CLINICAL TRIAL EVALUATION

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A UK registry study of the effectiveness of a new over-the-counter chronic pain therapy

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Practice points

- Musculoskeletal pain is widespread in the community.
- Wearable pulsed shortwave therapy is a new over-the-counter pain therapy in the UK and has not been shown to have any significant side effects, even in the elderly or subjects with diabetes.
- This registry study included 44,000 subjects who tried the device, with 5000 submitting an assessment.
- Subjects reported on average severe baseline pain which was present despite using on average two pain modalities including analgesics, heat wraps, transcutaneous electrical nerve stimulation and other pain therapies.
- Current pain modalities appear to be inadequate and ineffective for many individuals.
- In the study over 65% reported a clinically meaningful reduction in pain from a wide variety of etiologies and locations of pain.
- The average pain reduction reported in these individuals was 57%.
- The 3-month follow-up showed sustained pain relief, decreased oral analgesic medication use and quality of life improvement.
- Pulsed shortwave therapy offers a new alternative safe chronic pain therapy.

Background: The ActiPatch® (BioElectronics Corporation, MD, USA) pulsed shortwave therapy device has been shown to be clinically effective in three double-blind randomized controlled pain studies. However, the effectiveness of this device in a broader population of chronic musculoskeletal pain sufferers, affected by a variety of etiologies in different regions of the body, has not been studied. **Aim:** The objective of this registry study was to assess the effectiveness and satisfaction of the ActiPatch device in the general population of chronic pain sufferers. **Methods:** A total of 44,000 subjects completed the trial, with 5000 assessments of the device collected. **Conclusion:** The ActiPatch device appears to provide a clinically meaningful reduction of chronic musculoskeletal pain affecting different locations of the body caused by a variety of etiologies.

Chronic pain is a major burden for individuals and poses a significant public health challenge [1]. Its incidence and prevalence are increasing with an aging population and the rise in obesity. Prevalence of chronic pain is estimated to be 37% in the USA, with an estimated annual cost of US$635 billion [2]. Similar estimates have been put forward for the EU, with an annual cost calculated to be

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around €300 billion [3]. In a large European pain survey, Breviek *et al.* [4] reported that nearly one-fifth (19%) of adults across Europe suffer from moderate to severe chronic pain. When considering the location of the pain and its etiology, back pain was the most common location with arthritis/osteoarthritis being the most common cause [4]. Chronic back pain has a high economic outlay due to the direct costs of treatment, lost productivity, employment and disability compensation and negative impacts on quality of life [5,6].

Options for treating pain appear to be diminishing with a recent report highlighting the lack of efficacy of paracetamol for spinal pain and osteoarthritis, as well as the lack of improved function and durability of response to opioids [7,8]. Guidelines for NSAID use recommend use for the shortest duration and lowest effective dose due to risk of adverse effects [9]. These adverse effects include gastrointestinal tract injury [10,11], kidney injury, worsening of heart failure and hypertension, increased risk of stroke, heart attack [12] and deep vein thrombosis, as well as death [10,13]. The use of poorly tolerated and ineffective medications is a major driver in direct healthcare costs [14]. Therefore, identification of new safe pain therapies that are efficacious and cost effective are urgently needed.

Nonpharmacological therapies for chronic pain including therapies such as transcutaneous electrical nerve stimulation [15], heat wraps, physical therapy, acupuncture, nutrition, biofeedback and cognitive behavioral therapy have been used for chronic pain with varying degrees of efficacy [16,17].

ActiPatch® (BioElectronics Corporation, MD, USA) has been recently introduced into the UK as an over-the-counter (OTC) 'topical' analgesic for localized musculoskeletal pain. Before this introduction, there was almost no awareness of this medical technology and device. ActiPatch is a noninvasive, low power, easy to use, pulsed shortwave therapy device for localized musculoskeletal pain. The device does not produce heat or any sensation. There are two basic requirements to use the device, switching it on via an on/off switch, and affixing the device over the target area of the body. The area of treatment is confined to the area within the 11.5-cm diameter loop antenna covering an area of 100 cm^2, the antennae is circular, soft and flexible and can be shaped to fit the area/location being treated as required.

As an acute muscle pain treatment, the ActiPatch device significantly reduced postoperative pain in submuscular breast augmentation patients, and significantly reduced the requirement for narcotic pain medications [18]. In two chronic musculoskeletal pain conditions, plantar fasciitis [19] and osteoarthritis of the knee [20], the device was found to significantly reduce pain and medication use [19,20]. However, the effectiveness of ActiPatch has not been studied in a large cohort of musculoskeletal pain subjects with pain in different locations due to a variety of etiologies. To achieve this goal we conducted a registry study of subjects who signed up to receive a trial device. The trial device, once activated has a 7-day power supply and is recommended to be used continuously for the 7 days. The study was designed to evaluate effectiveness (where a treatment is defined to be effective if the user reports a significant reduction in pain when used in real life and in nonideal circumstances) of the device in the common areas of the body affected by different causes of musculoskeletal pain as well as acceptance of subsequent use of the device by the subjects.

Methods

• Subjects

A registry of 44,000 subjects who submitted a request via the ActiPatch website to try a trial device was established between July 2014 and April 2015. Most of these consumers first heard of this medical device via a company sponsored message found on Facebook or a direct response TV testimonial message, although some first heard of the trial offer from a friend or family or a few magazine advertisements. All subjects were from the UK and Ireland, ActiPatch is classified as a class IIa over the counter medical device in the EU but is not available in the USA over the counter. Subjects paid GB£2.95 to obtain the device that was shipped to their home.

• ActiPatch

ActiPatch is a low power pulsed shortwave therapy device operating at 27.12 MHz, emitting pulses at a rate of 1000 pulses per second, each sustained for a 100 µs. The peak power is 73 µWatts/cm^2 with an electromagnetic flux density of 30 µT. The mechanism of action is beginning to be elucidated. Unpublished data suggest a noninvasive neuromodulation effect, with the ability to stimulate afferent nerves through inductive coupling and stochastic resonance. The device

can be used up to 24 h per day and is placed over the area of localized pain either using medical tape or a specifically designed wrap.

• Data collection & processing

The survey objectives were to assess self-reported effects of ActiPatch on chronic pain from an array of etiologies. Three to four weeks after receiving a trial device, subjects were emailed a web-based assessment form using Constant Contact email software. An initial email was followed by a second reminder email 6 days later.

A total of 44,000 subjects registered, and received a trial device and the email assessment form generated 5002 responses, a response rate of approximately 11%. Raw data were outputted and analyzed with Excel 2013 (Microsoft Corp. WA, USA). The trial device was considered effective or of benefit when there was a reported 2 or greater visual analogue scale (VAS) point reduction (0–10 scale). The defined minimal VAS pain reduction for a treatment to be deemed clinically significant has been reported to be between 9 and 14 mm (0–100 mm scale) or 0.9–1.4 on the 0–10 scale [21] and so the 2-point VAS cut off level for determining the effectiveness is conservative. Tests for non-response bias were conducted by using the well validated approach of comparing first wave and second wave responses [22]. Validation was also done by grouping data by month to show the consistency of the data, and conducting a second assessment, after a minimum of 3 months, to determine durability of pain management, impact on quality of life and pain medication use. This assessment was sent to those reporting an intention to purchase the commercial device.

According to European regulations on non-interventional studies with medical devices (CE directive 93/42 and ISO 13485), this survey did not require ethics committee approval.

Results

A total of 5002 responses were acquired between June 2014 and April 2015. All responses were included in the data with the exception of responses that included comments that stated that the trial ActiPatch had not been received or used. There was a total of 250 exceptions with the majority reporting that they had not received the trial device and these were not included in the total of responses. There was a preponderance of females (74%), compared with males in the respondent population (26%), with the majority of subjects over the age of 35 years **(Box 1)**.

Box 1. Demographics of the trial device subjects.

- Gender:
  - Male: 26%
  - Female: 74%
- Age:
  - 18–24 years: 0.9%
  - 25–34 years: 2.9%
  - 35–44 years: 15%
  - 45–54 years: 25.4%
  - 55–64 years: 29.5%
  - 65 years or over: 26.3%

• Cause of pain

In a number a cases multiple causes of pain were reported with an overall average of 1.1 per subject **(Box 2)**. The most frequently reported etiologies were osteoarthritis (31%), rheumatoid arthritis 15% and fibromyalgia (15%).

• Location of pain

Multiple concurrent locations of pain were reported with an average of 1.7 per subject **(Table 1)**. Back pain was reported by 58% of respondents and sample use of the device for back pain was 44%; the knee and shoulder were the next most frequent areas of use at 21 and 15%, respectively. If it is assumed the sample user applied the device on the area that was causing the most pain, conditional that they reported that that location was causing some pain. The 'other' group mainly consisted of elbow, wrist, ankle, foot and legs for locations of use.

• Baseline pain

Baseline VAS score pain for all the responses was an average of 8.02, indicating the majority of

Box 2. Causes of chronic pain.

Percentage reporting

- Osteoarthritis: 31%
- Rheumatoid arthritis: 15%
- Fibromyalgia: 15%
- Sports injury: 8%
- Postsurgery pain: 6%
- Tendonitis: 3%
- Neuropathy: 5%
- Other: 29%

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Table 1. Location of pain and location of sample use.

Location	Location of pain (%)	Location of sample use (%)
Back	58	44
Knee	34	21
Neck	17	5
Shoulder	26	14
Hip	20	7
Other	14	8

subjects were experiencing severe pain. Baseline pain was present despite the use of on average of 1.97 pain modalities being used per subject. These were 84% analgesic tablets, 20% transcutaneous electrical nerve stimulation, 27% heat wrap, 32% topicals, 19% physical therapy and 10% other. Paracetamol and NSAIDs were the most frequently used medications at 43 and 48%, respectively (Box 3). For subjects who took pain medications, an average of 1.9 different pain medications were used.

• Pain data

The assessment of pain duration shows that chronic pain is a long standing issue for many individuals (Figure 1). Baseline pain increased with the duration of pain, with subjects reporting pain for more than 20 years recording the highest baseline pain at 8.48 (Figure 1) and less than 6 months the lowest baseline pain 7.63. There is a clear trend of increasing baseline pain with the duration of pain.

Assessment of the trial device

• Pain duration

Using the 2 VAS reduction criteria for benefit, the percentage reporting benefit from the trial device was 65% with an average pain reduction of 57% (Table 2). The percentage reporting benefit was consistent through the range of pain duration groups. However, there was a steady decrease in percentage effectiveness with duration of pain. With pain present for 20 years plus, these subjects reported an average 50% decrease in pain, compared with a 60% average reduction in pain for those with pain present for less than 2 years. Baseline pain shown in Table 2 is the baseline pain of those reporting benefit and is, therefore, slightly different than the baseline pain shown in Figure 1.

Box 3. Analgesic medications being used.

Analgesic: percentage using

- Paracetamol (acetaminophen): 43%
- NSAIDs: 48%
- COX-2 inhibitors: 2%
- Weak opioids: 23%
- Strong opioids: 21%
- Other: 22%

• Gender

Gender comparisons show that females have higher baseline pain (8.11) compared with males 7.79 (Table 3). The percentage reporting that the trial device was beneficial was higher in females at 67%, whereas with males it was 59%. However, there was no difference in the effectiveness between the genders for those reporting benefit, with females posting only a slightly higher VAS reduction (Table 3).

• Pain response by location

The following results represent data from the >6 month or chronic pain group only, a total of 4308 responses were subgrouped by location of sample use (Table 4). The percentage that reported benefit of the trial device and the level of pain reduction was consist in the major areas of the body varying from 61 to 70% effectiveness with a 4.37–4.81 VAS decrease or a 53–60% reduction in the reported pain level. The 'other' locations of use, consisted of use of the trial devices in areas of the body such as ankle, foot, elbow, wrist and hand and had the lowest effectiveness rate – 51% but highest percentage pain reduction at 60% (4.93 VAS points).

• Pain response by cause of pain

Average baseline pain was reported to be in the 8 VAS range for all causes of pain except sports injury (Table 5). The percentage reporting benefit was highest in rheumatoid arthritis and tendonitis at 71% and lowest in neuropathic pain at 59%. Effectiveness was fairly consistent with all causes of pain showing a greater than 50% pain reduction. To confirm the pain reductions were significant, a T-test was performed on the data, all locations of use and causes of pain reported in Tables 4 & 5 were statistically significant $p < 0.001$.

• VAS score distribution

The distribution of VAS scores for the 5002 respondents at baseline are predominantly in the 6–10 VAS point range totaling 4689 in this range, indicating that the registry was composed of mostly people in moderate to severe pain. However, after trial device use, repørted VAS

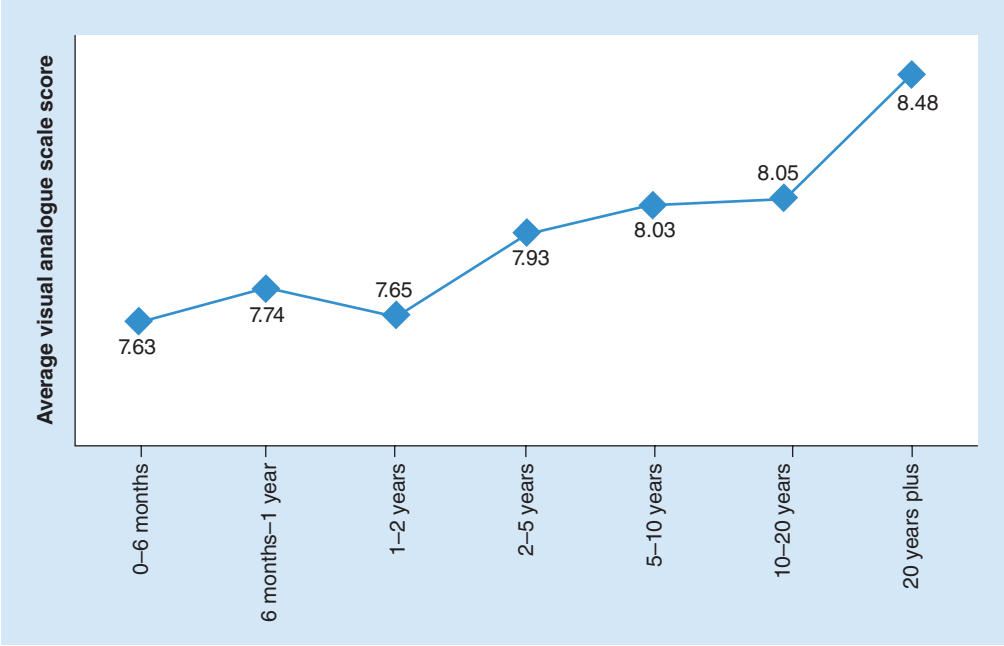

Figure 1. Baseline pain in relation to duration. Baseline pain showed a trend of increasing with the duration of pain.

scores have shifted and are fairly evenly distributed from 0 to 10, with 2879 in the 0–5 range and 2123 in the 6–10 range (Figure 2).

• Days to pain relief

The time in days needed for pain relief over the 7-day trial varied with the most reporting pain reductions by day 1 (31%) and day 2 (31%) followed by day 3 (19%). Therefore the majority, 81% required 3 days to experience pain relief (Figure 3). The data were from subjects that reported pain relief of two or more VAS points.

• Validation of the data

Baseline pain, the percentage reporting benefit and effectiveness of pain reduction with the responses are grouped by month (Table 6). These data show very strong consistency when compared across different assessment time periods. The percentage reporting benefit varied between 61 and 70% and percentage of pain reduction 53–59%.

• Non-response bias testing

Non-response bias testing was used to help validate the data [22]. This consisted of comparing the responses from the first email containing the survey – the first wave, to responses from a second reminder email 1 week later – the second wave (Table 7). The non-response testing shows only very small differences in first wave and second wave responses.

Table 2. Effectiveness and percentage benefiting from the trial device by duration of pain.

Pain duration	Percentage	Benefit (%)	Baseline VAS	Trial device VAS	VAS difference	Pain reduction (%)
0–6 months	13	65	7.83 ± 1.56	2.94 ± 1.83	4.89	62
6 months to 1 year	11	62	7.92 ± 1.47	3.14 ± 1.91	4.78	60
1–2 years	14	61	7.81 ± 1.49	3.15 ± 1.75	4.66	60
2–5 years	20	69	8.10 ± 1.49	3.29 ± 1.82	4.81	59
5–10 years	21	67	8.16 ± 1.38	3.41 ± 1.90	4.75	58
10–20 years	12	66	8.02 ± 1.59	3.51 ± 1.86	4.51	56
20 years plus	9	70	8.51 ± 1.59	4.14 ± 2.13	4.29	50
All	100	65	8.17 ± 1.50	3.49 ± 1.98	4.68	57

VAS: Visual analogue scale.

Table 3. Effectiveness by gender.

Gender	Response number	Benefit (%)	Baseline VAS	Trial device VAS	VAS difference	Pain reduction (%)
Female	3641	67	8.24 ± 1.45	3.51 ± 2.00	4.73	57
Male	1337	59	7.95 ± 1.62	3.37 ± 1.92	4.58	58

VAS: Visual analogue scale.

• Consumer acceptance

Of the responses 49% indicated that they would purchase, 22% indicated that they might purchase and 29% indicated that they did not plan to purchase the retail ActiPatch device. This response was highly correlated with the percentage improvement reported. Thus, those who reported substantial improvement in pain level also indicated a higher likelihood of purchasing the retail device. Similar patterns were found when asked if they would recommend to a friend or family member, 52% very likely recommend, 19% somewhat likely, 11% somewhat unlikely and 17% very unlikely to recommend the device.

• Three month follow-up survey data

A second follow-up assessment was sent to the 71% who reported an intention to purchase/maybe purchase the retail ActiPatch device. The assessments were sent after a minimum 3-month interval. The data from these surveys indicated a high purchase rate of 80% of the retail device. (Approximately half of 20% indicated that the reason for not purchasing was financial limitations, the retail cost is GB£19.99 equating to 66p a day) Long-term pain control was reported with 93% experiencing sustained benefit. Asked again for baseline pain, this was on average 8.34, very close to the baseline pain in the 7-day survey of 8.21 and was not significantly different ($p = 0.24$). Directly comparing the two baseline scores from the subjects 83% were either 0 or 1 point difference, with an average variation of 0.84 VAS points for all the subjects offering a strong validation to the VAS scoring used in this study. Pain levels at the 3-month time point with ActiPatch use were on average 3.99 or 51% lower than the reported baseline. Quality of life improvement was also reported with 84% reporting a moderate to a great improvement in quality of life. Along with this pain control, systemic medication use was reduced on average by 50%. These data are currently from 658 responses and data collection is ongoing.

• Attachment issues

The sample was sent with adhesive medical strips for attachment. This attachment method is adequate for most individuals, but a number of individuals, estimated at 3–6% commented on the difficulty of use.

• Safety

No major adverse events were reported. Minor issues centered on attachment of the device and a reaction to the adhesive medical tape and occurred in 0.4% of the responses. This issue can be mitigated by attachment of the device to clothing instead of directly to skin. The commercial device is supplied with wraps for back or knee to help with attachment issues.

Discussion

This registry survey provides data on a large cohort of over 5002 predominantly severe pain sufferers regarding the new OTC pain therapy device in terms of its effectiveness in the general musculoskeletal pain population. Therefore, the

Table 4. Pain reduction and effectiveness in relation to location of use for those reporting chronic pain (>6 months).

Location	Response number	Benefit (%)	Baseline VAS	Trial device VAS	VAS difference	Pain reduction (%)
Back	2080	65	8.17 ± 1.51	3.61 ± 2.03	4.56	56
Knee	946	69	8.22 ± 1.52	3.41 ± 1.89	4.81	59
Neck	211	61	7.97 ± 1.46	3.71 ± 1.89	4.26	53
Shoulder	603	68	8.11 ± 1.41	3.48 ± 1.94	4.63	57
Hip	339	70	8.25 ± 1.44	3.48 ± 2.00	4.77	58
Other	351	54	8.24 ± 1.47	3.31 ± 2.10	4.93	60

VAS: Visual analogue scale.

Table 5. Effectiveness and pain reduction by cause of chronic pain for those reporting chronic pain (>6 months).

Etiology	Response number	Benefit (%)	Baseline VAS	Trial device VAS	VAS difference	Pain reduction (%)
Rheumatoid arthritis	688	71	8.54 ± 1.41	3.62 ± 2.06	4.92	58
Osteoarthritis	1519	66	8.32 ± 1.38	3.63 ± 2.03	4.67	56
Fibromyalgia	787	68	8.57 ± 1.33	4.16 ± 2.09	4.41	51
Sports injury	370	69	7.68 ± 1.62	3.23 ± 1.81	4.45	58
Postsurgery pain	270	65	8.26 ± 1.62	3.72 ± 2.08	4.54	55
Tendonitis	128	67	8.38 ± 1.50	3.84 ± 1.85	4.54	54
Neuropathic	241	59	8.39 ± 1.36	3.82 ± 2.21	4.57	54
Other	1414	63	8.00 ± 1.57	3.36 ± 1.92	4.64	58

VAS: Visual analogue scale.

study population was defined by having musculoskeletal pain and not by a specific medical diagnosis as to the cause of pain. Demographics of the cohort favored females by 74% to 26% male and these percentages differ substantially from the reported epidemiology of chronic pain [4] (56% female/44% male) though chronic pain syndromes generally have a higher prevalence in women [1,4,23]. However, they were in line with the population segment targeted by the company with its messages concerning the opportunity to obtain the trial medical device. Specifically, the messages were targeted at women over 35 years of age who indicated on Facebook that they had some interest in pain or causes of pain, for example they were likely to discuss issues associated with arthritis. The locations of use of the trial device are similar to those reported in general surveys of chronic pain [4], with back pain being the most prominent issue reported by the subjects and the highest area of use of the trial device. The frequencies of the causes of pain reported in the registry also reflect a strong similarity to the general population of chronic pain sufferers surveyed in prior studies. However, some targeted marketing, for example, for fibromyalgia may have increased the percentage reporting this etiology as the cause of their pain.

The data presented here show a very high baseline pain scores among the respondents, with the majority – 89% reporting severe pain and the average pain score falling in the severe end of pain

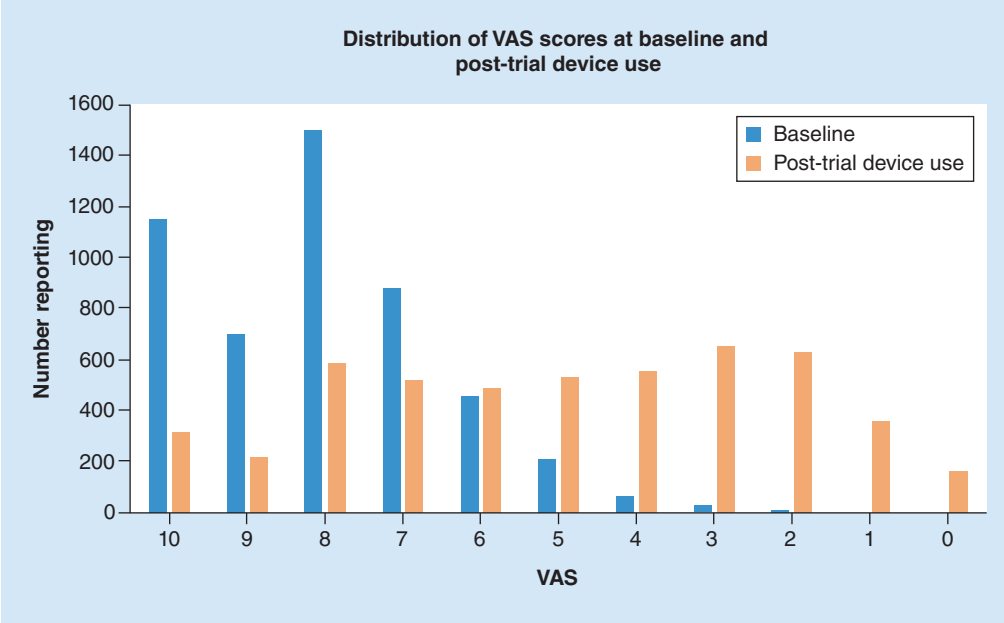

Figure 2. Distribution of visual analogue scale scores at baseline and after trial device use for all the subjects.
VAS: Visual analogue scale.

Table 6. Response data grouped by month.

Month and year	Response number	Benefit (%)	Baseline VAS	Trial device VAS	VAS difference	Pain reduction (%)
Jun–August 2014	444	70	8.47 ± 1.44	3.72 ± 2.16	4.75	56
September 2014	231	67	8.35 ± 1.40	3.95 ± 2.05	4.4	53
October 2014	611	62	8.22 ± 1.50	3.47 ± 2.02	4.75	58
November 2014	344	61	8.11 ± 1.39	3.36 ± 1.86	4.75	59
December 2014	452	68	8.10 ± 1.48	3.32 ± 1.91	4.78	59
January 2015	800	63	8.16 ± 1.55	3.51 ± 2.04	4.65	57
February 2015	441	69	8.11 ± 1.56	3.34 ± 2.00	4.77	59
March 2015	1216	63	8.08 ± 1.53	3.41 ± 1.93	4.62	58
April 2015	460	68	7.98 ± 1.48	3.39 ± 1.83	4.59	58
Other	5002	65	8.17 ± 1.50	3.49 ± 1.98	4.68	57

VAS: Visual analogue scale.

scale (8.02). This high baseline pain is present despite the use, on average, of two concurrent pain therapy modalities. This clearly demonstrates that pain treatment is often ineffective and inadequate in many individuals. Underscoring this point is the fact that 84% reported taking pain medications, and these subjects used on average 1.9 types of medication per individual clearly demonstrating that many patients respond poorly to a pharmacological approach for chronic pain [7,14]. Given this severe chronic pain segment of the general population has not found any solution to reducing this pain to an acceptable level, it is clear that there is a need for new innovative pain therapies that are effective, safe and economically acceptable. While reported baseline pain levels may seem to be high, baseline pain levels were duplicated in the 3-month follow-up assessment, suggesting the VAS scoring is reflected of the pain being experienced. These data indicate that ActiPatch is an effective pain modality; for those reporting benefit (2 or > VAS reduction) for all the responses was 65%, with an average pain reduction of 4.68 VAS points or 57%. The percentage reporting benefit from those reporting chronic pain, pain >6 months, was 65% with a 57% pain reduction demonstrating equal effectiveness for chronic pain. This is true regardless of the length of time pain was present, with only a slight decrease in effectiveness with the increased time of the chronic pain. The percentage reporting benefit was also consistent across all major areas of the body varying between 61 and 70%, except the option 'other' which included elbow, wrist, hand, fingers, legs, ankle and feet, where the benefit was reported by 54% (though the extent of effectiveness was higher at 60% or 4.93 VAS point pain decrease). This may be due to the difficulty of attachment of the device to these areas of the body and only those experiencing rapid pain relief persisted with the use of the sample device.

The percentage reporting that the device was beneficial showed consistency with different causes of pain, rheumatoid arthritis showed the highest rate of benefit at 71%, whereas neuropathy was the lowest reported at 55%. Effectiveness of the trial device was shown, with average VAS point decreases ranging from 4.41 to 4.92, with rheumatoid arthritis at 4.92 the largest VAS point decrease. Effectiveness of the ActiPatch sample was matched by subject interest in purchasing the full retail device, with 71% reporting a 'yes' or maybe purchase and consumer likelihood of recommending the device to family and friends.

The VAS scale has been used widely in clinical and research settings where a quick index of pain intensity is required and to which a numerical rating can be assigned. VAS scoring has been shown to have reliability and validity [24]. It is accepted

Table 7. Non-response bias testing.

Response number	Benefit (%)	Baseline VAS	Trial device VAS	VAS difference	Pain reduction (%)
Total 1231 responses (both waves)	63	8.05 ± 1.49	3.34 ± 2.78	4.71	59
First wave 829 responses	62	8.12 ± 1.49	3.36 ± 2.77	4.76	59
Second wave 319 responses	66	7.92 ± 1.56	3.25 ± 2.95	4.67	59

VAS: Visual analogue scale.

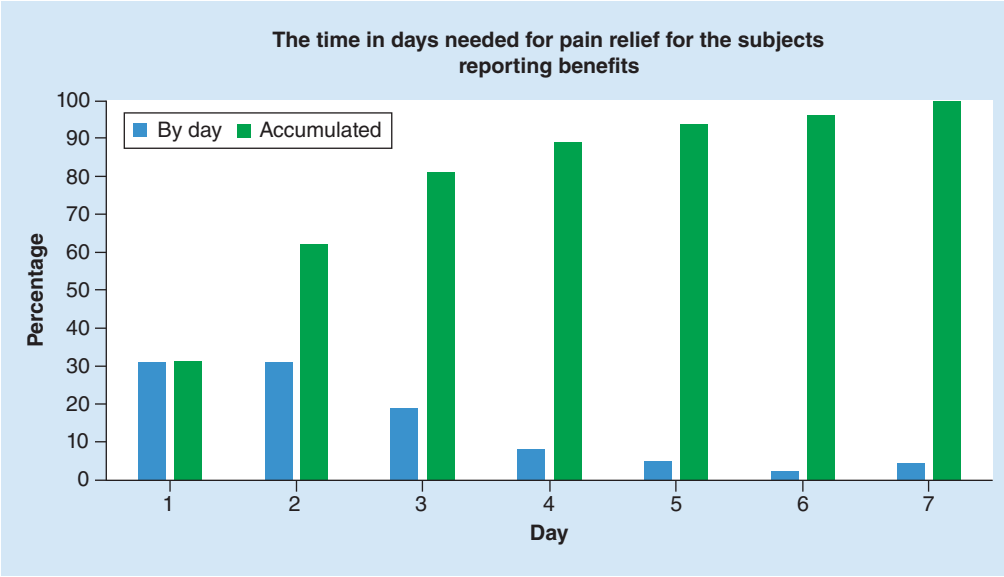

Figure 3. The days needed to experience pain relief shown as the percentage reporting pain relief by day, and accumulated percentage.

by the authors that it is a unidimensional pain rating scale that does not fully capture the complexity of the pain. Note, however, that the follow-up study also assessed the quality of life and the use of medication which are other indicators of the person's pain level [25].

While this study is not a randomized controlled trial, and lacks in this regard, there are strengths to this study. This is a large-scale report of a new OTC pain device being used in the community. The registry data come from 58 separate assessments that generate remarkably consistent results when grouped on a month by month basis. Baseline pain scores vary by only a few tenths between each of the sets of data collected, as does the extent of reported benefit in terms of both the level of and average pain reduction, and the effectiveness of the device. The data were also non-response bias tested. Non-response bias testing was conducted by examining trends in data over successive waves of data collection, and is a validated approach for determining non-response bias from just the obtained data [22]. Non-response bias testing did not reveal bias in the data as first wave and second wave baseline and device use VAS scores were very closely matched, as well as having the same level of effectiveness in percentage pain reduction. In fact, we noted that the second wave there was slight improvement in the percentage that reported benefit. Thus, the data suggest that the first wave contains a slightly higher level of people reporting no change in their pain levels. This may reflect that they were disappointed or frustrated that another pain therapy had failed for them and thus were quick to respond.

• Study limitations

This study involved participants who self-selected into the sample and thus may not represent a random sample of all chronic pain sufferers. In this way it is similar to many clinical trials where the patient volunteers to participate. In addition, our results are based only on users who responded to our survey. Although non-response bias testing did not reveal evidence of responder bias, it is still possible that bias could have been present.

Due to the open nature of the study, it could be argued that the reported benefit is due to a strong placebo effect. However, there is no evidence for placebo analgesia except for early time points in chronic pain [26]. Also the 3-month follow-up survey on subjects who reported effectiveness with the trial device indicated a substantial relationship between reported pain relief and actual consumer behavior. This was shown by subjects acquiring the commercial device as well as continued benefit over the longer period, with 93% who purchased the commercial device reporting continued benefit. Moreover, pain control was consistent with an average 51% reduction in pain. Pain control was matched by improvements in quality of life and reductions of systemic medication use. These data indicate that the benefit

experienced with the trial device was not due to a placebo effect. Furthermore, three published randomized controlled trials using placebo controls indicate that the placebo effect is minimal with this medical device. In plantar fasciitis the placebo effect was reported to be 7% in the control group [19], compared with a 40% pain reduction in the study group. In a knee osteoarthritis study placebo effect was reported to be small compared with the reduction in the study group [20]. Therefore, it would appear unlikely that a placebo effect had a major role in the reported effectiveness of the ActiPatch device though it can not be entirely ruled out as a contributing factor. What is clear overall, is that by using the device, subjects reported that they were in less pain and that they went on to purchase the commercially available device to continue to obtain the therapeutic benefit of pain reduction and as a result reported improvements in their quality of life.

The mechanism of action of ActiPatch is thought to be through a mechanism of noninvasive neuromodulation via stimulation of afferent nerves [McLeod KJ, Unpublished Data]. Though ActiPatch is a very low power device, the pulsed signal is adapted to influence afferent nerve firing through inductive coupling and stochastic resonance. Stochastic resonance is a process where the background noise amplifies the signal, in this case the inherent noise of the body amplifying the signal from the ActiPatch. The time response to pain relief reported supports the mechanism of neuromodulation as the potential mechanism of action. The time for pain relief was spread out over the 7-day trial period though the majority (81%) experienced pain relief by 3 days of use of the trial device.

Conclusion & future perspective

This registry study of 5002 individuals, of which 4301 reported chronic pain, demonstrated that 65% experienced a 2 or greater VAS point reduction, a clinically meaningful reduction in chronic musculoskeletal pain. Along with an excellent risk/benefit ratio profile of ActiPatch, the data supports its use in the community as an OTC product.

The completion of further randomized controlled studies of this device in chronic musculoskeletal pain are needed, as well as presenting a clear mechanism of action, which is believed to be noninvasive neuromodulation. This will help gain acceptance of the technology by patients and in the medical community. Further research and refinement of the technology may well enhance its clinical effect and offer a safe alternative chronic musculoskeletal pain therapy for many individuals in the years ahead.

Financial & competing interests disclosure

IM Rawe and DC Kotak are paid employees of BioElectronics Corporation. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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References

Papers of special note have been highlighted as:
• of interest; •• of considerable interest

1 Baker M, Collett B, Fischer A *et al.* Improving the current and future management of chronic pain. A European Concensus Report (2010). www.efic.org/userfiles/file/pain_proposal.pdf

•• **The concensus report clearly lays out the scale of chronic pain in the European community. Describes the challenges faced by those experiencing chronic pain and the challenges in providing pain management.**

2 Gaskin DJ, Richard P. The economic costs of pain in the United States. *J. Pain* 13(8), 715–724 (2012).

• **The actual cost of chronic pain is estimated showing the enormous economic burden of chronic pain in the USA.**

3 Wenig CM, Schmidt CO, Kohlmann T, Schweikert B. Costs of back pain in Germany. *Eur. J. Pain* 13(3), 280–286 (2009).

4 Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur. J. Pain* 10(4), 287–333 (2006).

•• **A comprehensive survey detailing the prevalence of chronic pain in European countries.**

5 Hong J, Reed C, Novick D, Happich M. Costs associated with treatment of chronic low back pain: an analysis of the UK General Practice Research Database. *Spine (Phila. PA 1976)* 38(1), 75–82 (2013).

6 Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain* 84(1), 95–103 (2000).

7 Machado GC, Maher CG, Ferreira PH *et al.* Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. *BMJ* 350, h1225 (2015).

• **Reviews paracetamol use and concludes that paracetamol is not an effective choice for spinal pain and osteoarthritis.**

8 Deyo RA, Von Korff M, Duhrkoop D. Opioids for low back pain. *BMJ* 350, g6380 (2015).

9 Hochberg MC, Altman RD, April KT *et al.* American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res. (Hoboken)* 64(4), 465–474 (2012).

10 Momeni M, Katz JD. Mitigating GI risks associated with the use of NSAIDs. *Pain Med.* 14(Suppl. 1), S18–S22 (2013).

11 Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal

antiinflammatory drugs. *N. Engl. J. Med.* 340(24), 1888–1899 (1999).

12 Gislason GH, Jacobsen S, Rasmussen JN *et al.* Risk of death or reinfarction associated with the use of selective cyclooxygenase-2 inhibitors and nonselective nonsteroidal antiinflammatory drugs after acute myocardial infarction. *Circulation* 113(25), 2906–2913 (2006).

13 Curiel RV, Katz JD. Mitigating the cardiovascular and renal effects of NSAIDs. *Pain Med.* 14(Suppl. 1), S23–S28 (2013).

14 Belsey J. Primary care workload in the management of chronic pain: a retrospective cohort study using a GP database to identify resource inplications for UK primary care. *J. Med. Econ.* 5, 39–50 (2002).

15 Vance CG, Dailey DL, Rakel BA, Sluka KA. Using TENS for pain control: the state of the evidence. *Pain Manag.* 4(3), 197–209 (2014)

16 Mathews M. Multimodal treatment of pain. *Neurosurg. Clin. N. Am.* 25, 803–808 (2014).

17 Turk DC, McCarberg B. Non-pharmacological treatments for chronic pain. *Dis. Manage. Health Outcomes* 13(1), 19–30 (2005).

18 Rawe IM, Lowenstein A, Barcelo CR, Genecov DG. Control of postoperative pain with a wearable continuously operating pulsed radiofrequency energy device: a preliminary study. *Aesthetic Plast. Surg.* 36(2), 458–463 (2012).

- **A small randomized control trial demonstrating efficacy of pulsed shortwave therapy for acute postoperative pain.**

19 Brook J, Dauphinee DM, Korpinen J, Rawe IM. Pulsed radiofrequency electromagnetic field therapy: a potential novel treatment of plantar fasciitis. *J. Foot Ankle Surg.* 51(3), 312–316 (2012).

- **A randomized controlled trial indicating the efficacy of pulsed shortwave therapy in recalcitrant plantar fasciitis.**

20 NCT Trials Database: NCT01877278. https://clinicaltrials.gov

21 Kelly AM. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. *Emerg. Med. J.* 18(3), 205–207 (2001).

22 Armstrong JB, Overton TS. Estimating nonresponse bias in mail surveys. *J. Market. Res.* 14, 396–402 (1977).

23 Mogil JS, Bailey AL. Sex and gender differences in pain and analgesia. *Prog. Brain Res.* 186, 141–157 (2010).

24 Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain. *Arthritis Care Res. (Hoboken)* 63(S11), 40–252 (2011).

25 Farrara JT, Young JP, LaMoreauxb *et al.* Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 94, 149–158 (2001).

26 Mbizvo GK, Nolan SJ, Nurmikko TJ, Goebel A. Placebo responses in long-standing complex regional pain syndrome: a systematic review and meta-analysis. *J. Pain* 16(2), 99–115 (2015).