SURVEY OF ACCUTANE USE IN WOMEN

Conducted by the Slone Epidemiology Unit,
Boston University School of Public Health,

Allen A. Mitchell, M.D., Principal Investigator
Carla Van Bennekom, R.N., M.P.H., Epidemiologist

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1371 Beacon Street
Brookline, MA 02146

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I. Historical Background

In 1982, isotretinoin (Accutane, Roche Laboratories) was first marketed in the U.S. for the treatment of severe recalcitrant cystic acne. Studies in animals had suggested a strong possibility that the drug would be teratogenic in humans, and from the outset it was contraindicated in women who were or might become pregnant during therapy or in the month following therapy. It was soon demonstrated that Accutane was indeed a human teratogen, affecting approximately 25-30% of exposed fetuses with craniofacial, heart, and central nervous system defects. Despite prominent warnings to physicians in direct mailings, advertisements, and the package insert, reports of pregnancies in exposed women continued to accumulate.

The problem of exposed pregnancies was reviewed in the spring of 1988 by the FDA Dermatologic Drugs Advisory Committee. While there was little question about the drug's teratogenicity, dermatologists and others argued that Accutane's unique efficacy and relatively short treatment course warranted its continued availability. In response to the problem, Roche proposed a unique and aggressive effort (the "Pregnancy Prevention Program", or PPP) designed to reduce the risk of pregnancy among women taking Accutane. The committee recommended that the major components of the PPP be implemented, and Roche launched the PPP in the fall of 1988.

The PPP was targeted to both prescribers and consumers. Every dermatologist in the U.S. and all nondermatologists identified as Accutane prescribers were sent the PPP materials. Among other items, these included guidelines for physicians, a patient qualification check list, patient brochure, true-false test, contraceptive information, information on the contraception referral program, and a consent form. In mid-1989, Roche replaced the traditional medication bottles with a 10-capsule blister pack that included information specifically directed at women—warnings about use in pregnancy, an "avoid pregnancy" icon behind each capsule, and drawings of malformations associated with Accutane.

While the PPP was widely recognized as innovative, unique, and aggressive, it was also recognized that there was no opportunity to pilot-test it, so that its efficacy could not be predicted. It was therefore necessary to assess compliance with the PPP among physicians and their female patients, and in particular to assess the rates of pregnancy during and immediately after treatment. The Slone Epidemiology Unit (SEU) of Boston University School of Public Health was asked to design and conduct that assessment (the "Accutane Survey"), which began in January, 1989 and is the subject of this report.

II. Survey Sponsorship

The Accutane Survey is supported exclusively by a contract with Hoffmann-LaRoche, Inc.

III. Survey Independence

The SEU has from the beginning and continues to be responsible for all aspects of the Survey, including the design, conduct, analysis and interpretation. Guidance to the Survey is provided by an SEU-appointed Accutane Advisory Committee (Appendix 1), which has met 16 times since the fall of 1988. While the advice given by the Committee is not binding on the Survey staff, nor is the Committee responsible for the Survey, their involvement has provided critically important guidance and insight that have contributed greatly to the Survey.

Summaries of the Survey's progress, problems, findings, and recommendations are forwarded to Roche each quarter; these reports are then included, unedited by Roche, in the manufacturer's quarterly reports to FDA. The most recent of the 46 quarterly reports, which covers the second quarter of 2000, is attached as Appendix 2.

IV. Objectives

The overall objective of the Survey is to assess compliance with the PPP among female users of Accutane. Specific objectives include determination of

- -awareness of the teratogenic risks of Accutane
- -history of prior acne therapy
- -rates of pregnancy during therapy and in the month following therapy
- -pregnancy outcomes
- -risk factors for the occurrence of pregnancy

For reasons detailed below, the objectives also include attempts to assess the representativeness of the Survey population.

V. Limitations

At the outset, we identified four limitations that faced the Survey. First, since the Survey was implemented contemporaneously with the PPP, baseline data on pregnancy prevention prior to the PPP would not be available, so a pre- and post-PPP comparison would not be possible. Second, like the PPP, implementation of the Survey was mandated without the benefit of pilot studies to test the effectiveness of its various components. Third, the Survey itself may be viewed as a form of intervention, making it difficult to separate the Survey's potential effect on compliance above and beyond the PPP.

Finally, as is the case for the PPP, participation in the Survey, is voluntary. We recognized, therefore, that women who participate in the Survey may not be representative of the larger population of women who take the drug. Responding to this concern has been an ongoing focus of the Survey.

VI. Survey Design

A. Background

Two considerations, both related to potential biases, influenced the design of the Survey. First, although it is impossible to assure representativeness in samples that are less than complete, an overall concern in designing the Survey was to maximize representativeness by maximizing Survey enrollment. Toward that end, the Survey used both traditional enrollment methods and a novel approach developed specifically for this effort (see below).

Second, we recognized that frequent follow-up of enrolled women would tend to minimize memory loss and biased recall, but multiple contacts could themselves serve to reinforce the PPP, blurring the Survey's ability to assess the PPP. On the other hand, avoiding follow-up contacts during the course of Accutane treatment would represent less of an intervention on the part of the Survey, but could result in biased recall of compliance-related information.

Given that the Survey is a research activity, approval was obtained from the Boston University Institutional Review Board, and written consent is obtained from every participant. No identifying information on Survey participants is provided to Roche, FDA, or others without specific written consent.

B. Subjects and Timing

Survey subjects are women of childbearing age (12 to 59 years) who are treated with Accutane. To identify compliance with the PPP, including the occurrence of pregnancy, the Survey covers the treatment period (typically, 5 months) and the subsequent 6 months (long enough to allow identification of pregnancies occurring as late as the first month after discontinuation of Accutane). A flow diagram describing the Survey is included; see Figure 1.

C. Enrollment

To maximize the proportion of women who participate in the Survey, we provide multiple opportunities for enrollment. One is a Survey Enrollment/Consent Form that is included among the PPP materials supplied to physicians. A toll-free telephone number provides another way to enroll in the Survey.

Recognizing at the outset that physicians might be too busy or unwilling to enroll or encourage their patients to enroll in the Survey, we developed a unique enrollment opportunity intended to enhance participation. Using a "direct-to-consumer" approach, each Accutane medication package includes an Enrollment/Consent Form; fashioned as much as possible to mimic a consumer rebate form, this approach does not involve the patient's physician. Indeed, the medication-package enrollment form was designed to encourage enrollment among women who were not enrolled through their physicians and

who might be at high risk for noncompliance. In all three enrollment approaches, patients are informed that they will receive a $10 payment for their participation.

D. Follow-Up

To minimize memory loss and biased recall, we collect information related to physician and patient compliance at the start of therapy as well as during treatment. However, as noted above, frequent inquiries might transform the observational intent of the Survey into a form of intervention. Therefore, women who enroll are assigned, at random, to be followed by one of two approaches. One involves multiple contacts both during and after therapy (see Figure 1); this provides information on physicians' and patients' compliance that is unaffected by any subsequent adverse events (e.g., pregnancy). Since these multiple contacts might themselves enhance compliance with the PPP, the remaining participants are sent a questionnaire after they complete their course of Accutane; the questionnaire obtains information on contraceptive practices during treatment and identifies the occurrence of pregnancy.

Enrollment forms are screened on arrival to the SEU to exclude those that are apparently fraudulent, men, and previously enrolled women. Eligible women are then randomly assigned so that 5000 women each year are to be followed during and after treatment (the "DAT" arm), and the remaining women are assigned to be followed by postal questionnaires only after treatment (the "AT" arm). Within two days of receipt of their enrollment, women are sent a check for $10 along with a letter indicating when to expect contact.

The DAT arm (n=5000 women per year) provides three contacts, both during and after treatment: At the start of therapy (within one month of enrollment), when we inquire about the patients' understanding of the hazards of Accutane and compliance with the PPP (including contraceptive practices); in the middle of therapy (between two and four months after starting Accutane), when we inquire about continued understanding of the drug's hazards and compliance; and six months after completion of Accutane treatment, when we ask about the occurrence of pregnancy. Women who cannot be reached within specified intervals are transferred to be followed in the AT cohort.

Women in the AT arm (the remaining enrollees) are sent a brief "tracking" questionnaire six months after starting Accutane to determine the date on which they completed or expect to complete treatment; the women are then sent a questionnaire six months after treatment stopped; this questionnaire is similar to the final interview in the DAT arm. Nonrespondents are contacted by air courier and, if necessary, by telephone.

Women who were pregnant at any time during treatment or in the month following treatment are interviewed by telephone regarding the pregnancy and its outcome, and permission is sought to obtain relevant medical records.

The design of the Survey changed in January, 1995. At that time, follow-up contacts in the DAT arm, previously conducted by telephone, were changed to postal questionnaires.

Thus, except for nonrespondents, both arms of the Survey use postal questionnaires as the primary method of contact.

VII. Survey Results

Findings from the Survey are presented in Tables 1-25 and Figure 2. Data on variables may come from the AT arm, the DAT arm, or both; also, within the different follow-up arms, data may derive from the various contacts (e.g., DAT_2, AT_{FINAL}). Further, the change in the DAT arm from telephone interview to postal questionnaire in 1995 involved limiting the detail of certain inquiries that had been part of the telephone interviews. Therefore, responses to questions in the telephone and postal questionnaire phases may not be directly comparable, and for clarity and simplicity of presentation most tables based on DAT information are limited to the last 5.5 years of the Survey (i.e., postal questionnaires beginning in 1995). A publication summarizing findings from the first years of the Survey (1989-1993) is provided as Appendix 3. Finally, data in tables may not add up to 100% due to rounding, and not all tables included in this report are described in the text that follows.

A. Enrollments

From the Survey's inception in January, 1989, through June 30, 2000, a total of 494,915 women had enrolled in the Survey. As reflected in Figure 2, 21,260 women enrolled in the first year, and enrollments steadily increased in each subsequent year, such that there were 53,383 women enrolled in 1999 (the last year with complete data) and a projected 54,000 women enrolled in 2000. Enrollment forms provided through physicians accounted for 21% of all Survey participants, and calls to the toll-free number accounted for 3%; over three-quarters of women (76%) have enrolled through the unique enrollment form made directly available to them in the medication package. These proportions have remained relatively constant over the years of the Survey (Figure 2).

B. Follow-up

1. DAT arm. As projected, approximately 5000 women each year were randomized to be followed during and after treatment (the DAT arm), for a total through June 30, 2000 of 61,659. Prior to 1995, 32,301women were assigned to be followed by telephone, and since 1995 another 29,358 have been assigned to be followed by postal questionnaire. After start-up problems in the first year, response rates to three telephone interviews were 98%, 98%, and 93%, respectively; with the postal questionnaire beginning in 1995, follow-up rates for the three contacts were 97-98%. Follow-up rates have remained consistently high since 1990.

2. AT arm. A total of 433,256 women *not* randomized to the DAT arm were followed by postal questionnaire after treatment was completed (AT arm). Follow-up rates for the questionnaire sent at this time have been 80-86% and have varied little over the years of the Survey.

C. Characteristics of Survey Participants and Their Physicians

1. Demographics

The median age of participants has declined somewhat, from 26 in the first years to 23 in recent quarters. From the early years of the Survey to more recent years, the proportions of participants in the under 16 year and the 16 through 19 year age groups have increased from 6% to 11%, and 18% to 24%, respectively; the proportions the 25 through 29 year, 30 through 34 year, and 35 through 39 year groups have decreased from 19% to 15%, 16% to 11%, and 12% to 9%, respectively. The proportions of women age 20 through 24 years and 40 years and older have changed little over time (Table 1). Over three quarters of the women had graduated from high school, and one third had completed college (Table 3). This relatively high level of education has remained constant since the Survey began.

Dermatologists were the prescribing physicians for 90% of enrollees (Table 4), with primary care providers (primarily family physicians and general practitioners) making up most of the remainder; these proportions have not changed appreciably over time. Over 90% of women had received at least one course of oral antibiotics prior to beginning Accutane (Table 5), and about three-quarters had received Retin-A and benzoyl peroxide. While the prevalences of exposure to antibiotics and benzoyl peroxide have remained constant since 1995, use of Retin-A has decreased, from 79% in 1995 to 68% in the most recent quarters; despite expectations that this decline was explained by use of more recently-introduced topical retinoids, this had not proved to be the case.

With respect to potential risks of pregnancy, 71% of women in 1995 reported that had ever had sexual intercourse, and this proportion has declined slightly since that time, to 68% in the current year (Table 6). The Survey classifies women according to pregnancy risk categories (Table 7). In the last 5.5 years, 57% reported that they were not sexually active (almost half of these women were using birth control); 39% reported that they were sexually active and using birth control, and 1% reported that they were sexually active but not using birth control (for ethical reasons, Survey staff contact this group of women to inform them of their high-risk behavior). These proportions have not changed appreciably over time.

2. Knowledge and Compliance

Enrollees' knowledge and compliance with the PPP reflect, to various degrees, the behavior of their prescribing physicians. As noted in Tables 9 and 10, virtually all women knew that Accutane was teratogenic and virtually all were told to avoid pregnancy; 43% knew that the drug could cause miscarriage. Over 75% signed a consent form provided by the physician, a proportion that has increased somewhat over time. In the current year, 67% of women postponed starting Accutane until results of a pregnancy test were known, and 58% postponed it until their next menstrual period. In the current year, 75% of women reported having a pregnancy test before starting Accutane (Table 11). These proportions have remained largely unchanged since 1995.

In the early years of the Survey, we asked women whether their physician had told them to wait to begin Accutane until the pregnancy test results were known and until the next menstrual period began (we subsequently revised those questions to inquire not about what their doctor *told* them but rather whether the women actually waited for test results and their menstrual period). In the first two years of the Survey, we observed lower-than-expected rates of instruction regarding waiting to begin Accutane and we observed a similar phenomenon for pregnancy testing. These findings prompted Roche in 1990 to revise the medication package so that the back of the package prominently displayed four instructions for female patients, each beginning with "You must…". These related to pregnancy testing and waiting to begin Accutane until the negative result comes back, waiting for the next menstrual period, using effective birth control, and enrolling in the Survey. In the three years following this modification in the medication package, we observed increases of about 10-20% in the proportion of women reporting pregnancy testing and in the proportions reporting that they were instructed to wait until their pregnancy test was negative and until their next menstrual period. For pregnancy testing in particular, the 1989-90 rate of 60% increased to 67% in 1991-1993, and subsequently increased to the current level of 75%.

Contraception. The distribution of contraceptive status, primary methods of contraception used by Survey participants, and distributions according to age are presented in Table 12. Overall, 18% of the women were surgically sterile, 30% did not use contraception (of which all but 1% reported not being sexually active), and 51% used non-surgical forms of contraception, whether they were sexually active or not. As expected, the prevalence of surgical sterility increased dramatically with age. Among non-surgical contraceptors, the oral contraceptive was the method used most commonly in all age groups, ranging from 40-45% among women 15-34 to 5% among women over 44.

Secular patterns are presented in Tables 13-15. Among women 15-24 and 25-34, there was an overall increase in contraception, virtually all of which was due to an increase in oral contraceptive use. Among women 35-44, there was more variability, with a relatively small increase in use of the oral contraceptive.

Among contraceptors, more than one form of contraception was used by 38% (Table 16), with a slight increase over time. Women using two or more forms reported approximately 200 different combinations. By far the most common combination among all contraceptors was the oral contraceptive and condom, used by 18%. Other specific combinations were used by 2% or fewer contraceptors. Distributions by age (Table 17) reflect that use of two or more methods was most common among women ages 15-34.

D. Pregnancies

While it is important to document compliance with various aspects of the PPP, the most critical measure of the PPP's success is the rate of pregnancy among women taking

Accutane. The Survey has therefore devoted considerable attention to identifying and following pregnancies among enrolled women.

Pregnancy rates during Accutane exposure are presented as the rate per 1000 treatment courses; a completed course, based on Survey data, is 140 days. Table 18 presents the overall rates of pregnancy among 339,944 women who had been followed to date. Among these women, there were 992 pregnancies over 134,715 person-years of Accutane exposure; the rate of pregnancy was 2.8 per 1000 140-day treatment courses. (The annualized rate is 7.4 pregnancies per 1000 person-years). The pregnancy rate has declined over time, from close to 4/1000 courses in 1989-90 to about 2.2/1000 in the 1997-98 cohorts. It is important to recognize that the preliminary rate for the 1999 cohort is 3.4, an anomalous increase relative to the trend observed over the previous 10 years; as was detailed in our last quarterly report (Appendix 2), a similarly increased preliminary rate was noted in the 1996 cohort, but with subsequent follow-up of that cohort, the rate decreased to 2.7/1000.

Among the women who were exposed to Accutane in pregnancy, 10% were pregnant at the start of therapy.

Pregnancy rates according to age are presented in Table 19. The highest rates were observed among women ages 25-34, and these distributions have remained largely unchanged over time.

Pregnancy rates according to primary method of contraception are presented in Table 20. It is important to note that while rates are quite low for the oral contraceptive relative to other methods, women using the oral contraceptive contribute the largest numbers of pregnancies (for example, in the AT arm, these pregnancies account for 33% of the total identified).

Among women who became pregnant in the 30 days following discontinuation of Accutane (i.e., women exposed before conception), the overall pregnancy rate for that 30 day period is 1.0 per 1000 women, and it has remained stable since the 1989 cohort (Table 21).

(NB: The numbers of women presented in Tables 11, 12, and 16 in our most recent quarterly report, which is attached as Appendix 4, contains minor numerical errors; they do not affect the rate calculations, however).

E. Pregnancy Outcomes

The outcomes of pregnancies exposed to Accutane are presented in Table 22. There were a total of 1019 pregnancies (this number is larger than that in Table 18 because Table 18 is limited to Accutane use lasting less than one year). Overall, the largest proportion--67%--resulted in a therapeutic abortion. Another 17% resulted in a spontaneous abortion, and 11% of pregnancies, or 117, were livebirths. Among the

livebirths (Table 23), examination of the infant and/or review of the medical records was conducted for 63; 19 had a malformation of any kind, and 8 had a major malformation.

There were 345 pregnancies occurring in the 30 days following cessation of Accutane (Table 24) (this number is larger than that in Table 21 for the reasons given immediately above). Among these, 46% were terminated, 11% resulted in a spontaneous abortion, and 39% of pregnancies resulted in a livebirth. Among the livebirths (Table 25), 68 had an examination and/or review of the medical record; of these, 7 had any malformation and none had a major malformation.

F. Differences According To Enrollment Method

As noted above, one purpose of the medication-package enrollment option was to recruit women to the Survey who might not have been enrolled by their physicians. Some differences between these women and those enrolling through their physicians are worth noting (there were too few women who enrolled through the toll-free telephone approach to include in this analysis). As noted in Table 26, women who enrolled through the medication package were 1.6 years older than those enrolling via their doctors, though education and region were similar in the two groups. On the other hand, women who enrolled through the package were less likely to be treated by a dermatologist than were women who enrolled through their doctor and the two groups differed according to their pregnancy risk status. Those enrolling via the medication package were less likely to have signed a consent form and less likely to have undergone pregnancy testing. Though pregnancy rates did not differ dramatically according to enrollment method (Table 27), the aggregate rate for women enrolling through the medication package was 2.8/1000 courses, while that for women who enrolled through their physicians was 2.5/1000.

VIII. Validity

With few exceptions, information in this Survey is based on self-report by the women who enrolled, and one must therefore consider whether the data are valid. Follow-up rates were high among women randomized to DAT and those randomized to AT; in the DAT arm 98-99% of women responded to the various contacts. Of note, responses regarding knowledge, behavior, and compliance were similar whether they were elicited at the start of treatment (in the first DAT contact) or six months after completion of treatment (in the final AT contact). Also, as noted in a separate report (Appendix 3), the low pregnancy rates during Accutane treatment were followed by an increase in pregnancy rates in each of the four months following cessation of therapy, such that the rate in the fourth month after therapy was more than triple that reported during therapy. Further, while two-thirds of pregnancies exposed to Accutane were terminated, that proportion diminished dramatically in each of the following four months. Both phenomena are consistent with intentional avoidance of pregnancy during the period of teratogenic risk. While underreporting of both pregnancies and therapeutic abortions is likely, these observations suggest that this concern is not likely to represent a major challenge to the validity of the Survey findings.

IX. Representativeness

The issue of validity is of course critical in the interpretation of findings related to women who participated in the Accutane Survey. It is a different matter, however, as to whether the findings from the Survey reflect the larger population of all women who take Accutane, whether or not they participate in the Survey. Clearly, if participation is universal, there is by definition no question about representativeness. In observational (epidemiologic) studies, concerns about representativeness are generally considered minimal if 70-80% of the target population participates. With lower participation, one must consider whether the enrolled sample represents the universe of women taking Accutane.

Our concern about representativeness predates the Survey and continues to be a major focus. To speak to that concern, one must know the proportion of users who enroll in the Survey and whether participants differ in critical ways from nonparticipants. The Survey staff have made numerous efforts to identify rates and characteristics of participants, but this has been a difficult challenge. Two early attempts to use computerized data for this purpose failed--one from Rhode Island (HDR) and another from a national dataset (HID). In both settings, these efforts failed because of small numbers of Accutane-exposed women and because of unanticipated difficulties in the technical aspects of matching Survey enrollees with health plan members. Working with Roche, our Advisory Committee and others, we sought additional data sources.

A Roche consumer survey of 400 women who received Accutane prescriptions in 1990-91 suggested that 60% (239/400) of users enrolled in the SEU Survey (details provided in pp. 5 & 6 and tables 45-52 of the appendix included in the 10th quarterly report, July 26, 1991). Comparison of women who enrolled with those who did not suggested that while educational levels were comparable, unenrolled women tended to be slightly older (31 vs. 29 years) and less likely to be sexually active (54% vs. 64%). Though the samples were small and constrained by methodologic limitations, these observations seemed to support anectodal reports from physicians that prescribers were less likely to encourage Survey participation for women at low risk of pregnancy. Further, only 20% of women over age 40 reported that their doctor encouraged them to enroll to enroll, while among younger women that rate varied from 41-52%. In addition, the prevalence of surgical sterility among enrolled women was 44%, whereas among those who did not enroll it was 65%.

Additional efforts to assess representativeness were advanced with the opportunity to work with United Health Care (UHC) to assess enrollment rates and characteristics of women prescribed Accutane. The detailed results of that inquiry are provided as Appendix 4, and only a brief summary is presented here.

The SEU contracted with UHC to identify a cohort of women who filled at least one prescription for Accutane between January, 1990 and June, 1996. Using an unusual blinding technique, SEU and UHC researchers were able to match individuals in 14 UHC health plans with those who participated in the Accutane Survey, preserving confidentiality of information from both sources. Among the 5095 women identified as

having filled an Accutane prescription, 38.4% were determined to be definite matches to the Accutane Survey, and an additional 7.5% were determined to be possible matches. Given the complexities of the process and the fact that true matches might have been underestimated, we concluded that in this population the Accutane Survey enrolled approximately 45% of women taking the drug.

As was noted in the consumer survey assessment, women from UHC plans who enrolled in the Accutane Survey tended to be younger than those who didn't—enrollment rates among 20-29 year old women were almost three times as high as those for women ages 45-59. Enrollees were more likely to be taking Accutane for longer times than those who did not enroll; prescriber specialty did not vary appreciably. Other characteristics were more difficult to compare, because even though the UHC data included more detail that other health plans, we were still limited by the amount and quality of information available; in particular, contraceptive use could not be interpreted because there was limited information in the claims database.

The analysis of the UHC dataset, while limited, provided more information than previous attempts and is, to our knowledge, the best source with which to assess Survey enrollment; it is our intent to repeat and, we hope, expand the above analysis as more data accumulate.

In summary, the UHC data suggest that approximately 45% of Accutane-treated women enroll in the Accutane Survey. While this proportion is remarkably high for a voluntary approach, the proportion is not high enough to itself assure representativeness. Though our *a priori* assumption was that women who enroll in the Survey would be those who are most compliant and least at risk of pregnancy, our experience suggests that this may not be the case. First, the 75% of women who enroll through the form on the medication package reflect less compliance with the PPP than do those who are enrolled through their prescribers. Second, assessments of representativeness using different databases with different strengths and limitations do not suggest that the Survey population is biased toward women at least risk of pregnancy; indeed, these preliminary findings suggest that, if anything, women who do not participate in the Survey are older and otherwise at lesser risk of pregnancy. Nonetheless, the importance of resolving the issue of representativeness demands ongoing attention and research.

X. Future Directions

Until the final format of revisions to the PPP is decided, it is difficult to project how the Survey that accompanies the PPP would itself be revised. However, there are certain components of the Survey that would benefit from enhancement or modification. These include increasing enrollments, enrolling women on subsequent courses of Accutane, increasing the power and value of the DAT arm, and modifying Survey questions. Each will be discussed briefly.

A. Increase Enrollments

As noted above, maximizing enrollment is a critical strategy to help assure the representativeness of the Survey population. Since inception of the Survey, we have offered a $10 payment for participation; a check in that amount is sent to each enrollee within 48 hours of our receiving the enrollment form. We propose to increase that payment to $20. In addition, we will pay each participant another $10 upon receipt of the final Survey form.

In addition, Roche will increase it's activities designed to encourage doctors and patients to enroll in the Survey. Among the proposals is to design a process that simplifies enrollment in the doctor's office. The Survey will itself promote the importance of enrollment to prescribers.

B. Enroll Women Who Receive Multiple Courses of Accutane

A limitation of the current Survey design is that is unable to follow more than one course of treatment for a given woman. The problem derives from the fact that women are asked to complete follow-up questionnaires six months after they have discontinued their Accutane treatment. Since a subsequent course can be initiated within that six-month period, there is the possibility of confusion on the part of the woman regarding the time-focus of the questions being asked. In the next year, we expect to develop and pilot-test an approach that will minimize this problem.

C. Increasing the Power and Value of the DAT Arm

In the present Survey, 5000 women each year are randomized to be followed both during and after treatment (the "DAT" arm). Since most information on information and compliance comes from this arm, we propose to increase the number of women assigned to this form of follow up from 5,000 each year to 50% of enrollees, with a minimum of 25,000 to be followed in the DAT arm each year. This 5-fold increase in numbers will substantially increase the statistical power of this approach, and in so doing it will help the Survey identify trends far earlier than in the past, enabling Roche, FDA, and prescribers to react more quickly to possible changes in patterns of Accutane use and compliance with the PPP.

D. Modify Questions Included in the Survey

In addition to modifications that will reflect changes made in the PPP, the Survey will inquire more specifically about concerns that have emerged in recent years. These include inquiries regarding the specific kinds of oral contraceptive being used and refinement of questions that permit the Survey to identify behaviors most likely to predict an increased risk of pregnancy.

ACCUTANE SURVEY

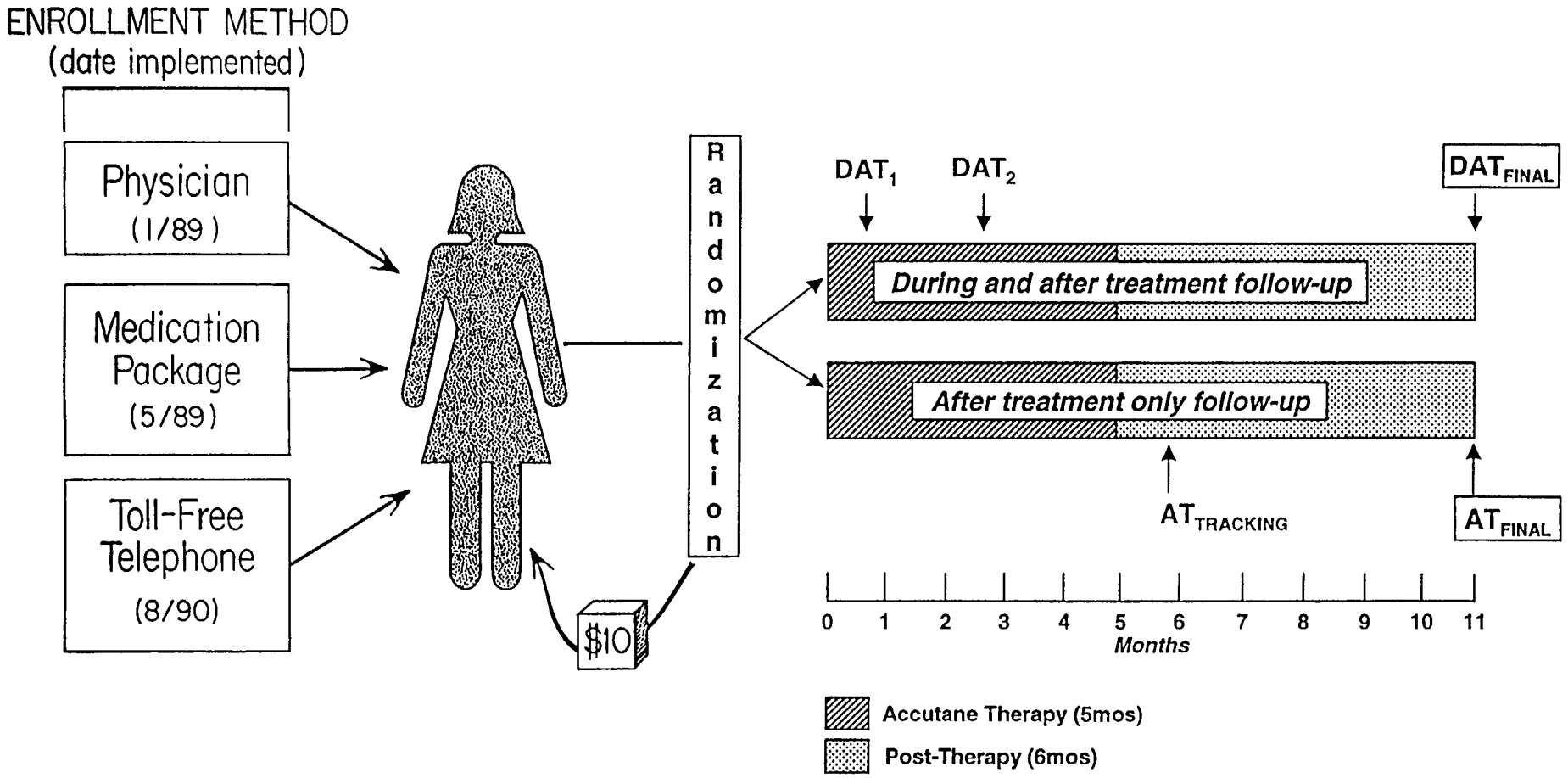


Figure 1

ACCUTANE SURVEY

RECEIPT OF ENROLLMENTS ACCORDING TO SURVEY YEAR

(1989 - Jun 2000)

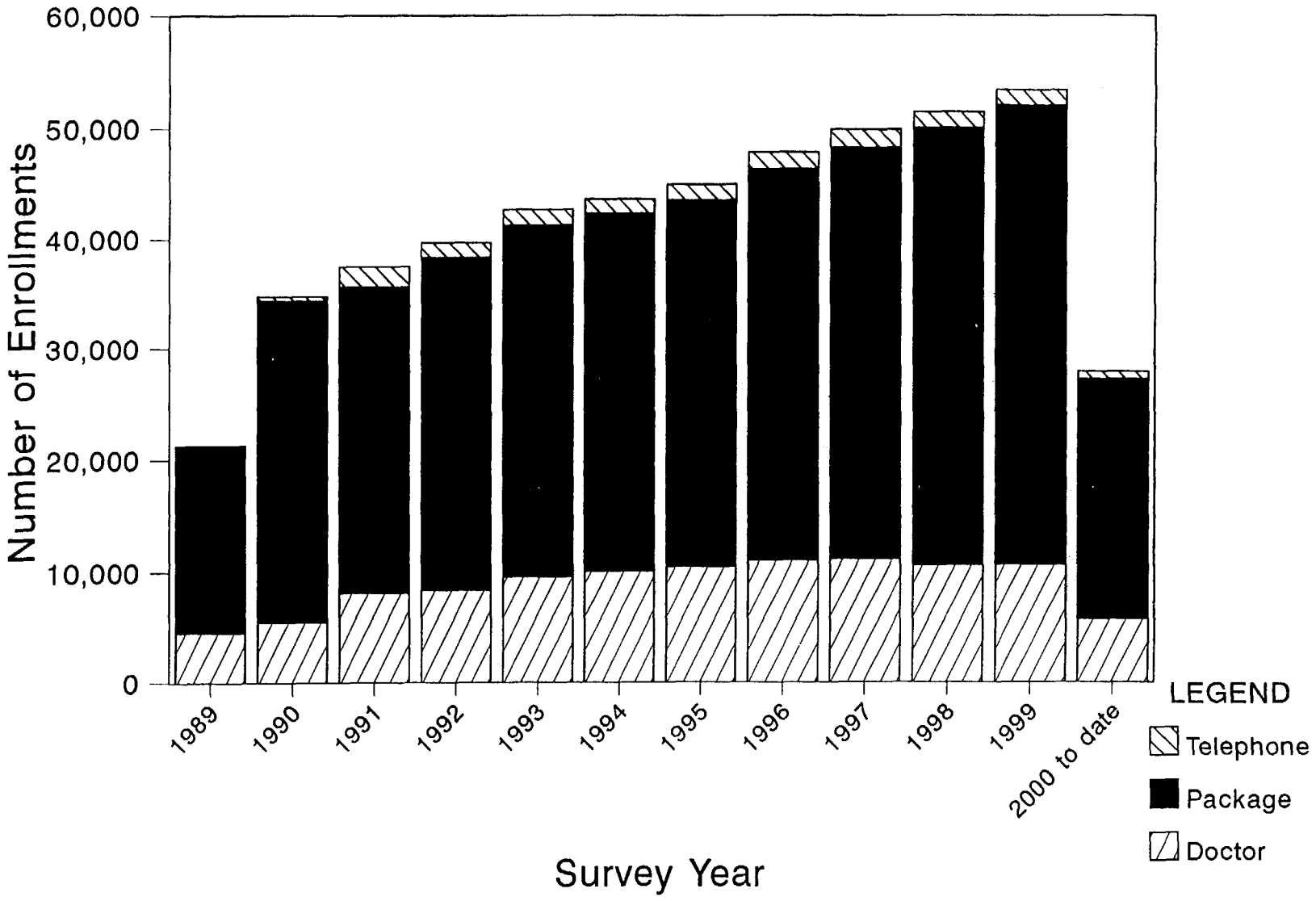


Figure 2

Table 1

Age of Enrollees by Enrollment Year
(1 of 2)

	1989 n=21260	1990 n=34768	1991 n=37461	1992 n=39641	1993 n=42690	1994 n=43608
Mean, years	26.8	26.7	26.4	26.0	25.6	25.7
Median, years	26	26	25	24	24	24
<16 years (%)	6	6	7	8	9	9
16-19 years (%)	18	18	19	20	21	21
20-24 years (%)	22	21	22	22	23	23
25-29 years (%)	19	19	18	17	16	17
30-34 years (%)	16	16	15	14	13	13
35-39 years (%)	12	12	11	10	10	10
40-44 years (%)	6	6	6	6	5	5
45-49 years (%)	2	2	2	2	2	2
50+ years (%)	1	1	1	1	1	1

Table 1

Age of Enrollees by Enrollment Year
(2 of 2)

	1995 n=44941	1996 n=47868	1997 n=49910	1998 n=51469	1999 n=53383	2000 n=27916	Total n=494915
Mean, years	25.5	25.3	25.2	25.2	25.1	25.1	25.6
Median, years	24	23	23	23	23	23	24
<16 years (%)	9	10	10	10	11	11	9
16-19 years (%)	22	23	24	24	24	24	22
20-24 years (%)	22	22	21	21	21	21	22
25-29 years (%)	16	17	16	16	16	15	17
30-34 years (%)	12	12	12	11	11	11	13
35-39 years (%)	9	9	9	9	9	9	10
40-44 years (%)	5	5	5	5	5	5	5
45-49 years (%)	2	2	2	2	2	2	2
50+ years (%)	1	1	1	1	1	1	1

Table 2

Region of Residence by Enrollment Year
%
(1 of 2)

	1989 n=21260	1990 n=34768	1991 n=37461	1992 n=39641	1993 n=42690	1994 n=43608
New England	4	4	4	5	5	5
Mid Atlantic	12	12	13	13	13	13
South Atlantic	17	18	18	18	18	17
East South Central	5	6	5	5	5	5
West South Central	12	12	12	11	11	11
Mountain	8	8	8	8	8	8
Pacific	21	20	19	19	19	19
West North Central	6	6	6	6	6	7
East North Central	13	13	14	13	14	14
Other	1	1	1	1	1	1

Table 2

Region of Residence by Enrollment Year
%
(2 of 2)

	1995 n=44941	1996 n=47868	1997 n=49910	1998 n=51469	1999 n=53383	2000 n=27916	Total n=494915
New England	5	5	5	5	5	6	5
Mid Atlantic	13	13	13	13	13	13	13
South Atlantic	18	18	18	18	18	18	18
East South Central	5	5	5	5	6	6	5
West South Central	10	11	10	10	10	10	11
Mountain	8	8	8	8	9	8	8
Pacific	18	18	18	18	16	16	18
West North Central	7	7	7	7	7	7	7
East North Central	14	14	14	14	15	15	14
Other	1	1	1	1	1	1	1

Table 3

Highest Level of Education by Enrollment Year*
%

	1995 n=4788	1996 n=5063	1997 n=5123	1998 n=4942	1999 n=5159	2000 n=1578	Total n=26653
<8 years	2	2	2	2	3	3	2
8-11 years	19	17	19	19	19	19	19
High school graduate	10	11	10	10	9	12	10
Some college or technical school	35	35	36	35	35	31	35
College graduate	23	24	21	23	23	24	23
Graduate school	10	11	11	10	10	11	10
Unknown	<1	<1	<1	1	<1	<1	<1

*Information from DAT-1 questionnaire, 1995-1996 and DAT-2 questionnaire, 1996-2000

Table 4

Type of Prescriber by Enrollment Year*
%

	1995 n=4788	1996 n=5063	1997 n=5123	1998 n=4942	1999 n=5159	2000 n=1578	Total n=26653
Dermatologist	92	90	90	90	90	91	90
General practitioner	2	3	3	3	3	3	3
Family practitioner	4	5	6	5	5	4	5
Gynecologist	<1	<1	<1	<1	<1	<1	<1
Internist	<1	1	1	<1	1	<1	1
Pediatrician	<1	<1	<1	<1	<1	<1	<1
Plastic surgeon	<1	<1	<1	<1	<1	<1	<1
Other	<1	<1	1	1	1	1	<1
Unknown	<1	<1	<1	<1	<1	<1	<1

*Information from DAT-1 questionnaire, 1995-1996 and DAT-2 questionnaire, 1996-2000

Table 5

Past Treatment for Acne by Enrollment Year*
% Yes

	1995 n=5108	1996 n=5157	1997 n=5206	1998 n=5047	1999 n=5283	2000 n=2585	Total n=28386
Any antibiotics	88	94	94	93	93	92	92
Oral vitamin A	12	11	12	11	10	9	11
Retin-A	79	78	77	77	73	70	76
Benzoyl peroxide	72	73	74	74	73	72	73

*Information from DAT-1 questionnaire, 1995-2000. Not mutually exclusive.

Table 6

Ever Had Sexual Intercourse, by Enrollment Year

	1995 n=5108	1996 n=5157	1997 n=5206	1998 n=5047	1999 n=5283	2000 n=2585	Total n=28386
No	28	29	31	32	32	31	31
Yes	71	70	68	67	67	68	69
Refused/ missing	<1	<1	1	1	1	1	1

Table 7

Pregnancy Risk Category by Enrollment Year[1]
% Yes

	1995 n=5023	1996 n=5087	1997 n=5144	1998 n=4987	1999 n=5220	2000 n=2555	Total n=28016
Hysterectomy or postmenopausal	3	3	4	3	3	3	3
Not sexually active, using birth control[2]	23	23	26	25	26	27	25
Not sexually active, not using birth control[3]	33	32	32	32	31	29	32
Sexually active, using birth control[4]	39	39	38	38	39	39	39
Sexually active, not using birth control[5]	1	1	1	1	1	<1	1
Unknown[6]	1	1	1	1	1	1	1

[1]Information from DAT-1 questionnaire, 1995-2000. Limited to women who started Accutane.
[2]Total includes 63 women who reported that they or their partners were infertile.
[3]Total includes 63 women who reported that they or their partners were infertile.
[4]Total includes 336 women who reported that they or their partners were infertile.
[5]Total includes 75 women who reported that they or their partners were infertile.
[6]Total includes 9 women who reported that they or their partners were infertile.

Table 8

Receipt of Information from PPP Kit by Enrollment Year*
% Yes

	1995 n=5108	1996 n=5157	1997 n=5206	1998 n=5047	1999 n=5283	2000 n=2585	Total n=28386
Patient brochure	92	92	91	91	92	92	92
True/false test	39	40	42	42	45	45	42
Birth control brochure	48	51	54	54	56	57	53

*Information from DAT-1 questionnaire, 1995-2000. Not mutually exclusive.

Table 9

Knowledge of Accutane Risk, by Enrollment Year*

	1995 n=5108	1996 n=5157	1997 n=5206	1998 n=5047	1999 n=5283	2000 n=2585	Total n=28386
May cause miscarriage	46	42	43	44	42	42	43
May cause birth defects	99	98	99	100	99	99	99

*Not mutually exclusive

Table 10

Compliance with Selected Measures of the PPP*
% Yes

	1995 n=5108	1996 n=5157	1997 n=5206	1998 n=5047	1999 n=5283	2000 n=2585	Total n=28386
Told to avoid pregnancy	99	99	99	99	99	99	99
Signed consent form	76	77	77	77	78	80	77
Postponed Accutane until results of pregnancy test known†	67	67	66	65	68	67	67
Postponed Accutane until next menstrual period†	57	57	57	57	57	58	57

*Information from DAT-1 questionnaire, 1995-2000. Not mutually exclusive.

†Women who had not yet started Accutane or who were identified as posthysterectomy or postmenopausal were excluded.

Table 11

Pregnancy Testing Before Starting Accutane by Enrollment Year*
%

	1995 n=4864	1996 n=4920	1997 n=4963	1998 n=4818	1999 n=5041	2000 n=2467	Total n=27073
Serum pregnancy test	55	56	55	56	56	55	56
Urine pregnancy test	10	8	9	9	10	10	9
Serum and urine pregnancy tests	8	9	8	7	8	7	8
Any pregnancy test†	75	76	76	76	77	75	76
No pregnancy test	25	24	24	24	23	25	24
Unknown	1	1	1	<1	<1	<1	1

*Information from DAT-1 questionnaire, 1995-2000. Women who had not yet started Accutane or who were identified as posthysterectomy or postmenopausal were excluded.

†Included in this category are 608 women who responded that they had a pregnancy test but were uncertain of the type of test; these women are not included in the preceding categories. See quarterly report for Jul-Sep 1995 for comment.

Table 12

Contraceptive Status and Primary Method by Age Group*
%

	<15 years n=1371	15-24 years n=13701	25-34 years n=7839	35-44 years n=4174	45+ years n=931	Total n=28016
Surgically sterile	<1	1	22	58	69	18
Female	<1	1	12	34	53	11
Male	0	1	10	24	16	7
Nonsurgically sterile†	<1	<1	<1	2	6	1
Nonuser	79	44	12	8	8	30
Not sexually active	79	44	12	8	8	30
Sexually active	<1	<1	<1	<1	1	<1
Nonsurgical contraceptors	17	54	65	33	16	51
Norplant or Depo-Provera injection	1	4	4	1	<1	3
Pill	11	40	45	16	5	35
IUD	<1	<1	1	2	1	1
Diaphragm	0	<1	1	3	2	1
Condoms	<1	5	9	7	5	6
Rhythm/natural family planning	<1	<1	<1	1	1	<1
Other methods	5	5	4	3	2	4
Unknown method	<1	<1	<1	<1	0	<1
Unknown	3	<1	<1	<1	1	<1

*Information from DAT-1 questionnaire, 1995-2000. Primary method determined using adaption of the schema of the National Survey of Family Growth (NCHS, March 20, 1990). Women who had not yet started Accutane were excluded.

†Defined as self-report of postmenopausal status or infertility in respondent or partner. Excludes women using contraception.

Table 13

Contraceptive Status and Primary Method by Enrollment Year*
Age 15-24 Years
%

	1995 n=2388	1996 n=2441	1997 n=2566	1998 n=2526	1999 n=2552	2000 n=1228	Total n=13701
Surgically sterile	1	1	1	1	1	1	1
Female	<1	<1	<1	1	<1	1	1
Male	<1	<1	<1	<1	<1	<1	<1
Nonsurgically sterile†	<1	<1	<1	<1	<1	<1	<1
Nonuser	48	46	44	43	42	40	44
Not sexually active	47	45	44	43	41	40	44
Sexually active	<1	<1	1	<1	<1	<1	<1
Nonsurgical contraceptors	51	53	54	55	56	58	54
Norplant or Depo-Provera injection	4	4	3	4	3	3	4
Pill	35	38	40	41	45	46	40
IUD	<1	<1	<1	<1	<1	<1	<1
Diaphragm	<1	1	<1	<1	<1	<1	<1
Condoms	6	5	6	5	4	3	5
Rhythm/natural family planning	<1	<1	0	<1	0	<1	<1
Other methods	6	5	5	5	4	5	5
Unknown method	<1	<1	<1	<1	<1	<1	<1
Unknown	<1	<1	<1	0	<1	<1	<1

*Information from DAT-1 questionnaire, 1995-2000. Primary method determined using adaption of the schema of the National Survey of Family Growth (NCHS, March 20, 1990). Women who had not yet started Accutane were excluded.

†Defined as self-report of postmenopausal status or infertility in respondent or partner. Excludes women using contraception.

Table 14

Contraceptive Status and Primary Method by Enrollment Year*
Age 25-34 Years
%

	1995 n=1446	1996 n=1504	1997 n=1418	1998 n=1343	1999 n=1410	2000 n=718	Total n=7839
Surgically sterile	22	21	22	22	21	23	22
Female	12	11	12	13	12	14	12
Male	10	10	10	9	8	9	10
Nonsurgically sterile†	1	<1	1	1	<1	<1	<1
Nonuser	14	14	12	11	11	11	12
Not sexually active	14	14	12	10	11	10	12
Sexually active	<1	<1	1	1	<1	1	<1
Nonsurgical contraceptors	62	64	66	66	67	67	65
Norplant or Depo-Provera injection	4	4	4	4	4	3	4
Pill	40	42	44	46	50	49	45
IUD	1	1	1	1	1	2	1
Diaphragm	2	2	2	2	1	1	1
Condoms	10	10	9	9	8	8	9
Rhythm/natural family planning	<1	<1	<1	<1	<1	<1	<1
Other methods	5	4	5	4	3	3	4
Unknown method	<1	<1	<1	<1	<1	1	<1
Unknown	0	<1	0	<1	<1	0	<1

*Information from DAT-1 questionnaire, 1995-2000. Primary method determined using adaption of the schema of the National Survey of Family Growth (NCHS, March 20, 1990). Women who had not yet started Accutane were excluded.

†Defined as self-report of postmenopausal status or infertility in respondent or partner. Excludes women using contraception.

Table 15

Contraceptive Status and Primary Method by Enrollment Year*
Age 35-44 Years
%

	1995 n=821	1996 n=764	1997 n=742	1998 n=704	1999 n=756	2000 n=387	Total n=4174
Surgically sterile	59	56	59	57	62	55	58
Female	35	34	34	33	38	31	34
Male	24	22	25	24	24	24	24
Nonsurgically sterile†	2	2	1	2	2	<1	2
Nonuser	8	8	8	9	8	9	8
Not sexually active	8	8	8	8	7	8	8
Sexually active	1	<1	<1	1	<1	<1	<1
Nonsurgical contraceptors	30	34	32	32	27	36	33
Norplant or Depo-Provera injection	<1	2	1	1	1	3	1
Pill	14	15	16	17	16	18	16
IUD	2	2	1	2	1	3	2
Diaphragm	3	3	3	2	1	2	3
Condoms	6	7	7	6	6	7	7
Rhythm/natural family planning	1	1	1	1	<1	1	1
Other methods	3	4	3	3	2	2	3
Unknown method	0	<1	0	0	<1	0	<1
Unknown	<1	0	<1	0	<1	<1	<1

*Information from DAT-1 questionnaire, 1995-2000. Primary method determined using adaption of the schema of the National Survey of Family Growth (NCHS, March 20, 1990). Women who had not yet started Accutane were excluded.

†Defined as self-report of postmenopausal status or infertility in respondent or partner. Excludes women using contraception.

Table 16

Number of Contraceptive Methods Reported by Contraceptors by Enrollment Year*
%

	1995 n=3214	1996 n=3299	1997 n=3343	1998 n=3272	1999 n=3415	2000 n=1732	Total n=18275
1	64	61	62	63	62	60	62
2	30	33	33	31	34	36	33
3+	6	6	5	6	5	4	5

*Information from DAT-1 questionnaire, 1995-2000. Women who had not yet started Accutane or who were identified as posthysterectomy or postmenopausal were excluded.

Table 17

Number of Contraceptive Methods Reported by Contraceptors by Age Group*
%

	<15 years n=233	15-24 years n=7583	25-34 years n=6652	35-44 years n=3338	45+ years n=469
1	88	62	57	70	78
2	11	33	37	26	20
3+	2	5	6	4	2

*Information from DAT-1 questionnaire, 1995-2000. Women who had not yet started Accutane or who were identified as posthysterectomy or postmenopausal were excluded.

Table 18

Pregnancy Rate According to Year of Enrollment
Risk Period: Accutane Course

	1989 Cohort[1]	1990 Cohort[2]	1991 Cohort[3]	1992 Cohort[4]	1993 Cohort[5]	1994 Cohort[6]	1995 Cohort[7]	1996 Cohort[8]	1997 Cohort[9]	1998 Cohort[10]	1999 Cohort[11]	Total
N	18294	30255	32228	33061	34110	34161	35093	36023	36556	35260	14903	339944
Pregnancies reported[12]	74	109	96	98	94	84	105	104	96	81	51	992
Person-years of Accutane exposure	7153	11463	12287	12676	13278	13470	14210	14777	15167	14508	5726	134715
Rate/1000 140-day courses of Accutane	4.0	3.6	3.0	3.0	2.7	2.4	2.8	2.7	2.4	2.1	3.4	2.8

[1]Excludes 900 women who reported use $\geq$ 1 year.

[2]Excludes 1109 women who reported use $\geq$ 1 year.

[3]Excludes 1059 women who reported use $\geq$ 1 year.

[4]Excludes 846 women who reported use $\geq$ 1 year.

[5]Excludes 762 women who reported use $\geq$ 1 year.

[6]Excludes 958 women who reported use $\geq$ 1 year.

[7]Excludes 945 women who reported use $\geq$ 1 year.

[8]Excludes 1019 women who reported use $\geq$ 1 year.

[9]Excludes 1043 women who reported use $\geq$ 1 year.

[10]Excludes 422 women who reported use $\geq$ 1 year.

[11]Excludes 30 women who reported use $\geq$ 1 year.

[12]Includes reports of pregnancies pending confirmation.

Table 19

Pregnancy Rates* by Age Group by Enrollment Year†
(1 of 2)

	1989		1990		1991		1992		1993		1994	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
<15 years	437	0	729	0	955	0	1109	2.5	1286	2.2	1273	0
15-24 years	6585	4.4	10820	4.0	12265	3.1	13199	2.8	14114	2.8	14055	2.2
25-34 years	5487	5.6	8801	5.0	9136	3.9	8859	3.8	8735	3.0	8629	3.0
35-44 years	2724	2.5	4490	1.1	4716	1.3	4554	2.7	4339	1.6	4476	1.5
45+ years	346	0	626	0	664	1.7	770	0	754	0	814	1.3

*Rate/1000 140-day courses of Accutane

†Excludes DAT arm and women using Accutane ≥365 days. 13 women with missing age data also excluded (none with report of pregnancy).

Table 19

Pregnancy Rates* by Age Group by Enrollment Year†
(2 of 2)

	1995		1996		1997		1998		1999		Total	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
<15 years	1392	1.3	1510	1.2	1484	1.2	1505	0	610	1.5	12290	1.0
15-24 years	14728	2.9	15346	2.7	15789	2.4	15359	2.2	6239	3.3	138499	2.8
25-34 years	8961	3.3	9064	3.9	9025	3.6	8689	2.9	3654	4.1	89040	3.7
35-44 years	4330	2.5	4412	0.9	4445	0.9	4314	1.6	1774	3.0	44574	1.7
45+ years	861	1.2	809	0	935	0	954	0	437	2.5	7970	0.5

*Rate/1000 140-day courses of Accutane

†Excludes DAT arm and women using Accutane ≥365 days. 13 women with missing age data also excluded (none with report of pregnancy).

Table 20

Pregnancy Rates* by Primary Method of Birth Control by Enrollment Year†
(1 of 2)

	1989		1990		1991		1992		1993		1994	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Tubal ligation	557	0	2769	0.7	2847	0	2692	0.4	2484	0	2296	0
Vasectomy	229	4.1	1678	1.2	1727	0.6	1730	0	1686	0	1691	0
Oral contraceptives	4583	4.2	7827	4.2	8868	3.2	9267	2.1	9627	2.1	9626	1.3
IUD	166	17.8	235	0	211	5.1	193	0	205	4.9	201	4.9
Diaphragm	555	5.3	749	6.8	669	9.0	559	10.8	409	0	378	5.3
Condom	1004	11.6	1571	9.0	1796	8.3	1866	11.4	1947	10.5	1852	9.0
Rhythm	73	29.5	97	19.8	103	9.8	82	37.2	82	0	90	0
Other method	1864	1.1	896	16.5	884	0	876	5.9	1143	1.7	1301	2.2
Unknown method	306	3.3	248	0	313	0	314	6.3	356	5.5	391	2.5
No method	6233	2.3	9392	1.7	10309	1.8	10904	1.8	11281	1.8	11414	1.8

*Rate/1000 140-day courses of Accutane

†Excludes DAT arm, women using Accutane $\geq$365 days, and women pregnant at start of Accutane. Primary method determined by adaptation of schema of the National Survey of Family Growth (NCHS, March 20, 1990)

Table 20

Pregnancy Rates* by Primary Method of Birth Control† by Enrollment Year
(2 of 2)

	1995		1996		1997		1998		1999		Total	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Tubal ligation	2347	1.7	2156	0	2110	0.4	2103	0.5	833	2.5	23194	0.5
Vasectomy	1742	0	1545	0.6	1605	0	1623	0	709	0	15965	0.3
Oral contraceptives	9941	2.6	10398	2.5	11132	2.0	11605	2.1	5021	2.8	97895	2.5
IUD	199	0	210	4.5	230	0	260	3.7	102	0	2212	3.6
Diaphragm	345	5.6	321	5.8	264	0	189	4.9	81	0	4519	5.9
Condom	1878	12.1	1973	11.5	1679	8.8	1404	10.7	505	20.3	17475	10.6
Rhythm	82	12.0	82	11.8	82	23.4	62	0	20	53.4	855	15.2
Other method	1353	3.5	1282	0.7	1197	3.2	1105	2.5	417	0	12318	3.1
Unknown method	464	4.0	641	1.4	617	0	680	2.7	292	3.3	4622	2.5
No method	11916	1.7	12528	1.6	12756	1.9	11785	1.0	4729	1.7	113247	1.7

*Rate/1000 140-day courses of Accutane

†Excludes DAT arm, women using Accutane ≥365 days, and women pregnant at start of Accutane. Primary method determined by adaptation of schema of the National Survey of Family Growth (NCHS, March 20, 1990)

Table 21

Pregnancy Rate According to Year of Enrollment
Risk Period: 30 Days Following Accutane Treatment

	1989 Cohort[1]	1990 Cohort[2]	1991 Cohort[3]	1992 Cohort[4]	1993 Cohort[5]	1994 Cohort[6]	1995 Cohort[7]	1996 Cohort[8]	1997 Cohort[9]	1998 Cohort[10]	1999 Cohort[11]	Total
N	18294	30255	32228	33061	34110	34161	35093	36023	36556	35260	14903	339944
Pregnancies reported[12]	23	41	26	34	31	30	32	25	44	36	16	338
Rate/1000 enrollees	1.3	1.4	0.8	1.0	0.9	0.9	0.9	0.7	1.2	1.0	1.1	1.0

[1]Excludes 900 women who reported use $\geq$ 1 year.

[2]Excludes 1109 women who reported use $\geq$ 1 year.

[3]Excludes 1059 women who reported use $\geq$ 1 year.

[4]Excludes 846 women who reported use $\geq$ 1 year.

[5]Excludes 762 women who reported use $\geq$ 1 year.

[6]Excludes 958 women who reported use $\geq$ 1 year.

[7]Excludes 945 women who reported use $\geq$ 1 year.

[8]Excludes 1019 women who reported use $\geq$ 1 year.

[9]Excludes 1043 women who reported use $\geq$ 1 year.

[10]Excludes 422 women who reported use $\geq$ 1 year.

[11]Excludes 30 women who reported use $\geq$ 1 year.

[12]Includes reports of pregnancies pending confirmation.

Table 22

Outcome of Pregnancies Exposed During Accutane Treatment*

	1989 Cohort (n=80)		1990 Cohort (n=111)		1991 Cohort (n=98)		1992 Cohort (n=99)		1993 Cohort (n=95)		1994 Cohort (n=89)		1995 Cohort (n=107)		1996 Cohort (n=109)		1997 Cohort (n=97)		1998 Cohort (n=83)		1999 Cohort (n=51)		Total (n=1019)	
Therapeutic abortion	65	(81%)	83	(75%)	60	(61%)	69	(70%)	62	(65%)	55	(62%)	69	(64%)	69	(63%)	65	(67%)	54	(65%)	30	(59%)	681	(67%)
Spontaneous abortion	7	(9%)	17	(15%)	20	(20%)	20	(20%)	17	(18%)	12	(13%)	16	(15%)	21	(19%)	16	(16%)	19	(23%)	12	(24%)	177	(17%)
Ectopic pregnancy	2	(2%)	3	(3%)	5	(5%)	3	(3%)	1	(1%)	3	(3%)	4	(4%)	3	(3%)	2	(2%)	1	(1%)	2	(4%)	29	(3%)
Stillbirth	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---
Livebirth	4	(5%)	7	(6%)	13	(13%)	7	(7%)	12	(13%)	17	(19%)	16	(15%)	14	(13%)	13	(13%)	9	(11%)	5	(10%)	117	(11%)
Pregnancy continuing	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---
Unknown†	2	(2%)	1	(1%)	0	---	0	---	3	(3%)	2	(2%)	2	(2%)	2	(2%)	1	(1%)	0	---	2	(4%)	15	(1%)

*Includes reports of pregnancies pending confirmation.

†Includes pregnancies pending follow-up or lost to follow-up.

Table 23

Status of Infants Born to Women
Exposed to Accutane After Conception (In Utero)

Number eligible*		119
Medical records status		
Refused**		50
Pending		6
Obtained		63
Examinations completed***		13
Results of medical record review/examinations		
No malformation		44
Minor malformation		11
Ear anomaly	2	
Hypoplastic scrotum	1	
Ear and craniofacial anomalies	2	
Craniofacial anomaly	1	
Mongolian spots	1	
Bilateral inguinal hernias	1	
Mild developmental delay	1	
Mild hydronephrosis on prenatal ultrasound	1	
Vesicoureteral reflux on prenatal ultrasound	1	
Major malformation		8
Ear, eye, craniofacial, and brain anomalies	1	
Ear and craniofacial anomalies	1	
Ear, eye, and heart anomalies	1	
Eye and brain anomalies	1	
? Deafness	1	
Ear, brain, and heart anomalies	1	
Brain and heart (deceased)	1	
Cystic kidney and hypospadias (also intrauterine growth retardation)	1	
Number with any malformations/number examined or with medical record review		19/63
Number with major malformations/number examined or with medical record review		8/63

*Includes 2 sets of twins: 1 normal, 1 minor kidney anomaly.
**Includes 1 death: maternal report of major birth defects.
***See text for explanation.

Table 24

Outcome of Pregnancy Among Women Who Conceived
Within 30 Days of Stopping Accutane Treatment*

	1989 Cohort (n=23)		1990 Cohort (n=43)		1991 Cohort (n=26)		1992 Cohort (n=35)		1993 Cohort (n=31)		1994 Cohort (n=32)		1995 Cohort (n=34)		1996 Cohort (n=25)		1997 Cohort (n=44)		1998 Cohort (n=36)		1999 Cohort (n=16)		Total (n=345)	
Therapeutic abortion	14	(61%)	23	(53%)	14	(54%)	22	(63%)	13	(42%)	17	(55%)	15	(43%)	8	(32%)	13	(30%)	16	(44%)	3	(19%)	158	(46%)
Spontaneous abortion	2	(9%)	7	(16%)	2	(8%)	2	(6%)	6	(19%)	1	(3%)	4	(11%)	3	(12%)	6	(14%)	4	(14%)	1	(6%)	38	(11%)
Ectopic pregnancy	1	(4%)	1	(2%)	1	(4%)	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	3	(1%)
Stillbirth	0	---	0	---	0	---	0	---	0	---	0	---	1	(3%)	0	---	0	---	0	---	0	---	1	(<1%)
Livebirth	6	(26%)	11	(26%)	8	(31%)	10	(28%)	12	(39%)	12	(35%)	12	(34%)	14	(56%)	25	(57%)	16	(42%)	9	(56%)	135	(39%)
Pregnancy continuing	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	1	(6%)	1	(<1%)
Unknown†	0	---	1	(2%)	1	(4%)	1	(3%)	0	---	2	(6%)	2	(6%)	0	---	0	---	0	---	2	(12%)	9	(3%)

*Includes reports of pregnancies pending confirmation.

†Includes pregnancies pending follow-up or lost to follow-up.

Table 25

Status of Infants Born to Women
Who Used Accutane Before Conception
(i.e., Conception Occurring in the 30 Days Following
Discontinuation of Accutane)

Number eligible*		137
Medical records status		
Refused**		54
Pending		15
Obtained		68
Examinations completed***		15
Results of medical record review/examinations		
No malformation		60
Minor malformation		7
Ear anomaly	1	
Craniofacial anomaly	2	
? Femoral anteversion	1	
Hydrocele	1	
Functional murmur, no follow-up required	1	
Murmur	1	
Major malformation		0
Other		1
Metabolic defect (deceased)	1	
Number with any malformations/number examined or with medical record review		7/68
Number with major malformations/number examined or with medical record review		0/68

*Includes 2 sets of twins: 3 normal, 1 minor ear anomaly.
**Includes one death: maternal report of complications from prematurity.
***See text for explanation.

Table 26

Characteristics of Enrollees by Enrollment Method
(1 of 2)

	Doctor-generated n=105292	Package generated n=375404	Toll-free telephone number n=14219
Age, years			
Mean	24.3	25.9	27.9
Median	22	24	27
Region, %			
New England	5	5	4
Mid Atlantic	13	13	14
South Atlantic	18	18	20
East South Central	5	5	6
West South Central	11	11	11
Mountain	9	8	7
Pacific	17	19	16
West North Central	6	7	6
East North Central	16	14	14
Other	1	1	1
Prescriber,* %			
Dermatologist	98	88	88
Other	2	12	12
Education,* %			
≤8 years	3	2	3
9-11 years	22	18	9
High school graduate	10	10	11
Some college or technical school	34	35	39
College graduate	22	23	27
Graduate school	9	11	12
Missing	<1	1	<1

*Limited to women in DAT arm, 1995-2000

Table 26

Characteristics of Enrollees by Enrollment Method
(2 of 2)

	Doctor-generated n=105292	Package generated n=375404	Toll-free telephone number n=14219
Prior acne treatments,* % Yes			
Antibiotics	94	92	92
Vitamin A	11	11	12
Retin-A	79	75	74
Benzoyl peroxide	73	73	74
Signed consent,* % Yes	98	71	73
Told to avoid pregnancy,* % Yes	100	99	99
Had pregnancy test before starting,* % Yes	84	69	69
Pregnancy risk category,* %			
Hysterectomy	1	4	5
Not sexually active, using birth control	28	24	25
Not sexually active, not using birth control	34	31	21
Sexually active, using birth control	33	40	47
Sexually active, not using birth control	<1	1	1
Unknown	3	1	1
Number of contraceptive methods used by contraceptors,* %			
1	59	63	60
2	35	32	34
3+	6	5	6

*Limited to women in DAT arm, 1995-2000

Table 27

Pregnancy Rates by Method of Enrollment by Enrollment Year*
(1 of 2)

	1989		1990		1991		1992		1993		1994	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Doctor-generated	3043	4.8	3942	3.0	6043	2.1	6125	3.4	6652	2.0	6864	1.5
Package-generated	12537	4.2	21265	3.8	20348	3.0	21474	2.8	21689	2.7	21623	2.3
Toll-free telephone number	---		259	2.1	1345	5.2	892	5.8	888	4.4	760	5.3

*Excludes women using Accutane ≥365 days and women in DAT arm

Table 27

Pregnancy Rates by Method of Enrollment by Enrollment Year*
(2 of 2)

	1995		1996		1997		1998		1999		Total	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Doctor-generated	7118	3.6	7334	1.9	7172	2.3	6497	1.5	2442	3.2	63232	2.5
Package-generated	22266	2.6	22916	2.9	23575	2.4	23595	2.2	9970	3.0	221258	2.8
Toll-free telephone number	888	3.2	893	3.2	935	5.2	732	5.3	304	17.4	7896	5.1

*Excludes women using Accutane ≥365 days and women in DAT arm

Slone Epidemiology Unit
Accutane Survey Advisory Committee
1988 – 2000

Paul D. Stolley, M.D., Chair*
The University of Maryland School of Medicine
Baltimore, M.D.

Edward L. Decker, Pharm.D.
New England Medical center
Boston, MA

Karen McKoy, M.D.
Lahey Clinic
Burlington, MA

John Melski, M.D.
Marshfield Clinic
Marshfield, WI

Peter Pochi, M.D.
Boston University School of Medicine
Boston, MA

Robert S. Stern, M.D.
Harvard Medical School
Boston, MA

Observers:

Charlotte Catz, M.D.
National Institute of Child Health and Human Development
Bethesda, MD

José F. Corderó, M.D.
Centers for Disease Control
Atlanta, GA

*Dr. Stolley resigned as Committee Chair on July 19, 2000 because he has joined the FDA as a Senior Consultant.

SURVEY OF ACCUTANE USE IN WOMEN

April 1, 2000 – June 30, 2000

July 27, 2000

A report of work conducted by the Slone Epidemiology Unit of the
School of Public Health, Boston University Medical School
Under contract to Hoffmann-La Roche, Inc.
Allen A. Mitchell, M.D., Principal Investigator
Carla M. Van Bennekom, M.P.H., Epidemiologist

I. INTRODUCTION

This report provides summary information concerning the Survey since its initiation on January 1, 1989, as well as more detailed information on activities for the current quarter, April 1, 2000 through June 30, 2000.

As in the past, data for enrollments are presented for the current quarter, the two previous quarters combined (October 1, 1999 through March 31, 2000), the period preceding the current and two previous quarters (January 1, 1989 through September 30, 1999) and the Survey to date (January 1, 1989 through June 30, 2000).

During the first quarter of 1995, we implemented the change from telephone interviews to mailed questionnaires for women surveyed during and after treatment, as described in the report for October through December, 1994 (i.e., the "telephone arm" has been replaced by the "during and after treatment" ["DAT"] arm). Preliminary data for the first mailed questionnaire (DAT-1) are presented for the same four time periods as the enrollment data (described above). The second mailed questionnaire (DAT-2) is not sent until 10 weeks after enrollment; as only a small number of women who enrolled in the current quarter are eligible for the DAT-2 questionnaire, preliminary data for that questionnaire are presented in the same format as the enrollment and DAT-1 data, but with the fourth quarter of 1999 providing the most recent information.

Given the relatively small number of pregnancies, pregnancy rates are presented for full-year periods--in this report, these include the 1989 through 1999 cohorts and these 11 cohorts combined.

In all tables, percentages may not total 100% because of rounding.

II. CURRENT STATUS OF SURVEY

A. Staffing, Facilities, and Data Management

During the current quarter, Kathleen O'Brien resigned from the position of Research Coordinator. Following her resignation, the supervisory responsibilities for the Survey were reorganized so that the responsibility for day-to-day operation of the study, previously shared by two Research Coordinators, was placed under a single Program Coordinator; Helen Bond, who previously worked as the Research Coordinator supervising the Survey's interviewers, was promoted to the new position of Program Coordinator. There were no other changes in staffing, facilities, or data management in the current quarter.

B. Enrollments

To date, we have enrolled 494,915 women in the Survey, including 11,995 in the current quarter. The distribution of enrollments by Survey quarter, according to enrollment method, is presented in Figure 1. For the current quarter, the proportions of enrollments generated by physicians, the medication package, and the toll-free telephone number were 20%, 77%, and 2%, respectively (Table 1).

Since 1990, we generally have observed an increase in enrollments for each quarter compared with the equivalent quarter of the previous year. For the current quarter compared with the equivalent quarter of 2000, however, we observed a very small decrease (<1%) in enrollments overall. Doctor-generated enrollments increased by 6%, and medication package-generated enrollments decreased by 1%. Such decreases often prove transient, as we have observed in several previous quarters; we will continue to closely monitor receipt of enrollments during the coming quarter.

C. "During and After Treatment" (DAT) Arm

As mentioned above, the change from the telephone interviews to the DAT arm mailed questionnaires began in 1995, and has been implemented in phases, beginning with the DAT-1, then DAT-2, then DAT-3, and then DAT-3 Follow-up. (The protocols for the DAT-1, DAT-2, DAT-3, and DAT-3 Follow-up questionnaires were described in the reports for January through March, 1995, April through June, 1995, April through June, 1996, and January through March, 1997, respectively.) The overall response rates for the DAT-1 and DAT-2 questionnaires continue to be over 98% (approximately 20% of women require telephone contact after failing to respond by mail). To date, the response rates to all mailings for the DAT-3 and DAT-3 Follow-up questionnaires are 90% and 80%, respectively, and we have successfully completed the questionnaire by telephone with an additional 8% and 16%, respectively. Thus, the total response rates for the DAT-3 and DAT-3 Follow-up questionnaires continue to be approximately 97-98%.

D. Characteristics of enrolled women and compliance with the PPP

Data for the DAT-1 and DAT-2 questionnaires are presented in Tables 3 through 10. Explanations of the changes in the format of Table 5, Pregnancy Risk Category at DAT-1, and Table 8, Contraceptive Status and Primary Method at DAT-1, were provided in the report for April through June, 1995; changes in the format of Table 10, Pregnancy Risk Category at DAT-2, were explained in the report for July through September, 1996 (NB: In that report, we mistakenly included the previous format for Table 10, which should be disregarded). In the following, we discuss only those data that we judged to warrant particular attention.

Table 4 presents past treatments for acne. In our recent reports, we noted a decrease in the proportion of women reporting prior use of Retin-A. For the current quarter compared with the

earlier time periods, we again note a decrease in this proportion (68%, 72%, and 77%, for the current quarter, the previous two quarters, and the preceding quarters, respectively). This decrease was not explained by an increase in the use of other topical retinoids. Further examination of aggregate Survey data revealed that Retin-A users (compared with non-users) tended to be younger, to enroll via forms from their physicians, to have higher rates of use of other medications for acne treatment before starting Accutane, and to be more compliant with the PPP; however, these factors varied little over time and do not explain the recent decrease in Retin-A use.

Information on pregnancy testing prior to starting Accutane treatment is presented in Table 6. For the current quarter compared to the previous two quarters and preceding quarters, we note a small increase in the proportion of women who reported that they had not had a pregnancy test before starting (26%, 24%, and 24%, respectively). This decrease in pregnancy testing is accounted for entirely by a small decrease in the proportion reporting having had a serum pregnancy test (53%, 56%, and 56%, for these three time periods respectively).

E. Pregnancy rates

Tables 11 through 13 present pregnancy rates, which include all eligible pregnancies reported among women enrolled through December 31, 1999. Because of continuing quality control, the total number of pregnancies may vary slightly from one report to another; however, in past quarters quality control-related changes have not materially affected pregnancy rates. The median duration of completed Accutane treatments among women enrolled in the Survey remains approximately 140 days, so rates continue to be calculated using the denominator of 1,000 140-day courses of Accutane. (See report for October through December, 1992 for a description of minor differences in the methods used to calculate pregnancy rates in the mail and telephone arms.)

The overall pregnancy rates for the risk period of Accutane use are shown in Table 11; for the 1989 through 1999 cohorts, there were 4.0, 3.6, 3.0, 3.0, 2.7, 2.4, 2.8, 2.7, 2.4, 2.1, and 3.4 pregnancies per 1,000 courses of Accutane, respectively; when expressed as annualized rates, these were 10.3, 9.5, 7.8, 7.7, 7.1, 6.2, 7.4, 7.0, 6.3, 5.6, and 8.9 per 1,000 person-years, respectively (in previous reports, rates were based on 100 person years). The rate for the most recent cohort appears to be higher than most previous cohorts; however, it is based on follow-up for less than 15,000 women, whereas we project that the final cohort will include well over 35,000 women. Further, similar experience with other recent cohorts suggests that the preliminary rate will decrease as more data become available. Indeed, preliminary data for the 1996 cohort also identified a rate of 3.4 based on follow-up of 15,610 women, but when follow-up reached the current total of 35,616 women, the rate declined to 2.7. We cannot predict that the 1996 pattern will repeat for the 1999 cohort, and we will carefully monitor changes in the pregnancy rate, if any, as we accumulate the majority of data for the 1999 cohort.

Pregnancies that begin in the 30 days following discontinuation of Accutane have been considered since the Survey's inception because of the potential risk for exposure associated with this time period (particularly if pregnancy occurs within days of discontinuing Accutane). Pregnancies occurring within 30 days of discontinuation of Accutane are identified as "pregnancies involving *use before conception*," in contrast to the situation of primary concern, in which Accutane exposure occurs *during pregnancy* (i.e., in utero exposure). The rates for pregnancies involving use before conception for the 1989 through 1999 cohorts were 1.3, 1.4, 0.8, 1.0, 0.9, 0.9, 0.9, 0.7, 1.2, 1.0, and 1.1 per 1,000 women, respectively (Table 12). Though recent rates are somewhat higher than for preceding years, the differences could be explained by sampling variation; we will closely monitor these rates in the coming months.

Table 13 presents the pregnancy rates for the 7,862 women in the 1989 through 1998 cohorts who reported using Accutane for one to two years (see report for April through June, 1993 for a description of how pregnancy rates are calculated for women using Accutane for this duration). There were 6, 2, 2, 1, 1, 5, 2, 5, 1, and 2 pregnancies reported in the 1989 through 1998 cohorts, respectively; the pregnancy rates were 6.4, 1.8, 1.9, 1.1, 1.2, 4.4, 1.8, 4.0, 0.8, and 4.1 per 1,000 person-years for the respective cohorts (in earlier reports, rates were based on 100 person years). Since rates are based on very small numbers of pregnancies (6 or fewer), instability in observed rates is not unexpected, and relatively high rates have not been observed in consecutive cohorts. Zero, 2, 0, 1, 0, 2, 2, 0, 0, and 0 pregnancies involving Accutane exposure before conception were reported in the 1989 through 1998 cohorts, respectively.

F. Pregnancy outcomes

The outcomes for pregnancies involving use of Accutane during gestation and those involving use before conception are presented in Tables 14 and 15, respectively. For the 1989 through 1999 cohorts combined, 11% of those women exposed during pregnancy and 39% of those exposed before conception have delivered liveborns, and these proportions have been relatively stable over time.

In our report for January through March, 1996, we noted that we had discontinued the direct examinations of the infants exposed to Accutane or those born of pregnancies involving use before conception and that instead we were concentrating our efforts on obtaining medical records for each infant. Tables 16 and 17 display information on the status of these infants, combining Survey examination results with the results of medical record reviews for those not examined.

Of the 118 infants (including two sets of twins) exposed to Accutane in utero, medical records or examinations were available for 63 (Table 16). Among these 63 infants, no anomalies were noted for 44. Minor anomalies were noted for 11, and major anomalies were noted for 8. Table 17 shows the status of the 127 infants (including two sets of twins) born to women who used Accutane before conception. Medical record reviews or examinations were available for 68 infants. No malformations were identified in 60 infants and minor malformations were

identified in 7. One infant is classified as "other"; the mother reported that her infant died of a metabolic defect at age six months, and the death certificate confirmed that the cause of death was congenital lactic acidemia. There were no major malformations noted in this group.

As indicated in the footnotes for Tables 11 through 15, pregnancies pending confirmation are included in the data presented. When the Survey's Senior Interviewer contacts these women, they sometimes provide more specific information that may change the exposure status of the pregnancy. In addition, improved computer software programs better identify re-enrollments for subsequent courses of Accutane, and this refinement will affect these tables (see report for April through June, 1995).

III. FUTURE ACTIVITIES

We will continue to closely monitor enrollments, re-enrollments, and rates of compliance with the Pregnancy Prevention Program in order to rapidly identify deviations that warrant modification in the Program or in the Sponsor's efforts aimed at encouraging use of the Program and enrollment in the Survey. Particular attention will be paid to changes (and their implications regarding compliance) in doctor-generated enrollments. Further, we will investigate whether the Sponsor's efforts to enhance PPP compliance (e.g., via mailings or sales representatives) correlate with changes in compliance observed in recent quarters.

Working with the Sponsor, we also will consider modifications in the Survey. These modifications will be undertaken in conjunction with changes in the PPP that may result from ongoing discussions involving the Survey staff, the Sponsor, and FDA. Among the changes we anticipate in the Survey are enhancement of the proportion of enrolled subjects and expansion of the number of subjects followed both during and after treatment—the latter intended to provide more statistical power and earlier evidence of changes in PPP compliance that may warrant prompt intervention or modification in the PPP.

IV. ADVISORY COMMITTEE ACTIVITIES

The Advisory Committee met on May 7, 1999. A conference call with the Committee will be scheduled shortly.

V. SUMMARY AND CONCLUSIONS

To date, 494,915 women have enrolled in the Accutane Survey since its inception in January, 1989. Over the past few years, compliance with elements of the Pregnancy Prevention Program has remained high and largely unchanged.

The most critical measure of the PPP is the occurrence of pregnancy, and based on completed follow-up of over 338,000 women, the overall pregnancy rate is 2.8 per 1,000 140-day courses of Accutane. This rate varied from 4.0 to 3.0 between 1989 and 1992, and then decreased from 1993 through 1998, ranging between 2.1 and 2.8. The preliminary rate for the 1999 cohort, while higher than most preceding cohorts, is based on incomplete data; experience with other recent cohorts suggests this rate will decline as more data become available. The general decline in pregnancy rates appears to result from a number of factors: the distribution of women enrolled in the Survey differs from that of the U.S. population in ways that would predict relatively high levels of compliance with the Pregnancy Prevention Program; women in the Survey are disproportionately not sexually active; and those who are sexually active appear to have high degrees of contraceptive compliance and efficacy. Further refinements of the PPP and the associated Survey will be proposed in an effort to enhance pregnancy prevention efforts.

ACCUTANE SURVEY

RECEIPT OF ENROLLMENTS ACCORDING TO SURVEY QUARTER

(Jan 1989 - Jun 2000)

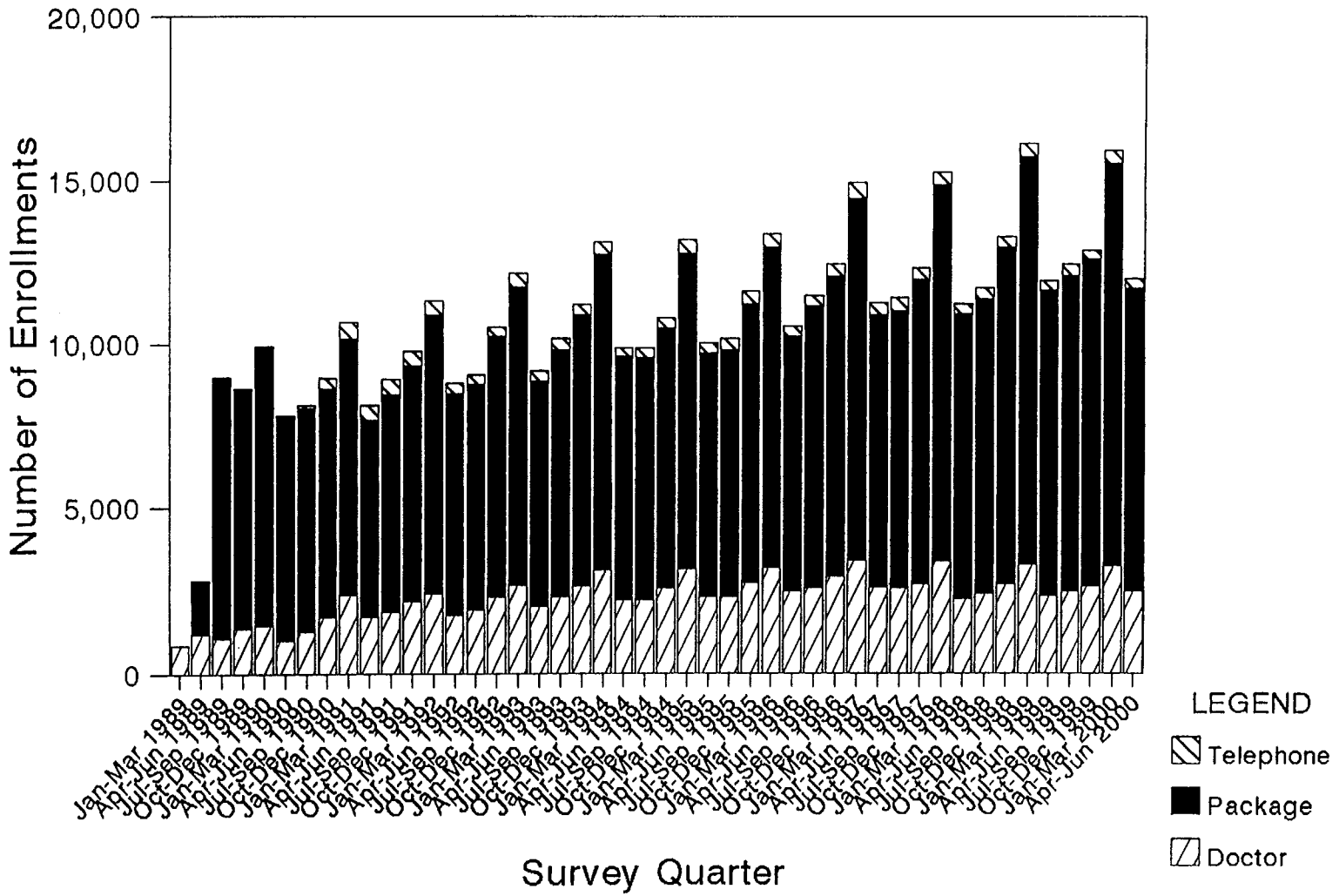


Figure 1

Table 1

Method of Enrollment

	Curr. Q. Apr-Jun 2000 (n=11995)		Prev. 2 Qs. Oct 1999-Mar 2000 (n=28776)		Preceding Qs. Jan 1989-Sep 1999 (n=454144)		Total 1/1/89-6/30/00 (n=494915)	
	N	%	N	%	N	%	N	%
Doctor	2453	20	5809	20	97030	21	105292	21
Package	9264	77	22298	78	343842	76	375404	76
Telephone	278	2	669	2	13272	3	14219	3

Table 2

Age of Enrollees

	Curr. Q. Apr-Jun 2000 (n=11995)	Prev. 2 Qs. Oct 1999-Mar 2000 (n=28776)	Preceding Qs. Jan 1989-Sep 1999 (n=454144)	Total 1/1/89-6/30/00 (n=494915)
Mean, years	25.5	24.9	25.7	25.6
Median, years	23	23	24	24

Table 3

During and After Treatment Arm (DAT-1)

Age at Onset of Acne*

Age (yrs)	Curr. Q Apr-Jun 2000 (n=991) N	%	Prev. 2 Qs. Oct 1999-Mar 2000 (n=2541) N	%	Preceding Qs. Jan 1995-Sep 1999 (n=24512) N	%	Total 1/1/95-6/30/00 (n=28044) N	%
<12	142	14	321	13	3339	14	3802	14
12-15	537	54	1453	57	13313	54	15303	55
16-19	122	12	351	14	3728	15	4201	15
20-24	81	8	174	7	1893	8	2148	8
25-29	46	5	108	4	1005	4	1159	4
30+	63	6	134	5	1234	5	1431	5

*342 women with missing information were excluded.

Table 4

During and After Treatment Arm (DAT-1)

Past Treatments for Acne*

	Curr. Q Apr-Jun 2000 (n=1006)		Prev. 2 Qs. Oct 1999-Mar 2000 (n=2563)		Preceding Qs. Jan 1995-Sep 1999 (n=24817)		Total 1/1/95-6/30/00 (n=28386)	
	N	%	N	%	N	%	N	%
Any antibiotic	927	92	2390	93	22935	92	26252	92
Oral vitamin A	97	10	237	9	2838	11	3172	11
Retin-A	688	68	1849	72	19082	77	21619	76
Benzoyl peroxide	725	72	1843	72	18146	73	20714	73

*Not mutually exclusive.

Table 5

During and After Treatment Arm (DAT-1)

Pregnancy Risk Category[1]

	Curr. Q Apr-Jun 2000 (n=988)		Prev. 2 Qs. Oct 1999-Mar 2000 (n=2540)		Preceding Qs. Jan 1995-Sep 1999 (n=24488)		Total 1/1/95-6/30/00 (n=28016)	
	N	%	N	%	N	%	N	%
Hysterectomy or postmenopausal	40	4	82	3	821	3	943	3
Not sexually active, using birth control[2]	262	26	667	26	6041	25	6970	25
Not sexually active, not using birth control[3]	284	29	742	29	7795	32	8821	32
Sexually active, using birth control[4]	388	39	1017	40	9406	38	10811	39
Sexually active, not using birth control[5]	7	1	8	<1	180	1	195	1
Unknown[6]	7	1	24	1	245	1	276	1

[1]Excludes 370 women who had not yet started Accutane.

[2]Total includes 63 women who reported that they or their partners were infertile.

[3]Total includes 63 women who reported that they or their partners were infertile.

[4]Total includes 336 women who reported that they or their partners were infertile.

[5]Total includes 75 women who reported that they or their partners were infertile.

[6]Total includes 9 women who reported that they or their partners were infertile.

Table 6

During and After Treatment Arm (DAT-1)

Compliance with Selected Measures of the PPP*

	Curr. Q. Apr-Jun 2000 (n=1006) % Yes	Prev. 2 Qs. Oct 1999-Mar 2000 (n=2563) % Yes	Preceding Qs. Jan 1995-Sep 1999 (n=24817) % Yes	Total 1/1/95-6/30/00 (n=28386) % Yes
Told to avoid pregnancy	99	99	99	99
Signed consent form	79	80	77	77
Postponed Accutane until results of pregnancy test known†	65	68	67	67
Postponed Accutane until next menstrual period†	58	58	57	57

*Not mutually exclusive.

†1313 women who had not yet started Accutane or who were identified as posthysterectomy or postmenopausal were excluded.

Table 7

During and After Treatment Arm (DAT-1)

Number of Women Who Reported Having a Pregnancy Test Before Starting Accutane*

	Curr. Q. Apr-Jun 2000 (n=948)		Prev. 2 Qs. Oct 1999-Mar 2000 (n=2458)		Preceding Qs. Jan 1995-Sep 1999 (n=23667)		Total 1/1/95-6/30/00 (n=27073)	
	N	%	N	%	N	%	N	%
Serum pregnancy test	506	53	1369	56	13209	56	15084	56
Urine pregnancy test	94	10	231	9	2180	9	2505	9
Serum and urine pregnancy tests	77	8	179	7	1850	8	2146	8
Any pregnancy test†	702	74	1848	75	17793	75	20343	75
No pregnancy test	243	26	603	24	5682	24	6528	24
Unknown	3	<1	7	<1	192	1	202	1

*1313 women who had not yet started Accutane or who were identified as posthysterectomy or postmenopausal were excluded.

†Included in this category are 608 women who responded that they had a pregnancy test but were uncertain of the type of test; these women are not included in the preceding categories. See report for Jul-Sep 1995 for comment.

Table 8

During and After Treatment Arm (DAT-1)

Contraceptive Status and Primary Method
According to Age Group*

	Age 15-24				Age 25-34				Age 35-44			
	1** (n= 438) %	2** (n= 1261) %	3** (n= 12002) %	4** (n= 13701) %	1** (n= 270) %	2** (n= 712) %	3** (n= 6856) %	4** (n= 7838) %	1** (n= 188) %	2** (n= 340) %	3** (n= 3646) %	4** (n= 4174) %
Surgically sterile	1	1	1	1	24	22	22	22	58	56	59	58
Female	<1	1	<1	1	15	14	12	12	32	32	35	34
Male	<1	<1	<1	<1	10	8	10	10	26	24	24	24
Nonsurgically sterile†	0	<1	<1	<1	1	0	<1	<1	<1	1	2	2
Nonuser	42	40	44	44	10	11	13	12	9	8	8	8
Not sexually active	42	40	44	44	9	10	12	12	8	8	8	8
Sexually active	<1	<1	<1	<1	1	1	<1	<1	<1	0	<1	<1
Nonsurgical contraceptors	57	58	54	55	64	67	65	65	31	35	31	32
Norplant or Depo-Provera injection	2	3	4	4	3	3	4	4	3	2	1	1
Pill	46	46	40	40	47	51	44	45	16	17	16	16
IUD	0	<1	<1	<1	1	2	1	1	3	2	2	2
Diaphragm	<1	<1	<1	<1	1	1	2	1	2	2	3	3
Condoms	2	4	5	5	8	7	10	9	5	9	8	7
Rhythm/natural family planning	0	<1	<1	<1	<1	<1	<1	<1	<1	1	1	1
Other methods	6	4	5	5	3	3	4	4	2	2	3	3
Unknown method	<1	<1	<1	<1	1	<1	<1	<1	0	0	<1	<1
Unknown	0	1	<1	<1	0	0	<1	<1	<1	<1	<1	<1

*Primary method determined using adaption of the schema of the National Survey of Family Growth (NCHS, March 20, 1990). 361 women who had not yet started Accutane were excluded.

**1 = Current Quarter (Apr-Jun 2000)
2 = Previous 2 Quarters (Oct 1999-Mar 2000)
3 = Preceding Quarters (Jan 1995-Sep 1999)
4 = Total (1/1/95-6/30/00)

†Defined as self-report of postmenopausal status or infertility in respondent or partner. Excludes women using contraception.

Table 9

During and After Treatment Arm (DAT-2)

Pregnancy Testing During Accutane Treatment

	Enrollment Quarter			Total
	Jan-Mar 2000 (n=1522) %	Jul-Dec-1999 (n=2286) %	Jan 1995-Jun 1999 (n=22794) %	1/1/95-3/31/00 (n=26602) %
Any pregnancy test	60	60	60	60
One	8	7	8	8
Two +	51	52	51	51
Unknown number	1	1	1	1
No pregnancy test	39	40	39	39
Unknown	1	1	1	1

Table 10

During and After Treatment Arm (DAT-2)

Pregnancy Risk Category

	Enrollment Quarter			
	Jan-Mar 2000 (n=1522) %	Jul-Dec-1999 (n=2286) %	Jan 1995-Jun 1999 (n=22794) %	Total 1/1/95-3/31/00 (n=26602) %
Hysterectomy or postmenopausal	3	4	3	3
Not sexually active, using birth control	24	21	21	22
Not sexually active, not using birth control	28	30	29	29
Sexually active, using birth control	44	43	44	44
Sexually active, not using birth control	1	1	1	1
Unknown	1	2	2	2

Table 11

Pregnancy Rate According to Year of Enrollment
Risk Period: Accutane Course

	1989 Cohort[1]	1990 Cohort[2]	1991 Cohort[3]	1992 Cohort[4]	1993 Cohort[5]	1994 Cohort[6]	1995 Cohort[7]	1996 Cohort[8]	1997 Cohort[9]	1998 Cohort[10]	1999 Cohort[11]	Total
N	18294	30255	32228	33061	34110	34161	35093	35616	36226	35013	14902	338959
Pregnancies reported[12]	74	109	96	98	94	84	105	104	96	81	51	992
Person-years of Accutane exposure	7153	11463	12287	12676	13278	13470	14210	14777	15167	14508	5726	134715
Rate/1000 140-day courses of Accutane	4.0	3.6	3.0	3.0	2.7	2.4	2.8	2.7	2.4	2.1	3.4	2.8

[1]Excludes 900 women who reported use ≥ 1 year.

[2]Excludes 1109 women who reported use ≥ 1 year.

[3]Excludes 1059 women who reported use ≥ 1 year.

[4]Excludes 846 women who reported use ≥ 1 year.

[5]Excludes 762 women who reported use ≥ 1 year.

[6]Excludes 958 women who reported use ≥ 1 year.

[7]Excludes 945 women who reported use ≥ 1 year.

[8]Excludes 1019 women who reported use ≥ 1 year.

[9]Excludes 1043 women who reported use ≥ 1 year.

[10]Excludes 422 women who reported use ≥ 1 year.

[11]Excludes 30 women who reported use ≥ 1 year.

[12]Includes reports of pregnancies pending confirmation.

Table 12

Pregnancy Rate According to Year of Enrollment
Risk Period: 30 Days Following Accutane Treatment

	1989 Cohort[1]	1990 Cohort[2]	1991 Cohort[3]	1992 Cohort[4]	1993 Cohort[5]	1994 Cohort[6]	1995 Cohort[7]	1996 Cohort[8]	1997 Cohort[9]	1998 Cohort[10]	1999 Cohort[11]	Total
N	18294	30255	32228	33061	34110	34161	35093	35616	36226	35013	14902	338959
Pregnancies reported[12]	23	41	26	34	31	30	32	25	44	36	16	338
Rate/1000 enrollees	1.3	1.4	0.8	1.0	0.9	0.9	0.9	0.7	1.2	1.0	1.1	1.0

[1]Excludes 900 women who reported use ≥ 1 year.

[2]Excludes 1109 women who reported use ≥ 1 year.

[3]Excludes 1059 women who reported use ≥ 1 year.

[4]Excludes 846 women who reported use ≥ 1 year.

[5]Excludes 762 women who reported use ≥ 1 year.

[6]Excludes 958 women who reported use ≥ 1 year.

[7]Excludes 945 women who reported use ≥ 1 year.

[8]Excludes 1019 women who reported use ≥ 1 year.

[9]Excludes 1043 women who reported use ≥ 1 year.

[10]Excludes 422 women who reported use ≥ 1 year.

[11]Excludes 30 women who reported use ≥ 1 year.

[12]Includes reports of pregnancies pending confirmation.

Table 13

Pregnancy Rate Among Women on Accutane 1-2 Years*

	1989 Cohort	1990 Cohort	1991 Cohort	1992 Cohort	1993 Cohort	1994 Cohort	1995 Cohort	1996 Cohort	1997 Cohort	1998 Cohort	Total
N	722	847	821	695	679	876	850	947	1017	408	7862
Pregnancies reported - during Accutane treatment**	6	2	2	1	1	5	2	5	1	2	27
- in 30 days following Accutane treatment**	0	2	0	1	0	2	2	0	0	0	7
Person-years of Accutane exposure after 12/31/88	933	1079	1071	928	865	1139	1093	1240	1293	483	9641
Rate/1000 person-years for risk period of Accutane treatment	6.4	1.8	1.9	1.1	1.2	4.4	1.8	4.0	0.8	4.1	2.8

*See previous report for explanation of change in method of rate calculation.

**Includes reports of pregnancies pending confirmation.

Table 14

Outcome of Pregnancies Exposed During Accutane Treatment*

	1989 Cohort (n=80)		1990 Cohort (n=111)		1991 Cohort (n=98)		1992 Cohort (n=99)		1993 Cohort (n=95)		1994 Cohort (n=89)		1995 Cohort (n=107)		1996 Cohort (n=109)		1997 Cohort (n=97)		1998 Cohort (n=83)		1999 Cohort (n=51)		Total (n=1019)	
Therapeutic abortion	65	(81%)	83	(75%)	60	(61%)	69	(70%)	62	(65%)	55	(62%)	69	(64%)	69	(63%)	65	(67%)	54	(65%)	30	(59%)	681	(67%)
Spontaneous abortion	7	(9%)	17	(15%)	20	(20%)	20	(20%)	17	(18%)	12	(13%)	16	(15%)	21	(19%)	16	(16%)	19	(23%)	12	(24%)	177	(17%)
Ectopic pregnancy	2	(2%)	3	(3%)	5	(5%)	3	(3%)	1	(1%)	3	(3%)	4	(4%)	3	(3%)	2	(2%)	1	(1%)	2	(4%)	29	(3%)
Stillbirth	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---
Livebirth	4	(5%)	7	(6%)	13	(13%)	7	(7%)	12	(13%)	17	(19%)	16	(15%)	14	(13%)	13	(13%)	9	(11%)	5	(10%)	117	(11%)
Pregnancy continuing	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---
Unknown†	2	(2%)	1	(1%)	0	---	0	---	3	(3%)	2	(2%)	2	(2%)	2	(2%)	1	(1%)	0	---	2	(4%)	15	(1%)

*Includes reports of pregnancies pending confirmation.

†Includes pregnancies pending follow-up or lost to follow-up.

Table 15

Outcome of Pregnancy Among Women Who Conceived
Within 30 Days of Stopping Accutane Treatment*

	1989 Cohort (n=23)		1990 Cohort (n=43)		1991 Cohort (n=26)		1992 Cohort (n=35)		1993 Cohort (n=31)		1994 Cohort (n=32)		1995 Cohort (n=34)		1996 Cohort (n=25)		1997 Cohort (n=44)		1998 Cohort (n=36)		1999 Cohort (n=16)		Total (n=345)	
Therapeutic abortion	14	(61%)	23	(53%)	14	(54%)	22	(63%)	13	(42%)	17	(55%)	15	(43%)	8	(32%)	13	(30%)	16	(44%)	3	(19%)	158	(46%)
Spontaneous abortion	2	(9%)	7	(16%)	2	(8%)	2	(6%)	6	(19%)	1	(3%)	4	(11%)	3	(12%)	6	(14%)	4	(14%)	1	(6%)	38	(11%)
Ectopic pregnancy	1	(4%)	1	(2%)	1	(4%)	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	3	(1%)
Stillbirth	0	---	0	---	0	---	0	---	0	---	0	---	1	(3%)	0	---	0	---	0	---	0	---	1	(<1%)
Livebirth	6	(26%)	11	(26%)	8	(31%)	10	(28%)	12	(39%)	12	(35%)	12	(34%)	14	(56%)	25	(57%)	16	(42%)	9	(56%)	135	(39%)
Pregnancy continuing	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	0	---	1	(6%)	1	(<1%)
Unknown†	0	---	1	(2%)	1	(4%)	1	(3%)	0	---	2	(6%)	2	(6%)	0	---	0	---	0	---	2	(12%)	9	(3%)

*Includes reports of pregnancies pending confirmation.

†Includes pregnancies pending follow-up or lost to follow-up.

Table 16

Status of Infants Born to Women
Exposed to Accutane After Conception (In Utero)

Number eligible*		118
Medical records status		
Refused**		49
Pending		6
Obtained		63
Examinations completed***		13
Results of medical record review/examinations		
No malformation		44
Minor malformation		11
Ear anomaly	2	
Hypoplastic scrotum	1	
Ear and craniofacial anomalies	2	
Craniofacial anomaly	1	
Mongolian spots	1	
Bilateral inguinal hernias	1	
Mild developmental delay	1	
Mild hydronephrosis on prenatal ultrasound	1	
Vesicoureteral reflux on prenatal ultrasound	1	
Major malformation		8
Ear, eye, craniofacial, and brain anomalies	1	
Ear and craniofacial anomalies	1	
Ear, eye, and heart anomalies	1	
Eye and brain anomalies	1	
? Deafness	1	
Ear, brain, and heart anomalies	1	
Brain and heart (deceased)	1	
Cystic kidney and hypospadias (also intrauterine growth retardation)	1	
Number with any malformations/number examined or with medical record review		19/63
Number with major malformations/number examined or with medical record review		8/63

*Includes 2 sets of twins: 1 normal, 1 minor kidney anomaly.
**Includes 1 death: maternal report of major birth defects.
***See text for explanation.

Table 17

Status of Infants Born to Women
Who Used Accutane Before Conception
(i.e., Conception Occurring in the 30 Days Following
Discontinuation of Accutane)

Number eligible*		137
Medical records status		
Refused**		54
Pending		15
Obtained		68
Examinations completed***		15
Results of medical record review/examinations		
No malformation		60
Minor malformation		7
Ear anomaly	1	
Craniofacial anomaly	2	
? Femoral anteversion	1	
Hydrocele	1	
Functional murmur, no follow-up required	1	
Murmur	1	
Major malformation		0
Other		1
Metabolic defect (deceased)	1	
Number with any malformations/number examined or with medical record review		7/68
Number with major malformations/number examined or with medical record review		0/68

*Includes 2 sets of twins: 3 normal, 1 minor ear anomaly.
**Includes one death: maternal report of complications from prematurity.
***See text for explanation.

Matching of Accutane Users:

A Collaborative Study Conducted by
The Slone Epidemiology Unit of Boston University
And Applied HealthCare Informatics at United HealthCare

July 1998

Matching of Accutane Users

Because the Survey of Accutane Users is voluntary, it has been recognized from the outset that enrollment will be incomplete. To estimate the proportion and characteristics of Accutane users who enroll in the Survey, the Slone Epidemiology Unit (SEU) contracted with United Health Care to identify a cohort of women who filled at least one prescription for Accutane between January 1990 and June 1996, and to determine the degree to which these Accutane users could be matched to participants in the SEU's Survey of Accutane Use in Women. Using an unusual blinding technique, researchers at SEU and at United HealthCare's Applied HealthCare Informatics were able to match individuals with relative confidence using only limited member and provider characteristics from the claims and SEU databases, thereby preserving member and Survey confidentiality. The study was approved by the Boston University Medical Center Institutional Review Board.

Methodology

All women who were enrolled in one of 14 United HealthCare fee-for-service IPA[1] health plans, covering the northeast, southeast, and midwest, who had filled a prescription for Accutane between 1/1/90 and 6/30/96 were eligible study subjects. Women who were not between the ages of 12 and 59 at their first Accutane prescription were excluded. The following data were abstracted: 1) Year of member birth, 2) Month of member birth, 3) Day of member birth, 4) Member's first name, 5) Member's first initial of last name, 6) Accutane fill dates, 7) Name of prescribing physician, 8) Member house number, and 9) Member zip code. SEU abstracted the same data elements from their Accutane Survey, except that dates of Accutane use were substituted for prescription fill dates. No written information was exchanged. Researchers at each site conducted the matching process on each of these variables. For each study subject identified by United HealthCare, researchers assigned one of four match values: 'definite match,' 'definite non-match,' 'other treatment,' and 'undetermined,' as defined by Carla Van Bennekom at SEU. "Definite match" was assigned when variables matched sufficiently to be confident of the match. "Definite

[1] Individual practice association model HMO

non-match" was assigned when variables did not match or did not match sufficiently to suggest a match. "Other treatment" was assigned when the UHC fill dates did not overlap with the survey dates of Accutane use, but other variables matched; this situation suggests that the woman had multiple Accutane treatments, though the survey treatment did not match the UHC treatment. "Undetermined" was assigned when some variables matched, but the matching information was insufficient to provide confidence that the subjects matched. Matching results were then imported into the United HealthCare study database and analyzed by the following variables: 1) Age at first Accutane prescription, 2) Year of first Accutane prescription, 3) Length of health plan enrollment prior to first Accutane prescription, 4) Duration of Accutane therapy, 5) Policy subscriber status, 6) Specialty of prescribing physician, and 7) Contraceptive use.

Results

A total of 5095 women between the ages of 12 and 59 had filled prescriptions for Accutane between 1/1/90 and 6/30/96. Table 1 summarizes this study population by plan membership and match status. Plans 11, 5, 1, 14, and 12 contributed 20%, 14%, 13%, 12% and 10% respectively of all subjects.

Of the 5095 women identified in the 14 plans, 1955 (38.4%) were determined to be definite matches to the SEU database. As shown in Table 1, 2758 (54.1%) were unmatched to the SEU database, and the remaining 382 (7.5%) were possible matches (those with either other treatment or undetermined match status). Rates of matching varied across plans. For non-matches, it ranged from 29.4% (Plan 7) to 69.2% (Plan 2); for plans with at least 300 Accutane users (with more stable estimates), non-matches ranged from 46.9% (Plan 4) to 61.3% (Plan 5).

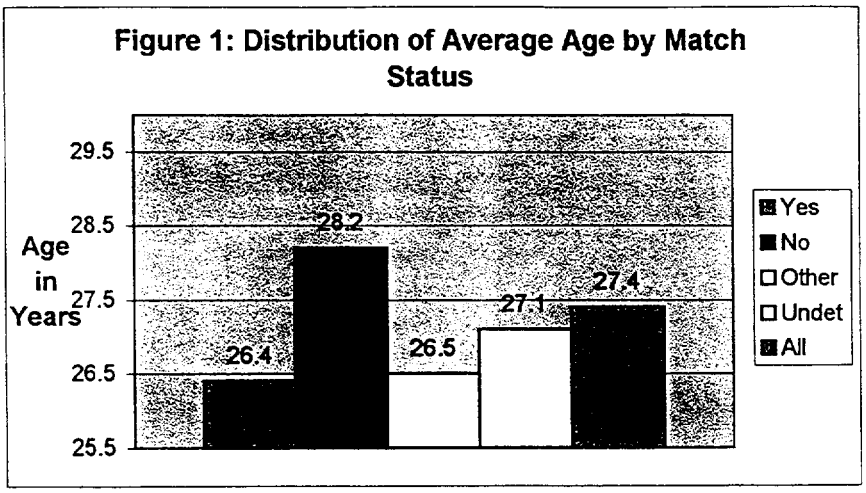
TABLE 1: PLAN BY MATCH STATUS

PLAN	YES		NO		OTHER		UNDET		ALL
	No.	%	No.	%	No.	%	No.	%	
1	204	30.7%	407	61.3%	36	5.4%	17	2.6%	664
2	19	29.2%	45	69.2%	1	1.5%	—		65
3	1	16.7%	4	66.7%	—		1	16.7%	6
4	120	37.7%	149	46.9%	35	11.0%	14	4.4%	318
5	237	32.1%	453	61.3%	39	5.3%	10	1.4%	739
6	94	35.9%	146	55.7%	17	6.5%	5	1.9%	262
7	24	70.6%	10	29.4%	—		—		34
8	20	42.6%	25	53.2%	—		2	4.3%	47
9	124	42.5%	155	53.1%	7	2.4%	6	2.1%	292
10	22	40.0%	27	49.1%	3	5.5%	3	5.5%	55
11	438	42.7%	507	49.5%	59	5.8%	21	2.0%	1025
12	217	40.9%	286	54.0%	17	3.2%	10	1.9%	530
13	201	44.4%	220	48.6%	24	5.3%	8	1.8%	453
14	234	38.9%	324	53.8%	37	6.1%	10	1.7%	605
ALL	**1955**	**38.4%**	**2758**	**54.1%**	**275**	**5.4%**	**107**	**2.1%**	**5095**

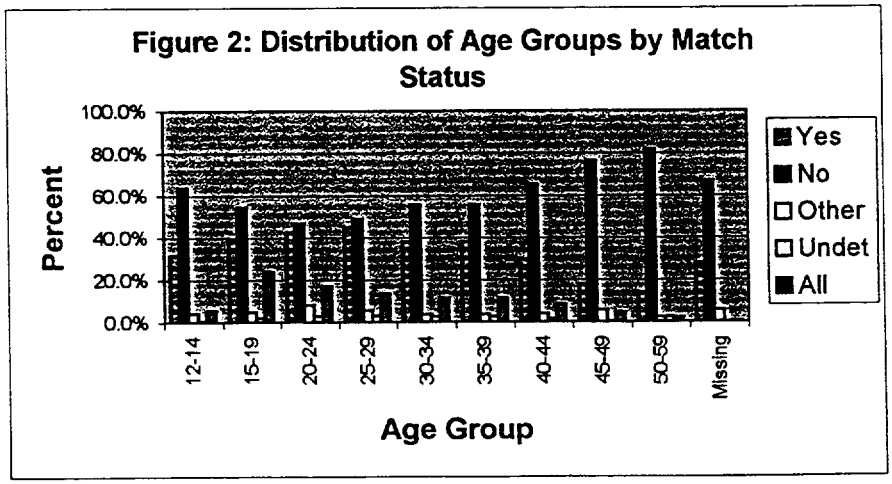
Because several of the plans have fewer than 100 members represented, only data on the combined plans will be presented and discussed with regard to the variables of interest in this report. The plan specific data are presented in Appendix A.

1) Match Status by Age

Age was calculated using the time of the first Accutane fill date. Average age of all study subjects was 27.4 and there was very little difference in the average ages for each match status across all 14 plans (Figure 1). Definite matches had an average age of 26.4 and definite non-matches had an average age of 28.2, a difference of 1.8 years. Those with a match status of 'other' had an average age of 26.5, and women with undetermined match status had an average age of 27.1. A total of 0.4% of the entire data set is missing data on age, with 12 missing from Plan 1 and six missing from Plan 12. (See Table 1A in Appendix A.) These women had been identified in an earlier study and we were unable to recapture their initial enrollment dates.



Match status was also analyzed within narrowly defined age groups. Figure 2 summarizes the distribution within these age groups by match status. Although, on average, women were in their late twenties at the time of first Accutane prescription, the largest proportion of women (23.8%) fell into the 15-19 year age group, with the 20-24 year age group as the second largest (17.1%). Match status varied appreciably with age at the time of first Accutane prescription. The highest match rates are in the 20-24 and 25-29 year age groups, with 42.7% and 45.1% definite matches, respectively. The lowest match rates are in the 45-49 and 50-59 year age groups, with 17.9% and 14.0% definite matches, respectively. (For data on age groups by match status by Plan, see Table 2A in Appendix A.)



2) Rate of Accutane Use

Table 2 summarizes the rate of Accutane use within each plan, across all match categories. The numerator was defined as all women between the ages of 12 and 59 enrolled in one of the 14 health plans who had filled a prescription for Accutane between 1/1/90 and 6/30/96. The denominator was defined as all women between the ages of 12 and 59 enrolled in the 14 health plans over the same time period. The overall prevalence rate of Accutane use is .0040 among women between the ages of 12 and 59 in 14 UHC health plans.

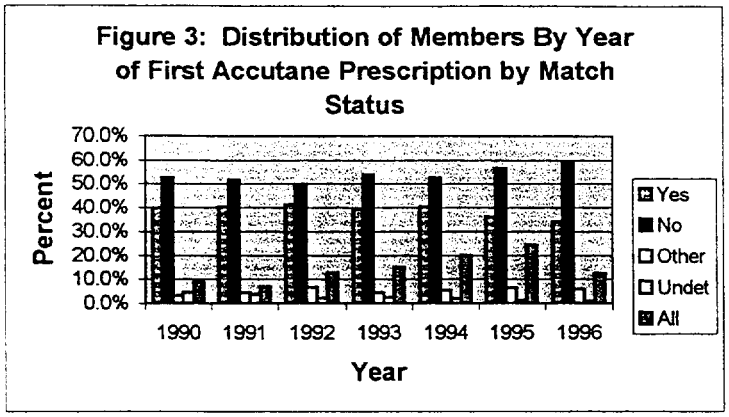
TABLE 2: RATE OF ACCUTANE USE BY PLAN

PLAN	Rate of Accutane Use
1	.0056
2	.0017
3	.0006
4	.0021
5	.0059
6	.0034
7	.0019
8	.0026
9	.0054
10	.0026
11	.0031
12	.0046
13	.0068
14	.0049
ALL	**.0040**

3) Match Status by Year of First Accutane Prescription

Figure 3 summarizes the year of first Accutane prescription in this study population and match status. The number of definite matches was relatively stable between 1990 and 1994, and decreased from 1994 to 1996. This decline was not due to a change in the number of questionable matches, but due to an increase in the number of confirmed non-matches. This study design did not permit us to assess whether characteristics of the women changed over time; the data have been archived, so another study could be undertaken to investigate this question. (The percent of other and undetermined matches was 7.3% in

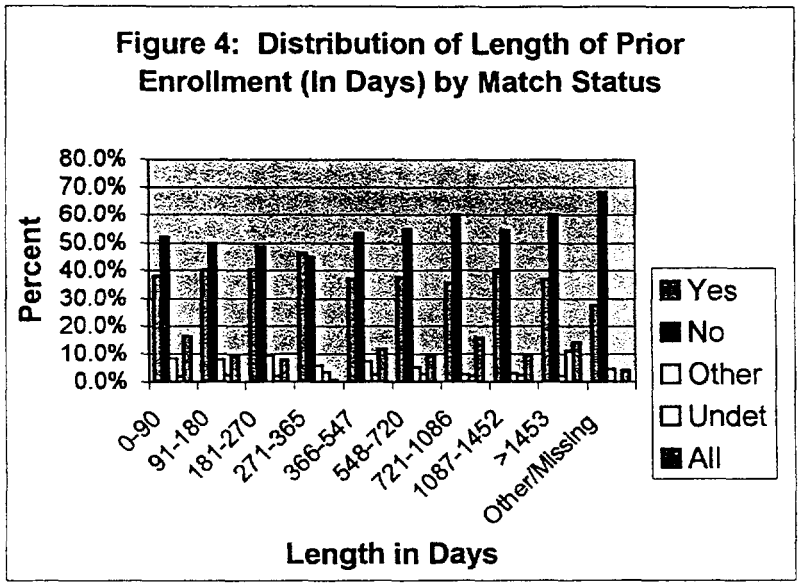
1994, 7.7% in 1995, and 6.9% in 1996, while the number of definite non-matches increased steadily from 52.5% in 1994 to 56.5% in 1995, and 59.1% in 1996.) (For data on year of first Accutane prescription by match status by plan, see Table 3A in Appendix A.)



4) Match Status by Length of Prior Enrollment

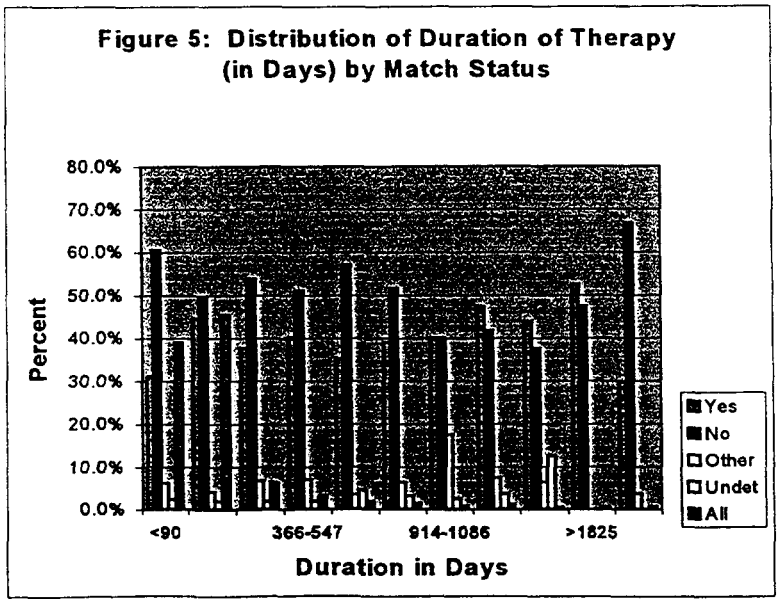
Match status was analyzed by length of prior membership in a health plan (Figure 4). It was hypothesized that women who had been enrolled with UHC for a short time prior to their Accutane treatment may have started Accutane therapy while covered by another insurance carrier, thereby reducing the likelihood of a definite match. Length of prior enrollment is defined as the number of days that a woman carried United HealthCare coverage prior to her first Accutane prescription. The largest proportion of women (16.3%) in our study population were enrolled in one of the 14 plans for 0-90 days before filling their first Accutane prescriptions. The fewest members (7.0%) were enrolled for 217-365 days prior to filling a prescription for Accutane. Overall match status varied little by length of prior enrollment, with definite matches ranging from a high of 46.2% in the 217-365 day category to a low of 35.6% in the 721-1086 day category[2]. (For data on length of prior enrollment by match status by plan, see Table 4A in Appendix A.)

[2] Four women fell into the category of 'other' due to lengths of enrollment of less than zero days. A total of 18 (0.4%) women who had been identified in an earlier study were missing data on length of prior enrollment, as we were unable to recapture their initial enrollment dates.



5) Match Status by Duration of Accutane Therapy

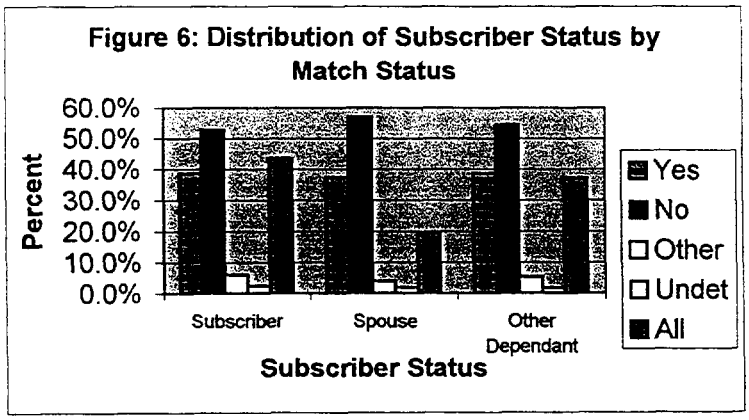
Figure 5 summarizes duration of Accutane therapy in days by match status. Overall, the largest proportion of women received Accutane therapy for six months or less. Duration of Accutane therapy in days appears to have minimal influence on match status. The highest definite match rates were found in women using Accutane for the longest durations, while the lowest definite match rate was found in



women using Accutane for three months or less. (For data on duration of therapy by plan match status, see Table 5A in Appendix A.)

6) Match Status by Subscriber Status

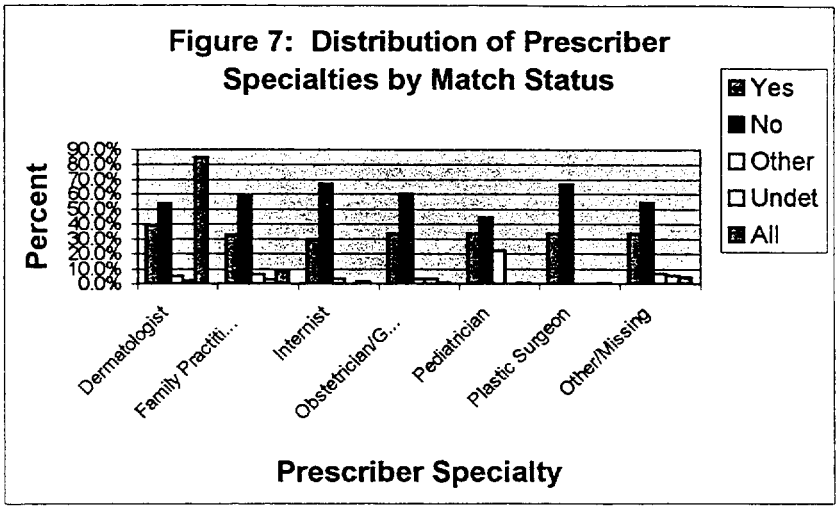
Member subscriber status was compared by match status as a possible indicator of problems with the matching process. A member may be a subscriber, a spouse or a dependent on the United HealthCare policy. The dependent status reflects children of the subscriber who may be covered on the UHC policy typically until they turn 24 if they are full-time students or until they turn 19 if they are not full-time students. Figure 6 summarizes subscriber status of this study population by match status, which varied minimally. (For data on subscriber status by plan by match status, see Table 6A in Appendix A.)



7) Match Status by Prescriber Specialty

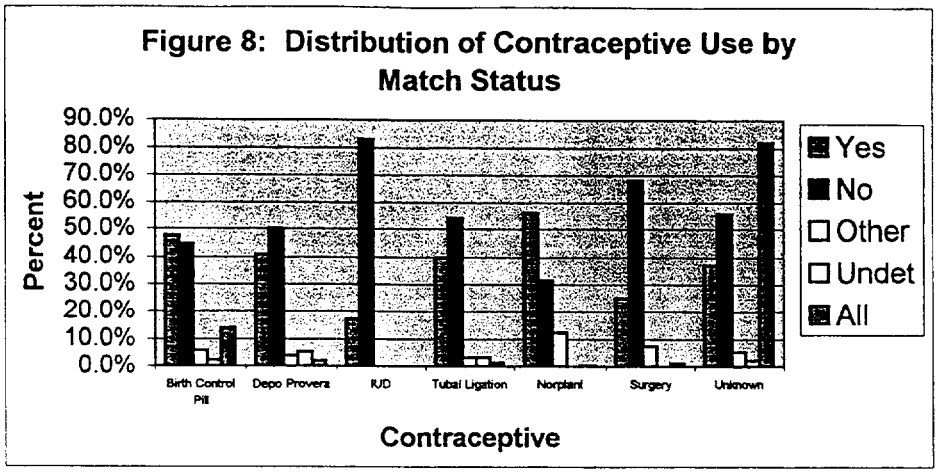
Match status was compared according to prescriber specialties (Figure 7). By far, the majority of prescriptions were written by dermatologists, with a total of 4298 (84.8%). In contrast, pediatricians wrote the fewest number of prescriptions for Accutane in this population, with a total of 9 (0.2%). Match status was almost constant across all prescriber specialties, with definite matches ranging from 39.4% to 29.5%. Finally, a total of 193 (3.8%) women had either missing data or their prescriptions were from other

prescriber specialties. (For data on prescriber specialty by match status by plan, see Table 7A in Appendix A).



8) Match Status by Selected Contraceptive Use

Contraceptive use was analyzed according to match status using only claims data (Figure 8). The vast majority of women (81.8%) fell into the category of "unknown", indicating that either 1) they do not use prescription birth control methods or 2) they went through a different provider or plan for birth control or 3) did not have health plan coverage for prescription contraceptives. In addition, we did not look at rates of vasectomy in these women's partners. Among those for whom we had information, birth control pills were used by 77%; the portion of definite matches among pill users was 47.4%. However, because the large proportion (82%) of women did not have information on their contraceptive status or method (because of the serious limitations noted above), matching according to contraceptive status or method cannot be accomplished in these data.. (For data on contraceptive use by match status by plan, see Table 8A in Appendix A).



Summary

A total of 5095 women between the ages of 12 and 59 filled at least one prescription for Accutane between 1/1/90 and 6/30/96. Roughly 38% were determined to be definite matches to the SEU database. An additional 7.5% were possible matches but could not be confirmed with certainty. Age appeared to influence the likelihood of matching, with older women matching less frequently. Other characteristics, including year of first Accutane prescription, length of prior enrollment in UHC plan, duration of therapy, subscriber status, and prescriber specialty, were found to have little influence. Contraceptive use could not be interpreted due to limited information on contraceptive use in the claims database.

Addendum – Follow-up to Pilot Matching Study

Matching of Plans 1 and 12 was originally conducted as a pilot phase to test the feasibility of the matching process. For matching, SEU restricted its database to records of women in the broad geographic area of these UHC plans. Because of concerns that matching might be underestimated because of participants moving out of those geographic areas, an additional study was conducted to estimate the magnitude of this problem. A sample of 100 women (50 each from Plans 1 and 12) that had originally been unmatched was re-examined using only the original identifiers to maintain comparability. For this study, SEU used its complete database of all women enrolled in the Survey; the database was sorted geographically

according to the area covered by a specific UHC plan to improve efficiency. There were two additional definite matches in Plan 1 and one additional definite match and one undetermined match in Plan 12. This suggests that the match rate may have been underestimated slightly because of the geographically restricted database used in the pilot phase. (SEU used the complete database with geographic sorting for the matching of the other 12 plans.)

Appendix A

TABLE 1A: AVERAGE AGE BY MATCH BY PLAN

PLAN	YES	NO	OTHER	UNDET	ALL
1	27.7*	29.6**	27.3***	31.2	28.9
2	24.3	30.7	22.0	----	28.7
3	22.0	21.0	----	47.0	25.5
4	26.0	27.5	25.7	27.0	26.7
5	25.4	27.7	27.4	23.0	26.9
6	28.3	28.4	27.9	26.4	28.3
7	25.7	27.8	----	----	26.3
8	23.9	30.2	----	16.5	27.0
9	26.6	29.1	19.1	27.7	27.8
10	22.0	25.7	19.3	25.0	23.9
11	27.3	29.3	26.2	27.1	28.3
12	27.0^	27.5^^	26.6	29.4	27.3
13	23.1	24.1	23.0	22.0	23.6
14	26.9	28.1	29.4	26.4	27.7
ALL	**26.4**	**28.2**	**26.5**	**27.1**	**27.4**

* 3 missing. ** 8 missing. *** 1 missing.
^ 2 missing. ^^ 4 missing.

TABLE 2A: AGE GROUPS BY MATCH BY PLAN

Plan	Match	12-14	15-19	20-24	25-29	30-24	35-39	40-44	45-49	50-59	MISSING
1	YES	5 18.5%	39 36.8%	34 36.6%	40 36.4%	33 26.6%	26 27.1%	20 32.3%	4 13.8%	----	3 25.0%
	NO	21 77.8%	62 58.5%	46 49.5%	63 57.3%	78 62.9%	61 63.5%	39 62.9%	24 82.8%	5 100%	8 66.7%
	OTHER	----	3 2.8%	11 11.8%	7 6.4%	7 5.6%	4 4.2%	1 1.6%	1 3.4%	----	1 8.3%
	UNDET	1 3.7%	2 1.9%	2 2.2%	----	6 4.8%	5 5.2%	2 3.2%	----	----	----
	ALL	27 4.1%	106 16.0%	93 14.0%	110 16.6%	124 18.7%	96 14.5%	62 9.3%	29 4.4%	5 0.8%	12 1.8%
2	YES	1 25.0%	9 56.3%	3 23.1%	----	1 16.7%	4 40.0%	----	1 11.1%	----	----
	NO	3 75.0%	7 43.8%	9 69.2%	1 100%	5 83.3%	6 60.0%	5 100%	8 88.9%	1 100%	----
	OTHER	----	----	1 7.7%	----	----	----	----	----	----	----
	UNDET	----	----	----	----	----	----	----	----	----	----
	ALL	4 6.2%	16 24.6%	13 20.0%	1 1.5%	6 9.2%	10 15.4%	5 7.7%	9 13.8%	1 1.5%	----
3	YES	----	----	1 100%	----	----	----	----	----	----	----
	NO	2 100%	1 100%	----	----	----	----	1 100%	----	----	----
	OTHER	----	----	----	----	----	----	----	----	----	----
	UNDET	----	----	----	----	----	----	----	1 100%	----	----
	ALL	2 33.3%	1 16.7%	1 16.7%	----	----	----	1 16.7%	1 16.7%	----	----
4	YES	3 21.4%	36 40.0%	20 37.7%	20 54.1%	15 34.9%	11 32.4%	12 40.0%	3 20.0%	----	----
	NO	9 64.3%	37 41.1%	23 43.4%	13 35.1%	24 55.8%	20 58.9%	12 40.0%	9 60.0%	2 100%	----
	OTHER	1 7.1%	12 13.3%	9 17.0%	3 8.1%	2 4.7%	1 2.9%	4 13.3%	3 20.0%	----	----
	UNDET	1 7.1%	5 5.6%	1 1.9%	1 2.7%	2 4.7%	2 5.9%	2 6.7%	----	----	----
	ALL	14 4.4%	90 28.3%	53 16.7%	37 11.6%	43 13.5%	34 10.7%	30 9.4%	15 4.7%	2 0.6%	----
5	YES	17 27.4%	62 29.7%	59 44.7%	29 45.3%	22 32.8%	26 37.1%	14 21.5%	4 8.7%	4 16.7%	----
	NO	43 69.4%	135 64.6%	61 46.2%	29 45.3%	38 56.7%	40 57.1%	49 75.4%	38 82.6%	20 83.3%	----
	OTHER	2 3.2%	8 3.8%	9 6.8%	6 9.4%	5 7.5%	3 4.3%	2 3.1%	4 8.7%	----	----
	UNDET	----	4 1.9%	3 2.2%	----	2 3.0%	1 1.4%	----	----	----	----
	ALL	62 8.4%	209 28.3%	132 17.9%	64 8.7%	67 9.1%	70 9.5%	65 8.8%	46 6.2%	24 3.2%	----
6	YES	4 36.4%	12 22.6%	20 47.6%	16 40.0%	19 50.0%	14 36.0%	6 28.6%	2 13.3%	1 33.3%	----
	NO	5 45.5%	37 69.8%	20 47.6%	20 50.0%	15 39.5%	21 53.8%	14 66.7%	12 80.0%	2 66.7%	----
	OTHER	2 18.2%	3 5.7%	2 4.8%	2 5.0%	2 5.3%	4 10.3%	1 4.8%	1 6.7%	----	----
	UNDET	----	1 1.9%	----	2 5.0%	2 5.3%	----	----	----	----	----
	ALL	11 4.2%	53 20.2%	42 16.0%	40 15.3%	38 14.5%	39 14.9%	21 8.0%	15 5.7%	3 1.2%	----
7	YES	1 50.0%	7 87.5 %	5 62.5%	1 50.0%	5 83.3%	4 80.0%	----	1 50.0%	----	----
	NO	1 50.0%	1 12.5 %	3 37.5%	1 50.0%	1 16.7%	1 20.0%	1 100%	1 50.0%	----	----
	OTHER	----	----	----	----	----	----	----	----	----	----
	UNDET	----	----	----	----	----	----	----	----	----	----
	ALL	2 5.9%	8 23.5%	8 23.5%	2 5.9%	6 17.6%	5 14.7%	1 2.9%	2 5.9%	----	----
8	YES	1 100%	7 50.0%	3 50.0%	4 57.1%	3 42.9%	2 20.0%	----	----	----	----
	NO	----	5 35.7%	3 50.0%	3 42.9%	4 57.1%	8 80.0%	2 100%	----	----	----
	OTHER	----	----	----	----	----	----	----	----	----	----
	UNDET	----	2 14.3%	----	----	----	----	----	----	----	----
	ALL	1 2.1%	14 29.8%	6 12.8%	7 14.9%	7 14.9%	10 21.3%	2 4.3%	----	----	----
9	YES	11 55.0%	31 43.1%	17 43.6%	17 42.5%	15 39.5%	22 62.9%	4 16.7%	6 30.0%	1 25.0%	----
	NO	7 35.0%	38 52.8%	18 46.2%	23 57.5%	20 52.6%	12 34.3%	20 83.3%	14 70.0%	3 75.0%	----
	OTHER	2 10.0%	2 2.8%	2 5.1%	----	1 2.6%	----	----	----	----	----
	UNDET	----	1 1.4%	2 5.1%	----	2 5.3%	1 2.9%	----	----	----	----
	ALL	20 6.8%	72 24.7%	39 13.4%	40 13.7%	38 13.0%	35 12.0%	24 8.2%	20 6.8%	4 1.4%	----
10	YES	1 50.0%	11 52.4%	3 23.1%	2 33.3%	3 100%	2 28.6%	----	----	----	----
	NO	1 50.0%	8 38.1%	7 53.8%	4 66.7%	----	4 57.1%	1 100%	1 100%	1 100%	----
	OTHER	----	1 4.8%	2 15.4%	----	----	----	----	----	----	----
	UNDET	----	1 4.8%	1 7.7%	----	----	1 14.3%	----	----	----	----
	ALL	2 3.6%	21 38.2%	13 23.6%	6 10.9%	3 5.5%	7 12.7%	1 1.8%	1 1.8%	1 1.8%	----
11	YES	6 31.6%	79 41.6%	91 48.4%	92 45.1%	89 50.6%	46 41.4%	26 32.5%	6 19.4%	3 11.5%	----
	NO	13 68.4%	97 51.1%	77 41.0%	90 44.1%	73 41.4%	61 55.0%	50 62.5%	24 77.4%	22 84.6%	----
	OTHER	----	10 5.3%	16 8.5%	16 7.8%	11 6.3%	2 1.8%	3 3.8%	1 3.2%	----	----
	UNDET	----	4 2.1%	4 2.1%	6 2.9%	3 1.7%	2 1.8%	1 1.3%	----	1 3.8%	----
	ALL	19 1.9%	190 18.5%	188 18.3%	204 19.9%	176 17.2%	111 10.8%	80 7.8%	31 3.0%	26 2.5%	----
12	YES	11 39.3%	40 37.4%	42 43.3%	42 46.7%	34 45.3%	25 37.9%	16 40.0%	4 36.4%	1 10.0%	2 33.3%
	NO	16 57.1%	63 58.9%	49 50.5%	41 45.6%	38 50.7%	37 56.1%	23 57.5%	7 63.6%	8 80.0%	4 66.7%
	OTHER	1 3.6%	2 1.9%	5 5.2%	4 4.4%	2 2.7%	2 3.0%	1 2.5%	----	----	----
	UNDET	----	2 1.9%	1 1.0%	3 3.3%	1 1.3%	2 3.0%	----	----	1 10.0%	----
	ALL	28 5.3%	107 20.2%	97 18.3%	90 17.0%	75 14.2%	66 12.5%	40 7.5%	11 2.1%	10 1.9%	6 1.1%
13	YES	11 44.0%	84 44.0%	35 42.2%	27 60.0%	19 59.4%	13 34.2%	11 35.5%	1 20.0%	----	----
	NO	14 56.0%	96 50.3%	36 43.4%	14 31.1%	10 31.3%	24 63.2%	20 64.5%	3 60.0%	3 100%	----
	OTHER	----	10 5.2%	7 8.4%	2 4.4%	3 9.4%	1 2.6%	----	1 20.0%	----	----
	UNDET	----	1 0.5%	5 6.0%	2 4.4%	----	----	----	----	----	----
	ALL	25 5.5%	191 42.2%	83 18.3%	45 9.9%	32 7.1%	38 8.4%	31 6.8%	5 1.1%	3 0.7%	----
14	YES	11 24.4%	56 41.5%	38 37.6%	40 46.5%	35 51.5%	27 46.6%	16 27.1%	8 20.5%	3 21.4%	----
	NO	32 71.1%	73 54.1%	53 52.5%	35 40.7%	27 39.7%	27 46.6%	38 64.4%	30 76.9%	9 64.3%	----
	OTHER	2 4.4%	5 3.7%	5 5.0%	10 11.6%	4 5.9%	4 6.9%	4 6.8%	1 2.6%	2 14.3%	----
	UNDET	----	1 0.7%	5 5.0%	1 1.2%	2 2.9%	----	1 1.7%	----	----	----
	ALL	45 7.4%	135 22.3%	101 16.7%	86 14.2%	68 11.2%	58 9.6%	59 9.8%	39 6.4%	14 2.3%	----
ALL	**YES**	**83 31.7%**	**473 39.0%**	**371 42.7%**	**330 45.1%**	**293 42.9%**	**222 38.3%**	**125 29.6%**	**40 17.9%**	**13 14.0%**	**5 27.8%**
	NO	**167 63.7%**	**660 54.4%**	**405 46.6%**	**337 46.0%**	**333 48.8%**	**322 55.6%**	**275 65.2%**	**171 76.3%**	**76 81.7%**	**12 66.7%**
	OTHER	**11 4.2%**	**56 4.6%**	**69 7.9%**	**50 6.8%**	**37 5.4%**	**21 3.6%**	**16 3.8%**	**12 5.4%**	**2 2.2%**	**1 5.6%**
	UNDET	**1 0.4%**	**24 2.0%**	**24 2.8%**	**15 2.0%**	**20 2.9%**	**14 2.4%**	**6 1.4%**	**1 0.4%**	**2 2.2%**	**----**
	ALL	**262 5.1%**	**1213 23.8%**	**869 17.1%**	**732 14.4%**	**683 13.4%**	**579 11.4%**	**422 8.3%**	**224 4.4%**	**93 1.8%**	**18 0.4%**

TABLE 3A: NUMBER OF MEMBERS BY YEAR OF FIRST ACCUTANE PRESCRIPTION BY MATCH STATUS BY PLAN

PLAN	MATCH	1990		1991		1992		1993		1994		1995		1996	
1	YES	45	30.0%	20	28.2%	41	43.2%	23	32.4%	32	39.5%	30	23.8%	13	18.6%
	NO	90	60.0%	44	62.0%	49	51.6%	46	64.8%	43	53.1%	83	65.9%	52	74.3%
	OTHER	5	3.3%	5	7.0%	3	3.2%	2	2.8%	5	6.2%	11	8.7%	5	7.1%
	UNDET	10	6.7%	2	2.8%	2	2.1%	---		1	1.2%	2	1.6%	----	
	ALL	150	22.6%	71	10.7%	95	14.3%	71	10.7%	81	12.2%	126	19.0%	70	10.5%
2	YES	1	100%	1	83.3%	1	25.0%	4	50.0%	5	38.5%	6	31.6%	1	7.1%
	NO	----		5	16.7%	3	75.0%	4	50.0%	8	61.5%	12	63.2%	13	92.9%
	OTHER	----		----		----		----		----		1	5.3%	----	
	UNDET	----		----		----		----		----		----		----	
	ALL	1	1.5%	6	9.2%	4	6.2%	8	12.3%	13	20.0%	19	29.2%	14	21.5%
3	YES	----		----		----		----		----		----		1	50.0%
	NO	----		----		----		----		----		4	100%	----	
	OTHER	----		----		----		----		----		----		----	
	UNDET	----		----		----		----		----		----		1	50.0%
	ALL	----		----		----		----		----		4	66.7%	2	33.3%
4	YES	----		----		20	43.5%	19	31.7%	31	39.2%	34	40.5%	16	32.7%
	NO	----		----		14	30.4%	34	56.7%	35	44.3%	38	45.2%	28	57.1%
	OTHER	----		----		8	17.4%	5	8.3%	8	10.1%	10	11.9%	4	8.2%
	UNDET	----		----		4	8.7%	2	3.3%	5	6.3%	2	2.4%	1	2.0%
	ALL	----		----		46	14.5%	60	18.9%	79	24.8%	84	26.4%	49	15.4%
5	YES	----		----		43	31.6%	62	36.9%	70	35.4%	42	27.1%	20	24.4%
	NO	----		----		76	55.9%	96	57.1%	118	59.6%	107	69.0%	56	68.3%
	OTHER	----		----		15	11.0%	8	4.8%	8	4.0%	3	1.9%	5	6.1%
	UNDET	----		----		2	1.5%	2	1.2%	2	1.0%	3	1.9%	1	1.2%
	ALL	----		----		136	18.4%	168	22.7%	198	26.8%	155	21.0%	82	11.1%
6	YES	5	35.7%	7	29.2%	8	36.4%	12	35.3%	24	40.7%	26	35.1%	12	34.3%
	NO	9	64.3%	14	58.3%	11	50.0%	19	55.9%	32	54.2%	42	56.8%	19	54.3%
	OTHER	----		3	12.5%	3	13.6%	---		2	3.4%	6	8.1%	3	8.6%
	UNDET	----		----		----		3	8.8%	1	1.7%	----		1	2.9%
	ALL	14	5.3%	24	9.2%	22	8.4%	34	13.0%	59	22.5%	74	28.2%	35	13.4%
7	YES	1	50.0%	1	20.0%	2	50.0%	3	60.0%	6	85.7%	6	66.7%	2	100%
	NO	1	50.0%	4	80.0%	2	50.0%	2	40.0%	1	14.3%	3	33.3%	----	
	OTHER	----		----		----		----		----		----		----	
	UNDET	----		----		----		----		----		----		----	
	ALL	2	5.9%	5	14.7%	4	11.8%	5	14.7%	7	20.6%	9	26.5%	2	5.9%
8	YES	3	75.0%	2	66.7%	5	45.5%	---		4	30.8%	3	37.5%	3	75.0%
	NO	1	25.0%	1	33.3%	5	45.5%	4	100%	8	61.5%	5	62.5%	1	25.0%
	OTHER	----		----		----		----		----		----		----	
	UNDET	----		----		1	9.1%	----		1	7.7%	----		----	
	ALL	4	8.5%	3	6.4%	11	23.4%	4	8.5%	13	27.7%	8	17.0%	4	8.5%
9	YES	18	36.7%	18	50.0%	22	57.9%	22	53.7%	16	31.4%	19	41.3%	9	29.0%
	NO	28	57.1%	17	47.2%	15	39.5%	18	43.9%	31	60.8%	25	54.3%	21	67.7%
	OTHER	----		----		1	2.6%	----		3	5.8%	2	4.3%	1	3.2%
	UNDET	3	6.1%	1	2.8%	----		1	2.4%	1	2.0%	----		----	
	ALL	49	16.8%	36	12.3%	38	13.0%	41	14.0%	51	17.5%	46	15.8%	31	10.6%
10	YES	2	33.3%	2	40.0%	3	37.5%	2	25.0%	4	40.0%	4	36.4%	3	42.9%
	NO	3	50.0%	2	40.0%	5	62.5%	6	75.0%	5	50.0%	6	54.5%	2	28.6%
	OTHER	----		----		----		----		1	10.0%	1	9.1%	1	14.3%
	UNDET	1	16.7%	1	20.0%	----		----		----		----		1	14.3%
	ALL	6	10.9%	5	9.1%	8	14.5%	8	14.5%	10	18.2%	11	20.0%	7	12.7%
11	YES	78	48.4%	44	39.3%	51	41.5%	60	41.1%	76	48.1%	79	36.7%	50	45.5%
	NO	72	44.7%	59	52.7%	67	54.5%	76	52.1%	69	43.7%	113	52.6%	51	46.4%
	OTHER	7	4.3%	4	3.6%	3	2.4%	5	3.4%	11	7.0%	21	9.8%	8	7.3%
	UNDET	4	2.5%	5	4.5%	2	1.6%	5	3.4%	2	1.3%	2	0.9%	1	0.9%
	ALL	161	15.7%		112	123	12.0%	146	14.2%	158	15.4%	215	21.0%	110	10.7%
					10.9%										
12	YES	20	45.5%	20	46.5%	22	33.3%	36	38.7%	39	44.3%	53	38.7%	27	45.8%
	NO	21	47.7%	21	48.8%	42	63.6%	52	55.9%	44	50.0%	78	56.9%	28	47.5%
	OTHER	1	2.3%	----		1	1.5%	4	4.3%	2	2.3%	5	3.6%	4	6.8%
	UNDET	2	4.5%	2	4.7%	1	1.5%	1	1.1%	3	3.4%	1	0.7%	----	
	ALL	44	8.3%	43	8.1%	66	12.5%	93	17.5%	88	16.6%	137	25.8%	59	11.1%
13	YES	----		15	62.5%	29	58.0%	28	41.8%	49	43.8%	52	40.9%	28	38.4%
	NO	----		5	20.8%	18	36.0%	34	50.7%	57	50.9%	65	51.2%	41	56.2%
	OTHER	----		2	8.3%	2	4.0%	5	7.5%	6	5.4%	6	4.7%	3	4.1%
	UNDET	----		2	8.3%	1	2.0%	---		---		4	3.1%	1	1.4%
	ALL	----		24	5.3%	50	11.0%	67	14.8%	112	24.7%	127	28.0%	73	16.1%
14	YES	7	35.0%	7	38.9%	17	40.5%	30	50.8%	51	36.4%	89	39.9%	33	32.0%
	NO	12	60.0%	10	55.6%	17	40.5%	21	35.6%	78	55.7%	119	53.4%	67	65.0%
	OTHER	1	5.0%	1	5.6%	7	16.7%	4	6.8%	7	5.0%	14	6.3%	3	2.9%
	UNDET	----		----		1	2.4%	4	6.8%	4	2.9%	1	0.4%	----	
	ALL	20	3.3%	18	3.0%	42	7.0%	59	9.8%	140	23.1%	223	37.0%	103	17.0%
ALL	**YES**	**180**	**39.9%**	**140**	**40.3%**	**266**	**41.2%**	**301**	**39.4%**	**407**	**40.3%**	**443**	**35.8%**	**218**	**34.0%**
	NO	**237**	**52.5%**	**179**	**51.6%**	**322**	**49.9%**	**412**	**53.9%**	**529**	**52.5%**	**700**	**56.5%**	**379**	**59.1%**
	OTHER	**14**	**3.1%**	**15**	**4.3%**	**43**	**6.7%**	**33**	**4.3%**	**53**	**5.3%**	**80**	**6.5%**	**37**	**5.8%**
	UNDET	**20**	**4.4%**	**13**	**3.7%**	**14**	**2.2%**	**18**	**2.4%**	**20**	**2.0%**	**15**	**1.2%**	**7**	**1.1%**
	ALL	**451**	**8.9%**	**347**	**6.8%**	**645**	**12.7%**	**764**	**15.0%**	**1009**	**19.8%**	**1238**	**24.3%**	**641**	**12.6%**

TABLE 4A: LENGTH OF PRIOR ENROLLMENT (IN DAYS) BY MATCH STATUS BY PLAN

PLAN	MATCH	0-90		91-180		181-270		217-365		366-547		548-720		721-1086		1087-1452		≥1453		Other/ Missing	
1	YES	46	31.3%	20	27.0%	20	35.7%	18	36.7%	17	26.6%	12	26.1%	26	27.7%	14	35.9%	28	33.7%	3	25.0%
	NO	88	59.9%	44	59.5%	31	55.4%	27	55.1%	41	64.1%	28	60.9%	63	67.0%	23	59.0%	54	65.1%	8	66.7%
	OTHER	10	6.8%	6	8.1%	3	5.4%	2	4.1%	6	9.4%	4	8.7%	2	2.1%	1	2.6%	1	1.2%	1	8.3%
	UNDET	3	2.0%	4	5.4%	2	3.6%	2	4.1%	----		2	4.3%	3	3.2%	1	2.6%	----		----	
	ALL	147	22.1%	74	11.1%	56	8.4%	49	7.4%	64	9.6%	46	6.9%	94	14.2%	39	5.9%	83	12.5%	12	1.8%
2	YES	5	35.7%	1	14.3%	----		3	37.5%	1	16.7%	2	50.0%	3	75.0%	----		4	25.0%	----	
	NO	8	57.1%	6	85.7%	5	100%	5	62.5%	5	83.3%	2	50.0%	1	25.0%	1	100%	12	75.0%	----	
	OTHER	1	7.1%	----		----		----		----		----		----		----		----		----	
	UNDET	----		----		----		----		----		----		----		----		----		----	
	ALL	14	21.5%	7	10.8%	5	7.7%	8	12.3%	6	9.2%	4	6.2%	4	6.2%	1	1.5%	16	24.6%	----	
3	YES	----		----		----		----		1	100%	----		----		----		----		----	
	NO	3	100%	----		1	100%	----		----		----		----		----		----		----	
	OTHER	----		----		----		----		----		----		----		----		----		----	
	UNDET	----		----		----		1	100%	----		----		----		----		----		----	
	ALL	3	50.0%	----		1	16.7%	1	16.7%	1	16.7%	----		----		----		----		----	
4	YES	21	36.2%	9	34.6%	15	51.7%	8	42.1%	16	37.2%	15	44.1%	19	29.2%	12	44.4%	5	29.4%	----	
	NO	22	37.9%	11	42.3%	8	27.6%	8	42.1%	18	41.9%	17	50.0%	43	66.2%	13	48.1%	9	52.9%	----	
	OTHER	12	20.7%	5	19.2%	5	17.2%	2	10.5%	7	16.3%	1	2.9%	2	3.1%	1	3.7%	----		----	
	UNDET	3	5.2%	1	3.8%	1	3.4%	1	5.3%	2	4.7%	1	2.9%	1	1.5%	1	3.7%	3	17.6%	----	
	ALL	58	18.2%	26	8.2%	29	9.1%	19	6.0%	43	13.5%	34	10.7%	65	20.4%	27	8.5%	17	5.3%	----	
5	YES	23	42.6%	14	41.2%	10	33.3%	20	41.7%	29	23.0%	29	32.2%	53	33.8%	39	31.5%	20	26.3%	----	
	NO	29	53.7%	19	55.9%	18	60.0%	22	45.8%	84	66.7%	55	61.1%	98	62.4%	74	59.7%	54	71.1%	----	
	OTHER	2	3.7%	1	2.9%	1	3.3%	5	10.4%	12	9.5%	4	4.4%	6	3.8%	6	4.8%	2	2.6%	----	
	UNDET	----		----		1	3.3%	1	2.1%	1	0.8%	2	2.2%	----		5	4.0%	----		----	
	ALL	54	7.3%	34	4.6%	30	4.1%	48	6.5%	126	17.1%	90	12.2%	157	21.2%	124	16.8%	76	10.3%	----	
6	YES	18	31.6%	7	25.9%	9	39.1%	8	36.4%	17	51.5%	6	33.3%	14	46.7%	11	40.7%	4	16.0%	----	
	NO	31	54.4%	17	63.0%	11	47.8%	13	59.1%	15	45.4%	9	50.0%	15	50.0%	16	59.3%	19	76.0%	----	
	OTHER	6	10.5%	3	11.1%	3	13.0%	1	4.5%	----		3	16.7%	----		----		1	4.0%	----	
	UNDET	2	3.5%	----		----		----		1	3.0%	----		1	33.3%	----		1	4.0%	----	
	ALL	57	21.8%	27	10.3%	23	8.8%	22	8.4%	33	12.6%	18	6.9%	30	11.5%	27	10.3%	25	9.5%	----	
7	YES	2	100%	2	100%	1	50.0%	2	100%	4	100%	3	60.0%	2	66.7%	2	50.0%	7	70.0%	----	
	NO	----		----		1	50.0%	----		----		2	40.0%	1	33.3%	2	50.0%	3	30.0%	----	
	OTHER	----		----		----		----		----		----		----		----		----		----	
	UNDET	----		----		----		----		----		----		----		----		----		----	
	ALL	2	5.9%	2	5.9%	2	5.9%	2	5.9%	4	11.8%	5	14.7%	3	8.8%	4	11.8%	10	29.4%	----	
8	YES	5	45.5%	2	66.7%	1	25.0%	----		3	75.0%	2	33.3%	5	55.6%	----		3	60.0%	----	
	NO	6	54.5%	1	33.3%	2	50.0%	3	100%	1	25.0%	4	66.7%	3	33.3%	2	100%	2	40.0%	----	
	OTHER	----		----		----		----		----		----		----		----		----		----	
	UNDET	----		----		1	25.0%	----		----		----		1	11.1%	----		----		----	
	ALL	11	23.4%	3	6.4%	4	8.5%	3	6.4%	4	8.5%	6	12.8%	9	19.1%	2	4.3%	5	10.6%	----	
9	YES	10	38.5%	6	40.0%	6	40.0%	8	57.1%	8	53.3%	4	36.4%	13	26.0%	22	61.1%	47	42.7%	----	
	NO	16	61.5%	7	46.7%	8	53.3%	4	28.6%	7	46.7%	4	36.4%	35	70.0%	13	36.1%	61	55.5%	----	
	OTHER	----		1	6.7%	1	6.7%	1	7.1%	----		----		1	2.0%	1	2.8%	2	1.8%	----	
	UNDET	----		1	6.7%	----		1	7.1%	----		3	27.3%	1	2.0%	----		----		----	
	ALL	26	8.9%	15	5.1%	15	5.1%	14	4.8%	15	5.1%	11	3.8%	50	17.1%	36	12.3%	110	37.7%	----	
10	YES	2	40.0%	----		2	50.0%	----		2	50.0%	2	66.7%	5	45.5%	3	42.9%	6	46.2%	----	
	NO	3	60.0%	4	57.1%	2	50.0%	1	100%	1	25.0%	----		5	45.5%	4	57.1%	7	53.8%	----	
	OTHER	----		2	28.6%	----		----		----		1	33.3%	----		----		----		----	
	UNDET	----		1	14.3%	----		----		1	25.0%	----		1	9.0%	----		----		----	
	ALL	5	9.1%	7	12.7%	4	7.3%	1	1.8%	4	7.3%	3	5.5%	11	20.0%	7	12.7%	13	23.6%	----	
11	YES	84	41.6%	41	45.1%	37	43.0%	42	58.3%	44	39.6%	37	45.1%	69	45.4%	28	37.8%	56	36.1%	----	
	NO	93	46.0%	40	44.0%	38	44.2%	27	37.5%	56	50.5%	40	48.8%	77	50.7%	44	59.5%	92	59.4%	----	
	OTHER	21	10.4%	7	7.7%	11	12.8%	1	1.4%	8	7.2%	4	4.9%	2	1.3%	----		5	3.2%	----	
	UNDET	4	2.0%	3	3.3%	----		2	2.8%	3	2.7%	1	1.2%	4	2.6%	2	2.7%	2	1.3%	----	
	ALL	202	19.8%	91	8.9%	86	8.4%	72	7.0%	111	10.8%	82	8.0%	152	14.8%	74	7.2%	155	15.1%	----	
12	YES	19	38.0%	23	54.8%	10	33.3%	10	43.5%	22	37.3%	19	34.5%	31	43.1%	23	44.2%	57	41.6%	3	30.0%
	NO	29	58.0%	18	42.9%	17	56.7%	7	30.4%	35	59.3%	32	58.2%	40	55.6%	25	48.1%	76	55.5%	7	70.0%
	OTHER	1	2.0%	1	2.4%	2	6.7%	3	13.0%	1	1.7%	2	3.6%	1	1.4%	3	5.8%	3	2.2%	----	
	UNDET	1	2.0%	----		1	3.3%	3	13.0%	1	1.7%	2	3.6%	----		1	1.9%	1	0.7%	----	
	ALL	50	9.4%	42	7.9%	30	5.7%	23	4.3%	59	11.1%	55	10.4%	72	13.6%	52	9.8%	137	25.8%	10	1.9%
13	YES	43	51.8%	22	40.0%	12	34.3%	18	40.0%	21	46.7%	25	47.2%	23	34.3%	20	62.5%	17	44.7%	----	
	NO	36	43.4%	28	50.9%	17	48.6%	24	53.3%	22	48.9%	23	43.4%	40	59.7%	10	31.3%	20	52.6%	----	
	OTHER	3	3.6%	4	7.3%	6	17.1%	2	4.4%	1	2.2%	3	5.7%	3	4.5%	1	3.1%	1	2.6%	----	
	UNDET	1	1.2%	1	1.8%	----		1	2.2%	1	2.2%	2	3.8%	1	1.5%	1	3.1%	----		----	
	ALL	83	18.3%	55	12.1%	35	7.7%	45	9.9%	45	9.9%	53	11.7%	67	14.8%	32	7.1%	38	8.4%	----	
14	YES	36	30.3%	37	48.7%	30	50.0%	28	56.0%	34	45.3%	17	31.5%	24	2.7%	14	33.3%	14	35.0%	----	
	NO	69	58.0%	33	43.4%	26	43.3%	19	38.0%	29	38.7%	36	66.7%	60	67.4%	27	64.3%	25	62.5%	----	
	OTHER	13	10.9%	6	7.9%	3	5.0%	3	6.0%	7	9.3%	1	1.9%	3	3.4%	1	2.4 %	----		----	
	UNDET	1	0.8%	----		1	1.7%	----		5	6.7%	----		2	2.2%	----		1	2.5%	----	
	ALL	119	19.7%	76	12.6%	60	10.0%	50	8.3%	75	12.4%	54	9.0%	89	14.7%	42	6.9%	40	6.6%	----	
ALL	**YES**	**314**	**37.8%**	**184**	**40.1%**	**153**	**40.3%**	**165**	**46.2%**	**219**	**37.1%**	**173**	**37.5%**	**286**	**35.6%**	**188**	**40.3%**	**267**	**36.8%**	**6**	**27.3%**
	NO	**433**	**52.1%**	**228**	**49.7%**	**185**	**48.7%**	**160**	**44.8%**	**314**	**53.2%**	**252**	**54.7%**	**482**	**60.0%**	**254**	**54.4%**	**435**	**60.0%**	**15**	**68.2%**
	OTHER	**69**	**8.3%**	**36**	**7.8%**	**35**	**9.2%**	**20**	**5.6%**	**42**	**7.1%**	**23**	**5.0%**	**20**	**2.5%**	**14**	**3.0%**	**15**	**2.1%**	**1**	**4.5%**
	UNDET	**15**	**1.8%**	**11**	**2.4%**	**7**	**1.8%**	**12**	**3.4%**	**15**	**2.5%**	**13**	**2.8%**	**15**	**1.9%**	**11**	**2.4%**	**8**	**1.1%**	**—**	
	ALL	831	16.3%	459	9.0%	380	7.5%	357	7.0%	590	11.6%	461	9.0%	803	15.8%	467	9.2%	725	14.2%	22	0.4%

TABLE 5A: DURATION OF THERAPY IN YEARS BY MATCH STATUS BY PLAN

PLAN	MATCH	≤.25	.25<D≤.5	.5<D≤1.0	1.0<D≤1.5	1.5<D≤2	2<D≤2.5	2.5<D≤3	3<D≤4	4<D≤5	>5	Other/ Missing
1	YES	62 22.1%	95 40.3%	13 27.1%	11 37.9%	2 14.3%	4 40.0%	3 33.3%	4 44.4%	2 40.0%	3 33.3%	5 33.3%
	NO	193 68.9%	125 53.0%	33 68.8%	15 51.7%	11 78.6%	5 50.0%	5 55.6%	4 44.4%	1 20.0%	6 66.7%	9 60.0%
	OTHER	18 6.4%	10 4.2%	2 4.2%	2 6.9%	----	1 10.0%	1 11.1%	----	1 20.0%	---	1 6.7%
	UNDET	7 2.5%	6 2.5%	----	1 3.4%	1 7.1%	----	----	1 11.1%	1 20.0%	---	----
	ALL	280 42.2%	236 35.5%	48 7.2%	29 4.4%	14 2.1%	10 1.5%	9 1.4%	9 1.4%	5 0.8%	9 1.4%	15 2.3%
2	YES	6 18.8%	12 42.9%	----	----	----	----	----	----	1 50.0%	----	----
	NO	25 78.1%	16 57.1%	1 100%	1 100%	1 100%	----	----	----	1 50.0%	----	----
	OTHER	1 3.1%	----	----	----	----	----	----	----	----	----	----
	UNDET	----	----	----	----	----	----	----	----	----	----	----
	ALL	32 49.2%	28 43.1%	1 1.5%	1 1.5%	1 1.5%	----	----	----	2 3.1%	----	----
3	YES	1 33.3%	----	----	----	----	----	----	----	----	----	----
	NO	1 33.3%	3 100%	----	----	----	----	----	----	----	----	----
	OTHER	----	----	----	----	----	----	----	----	----	----	----
	UNDET	1 33.3%	----	----	----	----	----	----	----	----	----	----
	ALL	3 50.0%	3 50.0%	----	----	----	----	----	----	----	----	----
4	YES	40 30.8%	72 46.2%	2 18.2%	2 28.6%	2 33.3%	----	----	2 50.0%	----	----	----
	NO	65 50.0%	69 44.2%	5 45.5%	3 42.9%	2 33.3%	2 66.7%	1 100%	2 50.0%	----	----	----
	OTHER	17 13.1%	12 7.7%	3 27.3%	2 28.6%	1 16.7%	----	----	---	----	----	----
	UNDET	8 6.2%	3 1.9%	1 9.1%	----	1 16.7%	1 33.3%	----	---	----	----	----
	ALL	130 40.9%	156 49.1%	11 3.5%	7 2.2%	6 1.9%	3 0.9%	1 0.3%	4 1.3%	----	----	----
5	YES	71 24.9%	139 39.8%	18 30.5%	4 28.6%	2 14.3%	1 9.1%	1 25.0%	1 33.3%	----	----	----
	NO	201 70.5%	184 52.7%	38 64.4%	8 57.1%	11 78.6%	9 81.8%	1 25.0%	1 33.3%	----	----	----
	OTHER	11 3.9%	20 5.7%	3 5.1%	1 7.1%	----	1 9.1%	2 50.0%	1 33.3%	----	----	----
	UNDET	2 0.7%	6 1.7%	----	1 7.1%	1 7.1%	----	----	----	----	----	----
	ALL	285 38.6%	349 47.2%	59 8.0%	14 1.9%	14 1.9%	11 1.5%	4 0.5%	3 0.4%	----	----	----
6	YES	27 28.7%	53 42.4%	5 27.8%	2 25.0%	2 40.0%	3 60.0%	----	1 25.0%	----	1 100%	----
	NO	58 61.7%	66 52.8%	11 61.1%	4 50.0%	2 40.0%	2 40.0%	----	2 50.0%	1 100%	----	----
	OTHER	7 7.4%	3 0.2%	2 11.1%	2 25.0%	1 20.0%	---	1 100%	1 25.0%	----	----	----
	UNDET	2 2.1%	3 0.2%	----	----	----	---	----	----	----	----	----
	ALL	94 35.9%	125 47.7%	18 6.9%	8 3.1%	5 1.9%	5 1.9%	1 0.4%	4 1.5%	1 0.4%	1 0.4%	----
7	YES	4 44.4%	18 85.7%	----	1 100%	----	----	1 50.0%	----	----	----	----
	NO	5 55.6%	3 14.3%	----	----	----	----	1 50.0%	1 100%	----	----	----
	OTHER	---	---	----	----	----	----	---	----	----	----	----
	UNDET	---	---	----	----	----	----	---	----	----	----	----
	ALL	9 26.5%	21 61.8%	----	1 2.9%	----	----	2 5.9%	1 2.9%	----	----	----
8	YES	7 33.3%	10 47.6%	2 66.7%	----	----	----	1 100%	----	----	----	----
	NO	13 61.9%	10 47.6%	1 33.3%	1 100%	----	----	----	----	----	----	----
	OTHER	----	----	---	----	----	----	----	----	----	----	----
	UNDET	1 4.8%	1 4.8%	---	----	----	----	----	----	----	----	----
	ALL	21 44.7%	21 44.7%	3 6.4%	1 2.1%	----	----	1 2.1%	----	----	----	----
9	YES	40 36.0%	62 45.6%	6 40.0%	7 63.6%	1 25.0%	4 57.1%	2 40.0%	----	1 50.0%	1 100%	----
	NO	67 60.4%	68 50.0%	8 53.3%	3 27.3%	3 75.0%	3 42.9%	2 40.0%	----	1 50.0%	----	----
	OTHER	3 2.7%	3 2.2%	1 6.7%	1 9.1%	---	---	----	----	----	----	----
	UNDET	1 0.9%	3 2.2%	----	----	---	---	1 20.0%	----	----	----	----
	ALL	111 38.0%	136 46.6%	15 5.1%	11 3.8%	4 1.4%	7 2.4%	5 1.7%	----	2 0.7%	1 0.3%	----
10	YES	5 20.0%	14 60.9%	3 50.0%	----	----	----	----	----	----	----	----
	NO	16 64.0%	8 34.8%	2 33.3%	----	----	----	----	1 100%	----	----	----
	OTHER	2 8.0%	1 4.3%	----	----	----	----	----	----	----	----	----
	UNDET	2 8.0%	----	1 16.7%	----	----	----	----	----	----	----	----
	ALL	25 45.5%	23 41.8%	6 10.9%	----	----	----	----	1 1.8%	----	----	----
11	YES	143 36.9%	226 46.4%	21 42.9%	13 39.4%	10 47.6%	7 50.0%	4 44.4%	8 53.3%	3 75.0%	3 60.0%	----
	NO	204 52.6%	230 47.2%	26 53.1%	18 54.5%	10 47.6%	6 42.9%	4 44.4%	6 40.0%	1 25.0%	2 40.0%	----
	OTHER	31 8.0%	22 4.5%	1 2.0%	2 6.1%	1 4.8%	1 7.1%	1 11.1%	----	----	----	----
	UNDET	10 2.6%	9 1.8%	1 2.0%	----	----	----	----	1 6.7%	----	----	----
	ALL	388 37.9%	487 47.5%	49 4.8%	33 3.2%	21 2.0%	14 1.4%	9 0.9%	15 1.5%	4 0.4%	5 0.5%	----
12	YES	83 37.2%	102 44.5%	11 39.3%	7 36.8%	3 60.0%	1 33.3%	2 100%	4 57.1%	----	1 50.0%	3 25.0%
	NO	125 56.1%	119 52.0%	14 50.0%	12 63.2%	2 40.0%	2 66.7%	----	2 28.6%	----	1 50.0%	9 75.0%
	OTHER	9 4.0%	4 1.7%	3 10.7%	---	---	---	----	1 14.3%	----	----	----
	UNDET	6 2.7%	4 1.7%	----	---	---	---	----	----	----	----	----
	ALL	223 42.1%	229 43.2%	28 5.3%	19 3.6%	5 0.9%	3 0.6%	2 0.4%	7 1.3%	----	2 0.4%	12 2.3%
13	YES	62 34.4%	107 48.2%	10 47.6%	8 72.7%	7 77.8%	3 75.0%	1 50.0%	3 100%	----	----	----
	NO	101 56.1%	104 46.8%	10 47.6%	2 18.2%	2 22.2%	1 25.0%	----	----	----	----	----
	OTHER	13 7.2%	8 3.6%	1 4.8%	1 9.1%	---	---	1 50.0%	----	----	----	----
	UNDET	4 2.2%	3 1.4%	----	----	---	---	----	----	1 100%	----	----
	ALL	180 39.7%	222 49.0%	21 4.6%	11 2.4%	9 2.0%	4 0.9%	2 0.4%	3 0.7%	1 0.2%	----	----
14	YES	67 31.9%	120 43.5%	30 46.9%	8 36.4%	3 25.0%	2 28.6%	1 25.0%	3 37.5%	----	----	----
	NO	131 62.4%	136 49.3%	25 39.1%	13 59.1%	8 66.7%	3 42.9%	2 50.0%	4 50.0%	1 100%	1 100%	----
	OTHER	---	15 5.4%	6 9.4%	1 4.5%	----	1 14.3%	1 25.0%	1 12.5%	----	----	----
	UNDET	1 0.5%	5 1.8%	3 4.7%	----	1 8.3%	1 14.3%	----	----	----	----	----
	ALL	210 34.7%	276 45.6%	64 10.6%	22 3.6%	12 2.0%	7 1.2%	4 0.7%	8 1.3%	1 0.2%	1 0.2%	----
ALL	**YES**	**618 31.0%**	**1030 44.6%**	**121 37.5%**	**63 40.1%**	**32 35.2%**	**25 39.1%**	**16 40.0%**	**26 47.3%**	**7 43.8%**	**10 52.6%**	**8 29.6%**
	NO	**1205 60.5%**	**1141 49.4%**	**174 53.9%**	**80 51.0%**	**52 57.1%**	**33 51.6%**	**16 40.0%**	**23 41.8%**	**6 37.5%**	**9 47.4%**	**18 66.7%**
	OTHER	**124 6.2%**	**98 4.2%**	**22 6.8%**	**11 7.0%**	**3 3.3%**	**4 6.3%**	**7 17.5%**	**4 7.3%**	**1 6.3%**	**—**	**1 3.7%**
	UNDET	**44 2.2%**	**43 1.9%**	**6 1.9%**	**3 1.9%**	**4 4.4%**	**2 3.1%**	**1 2.5%**	**2 3.6%**	**2 12.5%**	**—**	**—**
	ALL	**1991 39.1%**	**2312 45.4%**	**323 6.3%**	**157 3.1%**	**91 1.8%**	**64 1.3%**	**40 0.8%**	**55 1.1%**	**16 0.3%**	**19 0.4%**	**27 0.5%**

TABLE 6A: SUBSCRIBER STATUS BY MATCH STATUS BY PLAN

PLAN	MATCH	SUBSCRIBER		SPOUSE		OTHER DEPENDENT	
1	YES	109	28.3%	36	33.6%	59	34.3%
	NO	238	61.8%	65	60.7%	104	60.5%
	OTHER	26	6.8%	3	2.8%	7	4.1%
	UNDET	27	3.1%	3	2.8%	2	1.2%
	ALL	385	58.0%	107	16.1%	172	25.9%
2	YES	5	21.7%	2	13.3%	12	44.4%
	NO	17	73.9%	13	86.7%	15	55.6%
	OTHER	1	4.3%	----		----	
	UNDET	----		----		----	
	ALL	23	35.4%	15	23.1%	27	41.5%
3	YES	----		1	100%	----	
	NO	1	100%	----		3	100%
	OTHER	----		----		----	
	UNDET	----		1	100%	----	
	ALL	1	16.7%	2	33.3%	3	50.0%
4	YES	40	37.7%	32	42.1%	48	35.3%
	NO	48	45.3%	39	51.3%	62	45.6%
	OTHER	13	12.3%	3	3.9%	19	14.0%
	UNDET	5	4.7%	2	2.6%	7	5.1%
	ALL	106	33.3%	76	23.9%	136	42.8%
5	YES	70	31.8%	53	32.7%	114	31.9%
	NO	127	57.8%	102	63.0%	224	62.7%
	OTHER	19	8.6%	5	3.1%	15	4.2%
	UNDET	4	1.8%	2	1.2%	4	1.1%
	ALL	220	29.8%	162	21.9%	357	48.3%
6	YES	52	38.8%	18	39.1%	24	29.3%
	NO	70	52.2%	26	56.5%	50	61.0%
	OTHER	9	6.7%	1	2.2%	7	8.5%
	UNDET	3	2.2%	1	2.2%	1	1.2%
	ALL	134	51.1%	46	17.6%	82	31.3%
7	YES	9	81.8%	3	50.0%	5	29.4%
	NO	2	18.2%	3	50.0%	12	70.6%
	OTHER	----		----		----	
	UNDET	----		----		----	
	ALL	11	32.4%	6	17.6%	17	50.0%
8	YES	5	29.4%	7	50.0%	8	50.0%
	NO	12	70.6%	7	50.0%	6	37.5%
	OTHER	----		----		----	
	UNDET	----		----		2	12.5%
	ALL	17	36.2%	14	29.8%	16	34.0%
9	YES	47	40.5%	22	36.7%	55	47.4%
	NO	63	54.3%	38	63.3%	54	46.6%
	OTHER	1	0.9%	----		6	5.2%
	UNDET	5	4.3%	----		1	0.9%
	ALL	116	39.7%	60	20.5%	116	39.7%
10	YES	7	41.2%	1	16.7%	14	43.8%
	NO	8	47.1%	5	83.3%	14	43.8%
	OTHER	----		----		3	9.4%
	UNDET	2	11.8%	----		1	3.1%
	ALL	17	30.9%	6	10.9%	32	58.2%
11	YES	251	44.3%	67	37.4%	120	42.9%
	NO	270	47.7%	101	56.4%	136	48.6%
	OTHER	33	5.8%	8	4.5%	18	6.4%
	UNDET	12	2.1%	3	1.7%	6	2.1%
	ALL	566	55.2%	179	17.5%	280	27.3%
12	YES	106	42.6%	42	38.2%	69	40.4%
	NO	129	51.8%	62	56.4%	95	55.6%
	OTHER	8	3.2%	4	3.6%	5	2.9%
	UNDET	6	2.4%	2	1.8%	2	1.2%
	ALL	249	47.0%	110	20.8%	171	32.3%
13	YES	54	42.5%	40	49.4%	107	43.7%
	NO	61	48.0%	36	44.4%	123	50.2%
	OTHER	10	7.9%	3	3.7%	11	4.5%
	UNDET	2	1.6%	2	2.5%	4	1.6%
	ALL	127	28.0%	81	17.9%	245	54.1%
14	YES	102	42.1%	46	35.7%	86	36.8%
	NO	120	49.6%	69	53.5%	135	57.7%
	OTHER	15	6.2%	12	9.3%	10	4.3%
	UNDET	5	2.1%	2	1.6%	3	1.3%
	ALL	242	40.0%	129	21.3%	234	38.7%
ALL	**YES**	**857**	**38.7%**	**370**	**37.3%**	**728**	**38.6%**
	NO		**1166**	**566**	**57.0%**	**1026**	**54.3%**
	OTHER		**52.7%**	**39**	**3.9%**	**101**	**5.3%**
	UNDET	**135**	**6.1%**	**18**	**1.8%**	**33**	**1.7%**
	ALL	**56**	**2.5%**	**993**	**19.5%**	**1888**	**37.1%**
			2214				
			43.5%				

TABLE 7A: PRESCRIBER SPECIALTIES BY MATCH STATUS BY PLAN

Plan	Match	Dermatologist		Family Practitioner		Internist		Obstetrician/ Gynecologist		Pediatrician		Plastic Surgeon		Other/ Missing	
1	YES	191	31.2%	4	21.1%	----		----		----		----		9	30.0%
	NO	371	60.6%	14	73.7%	1	100%	2	100%	----		----		19	63.3%
	OTHER	35	5.7%	----		----		----		----		----		----	
	UNDET	15	2.5%	1	5.3%	----		----		----		----		2	6.7%
	ALL	612	92.2%	19	2.9%	1	0.2%	2	0.3%	----		----		30	4.5%
2	YES	17	38.6%	1	16.7%	----		----		----		----		1	33.3%
	NO	27	61.4%	5	83.3%	11	100%	1	100%	----		----		1	33.3%
	OTHER	----		----		----		----		----		----		1	33.3%
	UNDET	----		----		----		----		----		----		----	
	ALL	44	67.7%	6	9.2%	11	16.9%	1	1.5%	----		----		3	4.6%
3	YES	1	50.0%	----		----		----		----		----		----	
	NO	----		1	100%	3	100%	----		----		----		----	
	OTHER	----		----		----		----		----		----		----	
	UNDET	1	50.0%	----		----		----		----		----		----	
	ALL	2	33.3%	1	16.7%	3	50.0%	----		----		----		----	
4	YES	72	40.2%	28	35.0%	2	33.3%	----		----		----		18	34.6%
	NO	81	45.3%	40	50.0%	4	66.7%	----		1	100%	----		23	44.2%
	OTHER	18	10.1%	10	12.5%	----		----		----		----		7	13.5%
	UNDET	8	4.5%	2	0.3%	----		----		----		----		4	7.7%
	ALL	179	56.3%	80	25.2%	6	1.9%	----		1	0.3%	----		52	16.4%
5	YES	209	33.0%	21	28.8%	1	33.3%	2	66.7%	----		----		4	15.4%
	NO	385	60.8%	45	61.6%	2	66.7%	1	33.3%	1	100%	----		19	73.1%
	OTHER	30	4.7%	6	8.2%	----		----		----		----		3	11.5%
	UNDET	9	1.4%	1	1.4%	----		----		----		----		----	
	ALL	633	85.7%	73	9.9%	3	0.4%	3	0.4%	1	0.1%	----		26	3.5%
6	YES	91	36.5%	1	16.7%	1	50.0%	----		----		----		1	20.0%
	NO	136	54.6%	5	83.3%	1	50.0%	----		----		----		4	80.0%
	OTHER	17	6.8%	----		----		----		----		----		----	
	UNDET	5	2.0%	----		----		----		----		----		----	
	ALL	249	95.0%	6	2.3%	2	0.8%	----		----		----		5	1.9%
7	YES	17	85.0%	1	25.0%	2	50.0%	----		----		----		4	66.7%
	NO	3	15.0%	3	75.0%	2	50.0%	----		----		----		2	33.3%
	OTHER	----		----		----		----		----		----		----	
	UNDET	----		----		----		----		----		----		----	
	ALL	20	58.8%	4	11.8%	4	11.8%	----		----		----		6	17.6%
8	YES	10	41.7%	7	38.9%	2	100%	----		----		----		1	50.0%
	NO	13	54.2%	11	61.1%	----		1	100%	----		----		----	
	OTHER	----		----		----		----		----		----		----	
	UNDET	1	4.2%	----		----		----		----		----		1	50.0%
	ALL	24	51.1%	18	38.3%	2	4.3%	1	2.1%	----		----		2	4.3%
9	YES	99	43.4%	20	37.0%	1	50.0%	----		1	100%	----		3	50.0%
	NO	118	51.8%	32	59.3%	1	50.0%	1	100%	----		----		3	50.0%
	OTHER	7	3.1%	----		----		----		----		----		----	
	UNDET	4	1.8%	2	3.7%	----		----		----		----		----	
	ALL	228	78.1%	54	18.5%	2	0.7%	1	0.3%	1	0.3%	----		6	2.1%
10	YES	19	48.7%	2	20.0%	----		----		----		----		1	20.0%
	NO	17	43.6%	7	70.0%	----		----		----		----		3	60.0%
	OTHER	1	2.6%	1	10.0%	1	100%	----		----		----		----	
	UNDET	2	5.1%	----		----		----		----		----		1	20.0%
	ALL	39	70.9%	10	18.2%	1	1.8%	----		----		----		5	9.1%
11	YES	382	44.3%	41	35.3%	2	25.0%	6	40.0%	----		----		7	31.8%
	NO	413	47.9%	65	56.0%	6	75.0%	9	60.0%	----		----		14	63.6%
	OTHER	50	5.8%	8	6.9%	----		----		1	100%	----		----	
	UNDET	18	2.1%	2	1.7%	----		----		----		----		1	4.5%
	ALL	863	84.2%	116	11.3%	8	0.8%	15	1.5%	1	0.1%	----		22	2.1%
12	YES	190	42.4%	7	30.4%	----		1	50.0%	----		5	33.3%	14	34.1%
	NO	237	52.9%	15	65.2%	1	100%	1	50.0%	----		10	66.7%	22	53.7%
	OTHER	15	3.3%	1	4.3%	----		----		----		----		1	2.4%
	UNDET	6	1.3%	----		----		----		----		----		4	9.8%
	ALL	448	84.5%	23	4.3%	1	0.2%	2	0.4%	----		15	2.8%	41	7.7%
13	YES	179	45.0%	8	25.8%	5	62.5%	----		----		----		9	69.2%
	NO	195	49.0%	17	54.8%	3	37.5%	1	100%	2	100%	----		2	15.4%
	OTHER	20	5.0%	2	6.5%	----		----		----		----		2	15.4%
	UNDET	4	1.0%	4	12.9%	----		----		----		----		----	
	ALL	398	87.9%	31	6.8%	8	1.8%	1	0.2%	2	0.4%	----		13	2.9%
14	YES	217	38.8%	10	47.6%	2	22.2%	1	25.0%	2	66.7%	----		2	22.2%
	NO	300	53.7%	10	47.6%	6	66.7%	1	25.0%	----		----		7	77.8%
	OTHER	33	5.9%	1	4.8%	1	11.1%	1	25.0%	1	33.3%	----		----	
	UNDET	9	1.6%	----		----		1	25.0%	----		----		----	
	ALL	559	92.4%	21	3.5%	9	1.5%	4	0.7%	3	0.5%	----		9	1.5%
ALL	**YES**	**1694**	**39.4%**	**151**	**32.7%**	**18**	**29.5%**	**10**	**33.3%**	**3**	**33.3%**	**5**	**33.3%**	**74**	**33.6%**
	NO	**2296**	**53.4%**	**270**	**58.4%**	**41**	**67.2%**	**18**	**60.0%**	**4**	**44.4%**	**10**	**66.7%**	**119**	**54.1%**
	OTHER	**226**	**5.3%**	**29**	**6.3%**	**2**	**3.3%**	**1**	**3.3%**	**2**	**22.2%**	—		**15**	**6.8%**
	UNDET	**82**	**1.9%**	**12**	**2.6%**	—		**1**	**3.3%**	—		—		**12**	**5.5%**
	ALL	**4298**	**84.4%**	**462**	**9.1%**	**61**	**1.2%**	**30**	**0.6%**	**9**	**0.2%**	**15**	**0.3%**	**220**	**4.3%**

TABLE 8A: CONTRACEPTIVE USE BY MATCH BY PLAN

Plan	Match	Birth Control Pill	Depo Provera	IUD	Tubal Ligation	Norplant	Surgery	Other/ Missing
1	Yes	27 35.1%	2 14.3%	----	2 15.4%	----	3	170 30.7%
	No	44 57.1%	11 79.%	----	9 69.2%	----	42.9%	339 61.3%
	Other	4 5.2%	---	----	1 7.7%	----	4	31 5.6%
	Undet	2 2.6%	1 7.1%	----	1 7.7%	----	57.1%	13 2.4%
	All	77 11.6%	14	----	13	----	----	553 83.3%
			2.1%		2.0%		----	
							7	
							1.1%	
2	Yes	4 26.7%	----	----	----	----	----	15 31.3%
	No	10 66.7%	----	----	----	----	2	33 68.8%
	Other	1 6.7%	----	----	----	----	100%	----
	Undet	----	----	----	----	----	----	----
	All	15 23.1%	----	----	----	----	----	48 73.8%
							2	
							3.1%	
3	Yes	----	----	----	----	----	----	1 16.7%
	No	----	----	----	----	----	----	4 66.7%
	Other	----	----	----	----	----	----	----
	Undet	----	----	----	----	----	----	1 16.7%
	All	----	----	----	----	----	----	6 100%
4	Yes	2 40.0%	2 50.0%	1 100%	1 50.0%	----	1	113 38.0%
	No	3 60.0%	----	----	1 50.0%	----	12.5%	139 46.8%
	Other	----	----	----	----	1 100%	6	33 11.1%
	Undet	----	2 50.0%	----	----	----	75.0%	12 4.0%
	All	5 1.6%	4 1.3%	1 0.3%	2 0.6%	1 0.3%	1	297 93.4%
							12.5%	

							8	
							2.5%	
5	Yes	51 43.2%	5 35.7%	----	2 22.2%	1 25.0%	----	176 29.9%
	No	56 47.5%	8 57.1%	----	6 66.7%	3 75.0%	4	378 64.2%
	Other	9 7.6%	----	----	----	----	80.0%	29 4.9%
	Undet	2 1.7%	1 7.1%	----	1 11.1%	----	1	6 1.0%
	All	118 16.0%	14	----	9 1.2%	4 0.5%	20.0%	589 79.7%
			1.9%				----	
							5	
							0.7%	
6	Yes	24 53.3%	----	----	2 66.7%	2 100%	1	65 31.6%
	No	18 40.0%	1 100%	----	1 33.3%	----	20.0%	123 59.7%
	Other	3 6.7%	----	----	----	----	3	13 6.3%
	Undet	----	----	----	----	----	60.0%	5 2.4%
	All	45 17.2%	1 0.4%	----	3 1.1%	2 0.8%	1	206 78.6%
							20.0%	

							5	
							1.9%	
7	Yes	2 66.7%	1 100%	----	----	----	1	20 69.0%
	No	1 33.3%	----	----	----	----	100%	9 31.0%
	Other	----	----	----	----	----	----	----
	Undet	----	----	----	----	----	----	----
	All	3 8.8%	1 2.9%	----	----	----	----	29 85.3%
							1	
							2.9%	

Plan	Match	Birth Control Pill	Depo Provera	IUD	Tubal Ligation	Norplant	Surgery	Other/ Missing
8	Yes	4 44.4%	----	----	----	----	----	16 43.2%
	No	5 55.6%	----	----	----	----	1	19 51.4%
	Other	----	----	----	----	----	100%	----
	Undet	----	----	----	----	----	----	2 5.4%
	All	9 19.1%	----	----	----	----	----	37 78.7%
							1	
							2.1%	
9	Yes	24 47.1%	3 33.3%	----	2 100%	----	----	95 41.9%
	No	22 43.1%	6 66.7%	1 100%	----	----	2	124 54.6%
	Other	2 3.9%	----	----	----	----	100%	5 2.2%
	Undet	3 5.9%	----	----	----	----	----	3 1.3%
	All	51 17.5%	9 3.1%	1 0.3%	2 0.7%	----	----	227 77.7%
							2	
							0.7%	
10	Yes	2 33.3%	----	----	1 50.0%	----	----	19 41.3%
	No	4 66.7%	1 100%	----	1 50.0%	----	----	21 45.7%
	Other	----	----	----	----	----	----	3 6.5%
	Undet	----	----	----	----	----	----	3 6.5%
	All	6 10.9%	1 1.8%	----	2 3.6%	----	----	46 83.6%
11	Yes	80 54.8%	11 57.9%	----	3 42.9%	1 50.0%	1	342 40.4%
	No	56 38.4%	6 31.6%	1 100%	4 57.1%	1 50.0%	33.3%	438 51.7%
	Other	8 5.5%	2 10.5%	----	----	----	1	48 5.7%
	Undet	2 1.4%	----	----	----	----	33.3%	19 2.2%
	All	146 14.2%	19 1.9%	1 0.1%	7 0.7%	2 0.2%	1	847 82.6%
							33.3%	
							----	
							3 0.3%	
12	Yes	50 50.5%	1 50.0%	----	2 22.2%	1 100%	2	161 39.1%
	No	41 41.4%	1 50.0%	1 100%	7 77.8%	----	33.3%	232 56.3%
	Other	5 5.1%	----	----	----	----	4	12 2.9%
	Undet	3 3.0%	----	----	----	----	66.7%	7 1.7%
	All	99 18.7%	2 0.4%	1 0.2%	9 1.7%	1 0.2%	----	412 77.7%
							----	
							6 1.1%	
13	Yes	24 60.0%	4 44.4%	----	5 62.5%	2 66.7%	3	163 42.4%
	No	13 32.5%	4 44.4%	1 100%	2 25.0%	----	37.5%	195 50.8%
	Other	2 5.0%	1 11.1%	----	1 12.5%	1 33.3%	5	19 4.9%
	Undet	1 2.5%	----	----	----	----	62.5%	7 1.8%
	All	40 8.8%	9 2.0%	1 0.2%	8 1.8%	3 0.7%	----	384 84.8%
							----	
							8 1.8%	
14	Yes	43 44.3%	2 100%	----	5 62.5%	----	1 20.0%	183 37.4%
	No	45 46.4%	----	1 100%	3 37.5%	3 100%	4 80.0%	268 54.8%
	Other	7 7.2%	----	----	----	----	----	30 6.1%
	Undet	2 2.1%	----	----	----	----	----	8 1.6%
	All	97 16.0%	2 0.3%	1 0.2%	8 1.3%	3 0.5%	5 0.8%	489 80.8%
ALL	**Yes**	**337 47.4%**	**31 40.8%**	**1 17%**	**25 39.7%**	**9 56.3%**	**13 25%**	**1539 36.9%**
	No	**318 44.7%**	**38 50.0%**	**5 83%**	**34 54.0%**	**5 31.3%**	**36 68%**	**2322 55.7%**
	Other	**41 5.8%**	**3 3.9%**	**—**	**2 3.2%**	**2 12.5%**	**4 7.5%**	**223 5.3%**
	Undet	**15 2.1%**	**4 5.3%**	**—**	**2 3.2%**	**—**	**—**	**86 2.1%**
	All	**711 14.0%**	**76 1.5%**	**6 0.1%**	**63 1.2%**	**16 0.3%**	**53 1.0%**	**4170 81.8%**