6 Months Observational Study

The purpose of this study is to determine the long term (six month) effectiveness of the ActiPatch device for chronic pain.

Methods

Study Subjects

The subjects in this study are a subset of the larger registry comprising 12,390 subjects, as discussed in the previous sections. Approximately 2 months after estimating the completion of the 7-day trial, subjects who indicated that they would definitely purchase the retail device were asked if they would consent to take part in an observational registry study, and if they had already purchased a retail ActiPatch®. Subjects who agreed to be part of the study were told they would need to answer three assessments at different points in time: 3, 4 months and 6 months after the initial 7-day trial. The objectives of the study were explained to the subjects, and as an incentive to complete the entirety of the study, they were offered a free retail ActiPatch unit (worth about $28 retail at today's exchange rate) upon completing the study.

Data collected previously in the original registry study indicated that those who reported they would definitely purchase the device also reported the largest reported pain decrease (other options to the intent to purchase question included: Probably, Possibly, Probably Not and Definitely Not). On average, those indicating they would definitely purchase a retail device reported a 5- point VAS reduction (60% reduction) in baseline pain. In contrast, those indicating "Probably" reported a 3.9 VAS reduction (49%), "Possibly" reported a 2.6 VAS reduction (34%), "Possibly not" reported a 0.9 VAS reduction (11%), and "definitely not" reported a 0.23 VAS reduction (3%). This implies that all the subjects who participated in the 6-month observational study were individuals who received substantial pain relief in the 7-day trial, i.e. positive responders to the ActiPatch therapy. Moreover, at the time of contacting them about this study the individuals had already been using the device as a pain therapy and this required purchase and/or repurchase of the device over the 6-month period. Also, use of the device was not dependent on any healthcare practitioner for instruction.

Data acquisition & analysis

The 3, 4 & 6-month Assessment

The questions in the assessments were designed to document reported changes in pain (visual analogue scores on a 0-10 scale), medication use, sleep quality, physical activity and overall quality of life. The data that were obtained from the 7-day trial assessment were compared to data from the follow up assessment to determine if the level of pain relief reported in the former assessment was maintained over a 6-month period. Data from the follow up assessment was also used to document temporal trends of behavioral changes or other factors that could indicate the effectiveness of ActiPatch® therapy.

The raw data from the assessments was exported into a comma-delimited (CSV) file and analyzed using Excel 2013 (Microsoft Corporation, Redmond, Washington).

Results

Of the 254 subjects who volunteered to participate in the study, 244 completed assessment-1 (3-month interval), 231 completed assessment-2 (4-month interval) and 225 completed assessment-3 (6-month interval). As of phase 3, 219 subjects completed at least two assessments and a total of 194 (88%) subjects completed all three assessments. (An analysis of study dropouts is provided below.)

Tables 1-4 provide a profile of the study participants based on their responses from the initial 7-day trial assessment. In general, this profile is very similar to the CBP registry. In Table 1 we see most subjects were female and over the age of 35 years old.

Table 1. Age and gender of the study participants.

Age	PERCENT	Gender	Percent
18-24	0.4%	Male	28%
25-34	2.9%	Female	72%
35-44	11.3%		
45-54	19.6%		
55-64	39.6%		
65 plus	25.4%		
Prefer not to answer	0.8%		

The distribution of pain duration is shown in Table 2. The vast majority (92%) of the pain was chronic in nature. Subjects also reported on the etiology of their pain, with arthritis being the most prevalent: osteoarthritis (36%), and rheumatoid arthritis (13%). Fibromyalgia was the next leading etiology (10%).

Table 2. Pain duration of the subjects recorded in the 7-day trial assessment.

Duration	PERCENT
0-6 months	8
6 m – 1 year	15
1-2 years	16
2-5 years	21
5-10 years	19
10-20 years	11
20 years plus	11

Baseline Analgesics

Analgesic medications were used by 96% of subjects as their main pain-relief therapy (Table 3), with a combination of over-the-counter analgesics such as paracetamol (55%) and NSAIDs (60%), as well as a number of prescription analgesics. Alternative pain relief modalities such as transcutaneous electrical nerve stimulation (TENS) – 16%, heat wraps – 28% and physical therapy – 24% were also utilized.

Table 3. Analgesic medications used by the study participants

Analgesics	PERCENT
NSAIDS e.g. ibuprofen	60
Paracetamol	55
Weak opioids (e.g. codeine)	43
Strong opioids (e.g. hydrocodone)	20
Cyclooxygenase (cox-2) inhibitors	1
Pregabalin (e.g. lyrica)	11
Amitriptyline	19
Topical opioid (e.g. morphine)	9
Topical NSAIDS e.g. Voltarol	22
Gabapentin	11
Other	1.7
No Analgesics	4%

Pain location/Device Use

Location of pain was predominantly in the back, followed by, knee, shoulder, hip, neck and other anatomical areas. (See Table 4.) Subjects reported device use on average in 1.1 locations.

Table 4. Device use location

	Device Use
Back	45%
Knee	36%
Shoulder	12%
Neck	3%
Hip	11%
Other	8%

Pain Response Over Time

The average baseline VAS pain score reported in the 7-day trial assessment was 8.24±1.4. The average baseline VAS pain score (i.e., the level of pain before using the medical device) was also collected during each of the three assessments conducted during the observational study and were consistent with the largest variation only 0.28 VAS points between the 7 day and 6 month assessments. After completing the 7-day trial the average reported VAS score was 3.03 (63% reduction). At the 3-month interval, the reported VAS score was 2.95 (65.5% reduction), 3.20 (62% reduction) at the 4-month interval and 3.36 (60.5% reduction) at the 6-month interval (Table 5 and Figure 1) from their respective baselines. All treatment average VAS scores were statistically significant different from the baseline average scores ($P = \leq 0.005$).

Table 5. The baseline pain and treatment scores for the four assessments, and percent pain reduction.

Assessment	Baseline	Treatment	Percent	P value
7 Day	8.24±1.40	3.03±1.87	63.0%	≤0.005
3 Month	8.31±1.22	2.95±1.66	65.5%	≤0.005
4 Month	8.40±1.23	3.20±1.86	62.0%	≤0.005
6 Month	8.52±1.28	3.36±1.92	60.5%	≤0.005

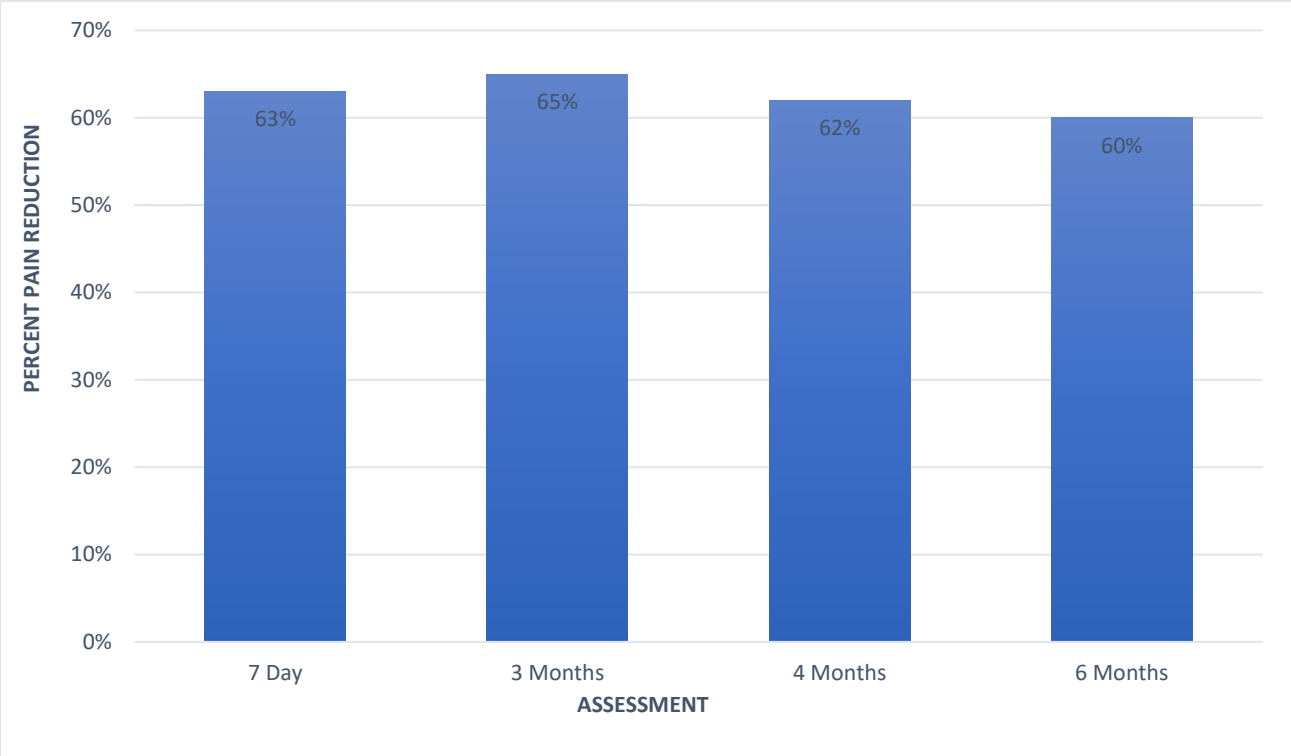

Figure 1. The reported reduction in pain was consistently above 60% at each of the assessments.

Figure 2 shows the paired baseline and treatment VAS scores of 105 subjects who used the device for chronic back pain as documented in assessment-3 (6 month interval) of the follow up assessment. The majority of these subjects (93%) reported severe baseline pain scores ranging from 7-10. Upon using the ActiPatch, these scores were reduced, such that 60% reported only mild pain (0-3), 35% moderate pain (4-6) and just 5% reported severe pain after six months of using the ActiPatch.

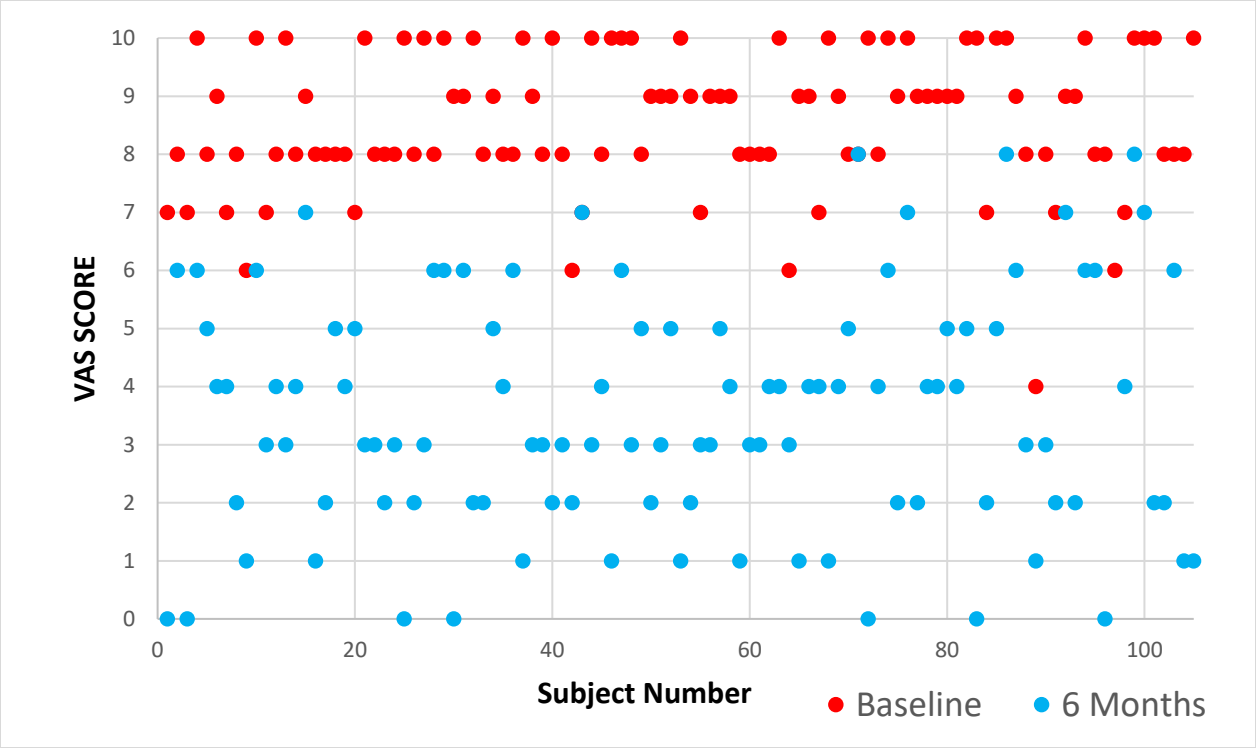

Figure 2. Paired baseline and treatment VAS scores documented in assessment-3 (6-month interval) from 105 subjects who used the device for chronic back pain. 93% reported severe baseline pain (VAS score 7-10), but after using the ActiPatch the number in this group was reduced to 6.6%.

Analgesics Reduction

As shown previously in Table 3, analgesics were widely used by the study subjects. At 6 months a majority (86%) reported a reduction in medication use (Figure 3), including 23% who reported eliminating medication use. Reduction in medication was not dependent on form of medication being used i.e. over-the-counter or prescription.

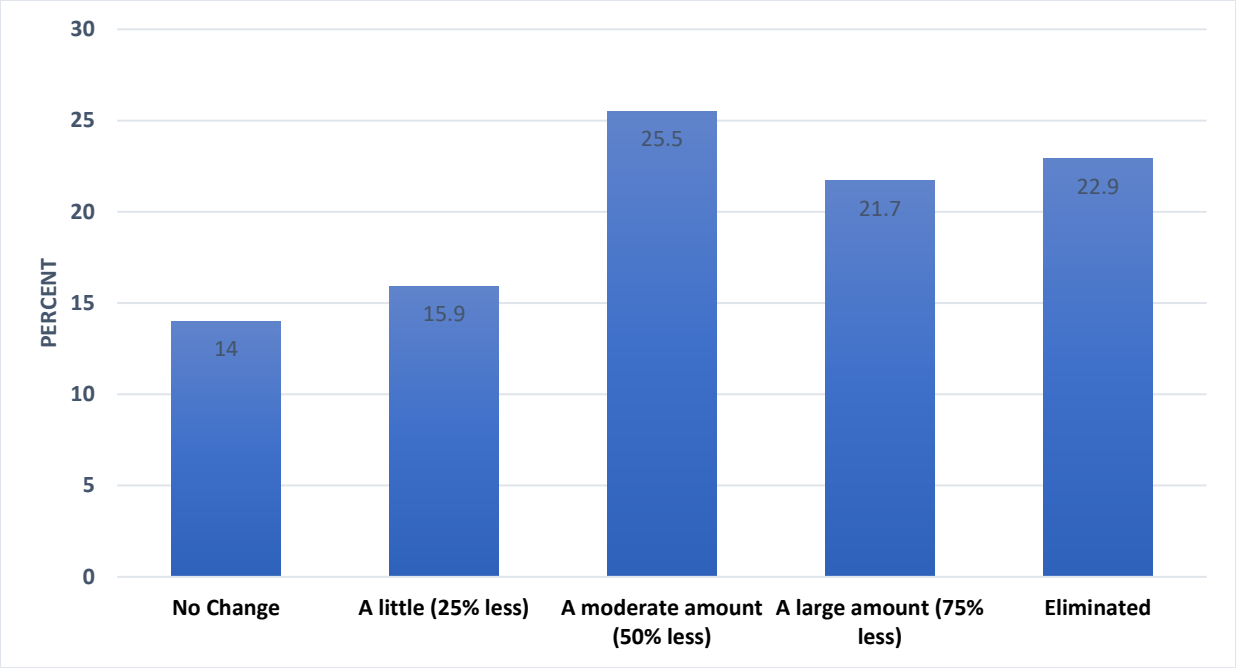

Figure 3. The majority of the subjects were able to reduce analgesic medication use, with 86% reporting at least a 25% reduction and 44.6% reporting a large (75%) reduction or elimination of medication use.

Quality of Life Measures

Quality of life (QOL) changes were evaluated in subjects over time using a standard QOL assessment consisting of seven responses, ranging from "no change" to "a great deal better" since using ActiPatch as a pain therapy. At the 6-month interval, 91.5% reported a "moderately better" to "great deal better" improvement in their quality of life (Figure 4.). These data include all the 194 subjects who completed all 3 follow up assessments. Improvements in sleep were reported by 90.6% of the study subjects at the 6-month interval. Similarly improvements in physical activity were reported by 90.5% by the six month time period.

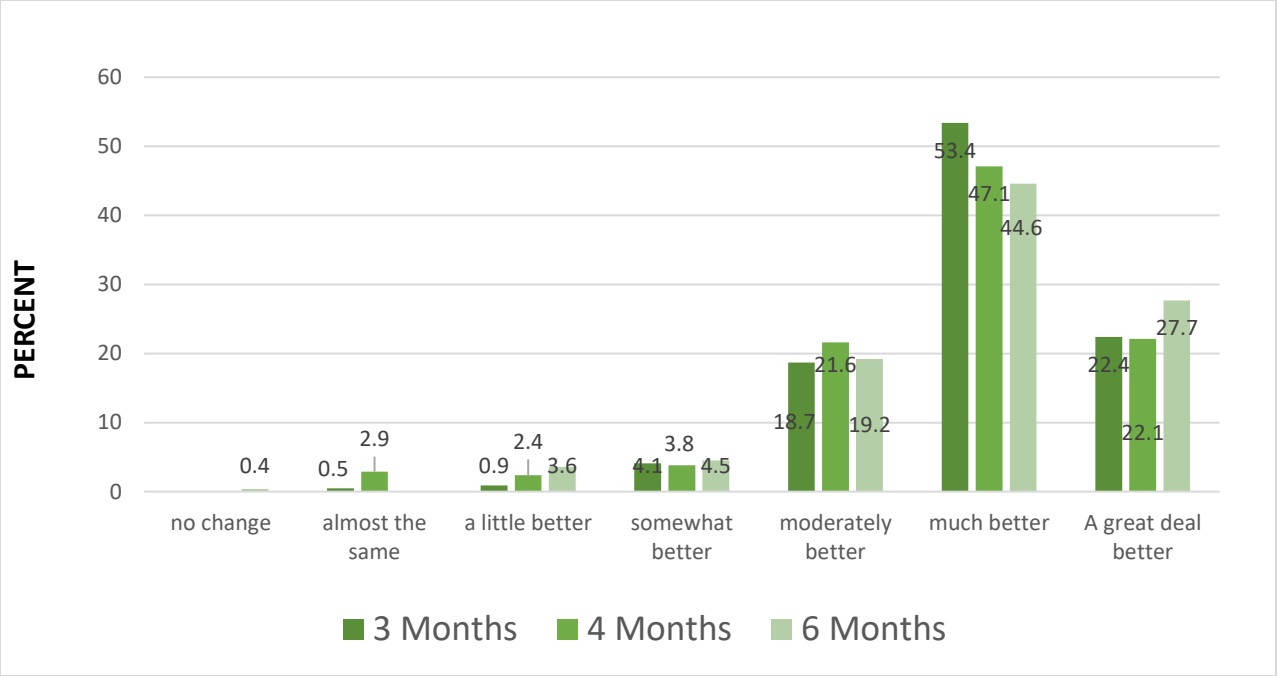

Figure 4. Quality of life was improved for a majority of the subjects, and was consistent over the 6 month study period.

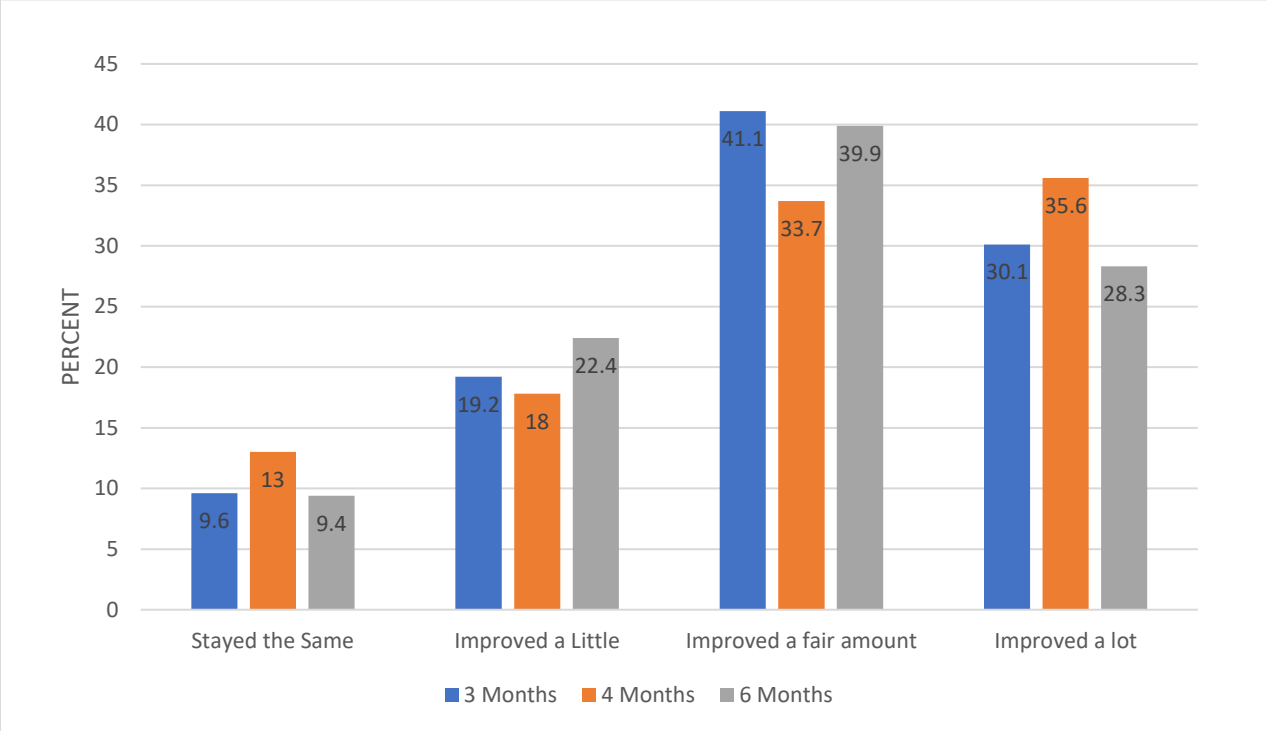

Figure 5. Sleep activity was reportedly improved in over 90% of the subjects at each of the assessments.

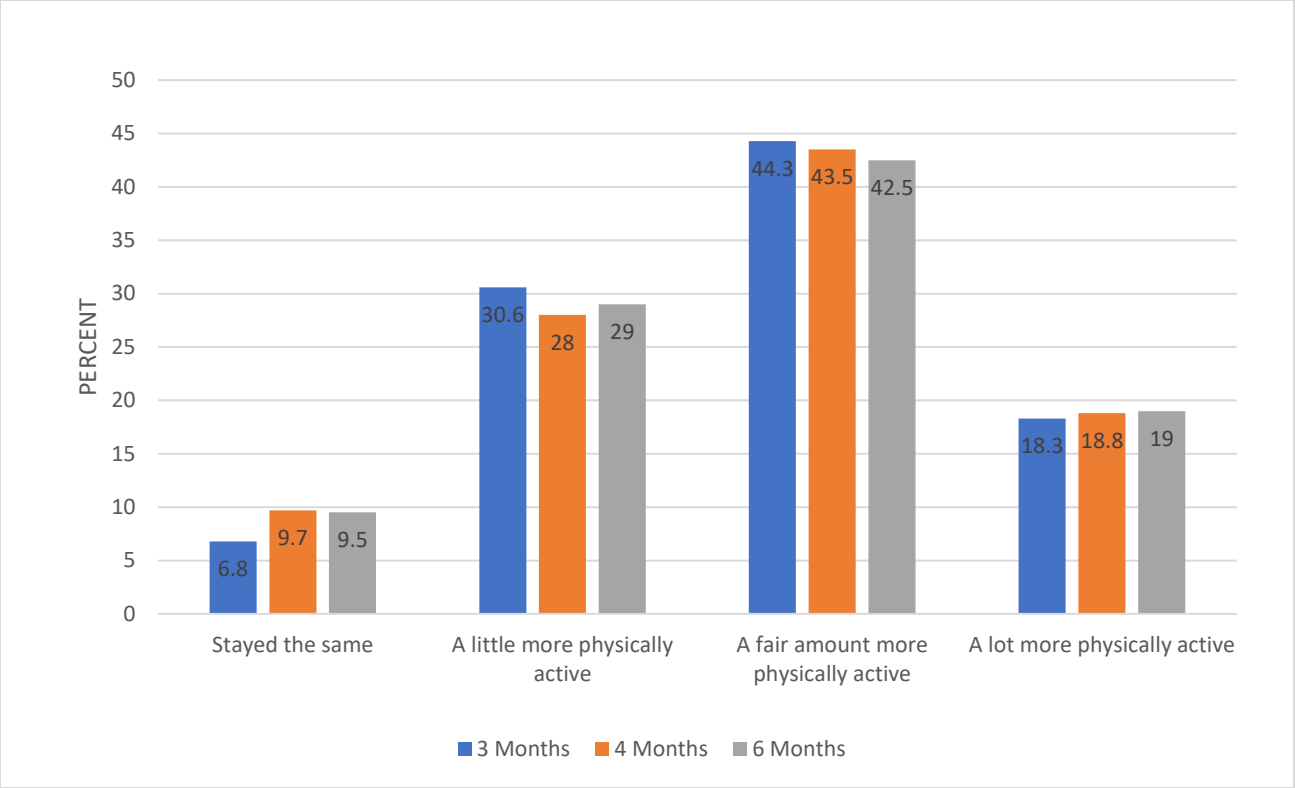

Figure 6. Physical activity was reportedly in over 90% of the subjects at each of the assessments.

Device Use

Over the 6-month period, the need to use the ActiPatch® decreased with time, with 60% reporting everyday use at the 3-month interval and only 36% reporting everyday use at the 6-month interval. A corresponding increase in those using the device only as needed was also seen, increasing from 20% at the 3-month interval to 37% at the 6-month interval.

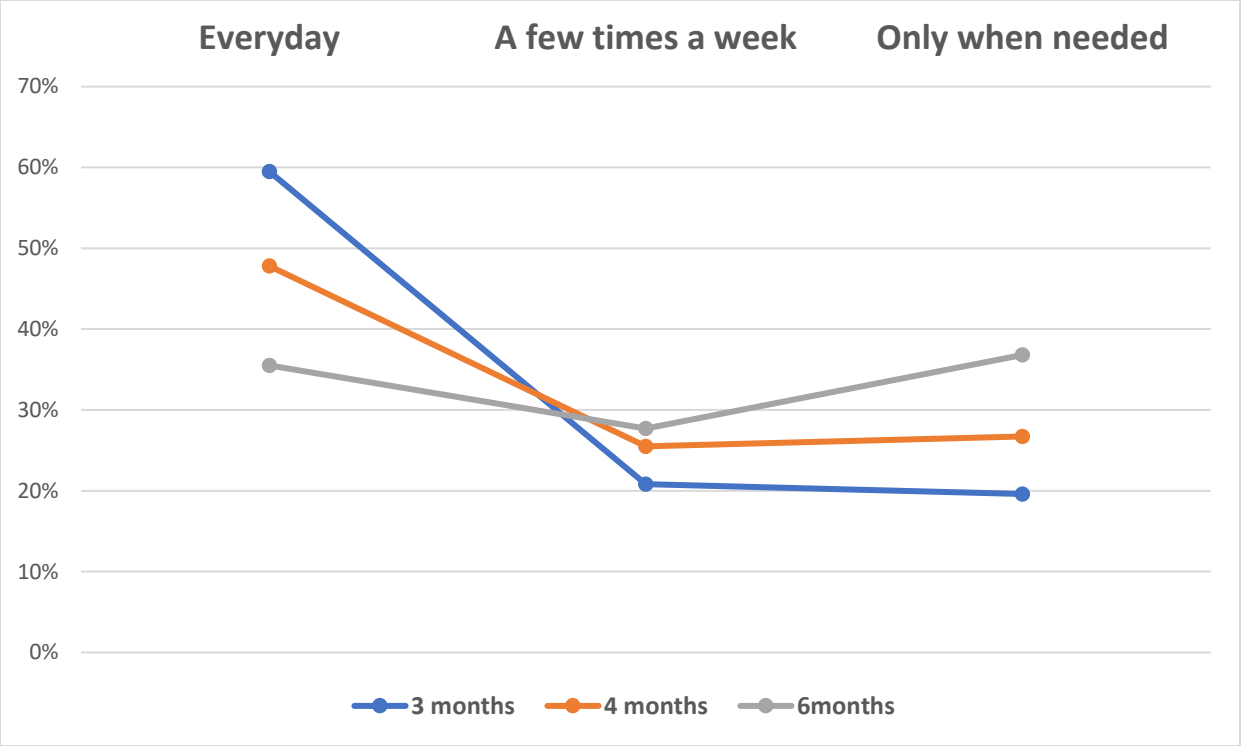

Figure 7. Device use decreased with time, with only 60% using it "Every Day" at 3 months and 36% at 6 months. Device use "Only When Needed" increased from 20% at 3 months to 37% at 6 months.

Health Economics

Of the subjects, 64% were able to reduce the number of visits to a physician and 69% indicated that they spent less money on pain therapies (Figure 8.).

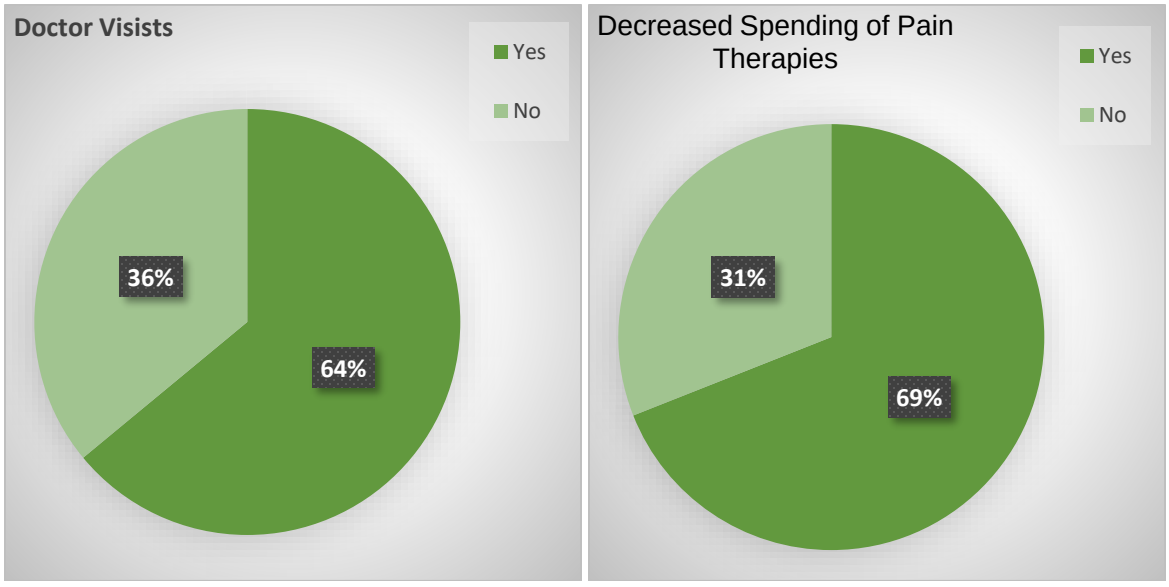

Figure 8. Visits to the physician were reduced in 64% of the subjects, and 69% spent less money on pain therapies.

Subject Drop Outs

A total of n = 21 of the 254 subjects who indicated they would be part of the longitudinal study only completed the 3 month's assessment. Eleven of these 21 subjects reported at that time their pain level was mild (0-3 VAS score), and these 11 subjects also reported either a much better or a great deal better QOL improvements (with the exception of one subject who reported a moderate QOL improvement). Based on these data we classified these subjects as having received a successful treatment and this lead them to "drop out" of the remaining assessments. (We note that the only compensation for completing the remaining two assessments was to receive a free device, the use of which was less valuable given that they were no longer in pain.) Of the remaining 10, nine reported moderate pain and 1 reported severe pain. These subjects are assumed to be treatment failures.

Another 21 completed the 3 and 4 months or the 4 month's assessment only. Of these 21 subjects, 3 subjects were not experiencing good pain relief. It's assumed that these subjects dropped out due to treatment failure or changes in the underlying condition. Another six subjects were experiencing moderate pain (4-6 VAS scores) and are assumed to be treatment failures, while the remaining 12 subjects reported mild pain and had an average 1.9 VAS score, and are therefore determined to be treatment successes. Thus, we estimate in total there were 19 treatment failures or 7.5% of the total sample that occurred for the 42 subjects who did not complete the six-month study.

Summary

- The vast majority of the subjects in the study continued to receive benefit at 6 months (83%) or achieved resolution (9%) of their pain to a degree that the use of ActiPatch was no longer needed. Conversely 7.5% of those subjects who initially indicated that they got substantial pain relief from the 7-day trial, were classified as not continuing to get relief over a longer period of time.
- Well maintained pain was reflected in improved quality of life measures.
- The data also show that pain management was achieved with a concurrent reduction in analgesic medications.
- Taken together well controlled pain and less use of analgesic drugs translated into meaningful improvements in quality of life for greater than 90% of the individuals in the study.
- Decreased device use over time is indicative of an improving underlying condition.
- The majority of subjects indicated less visits to Doctors and less spending on pain therapies.

ActiPatch Sleep Study

Overview and Methods

In this section of the Registry data, we investigate the impact of pain levels on sleep quality, and if using the 7-day trial device changed sleep quality. Pain data pertaining to individuals in this subset were not included in the larger, 5244 subject data set provided in section 1 since these data were recently collected using a somewhat different set of questions. The impact of pain on a subject's sleep quality was assessed on a visual analogue scale of 0-10, 0 being no impact from pain and 10 being the worst impact from pain. Data were collected for all individuals suffering with chronic pain, but this section only reports on data for individuals suffering with chronic back pain. With this noted, the data collection procedure and sample used is similar in all respects to the procedure used in the 5244 person CBP registry.

Chronic Pain and Sleep

In recent years, there has been more attention drawn to an interesting hypothesis: that disturbance in sleep can cause or modulate both acute and chronic pain levels. Laboratory based sleep deprivation studies have indicated that reductions in total sleep time are accompanied by increased sensitivity to noxious stimuli (secondary hyperalgesia) and by decrements in endogenous pain-inhibitory processes. This could help explain why many chronic pain conditions have a pathology that can be linked to central sensitization (CS). More than 50% of osteoarthritis patients experience pain during the night, resulting in sleep disruption, poor sleep quality, sleep fragmentation and frequent shifts between sleep cycles[1]. Recent studies have shown that sleep disruption can be a predictor of pain severity. As such, in individuals suffering with chronic pain, sleep disruption could be associated with increased pain sensitivity and reduced pain inhibition. Literature evidence indicates that the severity of sleep disruption is associated with altered pain processing, and that improving sleep quality for persons with knee OA-related pain might contribute to pain reductions. In summary, individuals with insomnia and other sleep issues have an increased sensitivity to pain. Sleep disruption appears to be associated with altered pain processing and central sensitization. With this in mind, we explored the association between pain reduction and improved sleep.

Results

A total of 233 subjects completed this study, with 138 (59%) of them suffering with chronic back pain. Tables 1-4 provide details about the study participants, categorized by age, pain duration, pain etiology and location of trial device use.

Table 1. Age and gender of the study participants.

Gender	All	CBP
Male	16%	16%

[1] Campbell CM, Buenaver LF, Finan P et al. Sleep, Pain Catastrophizing, and Central Sensitization in Knee Osteoarthritis Patients With and Without Insomnia. Arthritis Care Res (Hoboken). 2015 Oct;67(10):1387-96.

Female	84%	84%
Age	**All**	**CBP**
18-24	0.4%	0.7%
25-34	2.1%	3.6%
35-44	21.0%	22.4%
45-54	29.6%	29.7%
55-64	26.6%	22.5%
65 plus	20.2%	21.7%
Prefer not to answer	0%	0%

Table 2. Pain duration as reported by subjects in the 7-day trial assessment.

Duration	All	CBP
0-6 months	N/A	N/A
6 m – 1 year	10.3%	10.9%
1-2 years	15.5%	11.6%
2-5 years	25.3%	23.9%
16.5-10 years	22.3%	19.6%
10-20 years	17.6%	22.5%
20 years plus	9%	10.1%

Table 3. Location of use of the trial device

	All
Back	57.9%
Knee	13.3%
Neck	8.6%
Shoulder	16.3%
Hip	10.3%
Ankle	2.6%
Foot	2.1%
Elbow	1.7%
Wrist	0.4%
Leg	1.7%
Hand	0
Other	2.1%

Table 4. Pain Etiology

Etiology	All	CBP
	N=233	N=138
Not sure	13.8%	16.7%
Accident	9.1%	10.9%

Ankylosing spondylitis	3.9%	5.8%
Cervical issues	3.0%	3.6%
CRPS	0.9%	0.7%
Disc issues	13.4%	21.0%
Fibromyalgia	15.9%	18.1%
Frozen shoulder	2.6%	1.4%
Ligament damage	1.3%	0.7%
Multiple Sclerosis	0.4%	0%
Neuropathy	3.9%	4.3%
Osteoarthritis	19.0%	13.0%
Osteoporosis	3.0%	3.6%
Rheumatoid arthritis	9.1%	8.0%
Sciatica	11.6%	15.9%
Sports injury	3.4%	2.2%
Surgery	3.9%	5.1%
Tendinitis	2.2%	0.7%
Trapped nerve	4.3%	5.1%
other	15.5%	13.8%

Pain Data/Sleep Data

Pain level and its impact on sleep quality were assessed on a 0-10 visual analogue scale (VAS), Table 5 shows average VAS scores for the entire group, and more specifically, for CBP subjects.

Table 5. Baseline and post-trial VAS scores, VAS difference and percent difference.

	N = 233 Pain	N = 233 Sleep	CBP N=138 Pain	CBP N=138 Sleep
Baseline VAS	8.19±1.42	6.66±3.14	8.14±1.31	6.61±2.95
Post-trial VAS	4.90±2.78	4.28±3.28	4.52±2.84	4.13±3.16
VAS Difference	3.29	2.38	3.62	2.48
Percent Improvement	40.2%	35.7%	44.5%	37.5%
P Value	<0.005	<0.005	<0.005	<0.005

Of the 138 subjects with CBP, 118 (85%) reported that pain interfered with their sleep. A majority of these individuals (72, 61%) reported that using the 7-day trial device enabled them to sleep better. In Tables 6 and 7 we show the association between reduction in pain and changes in sleep scores by categorizing the data into three groups: those who reported better sleep (N=72), those who reported that their sleep was affected by their pain, but did not notice improvements with device use (N=45), and those who indicated that their chronic pain did not affect their sleep (N=21).

Table 6. VAS scores before and after using 7-day trial device for both types of individuals: those who reported sleep improvements and those who did not.

Improved sleep	CBP Pain Score	CBP Sleep Interference score
Improved sleep	**N=72**	**N=72**
Baseline VAS	8.10±1.46	7.29±2.04
Post-trial VAS	3.14±2.11	2.85±2.16
VAS Difference	4.96	4.44
Percent Improvement	61.2%	60.9%
No improved sleep	**N=45**	**N=45**
Baseline VAS	8.46±1.13	7.87±1.76
Post-trial VAS	7.57±2.12	7.53±1.88
VAS Difference	0.89	0.34
Percent Reduction	10.5%	4.3%

Table 7. Pain data for the (n = 24) subjects who reported that their pain didn't interfere with their sleep.

	CBP Pain Score – no sleep interference
No sleep interference	**N=21**
Baseline VAS	7.48 ± 1.21
Post-trial VAS	3.95 ± 2.62
VAS Difference	3.53
Percent Improvement	47.2%

Discussion and Conclusions

Tables 6 shows a strong correlation between pain reduction and improved sleep. For chronic back pain sufferers who reported sleep quality improvements from using the 7-day trial device (52.1%), their pain was decreased by 61.2% and sleep quality improved by 60.9%. Conversely, those who indicated no significant increase in sleep quality (32.6%) indicated that the device provided little relief in their pain levels. In individuals with no sleep interference due to their pain (15.2%), using the 7-day device nearly halved their pain, a figure that is slightly higher than the average reduction noted in the CBP registry study.

In summary, these data provide strong evidence of a correlation between chronic pain and sleep quality. When pain levels decrease sleep quality increases. Conversely when sleep increases we also see decreases in pain levels. Thus, the two observations go hand in hand. As a result, we see that using the 7-day ActiPatch device not only significantly reduces pain levels for a large number of individuals, but also improves sleep quality which has important implication for subject quality of life.