with stage I–III clear cell renal cell carcinoma who had undergone a nephrectomy. The panel was significantly associated with recurrence after stratifying by stage and adjusting for grade, tumour size, and Leibovich score.

Several obstacles exist to the incorporation of biomarkers into clinical use. First, the benefit of adjuvant therapies needs to be established. Markers that are prognostic might not be predictive such that identifying patients at increased risk of recurrence does not immediately translate into a greater likelihood of them benefiting from therapy. Clinical trials are needed to show a benefit of adjuvant therapies on the basis of markers rather than clinical data alone, which is a difficult challenge. Additionally, there will be regulatory and financial burdens. Despite these obstacles, incorporation of molecular markers into clinical practice is important to facilitate a personalised medicine approach so that patients are not treated with a one-size-fits-all approach, which results in over-treatment for some and under-treatment for others.

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Use of medical cannabis: perceptions of Israeli oncologists

The use of the cannabis plant (*Cannabis sativa*) for the treatment of various cancer-related symptoms, including pain, cachexia, anxiety, and chemotherapy-induced nausea and vomiting, is constantly increasing worldwide.[1,2] The plant contains hundreds of active compounds, of which Δ–9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are considered the most clinically relevant.[2] The activity of the natural plant against cancer-related symptoms has not yet been tested in prospective clinical trials.

Since 2010, Israeli patients with cancer can receive a permit for cannabis use for palliation after a recommendation by their treating oncologist. According to the Israeli Ministry of Health, more than 10 000 patients with cancer receive permits annually, making it the most commonly prescribed medication by the Israeli oncologists. Thus, Israeli oncologists are unique in terms of their vast expertise in the use of cannabis for cancer-associated symptoms.[3,4]

To examine the experience, perceptions, and attitudes of Israeli oncologists towards the use of cannabis, we did a national web-based survey among all those oncologists who are registered with the Israeli Society of Clinical Oncology and Radiation Therapy.

126 (53%) of 238 registered oncologists responded to the survey. Cannabis is extensively used, with 110 (87%) of 126 oncologists prescribing cannabis regularly (table). The indications judged most suitable for starting cannabis were loss of appetite (100 [79%] of 126), nausea (97 [77%]), pain (95 [75%]), and mood disorder (78 [62%]; figure). 115 (91%) of 126 responders have found cannabis effective at least to some degree and most perceived it as safe, with 53 (42%) responders stating they have encountered mild or no side-effects in patients and 63 (50%) responders reporting serious adverse effects but only in a few patients. Despite the extensive use, nearly 90% (111/126) of responders admitted a paucity of

knowledge regarding cannabis use and relied mostly on personal clinical experience as a guide for dosing.

Importantly, pattern of use was affected by personal views. Thus, although physicians favouring legalisation (n=46) and opposing legalisation (n=78) had similar views regarding indications, contraindications, activity, safety, and knowledge, those favouring legalisation reported recommending more permits per year than those opposing it (p=0·045; table). Views regarding the role of cannabis in the treatment of cancer-related pain were also intriguing. As expected from clinical guidelines, only 33 (26%) of 126 responders stated that cannabis should be used before opiates for pain relief among patients with cancer. Yet, most physicians perceived cannabis as safer than opiates and 61 (53%) respondents would prefer cannabis over opiates as a first treatment option, if pain relief was needed by a close relative.

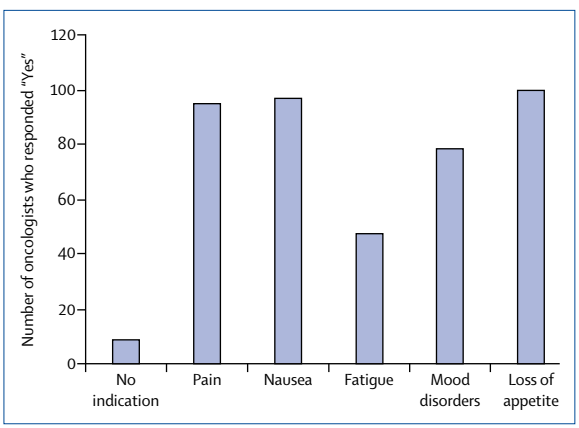

Figure: **Most appropriate indications for cannabis use as perceived by Israeli oncologists**

A survey[5] of 237 oncologists in the USA, of whom only 125 (55%) were practicing in a state where medical cannabis has been legalised, noted highly variable perceptions regarding cannabis use, with only 80 (33%) perceiving it effective for pain relief compared with standard treatment. Similarly to our findings, attitudes toward cannabis use were affected by non-medical variables, including practicing in southern versus northern states and working in hospitals or community-based clinics. These data suggest that in

	All	Oppose legalisation (n=78)*	Favour legalisation (n=46)*	p value
How many new permits for cannabis do you prescribe per year? (n=124)				
Never	16 (13%)	11 (14%)	5 (11%)	0·045†
<20	26 (21%)	21 (27%)	5 (11%)	
20–50	46 (37%)	25 (32%)	21 (46%)	
>50	36 (29%)	21 (27%)	15 (33%)	
In your experience, how frequent are the side-effects from cannabis use? (n=124)				
No side-effects	4 (3%)	4 (5%)	0	0·22
Major side-effect in few patients	48 (39%)	36 (46%)	15 (33%)	
Minor side-effects	62 (50%)	33 (42%)	26 (57%)	
Major side-effects in many patients	10 (8%)	5 (6%)	5 (11%)	
What should be the first-line of treatment for cancer-related pain? (n=120)				
Cannabis	33 (28%)	20 (26%)	13 (11%)	0·022
Opioids	74 (62%)	52 (68%)	22 (50%)	
Cannabis should never be prescribed	13 (11%)	4 (5%)	9 (21%)	
Which medication is more hazardous? (n=122)				
Cannabis is more hazardous	14 (12%)	10 (13%)	4 (9%)	0·205
Opioids are more hazardous	55 (45%)	30 (39%)	25 (56%)	
Both equally hazardous	53 (44%)	37 (48%)	16 (36%)	
What would you recommend first for a relative with cancer-related pain? (n=114)				
Cannabis	61 (54%)	32 (46%)	29 (64%)	0·059
Opioids	53 (46%)	37 (54%)	16 (36%)	

Data are n (%). *Of the 126 respondents, two did not answer the question regarding legalisation. †p value is calculated for respondents who prescribe many permits versus those who prescribe few or no permits.

Table: **Survey on use, perceived activity, and safety of cannabis among Israeli oncologists**

the absence of clear scientific evidence or guidelines, physicians might rely on personal attitudes and moral judgment. Similar findings were noted among Israeli pain specialists and palliative care providers.[3,6–8]

Discussing cannabis treatment with patients has become another time-consuming task for oncologists, with 105 (84%) of 126 reporting having such discussions at every visit and with 25 (20%) stating spending more than 6 min each visit on this subject. Thus, the extensive use of cannabis might also have a direct effect on the use and demand of oncology services. We noted that the demand for cannabis is often driven by the patients themselves, who, based on extensive coverage in social networks, perceive it as a potent cancer treatment.[4] Indeed, Israeli oncologists often report informally on patients who ask for cannabis for symptom control but intend to use it as a direct treatment of cancer. Because the use of cannabis for such purpose is not allowed, according to the Israeli Ministry of Health guidelines, and is not reported to oncologists, the magnitude of the phenomenon could not be assessed in this survey.

Since no prospective clinical data regarding the efficacy of cannabis for cancer-related symptoms are available, the knowledge of oncologists who are experienced in its use is highly valuable. The Israeli oncologists who have vast experience with the use of cannabis perceive it as effective, mostly for loss of appetite, nausea, pain, and mood disorder, and they regard it as safe. However, our survey also indicates a paucity of knowledge and a unique role for moral attitudes affecting clinical decisions. These findings call for the implementation of an educational programme and the generation of practice guidelines to enable a more consistent and rational approach towards the use of cannabis in oncology.

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