



## Original Article

## Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly

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## ARTICLE INFO

## Keywords:

Medical cannabis  
 Medical marijuana  
 Elderly  
 Aged  
 Opioids

## ABSTRACT

**Introduction:** There is a substantial growth in the use of medical cannabis in recent years and with the aging of the population, medical cannabis is increasingly used by the elderly. We aimed to assess the characteristics of elderly people using medical cannabis and to evaluate the safety and efficacy of the treatment.

**Methods:** A prospective study that included all patients above 65 years of age who received medical cannabis from January 2015 to October 2017 in a specialized medical cannabis clinic and were willing to answer the initial questionnaire. Outcomes were pain intensity, quality of life and adverse events at six months.

**Results:** During the study period, 2736 patients above 65 years of age began cannabis treatment and answered the initial questionnaire. The mean age was  $74.5 \pm 7.5$  years. The most common indications for cannabis treatment were pain (66.6%) and cancer (60.8%). After six months of treatment, 93.7% of the respondents reported improvement in their condition and the reported pain level was reduced from a median of 8 on a scale of 0–10 to a median of 4. Most common adverse events were: dizziness (9.7%) and dry mouth (7.1%). After six months, 18.1% stopped using opioid analgesics or reduced their dose.

**Conclusion:** Our study finds that the therapeutic use of cannabis is safe and efficacious in the elderly population. Cannabis use may decrease the use of other prescription medicines, including opioids. Gathering more evidence-based data, including data from double-blind randomized-controlled trials, in this special population is imperative.

## 1. Introduction

The use of medical cannabis in recent years is growing substantially [1–3], with varied indications such as: chronic pain, chemotherapy-induced nausea and vomiting, multiple sclerosis, Alzheimer's disease, anorexia nervosa, anxiety, dementia, dystonia, Huntington's disease, Parkinson's disease, post-traumatic stress disorder (PTSD), psychosis, Tourette syndrome, epilepsy and more [4–6]. The number of people aged 60 years and over is expected to double by 2025 worldwide and by 2050 in the United States [7–9]. Epidemiological data show that the older population constitutes a growing segment of medical cannabis users, ranging from approximately 7% to more than one third, depending on the country [10–12].

It is well known that aging is associated with substantial changes in pharmacokinetics and pharmacodynamics; for instance, hepatic drug clearance as well as renal elimination are both decreased in the elderly. Furthermore, aging is associated with increased body fat and decreased

lean body mass [13,14], which increase the volume of distribution for lipophilic drugs, such as cannabis. Only a small number of studies have evaluated the pharmacokinetics of cannabis and cannabinoids in the elderly population [15–17]. Interaction of cannabis and other drugs is also largely unknown, as the current evidence is scarce. Concomitant administration of cannabis with other drugs that influence the hepatic CYP family enzymes may greatly alter the metabolism of the cannabinoids. This issue is especially important in the elderly population, where polypharmacy is common [18,19]. Common adverse events patients experience due to cannabis use include dizziness, euphoria, drowsiness, confusion and disorientation [4,20]. These events are particularly important in the elderly population, which may suffer from conditions such as dementia, frequent falls, mobility problems, hearing or vision impairments [21,22]. Thus, studies conducted on younger adults cannot be simply extrapolated to the elderly population.

Despite the significant rise in use, the current evidence on the efficacy and safety of medical cannabis in elderly is scarce. Only a small

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number of studies included elderly patients or analyzed them separately [20]. The aim of this study was to assess the characteristics of the older population receiving medical cannabis for a wide variety of diseases as well as evaluate the safety and efficacy of short and medium-term use.

## 2. Materials and methods

### 2.1. Study design and population

In Israel, most physicians who wish to prescribe medical cannabis for their patients send an authorization request to the Israel Medical Cannabis Agency (IMCA), a unit within the Israeli Ministry of Health (IMOH) [42]. Following the authorization for use patients are asked to contact one of the eight specified medical cannabis suppliers in Israel. To date, over 32,000 medical cannabis licenses were given in Israel, and approximately 33% of the patients receive their cannabis from “Tikun Olam Ltd.”, the largest medical cannabis supplier in Israel.

The study included all the patients who initiated treatment with medical cannabis at “Tikun Olam” from January 20, 2015 to October 30, 2017, that were willing to answer the initial questionnaire and were 65 years of age or older at the initiation of treatment. The study was approved by the “Soroka University Medical Center” institutional review board (IRB) Committee. All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. All the patients gave informed consent to participate in the study.

### 2.2. Data sources and collection

As part of the routine treatment process, every patient who begins treatment with medical cannabis from “Tikun Olam” receives thorough instructions from a certified nurse on the use of the drug, possible side effects, route of administration and the regulatory process that the use of medical cannabis entails. The medical cannabis license specifies two possible routes of administration: oil and inflorescence, delivered as flowers, capsules and cigarettes. During this intake session, following the patient's consent, the patient's medical history, medication use, habits, detailed symptoms list, quality of life assessment, indication for cannabis treatment and demographic data are evaluated by the nurse. At the end of the intake session the nurse recommends, out of the 15 available cannabis strains, specific strains suitable to the patient's condition. Every patient is eligible for either a single strain or several strains.

All the patients were followed up at one month and at six months from treatment initiation by a telephone interview. The interview after six months is extensive and includes an assessment of adverse events, treatment satisfaction, changes in symptoms and in drug regimens.

### 2.3. Study outcomes

For safety analysis, at six months of treatment, we assessed the occurrence and frequency of any adverse events and specifically the following: headache, dizziness, nausea, vomiting, stomach ache, dry mouth, somnolence, weakness, confusion and disorientation, restlessness, hallucinations, red eyes, palpitations, drop in sugar levels and cough. The patients were asked to provide details of the incidence, duration and severity of the reported adverse event.

For efficacy analysis, after six months of treatment, we assessed the following parameters:

- Quality of life – global assessment by the patient using the Likert scale with five options: very good, good, not good nor bad, bad or very bad.
- Pain intensity – assessment by the numeric visual analog scale with an 11-point scale (0 = no pain, 10 = worst pain imaginable).
- Perception of the general effect of cannabis – global assessment by using the Likert scale with seven options: significant improvement,

moderate improvement, slight improvement, no change, slight deterioration, moderate deterioration or significant deterioration.

- Treatment success – treatment success was defined as moderate or significant improvement in the patient's condition and compliance with the treatment.

### 2.4. Statistical analysis

Continuous variables with normal distribution were presented as means with standard deviation. Ordinary variables or continuous variable with non-normal distribution were presented as medians with an interquartile range (IQR). Categorical variables were presented as counts and percent of the total.

When appropriate, univariate comparisons were made using  $\chi^2$ -test or Fisher's exact test for categorical variables, and using Student's *t*-test or Mann–Whitney test for quantitative variables. Paired Wilcoxon test was used to compare ordinal variables.

A *p*-value of 0.05 or less (two-sided) was considered statistically significant. IBM SPSS software, version 24.0, was used for statistical analysis.

## 3. Results

### 3.1. Characteristics of the cohort

We identified 2736 patients over the age of 65 who initiated treatment with medical cannabis from “Tikun Olam” during the study period and were willing to answer the initial questionnaire. During the six months follow-up period, 564 patients died, 661 had been treated for less than six months, 297 stopped the treatment within six months and 28 patients switched to a different cannabis supplier. Thus, of the entire cohort, 1186 (43.3%) were eligible to answer the follow-up questionnaire after six months of treatment. Of the eligible patients, 901 (76.0%) responded to the questionnaire (Fig. 1). Of the entire population, 334 patients (12.2%) used medical cannabis from a different supplier prior to the initiation of treatment with “Tikun Olam”. The elderly population comprises 34.2% of all the patients who initiated cannabis treatment with “Tikun Olam” in the study period (data not shown).

Table 1 shows demographic characteristics of the cohort. The mean age was  $74.5 \pm 7.5$  years, with a slight female predominance (1463, 53.5%). The most common route of administration was oil (1022, 37.3%), followed by smoking (669, 24.4%) and vaporization (176, 6.4%).

Table 2 shows the indications for the medical cannabis. The most common indications were pain (1822, 66.6%) and cancer (1482, 60.8%), with a significant overlap between the two groups (cancer associated pain). All other indications comprise < 10% of the indications in the cohort. Cancer was also the most prevalent diagnosis at treatment initiation, followed by cardiovascular diseases (Supplementary data Table 1).

### 3.2. Strains of cannabis

Out of the 901 respondents at six months, 264 (29.3%) used one strain, 482 (53.5%) used two strains and 141 (15.6%) used between three to six strains. Most of the patients were using THC (tetrahydrocannabinol) rich strains of cannabis, whether the origin is from a *sativa* dominant species (“Erez” was used by 54.6% of the patients) or an *indica* dominant species (“Alaska” was used by 27.4% of the patients), regardless of the indication for cannabis use (Supplementary data Table 2). CBD (cannabidiol) rich strains were used by patients who suffer from pain (23.3%), chemotherapy side effects (30.9%), Parkinson's disease (45.7%) and inflammatory bowel disease (40%).

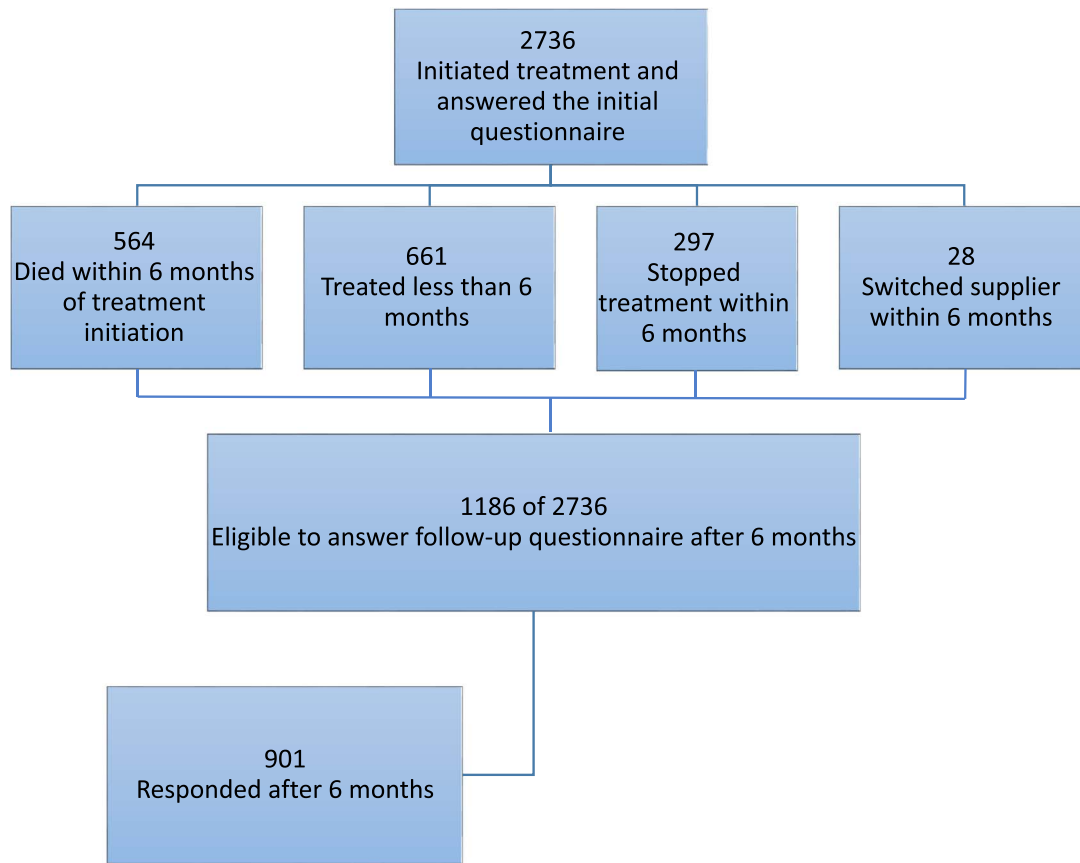


Fig. 1. Flow chart for the selection of the study population.

**Table 1**  
Baseline characteristics of the patients at treatment initiation.

Variable	Number of patients (N = 2736)
Age (years)	65–74 – 1525 (55.7%) 75–84 – 885 (32.3%) ≥ 85 – 326 (11.9%)
Male	1273 (46.5%)
BMI	25.2 ± 5.0
Driving a car	986 (36.0%)
Approved monthly dosage of cannabis (grams)	28.8 ± 14.9
Approved route of administration	Oil - 737 (26.9%) Inflorescence - 640 (23.4%) Oil + Inflorescence – 1331 (48.6%)
Previous experience with cannabis	694 (25.4%)
Cigarettes smokers	424 (15.5%)
Number of regularly used medications	6 (3,9)
Number of days hospitalized in the past six months	0 (0,9)

### 3.3. Outcomes of cannabis treatment

The treatment with cannabis induced a significant reduction in the intensity of the reported pain, from a median of 8 on a scale of 0–10 to a median of 4 after six months of treatment (Fig. 2). Moreover, prior to the treatment, 573 (66.8% of the respondents) reported high pain intensity of 8–10 and at six months of treatment only 65 (7.6%) reported high pain intensity ( $p < .001$ ).

The general assessment of quality of life was improved with the treatment. At baseline, 540 (79.3% of respondents) defined their quality of life as either bad or very bad, while after the treatment, 505 (58.6%) defined their quality of life as either good or very good ( $p < .001$ , Fig. 3).

**Table 2**  
Indications for receiving cannabis prescription.

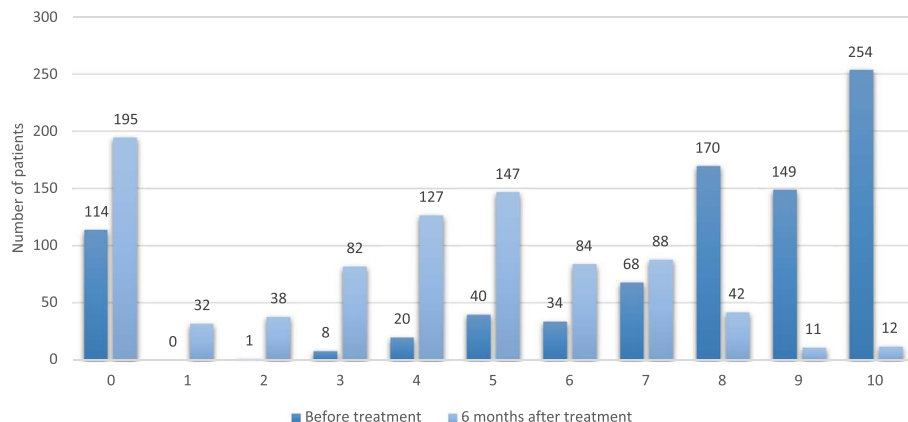
Indication	Number of patients (N = 2736)
Cancer associated pain	1001 (36.6%)
Nonspecific pain	821 (30.0%)
Cancer – chemotherapy treatment	661 (24.2%)
Parkinson's disease	146 (5.3%)
Others	49 (1.8%)
Post-traumatic stress disorder	21 (0.8%)
Crohn's disease	10 (0.4%)
Amyotrophic lateral sclerosis	9 (0.3%)
Compassion treatment	7 (0.3%)
Ulcerative colitis	5 (0.2%)
Alzheimer's disease	4 (0.1%)
Multiple sclerosis	2 (0.1%)

The following indications were aggregated into the category 'Others': epilepsy, tic disorder, multiple system atrophy, essential tremor, dementia, tension headache, cluster headache, peripheral vascular disease, myelodysplastic syndrome, fibromyalgia and rheumatoid arthritis.

In addition to the general improvement in the quality of life, the patients perceived the treatment as effective for their condition. When asked to globally assess the effects of the treatment on their condition, 844 patients (93.7% of the respondents) reported improvement and 378 of them (41.9% of the total respondents) defined it as a significant improvement (Fig. 4).

Overall, in 708 out of 1198 patients (59.1%), the treatment was considered successful (identified by at least a moderate improvement in their condition while still receiving treatment). The denominator included all the patients who answered the follow-up questionnaire and the patients who stopped treatment, for any cause.

**Pain intensity scale,  $p < 0.001$  (n=858)**



**Fig. 2.** Assessment of the pain intensity on a 0–10 scale before and after six months of cannabis therapy.

**3.4. Cannabis safety and treatment adherence**

Of the 297 that stopped the treatment (10.8% of the entire group, Fig. 1), 162 provided a reason for their discontinuation: 44 (1.6%) stopped the treatment because of ineffectiveness; 38 (1.4%) stopped due to adverse effects; 22 (0.8%) because of the bureaucracy that the treatment continuation entails; 25 (0.9%) because their indication for cannabis was temporary, such as chemotherapy treatments; 33 (1.2%) for other various reasons.

Of the 901 patients who responded to the follow-up questionnaire (still receiving the treatment at six months), 286 (31.7%) reported at least one adverse event due to the treatment after six months (Table 3). The most common adverse events were dizziness (9.7%) and dry mouth (7.1%). Of the 286 patients that reported adverse events, 33 (11.5%) rated their severity as 7–10 on a scale of 1–10).

Of the 515 patients that responded to the question regarding falls, 275 (53.4%) reported falling once or more in the six months preceding treatment initiation (median number of falls – 1, interquartile range [0–2]) and 113 (21.9%) reported falling once or more within the six months after treatment initiation (median number of falls – 0, interquartile range [0–0],  $p < .001$ ).

**3.5. Effect on medications regimen**

Of the patients who responded to the questionnaire, 791 of the patients (87.8%) answered the questions regarding changes in

medication regimen at six months: 463 patients (58.5%) reported no change in the total number of chronic medications they use, and 104 (13.1%) began treatment with a new chronic drug (Table 4). 278 patients (35.1%) reported a decrease in the number of drugs or their dosage, and 47 patients (5.9%) reported an increase in the number of drugs or their dosage. Moreover, 143 patients (18.1%) stopped using opioid analgesics or reduced their dose, while only 32 (4.0%) increased the dose of opioids or began using them after the initiation of cannabis treatment.

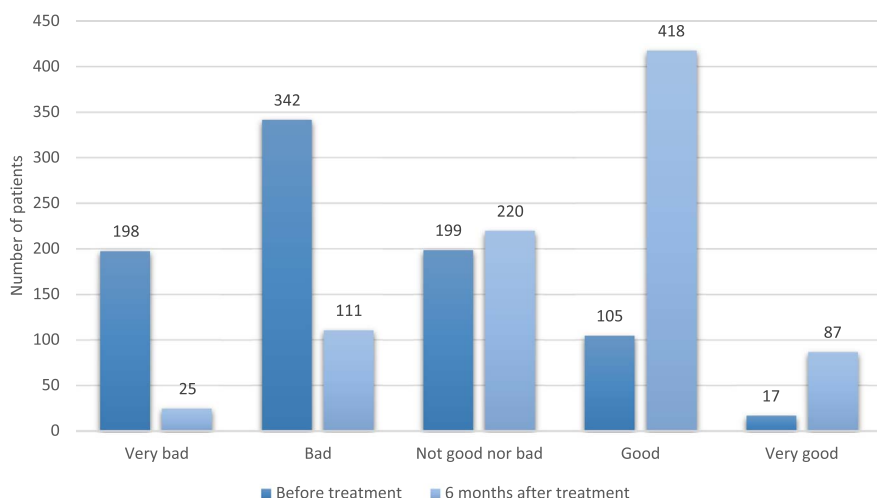
**4. Discussion**

In this study of elderly patients treated with medical cannabis, we have shown that the treatment is effective in improving pain and quality of life, was not associated with serious adverse events and was characterized by a low discontinuation rate.

**4.1. Cohort characteristics**

The characteristics of our cohort are different from those of previous studies. Several studies conducted in California found that most medical cannabis users were males and that the older population constitute a small minority [23–25]. Studies conducted in Canada and in an international survey showed similar results [12,26]. It should be noted that these studies were held between 2006 and 2012, and more recent data from six states in the United States showed a substantial increase in the

**Quality of life,  $p < 0.001$  (n=861)**



**Fig. 3.** Quality of life prior and six months after the initiation of cannabis treatment.

### Perception of the general effect of cannabis on the patient's condition after 6 months (N=901)

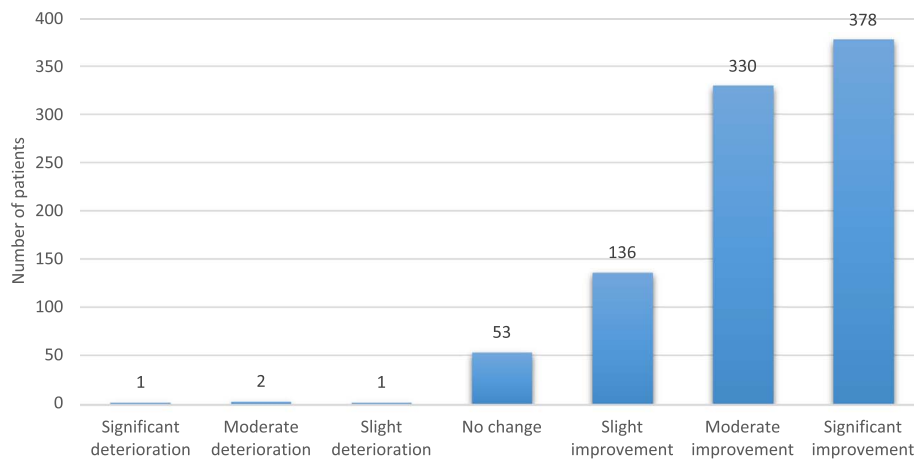


Fig. 4. Perception of the general effect of cannabis on the patient's condition after six months of treatment.

**Table 3**  
Adverse events after six months of treatment with cannabis.

Adverse event	Number of patients (N = 901)
Dizziness	87 (9.7%)
Dry mouth	64 (7.1%)
Somnolence	35 (3.9%)
Weakness	21 (2.3%)
Nausea	20 (2.2%)
Confusion and disorientation	17 (1.9%)
Drop in sugar levels	16 (1.8%)
Cough	13 (1.4%)
Headache	10 (1.1%)
Vomiting	10 (1.1%)
Sore throat	9 (1.0%)
Restlessness	8 (0.9%)
Hallucinations	7 (0.8%)

use of cannabis by the elderly population [11]. Hazekamp et al. [10] reported that in the Netherlands between 2003 and 2010, a third of the medical cannabis population was the elderly. None of these studies analyzed the elderly population separately, or focused on its unique characteristics.

In the majority of the previous studies the main indications for using medical cannabis were chronic pain, anxiety, sleep disturbances and

arthritis whereas cancer was the indication for only a small percent of the patients. In our cohort, pain was the most common indication, but cancer was almost as common; all other indications comprised only a small part of the cohort. The noted differences in study populations may be attributed to variable definitions of medical cannabis users. While we included only patients who received an authorization for cannabis from a physician, some of the other studies include patients who self-treated their conditions with cannabis [24,26]. Furthermore, we should emphasize that the nature of our cohort is largely determined by the indications and restrictions that the Israeli Ministry of Health sets to prescribing medical cannabis [27]. For example, sleep disturbances, arthritis and depression, also very common in the elderly population, are not authorized indications for medical cannabis use in Israel. The high death rate in our study might reflect the severity of the patients' condition and the fact that cannabis in Israel is mainly prescribed as a palliation treatment.

#### 4.2. Cannabis efficacy

The rates of treatment satisfaction were high, with a significant relief of pain (most common indication) for most patients and a significant improvement in the overall quality of life. Clinically meaningful pain reduction is defined as a decrease of 2 points on a 0-to-10 numerical pain rating or a 30% improvement in pain intensity [28,29].

**Table 4**  
Changes in drug regimens after six months of treatment with cannabis (n = 791).

Drug class	Number of patients who stopped using a certain drug	Number of patients who reduced the dose of a certain drug	Number of patients who increased the dose of a certain drug	Number of patients who added a new drug
Opioid analgesics <sup>a</sup>	114 (14.4%)	29 (3.7%)	6 (0.8%)	26 (3.3%)
Other analgesic drugs <sup>b</sup>	58 (7.3%)	17 (2.1%)	0 (0%)	6 (0.8%)
Benzodiazepines	59 (7.5%)	14 (1.8%)	1 (0.1%)	5 (0.6%)
Neuropathic pain drugs <sup>c</sup>	32 (4%)	14 (1.8%)	0 (0%)	6 (0.8%)
SSRI or SNRI	17 (2.1%)	2 (0.3%)	2 (0.3%)	7 (0.9%)
Antihypertensive drugs	90 (11.4%)	13 (1.6%)	4 (0.5%)	9 (1.1%)
Antidiabetic drug	23 (2.9%)	6 (0.8%)	0 (0%)	4 (0.5%)
Anti-psychotics	15 (1.9%)	1 (0.1%)	0 (0%)	9 (1.1%)
Anti-emetics	15 (1.9%)	2 (0.3%)	0 (0%)	0 (0%)
All other drugs	242 (30.6%)	36 (4.6%)	19 (2.4%)	76 (9.6%)
Total	665 (84.1%)	134 (16.9%)	32 (4%)	148 (18.7%)

SSRI – Selective Serotonin Reuptake Inhibitor; SNRI – Serotonin–Norepinephrine Reuptake Inhibitor.

<sup>a</sup> Includes: Morphine, Tramadol, Fentanyl, Oxycodone, Buprenorphine, Oxycodone-naloxone (Targin), Acetaminophen-Oxycodone (Percocet), Codeine-Caffeine-Paracetamol (Rokacet).

<sup>b</sup> Includes: NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), Paracetamol, Dipyron.

<sup>c</sup> Includes: Pregabalin, Gabapentin, Amitriptyline.



Our study shows a median decrease of 4 points, which represents a substantial improvement. These findings are consistent with other similar studies [30–32]. A recent systematic review and meta-analysis found limited evidence for the use of cannabis as a treatment for chronic pain, but it should be noted that many of the reviewed studies used cannabinoid-based medicines and not herbal cannabis [33]. Nevertheless, large randomized trials are still needed to determine the utility of cannabis in chronic pain management. The significant improvement in the quality of life and the broad perception that cannabis is helpful for the patients' illnesses as found in our study are consistent with other reports [24,30].

#### 4.3. Cannabis safety

Our study showed that cannabis treatment was not associated with a high number of adverse events in the short and medium-term of the follow-up. Only a small number of patients stopped the treatment due to adverse events. Most common adverse events were related to the central nervous system and the gastrointestinal system. These findings are consistent with other studies that showed that medical cannabis adverse events are mostly non-serious [4,31–34]. Dizziness is reported as one of the most common adverse events of cannabis use, as it was in our study. It is especially important in the elderly and frail population since dizziness can increase the risk of falls. Nevertheless, the number of falls in our study was significantly lower after the treatment in comparison to before treatment. Long-term adverse effects of chronic cannabis use should be elucidated in further studies, both in young and elderly populations.

After six months of treatment with cannabis, the vast majority of the patients stopped using a certain chronic medication or reduced the doses of the chronic drugs. The most common medications that were stopped or reduced were analgesics, and specifically opioids. Use of cannabis as a substitute for prescription medication has been shown by a number of studies, with higher rates of reduction and discontinuation than seen in our study [30,31,35–39]. Opioids are known to cause a plethora of serious adverse events especially in chronic use and in the elderly [40]. The adverse effects of opioids appear to be more frequent and severe than those induced by cannabis. However, randomized-controlled trials are still required to determine if cannabis can truly aid in reducing the impact of the opioid epidemic and in which ways [41].

#### 4.4. Strengths and limitations of the study

The strengths of this study include the large cohort of patients and the focus on the elderly population. All the patients were seen by a physician prior to receiving their medical cannabis license, thus eliminating 'self-treating' patients. The study does not exclude specific diagnoses and reflects a large part of elderly medical cannabis users in Israel.

Our study has several limitations. The observational nature of our study can only allow us to determine association and not causality. We did not include elderly patients who began treatment with "Tikun Olam" and refused to answer our initial questionnaire. Our follow-up period is rather short, only six months. We also had a substantial number of patients who did not respond to the follow-up questionnaire (24%). Most of the patients are using a mixture of cannabis strains and we cannot determine the exact dose of active components each patient is receiving. The characteristics of our cohort are limited by the regulations of the Israeli Ministry of Health.

#### 5. Conclusions

The older population is a large and growing part of medical cannabis users. Our study finds that the therapeutic use of cannabis is safe and efficacious in this population. Cannabis use can decrease the use of other prescription medicines, including opioids. Gathering more

evidence-based data, including from double-blind randomized-controlled trials, in this special population is imperative.

#### Conflict of interest statement

The study was supported by 'Tikun Olam Ltd.', cannabis supplier in Israel. Victor Novack serves in the scientific advisory board of 'Tikun Olam Ltd.' and Lihi Bar-Lev Schleider is an employee of 'Tikun Olam Ltd.'. Ran Abuhasira has no conflicts of interests to declare.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejim.2018.01.019>.

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