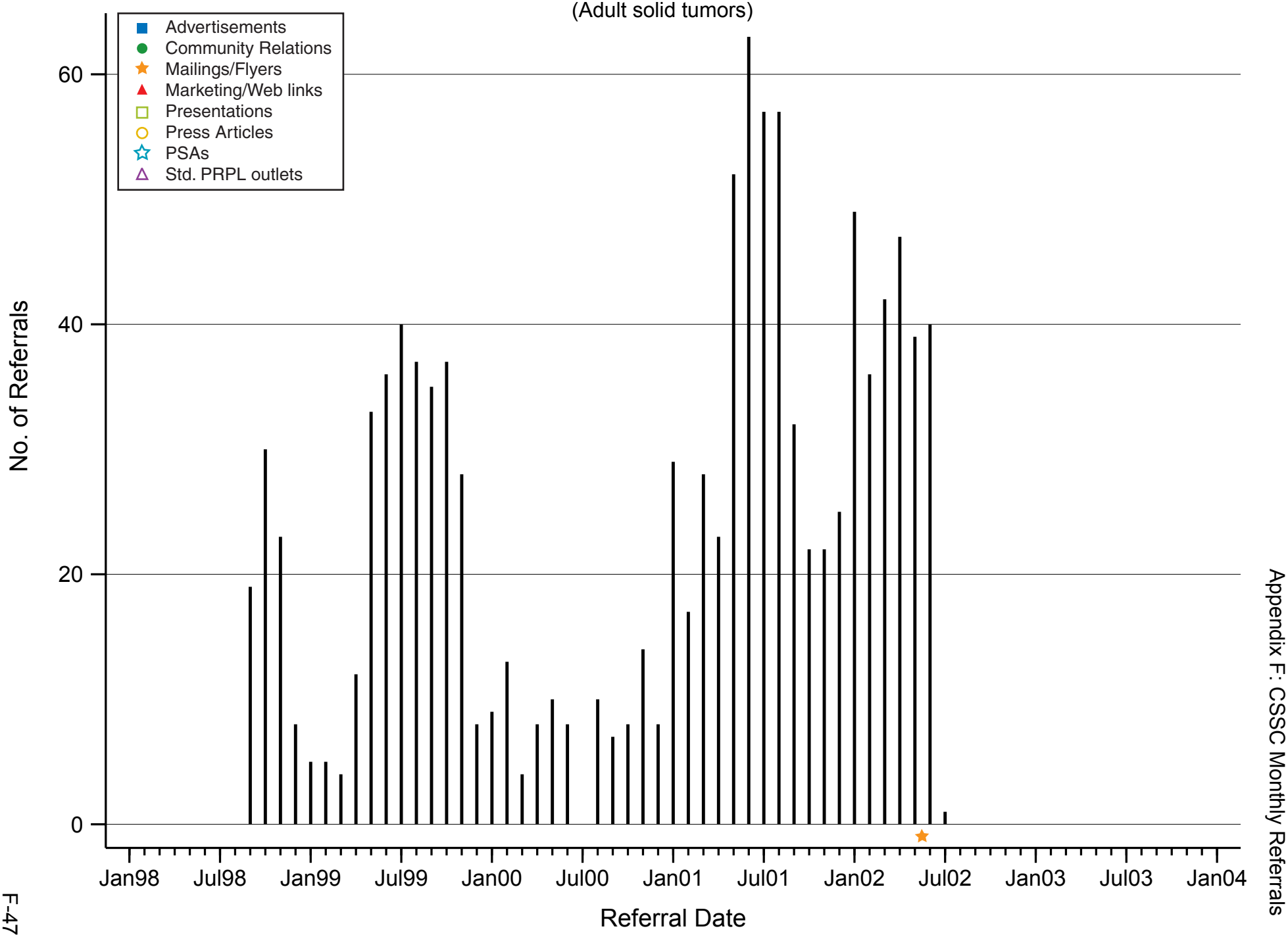
Monthly Referral Distribution of 97-C-0068

(Recurrent colorectal cancer)



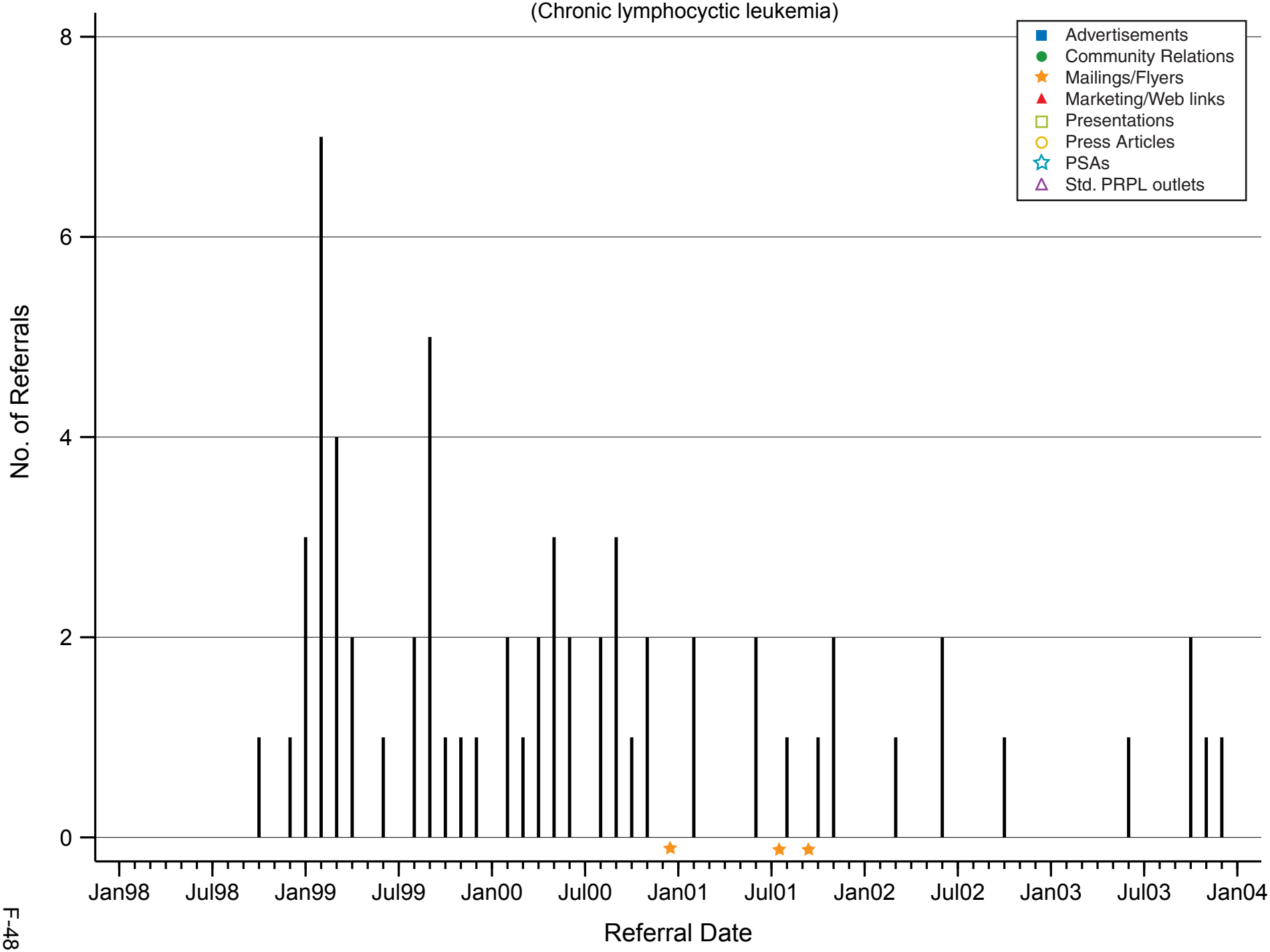
Monthly Referral Distribution of 97-C-0141

(Adult solid tumors)



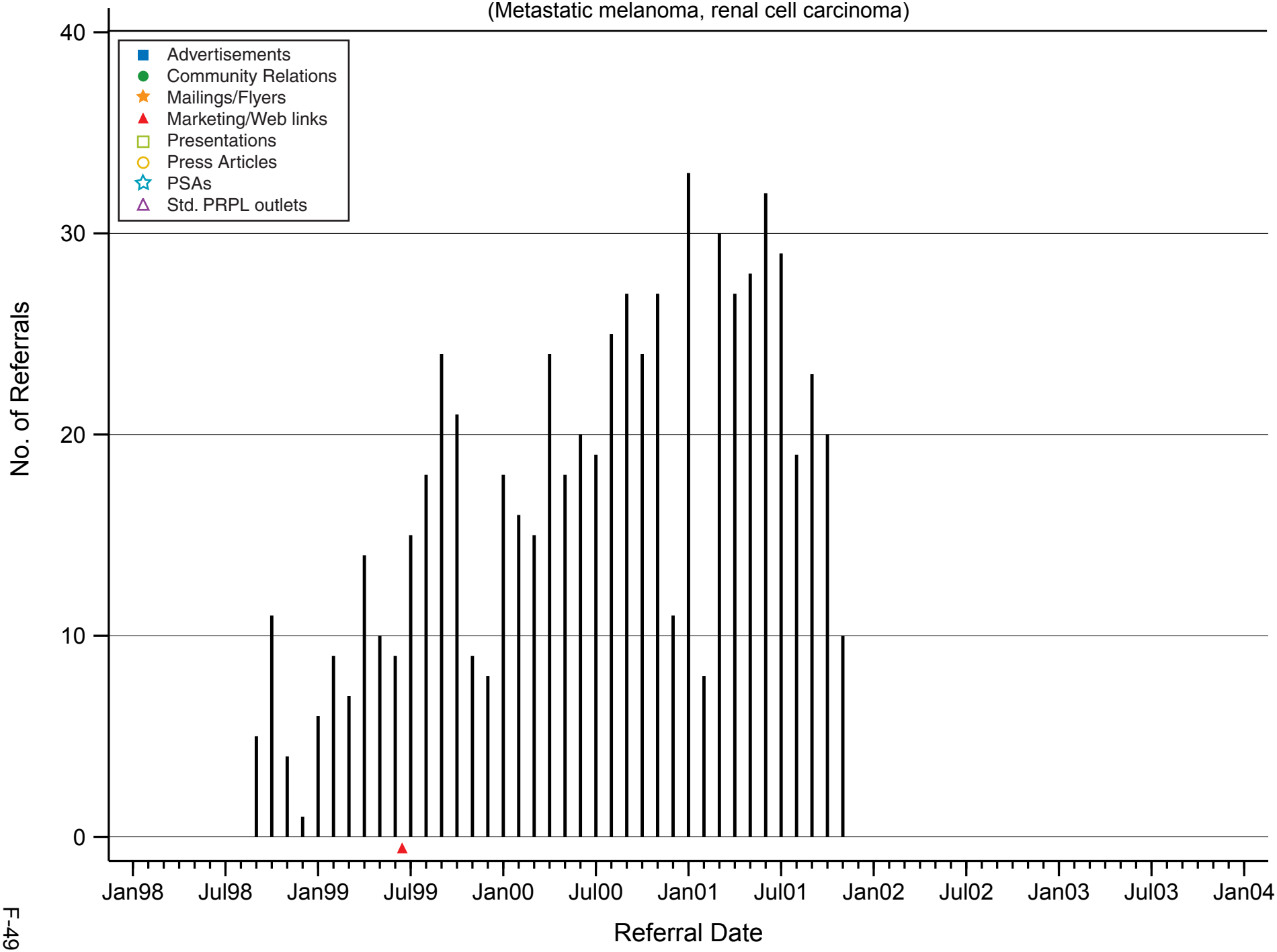
Monthly Referral Distribution of 97-C-0178

(Chronic lymphocyctic leukemia)



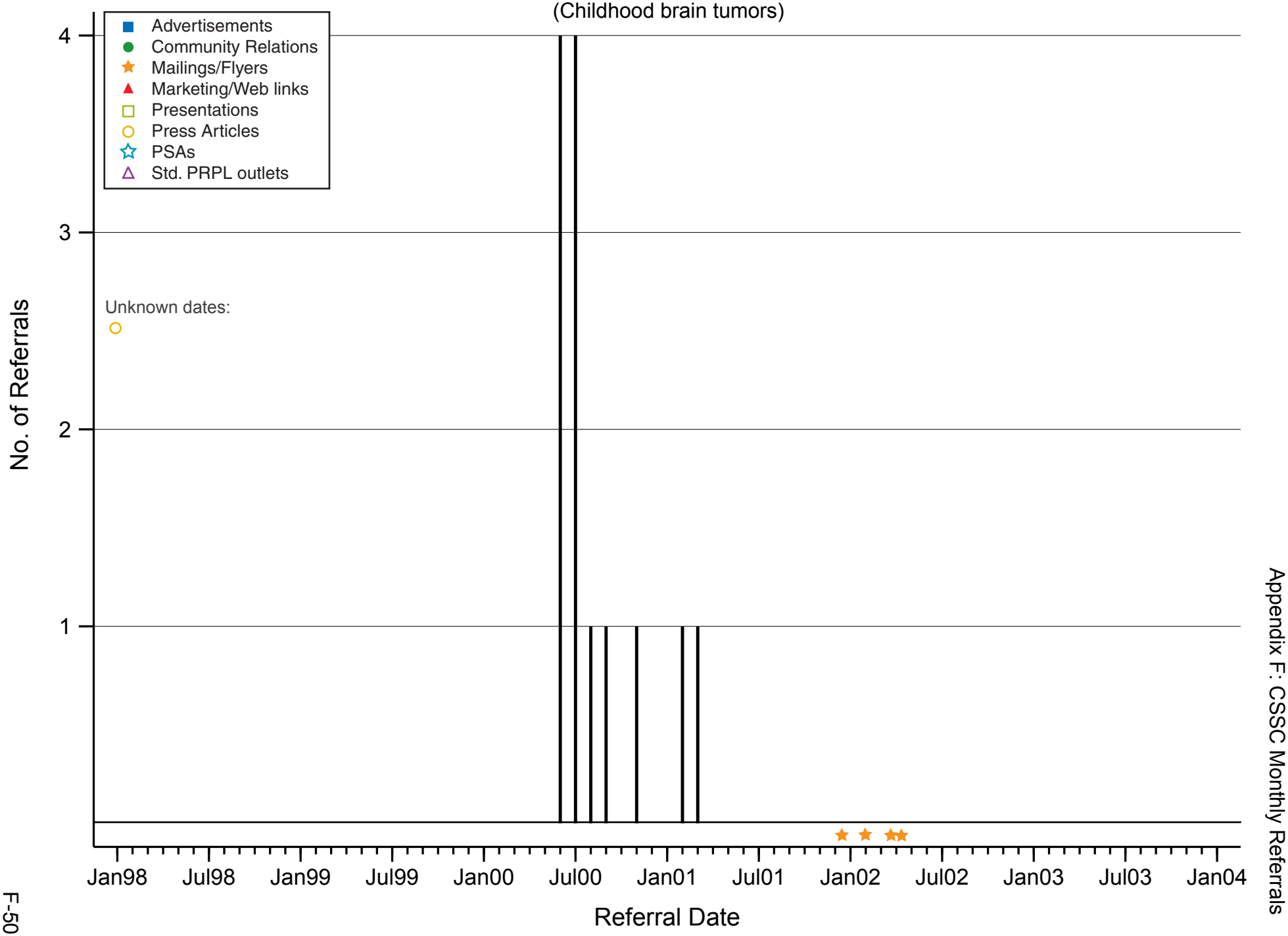
Monthly Referral Distribution of 98-C-0040

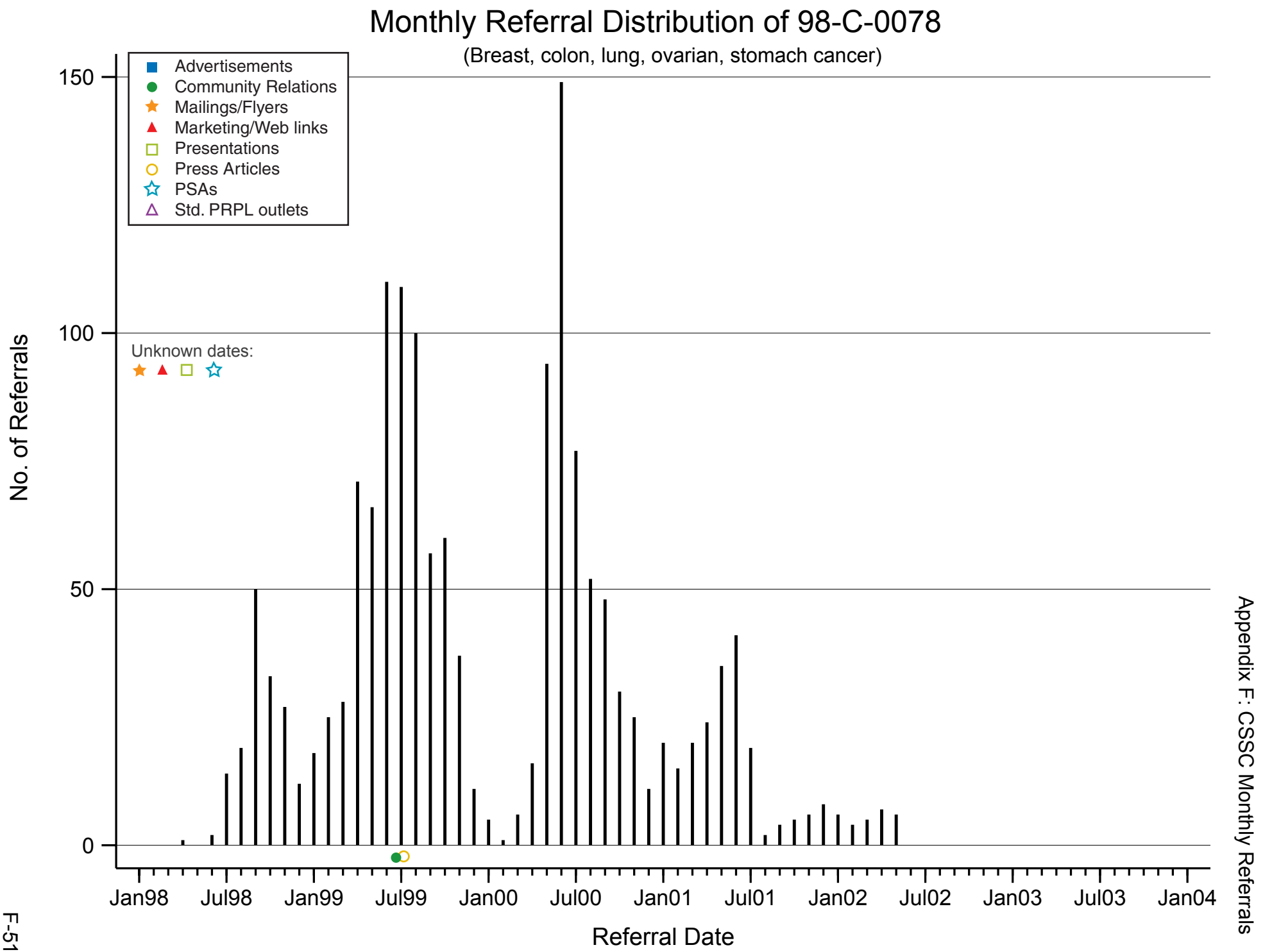
(Metastatic melanoma, renal cell carcinoma)



Monthly Referral Distribution of 98-C-0074

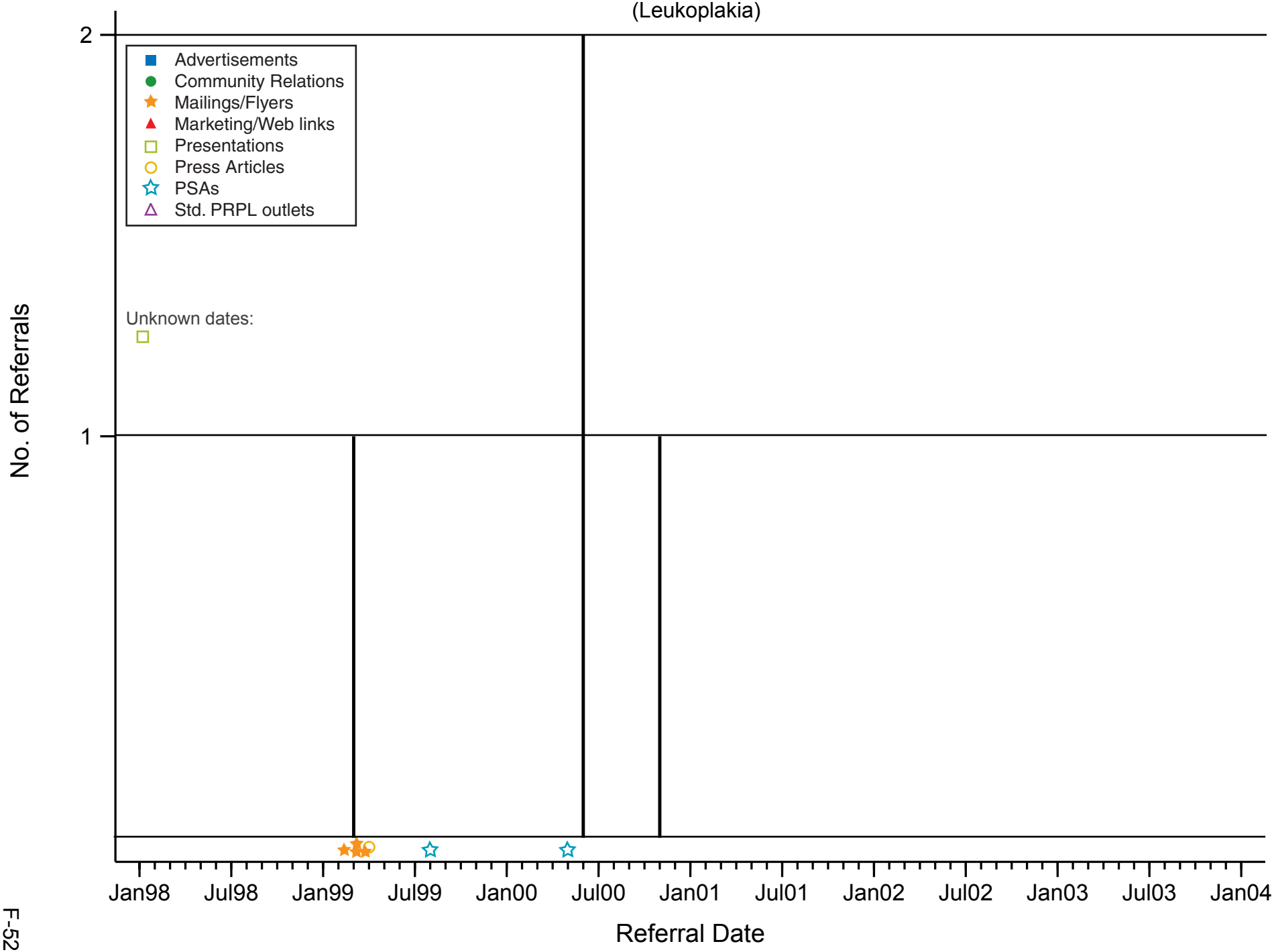
(Childhood brain tumors)




Monthly Referral Distribution of 98-C-0078
(Breast, colon, lung, ovarian, stomach cancer)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown dates:
150
100
50
0
No. of Referrals
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

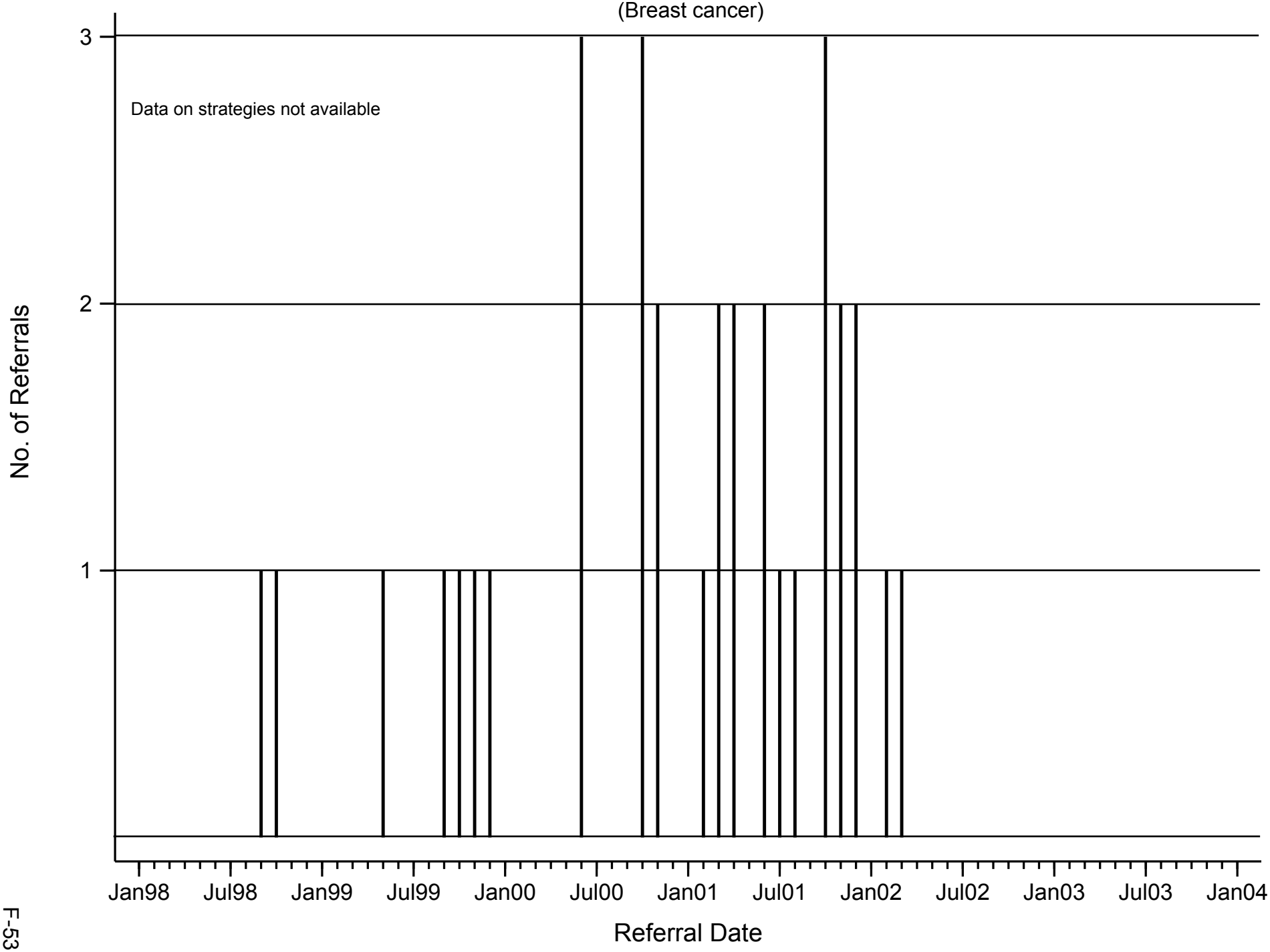
Monthly Referral Distribution of 98-C-0118

(Leukoplakia)



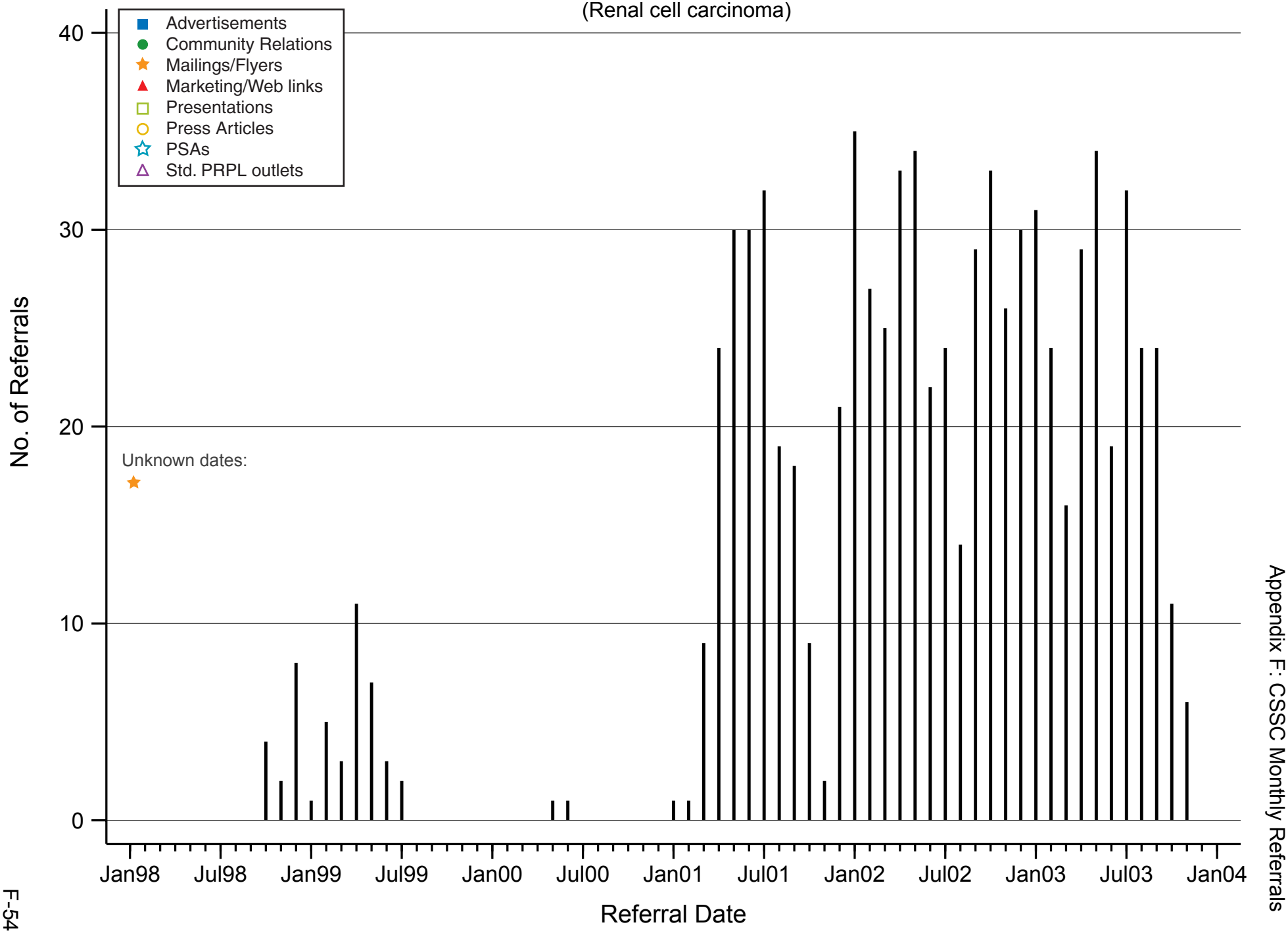
Monthly Referral Distribution of 98-C-0123

(Breast cancer)



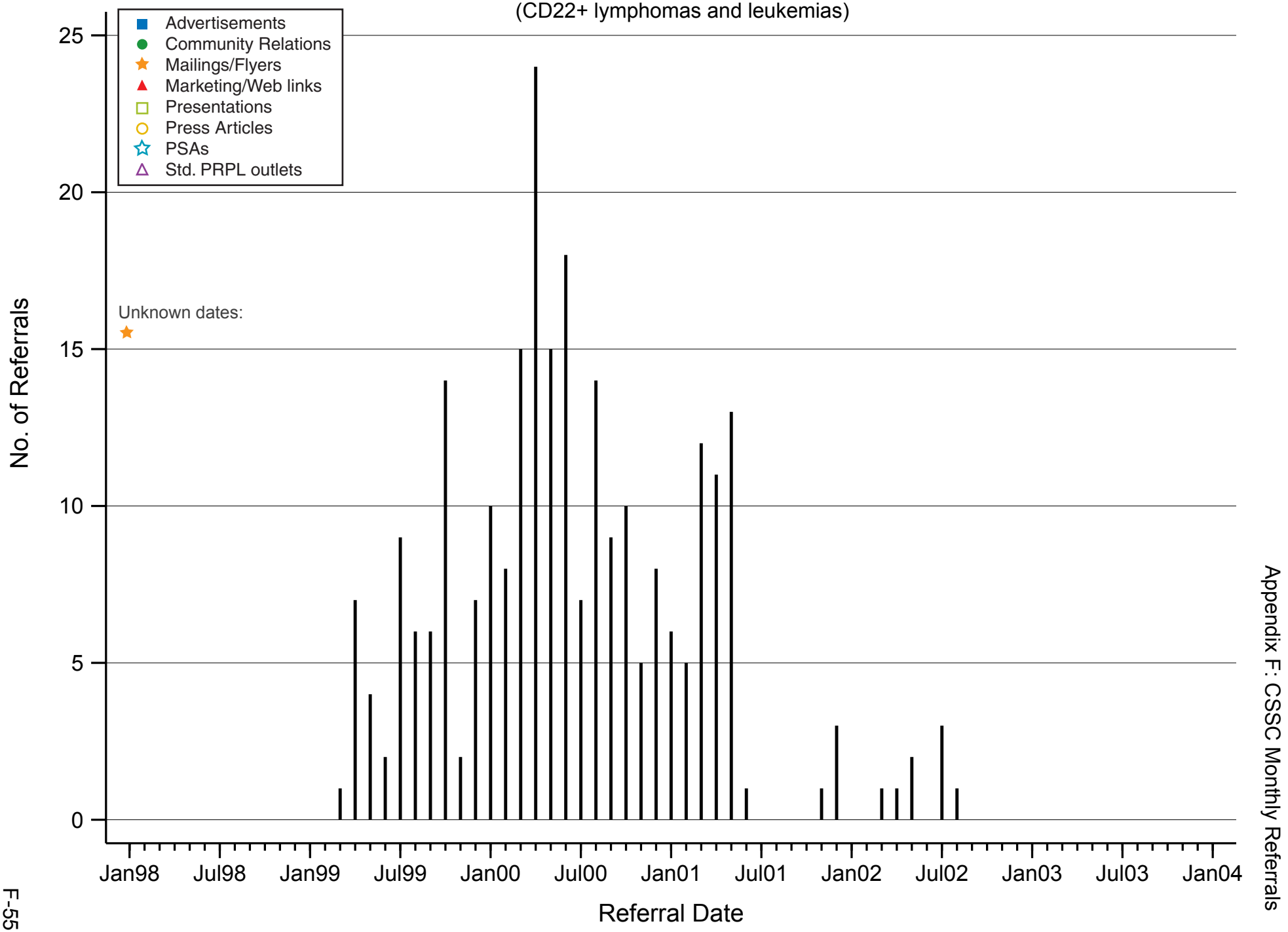
Monthly Referral Distribution of 98-C-0139

(Renal cell carcinoma)



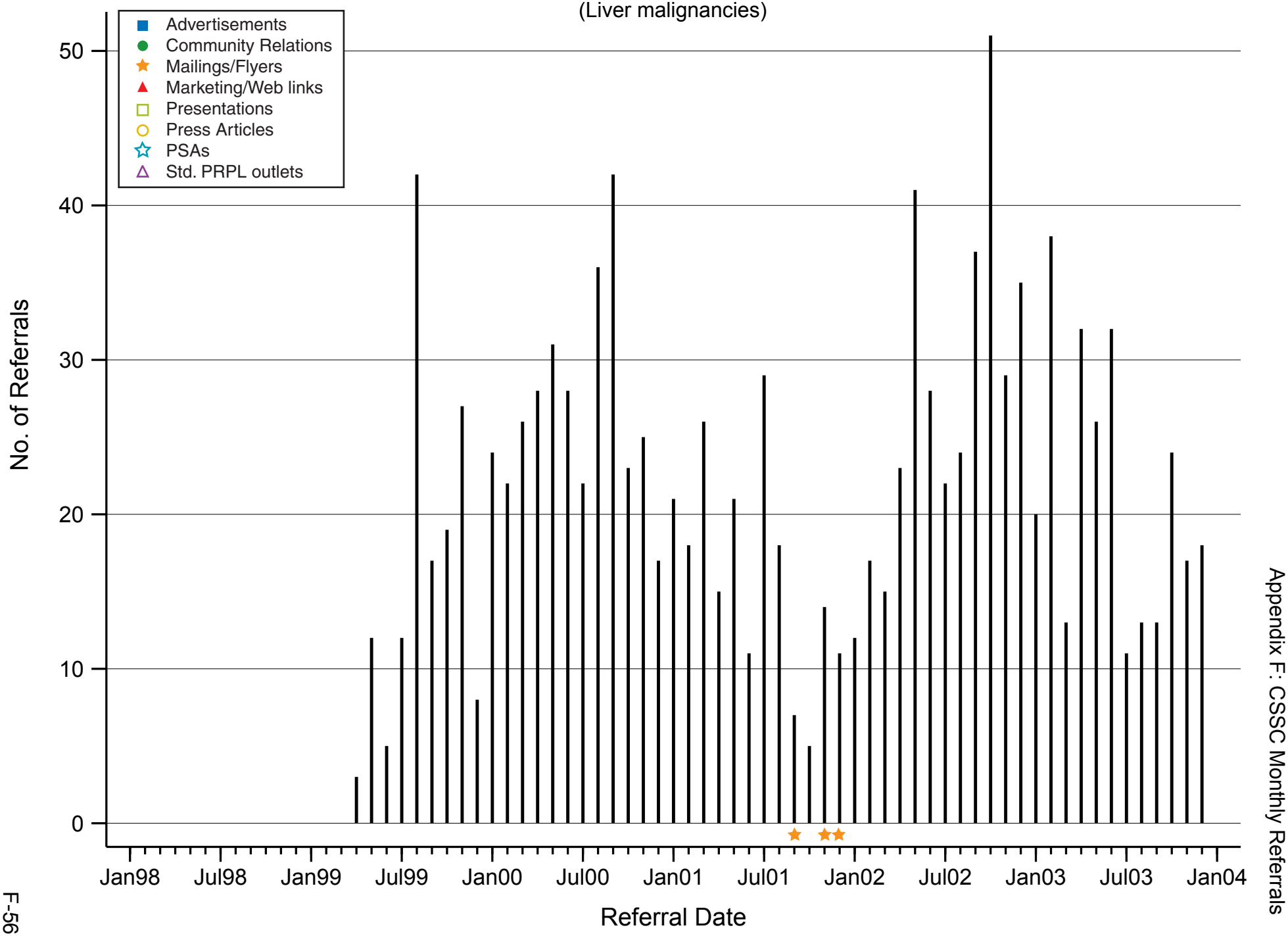
Monthly Referral Distribution of 99-C-0014

(CD22+ lymphomas and leukemias)



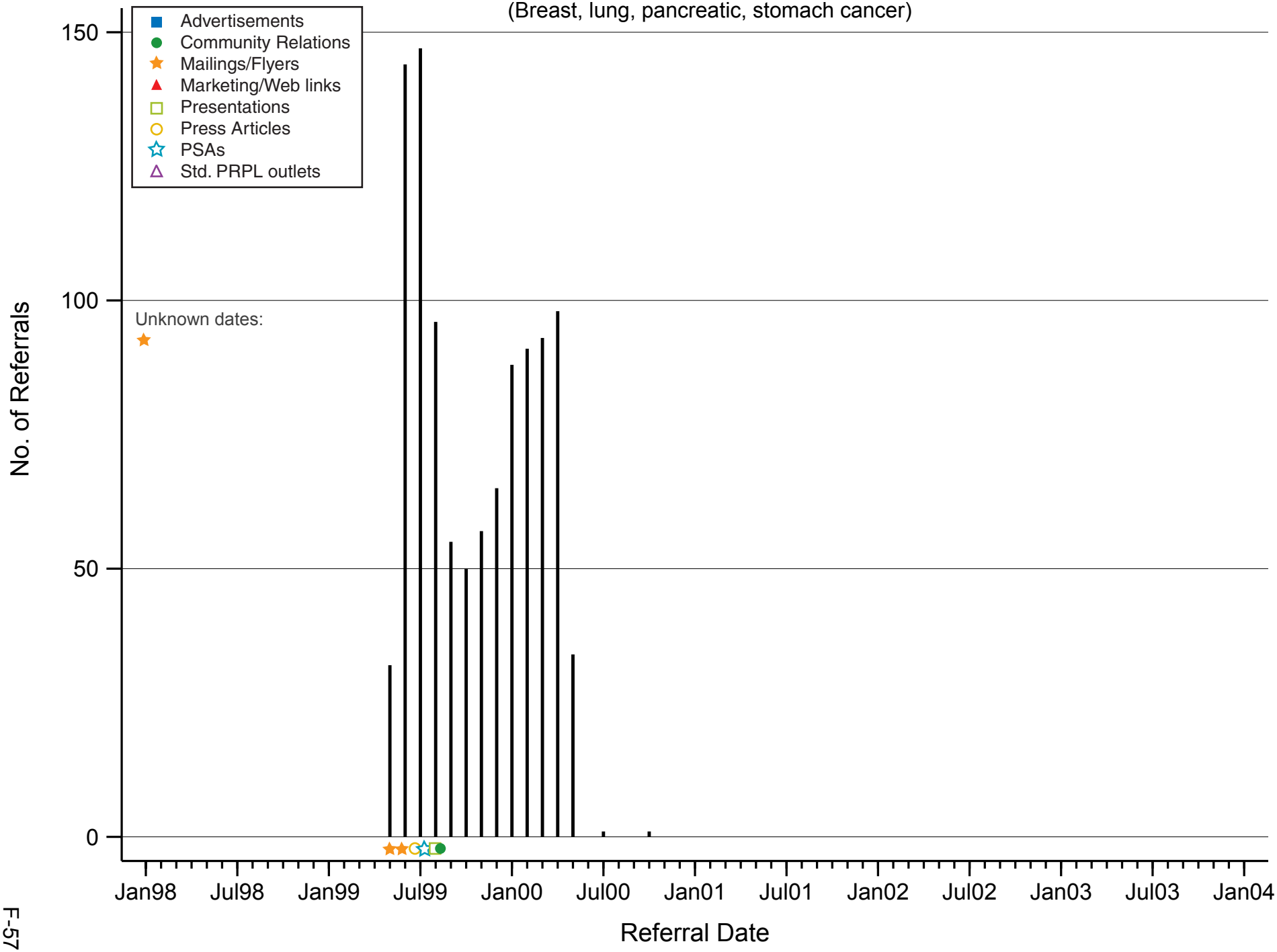
Monthly Referral Distribution of 99-C-0025

(Liver malignancies)



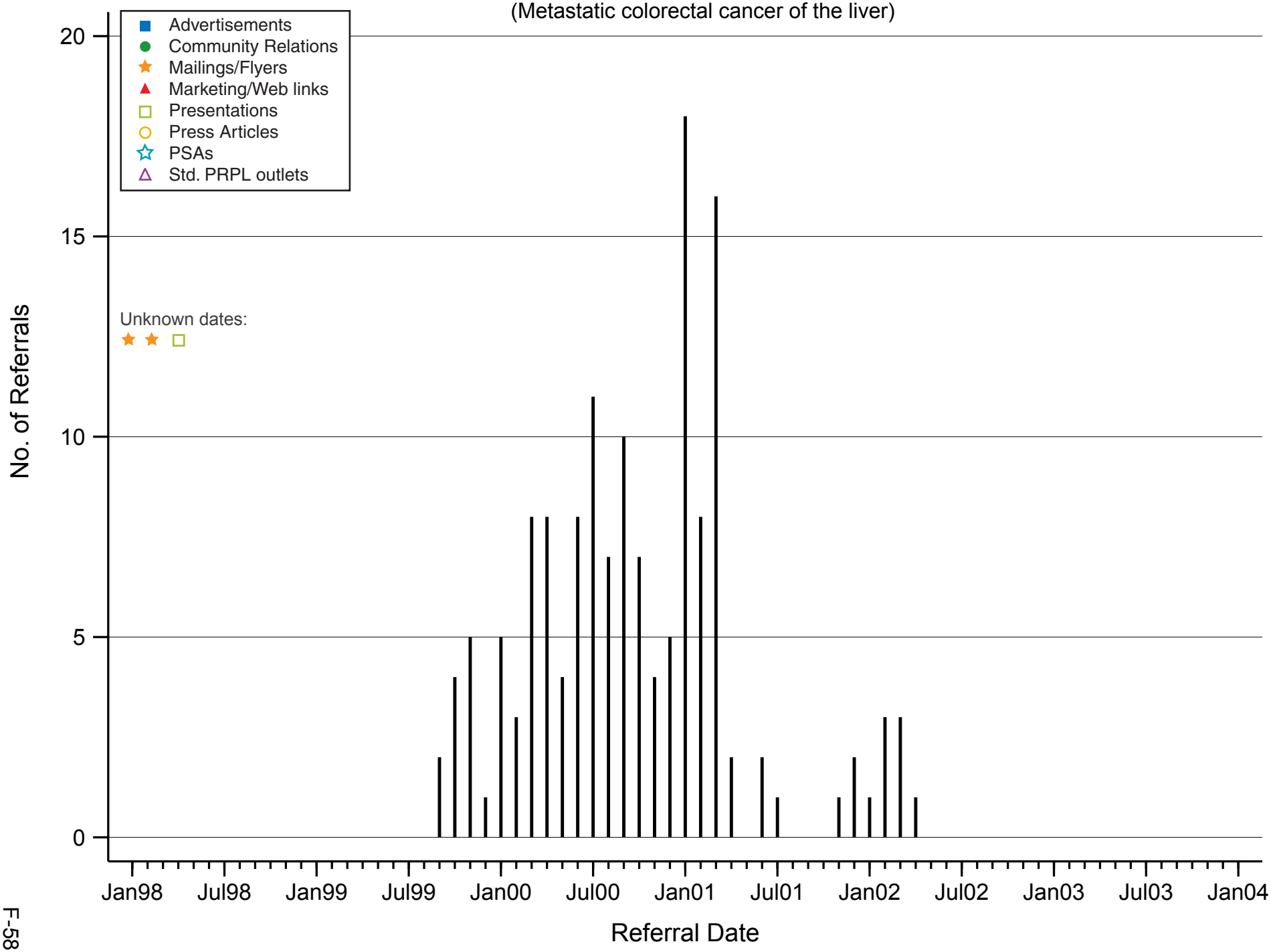
Monthly Referral Distribution of 99-C-0071

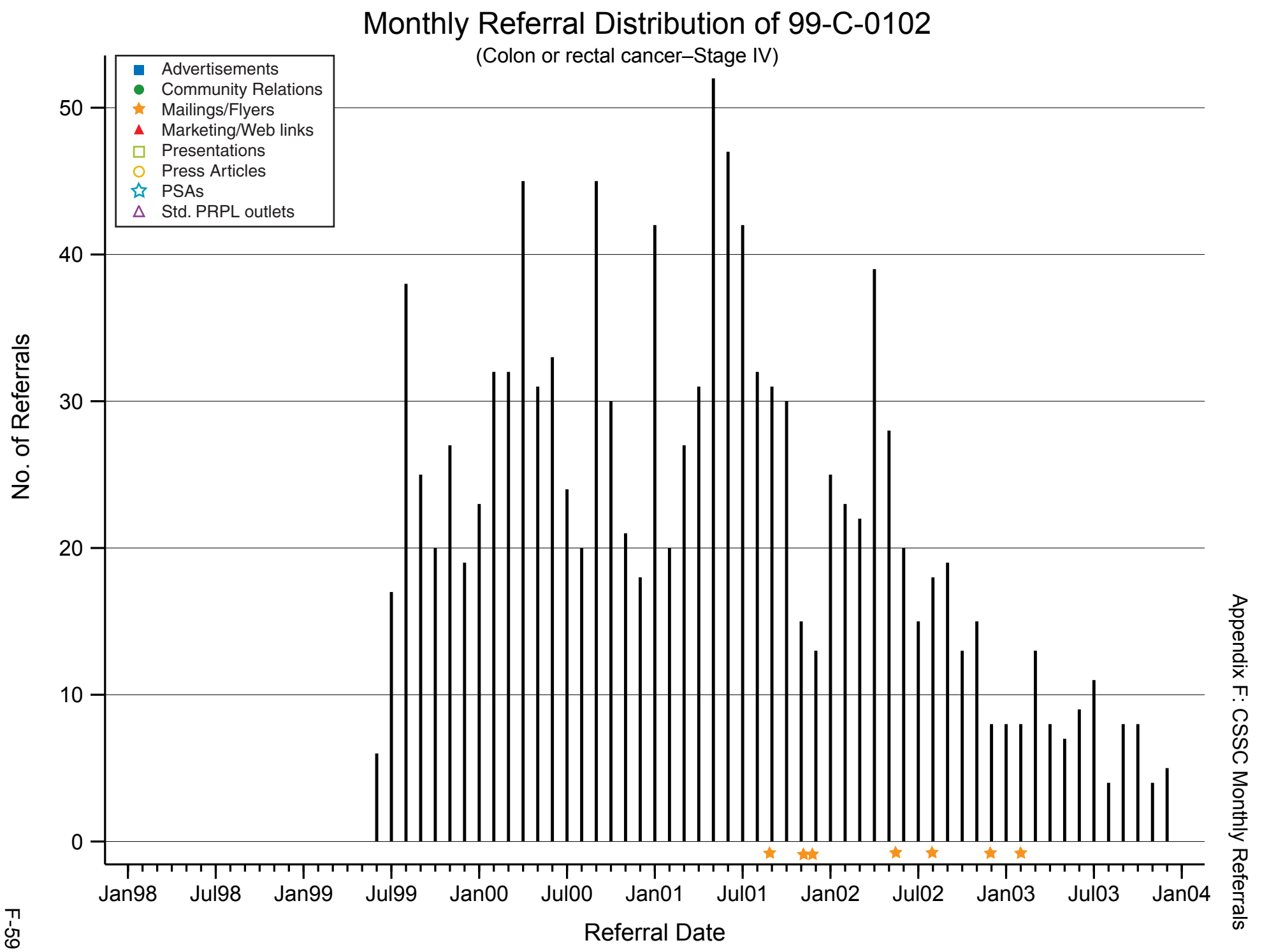
(Breast, lung, pancreatic, stomach cancer)



Monthly Referral Distribution of 99-C-0093

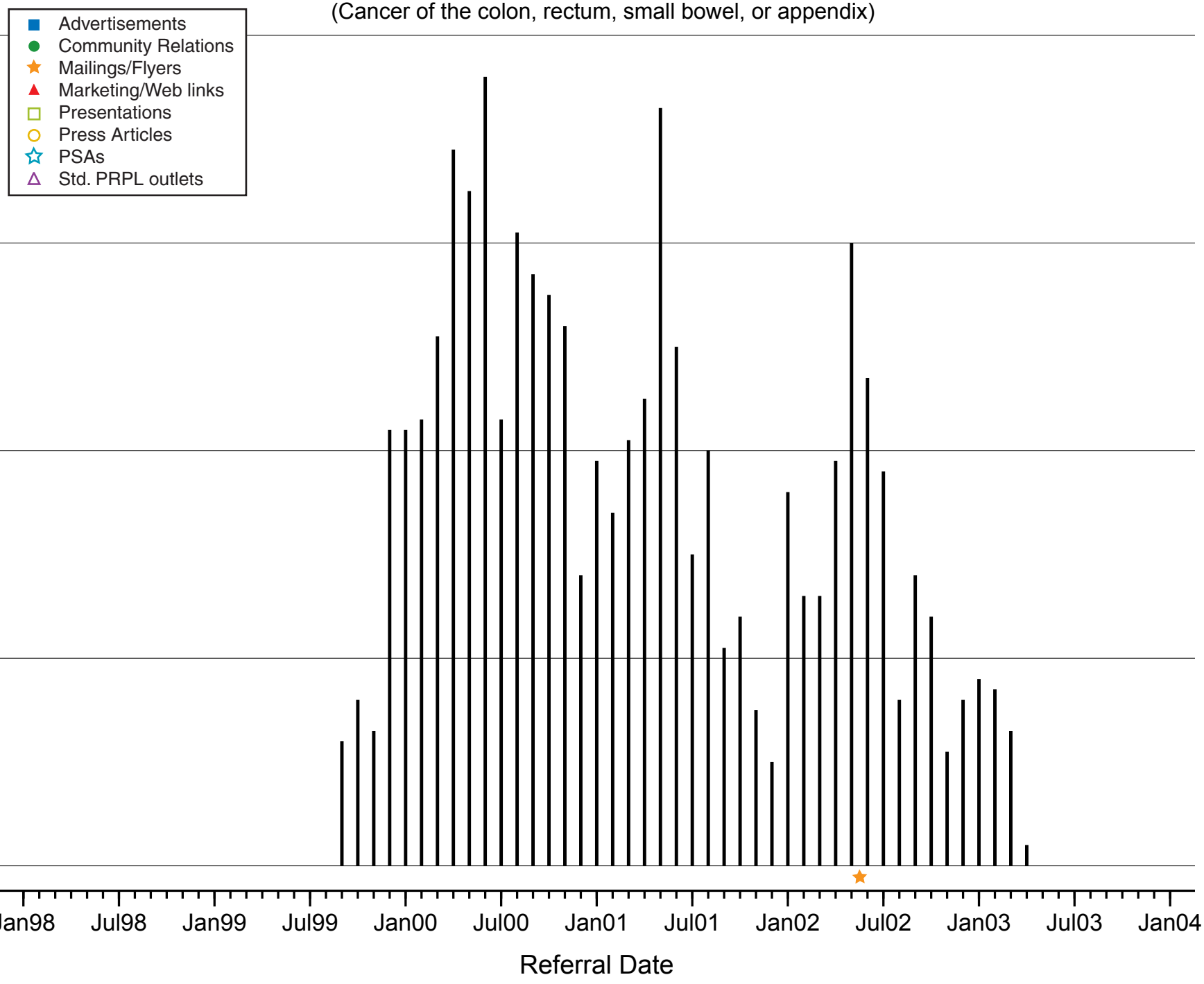
(Metastatic colorectal cancer of the liver)




Monthly Referral Distribution of 99-C-0102
(Colon or rectal cancer–Stage IV)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
0
10
20
30
40
50
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

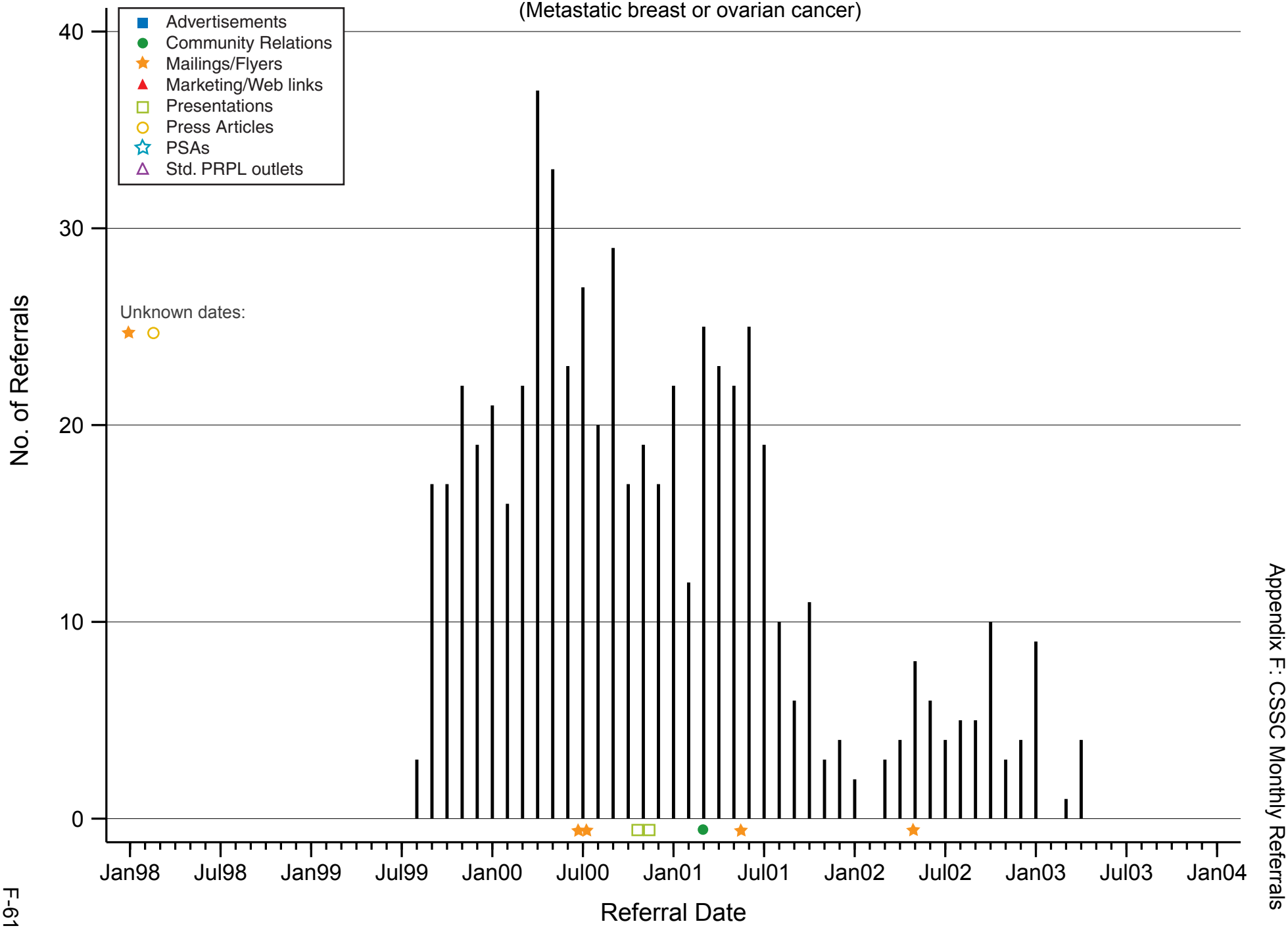
Monthly Referral Distribution of 99-C-0117

(Cancer of the colon, rectum, small bowel, or appendix)



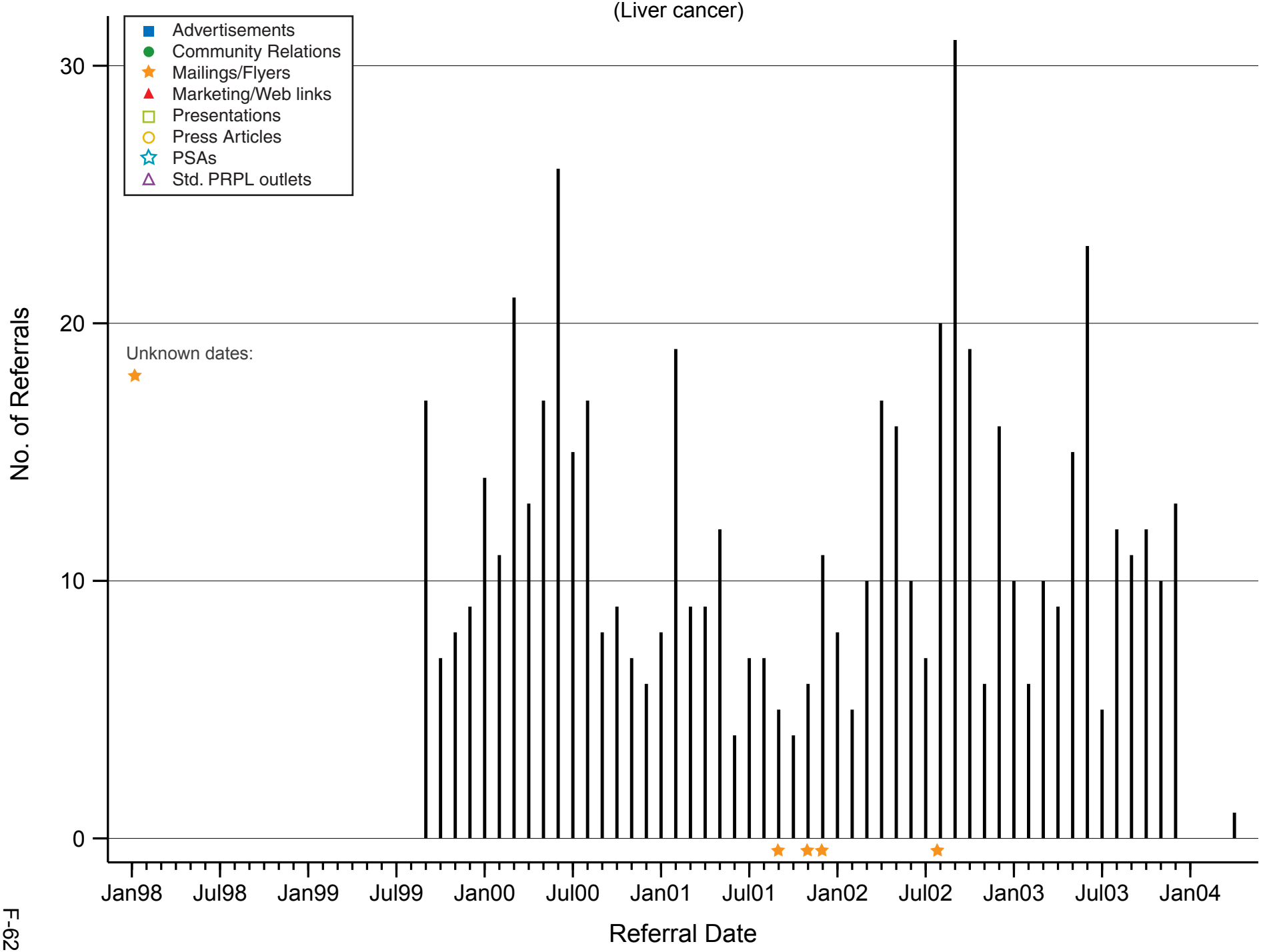
Monthly Referral Distribution of 99-C-0121

(Metastatic breast or ovarian cancer)



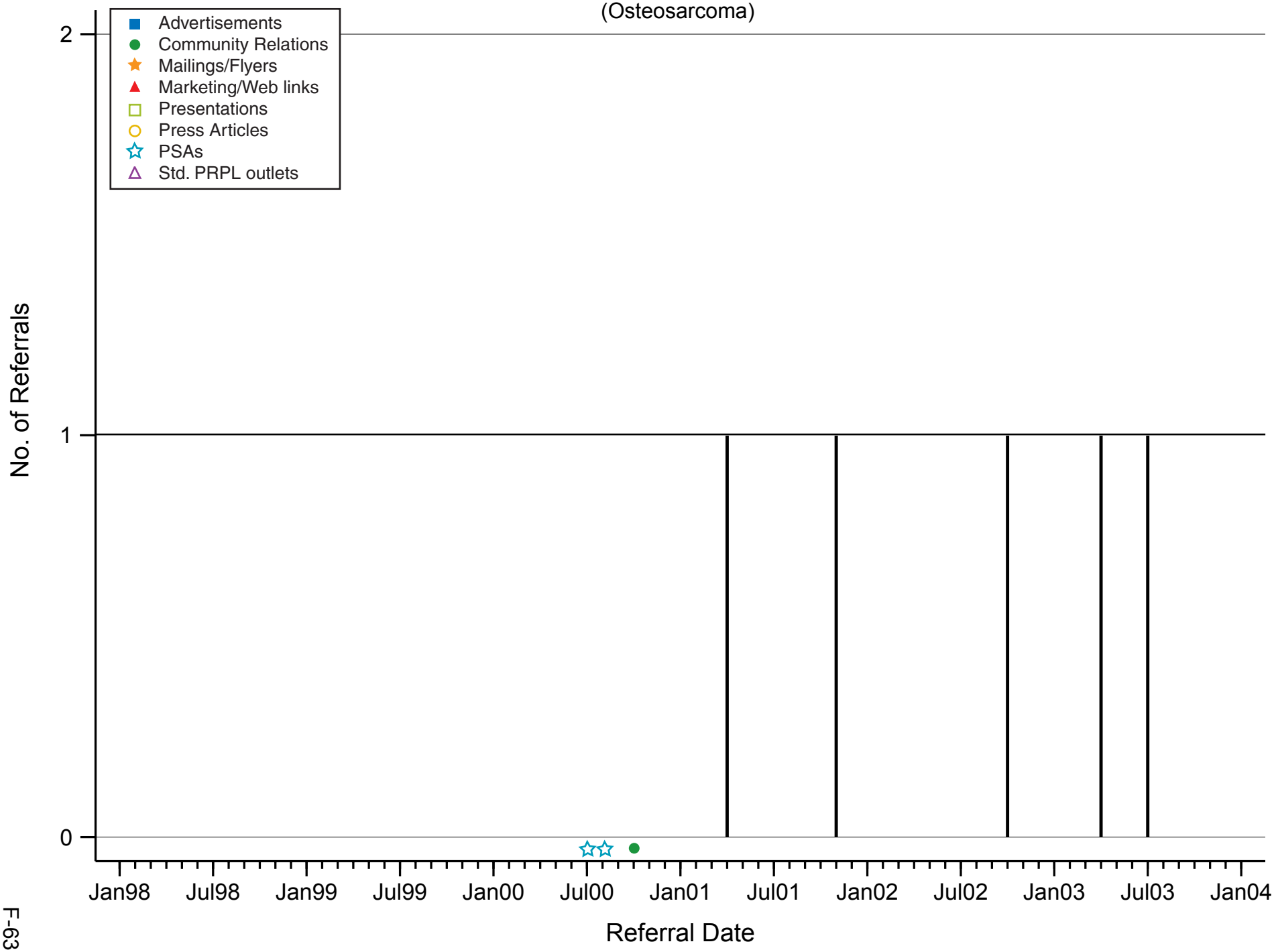
Monthly Referral Distribution of 99-C-0123

(Liver cancer)



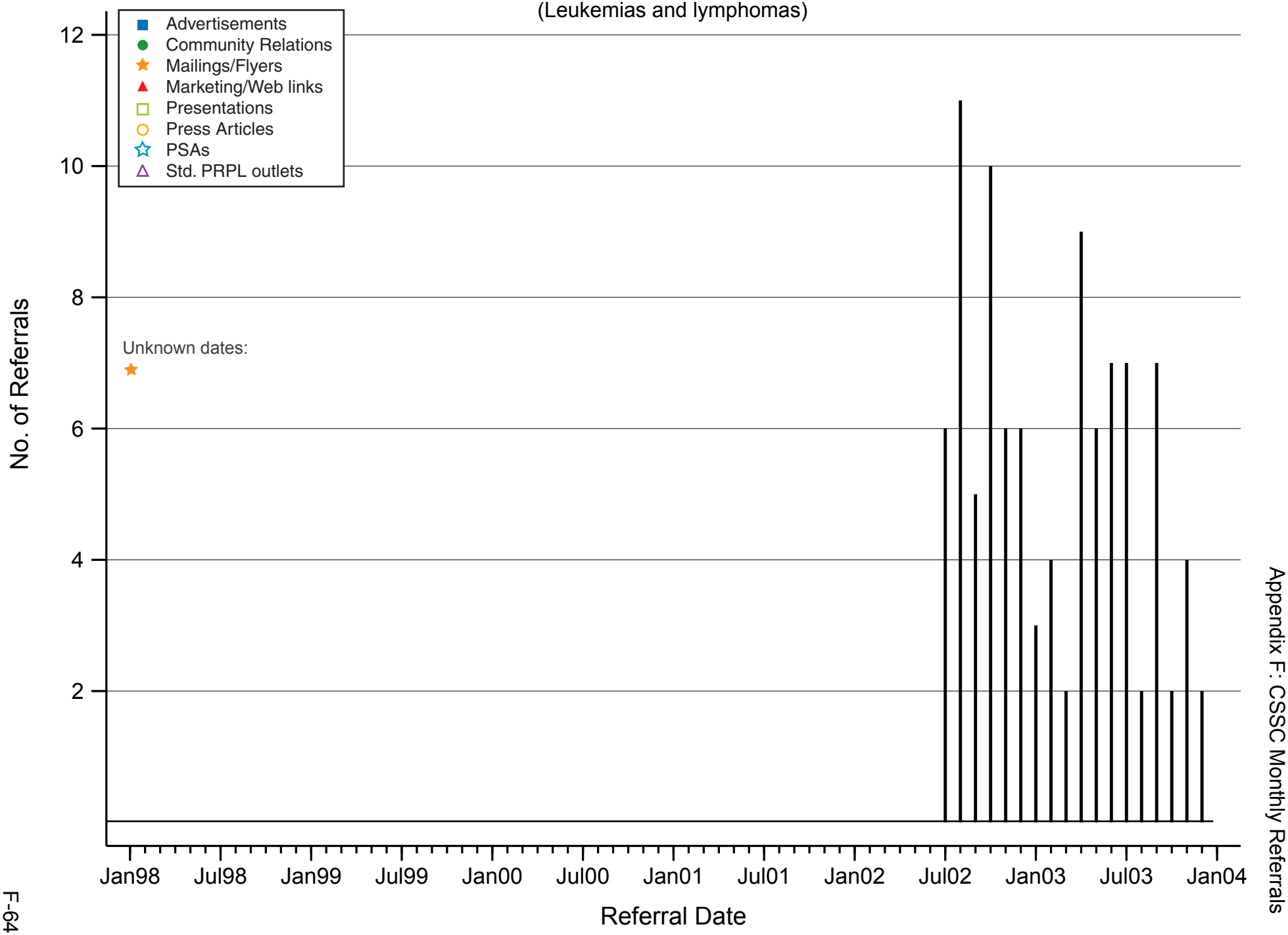
Monthly Referral Distribution of 99-C-0125

(Osteosarcoma)



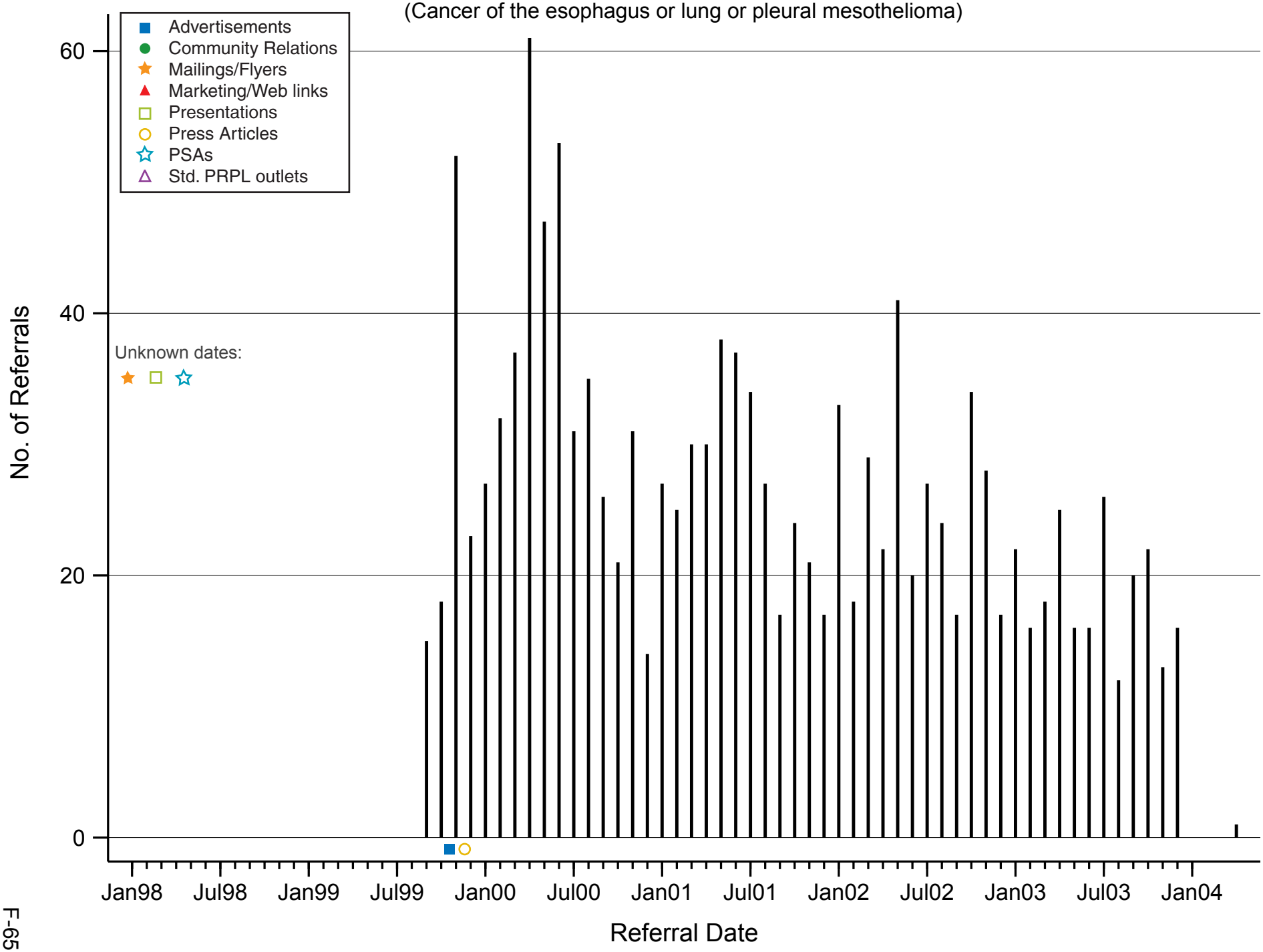
Monthly Referral Distribution of 99-C-0127

(Leukemias and lymphomas)



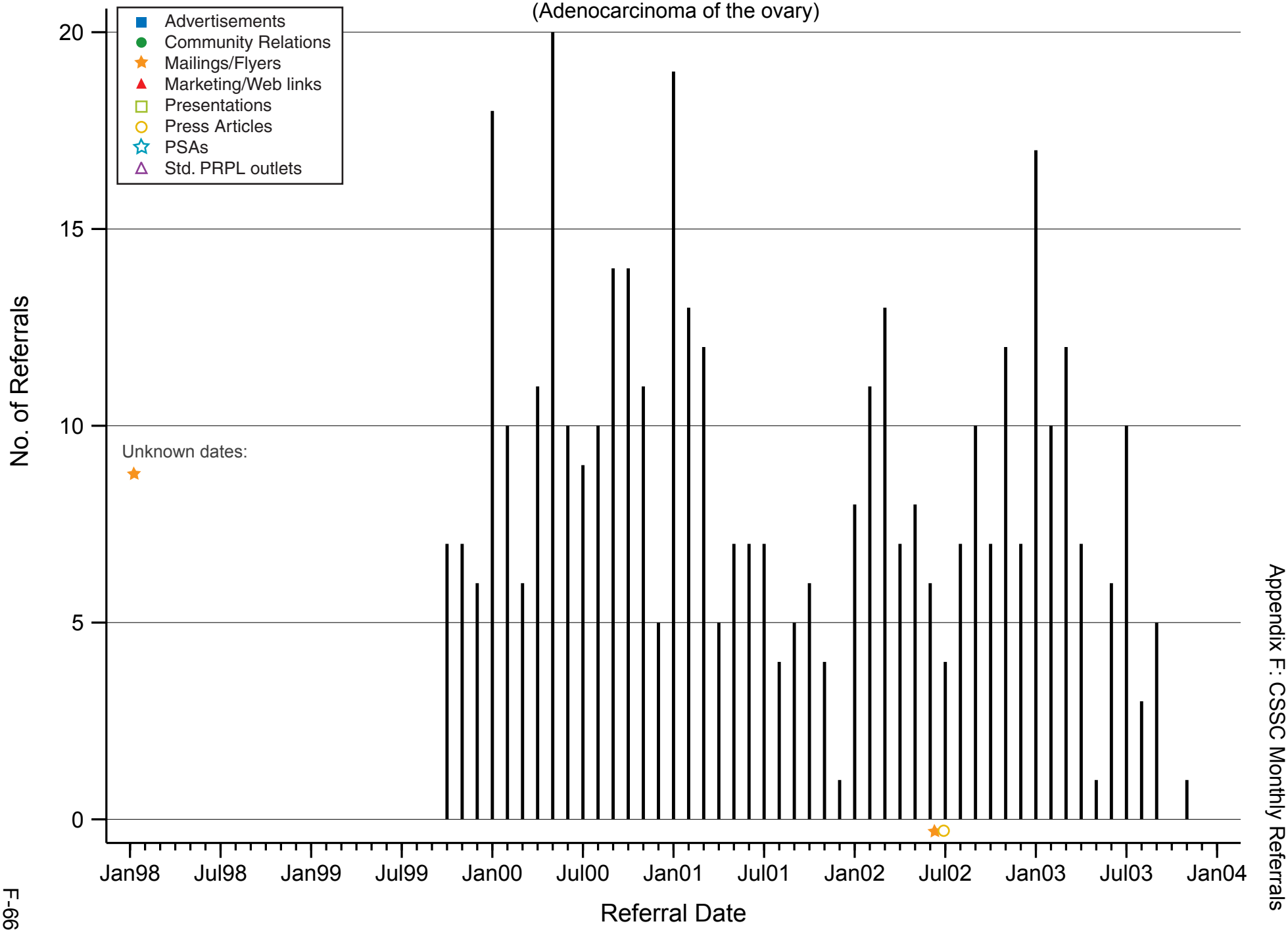
Monthly Referral Distribution of 99-C-0129

(Cancer of the esophagus or lung or pleural mesothelioma)



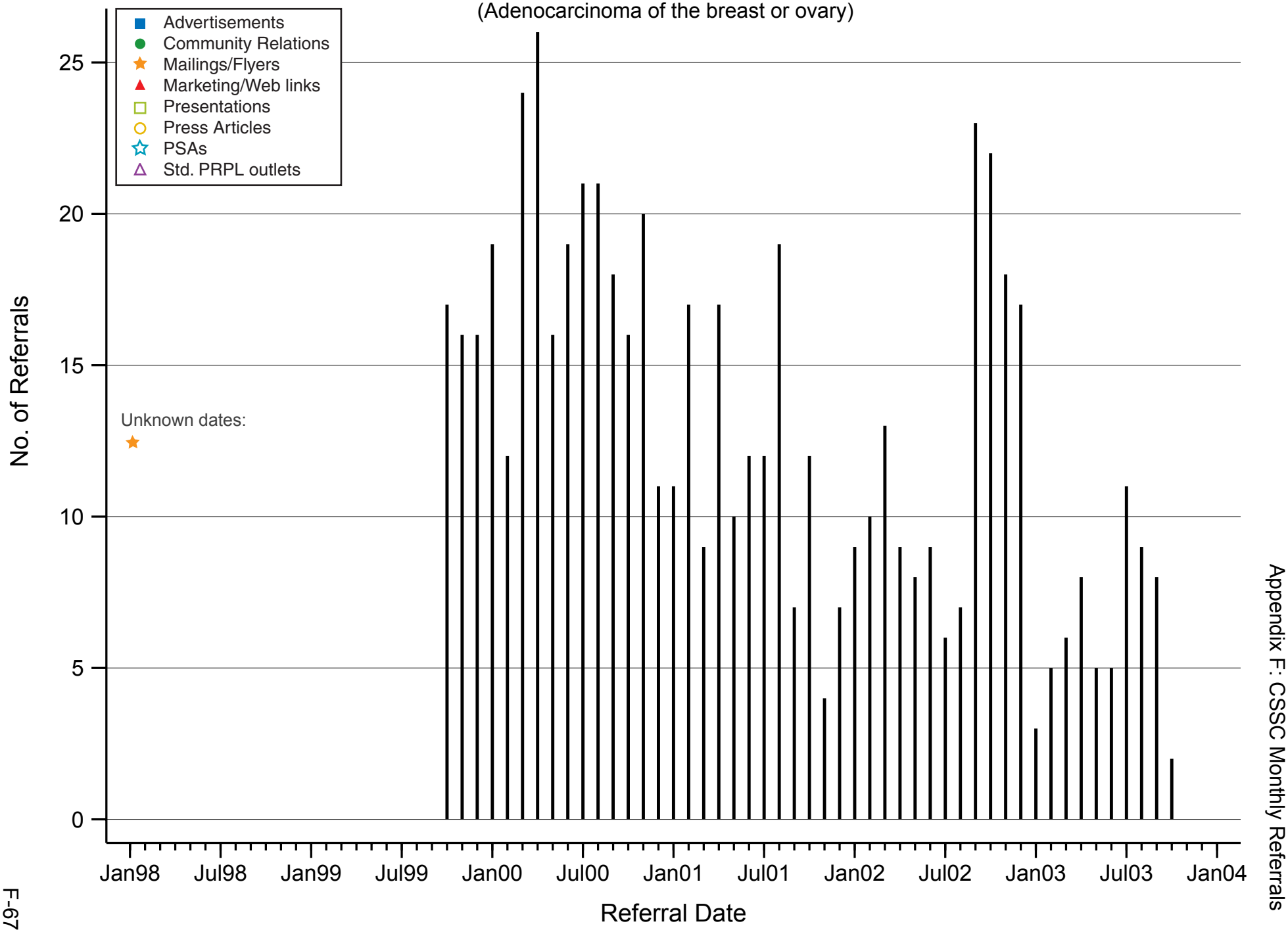
Monthly Referral Distribution of 99-C-0137

(Adenocarcinoma of the ovary)



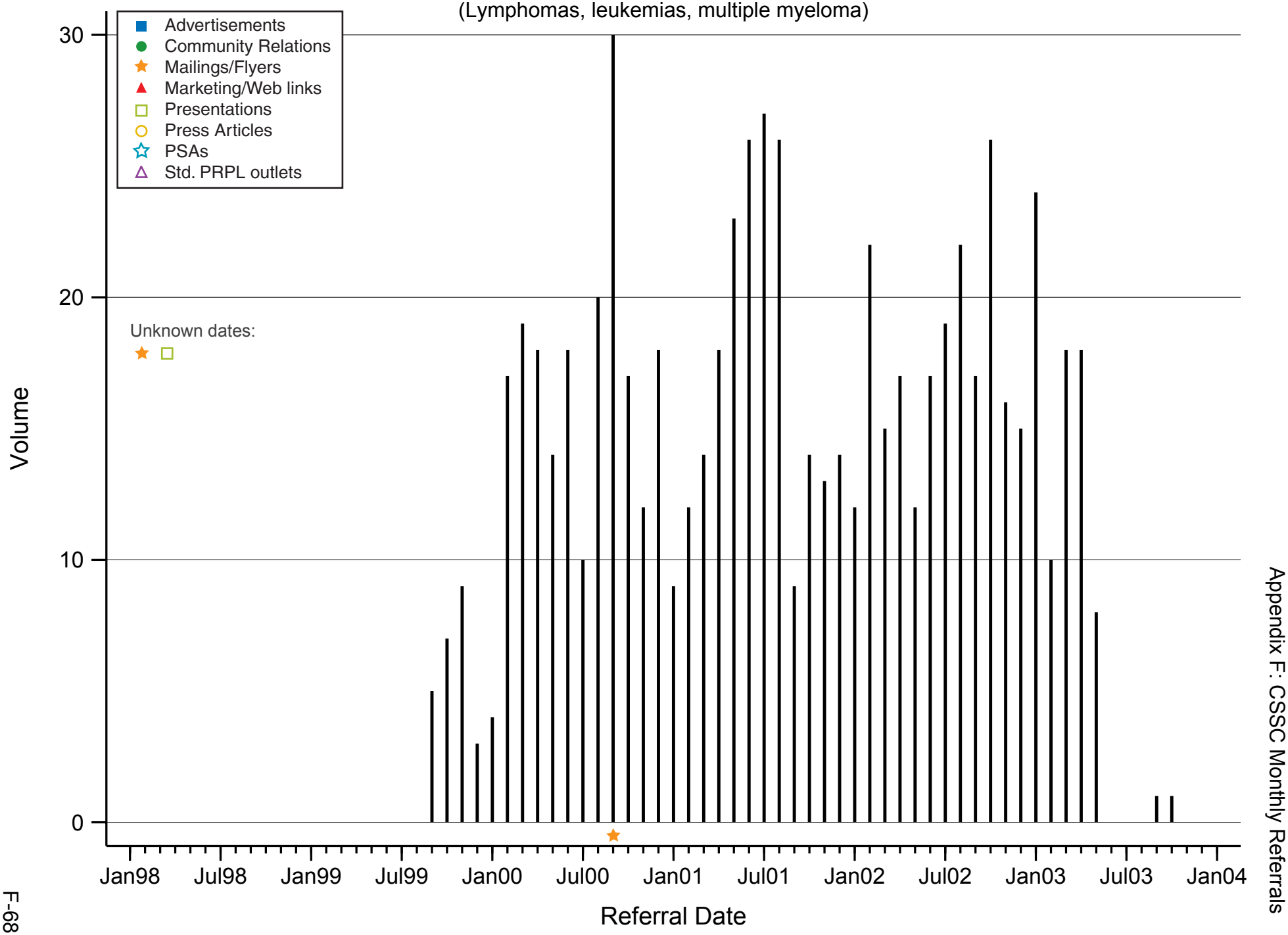
Monthly Referral Distribution of 99-C-0138

(Adenocarcinoma of the breast or ovary)



Monthly Referral Distribution of 99-C-0143

(Lymphomas, leukemias, multiple myeloma)

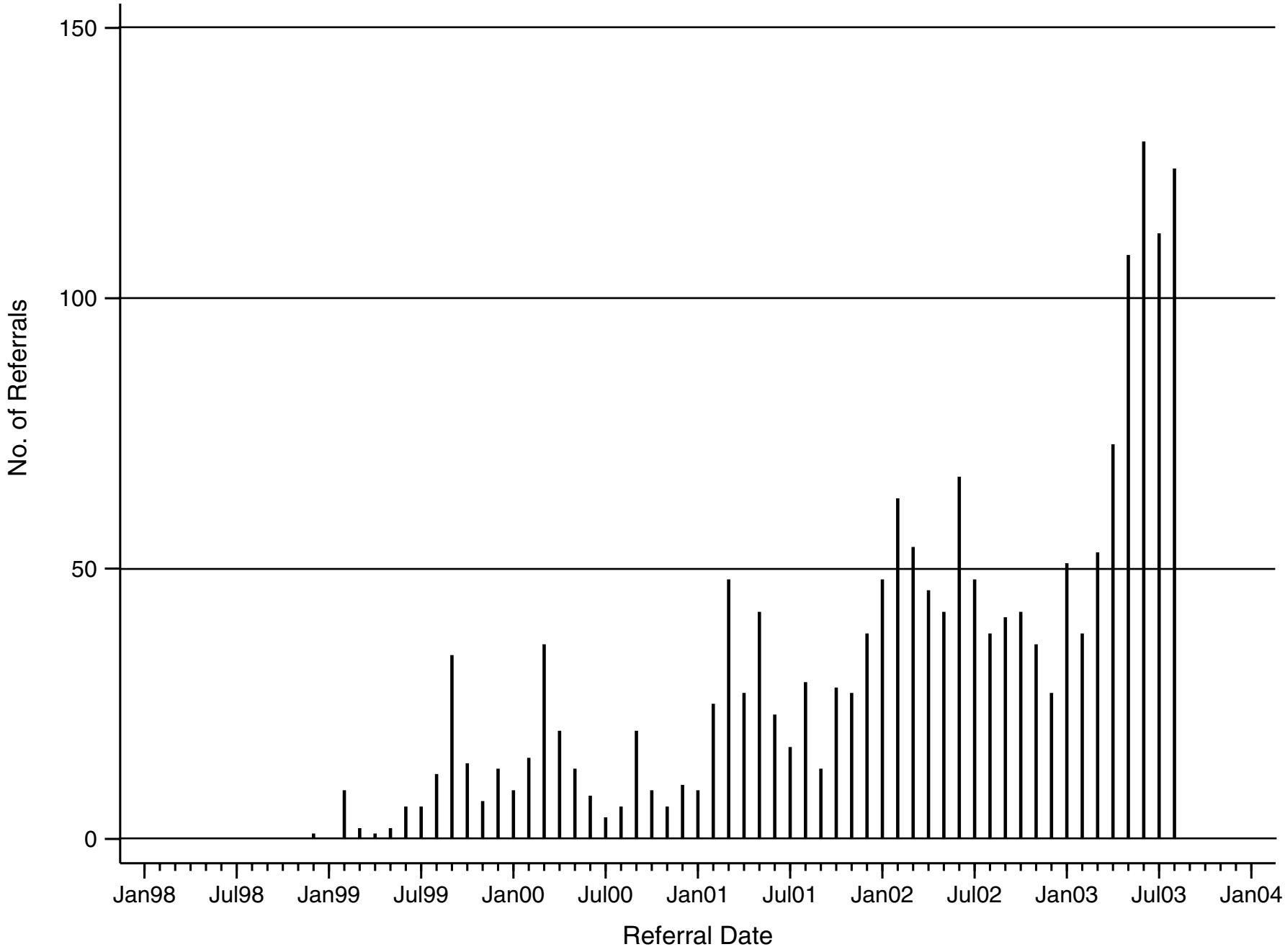


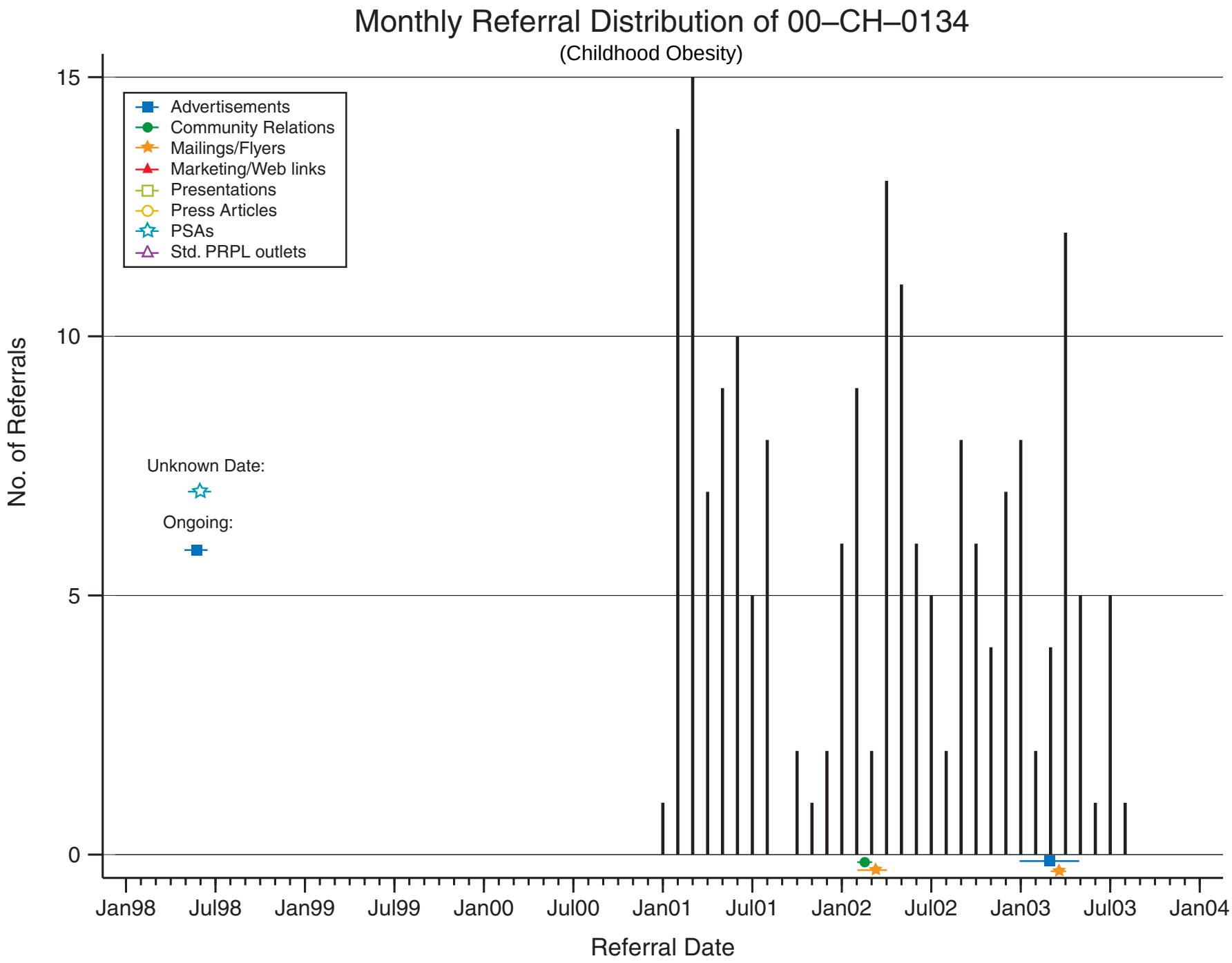
Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

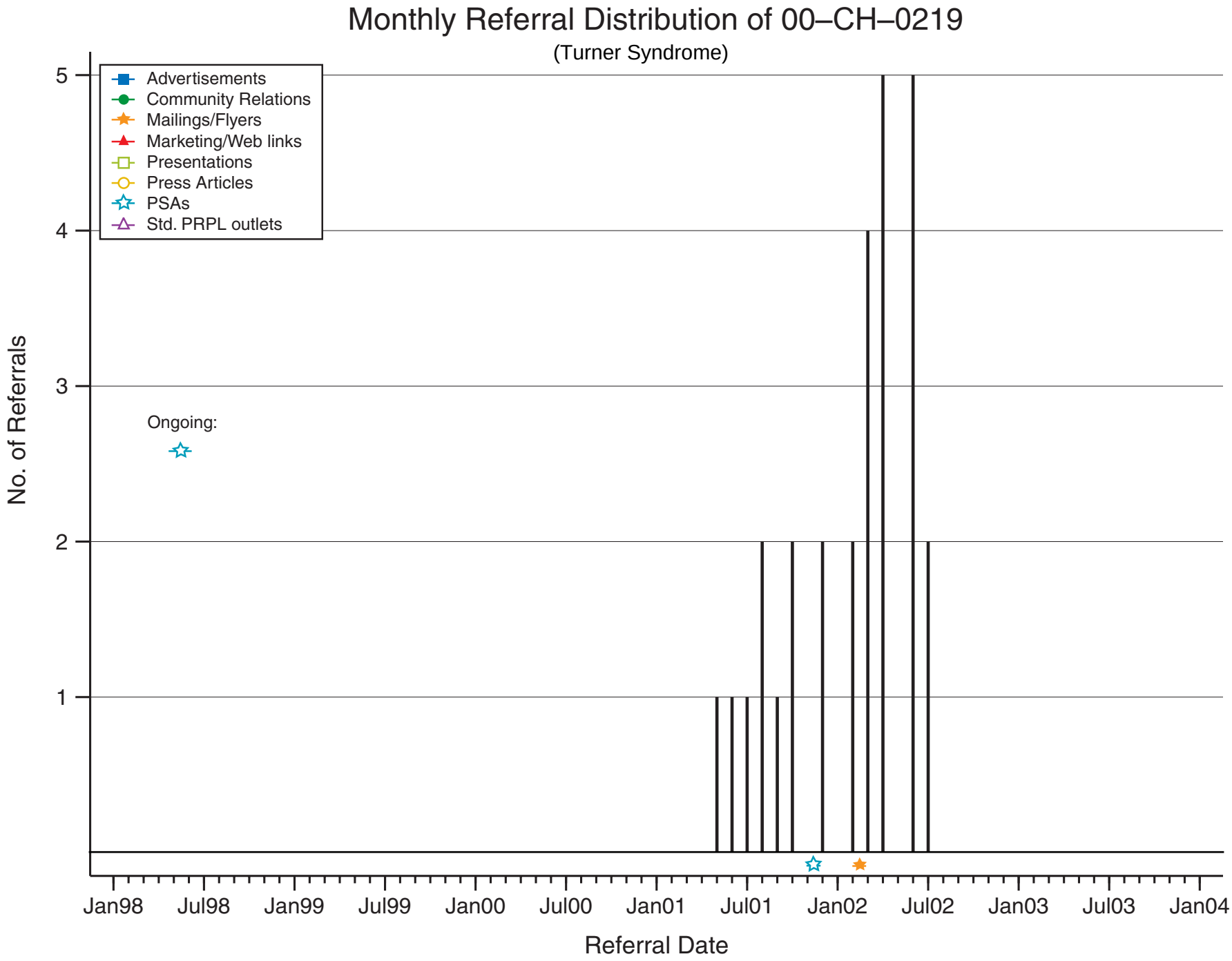
Appendix G: PRPL Monthly Referrals

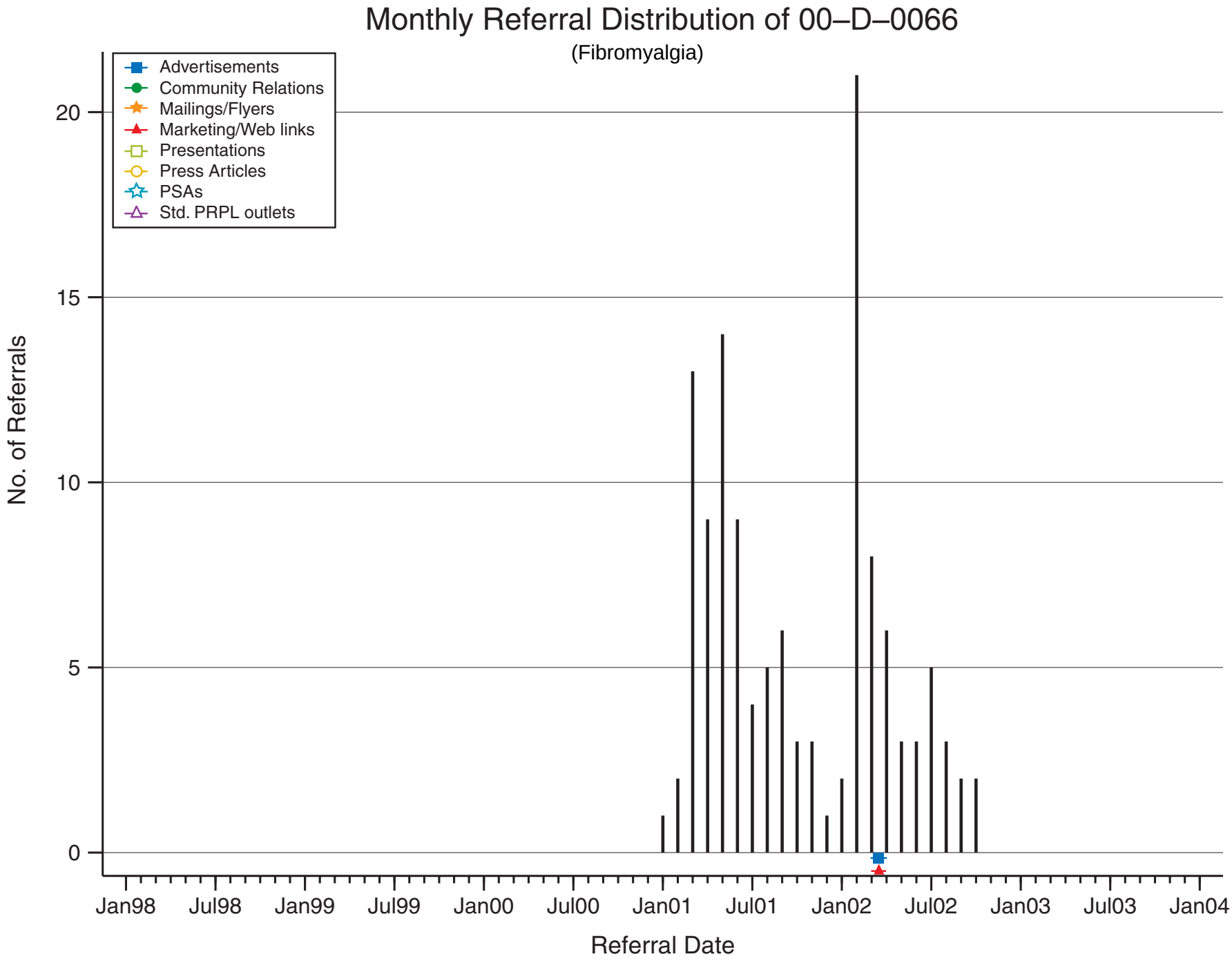
CSR Incorporated
Consulting Services & Research

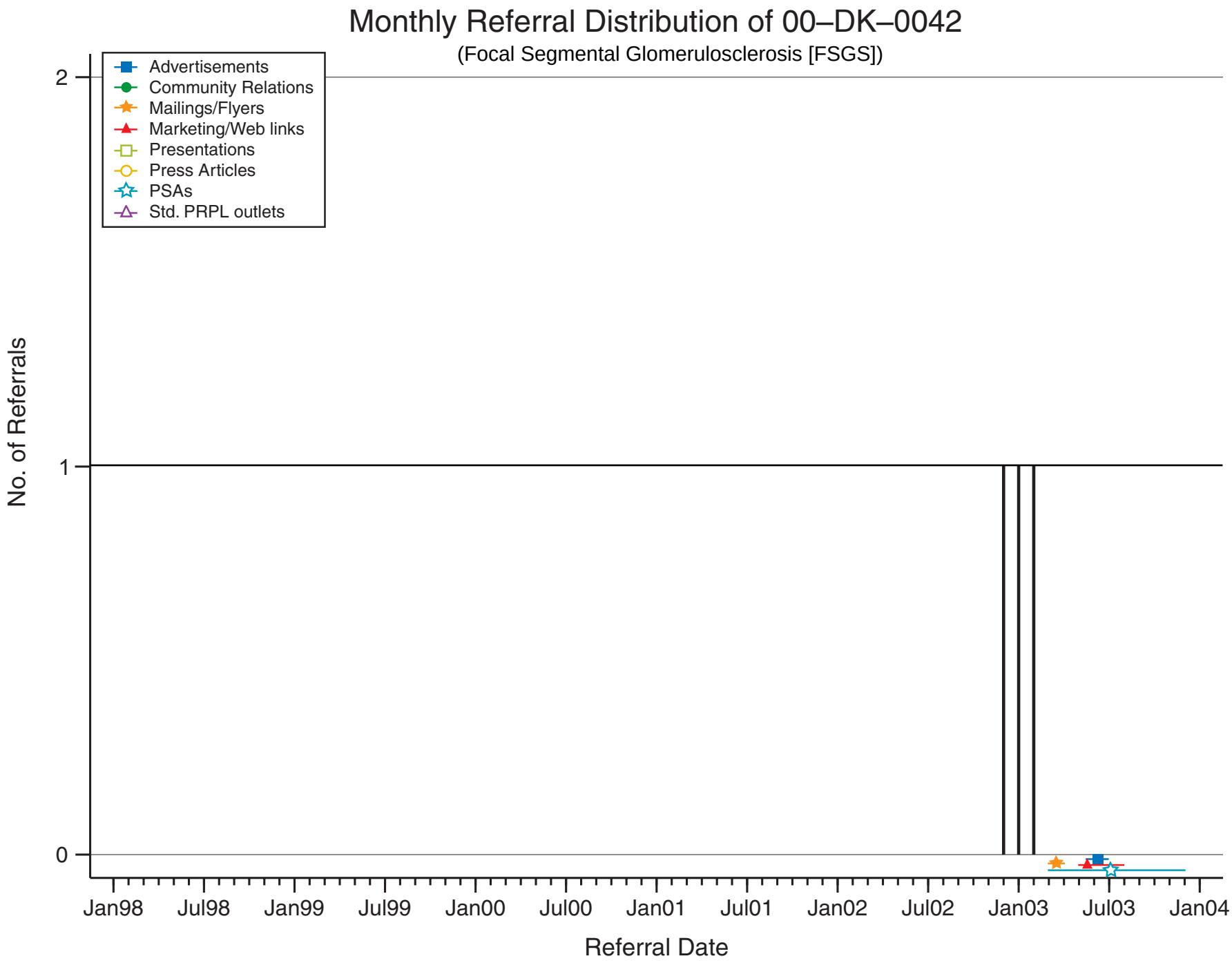
Appendix G: PRPL Monthly Referrals: Distribution of 34 PRPL Protocols

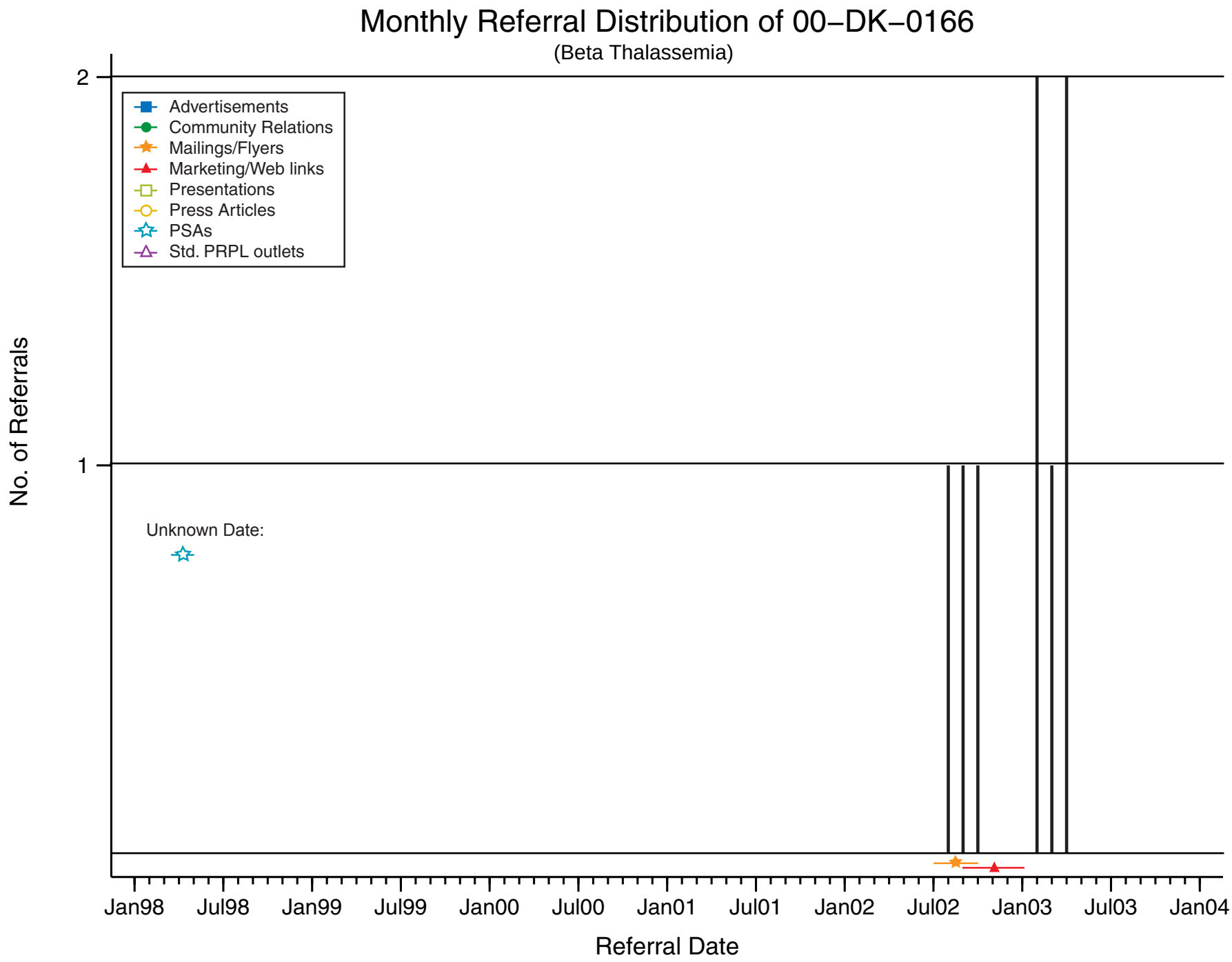


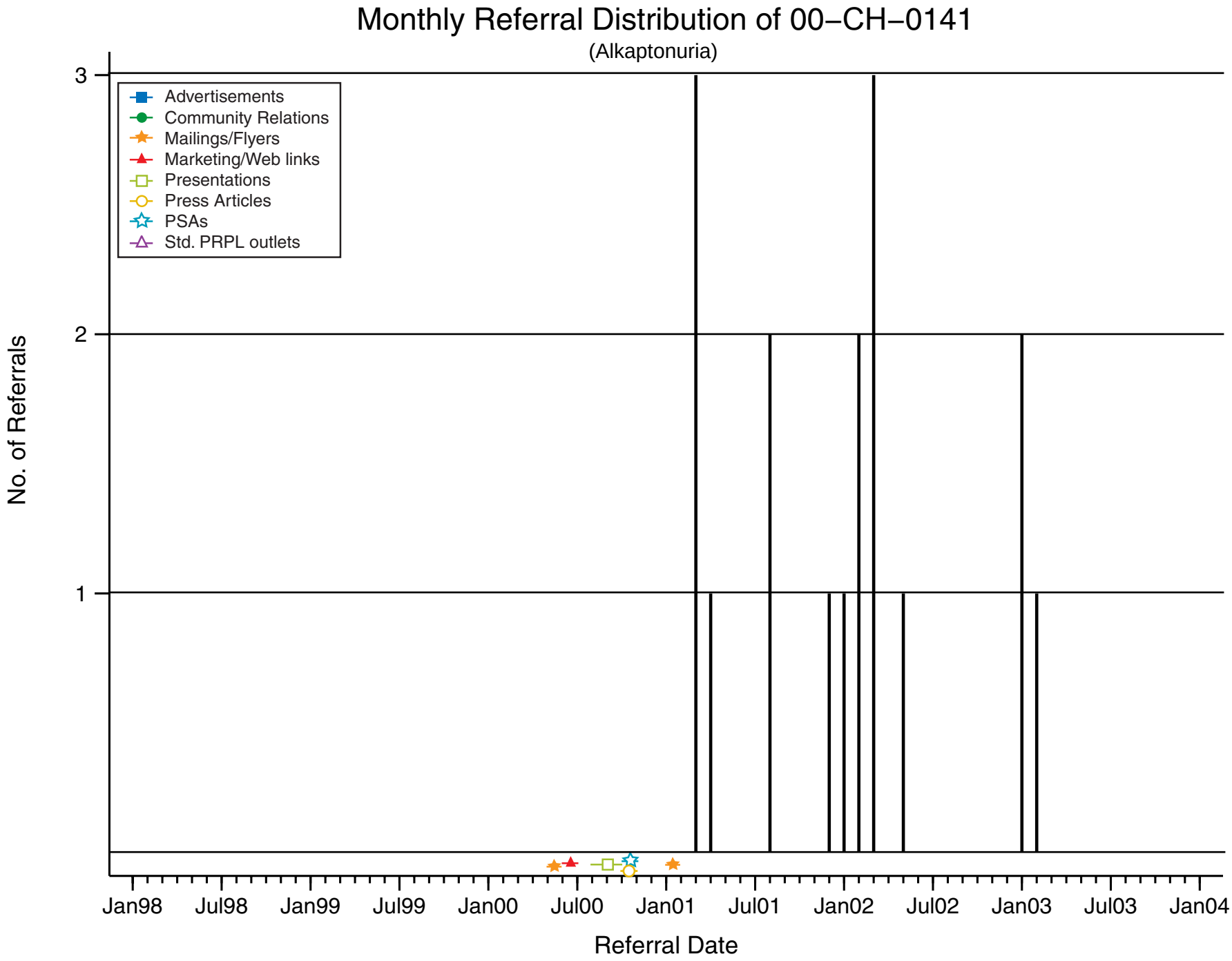

Monthly Referral Distribution of 00–CH–0134
(Childhood Obesity)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown Date:
Ongoing:
No. of Referrals
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

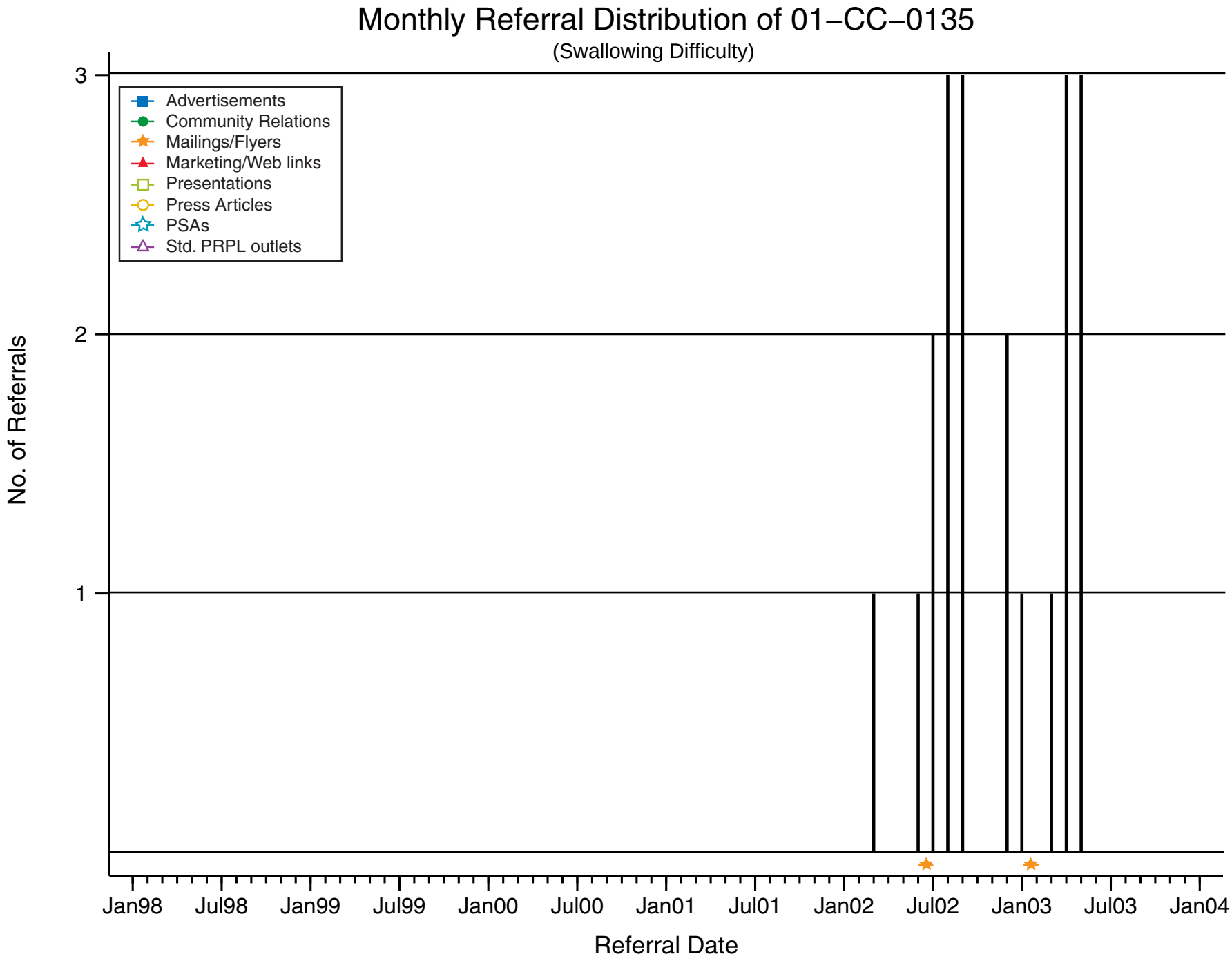

Monthly Referral Distribution of 00–CH–0219
(Turner Syndrome)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

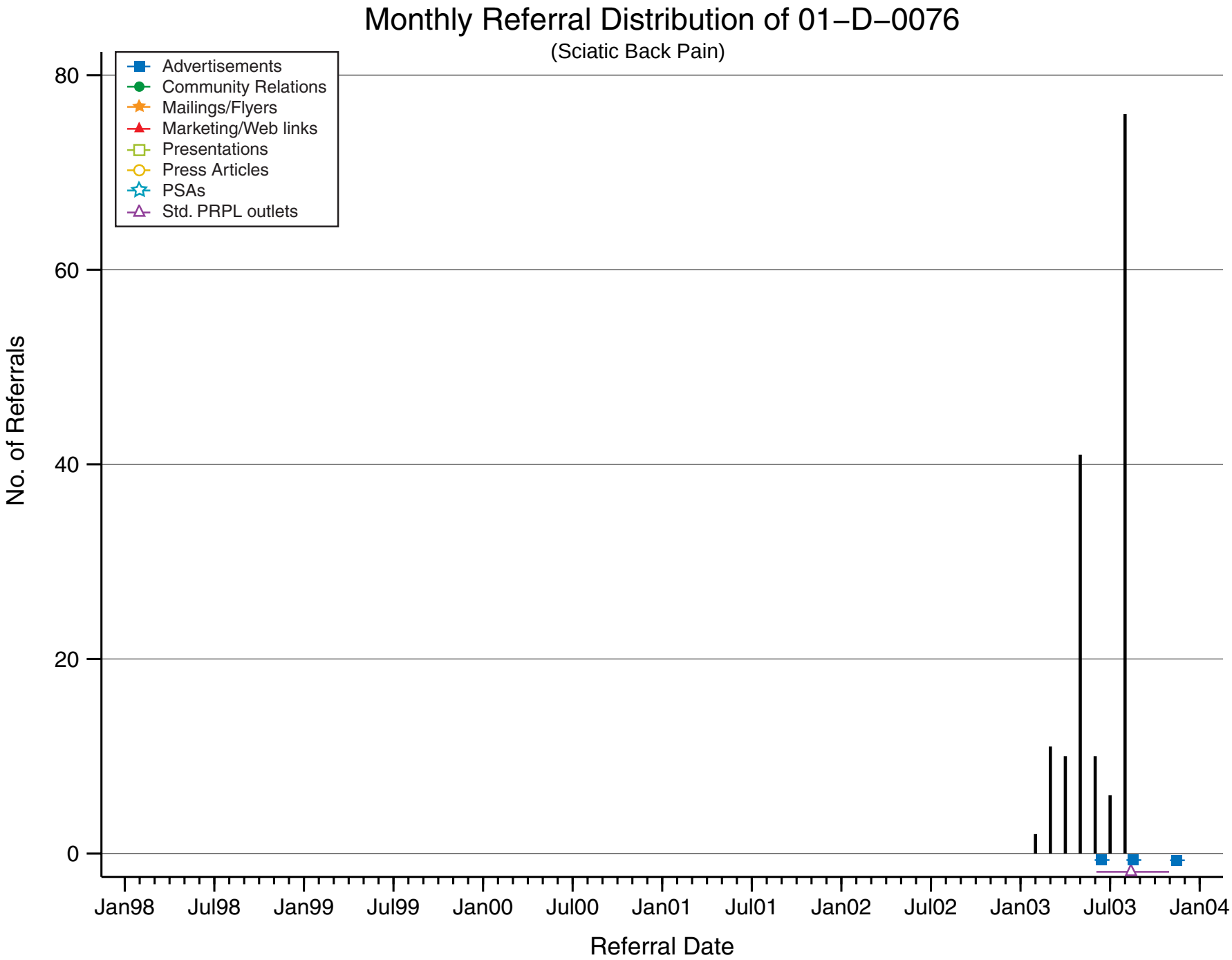

Monthly Referral Distribution of 00–D–0066
(Fibromyalgia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
0
5
10
15
20
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

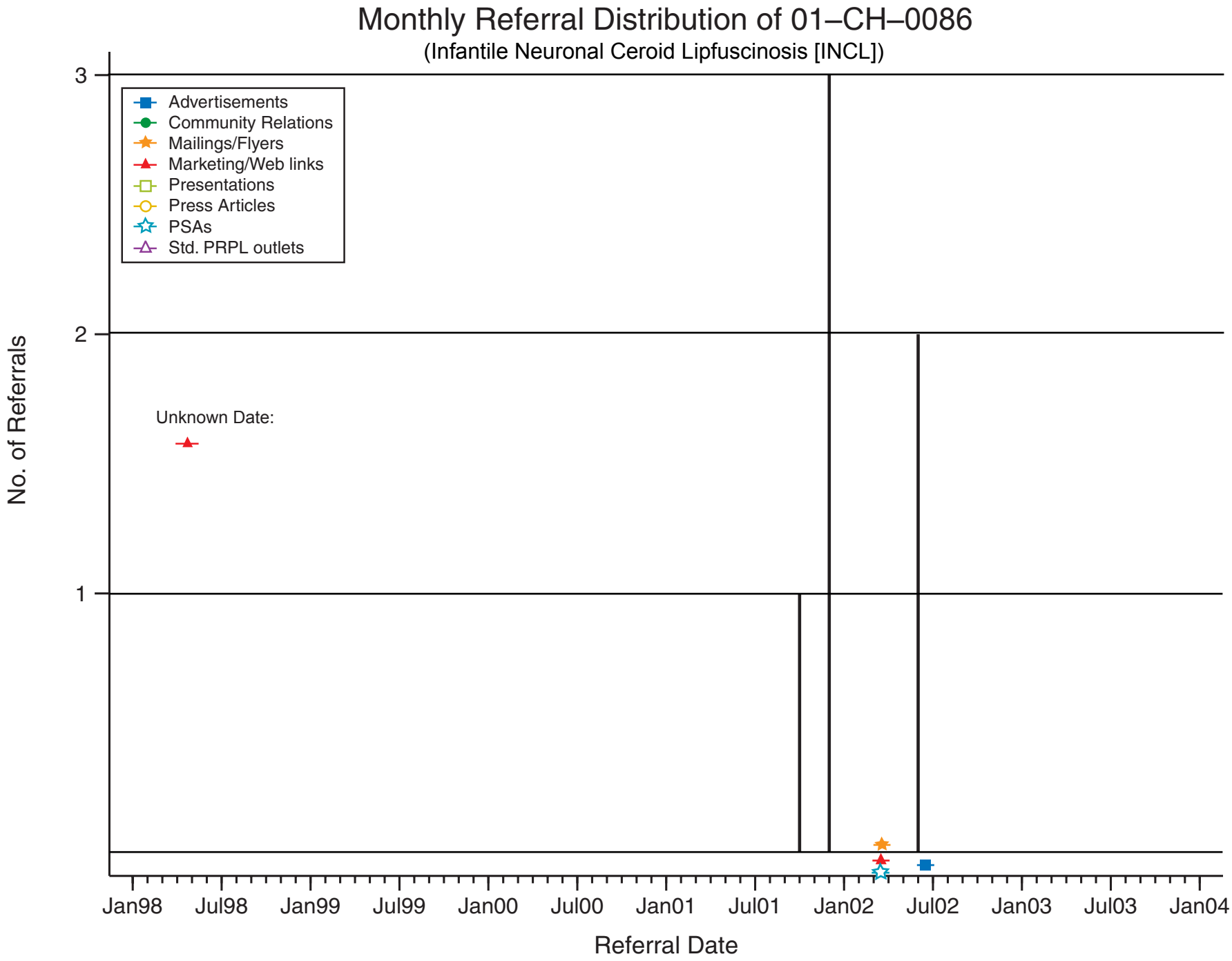

Monthly Referral Distribution of 00–DK–0042
(Focal Segmental Glomerulosclerosis [FSGS])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

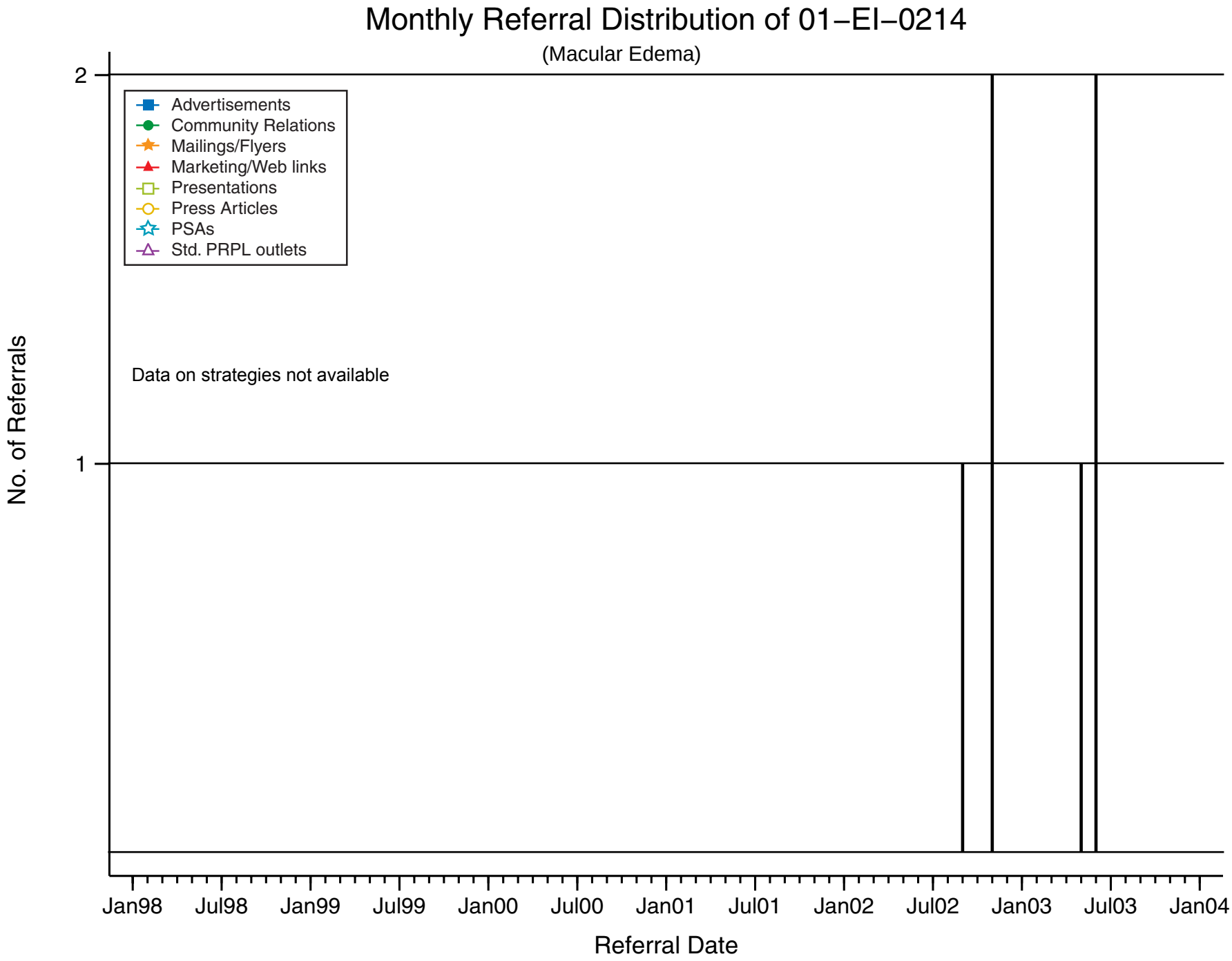

Monthly Referral Distribution of 00–DK–0166
(Beta Thalassemia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
2
1
Unknown Date:
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

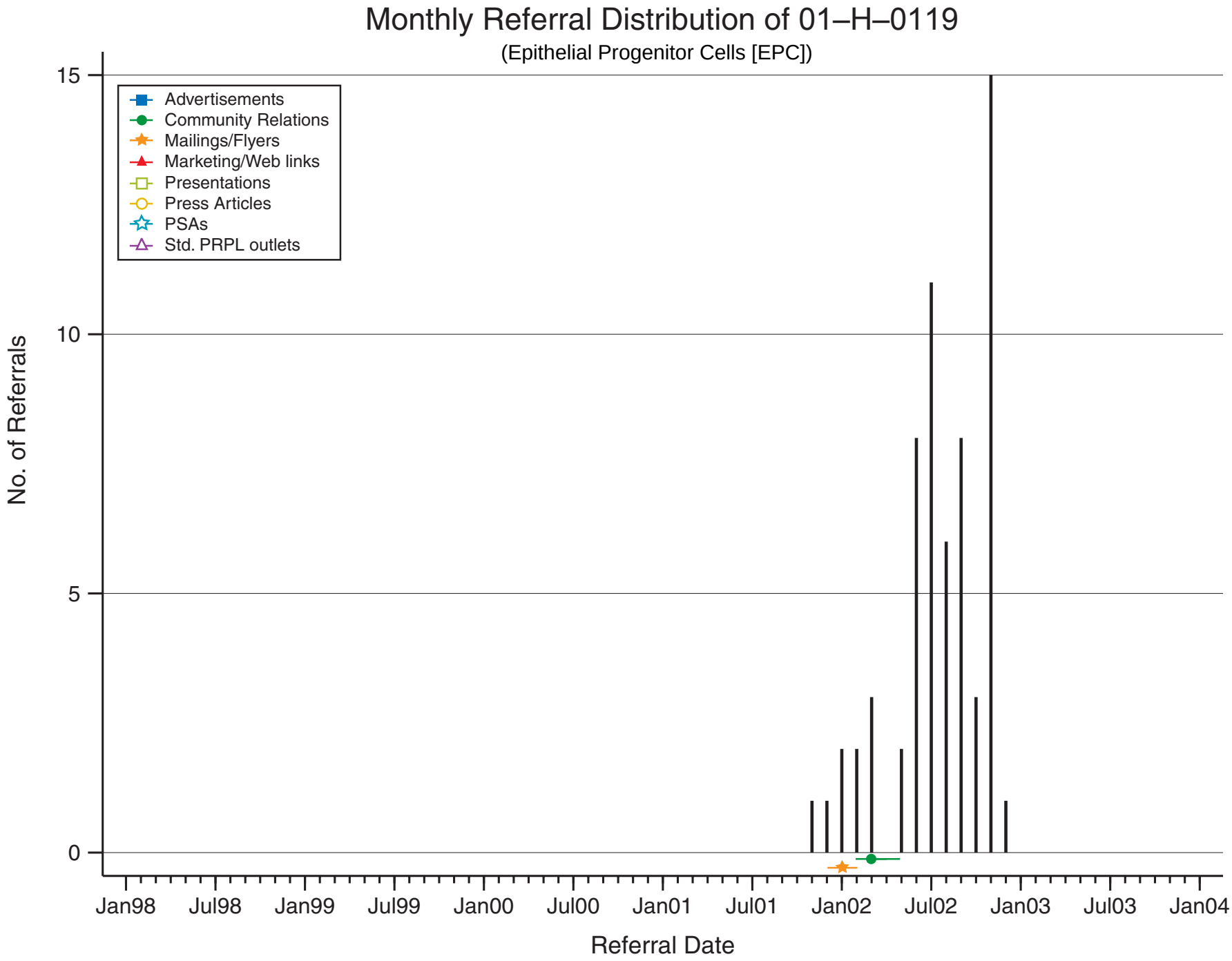

Monthly Referral Distribution of 00–CH–0141
(Alkaptonuria)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

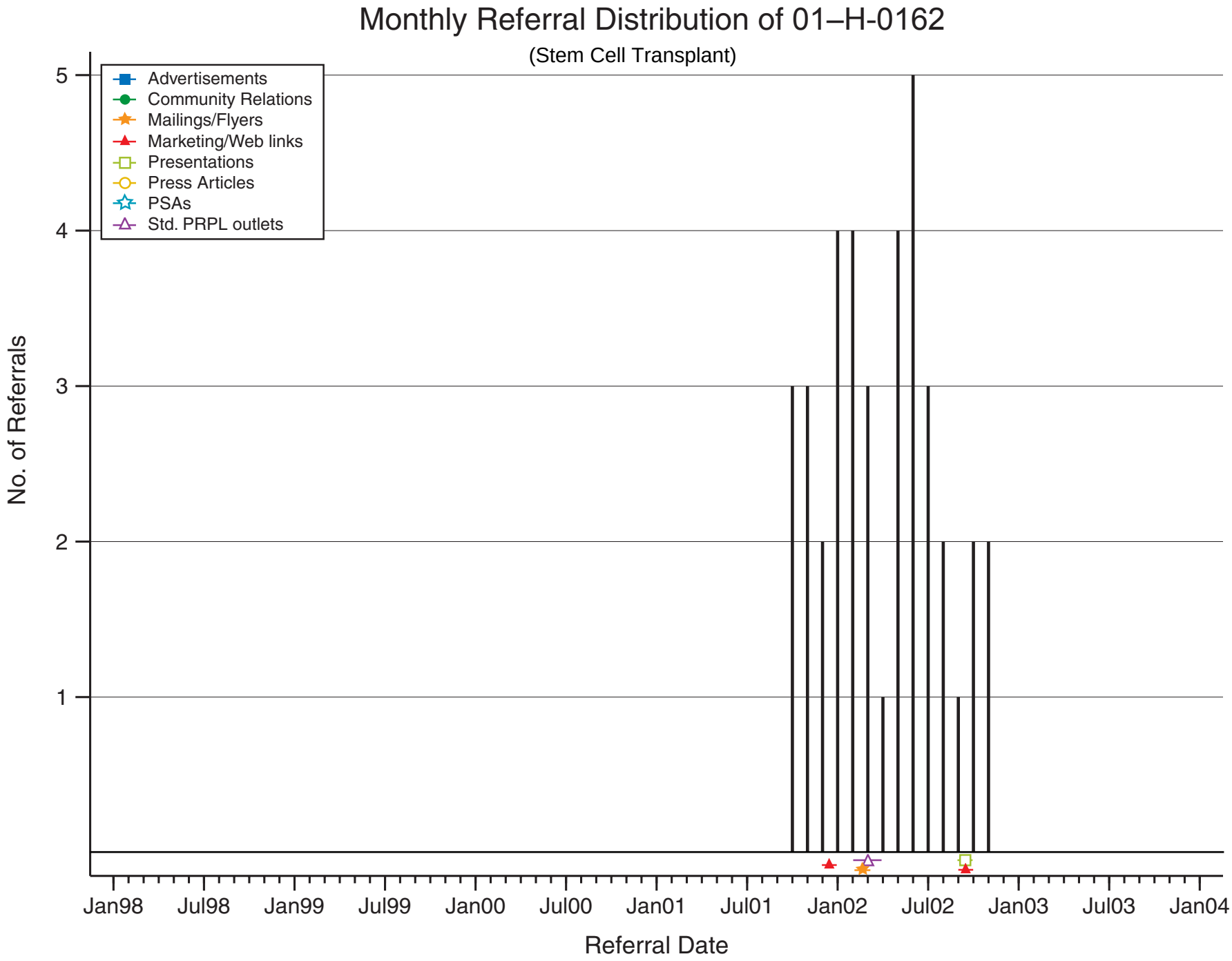

Monthly Referral Distribution of 01–CC–0135
(Swallowing Difficulty)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

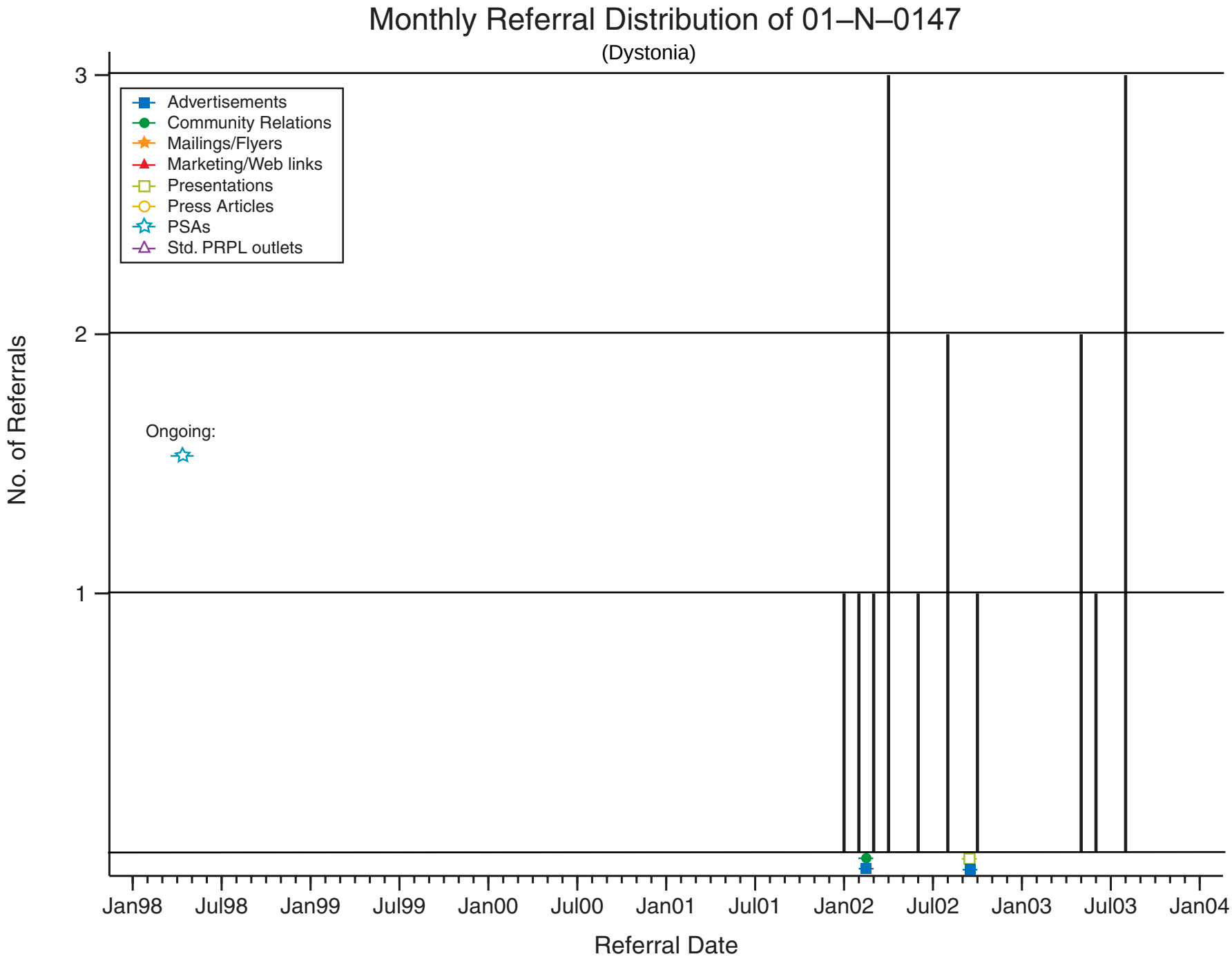

Monthly Referral Distribution of 01–D–0076
(Sciatic Back Pain)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
80
60
40
20
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

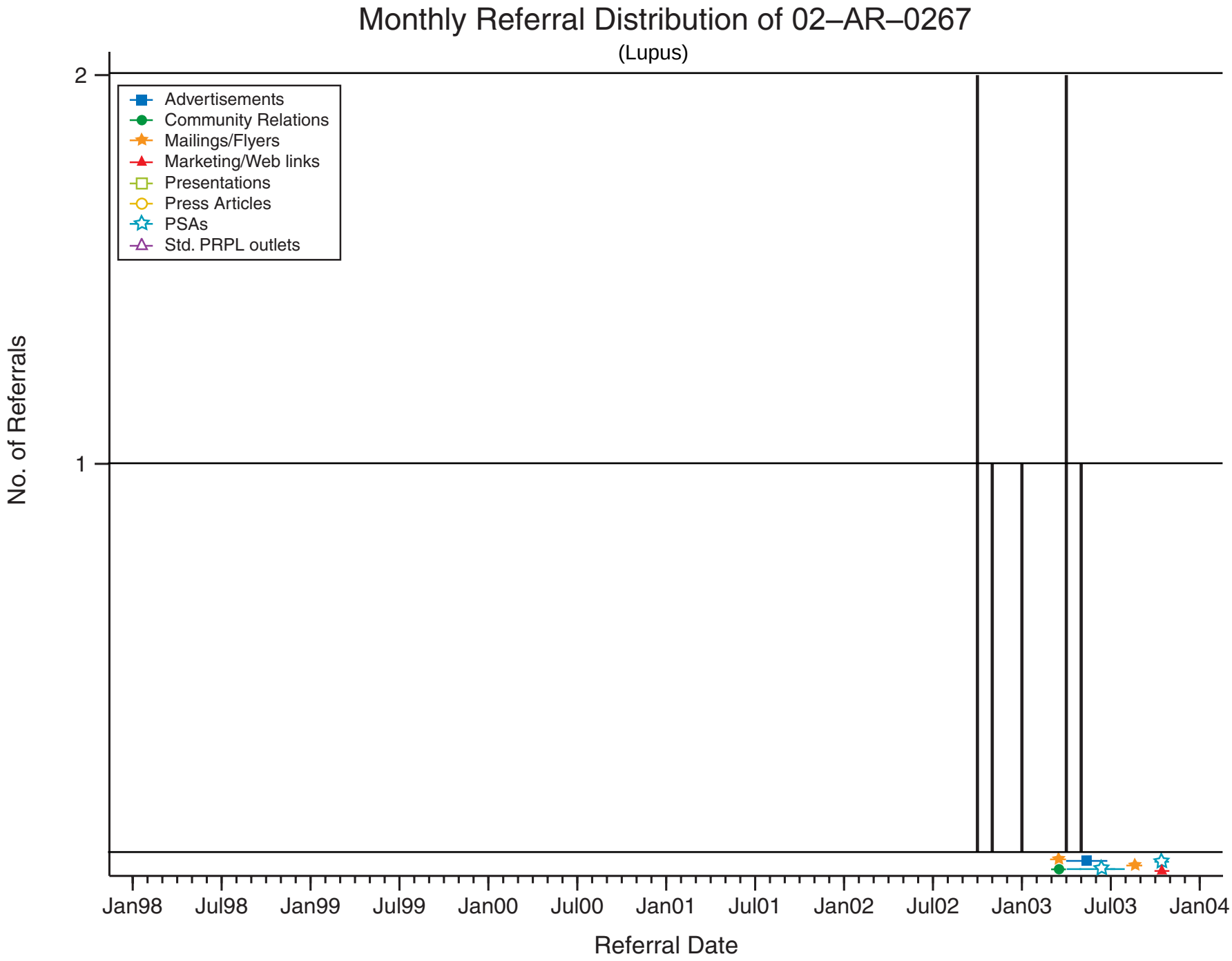

Monthly Referral Distribution of 01–CH–0086
(Infantile Neuronal Ceroid Lipfuscinosis [INCL])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown Date:
No. of Referrals
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

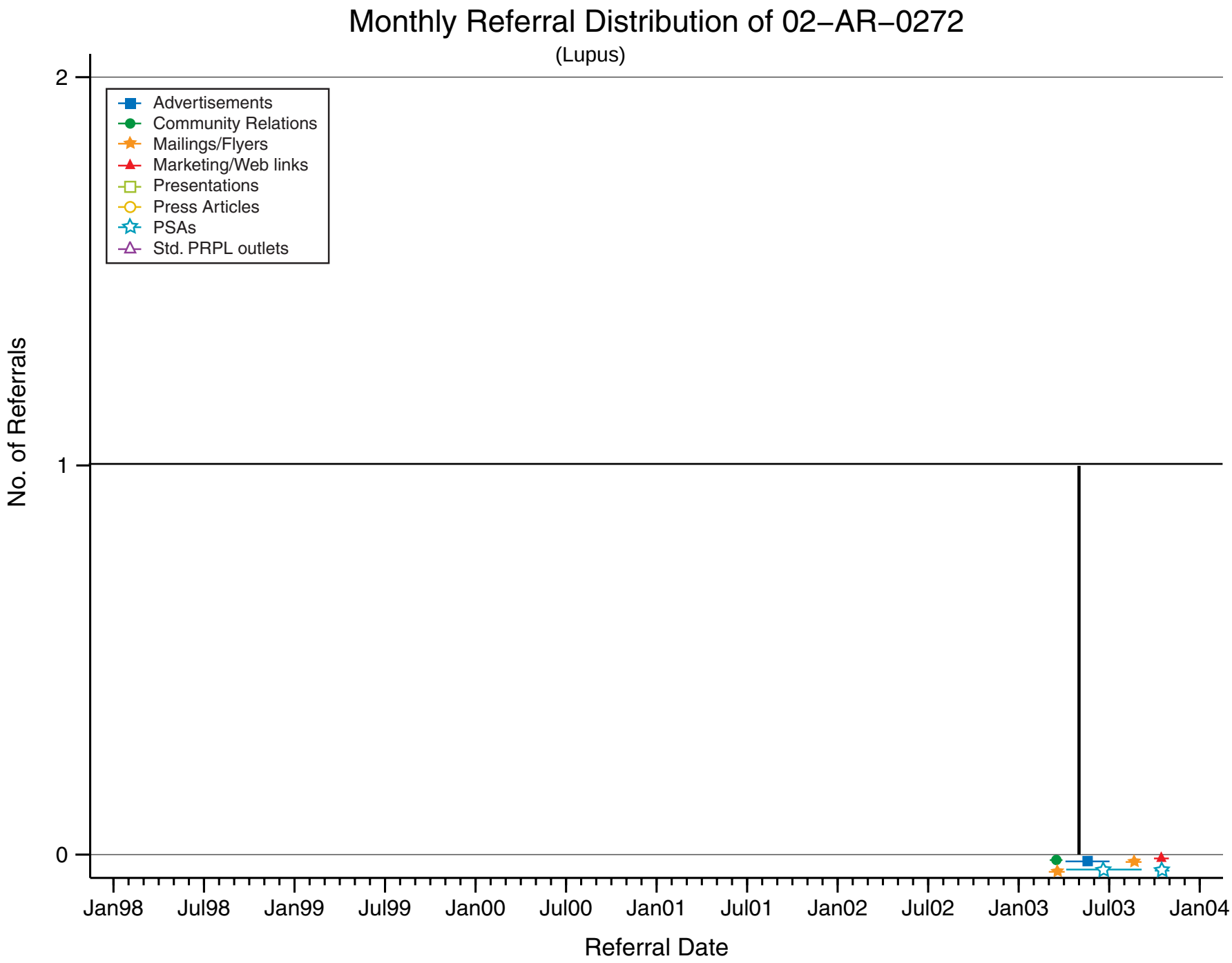

Monthly Referral Distribution of 01–EI–0214
(Macular Edema)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Data on strategies not available
No. of Referrals
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

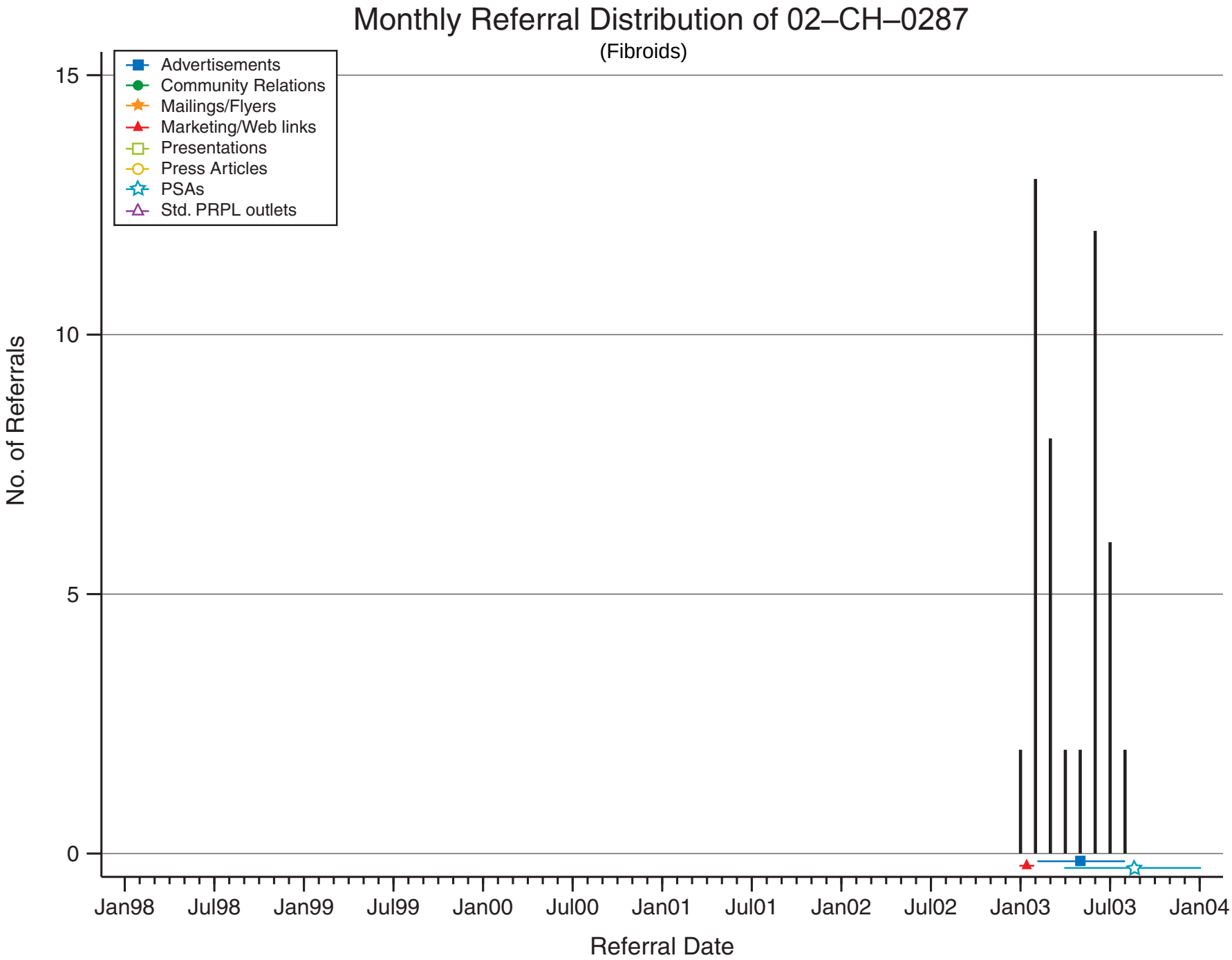

Monthly Referral Distribution of 01–H–0119
(Epithelial Progenitor Cells [EPC])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

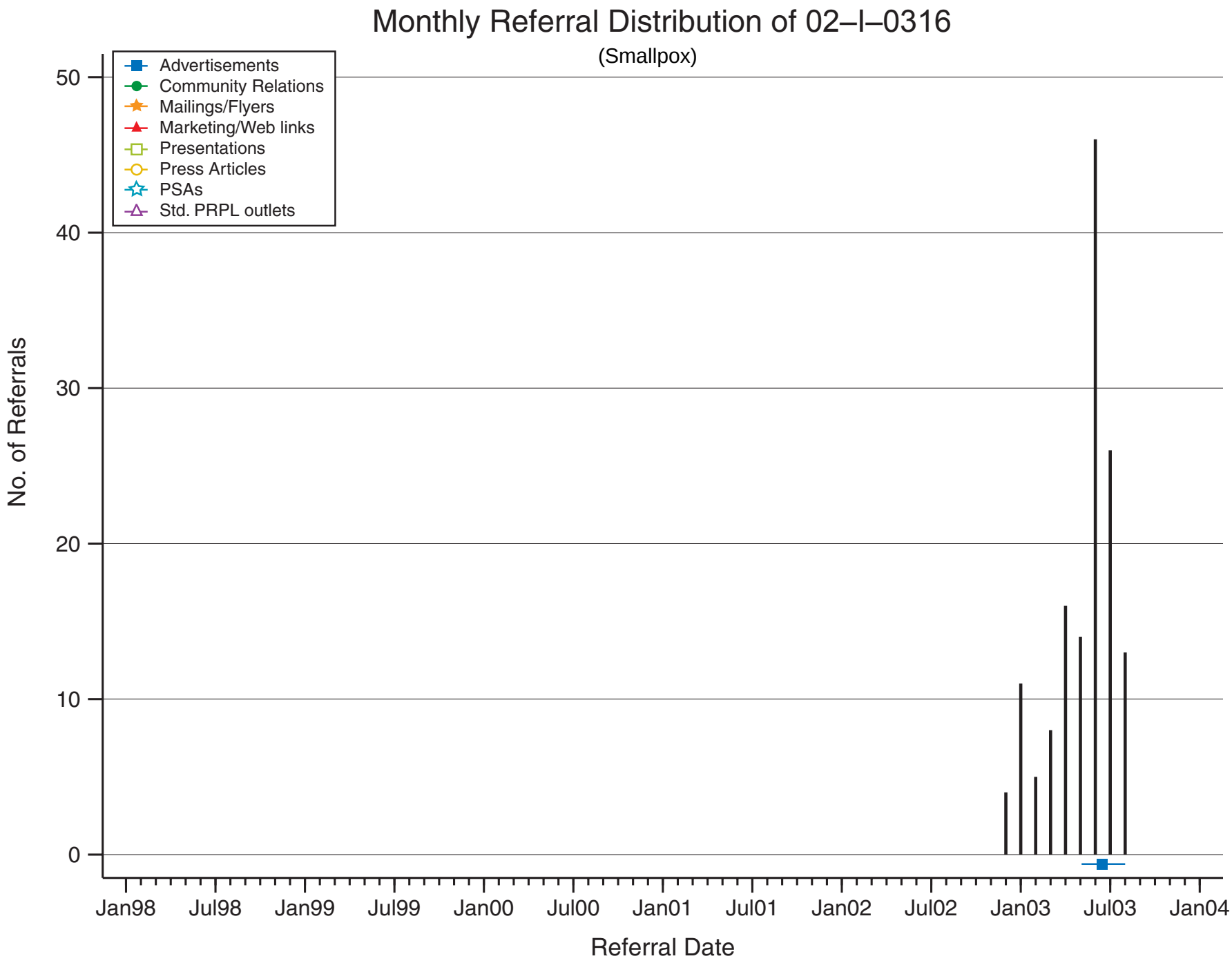

Monthly Referral Distribution of 01–H-0162
(Stem Cell Transplant)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 01–N–0147
(Dystonia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 02–AR–0267
(Lupus)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

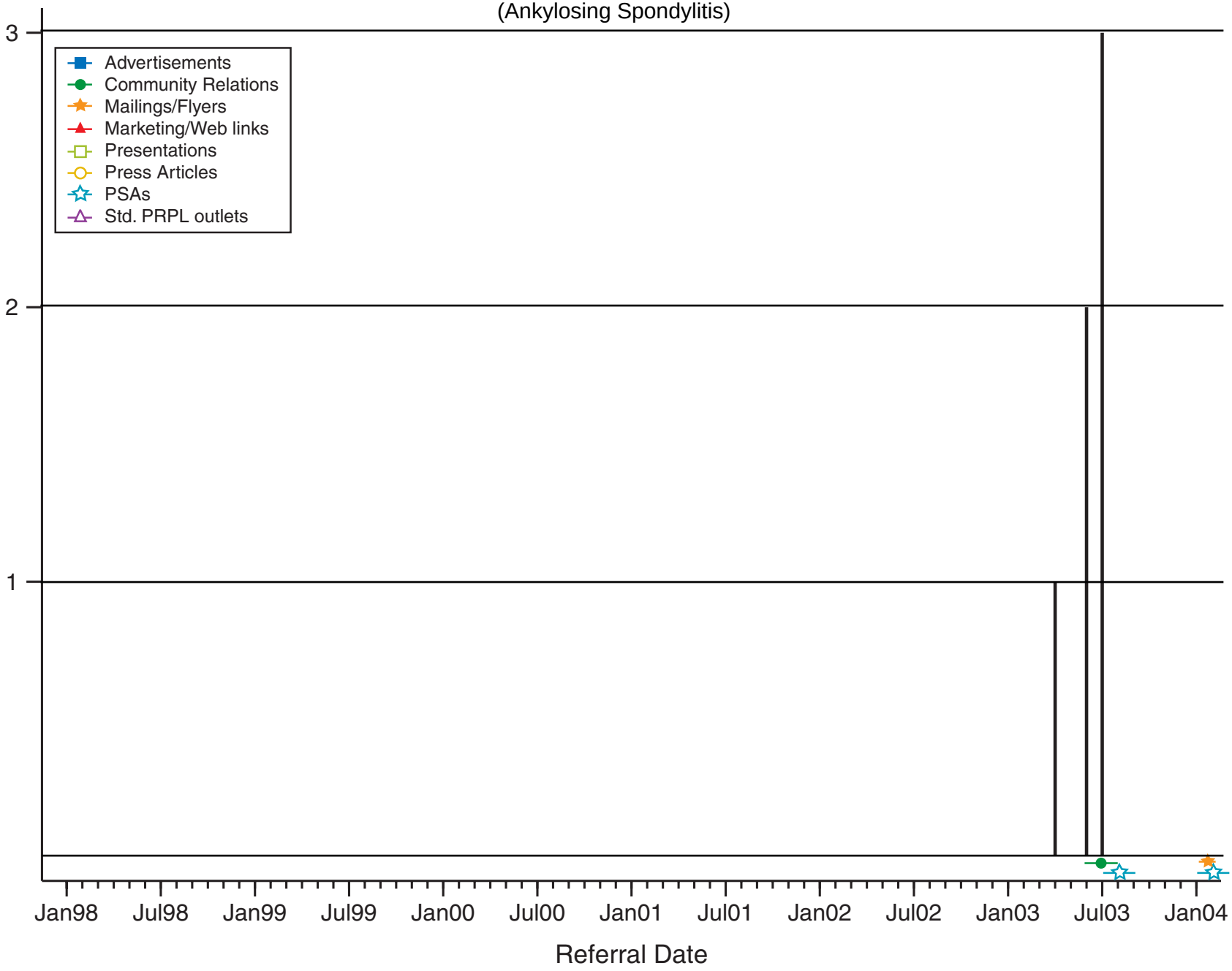

Monthly Referral Distribution of 02–AR–0272
(Lupus)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

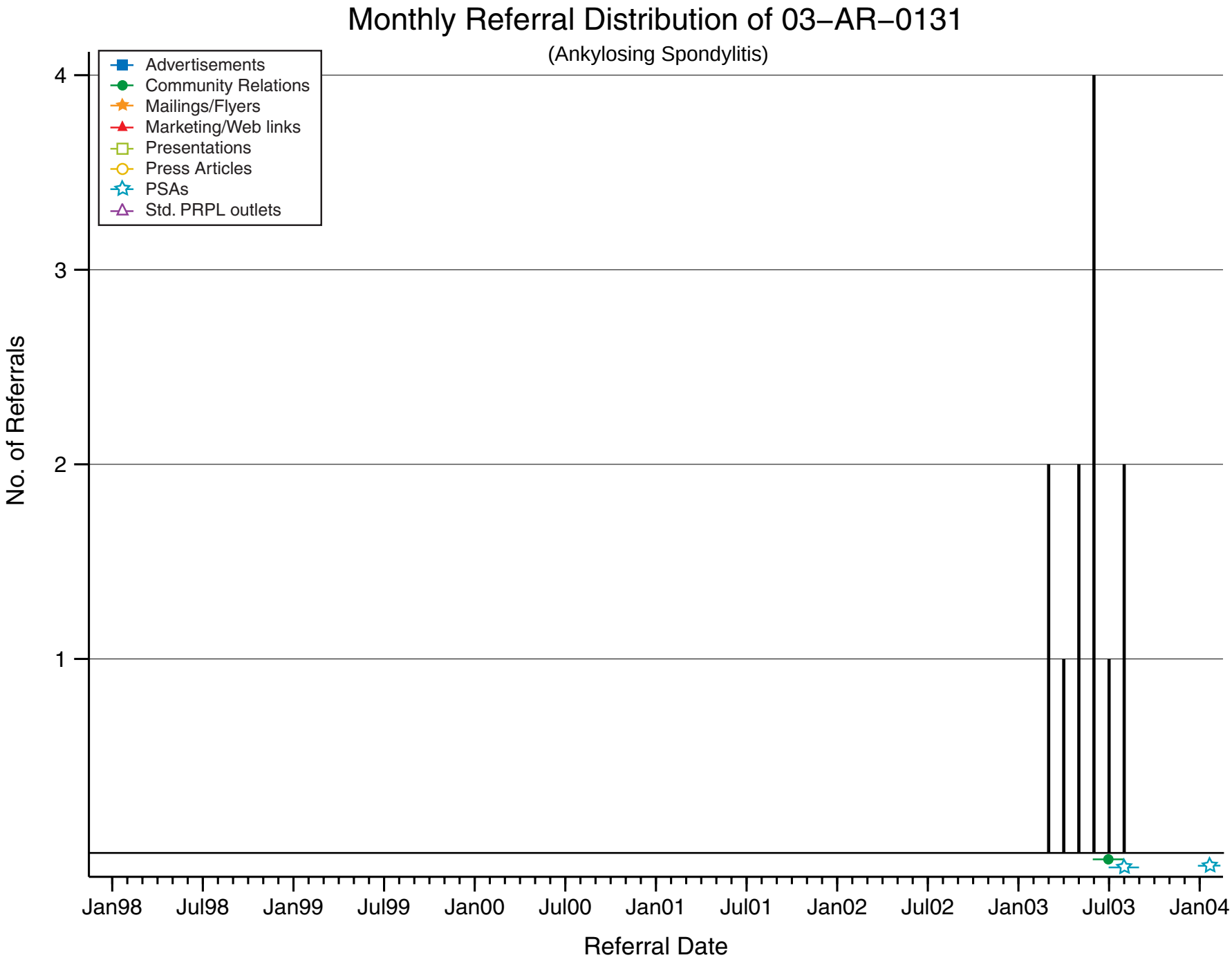

Monthly Referral Distribution of 02–CH–0287
(Fibroids)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

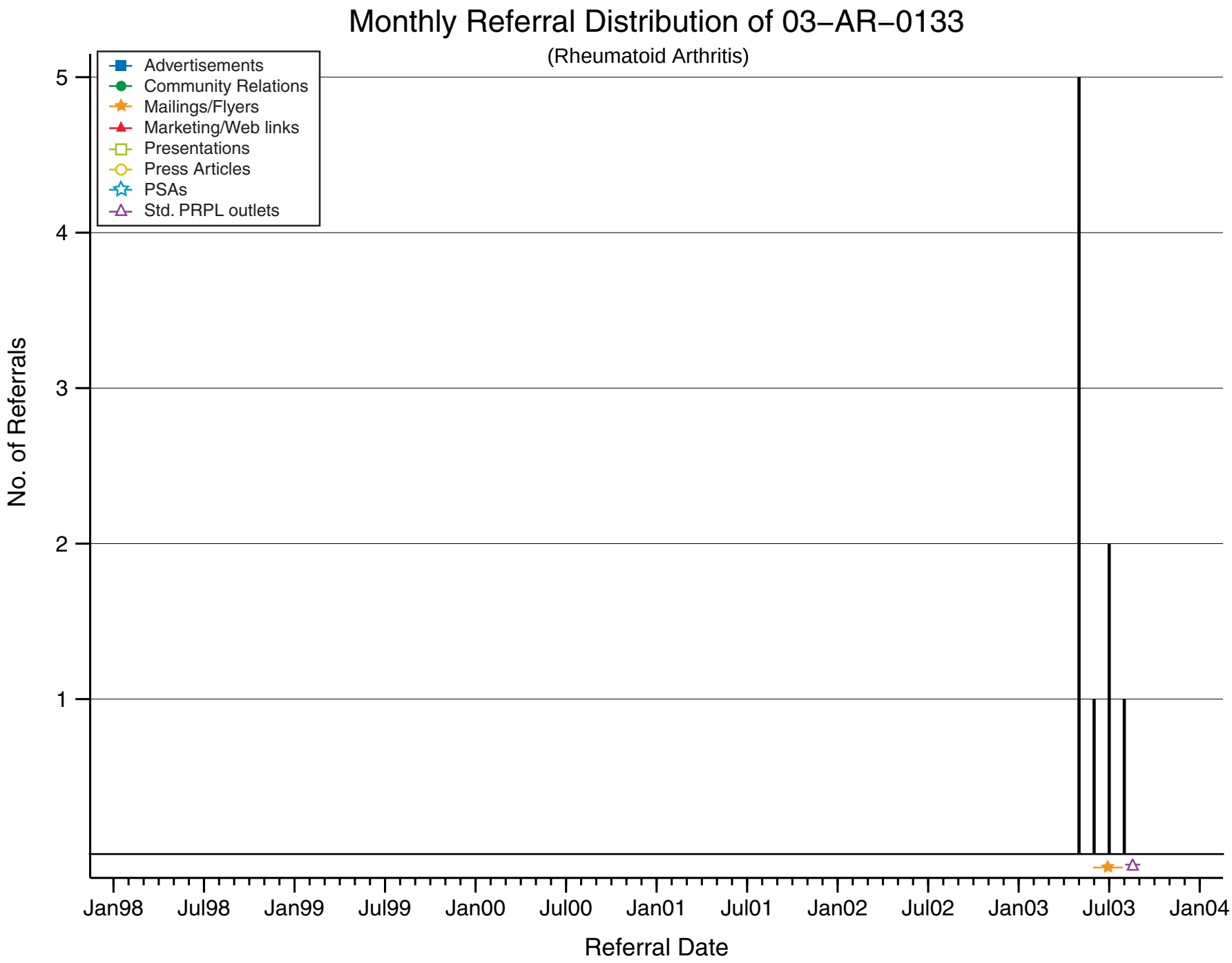

Monthly Referral Distribution of 02–I–0316
(Smallpox)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
50
40
30
20
10
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

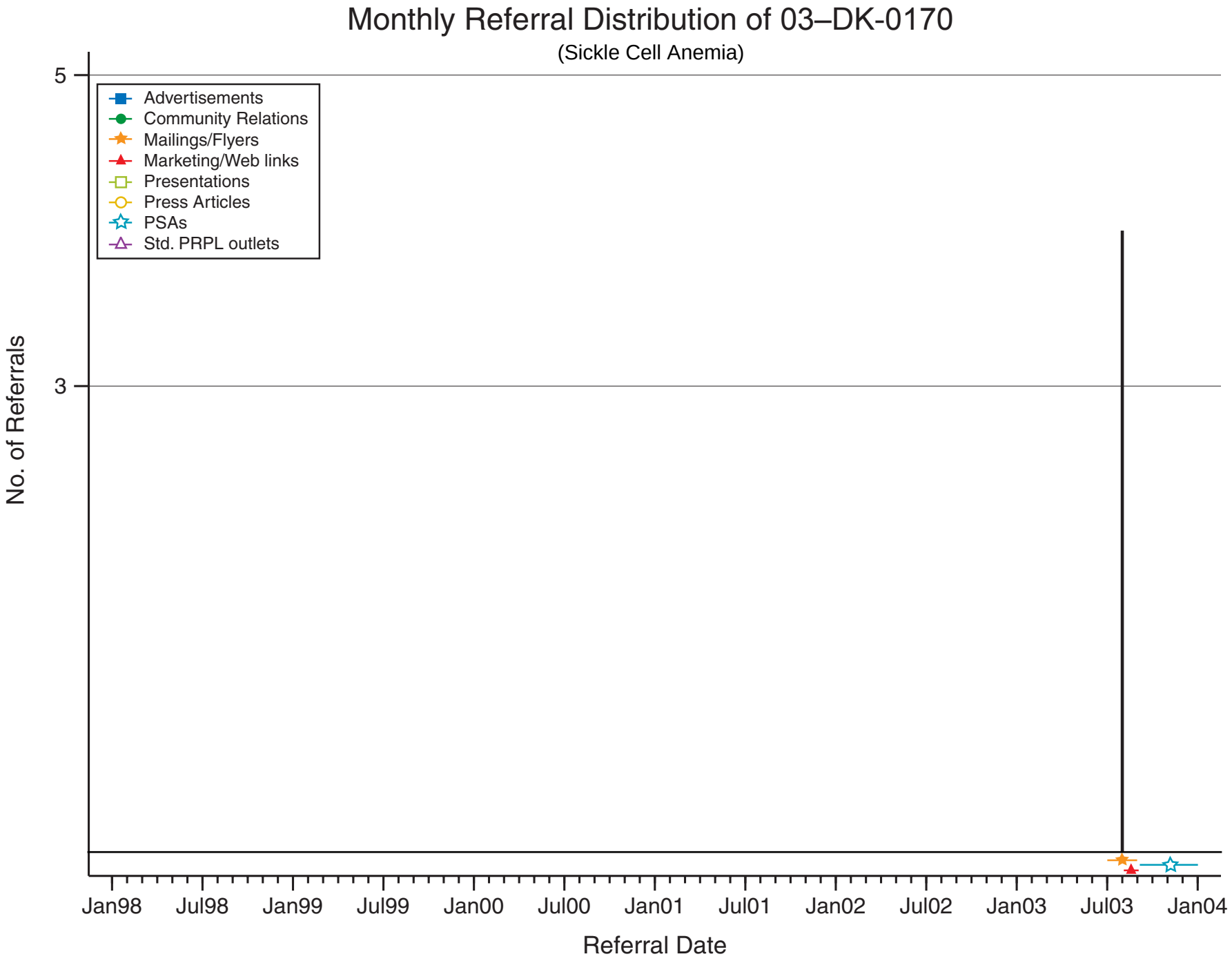
Monthly Referral Distribution of 03–AR–0130

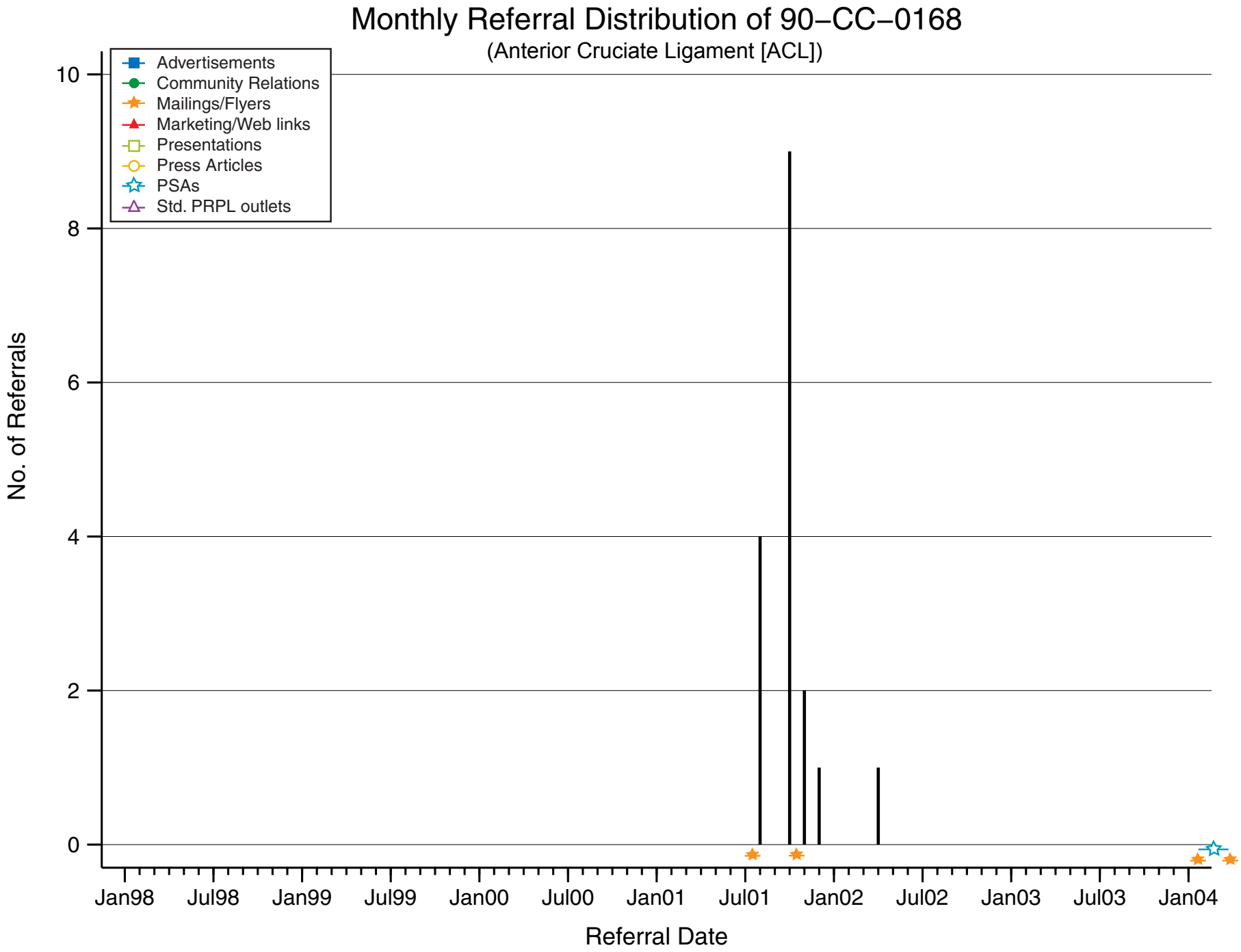
(Ankylosing Spondylitis)




Monthly Referral Distribution of 03–AR–0131
(Ankylosing Spondylitis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

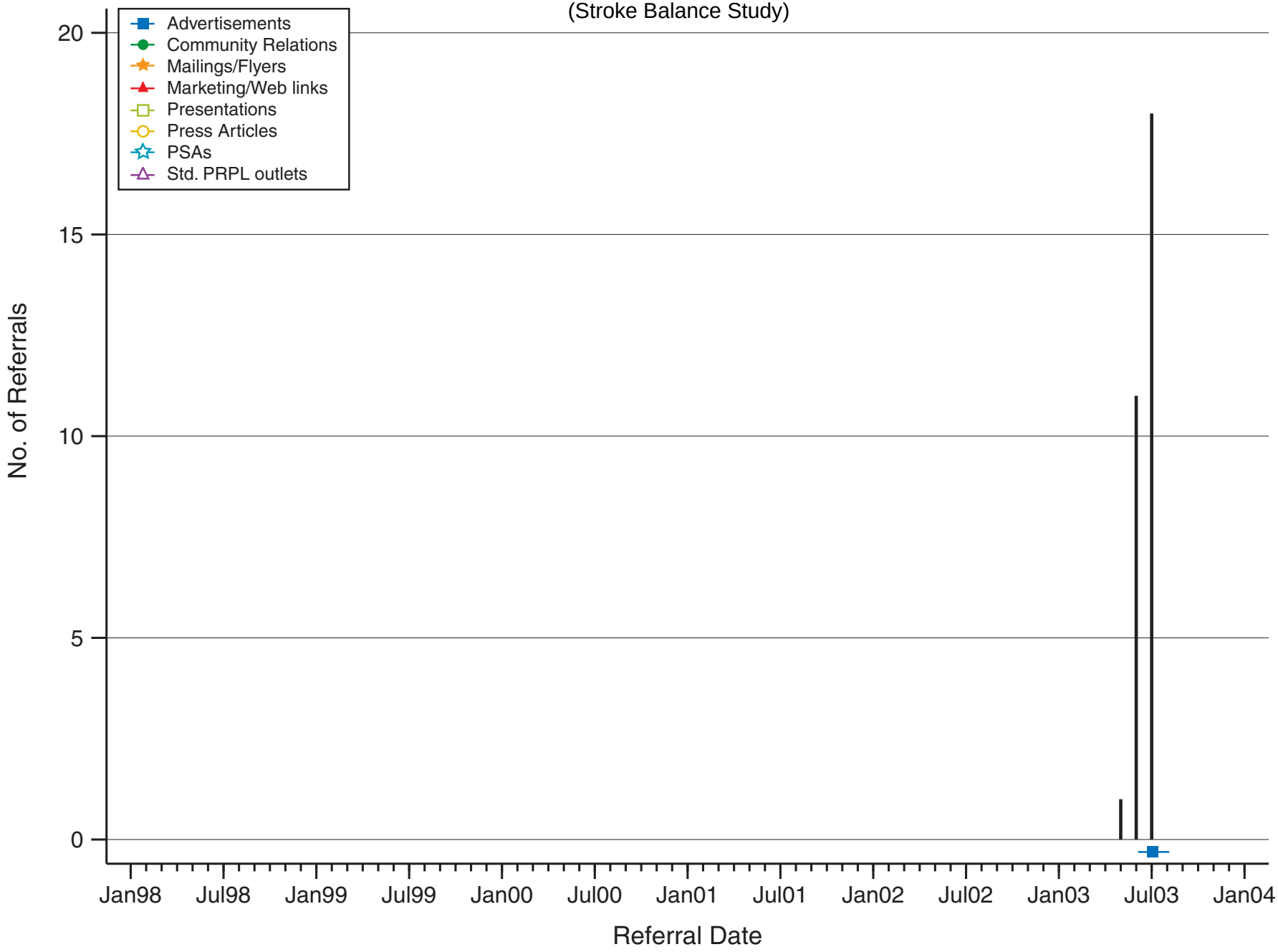

Monthly Referral Distribution of 03–AR–0133
(Rheumatoid Arthritis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

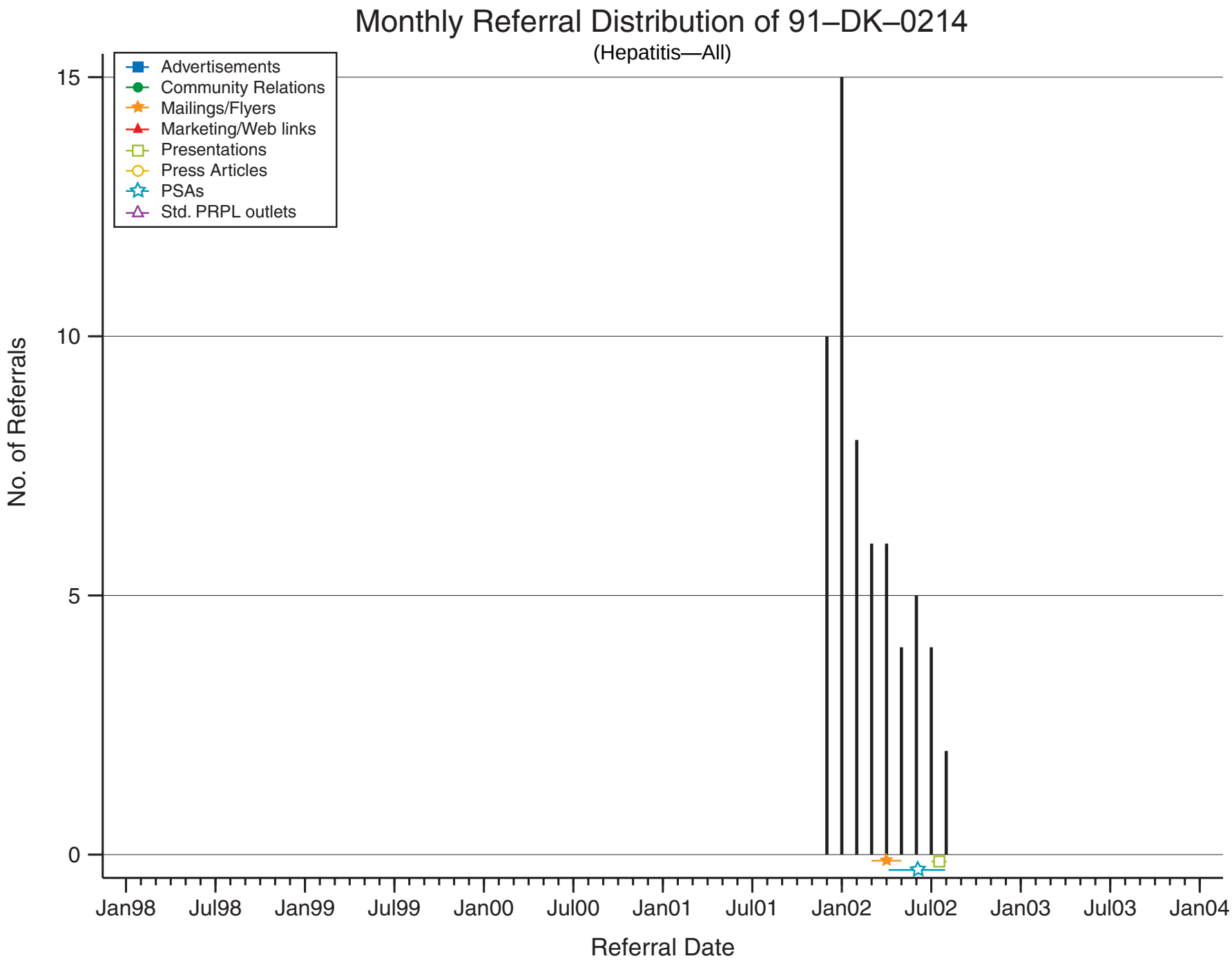

Monthly Referral Distribution of 03–DK-0170
(Sickle Cell Anemia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
5
3
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

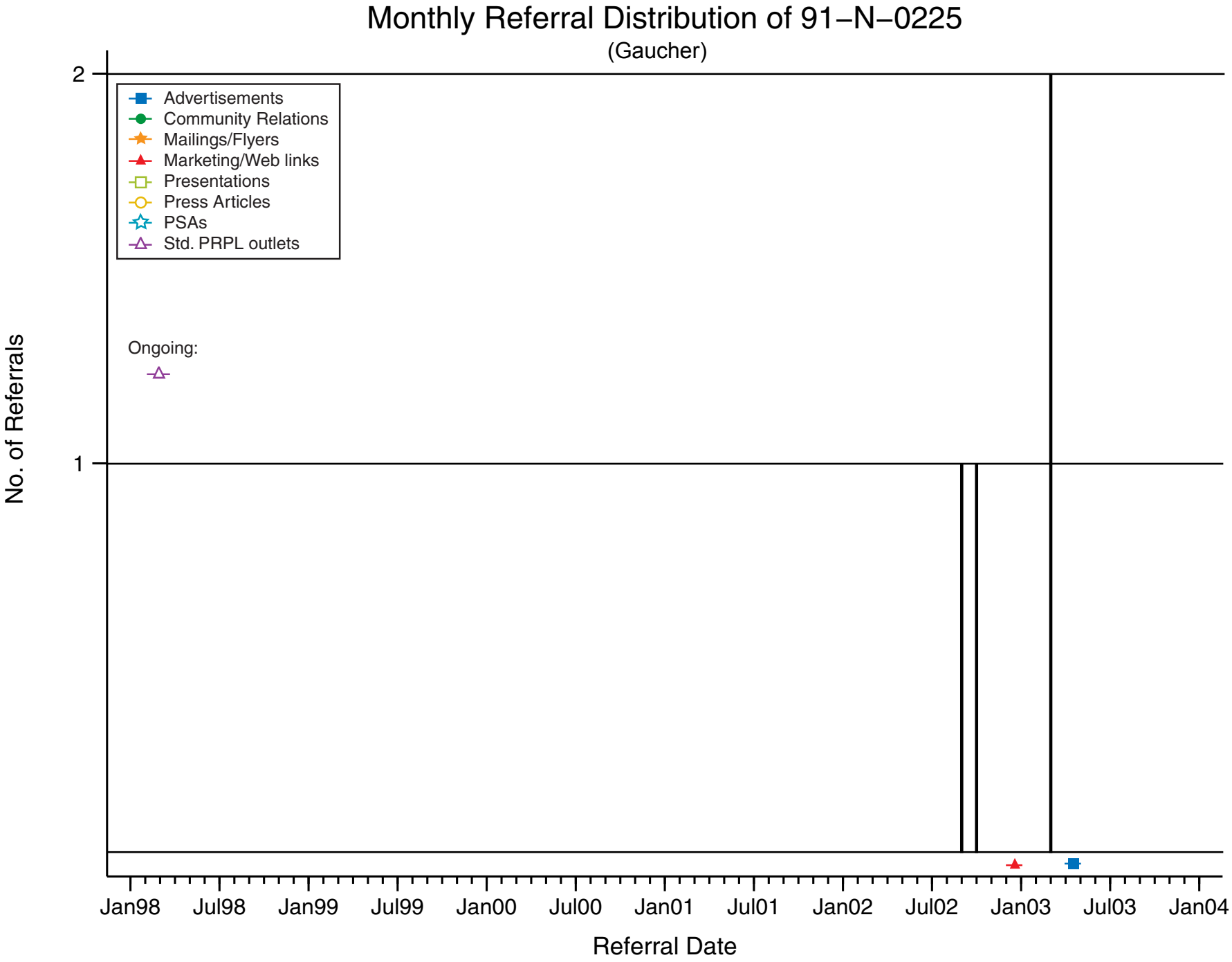

Monthly Referral Distribution of 90–CC–0168
(Anterior Cruciate Ligament [ACL])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
0
2
4
6
8
10
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

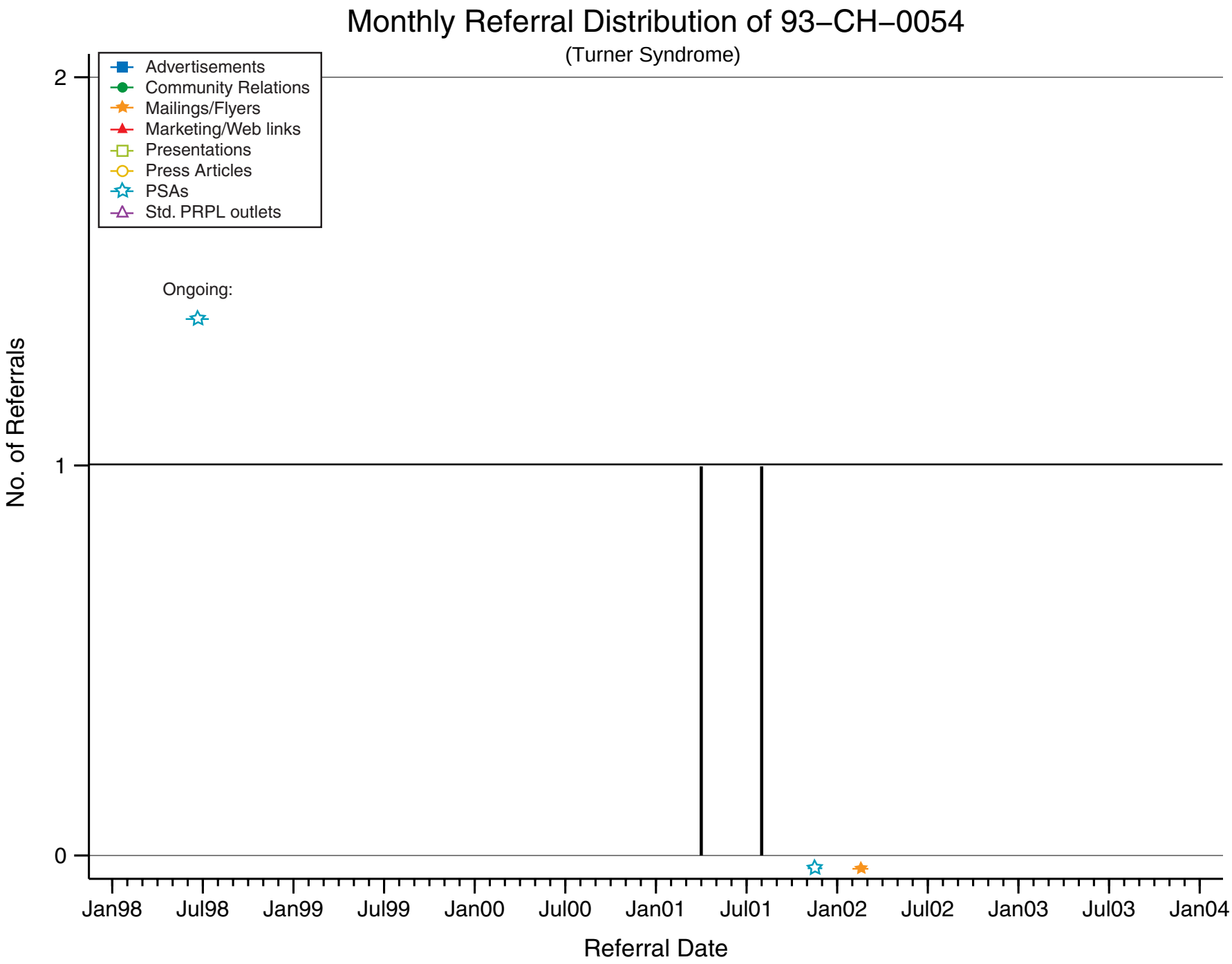
Monthly Referral Distribution of 90–CC–0168B

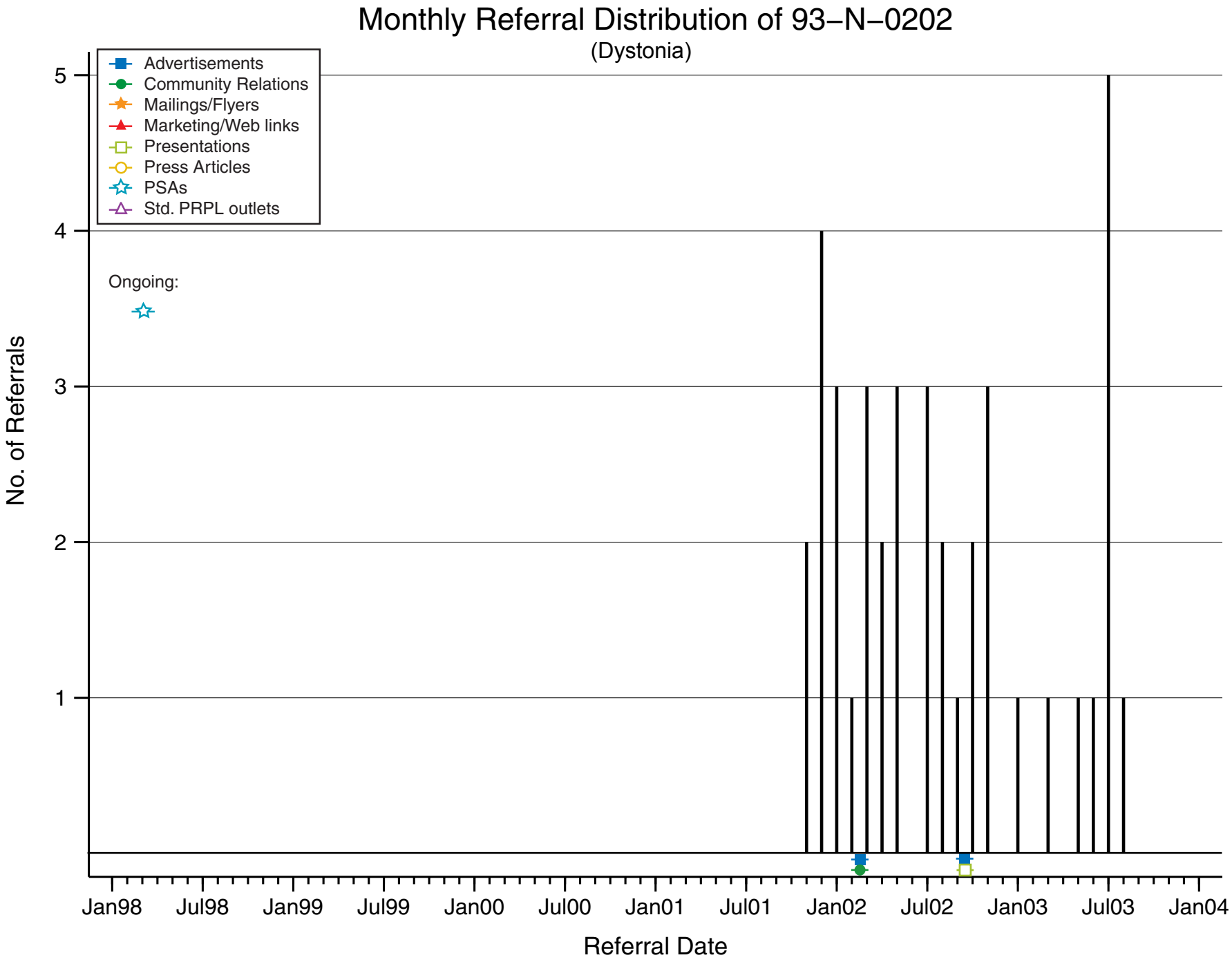
(Stroke Balance Study)




Monthly Referral Distribution of 91–DK–0214
(Hepatitis—All)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 91–N–0225
(Gaucher)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 93–CH–0054
(Turner Syndrome)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 93–N–0202
(Dystonia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
5
4
3
2
1
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Jul98
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Jul99
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Jan02
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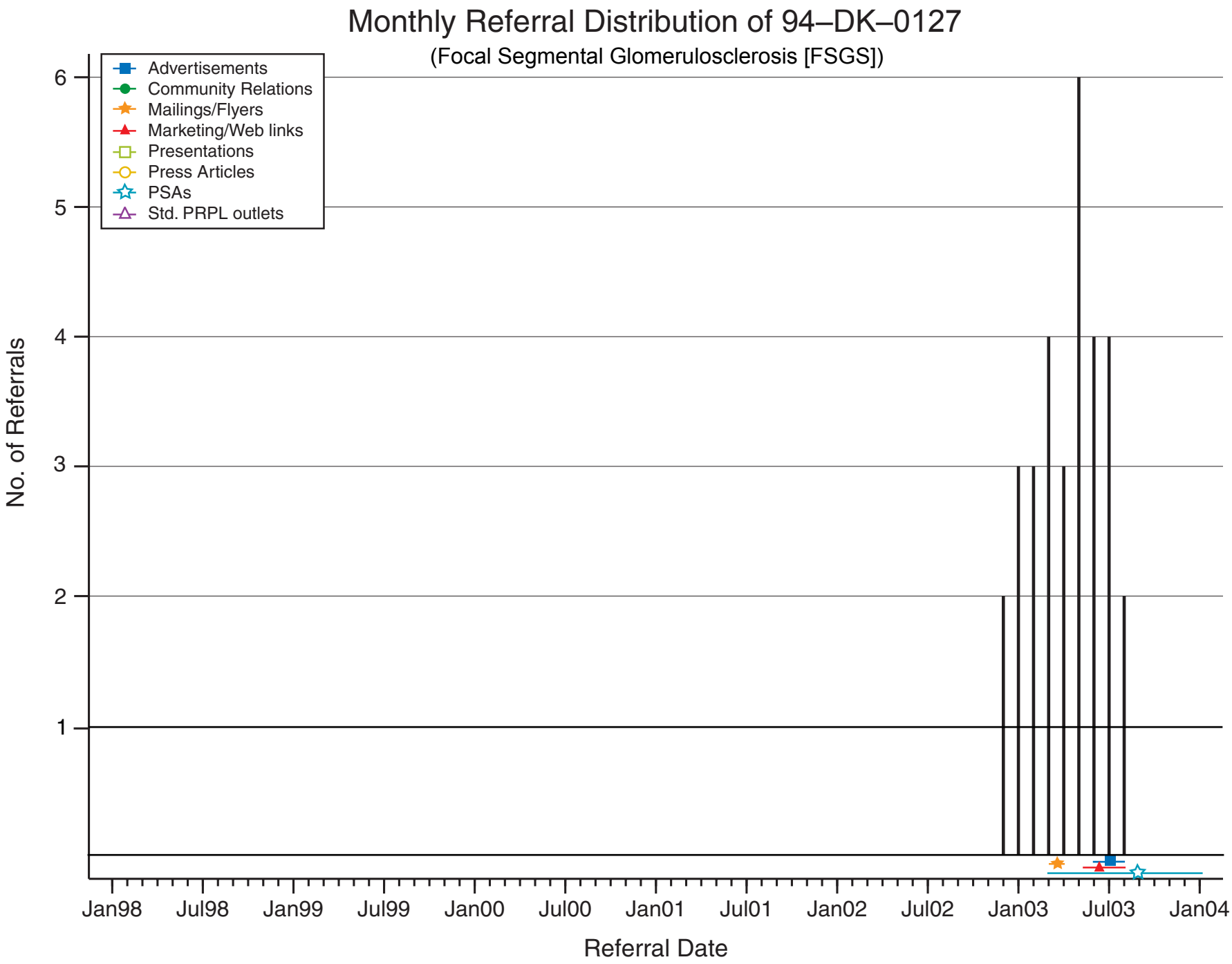
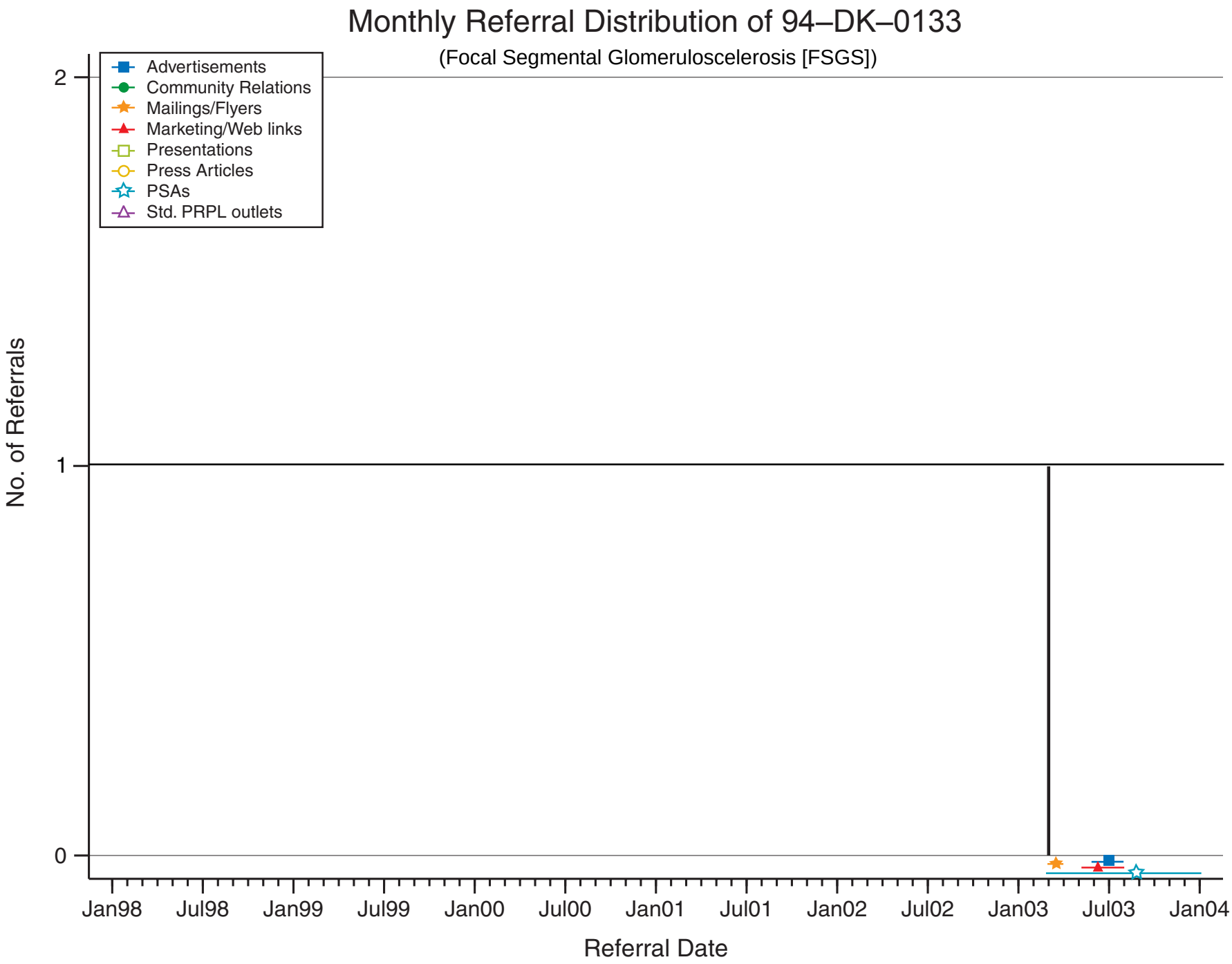
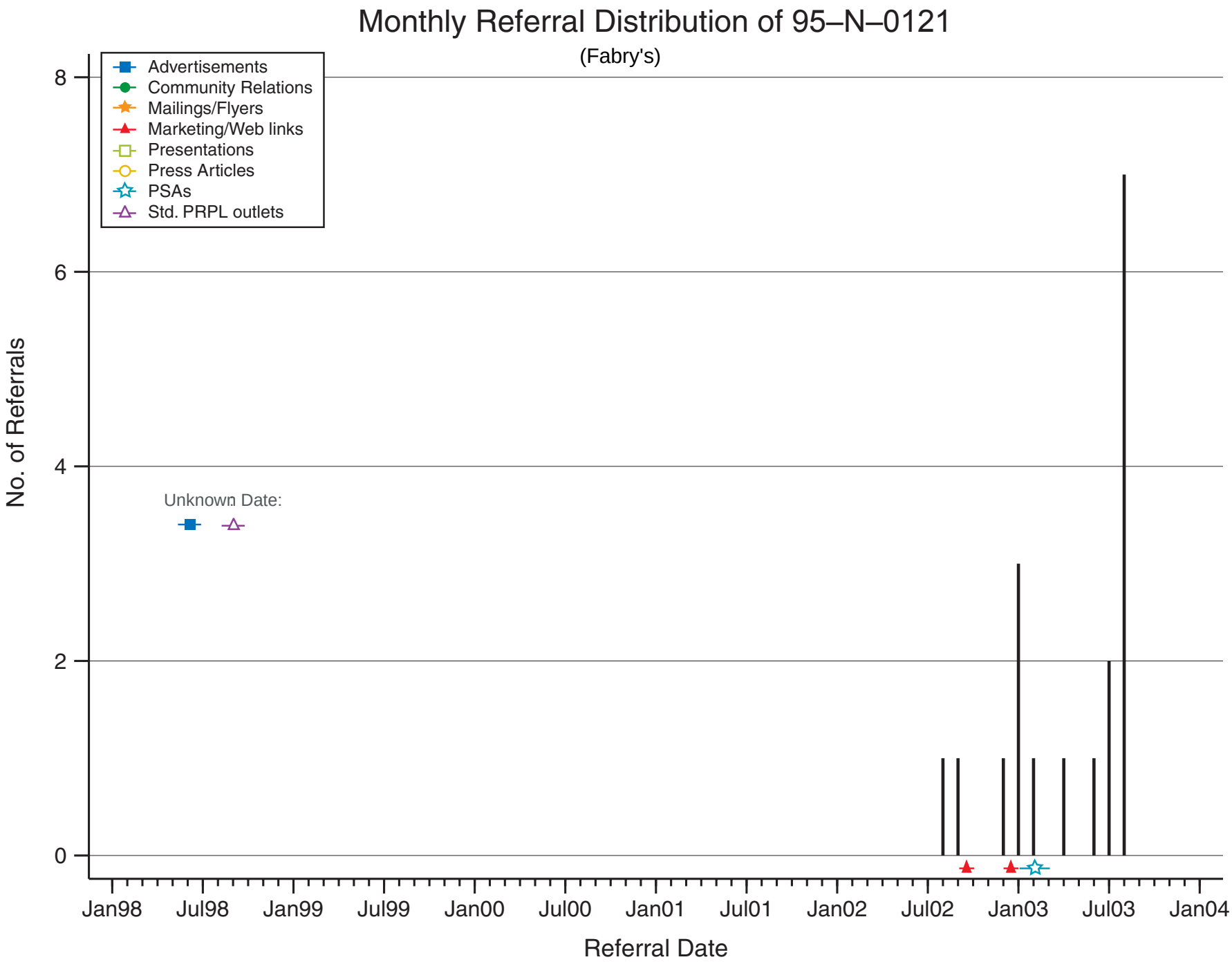
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 94–DK–0127
(Focal Segmental Glomerulosclerosis [FSGS])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
6
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 94–DK–0133
(Focal Segmental Glomeruloscelerosis [FSGS])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 95–N–0121
(Fabry's)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
8
6
4
2
0
Unknown Date:
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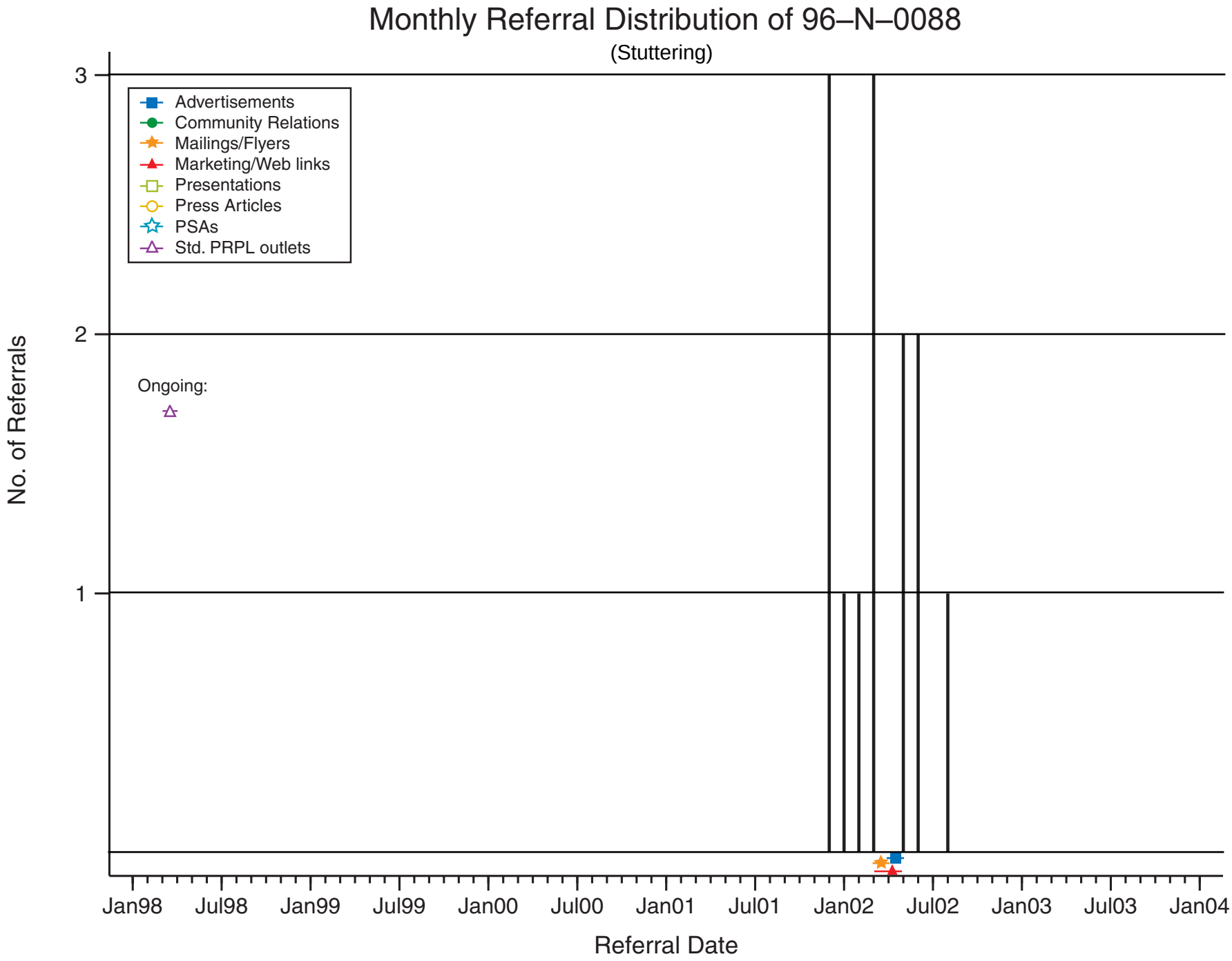
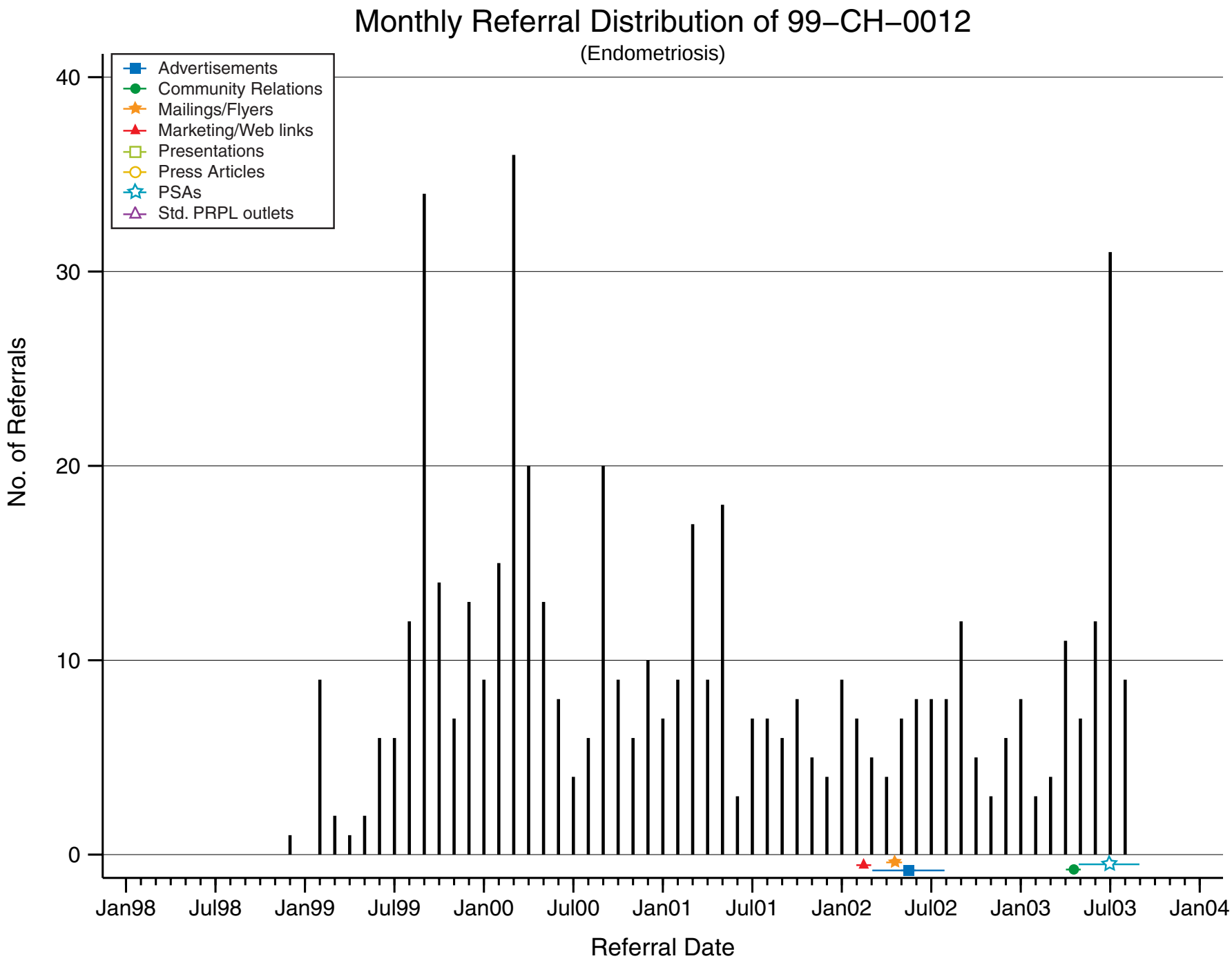
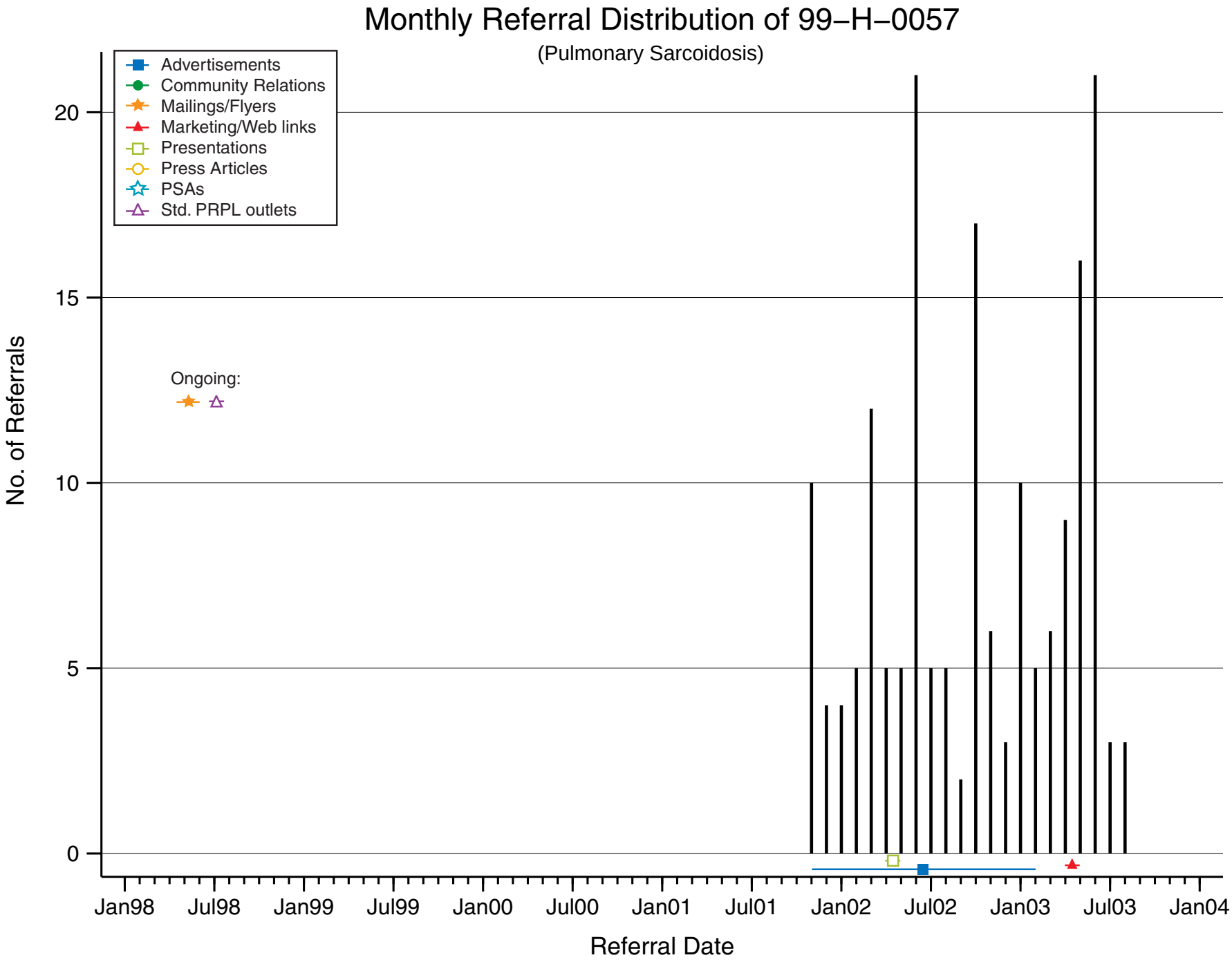
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 96–N–0088
(Stuttering)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date


Monthly Referral Distribution of 99–CH–0012
(Endometriosis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of Referrals
0
10
20
30
40
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

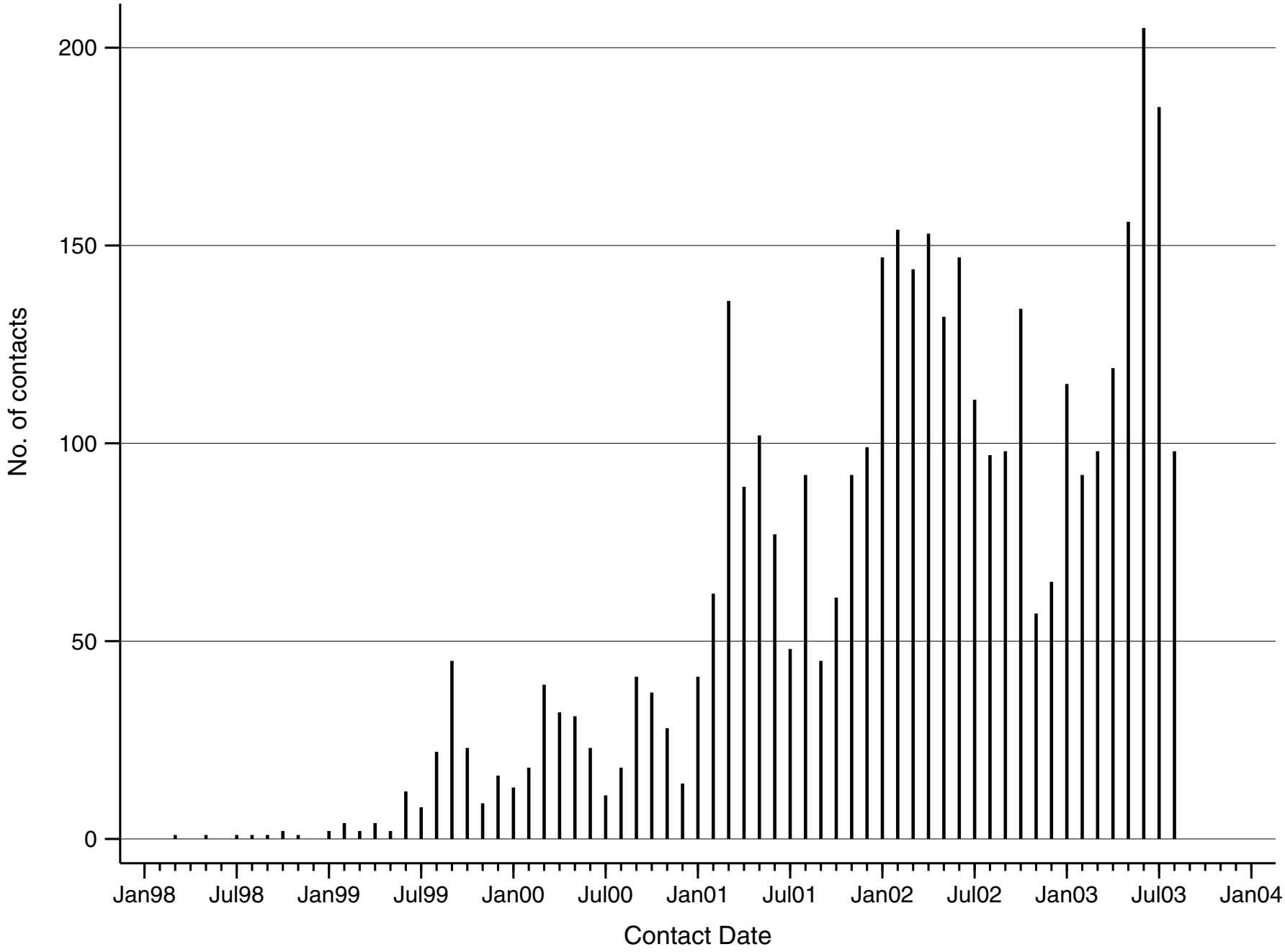

Monthly Referral Distribution of 99–H–0057
(Pulmonary Sarcoidosis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of Referrals
0
5
10
15
20
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Referral Date

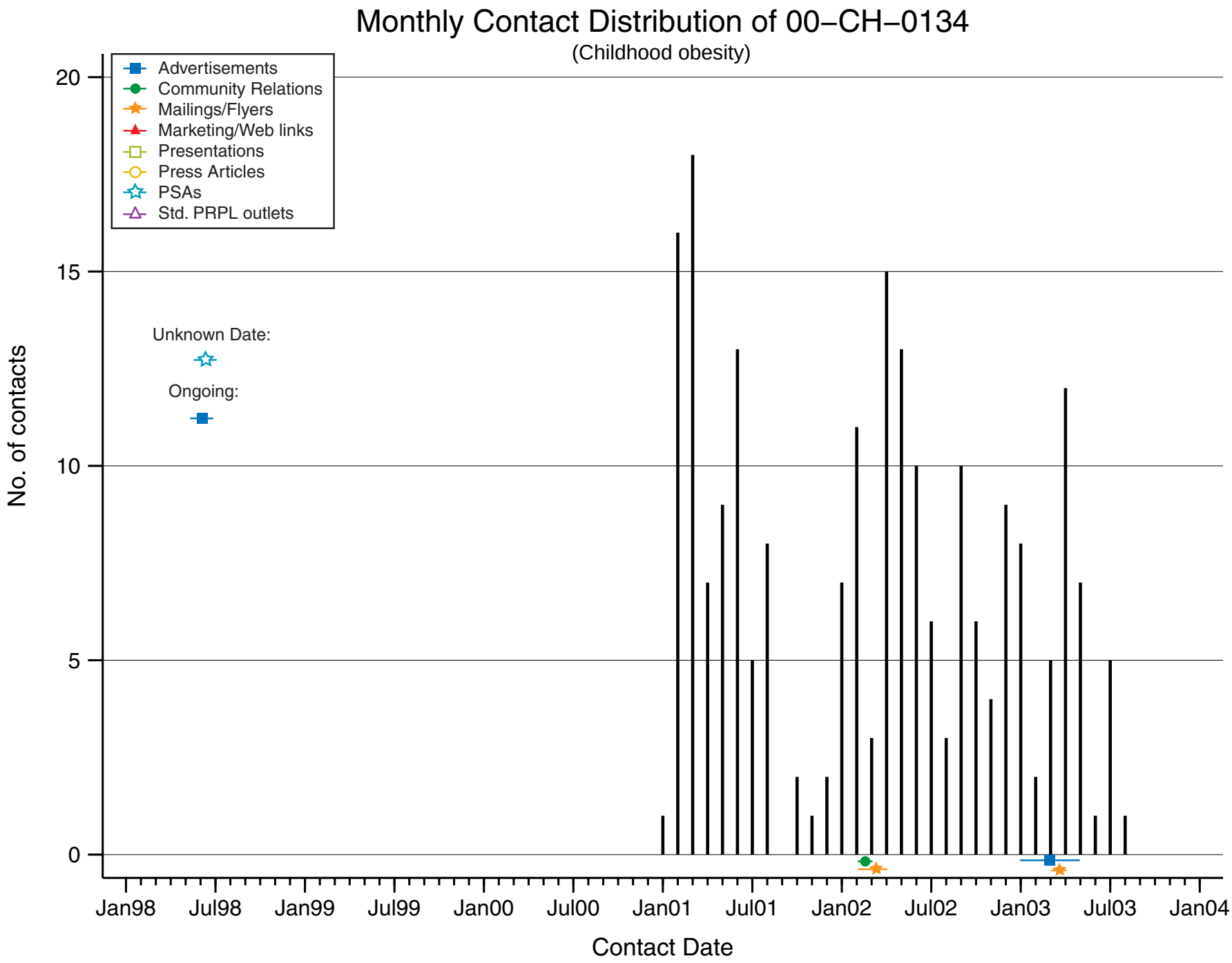
Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

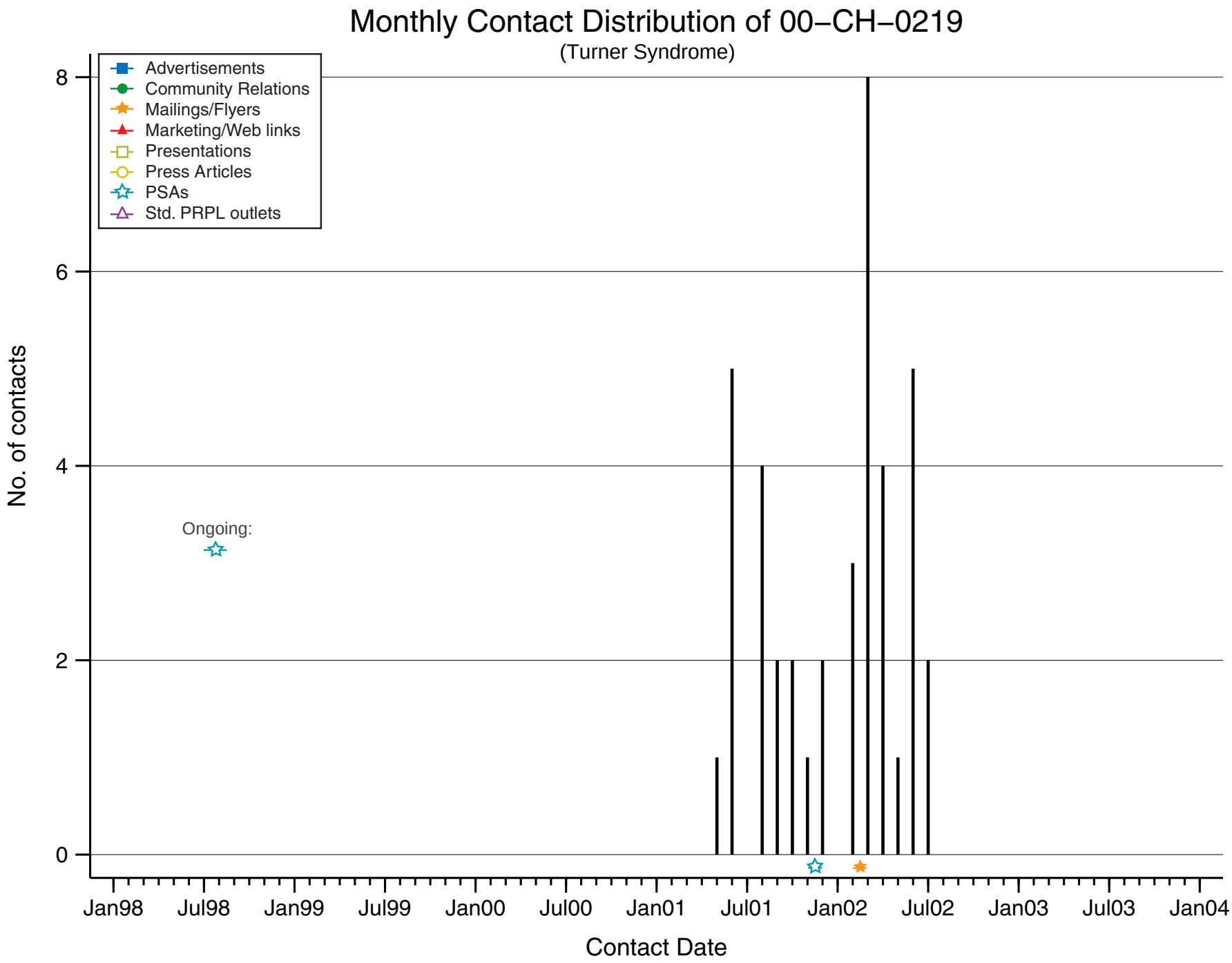
Appendix H: PRPL Monthly Contacts

CSR Incorporated
Consulting Services & Research

Appendix H: PRPL Monthly Contacts: Distribution of 34 PRPL Protocols




Monthly Contact Distribution of 00–CH–0134
(Childhood obesity)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown Date:
Ongoing:
No. of contacts
20
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 00–CH–0219
(Turner Syndrome)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
0
2
4
6
8
Ongoing:
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
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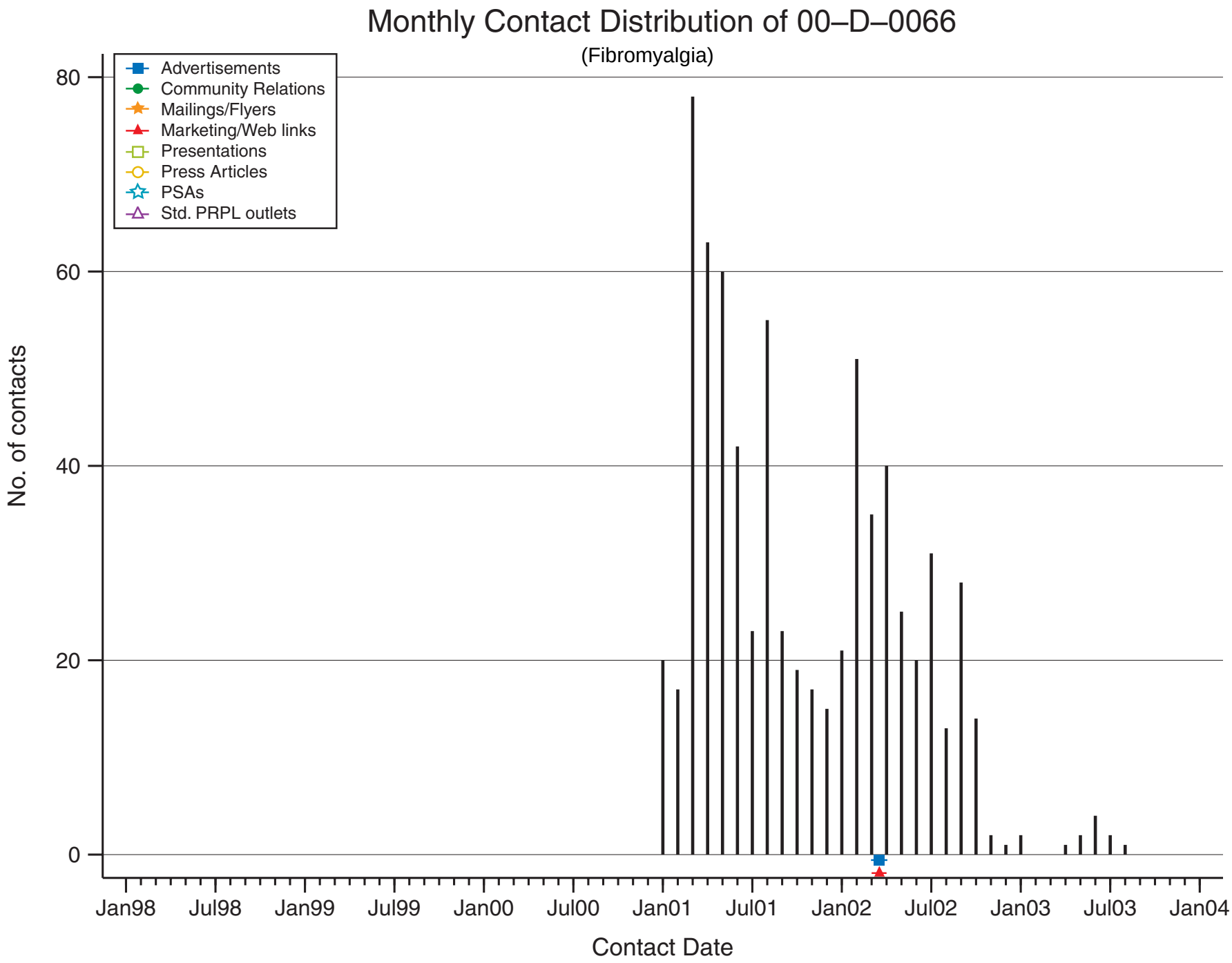
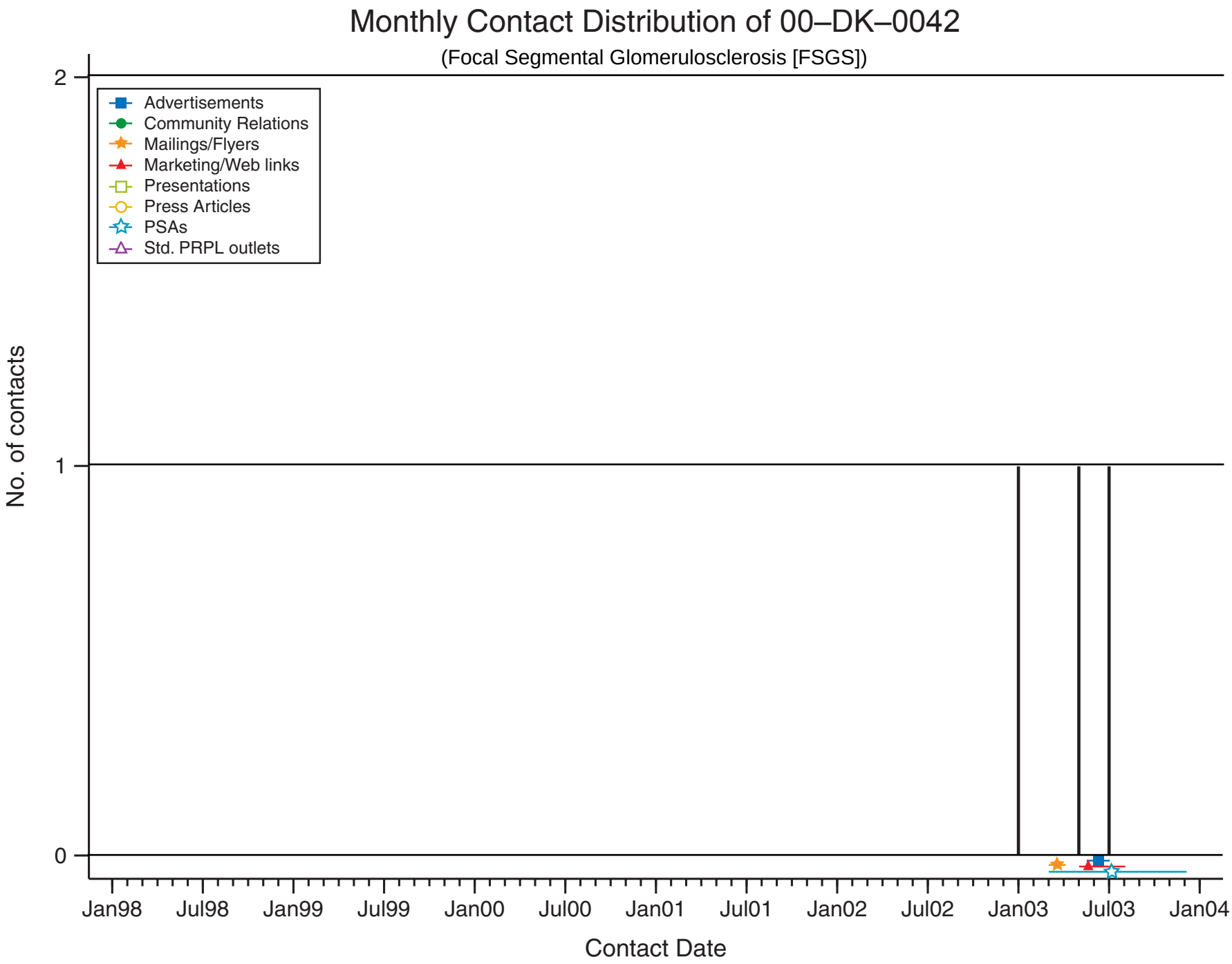
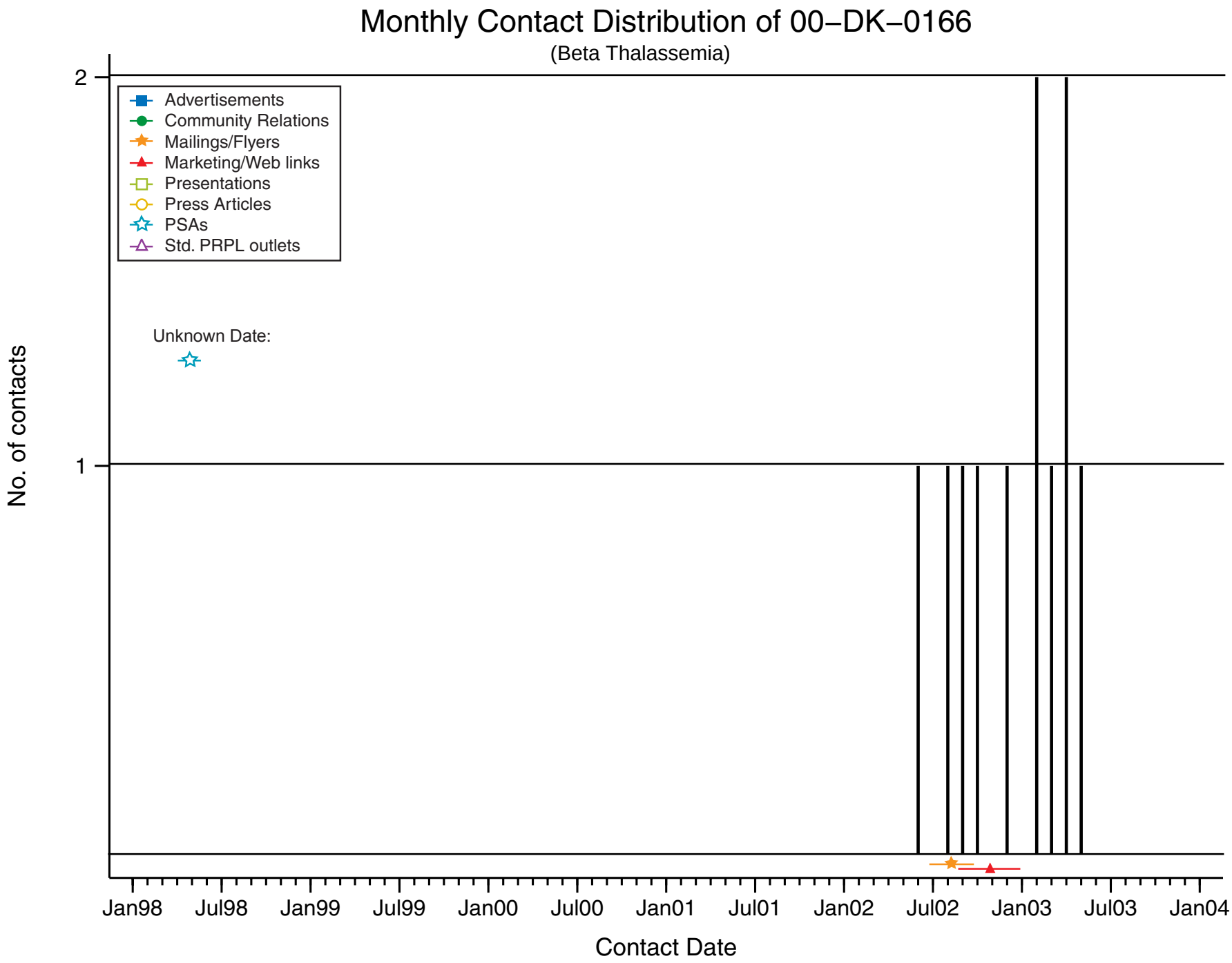
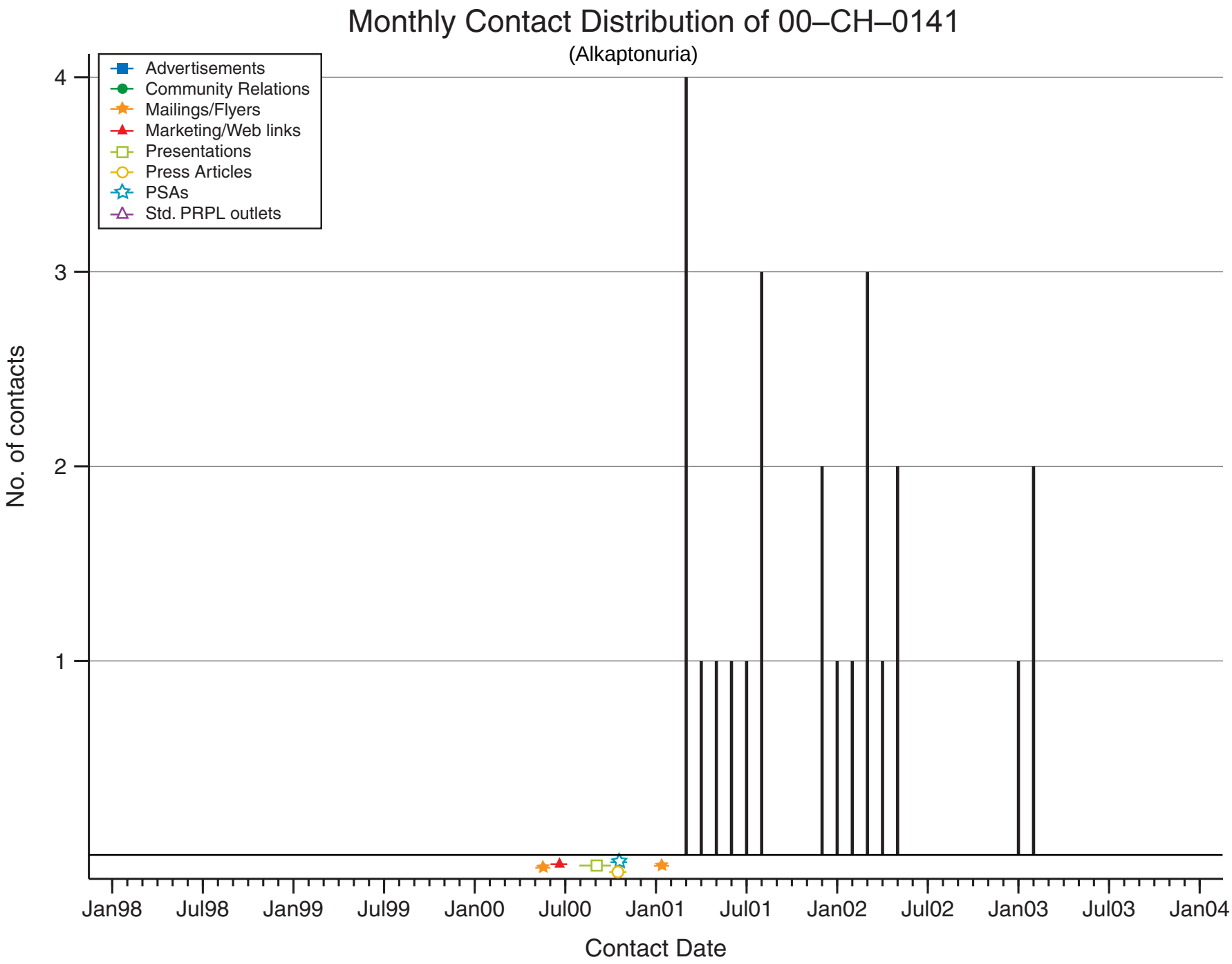
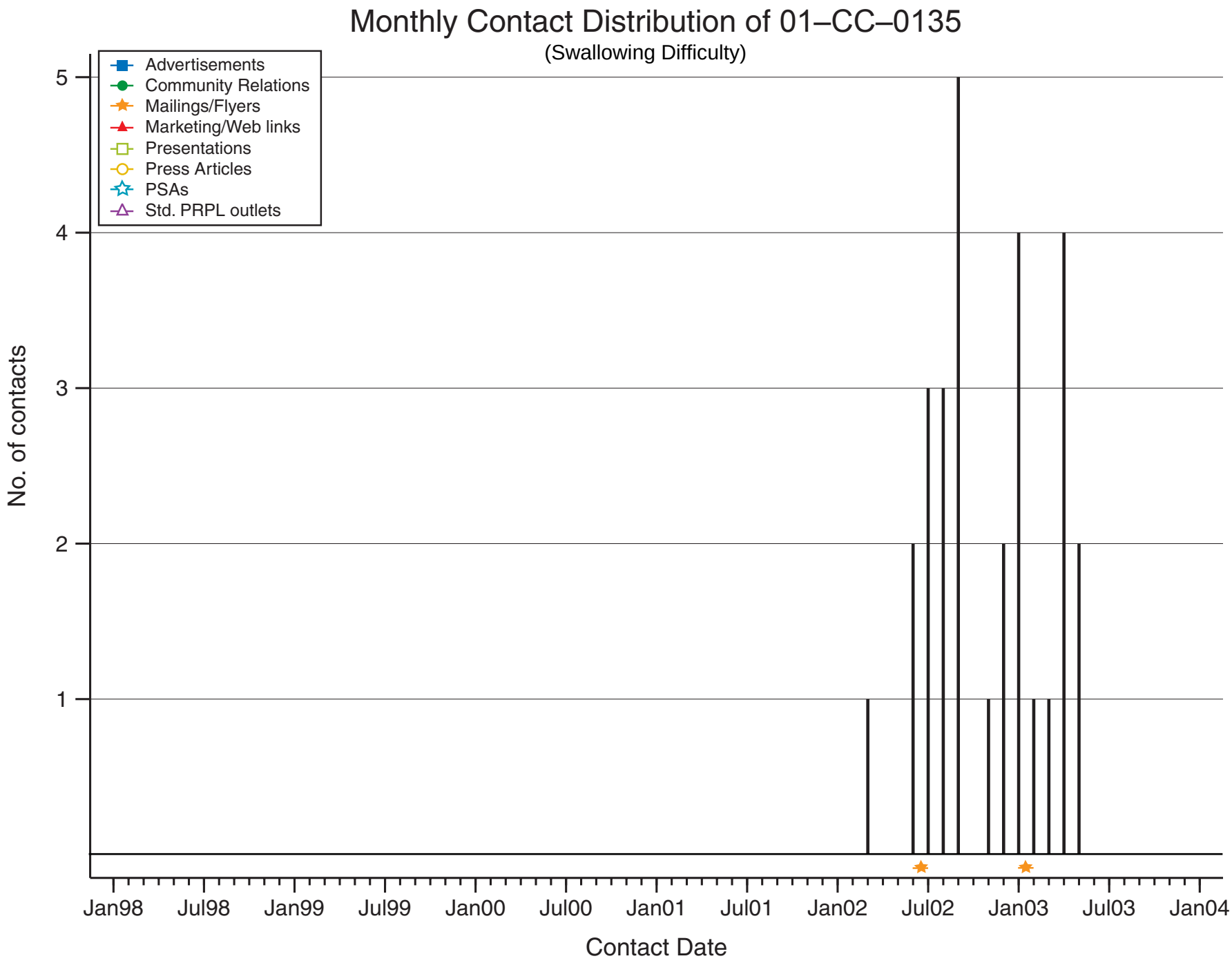
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 00–D–0066
(Fibromyalgia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
80
60
40
20
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 00–DK–0042
(Focal Segmental Glomerulosclerosis [FSGS])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 00–DK–0166
(Beta Thalassemia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown Date:
No. of contacts
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 00–CH–0141
(Alkaptonuria)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–CC–0135
(Swallowing Difficulty)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
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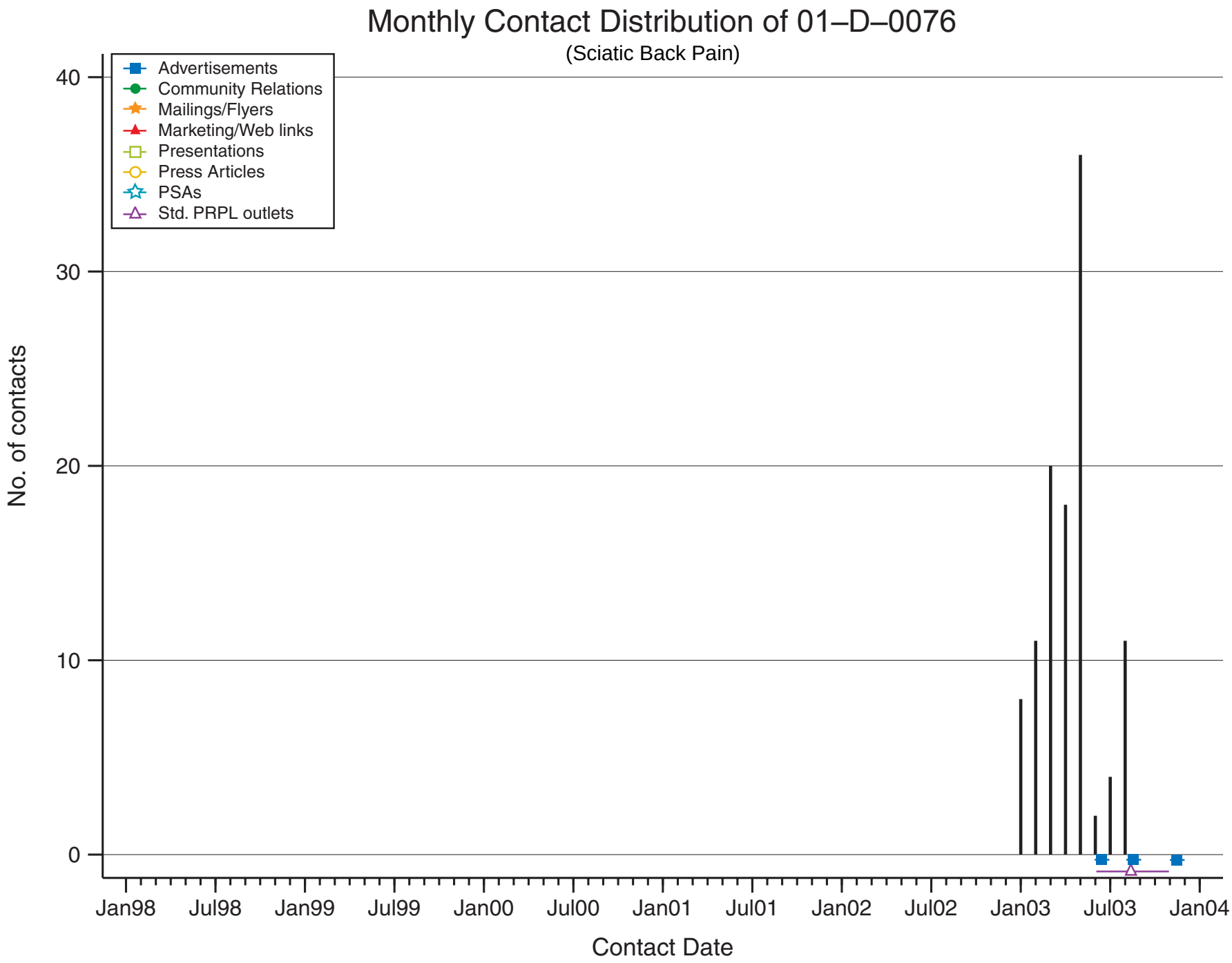
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–D–0076
(Sciatic Back Pain)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
40
30
20
10
0
Jan98
Jul98
Jan99
Jul99
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Jul00
Jan01
Jul01
Jan02
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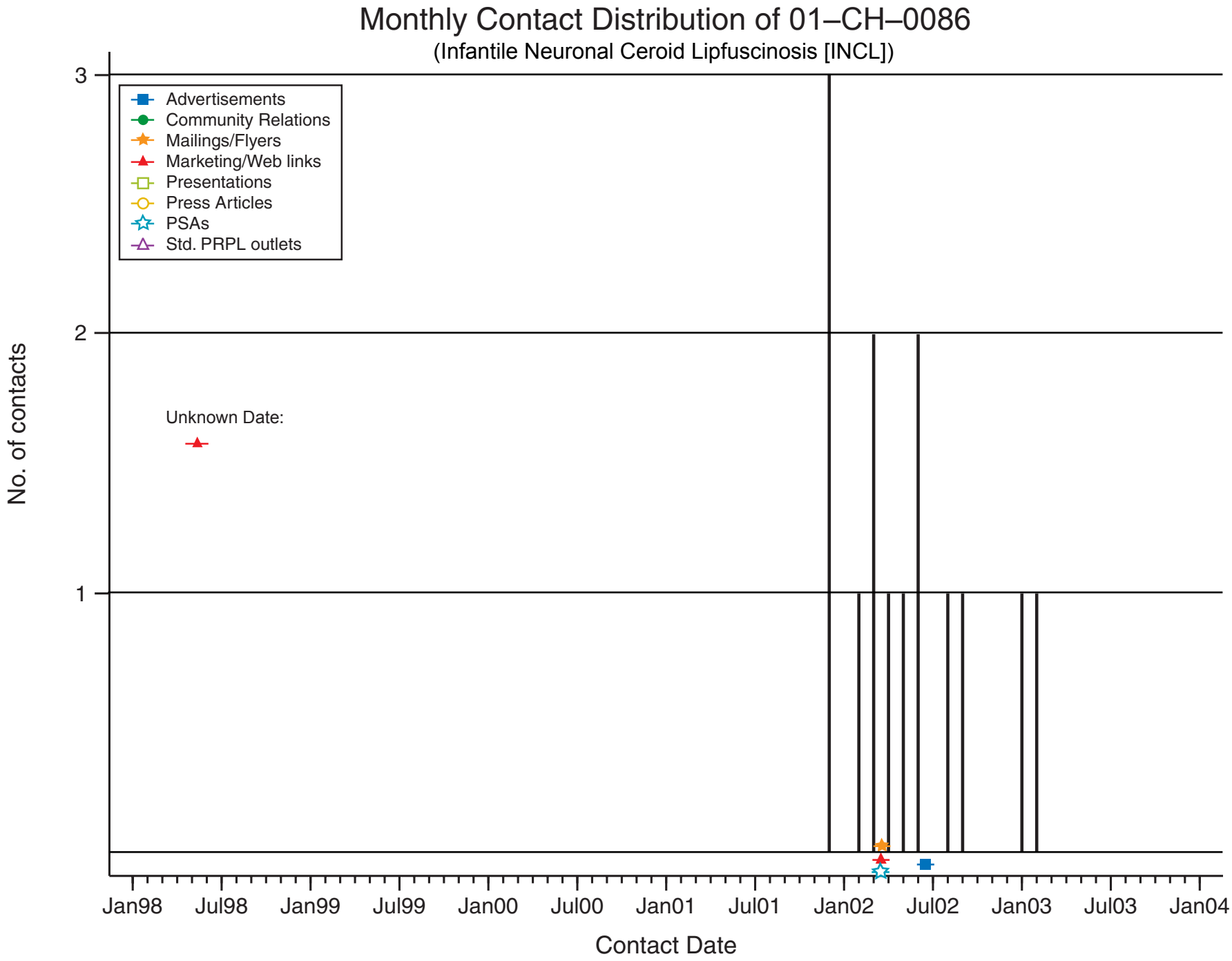
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–CH–0086
(Infantile Neuronal Ceroid Lipfuscinosis [INCL])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Unknown Date:
No. of contacts
3
2
1
Jan98
Jul98
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Jan02
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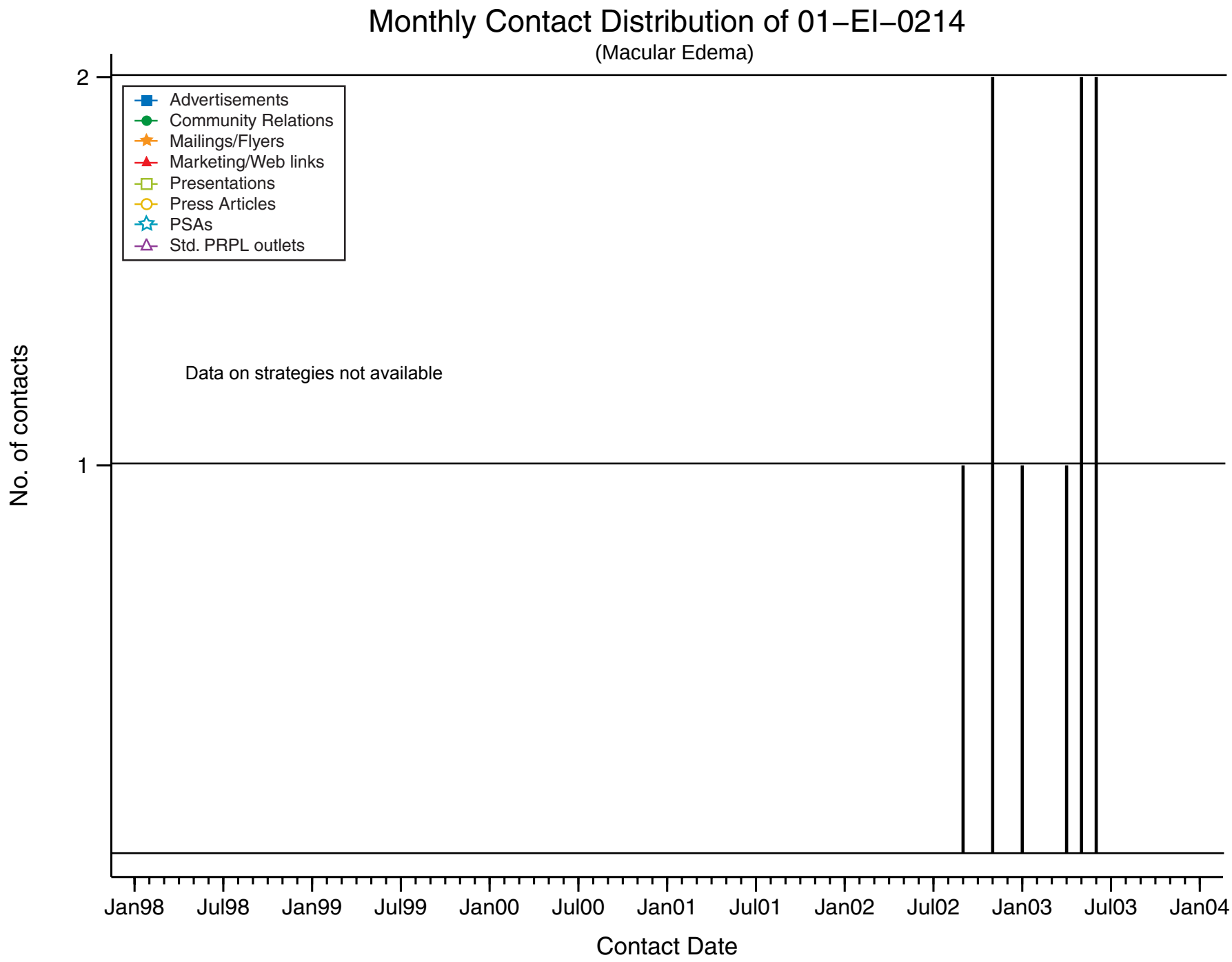
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–EI–0214
(Macular Edema)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Data on strategies not available
No. of contacts
2
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Jul00
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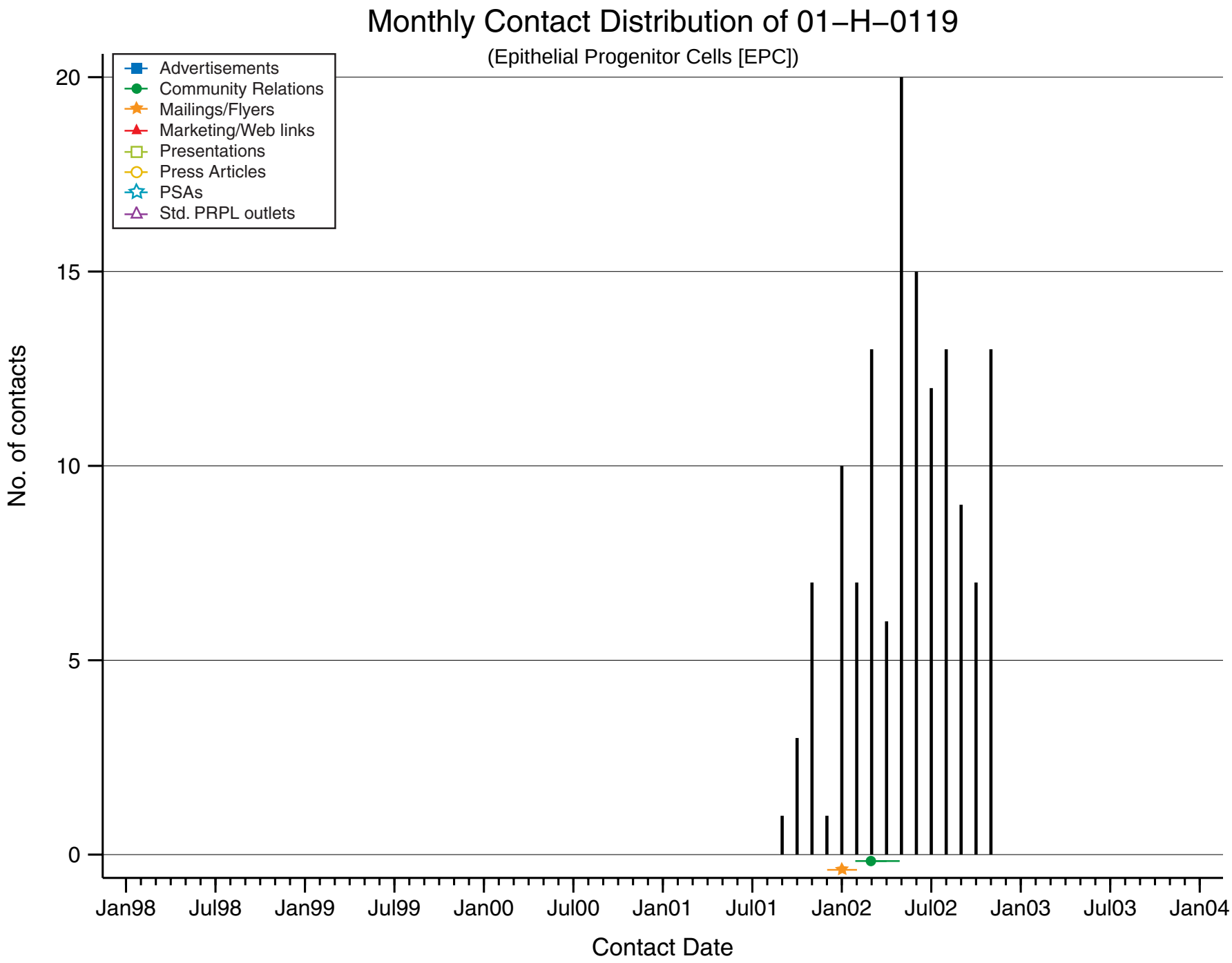
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–H–0119
(Epithelial Progenitor Cells [EPC])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
20
15
10
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Jan98
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Jan99
Jul99
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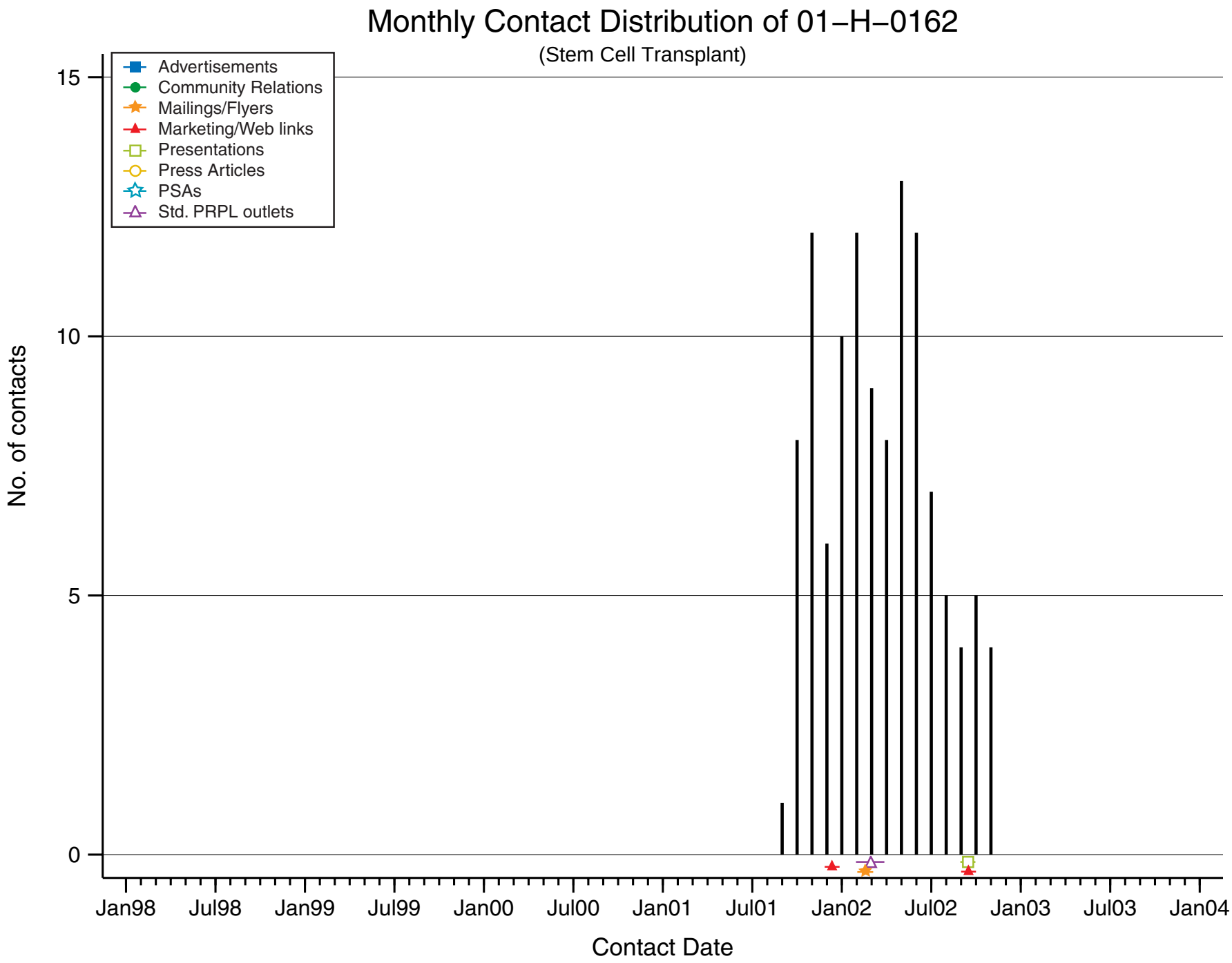
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–H–0162
(Stem Cell Transplant)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
15
10
5
0
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Jul98
Jan99
Jul99
Jan00
Jul00
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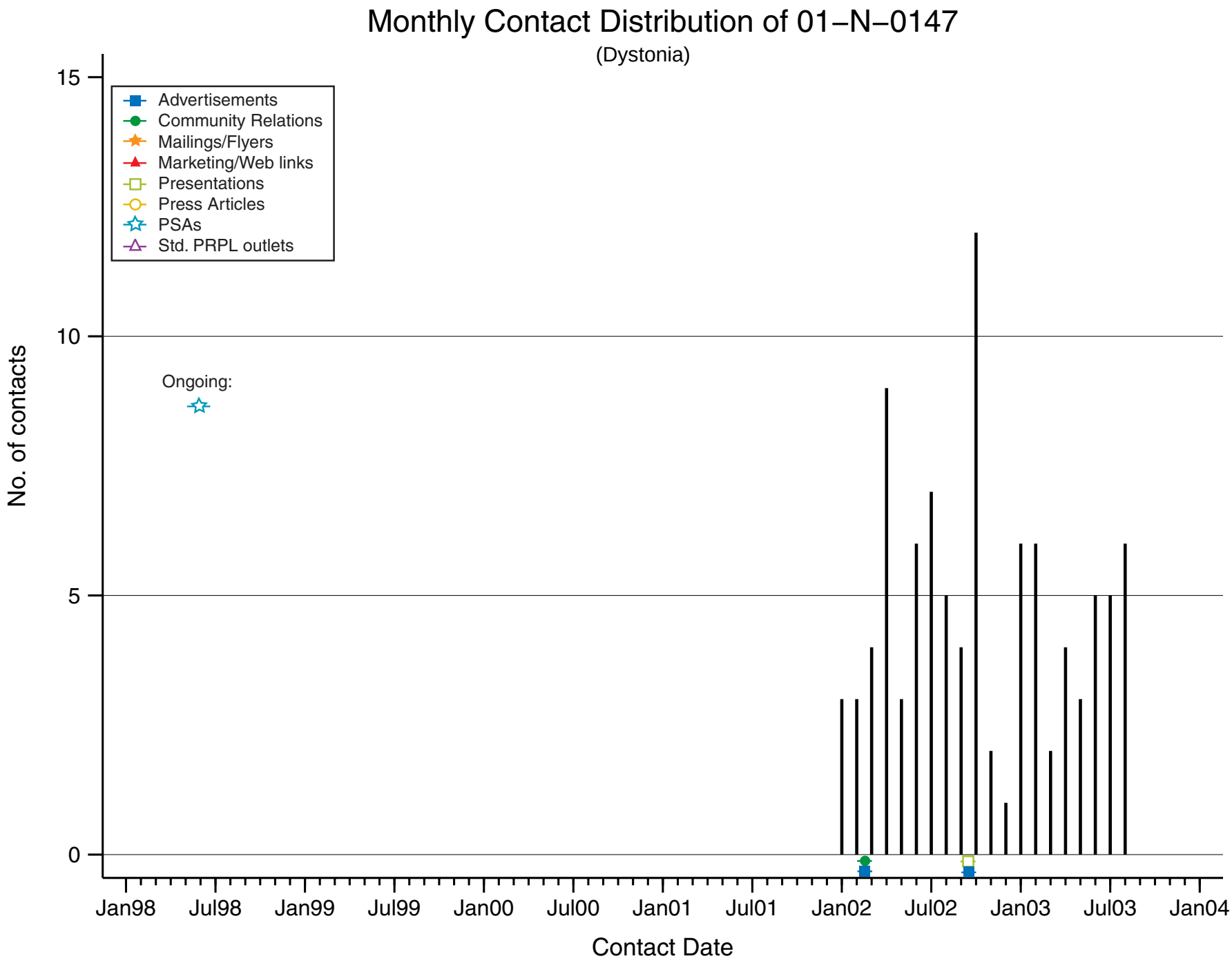
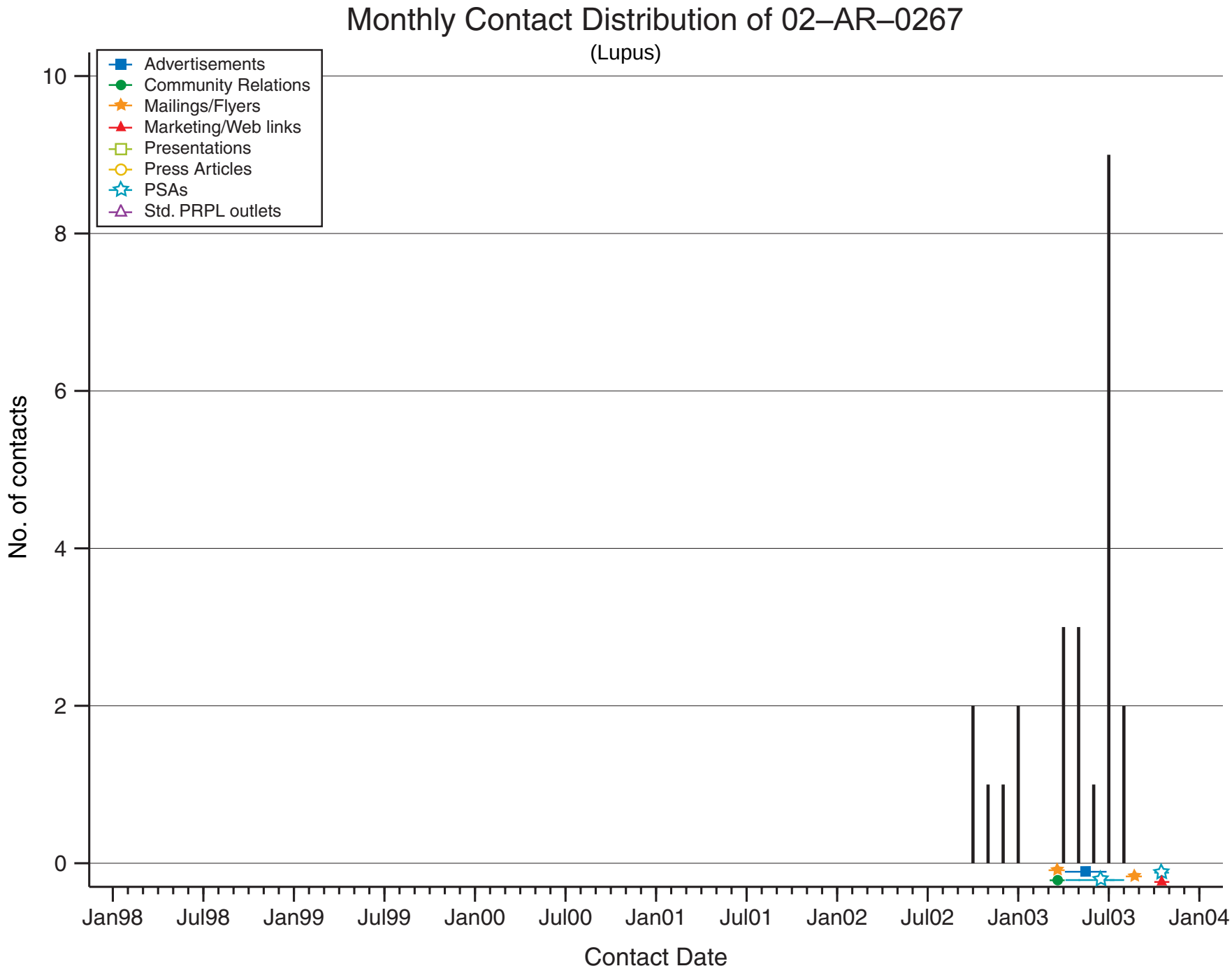
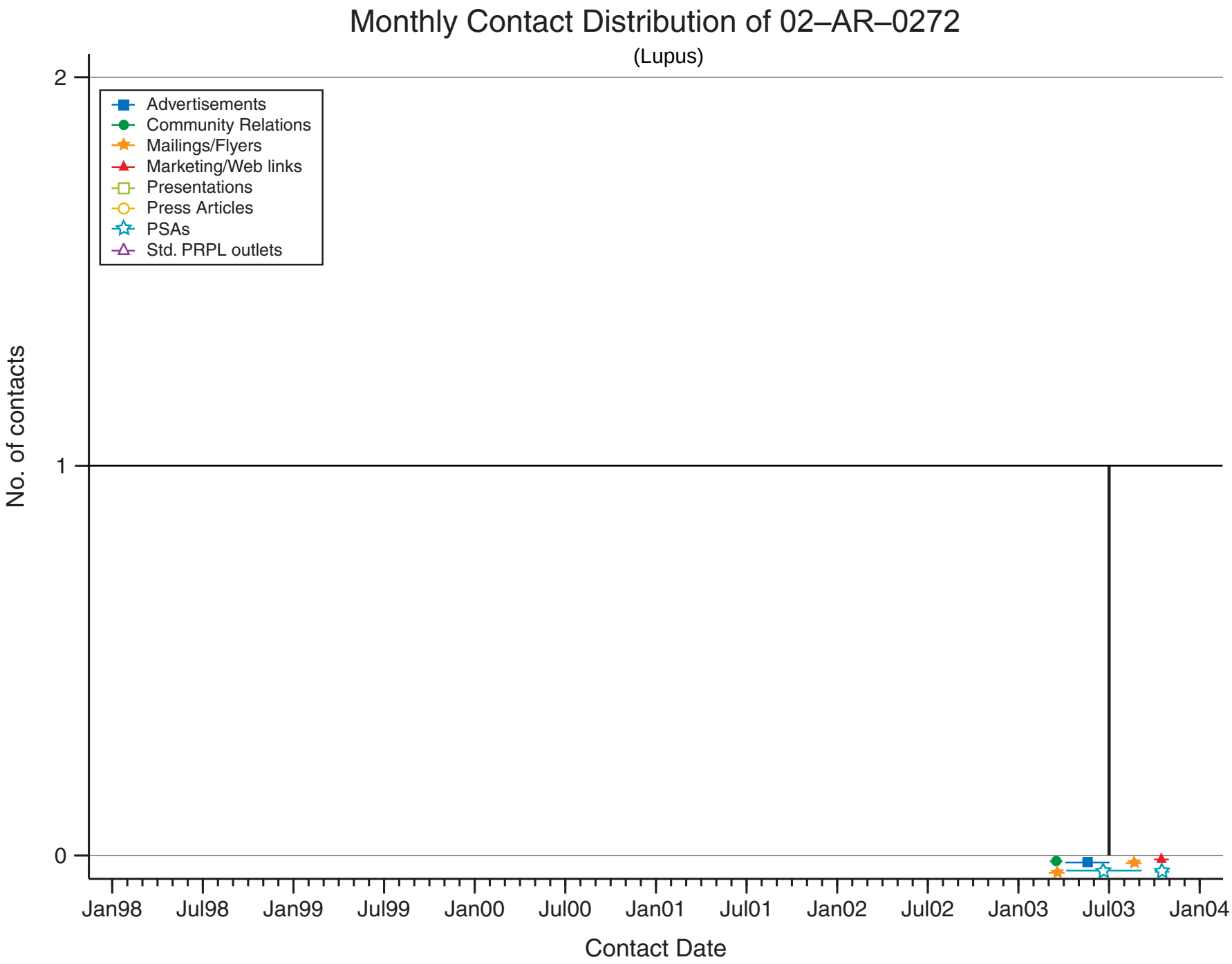
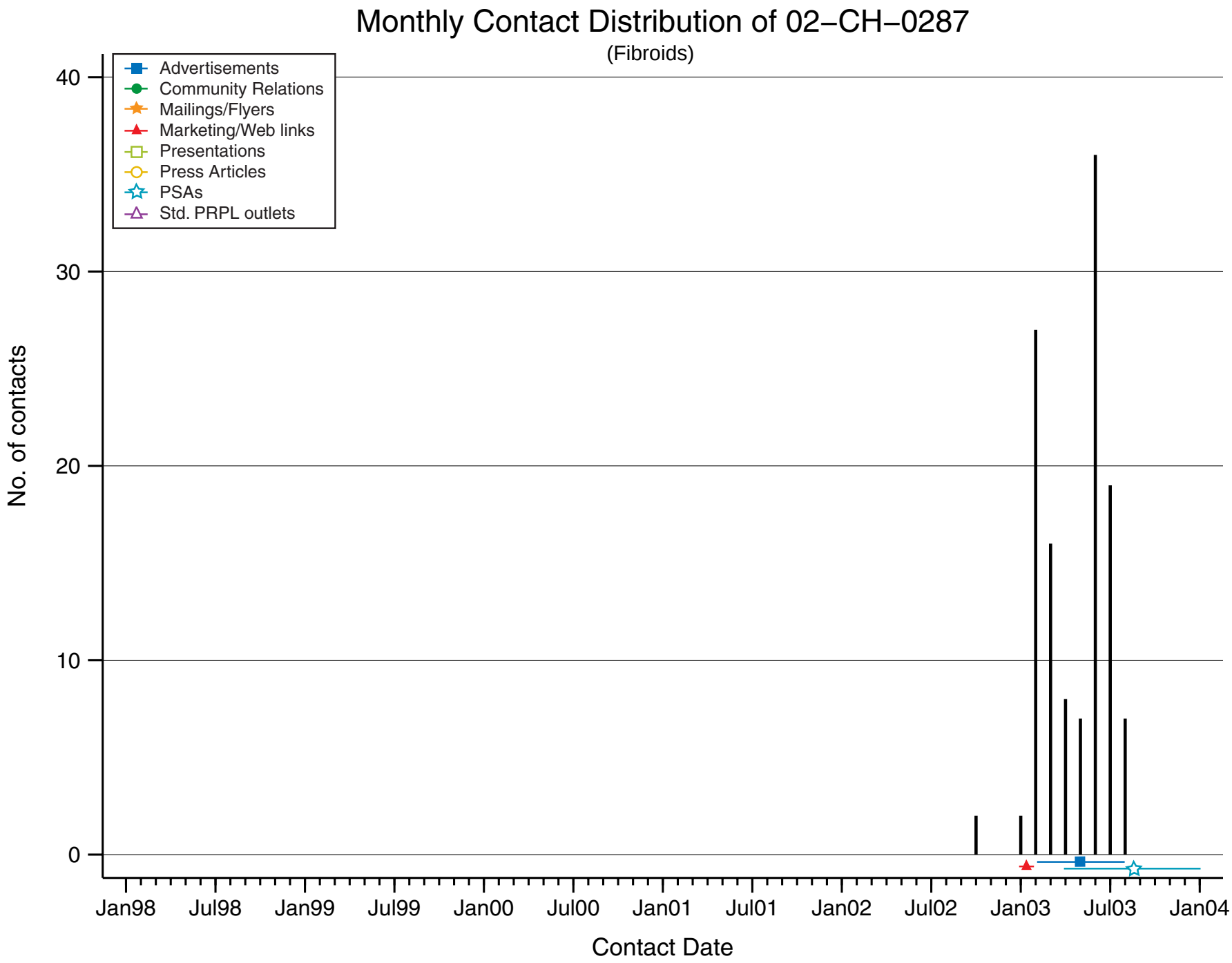
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 01–N–0147
(Dystonia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of contacts
15
10
5
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 02–AR–0267
(Lupus)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
0
2
4
6
8
10
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 02–AR–0272
(Lupus)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 02–CH–0287
(Fibroids)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
40
30
20
10
0
Jan98
Jul98
Jan99
Jul99
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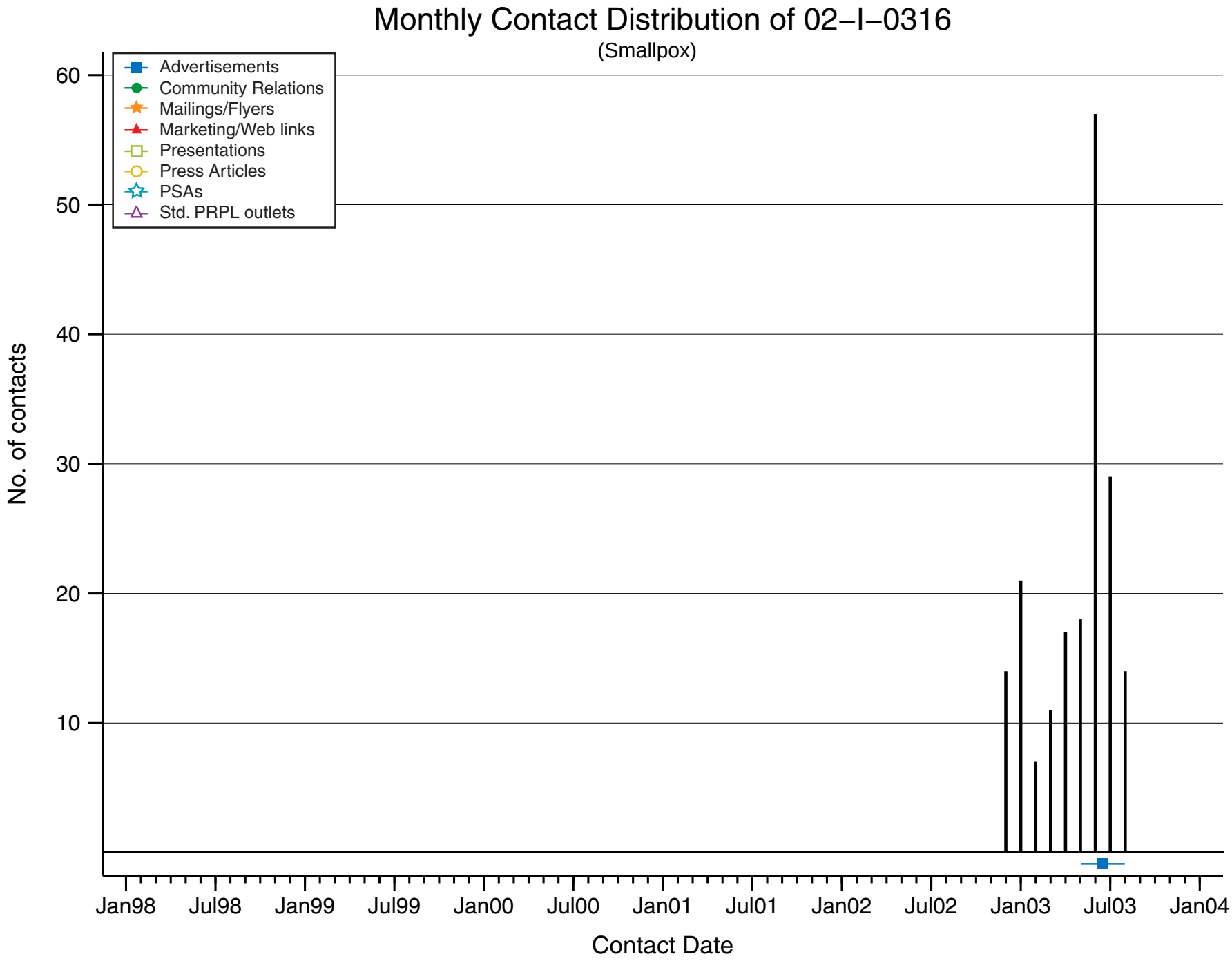
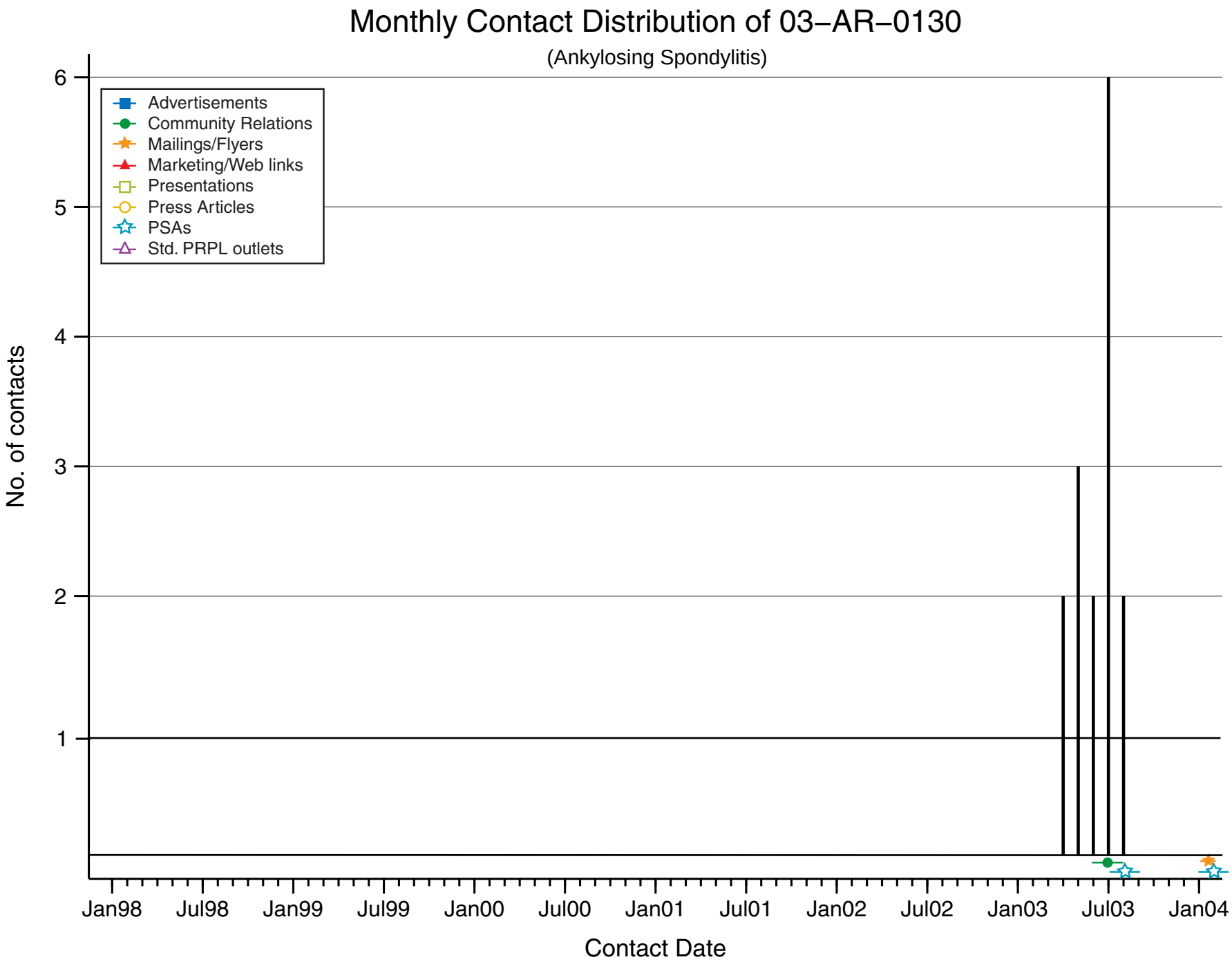
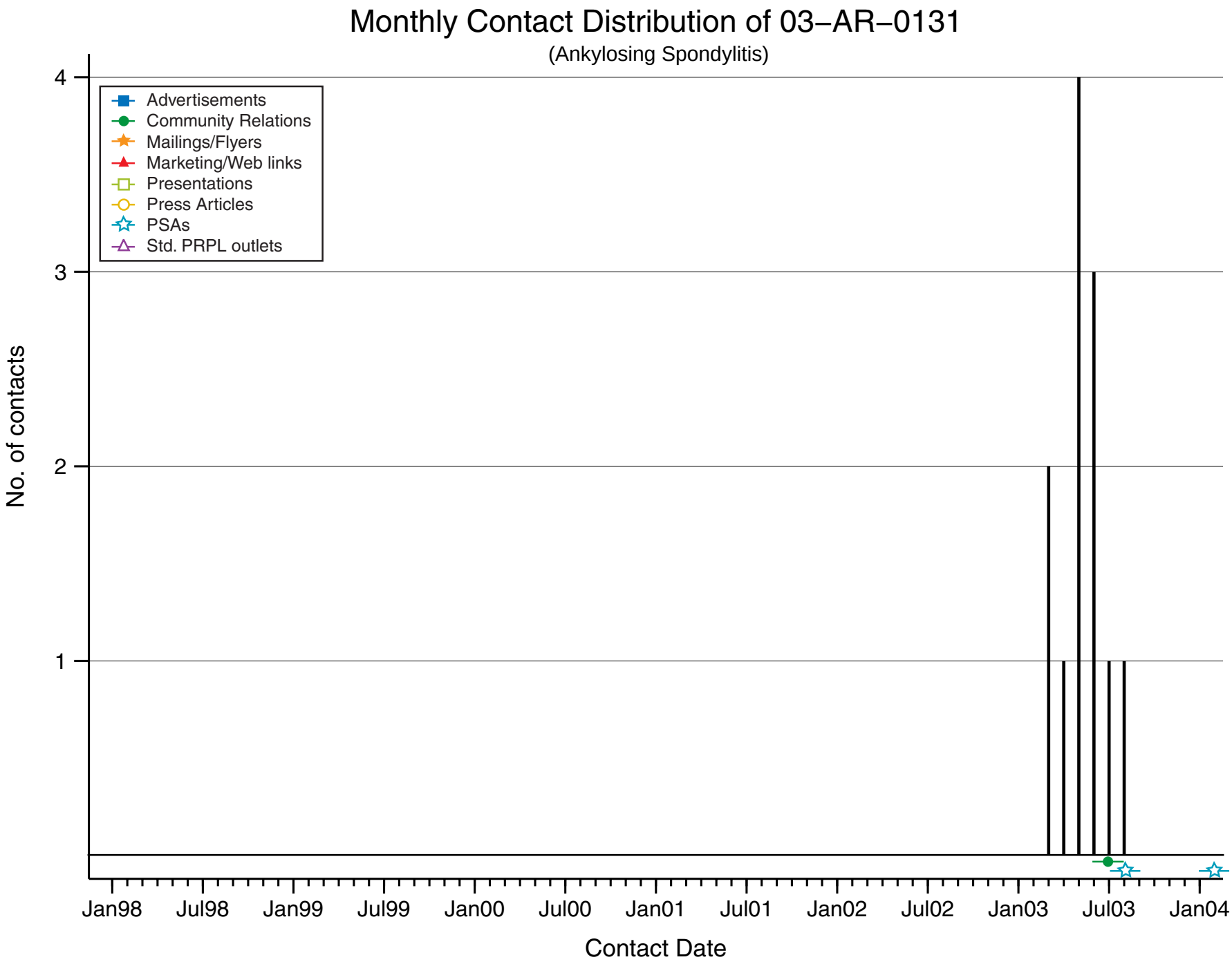
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 02–I–0316
(Smallpox)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
60
50
40
30
20
10
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 03–AR–0130
(Ankylosing Spondylitis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
6
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 03–AR–0131
(Ankylosing Spondylitis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
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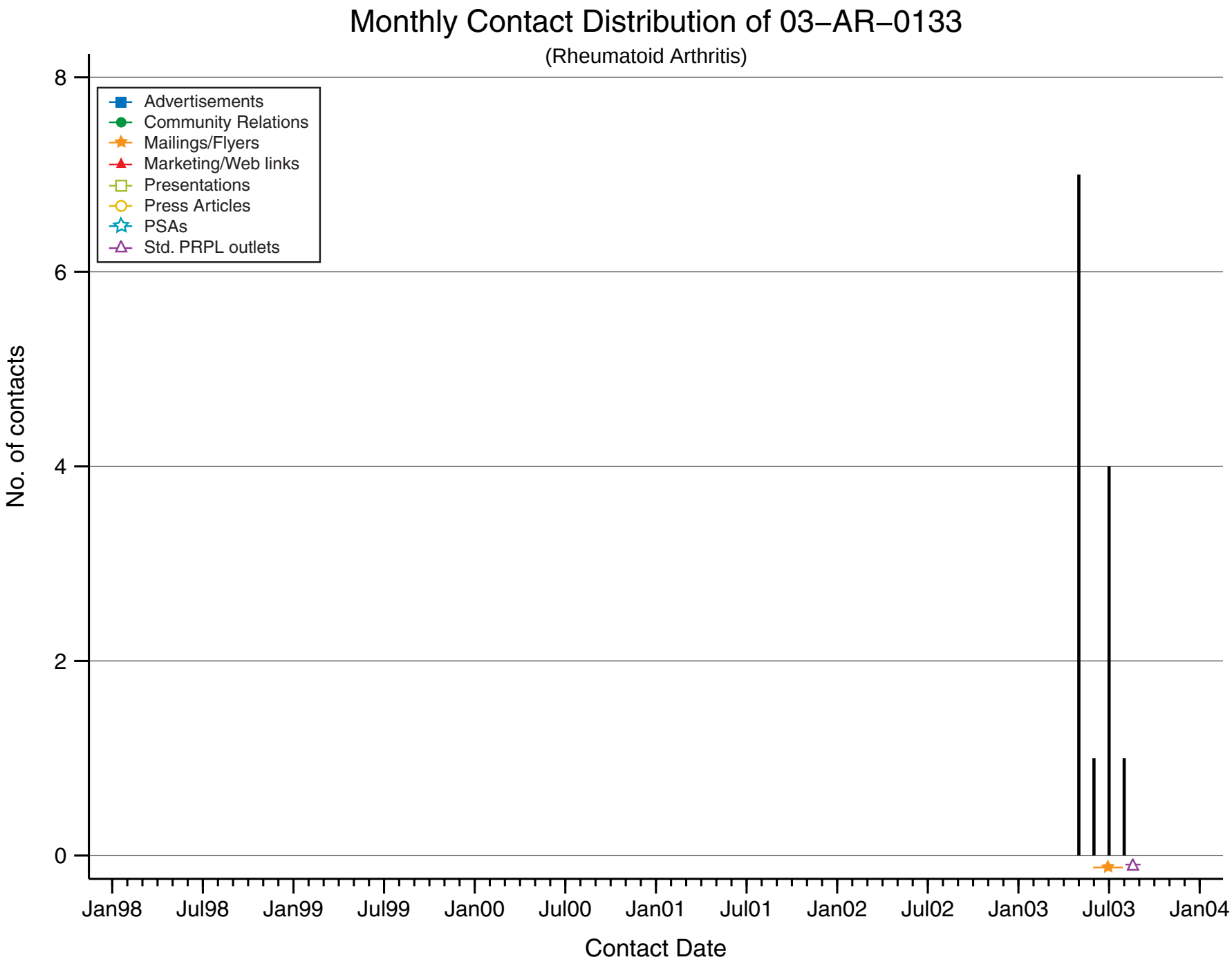
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 03–AR–0133
(Rheumatoid Arthritis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
0
2
4
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8
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Jul98
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Jan02
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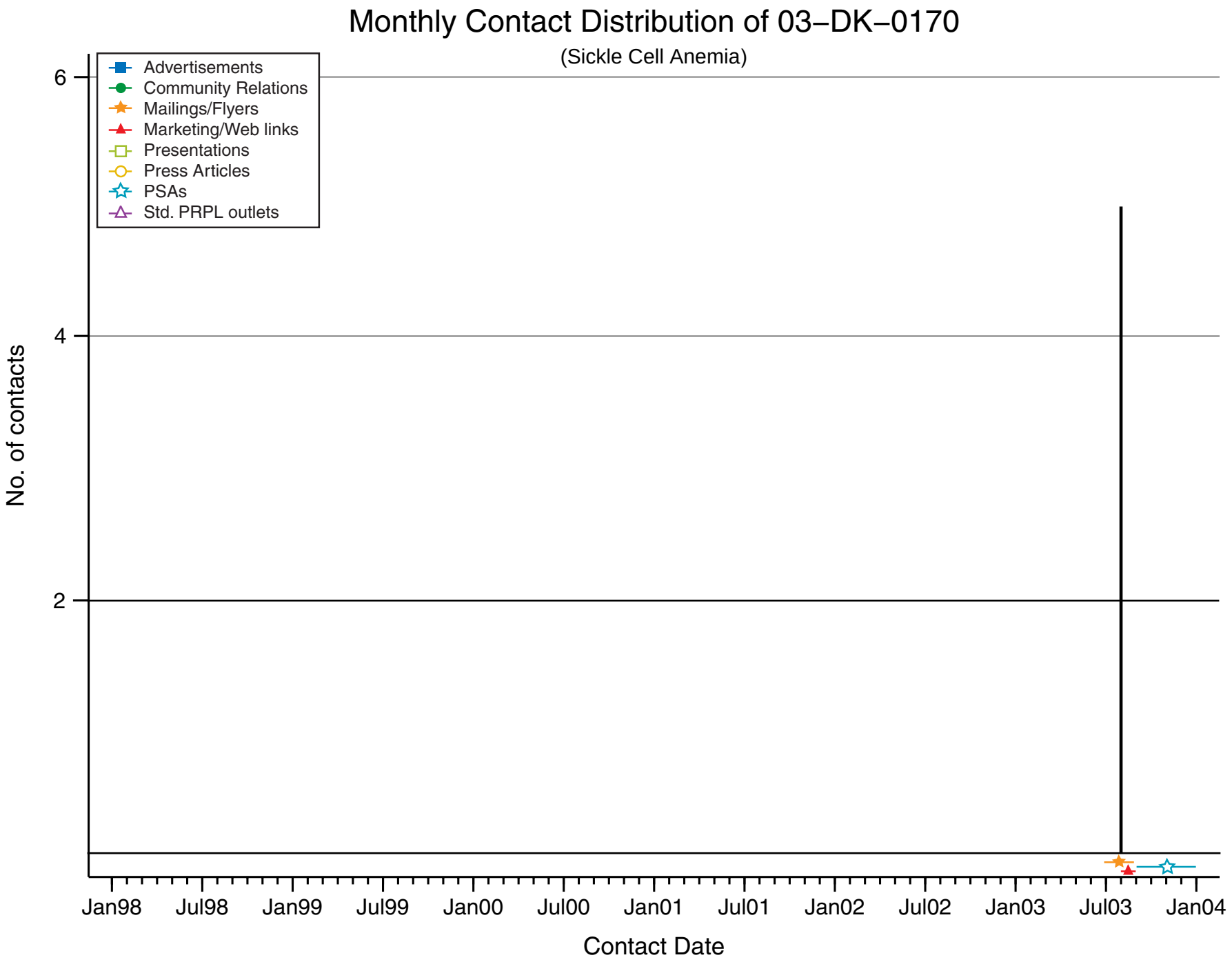
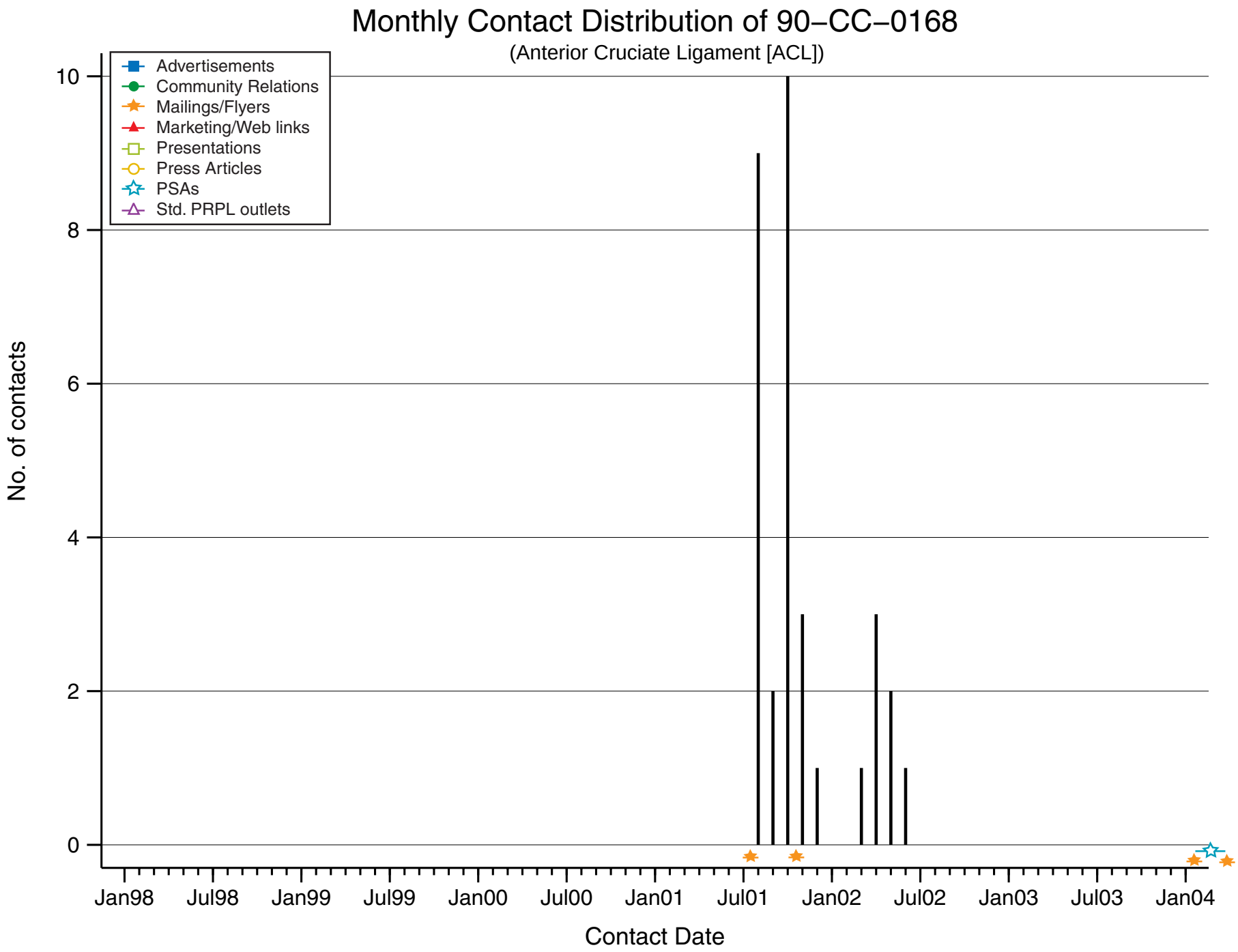
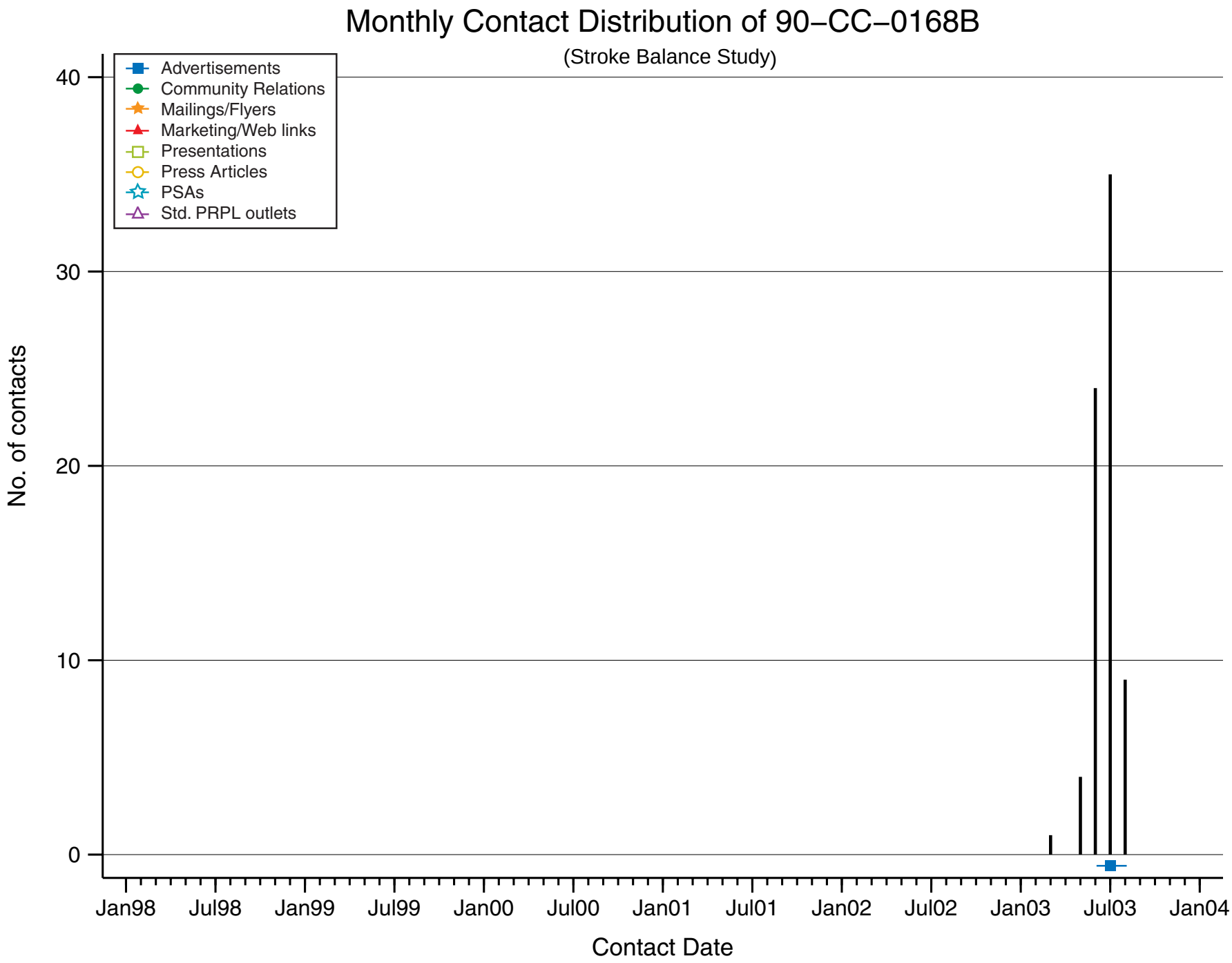
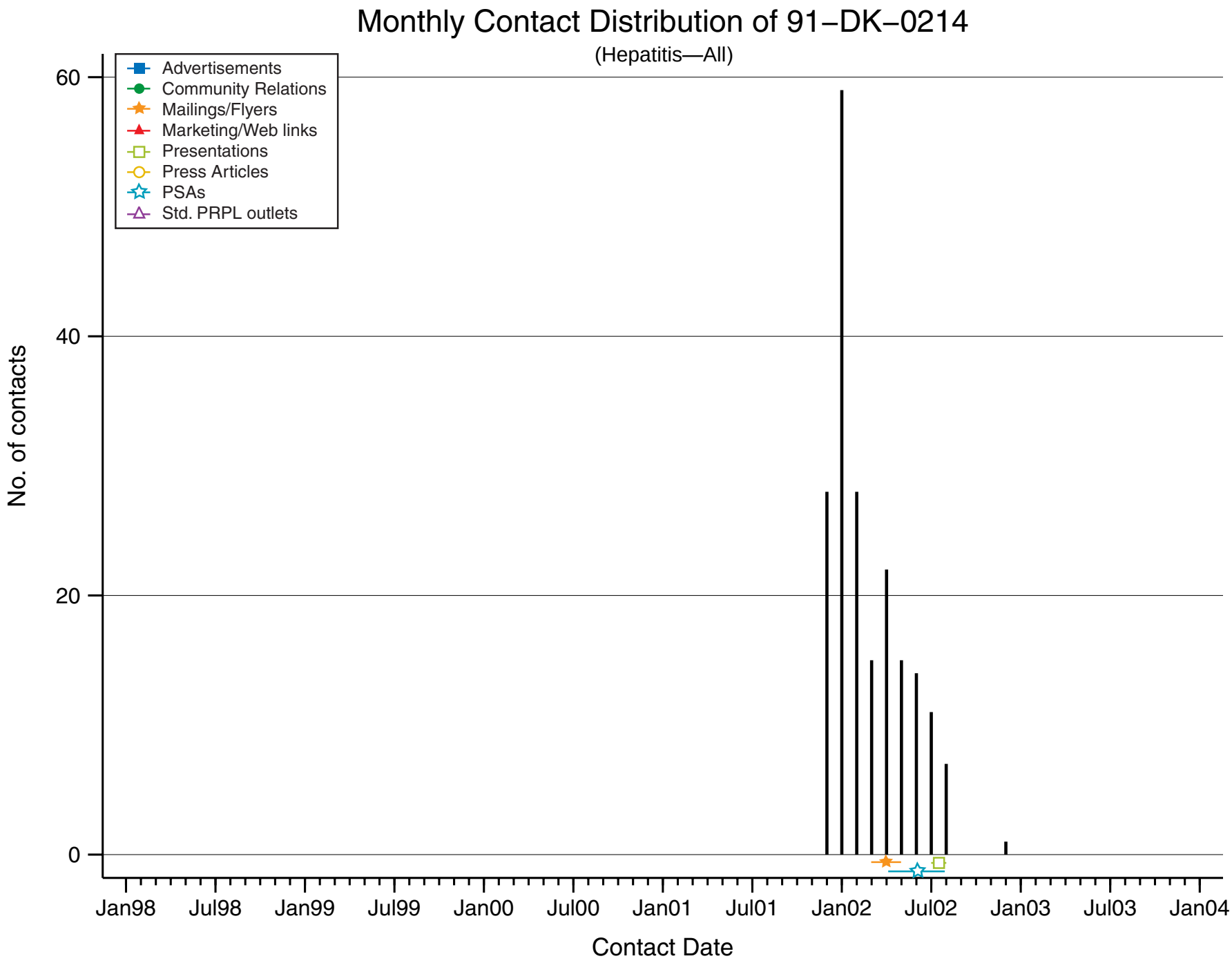
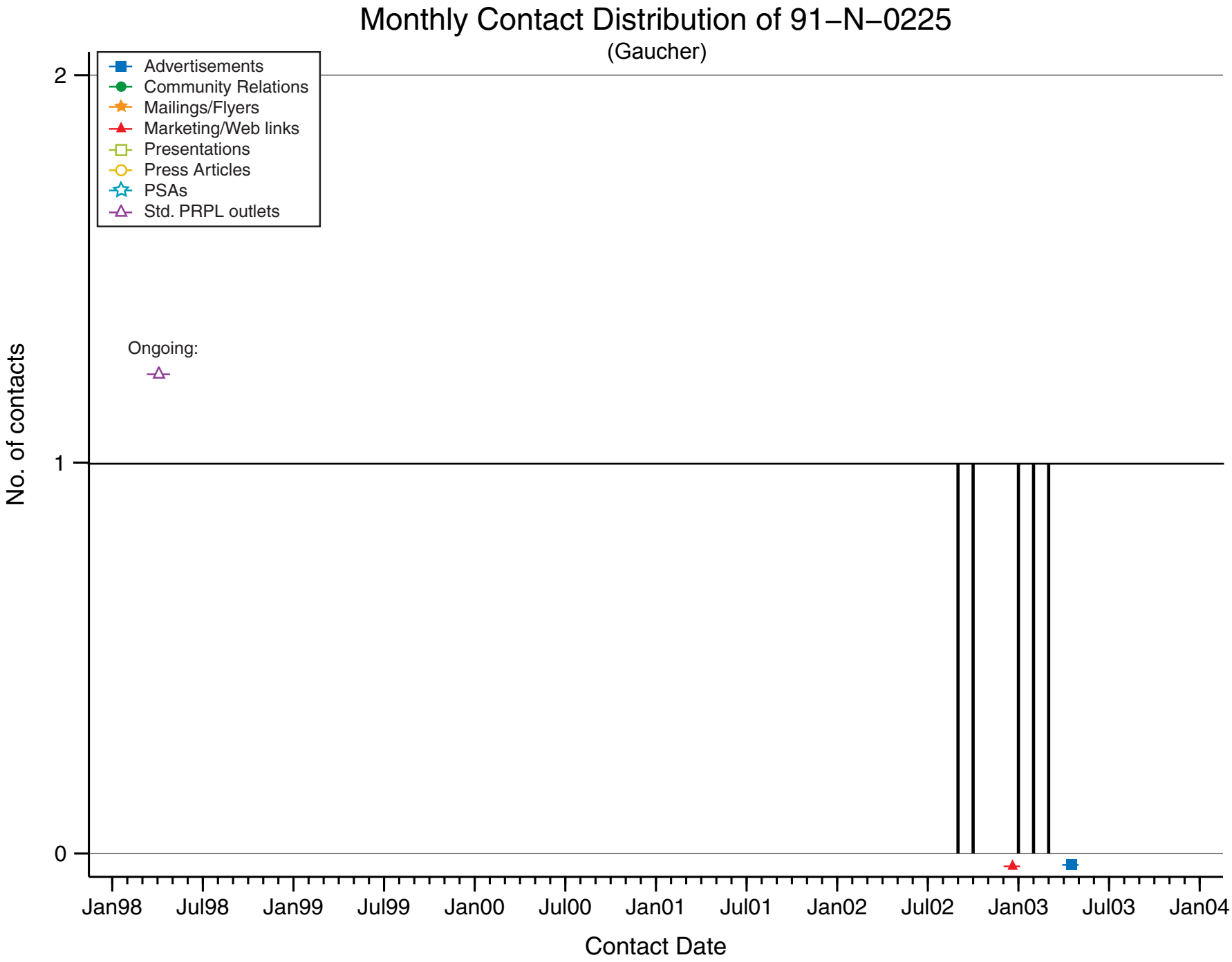
Jul03
Jan04
Contact Date

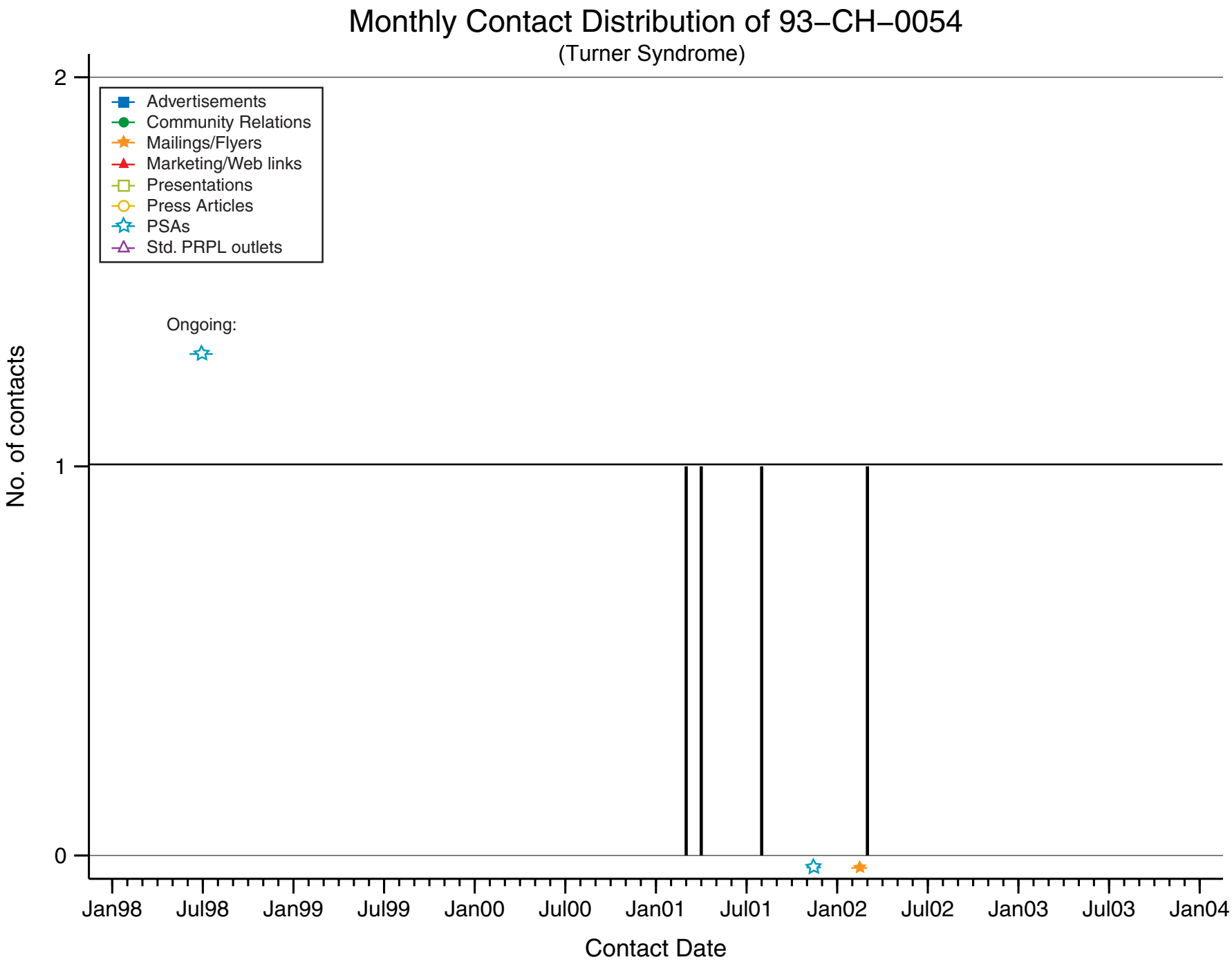

Monthly Contact Distribution of 03–DK–0170
(Sickle Cell Anemia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
6
4
2
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date

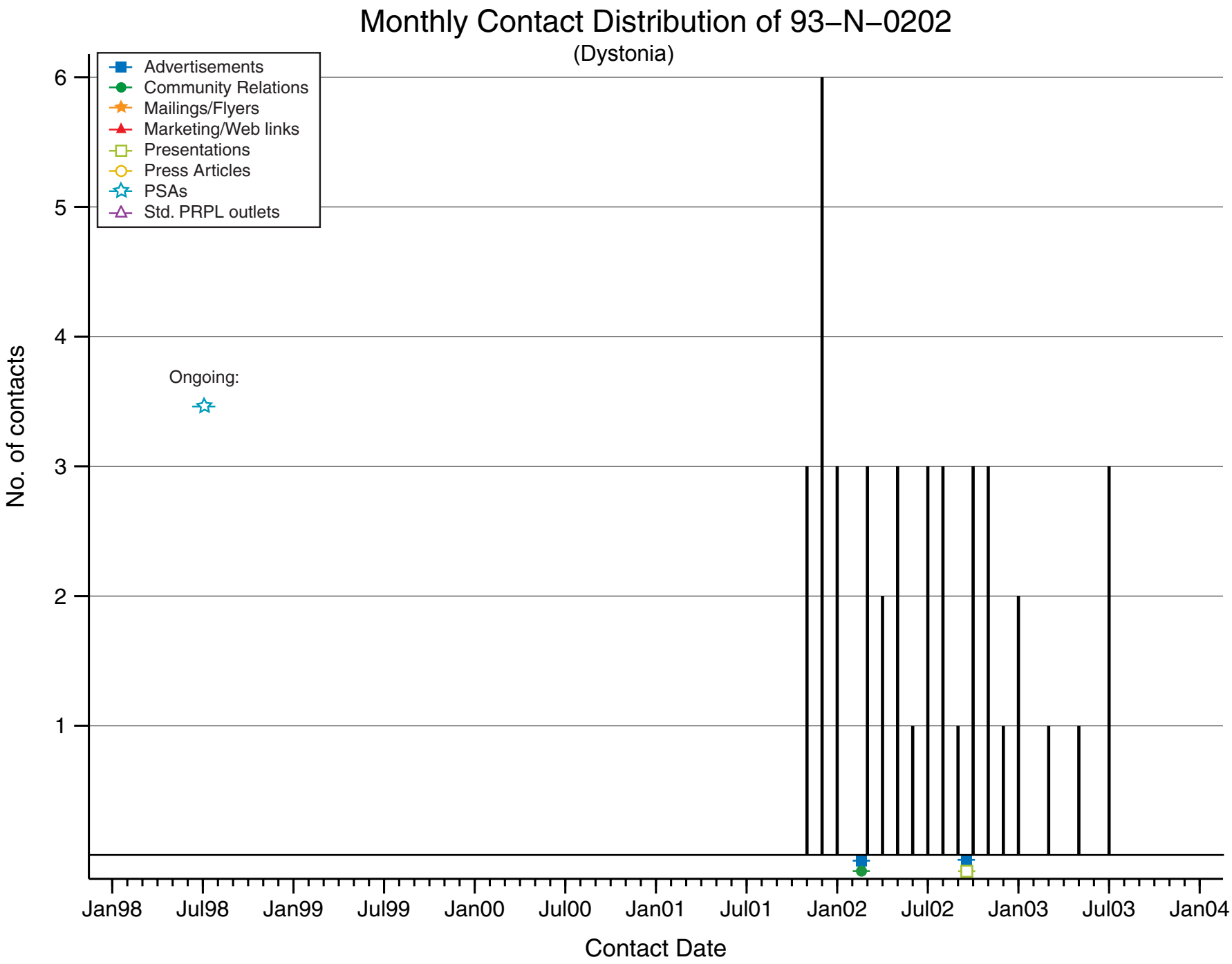

Monthly Contact Distribution of 90–CC–0168
(Anterior Cruciate Ligament [ACL])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
0
2
4
6
8
10
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date

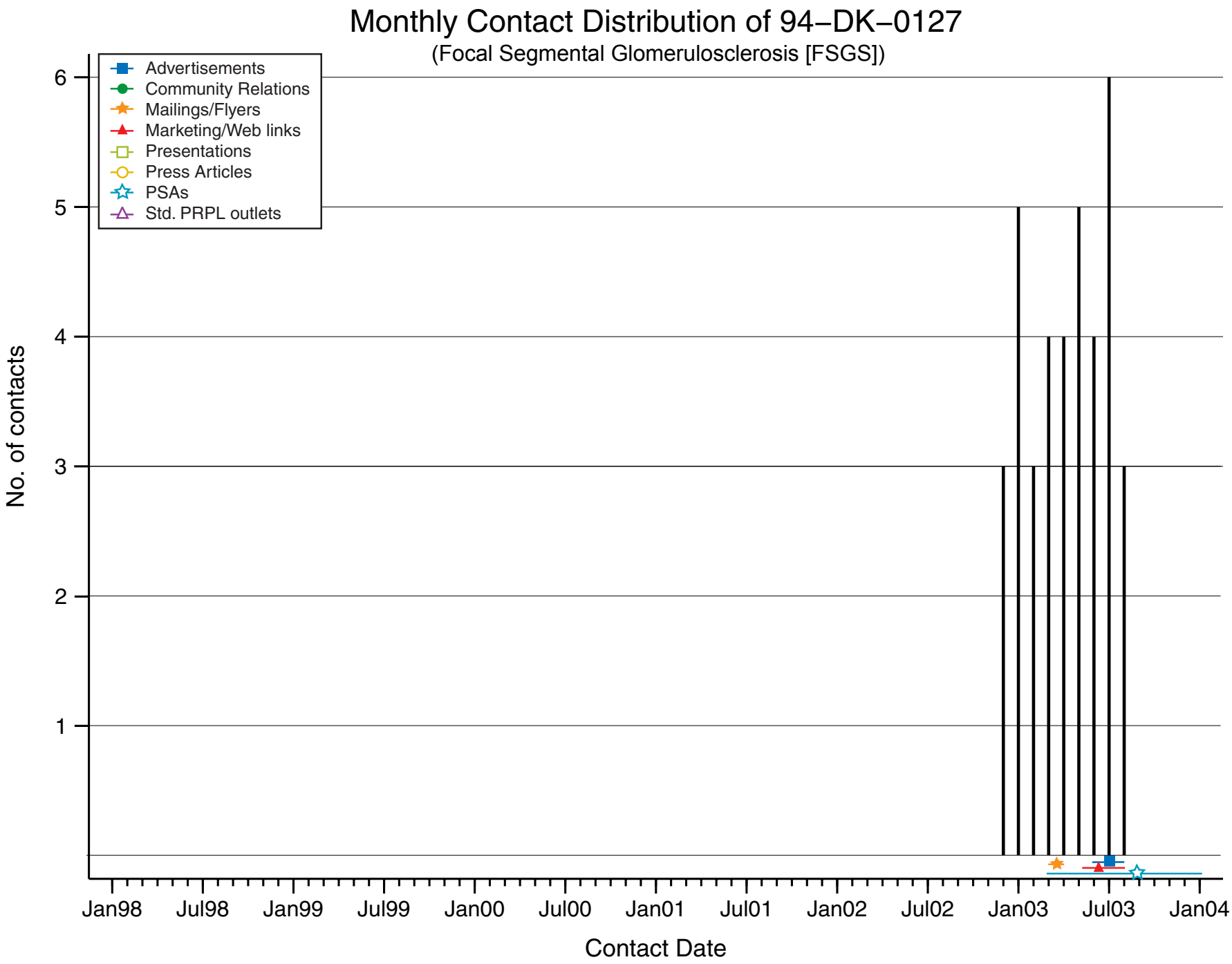

Monthly Contact Distribution of 90–CC–0168B
(Stroke Balance Study)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
40
30
20
10
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date

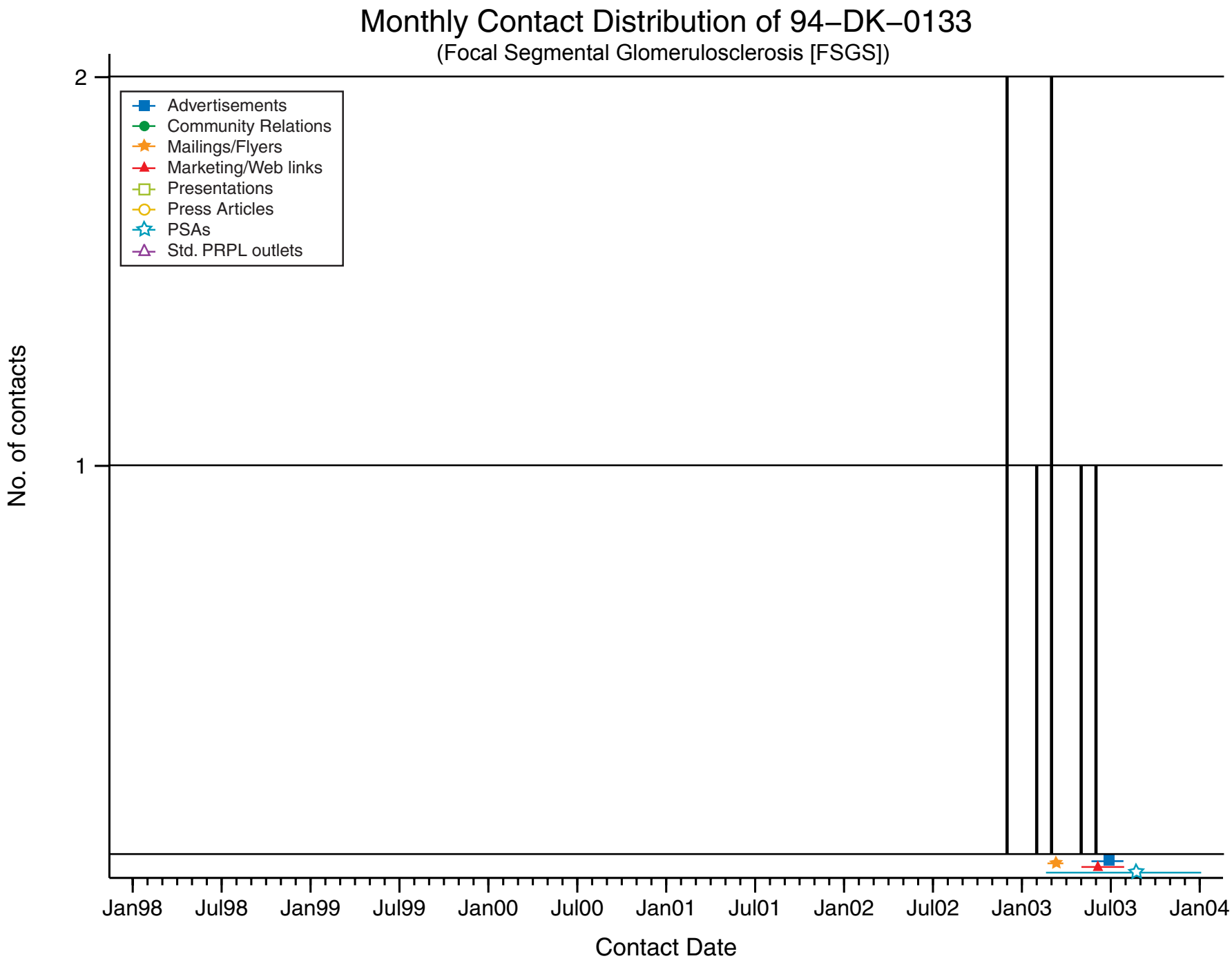

Monthly Contact Distribution of 91–DK–0214
(Hepatitis—All)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
60
40
20
0
No. of contacts
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date

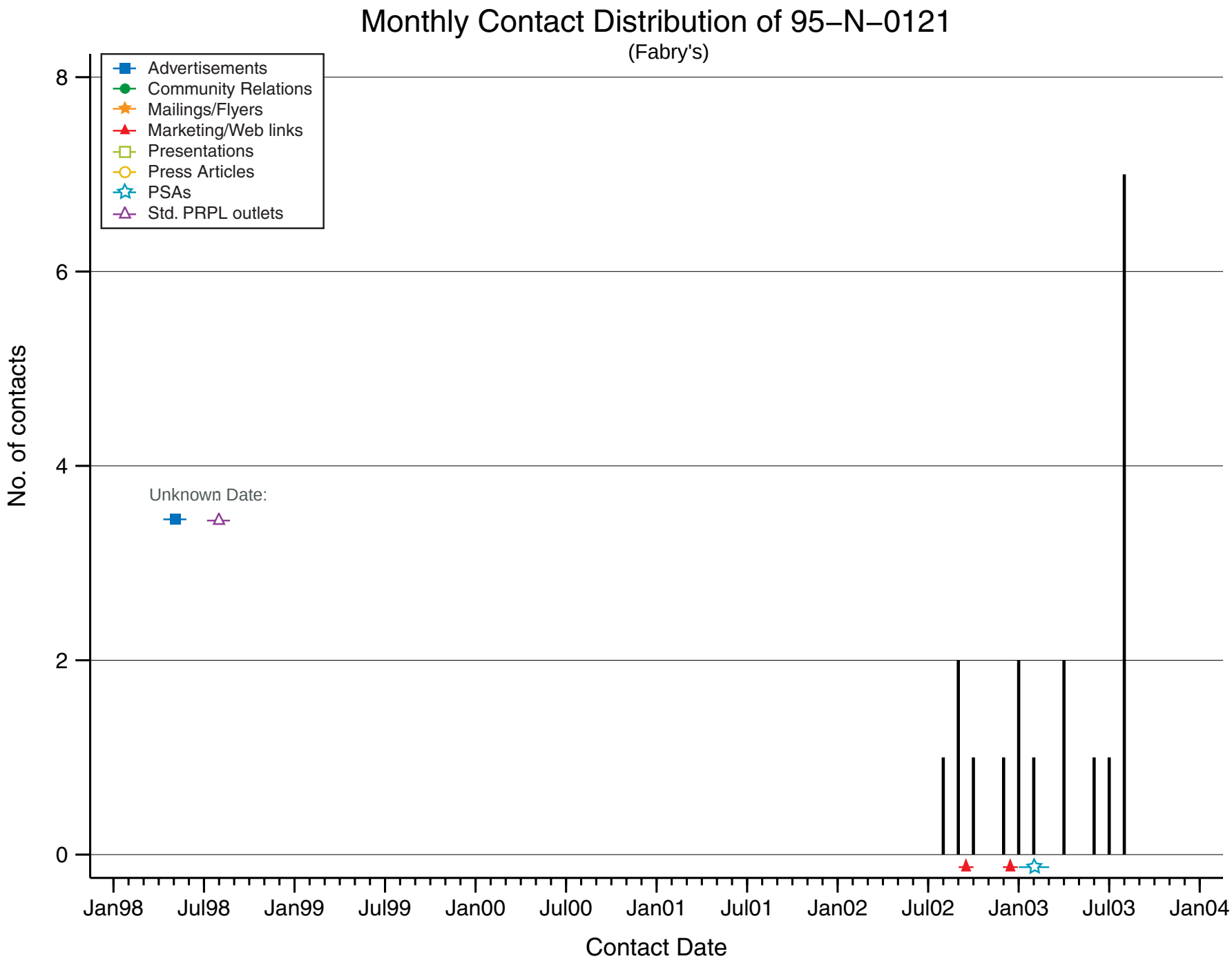

Monthly Contact Distribution of 91–N–0225
(Gaucher)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of contacts
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 93–CH–0054
(Turner Syndrome)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of contacts
2
1
0
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 93–N–0202
(Dystonia)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of contacts
6
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 94–DK–0127
(Focal Segmental Glomerulosclerosis [FSGS])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
6
5
4
3
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 94–DK–0133
(Focal Segmental Glomerulosclerosis [FSGS])
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
2
1
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 95–N–0121
(Fabry's)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
0
2
4
6
8
Unknown Date:
Jan98
Jul98
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Jul99
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Jul01
Jan02
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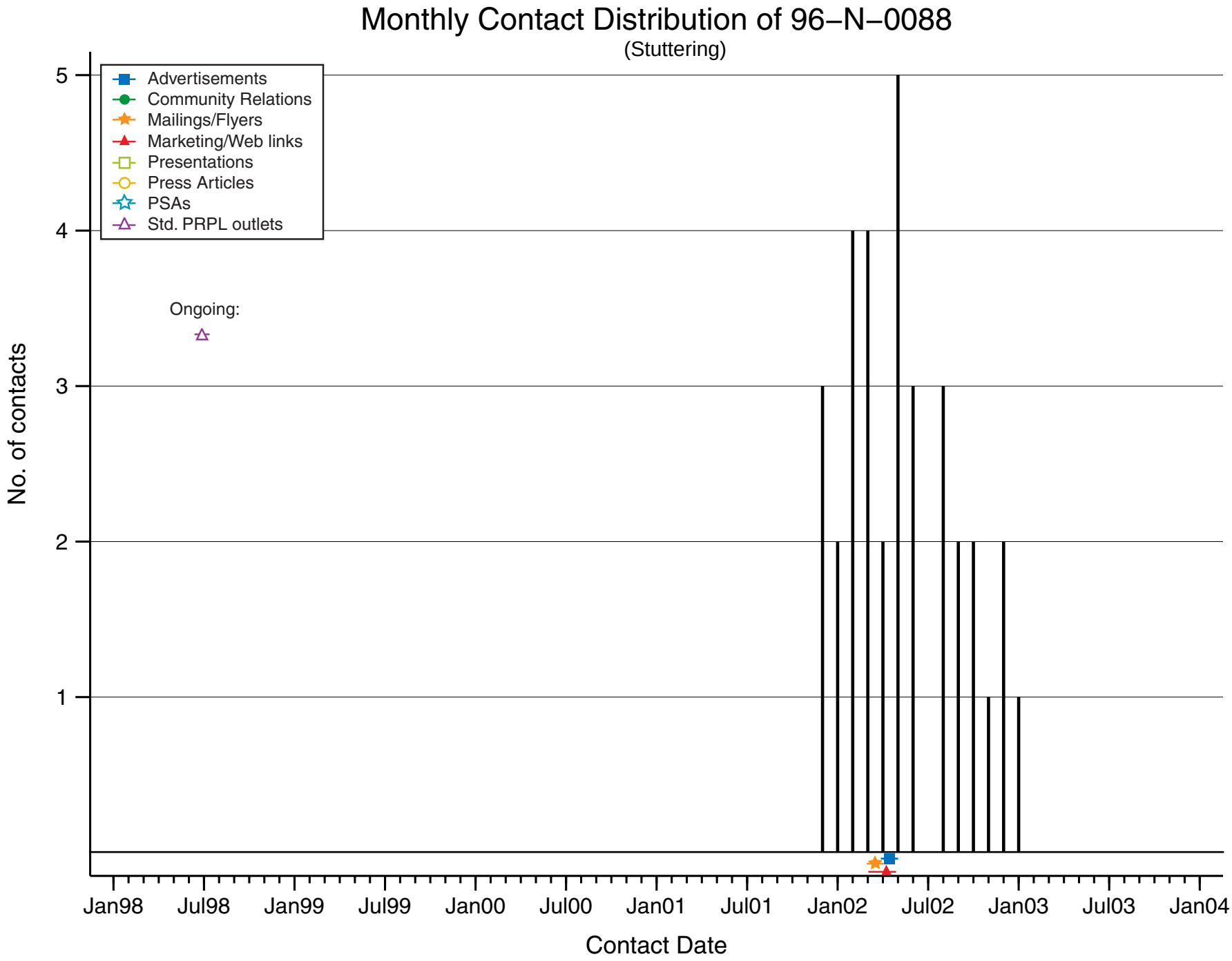
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 96–N–0088
(Stuttering)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of contacts
5
4
3
2
1
Jan98
Jul98
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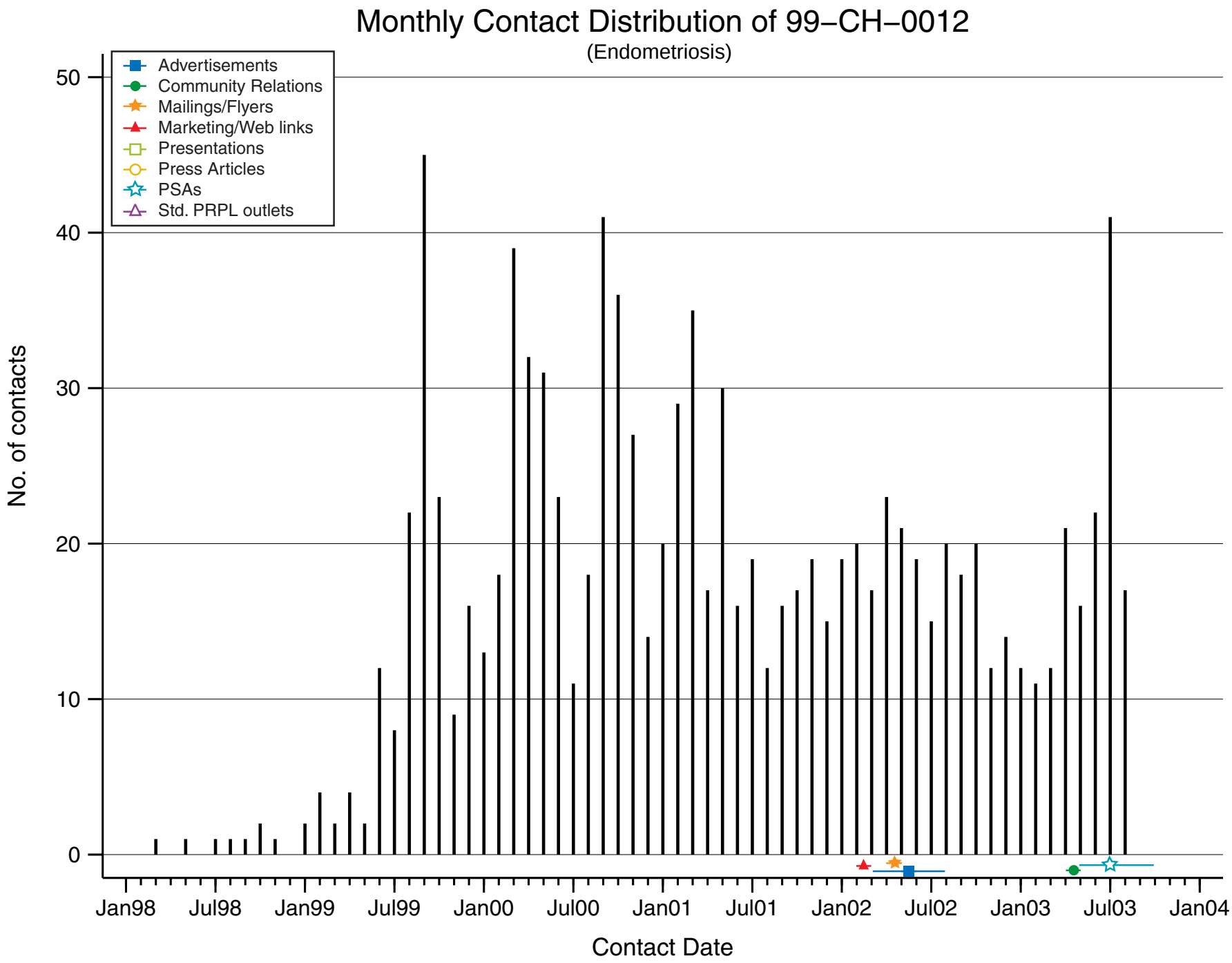
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date


Monthly Contact Distribution of 99–CH–0012
(Endometriosis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
No. of contacts
0
10
20
30
40
50
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
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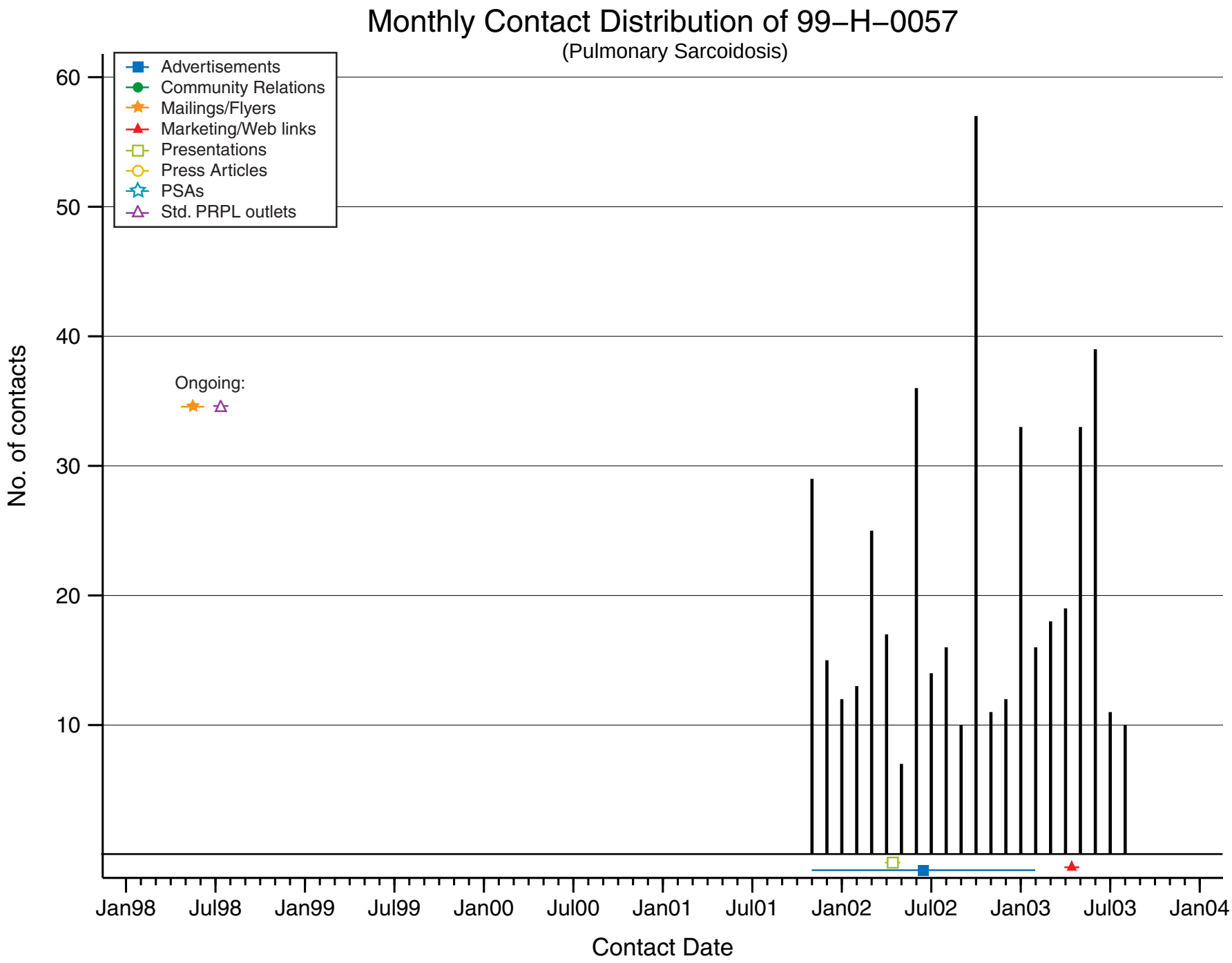
Jan04
Contact Date


Monthly Contact Distribution of 99–H–0057
(Pulmonary Sarcoidosis)
Advertisements
Community Relations
Mailings/Flyers
Marketing/Web links
Presentations
Press Articles
PSAs
Std. PRPL outlets
Ongoing:
No. of contacts
60
50
40
30
20
10
Jan98
Jul98
Jan99
Jul99
Jan00
Jul00
Jan01
Jul01
Jan02
Jul02
Jan03
Jul03
Jan04
Contact Date

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix I: CSSC: Referrals by Patient (Self-Reported) Source of Income

CSR Incorporated
Consulting Services & Research

Appendix I: CSSC: Referrals by Patient (Self-Reported) Source of Information

Protocol			CIS	NIH main office–PRPL	Internet	Physician	Healthcare provider	Word of mouth	Community outreach	Professional journal	Magazine	Newspaper	Newsletter	Radio	TV	Other	Missing	Total
Total		N	8,167	3,426	5,099	3,538	1,438	1,775	1,134	36	163	365	10	8	336	4,307	53	29,855
		%	(27.4)	(11.5)	(17.1)	(11.9)	(4.8)	(5.9)	(3.8)	(0.1)	(0.5)	(1.2)	(0.0)	(0.0)	(1.1)	(14.4)	(0.2)	
00-C-0044	Breast cancer, lung cancer, ovarian cancer	n	236	49	79	52	39	32	26	1	1	7			3	60		585
		%	(40.3)	(8.4)	(13.5)	(8.9)	(6.7)	(5.5)	(4.4)	(0.2)	(0.2)	(1.2)			(0.5)	(10.3)		
00-C-0069	Peritoneal cancer confined to the abdomen	n	74	36	76	28	10	14	10		2	4		1		64		319
		%	(23.2)	(11.3)	(23.8)	(8.8)	(3.1)	(4.4)	(3.1)		(0.6)	(1.3)		(0.3)		(20.1)		
00-C-0088	Primary lung cancer or cancers spread to the lung	n	238	90	135	98	29	53	28		4	5			9	114		803
		%	(29.6)	(11.2)	(16.8)	(12.2)	(3.6)	(6.6)	(3.5)		(0.5)	(0.6)			(1.1)	(14.2)		
00-C-0119	Breast cancer–metastatic	n	85	33	68	30	16	27	9		3	5			9	57		342
		%	(24.9)	(9.6)	(19.9)	(8.8)	(4.7)	(7.9)	(2.6)		(0.9)	(1.5)			(2.6)	(16.7)		
00-C-0121	Advanced solid tumor cancers	n	1,089	488	786	500	238	231	166	5	10	34	1		36	650	4	4,238
		%	(25.7)	(11.5)	(18.5)	(11.8)	(5.6)	(5.5)	(3.9)	(0.1)	(0.2)	(0.8)	(0.0)		(0.8)	(15.3)	(0.1)	
00-C-0128	Recurrent or metastatic squamous cell carcinoma of the head and neck	n	57	31	43	40	5	15	9			4			2	55		261
		%	(21.8)	(11.9)	(16.5)	(15.3)	(1.9)	(5.7)	(3.4)			(1.5)			(0.8)	(21.1)		
00-C-0133	Mantle cell lymphoma	n	3	12	3	5	1	3								4		31
		%	(9.7)	(38.7)	(9.7)	(16.1)	(3.2)	(9.7)								(12.9)		
00-C-0137	Prostate cancer–advanced	n	25	16	11	25	6	3	6		1	4			1	64		162
		%	(15.4)	(9.9)	(6.8)	(15.4)	(3.7)	(1.9)	(3.7)		(0.6)	(2.5)			(0.6)	(39.5)		
00-C-0149	Breast cancer	n	8	6	6	4		8	1		2	3				10		48
		%	(16.7)	(12.5)	(12.5)	(8.3)		(16.7)	(2.1)		(4.2)	(6.3)				(20.8)		
00-C-0154	Prostate cancer–confined to prostate	n	39	30	22	17		10	3	1	1	19	1			26		169
		%	(23.1)	(17.8)	(13.0)	(10.1)		(5.9)	(1.8)	(0.6)	(0.6)	(11.2)	(0.6)			(15.4)		
00-C-0173	Malignant gliomas and benign and malignant meningiomas	n		2	1	1	1									1		6
		%		(33.3)	(16.7)	(16.7)	(16.7)									(16.7)		
00-C-0206	Breast cancer–Stage IV	n	41	15	28	25	7	15	5		2	1			5	32		176
		%	(23.3)	(8.5)	(15.9)	(14.2)	(4.0)	(8.5)	(2.8)		(1.1)	(0.6)			(2.8)	(18.2)		
00-C-0218	Pancreatic cancer–advanced	n	32	19	8	8	6	9	4							14		100
		%	(32.0)	(19.0)	(8.0)	(8.0)	(6.0)	(9.0)	(4.0)							(14.0)		
00-C-0224	Cancer	n	290	115	188	138	82	61	39	1	7	11				184		1,116
		%	(26.0)	(10.3)	(16.8)	(12.4)	(7.3)	(5.5)	(3.5)	(0.1)	(0.6)	(1.0)				(16.5)		
01-C-0011	Malignant mesothelioma, ovarian cancer, pancreatic cancer, squamous cell ca head and neck and cervix	n	179	84	116	83	27	43	21		8	4			4	93		662
		%	(27.0)	(12.7)	(17.5)	(12.5)	(4.1)	(6.5)	(3.2)		(1.2)	(0.6)			(0.6)	(14.0)		
01-C-0021	B cell lymphoma	n	12	13	27	4	2	5	5	1	5	4			3	17		98
		%	(12.2)	(13.3)	(27.6)	(4.1)	(2.0)	(5.1)	(5.1)	(1.0)	(5.1)	(4.1)			(3.1)	(17.3)		

Protocol			CIS	NIH main office–PRPL	Internet	Physician	Healthcare provider	Word of mouth	Community outreach	Professional journal	Magazine	Newspaper	Newsletter	Radio	TV	Other	Missing	Total
01-C-0049	Cutaneous T cell lymphoma	n	6	5	18	14	3	4	2			1			1	15		69
		%	(8.7)	(7.2)	(26.1)	(20.3)	(4.3)	(5.8)	(2.9)			(1.4)			(1.4)	(21.7)		
01-C-0067	HIV-associated Kaposi's sarcoma	n		2	4	7	1	1	2							4		21
		%		(9.5)	(19.0)	(33.3)	(4.8)	(4.8)	(9.5)							(19.0)		
01-C-0082	Solid tumors unresposive to standard therapy	n	135	72	112	47	26	36	20		4	3			6	87		548
		%	(24.6)	(13.1)	(20.4)	(8.6)	(4.7)	(6.6)	(3.6)		(0.7)	(0.5)			(1.1)	(15.9)		
01-C-0104	Squamous cell carcinoma head and neck	n	30	15	24	29	2	9	4			4			2	28		147
		%	(20.4)	(10.2)	(16.3)	(19.7)	(1.4)	(6.1)	(2.7)			(2.7)			(1.4)	(19.0)		
01-C-0173	Breast cancer–inflammatory or locally advanced	n	2	2	15			3							1	5		28
		%	(7.1)	(7.1)	(53.6)			(10.7)							(3.6)	(17.9)		
01-C-0213	Lymphomas	n	19	7	24	7	8	10	4		2	4			3	20		108
		%	(17.6)	(6.5)	(22.2)	(6.5)	(7.4)	(9.3)	(3.7)		(1.9)	(3.7)			(2.8)	(18.5)		
01-C-0256	Solid malignancies unresectable or metastatic	n	385	213	388	185	100	116	64	4	16	25	1	2	29	339	2	1,869
		%	(20.6)	(11.4)	(20.8)	(9.9)	(5.4)	(6.2)	(3.4)	(0.2)	(0.9)	(1.3)	(0.1)	(0.1)	(1.6)	(18.1)	(0.1)	
02-C-0006	HIV–pediatric	n			2													2
		%			(100)													
02-C-0083	Adult solid tumors or lymphomas	n	152	81	176	84	40	33	28		1	13			11	170		789
		%	(19.3)	(10.3)	(22.3)	(10.6)	(5.1)	(4.2)	(3.5)		(0.1)	(1.6)			(1.4)	(21.5)		
02-C-0149	Prostate cancer	n	35	27	25	29	7	4	2		2	9	1		3	27	1	172
		%	(20.3)	(15.7)	(14.5)	(16.9)	(4.1)	(2.3)	(1.2)		(1.2)	(5.2)	(0.6)		(1.7)	(15.7)	(0.6)	
02-C-0190	Ovarian, pelvic or peritoneal cancer	n	20	10	40	17	6	12	9		3	2	1		4	25		149
		%	(13.4)	(6.7)	(26.8)	(11.4)	(4.0)	(8.1)	(6.0)		(2.0)	(1.3)	(0.7)		(2.7)	(16.8)		
02-C-0207	Prostate cancer	n	5	7	7	6		2	2			5				12		46
		%	(10.9)	(15.2)	(15.2)	(13.0)		(4.3)	(4.3)			(10.9)				(26.1)		
02-C-0215	Prostate cancer	n	6	6		6		2	1			4				9		34
		%	(17.6)	(17.6)		(17.6)		(5.9)	(2.9)			(11.8)				(26.5)		
02-C-0218	Prostate cancer	n	23	14	18	19	4	3				8	1		2	17		109
		%	(21.1)	(12.8)	(16.5)	(17.4)	(3.7)	(2.8)				(7.3)	(0.9)		(1.8)	(15.6)		
02-C-0229	Breast cancer, male breast cancer	n	38	16	50	10	6	23	4		4	2			11	36		200
		%	(19.0)	(8.0)	(25.0)	(5.0)	(3.0)	(11.5)	(2.0)		(2.0)	(1.0)			(5.5)	(18.0)		
03-C-0005	Breast cancer–stage II or III	n	1													3		4
		%	(25.0)													(75.0)		
03-C-0077	Lymphoma, leukemia	n	26	17	26	14	5	8	1			1		1		17		116
		%	(22.4)	(14.7)	(22.4)	(12.1)	(4.3)	(6.9)	(0.9)			(0.9)		(0.9)		(14.7)		
93-C-0133	Non-Hodgkin's lymphoma	n	11	17	23	12	5	8	5			2			5	13	3	104
		%	(10.6)	(16.3)	(22.1)	(11.5)	(4.8)	(7.7)	(4.8)			(1.9)			(4.8)	(12.5)	(2.9)	
94-C-0074	Lymphomatoid granulomatosis	n	1	3	4	2										1		11
		%	(9.1)	(27.3)	(36.4)	(18.2)										(9.1)		
94-C-0096	Adult solid tumors	n	56	47	27	40	13	16	10	1		6			5	32	4	257
		%	(21.8)	(18.3)	(10.5)	(15.6)	(5.1)	(6.2)	(3.9)	(0.4)		(2.3)			(1.9)	(12.5)	(1.6)	

Protocol			CIS	NIH main office–PRPL	Internet	Physician	Healthcare provider	Word of mouth	Community outreach	Professional journal	Magazine	Newspaper	Newsletter	Radio	TV	Other	Missing	Total
95-C-0054	T cell large granular lymphocytic leukemia	n	12	15	10	9	5	3	4							11		69
		%	(17.4)	(21.7)	(14.5)	(13.0)	(7.2)	(4.3)	(5.8)							(15.9)		
95-C-0119	Osteosarcoma	n	2		1	2										1	2	8
		%	(25.0)		(12.5)	(25.0)										(12.5)	(25.0)	
95-C-0154	Cervial cancer and other cancers carrying HPV	n	117	54	71	67	13	28	12		1	4			5	45	1	418
		%	(28.0)	(12.9)	(17.0)	(16.0)	(3.1)	(6.7)	(2.9)		(0.2)	(1.0)			(1.2)	(10.8)	(0.2)	
96-C-0004	Breast cancer	n	1	2		1	1									2		7
		%	(14.3)	(28.6)		(14.3)	(14.3)									(28.6)		
96-C-0011	HIV-associated Kaposi's sarcoma	n	103	31	58	39	30	27	15	2	2	6			3	39	2	357
		%	(28.9)	(8.7)	(16.2)	(10.9)	(8.4)	(7.6)	(4.2)	(0.6)	(0.6)	(1.7)			(0.8)	(10.9)	(0.6)	
96-C-0064	Ovarian cancer	n	130	82	73	66	20	42	36	5	2	9			16	78	6	565
		%	(23.0)	(14.5)	(12.9)	(11.7)	(3.5)	(7.4)	(6.4)	(0.9)	(0.4)	(1.6)			(2.8)	(13.8)	(1.1)	
97-C-0024	Lymphomas and rare leukemias	n	1	2	2	2	1									2		10
		%	(10.0)	(20.0)	(20.0)	(20.0)	(10.0)									(20.0)		
97-C-0040	AIDS-related lymphoma	n	1	2	2	4	1	2								3		15
		%	(6.7)	(13.3)	(13.3)	(26.7)	(6.7)	(13.3)								(20.0)		
97-C-0068	Recurrent colorectal cancer	n	1	3	1	3					1					2		11
		%	(9.1)	(27.3)	(9.1)	(27.3)					(9.1)					(18.2)		
97-C-0141	Adult solid tumors	n	329	169	162	135	68	70	33	1	2	13			7	175	3	1,167
		%	(28.2)	(14.5)	(13.9)	(11.6)	(5.8)	(6.0)	(2.8)	(0.1)	(0.2)	(1.1)			(0.6)	(15.0)	(0.3)	
97-C-0178	Chronic lymphocytic leukemia	n	14	13	17	3	4	2	3	1		2			1	4		64
		%	(21.9)	(20.3)	(26.6)	(4.7)	(6.3)	(3.1)	(4.7)	(1.6)		(3.1)			(1.6)	(6.3)		
98-C-0040	Metastatic melanoma, renal cell carcinoma	n	136	83	100	134	35	20	81	1	1	3			10	78	4	686
		%	(19.8)	(12.1)	(14.6)	(19.5)	(5.1)	(2.9)	(11.8)	(0.1)	(0.1)	(0.4)			(1.5)	(11.4)	(0.6)	
98-C-0074	Childhood brain tumors	n	4	4	2		1	1								1		13
		%	(30.8)	(30.8)	(15.4)		(7.7)	(7.7)								(7.7)		
98-C-0078	Breast, colon, lung, ovarian, stomach cancer	n	575	227	185	169	85	101	43	2		10			18	162	19	1,596
		%	(36.0)	(14.2)	(11.6)	(10.6)	(5.3)	(6.3)	(2.7)	(0.1)		(0.6)			(1.1)	(10.2)	(1.2)	
98-C-0118	Leukoplakia	n				4		1		1						1		7
		%				(57.1)		(14.3)		(14.3)						(14.3)		
98-C-0123	Breast cancer	n	9	1	6	18	1		6							5		46
		%	(19.6)	(2.2)	(13.0)	(39.1)	(2.2)		(13.0)							(10.9)		
98-C-0139	Renal cell carcinoma	n	128	118	162	132	48	32	59	2		4			5	146		836
		%	(15.3)	(14.1)	(19.4)	(15.8)	(5.7)	(3.8)	(7.1)	(0.2)		(0.5)			(0.6)	(17.5)		
99-C-0014	CD22+ lymphomas and leukemias	n	66	26	51	35	2	21	16	2	4	9			12	26	1	271
		%	(24.4)	(9.6)	(18.8)	(12.9)	(0.7)	(7.7)	(5.9)	(0.7)	(1.5)	(3.3)			(4.4)	(9.6)	(0.4)	
99-C-0025	Liver malignancies	n	354	133	236	155	62	79	46		5	12		2	18	163		1,265
		%	(28.0)	(10.5)	(18.7)	(12.3)	(4.9)	(6.2)	(3.6)		(0.4)	(0.9)		(0.2)	(1.4)	(12.9)		
99-C-0071	Breast, lung, pancreatic, stomach cancer	n	402	127	131	127	44	68	43	2		11			9	88		1,052
		%	(38.2)	(12.1)	(12.5)	(12.1)	(4.2)	(6.5)	(4.1)	(0.2)		(1.0)			(0.9)	(8.4)		

Protocol			CIS	NIH main office–PRPL	Internet	Physician	Healthcare provider	Word of mouth	Community outreach	Professional journal	Magazine	Newspaper	Newsletter	Radio	TV	Other	Missing	Total
99-C-0093	Colorectal cancer of the liver	n	51	12	22	13	6	10	2						1	33		150
		%	(34.0)	(8.0)	(14.7)	(8.7)	(4.0)	(6.7)	(1.3)						(0.7)	(22.0)		
99-C-0102	Colon or rectal cancer–Stage IV	n	419	110	218	166	59	59	30		2	9		1	13	154		1,240
		%	(33.8)	(8.9)	(17.6)	(13.4)	(4.8)	(4.8)	(2.4)		(0.2)	(0.7)		(0.1)	(1.0)	(12.4)		
99-C-0117	Cancer of the colon, rectum, small bowel, or appendix	n	567	142	235	210	70	98	39		3	6		1	10	203	1	1,585
		%	(35.8)	(9.0)	(14.8)	(13.2)	(4.4)	(6.2)	(2.5)		(0.2)	(0.4)		(0.1)	(0.6)	(12.8)	(0.1)	
99-C-0121	Metastatic breast or ovarian cancer	n	209	62	92	64	35	46	26	1	1	4			5	65		610
		%	(34.3)	(10.2)	(15.1)	(10.5)	(5.7)	(7.5)	(4.3)	(0.2)	(0.2)	(0.7)			(0.8)	(10.7)		
99-C-0123	Liver cancer	n	196	64	124	59	27	39	18		1	3			7	85		623
		%	(31.5)	(10.3)	(19.9)	(9.5)	(4.3)	(6.3)	(2.9)		(0.2)	(0.5)			(1.1)	(13.6)		
99-C-0125	Osteosarcoma	n	2	1	1		1	1	1									7
		%	(28.6)	(14.3)	(14.3)		(14.3)	(14.3)	(14.3)									
99-C-0127	Leukemias and lymphomas	n	14	13	26	10	4	5	4		4	4	1			17		102
		%	(13.7)	(12.7)	(25.5)	(9.8)	(3.9)	(4.9)	(3.9)		(3.9)	(3.9)	(1.0)			(16.7)		
99-C-0129	Cancer of the esophagus or lung or pleural mesothelioma	n	501	153	217	122	62	88	44		6	37			20	153		1,403
		%	(35.7)	(10.9)	(15.5)	(8.7)	(4.4)	(6.3)	(3.1)		(0.4)	(2.6)			(1.4)	(10.9)		
99-C-0137	Adenocarcinoma of the ovary	n	102	41	79	41	16	20	21		38	8	2		3	50		421
		%	(24.2)	(9.7)	(18.8)	(9.7)	(3.8)	(4.8)	(5.0)		(9.0)	(1.9)	(0.5)		(0.7)	(11.9)		
99-C-0138	Adenocarcinoma of the breast or ovary	n	184	60	110	68	25	45	24		4	7			9	91		627
		%	(29.3)	(9.6)	(17.5)	(10.8)	(4.0)	(7.2)	(3.8)		(0.6)	(1.1)			(1.4)	(14.5)		
99-C-0143	Lymphomas, leukemias, multiple myeloma	n	178	76	125	94	17	48	38	2	8	10	1		9	119		725
		%	(24.6)	(10.5)	(17.2)	(13.0)	(2.3)	(6.6)	(5.2)	(0.3)	(1.1)	(1.4)	(0.1)		(1.2)	(16.4)		

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix J: CSSC: Patient Recruitment Strategies by Protocol

CSR incorporated
Consulting Services & Research

Appendix J: CSSC: Patient Recruitment Strategies by Protocol

Protocol		Mailing/flyers	Advertisements	Presentation	Press articles	PSA	Marketing web links	Community relations	Total strategies	Total strategy types
00-C-0044	Breast cancer, lung cancer, ovarian cancer	2	0	0	0	0	0	0	2	1
00-C-0069	Peritoneal cancer confined to the abdomen	5	0	0	0	0	0	0	5	1
00-C-0088	Primary lung cancer or cancers spread to the lung	0	1	1	0	1	0	1	4	4
00-C-0119	Breast cancer–metastatic	5	0	0	1	0	0	0	6	2
00-C-0121	Advanced solid tumor cancers	2	0	0	0	0	0	0	2	1
00-C-0128	Recurrent or metastatic squamous cell carcinoma of the head and neck	3	0	0	0	0	0	0	3	1
00-C-0133	Mantle cell lymphoma	5	0	1	1	0	0	1	8	4
00-C-0137	Prostate cancer–advanced	4	0	0	0	0	1	0	5	2
00-C-0149	Breast cancer	4	0	1	0	0	0	0	5	2
00-C-0154	Prostate cancer–confined to prostate	2	0	0	0	0	1	0	3	2
00-C-0173	Malignant gliomas and benign and malignant meningiomas	2	0	0	1	0	0	0	3	2
00-C-0206	Breast cancer–Stage IV	4	0	0	0	0	0	0	4	1
00-C-0218	Pancreatic cancer–advanced	2	0	0	0	0	0	0	2	1
00-C-0224	Cancer	2	0	0	0	0	0	0	2	1
01-C-0011	Malignant mesothelioma, ovarian cancer, pancreatic cancer, squamous cell ca head and neck and cervix	2	0	0	1	0	0	0	3	2
01-C-0021	B cell lymphoma	1	0	0	1	0	0	0	2	2
01-C-0049	Cutaneous T cell lymphoma	4	0	0	0	0	0	1	5	2
01-C-0067	HIV-associated Kaposi's sarcoma	2	0	0	0	0	0	1	3	2
01-C-0082	Solid tumors unresposive to standard therapy	1	0	0	0	0	0	0	1	1
01-C-0104	Squamous cell carcinoma head and neck	3	0	0	0	0	0	0	3	1
01-C-0173	Breast cancer-inflammatory or locally advanced	2	0	0	0	0	0	0	2	1
01-C-0213	Lymphomas	0	0	0	0	0	0	0	0	0
01-C-0256	Solid malignancies, unresectable or metastatic	1	0	0	0	0	0	0	1	1
02-C-0006	HIV-pediatric	1	0	0	0	0	0	1	2	2
02-C-0083	Adult solid tumors or lymphomas	1	0	0	0	0	0	0	1	1
02-C-0149	Prostate cancer	1	0	0	0	0	0	0	1	1
02-C-0190	Ovarian, pelvic, or peritoneal cancer	1	0	0	2	0	0	0	3	2
02-C-0207	Prostate cancer	1	0	0	0	0	1	0	2	2
02-C-0215	Prostate cancer	1	0	0	0	0	1	0	2	2
02-C-0218	Prostate cancer	1	0	0	0	0	0	0	1	1
02-C-0229	Breast cancer, male breast cancer	0	0	0	0	0	0	0	0	0
03-C-0005	Breast cancer–stage II or III	0	0	0	0	0	0	0	0	0
03-C-0077	Lymphoma, leukemia	0	0	0	0	0	0	0	0	0
93-C-0133	Non-Hodgkin's lymphoma	5	0	1	1	0	0	1	8	4
94-C-0074	Lymphomatoid granulomatosis	5	0	1	1	0	0	1	8	4

Protocol		Mailing/flyers	Advertisements	Presentation	Press articles	PSA	Marketing web links	Community relations	Total strategies	Total strategy types
94-C-0096	Adult solid tumors	1	0	0	0	0	0	0	1	1
95-C-0054	T cell large granular lymphocytic leukemia	1	0	0	0	0	0	0	1	1
95-C-0119	Osteosarcoma	1	0	0	0	2	0	0	3	2
95-C-0154	Cervial cancer and other cancers carrying HPV	2	0	0	1	0	0	0	3	2
96-C-0004	Breast cancer	1	0	0	0	0	0	0	1	1
96-C-0011	HIV-associated Kaposi's sarcoma	0	0	0	1	0	0	0	1	1
96-C-0064	Ovarian cancer	1	0	0	0	0	0	0	1	1
97-C-0024	Lymphomas and rare leukemias	2	0	0	0	0	0	0	2	1
97-C-0040	AIDS-related lymphoma	1	0	0	0	0	0	0	1	1
97-C-0068	Recurrent colorectal cancer	1	0	0	0	0	0	0	1	1
97-C-0141	Adult solid tumors	1	0	0	0	0	0	0	1	1
97-C-0178	Chronic lymphocytic leukemia	3	0	0	0	0	0	0	3	1
98-C-0040	Metastatic melanoma, renal cell carcinoma	0	0	0	0	0	1	0	1	1
98-C-0074	Childhood brain tumors	4	0	0	1	0	0	0	5	2
98-C-0078	Breast, colon, lung, ovarian, stomach cancer	1	0	1	1	1	1	1	6	6
98-C-0118	Leukoplakia	4	0	1	1	2	0	1	9	5
98-C-0123	Breast cancer	0	0	0	0	0	0	0	0	0
98-C-0139	Renal cell carcinoma	1	0	0	0	0	0	0	1	1
99-C-0014	CD22+ lymphomas and leukemias	1	0	0	0	0	0	0	1	1
99-C-0025	Liver malignancies	3	0	0	0	0	0	0	3	1
99-C-0071	Breast, lung, pancreatic, stomach cancer	3	0	1	1	1	0	1	7	5
99-C-0093	Colorectal cancer of the liver	2	0	1	0	0	0	0	3	2
99-C-0102	Colon or rectal cancer–Stage IV	4	0	0	0	0	0	0	4	1
99-C-0117	Cancer of the colon, rectum, small bowel, or appendix	1	0	0	0	0	0	0	1	1
99-C-0121	Metastatic breast or ovarian cancer	5	0	2	1	0	0	1	9	4
99-C-0123	Liver cancer	5	0	0	0	0	0	0	5	1
99-C-0125	Osteosarcoma	0	0	0	0	2	0	1	3	2
99-C-0127	Leukemias and lymphomas	1	0	0	0	0	0	0	1	1
99-C-0129	Cancer of the esophagus or lung or pleural mesothelioma	1	1	1	1	1	0	0	5	5
99-C-0137	Adenocarcinoma of the ovary	2	0	0	1	0	0	0	3	2
99-C-0138	Adenocarcinoma of the breast or ovary	1	0	0	0	0	0	0	1	1
99-C-0143	Lymphomas, leukemias, multiple myeloma	2	0	1	0	0	0	0	3	2

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix K: PRPL: Referrals by Patient Self-Reported Source of Information

CSR Incorporated
Consulting Services & Research

Appendix K: PRPL: Referrals by Patient Self-Reported Source of Information

Protocol			Book	Community outreach	Direct mail/letter	Healthcare provider	Internet	Magazine	Newsletter	Newspaper	Physician	Professional journal	Radio	TV	Word of mouth	Missing	Total
00-CH-0134	Childhood obesity	N	1	9	0	4	19	36	10	48	21	0	2	2	37	2	191
		%	(0.52)	(4.71)	(0.00)	(2.09)	(9.95)	(18.85)	(5.24)	(25.13)	(10.99)	(0.00)	(1.05)	(1.05)	(19.37)	(1.05)	(10.42)
00-CH-0141	Alkaptonuria	N	0	2	0	0	13	0	0	0	0	0	0	0	2	0	17
		%	(0.00)	(11.76)	(0.00)	(0.00)	(76.47)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(11.76)	(0.00)	(0.93)
00-CH-0219	Turner syndrome	N	0	3	1	0	13	0	3	4	0	0	0	0	3	1	28
		%	(0.00)	(10.71)	(3.57)	(0.00)	(46.43)	(0.00)	(10.71)	(14.29)	(0.00)	(0.00)	(0.00)	(0.00)	(10.71)	(3.57)	(1.53)
00-D-0037	TMJ	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		%	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
00-D-0066	Fibromyalgia	N	0	8	0	2	32	2	2	34	5	1	0	0	39	0	125
		%	(0.00)	(6.40)	(0.00)	(1.60)	(25.60)	(1.60)	(1.60)	(27.20)	(4.00)	(0.80)	(0.00)	(0.00)	(31.20)	(0.00)	(6.82)
00-DK-0042	FSGS	N	0	0	0	0	3	0	0	0	0	0	0	0	0	0	3
		%	(0.00)	(0.00)	(0.00)	(0.00)	(100.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.16)
00-DK-0166	Beta thalassemia	N	0	2	1	0	1	1	1	0	0	0	0	0	2	0	8
		%	(0.00)	(25.00)	(12.50)	(0.00)	(12.50)	(12.50)	(12.50)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(25.00)	(0.00)	(0.44)
01-CC-0135	Swallowing difficulty	N	1	0	1	1	6	1	4	0	0	0	0	0	6	0	20
		%	(5.00)	(0.00)	(5.00)	(5.00)	(30.00)	(5.00)	(20.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(30.00)	(0.00)	(1.09)
01-CH-0086	INCL	N	0	0	0	0	5	0	0	0	0	1	0	0	0	0	6
		%	(0.00)	(0.00)	(0.00)	(0.00)	(83.33)	(0.00)	(0.00)	(0.00)	(0.00)	(16.67)	(0.00)	(0.00)	(0.00)	(0.00)	(0.33)
01-D-0076	Sciatic back pain	N	2	4	0	0	21	1	3	116	1	0	0	0	8	0	156
		%	(1.28)	(2.56)	(0.00)	(0.00)	(13.46)	(0.64)	(1.92)	(74.36)	(0.64)	(0.00)	(0.00)	(0.00)	(5.13)	(0.00)	(8.51)
01-EI-0214	Macular edema	N	0	0	0	0	4	0	0	0	2	0	0	0	0	0	6
		%	(0.00)	(0.00)	(0.00)	(0.00)	(66.67)	(0.00)	(0.00)	(0.00)	(33.33)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.33)
01-H-0119	EPC	N	3	5	0	1	12	0	13	6	2	0	2	0	20	0	64
		%	(4.69)	(7.81)	(0.00)	(1.56)	(18.75)	(0.00)	(20.31)	(9.38)	(3.13)	(0.00)	(3.13)	(0.00)	(31.25)	(0.00)	(3.49)
01-H-0162	Stem cell transplant	N	0	2	0	0	11	1	0	9	0	0	0	0	16	0	39
		%	(0.00)	(5.13)	(0.00)	(0.00)	(28.21)	(2.56)	(0.00)	(23.08)	(0.00)	(0.00)	(0.00)	(0.00)	(41.03)	(0.00)	(2.13)
01-N-0147	Dystonia	N	0	0	0	0	10	1	1	1	0	0	0	0	3	0	16
		%	(0.00)	(0.00)	(0.00)	(0.00)	(62.50)	(6.25)	(6.25)	(6.25)	(0.00)	(0.00)	(0.00)	(0.00)	(18.75)	(0.00)	(0.87)
02-AR-0267	Lupus	n	0	0	0	0	1	0	0	0	1	0	0	1	4	0	7
		%	(0.00)	(0.00)	(0.00)	(0.00)	(14.29)	(0.00)	(0.00)	(0.00)	(14.29)	(0.00)	(0.00)	(14.29)	(57.14)	(0.00)	(0.38)
02-AR-0272	Lupus	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
		%	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(100.00)	(0.00)	(0.05)
02-CH-0287	Fibroids	N	1	4	0	0	9	1	2	18	2	0	0	1	9	0	47
		%	(2.13)	(8.51)	(0.00)	(0.00)	(19.15)	(2.13)	(4.26)	(38.30)	(4.26)	(0.00)	(0.00)	(2.13)	(19.15)	(0.00)	(2.56)
02-I-0316	Small Pox	N	0	19	0	0	9	0	3	67	0	0	23	1	20	1	143
		%	(0.00)	(13.29)	(0.00)	(0.00)	(6.29)	(0.00)	(2.10)	(46.85)	(0.00)	(0.00)	(16.08)	(0.70)	(13.99)	(0.70)	(7.80)
03-AR-0130	Ankylosing spondylitis	N	0	0	0	0	4	0	0	1	0	0	0	0	1	0	6
		%	(0.00)	(0.00)	(0.00)	(0.00)	(66.67)	(0.00)	(0.00)	(16.67)	(0.00)	(0.00)	(0.00)	(0.00)	(16.67)	(0.00)	(0.33)
03-AR-0131	Ankylosing spondylitis	N	0	1	0	0	10	0	0	0	0	0	0	0	1	0	12
		%	(0.00)	(8.33)	(0.00)	(0.00)	(83.33)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(8.33)	(0.00)	(0.65)
03-AR-0133	RA	N	0	0	0	0	0	0	1	5	1	0	0	0	2	0	9
		%	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(11.11)	(55.56)	(11.11)	(0.00)	(0.00)	(0.00)	(22.22)	(0.00)	(0.49)

Protocol			Book	Community outreach	Direct mail/letter	Healthcare provider	Internet	Magazine	Newsletter	Newspaper	Physician	Professional journal	Radio	TV	Word of mouth	Missing	Total
03-DK-0170	Sickle-cell anemia	N	0	2	2	0	0	0	0	0	0	0	0	0	0	0	4
		%	(0.00)	(50.00)	(50.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.22)
90-CC-0168	Anterior Cruciate Ligament (ACL)	N	0	4	0	0	0	0	7	0	0	0	0	0	6	0	17
		%	(0.00)	(23.53)	(0.00)	(0.00)	(0.00)	(0.00)	(41.18)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(35.29)	(0.00)	(0.93)
90-CC-0168B	Stroke Balance Study	N	0	1	0	0	1	0	1	24	1	0	0	0	2	0	30
		%	(0.00)	(3.33)	(0.00)	(0.00)	(3.33)	(0.00)	(3.33)	(80.00)	(3.33)	(0.00)	(0.00)	(0.00)	(6.67)	(0.00)	(1.64)
91-DK-0214	Hepatitis–All	N	2	4	0	1	29	0	2	3	6	0	0	0	12	1	60
		%	(3.33)	(6.67)	(0.00)	(1.67)	(48.33)	(0.00)	(3.33)	(5.00)	(10.00)	(0.00)	(0.00)	(0.00)	(20.00)	(1.67)	(3.27)
91-N-0225	Gaucher	N	0	0	0	0	4	0	0	0	0	0	0	0	0	0	4
		%	(0.00)	(0.00)	(0.00)	(0.00)	(100.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.22)
93-CH-0054	Turner syndrome	N	0	0	0	0	1	0	0	0	0	0	0	0	1	0	2
		%	(0.00)	(0.00)	(0.00)	(0.00)	(50.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(50.00)	(0.00)	(0.11)
93-N-0202	Dystonia	N	0	2	0	1	18	1	1	1	5	0	0	0	9	1	39
		%	(0.00)	(5.13)	(0.00)	(2.56)	(46.15)	(2.56)	(2.56)	(2.56)	(12.82)	(0.00)	(0.00)	(0.00)	(23.08)	(2.56)	(2.13)
94-DK-0127	FSGS	N	0	0	0	0	24	0	0	1	1	0	0	1	4	0	31
		%	(0.00)	(0.00)	(0.00)	(0.00)	(77.42)	(0.00)	(0.00)	(3.23)	(3.23)	(0.00)	(0.00)	(3.23)	(12.90)	(0.00)	(1.69)
94-DK-0133	FSGS	N	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
		%	(0.00)	(0.00)	(0.00)	(0.00)	(100.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.05)
95-N-0121	Fabry's	N	0	0	0	0	10	0	1	0	0	0	0	0	7	0	18
		%	(0.00)	(0.00)	(0.00)	(0.00)	(55.56)	(0.00)	(5.56)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(38.89)	(0.00)	(0.98)
96-N-0088	Stuttering	N	0	0	0	0	3	4	0	1	2	0	0	0	3	0	13
		%	(0.00)	(0.00)	(0.00)	(0.00)	(23.08)	(30.77)	(0.00)	(7.69)	(15.38)	(0.00)	(0.00)	(0.00)	(23.08)	(0.00)	(0.71)
99-CH-0012	Endometriosis	N	5	20	9	1	286	5	13	57	10	0	19	9	96	3	533
		%	(0.94)	(3.75)	(1.69)	(0.19)	(53.66)	(0.94)	(2.44)	(10.69)	(1.88)	(0.00)	(3.56)	(1.69)	(18.01)	(0.56)	(29.08)
99-H-0057	Pulmonary sarcoidosis	N	0	8	1	1	51	1	2	27	7	0	12	24	43	0	177
		%	(0.00)	(4.52)	(0.56)	(0.56)	(28.81)	(0.56)	(1.13)	(15.25)	(3.95)	(0.00)	(6.78)	(13.56)	(24.29)	(0.00)	(9.66)
Total		N	15	100	15	12	611	55	70	423	67	2	58	39	357	9	1,833

Evaluation of Patient Recruitment Strategies—Phase I Feasibility Study

Appendix L: PRPL: Patient Recruitment Strategies by Protocol

CSR Incorporated
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Appendix L. PRPL: Patient Recruitment Strategies by Protocol

Protocol		Advertisements	Community relations	Mailings/Flyers	Marketing/Web links	Presentations	Press articles	PSA	Standard PRPL outlets	Total	Total strategy types
00-CH-0134	Childhood Obesity	2	1	2	0	0	0	1	0	6	4
00-CH-0141	Alkaptonuria	0	0	3	1	1	1	1	0	7	5
00-CH-0219	Turner's Syndrome	0	0	1	0	0	0	2	0	3	2
00-D-0037	TMJ	2	0	1	0	0	0	1	0	4	3
00-D-0066	Fibromyalgia	1	0	0	1	0	0	0	0	2	2
00-DK-0042	FSGS	1	0	1	1	0	0	1	0	4	4
00-DK-0166	Beta Thalassemia	0	0	2	1	0	0	2	0	5	3
01-CC-0135	Swallowing Difficulty	0	0	2	0	0	0	0	0	2	1
01-CH-0086	INCL	1	0	1	1	0	0	1	1	5	5
01-D-0076	Sciatic Back Pain	4	0	0	0	0	0	0	1	5	2
01-EI-0214	Macular Edema	0	0	0	0	0	0	0	0	0	0
01-H-0119	EPC	0	1	1	0	0	0	0	0	2	2
01-H-0162	Stem Cell Transplant	0	0	1	2	1	0	0	1	5	4
01-N-0147	Dystonia	2	1	0	0	1	0	1	0	5	4
02-AR-0267	Lupus	1	1	2	1	0	0	2	0	7	5
02-AR-0272	Lupus	1	1	2	1	0	0	2	0	7	5
02-CH-0287	Fibroids	1	0	1	0	0	0	1	0	3	3
02-I-0316	Small Pox	1	0	0	0	0	0	0	0	1	1
03-AR-0130	Ankylosing Spondylitis	0	1	1	0	0	0	4	0	6	3
03-AR-0131	Ankylosing Spondylitis	0	1	0	0	0	0	4	0	5	2
03-AR-0133	RA	0	0	1	0	0	0	0	1	2	2
03-DK-0170	Sickle Cell Anemia	0	0	1	1	0	0	1	0	3	3
90-CC-0168	Anterior Cruciate Ligament (ACL)	0	0	4	0	0	0	1	0	5	2
90-CC-0168B	Stroke Balance Study	1	0	0	0	0	0	0	0	1	1
91-DK-0214	Hepatitis-All	0	0	1	0	1	0	1	1	4	4
91-N-0225	Gaucher	1	0	0	1	0	0	0	1	3	3
93-CH-0054	Turner's Syndrome	0	0	1	0	0	0	2	0	3	2
93-N-0202	Dystonia	2	1	0	0	1	0	1	0	5	4
94-DK-0127	FSGS	1	0	1	1	0	0	1	0	4	4
94-DK-0133	FSGS	1	0	1	1	0	0	1	0	4	4
95-N-0121	Fabry's	1	0	0	2	0	0	1	1	5	4
96-N-0088	Stuttering	1	0	1	1	0	0	0	1	4	4
99-CH-0012	Endometriosis	1	1	1	1	0	0	1	0	5	5
99-H-0057	Pulmonary Sarcoidosis	1	0	1	1	1	0	0	1	5	5
Total		27	9	34	18	6	1	33	9	137	