



## From farm to bedside: Potential of medical cannabis in global health



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### ABSTRACT

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**Introduction:** The growing opioid crisis and persistent global health disparities underscore the urgent need for alternative therapeutic strategies. *Cannabis*, with its long-standing historical use and recent legislative developments, presents a potentially significant avenue for addressing these challenges. This review examines the

**Abbreviations:** THC,  $\Delta$ -trans- $\Delta^9$ -tetrahydrocannabinol; ACRC, Academic Clinical Research Center; CBD, Cannabidiol; CORE, Care, Outreach, Research, and Education; FDA, Food and Drug Administration; GACP, Agricultural and Collection Practices; GAP, Good Agricultural Practice; GHC, Global Health Catalyst; IPI, International Phytomedicine and Medical Cannabis Institute; LMICs, Low- and middle-income countries; MC, Medicinal Cannabis; MCRC, Medicinal Cannabis Research Collaboration; NASEM, National Academies of Sciences, Engineering, and Medicine; USA, United States of America; USD, United States Dollar; UM, University of Mississippi; UN, United Nations; SAHPRA, South African Health Products Regulatory Authority; WHO, World Health Organization.

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evolving landscape of medicinal cannabis, drawing from historical ethnopharmacological data and contemporary scientific discussions.

**Methods:** This review synthesized evidence from historical ethnobotanical records, peer-reviewed studies, and outcomes derived from recent Global Health events. These events facilitated discussions among diverse stakeholders, including healthcare professionals, policymakers, researchers, industry representatives, farmers, and patient advocates. Case studies and successful models from the USA and Africa, including the recent FDA approval for first-in-human clinical trials of a medicinal cannabis derivative for pancreatic cancer, were analysed.

**Results:** Successful models include collaborative platforms fostering stakeholder engagement, such as partnerships between African farmers and biotech firms to standardize cultivation. Successful models demonstrate the potential for adaptation and scaling in diverse healthcare settings. The FDA trial approval exemplifies progress in clinical translation. However, disparities persist, with patients within Africa facing systemic barriers to medical *Cannabis* certification and higher rates of punitive opioid discontinuation.

**Conclusion:** Medicinal *Cannabis* presents a complex yet promising solution for reducing opioid-related mortality and addressing healthcare inequities. Implementing strategic frameworks like CORE (Care, Outreach, Research, Education) is essential for developing safe, high-quality, evidence-based cannabis products. Through fostering collaboration and addressing existing obstacles, the therapeutic potential of medicinal *Cannabis* can be harnessed to mitigate the opioid crisis and reduce global health disparities, effectively translating research from farm to bedside.

## 1. Introduction

*Cannabis*, a medicinal plant from the Cannabaceae family, has a well-documented history of therapeutic use dating back millennia, with historical evidence indicating its potential in treating various ailments<sup>96, 21, 41, 42</sup>. *Cannabis*' adaptability to diverse climates has facilitated its global spread, leading to genetic, morphological, and chemical diversity<sup>64</sup>. This diversity has presented challenges in taxonomic classification, with differing proposals suggesting distinct species or subspecies within the *Cannabis* genus<sup>12, 21</sup>. Proposals range from distinct three-species (*C. sativa*, *C. indica*, *C. ruderalis*),<sup>98, 21, 36</sup> to two-species (*C. sativa* and *C. indica*)<sup>21</sup> or even a single species (*C. sativa*) with various subspecies (*C. sativa* ssp. *indica*, *C. sativa* ssp. *ruderalis* and *C. sativa* ssp. *Afghanica*)<sup>6, 63, 65</sup>; Small, 2015;<sup>103, 124</sup>). The current consensus leans towards *Cannabis* being a monospecific genus<sup>16, 45</sup>. Regardless of the ongoing taxonomic debate, for this research, we will focus on *Cannabis* at the genus level.

In the mid-20th century, research on cannabis declined significantly due to legal restrictions in many countries<sup>32</sup>, resulting in a substantial knowledge gap<sup>95, 32</sup>. However, recent years have witnessed a resurgence of interest in cannabis research,<sup>9</sup> particularly regarding its therapeutic potential in addressing conditions such as depression, inflammation and chronic pain<sup>37</sup>. This renewed focus is justified by the complex chemical composition of *Cannabis*, containing over 550 bioactive compounds across various (flavonoid, cannabinoids, stilbenoid, alkaloid, lignanamide, carotenoid, and terpenoid) classes<sup>47</sup>. Cannabinoids, the most notable group,<sup>85</sup> offer promising applications in various medical fields such as oncology and microbiology, with potential to target viruses, fungi, and bacteria<sup>119, 85</sup>.

The increasing body of scientific evidence supporting the efficacy of medical *Cannabis* products is driving recognition of their potential to enhance global health and development<sup>28</sup>. Research conducted in an institution like the National Academies of Sciences, Engineering, and Medicine (NASEM) and others<sup>40</sup>; Mary E Lynch & Fiona Campbell, 2011;<sup>74, 101</sup>) have demonstrated the effectiveness of *Cannabis* in treating various conditions, including childhood epilepsy, chemotherapy-induced nausea, chronic pain, and multiple sclerosis spasticity<sup>(11; Daniela 30, 59, 68, 101, 107)</sup>. In addition to these therapeutic benefits, medical *Cannabis* may also offer advantages such as stress reduction, improved sleep outcomes, and a potential decrease in reliance on harmful medications<sup>99, 101, 109, 18, 22, 50, 75</sup>. However, it is essential to approach medical *Cannabis* use with caution due to potential drawbacks, including respiratory problems, impaired driving ability, and mental health issues<sup>101</sup>. Thus, careful consideration of both benefits and risks, alongside ongoing research, is crucial for informed

decision-making regarding medical *Cannabis* use.

Recognizing the growing interest in medical *Cannabis* and its potential to address global health disparities, recent summits organized by the Global Health Catalyst (GHC) brought together stakeholders worldwide<sup>76</sup>. These summits, spearheaded by institutions like Harvard, Johns Hopkins, and the University of Pennsylvania, aimed to foster knowledge sharing, strategic discussions, and collaboration around translating evidence-based research into clinical practice<sup>76</sup>. Their focus lies on maximizing the benefits, minimizing risks, and reducing disparities in access to safe and effective *Cannabis*. The summits identified four core areas (Care, Outreach, Research, and Education) for advancing global health collaborations in this field,<sup>76</sup> which will be explored in this work.

The landscape of medical *Cannabis* is undergoing a significant transformation, driven by both policy changes and a surge in research interest. A pivotal moment came in November 2020 when the UN Commission on Narcotic Drugs, following the World Health Organization's recommendation, removed *Cannabis* from a restrictive schedule<sup>(81; WHO, 2020)</sup>. This decision, coupled with the USA's Medical Marijuana and Cannabidiol Research Expansion Act of 2022<sup>92</sup>, has resulted in renewed interest. Furthermore, the projected growth of the legal *Cannabis* market, particularly for medical use,<sup>114</sup> necessitates improved research and infrastructure, especially in low- and middle-income countries (LMICs). In light of these developments, this review will probe into the evolving legal landscape surrounding *Cannabis*. We will explore the growing interest in global health and development opportunities it presents, with a particular focus on Africa. Additionally, we will highlight activities and potential areas for collaboration within the CORE framework (Care, Outreach, Research, and Education) to maximize the benefits and minimize the risks of *Cannabis* use on a global scale.

## 2. Landscape on medical cannabis for global health and development

The legal and economic landscape of *Cannabis* is shaped by a complex interplay of cultural, social, economic, and political factors worldwide<sup>118</sup>. The International Narcotics Control Board (INCB) plays a key role in regulating *Cannabis* for medical and scientific purposes. In 2021, the INCB convened a meeting with representatives from over 36 countries, including the European Union, African Union, Organization of American States, and the United Nations Office on Drugs and Crime, to discuss control and reporting mechanisms for the medical and scientific use of *Cannabis* (WHO, 2014). International drug control treaties allow for medical use of cannabinoids, complying with regulations

designed to prevent diversion for non-medical purposes. These regulations require governments to license and control production, estimate national medical Cannabis needs, and ensure medicinal cannabinoids are used under medical supervision and in accordance with evidence-based practices regarding safety and efficacy. Adherence to these measures is crucial for maintaining the integrity of the pharmaceutical regulatory system (19; WHO, 2014).

In recent years, a notable shift towards Cannabis law liberalization has emerged in several countries<sup>94</sup>. This trend is driven by evolving perceptions of Cannabis, including its potential medicinal value, economic opportunities, and social justice considerations. The legal Cannabis industry is projected to experience significant global expansion. Projections indicate that global spending on legal Cannabis will reach \$57 billion by 2027. The recreational market is expected to be the dominant sector, accounting for 67 % of spending, with medical Cannabis representing the remaining 33 %. The most noteworthy growth is anticipated in markets outside of established regions, with spending projected to surge from \$52 million in 2017 to \$2.5 billion in 2027 (24; Pellechia, 2018). This global shift is reflected in the increasing number of countries adopting various regulatory models for medical Cannabis (MC)<sup>94</sup>.

However, despite this trend towards legalization and acceptance, some regions, particularly in Asia and the Middle East, still maintain strict prohibitions and harsh penalties for Cannabis use, even for medicinal purposes (Fig. 1). This highlights the ongoing geographical disparity in Cannabis policies. While growing evidence for the therapeutic benefits of Cannabis is driving legalization efforts in many parts of the world, significant challenges remain in achieving global uniformity on Cannabis regulations<sup>94</sup>.

Canada pioneered a centralized MC program in 1999, offering patients access through prescriptions<sup>94,49,87</sup>. Similarly, California became the first USA state to legalize MC in 1996, with most states following suit by 2016<sup>82</sup>. Many states have enacted their own Cannabis laws. As of today, 36 out of 50 states, including Washington D.C., allow for Cannabis use. Eighteen of these states permit recreational use, while the others allow Cannabis for medical purposes only<sup>88</sup>. Thailand amended its strict Cannabis prohibition laws in 2019 to allow for controlled medical use<sup>91</sup>. Uruguay stands out as the first nation to legalize Cannabis entirely through government public health initiatives in 2013<sup>2</sup>. While

some countries like Argentina, Brazil, and Mexico haven't reached the same level of regulation, legislative reforms are pushing for change. As of today, numerous countries have established MC programs, including Canada, Colombia, Chile, Germany, Israel, Italy, Jamaica, Netherlands, Switzerland, Thailand, the United Kingdom and Uruguay<sup>91</sup>. With over 70 countries globally legalizing Cannabis for medical use (Kacey Morrissey, 2021), a growing acceptance of its potential therapeutic applications is evident (Box 1). This global shift is further highlighted by the increasing number of African countries exploring the legalization of MC<sup>97</sup>.

Africa represents a prime example where the landscape of *Cannabis* is changing significantly<sup>43,83</sup>. Prohibition Partners (a UK-based research firm) predicted the African Cannabis market (legal) could reach USD 7.1 billion by 2023<sup>83</sup>. Strong laws and regulations alongside a streamlined legal status to grow and use Cannabis for research and medicinal purposes are expected to significantly boost the African economy<sup>43</sup>, reduce criminal activities around illicit Cannabis-derived drugs, and potentially contribute to people's health. The cultivation and use of Cannabis within the continent show a trend toward legalization. Fig. 2 and Supplementary Table 1 show the legal status of the medical/recreational use of Cannabis in African countries.

Cannabis is grown widely within African grasslands, even though many countries label it illegal<sup>102</sup>. There is growing interest in Cannabis as an economic crop as seen in recent exports, owing to its legalized cultivation, and growing debates to allow its medicinal use<sup>62</sup>. In 2021, Morocco and Zambia relaxed their laws against Cannabis cultivation, among 13 other nations in Africa (Petrack). Lesotho was the first African country to legalize Cannabis, in 2008, for medicinal purposes, but has recently increased the cultivation license fee and most farmers are unable to afford the license (Clemence Rusenga, 2022). In September 2018, South Africa's (SA) Constitutional Court ruled that the recreational use of Cannabis was no longer a criminal offence<sup>48</sup>.

Driven by recent policy changes and strategic approaches by some African governments, the continent's Cannabis industry is experiencing growth. This expansion is creating new employment opportunities that contribute to development and healthcare initiatives<sup>121,38</sup>. As this industry continues to grow, governments are looking to set up appropriate regulations to protect patients and/or consumers, whilst not stymieing research and development. Fig. 3 provides an overview of the key factors

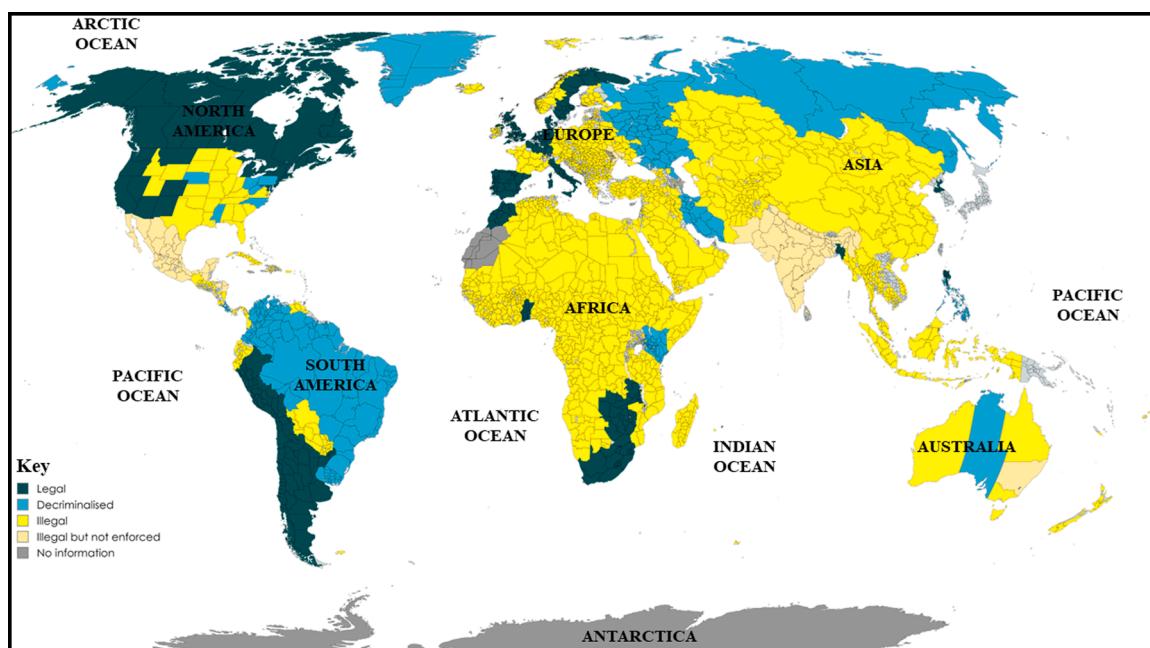


Fig. 1. An illustration of the legal status of *Cannabis* and Cannabis-based pharmaceutical products varies globally.

**Box 1**

Legislation and regulations related to medical Cannabis across various regions.

- North America, with a population of 368 million, has 49.6 million Cannabis consumers, with 4.4 million listed *Cannabis* patients (Kacey Morrissey, 2021).
  - The *Cannabis* Act in Canada (Canada, 2022) dictates advertising and marketing restrictions, age regulations, packing and labelling, and testing for the recreational use of Cannabis in Canada.
  - In the United States, *Cannabis* has been legalized for medical use in at least 39 states and Washington D.C.<sup>89</sup>. The Marijuana and Cannabidiol Research Expansion Act<sup>90</sup>, signed into law in December 2022, is the first standalone Cannabis reform legislation that does three significant things:
    - a. Provides a mechanism for the scientific study of cannabidiol and Cannabis for medical purposes, effectively facilitating research.
    - b. Organizes a pathway for the FDA to approve the commercial production of drugs containing or derived from Cannabis.
    - c. Allows doctors to discuss the benefits and harms of using Cannabis and its derivatives.
  - American states with *Cannabis* laws in action have an approximately 25 % lower mean annual opioid overdose mortality rate (over the period 1990–2010) than those without *Cannabis* laws.<sup>10</sup>
- Europe, with a population of about 869 million, has 44.2 million Cannabis consumers and 107,356 listed *Cannabis* users. The *Cannabis* market in Europe is expected to grow from USD 4.96 billion in 2022 to USD 13.37 billion by 2027 (Kacey Morrissey, 2021).
  - The Netherlands has legalized *Cannabis* prescription for a list of conditions for which the use of Cannabis has been scientifically established (Kacey Morrissey, 2021).
  - Other countries, including Finland, Denmark, Italy, Luxembourg, Norway, Malta, Poland, Portugal, United Kingdom, have also legalized Cannabis with or without an established set of medical conditions for which Cannabis can be prescribed or used (Kacey Morrissey, 2021).
  - The Czech Republic legalized *Cannabis* in 2013 and has provided insurance coverage to boost patient participation (covering 90 % of *Cannabis* charges) since 2020. Germany adds to this list, allowing insurance reimbursements for *Cannabis* (Kacey Morrissey, 2021).
  - Europe has strict (–)-trans- $\Delta^9$ -tetrahydrocannabinol (THC) regulations but those on cannabidiol (CBD) are typically lower. Germany and Austria have set their upper THC limit to 0.2 % and 0.3 %, respectively. Switzerland marketers can sell CBD products without restriction as long as their THC concentration remains below 1 %<sup>58</sup>.
  - Luxembourg announced the legalization of Cannabis for recreational use in 2021, permitting adults to grow up to four plants domestically for personal use and trade seeds with no limit content of THC<sup>20</sup>.
  - Russia introduced and adopted changes to Federal Law N 168-F3 in 2019, allowing licensed state enterprises/experts to grow narcotic drug-containing plants for research and scientific purposes in medicine and veterinary sciences<sup>4</sup>.
  - Lithuania legalized the use of Cannabis for medicinal purposes in 2019. Georgia decriminalized the use of Cannabis within their constitution as long as it is used for recreational purposes privately<sup>4</sup>.
  - Estonia allows the import of Cannabis for medicinal reasons and does not hold any criminal responsibility for personal possession of up to 7.5 g of dried flower<sup>4</sup>.
- Asia-Pacific
  - The Australian Capital Territory has legalized the recreational use of Cannabis. New Zealand and Thailand have approved its medical use and, South Korea and Singapore have limited use. China and Japan will likely open themselves up for medicinal use soon<sup>7</sup>.
  - In India, strict laws disapprove of its use and prohibit consuming all psychoactive substances except for medicinal or scientific reasons. However, an indigenous Cannabis preparation called 'Bhang' (an edible mixture of seeds and leaves) is legal<sup>13</sup>.
- South America
  - Uruguay in 2013 legalized Cannabis completely, being the first in the world to do so. The law allows users to buy 40 g of Cannabis monthly and to grow up to six plants at home or more through users' cooperatives or licensed producers<sup>13</sup>.

that the industry considers when establishing a Cannabis business in Africa.

The emerging MC industry in Africa presents significant opportunities for collaboration and growth. South Africa is a frontrunner in this field,<sup>8</sup>, with its legalized Cannabis industry poised to potentially surpass USD 1.7 billion in value<sup>34</sup>. Notably, South Africa is making significant strides in translating research into practical applications. This "farm-to-bedside" approach focuses on establishing MC as a commercially available product supported by ongoing research, including clinical trials (as detailed in **Box 1** and **Fig. 4**)<sup>86,122</sup>. Opening windows for developing core opportunities in the global landscape. These advancements position Africa to develop core competencies within the global *Cannabis* landscape.

### 3. Recommendations from farm to bedside

The emerging consensus of experts during global health summits includes the significant potential of medical Cannabis for global health. Carefully integrating evidence-based Cannabis products in medical practice could provide low-cost and accessible approaches for patients. There is a tremendous opportunity to develop evidence-based high-quality products accessible to such patients to manage their symptoms.

**Fig. 5** illustrates the recommendations. One recommendation is to establish uniform government regulations to maximize the benefits of *Cannabis*. An example of compliant cultivation practices, based on South Africa's example highlighted above is a valuable reference to other countries. Farmers with a license may farm indoors or outdoors. Once

**Box 2**

Key steps in building a *Cannabis* endeavour in South Africa that serves as an example.

- Working with the South African Health Products Regulatory Authority (SAHPRA)
  - Approves/permits health supplement products containing less than 0.001 % THC ((–)-trans- $\Delta^9$ -tetrahydrocannabinol) and a maximum daily dosage of 20 mg cannabidiol (CBD) for individuals over 18. Only one synthetic medical Cannabis product: dronabinol, has been approved to date<sup>113</sup>.
  - The evolving regulatory and legal landscape on the use of *Cannabis* will guide prescription and recreational use in the coming years<sup>60</sup>.
- Securing a License for Cannabis farming (*How to Get a Cannabis License in South Africa*,<sup>53</sup>)
  - To secure a Cannabis cultivation license in South Africa (Fig. 3), the applicant needs to acquire appropriate land. All facilities for processing (such as industrial plants and storage houses) should be built on the premises before the start of the contract.
  - The land should be well connected with the major roadways and link circuits via which the main transportation is expected.
  - The cultivator must have the documented right to grow Cannabis.
  - Soil tests for various minerals essential for plant growth should be performed. Water quality and power supply should be checked, and emergency backups should be identified and established.
  - Challenges include huge expenses in setting up an in-country, regulatory-compliant medicinal Cannabis cultivation site, and growing operations to a high standard<sup>46</sup>.
  - Despite the South African (SA) authorities providing much guidance and being thorough in their audits, ensuring compliance takes work.
  - Partnering with other entities, such as accredited, third-party verification institutions, is imperative as part of the validation process.
- Compliance
  - Appropriate compliance personnel should be included in the plan to ensure there is no compliance breach and actions against the set and prescribed regulations.
- Quality assurance from farm to bedside
  - Farming at the highest standard using Good Agricultural Practice (GAP) is crucial for determining the product quality for patients/consumers. There is, therefore, a need to establish standards for quality assurance.
  - A pharmacist registered with the South Africa Pharmacy Council should comply with all the provisions of the Pharmacy Acts and other legislations. The pharmacist would be responsible for checking the product quality, dosage, labelling, and release within the requirements of the law. The pharmacist would also recall the products, investigate the problems, and provide solutions for record-keeping.

harvested, the crop should be subjected to quality checks and consistency in phytochemical ratio. The Good Agricultural and Collection Practices (GACP) guidelines establish a structured framework that guarantees the appropriate and consistent quality of cultivated and produced medicinal plant material. To ensure a safe and effective journey of medicinal products "From Farm to Bedside," heightened attention must be devoted to quality assurance and control with a stringent documentation process, guaranteeing the integrity of the supply chain and, more importantly, safeguarding patients. A robust track-and-trace system that systematically tracks and records every activity throughout the supply chain, ensures not only consistent and reliable market access of products but also reinforces patient protection by preserving product quality. Another recommendation is to establish a center of excellence or an entity such as the scientific research institutions in every country to check quality and consistency, followed by clinical trials. Regulatory bodies such as the FDA, institutional review board, and similar are essential for clinical translation. Finally, the product may proceed to commercialization and market penetration via a collaboration between business liaisons and health experts. This process may take a few months to years, depending on the product and intervention for which it is being developed. Another recommendation is to integrate educational programs into each country's centers of excellence/academic institutions. One example is a master's course on, "Medical Science Cannabis and Therapeutics," at the University of Maryland, USA<sup>121</sup>. Education and awareness amongst the general public, medical specialists, and pharmacists for responsible use is important.

With a vision of "Unprecedented Health and Wealth from Medicinal Plants", an International Phytomedicine and Medical Cannabis Institute (IPI) represents one example with a mission to support research and

education on medical cannabis products. The IPI model (Fig. 6) follows a collaborative model with a virtual platform linked to labs of faculty and investigators at different institutions and industry partners. The four interrelated IPI cores on Care, Outreach, Research and Education provide complementary areas for facilitating the translation of evidence-based products from farm to bedside, which are discussed in detail in the following section.

CMC: Chemistry, Manufacturing and Control

#### 4. Core opportunities in global health

The new regulations and increasingly favourable legal landscape for medical *Cannabis* provide major opportunities for global health that have resulted in regular presentations at Global Health conferences like the GHC summits. These opportunities can be considered under Care, Outreach, Research, and Education.

##### 4.1. Care

###### 4.1.1. Opportunity for closing the pain divide

Chronic pain is a major health problem<sup>104</sup>. Disparities in access to pain relief medication, are considered one of the most heinous, hidden inequities in global health. The Lancet Commission on global access to palliative care and pain relief has called for urgent action to address the so-called 10–90 pain divide—that the wealthiest 10 % of countries possess 90 % of opioids according to oral morphine equivalent values<sup>44</sup>. Although opioids are widely used for clinical management of pain, their long-term use is accompanied by side effects that diminish the quality of life in many patients, and have caused a concomitant rise in prescription

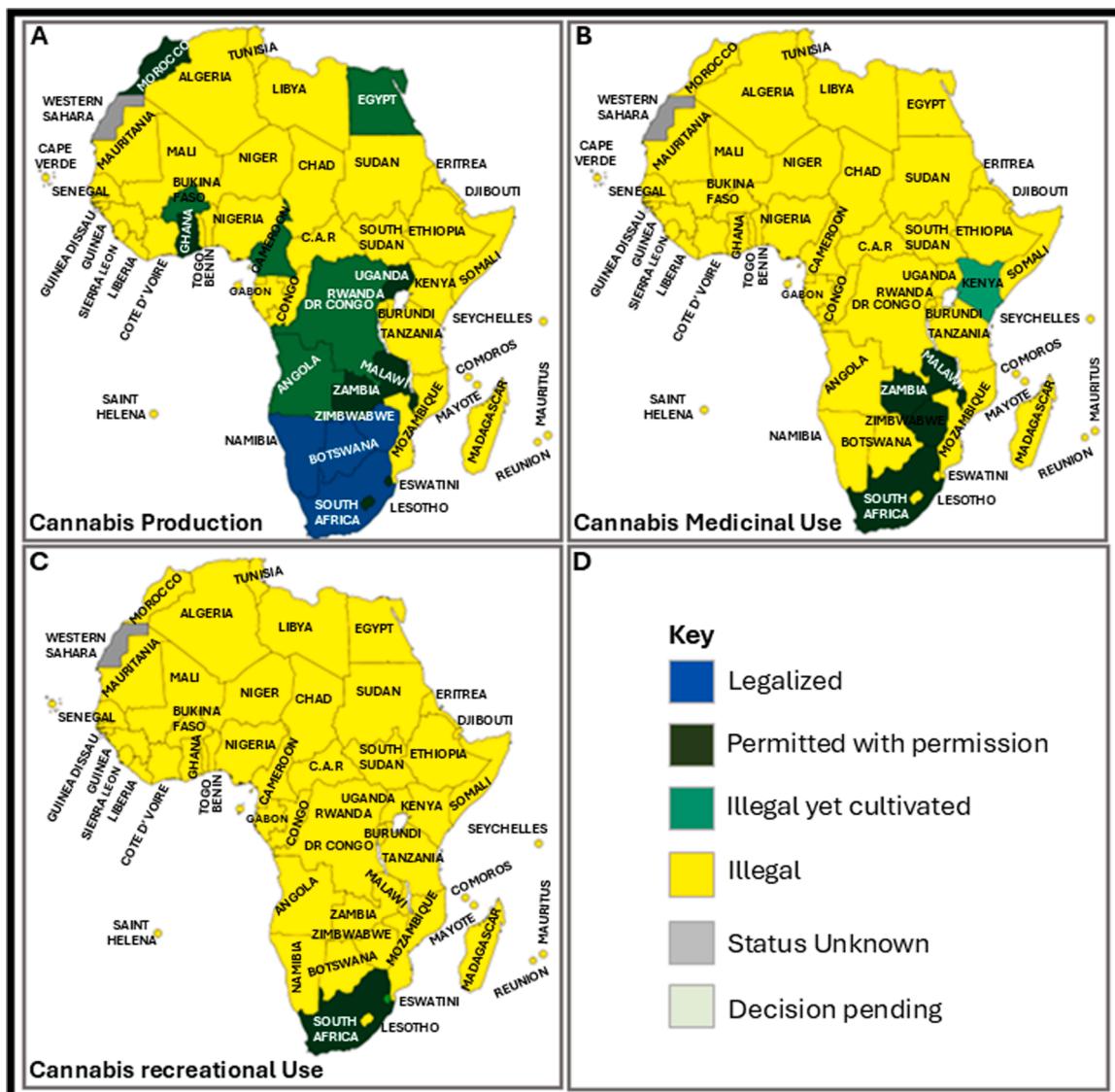


Fig. 2. An illustration country specific laws for *Cannabis*; A) production, B) Medicinal use and recreation in Africa.



Fig. 3. Strengths Weaknesses Opportunities and Threats (SWOT) analysis on setting up the Cannabis industry in Africa highlighted during Global Health Catalyst summits. GAP - good agricultural practice; GMP – good manufacturing practice.

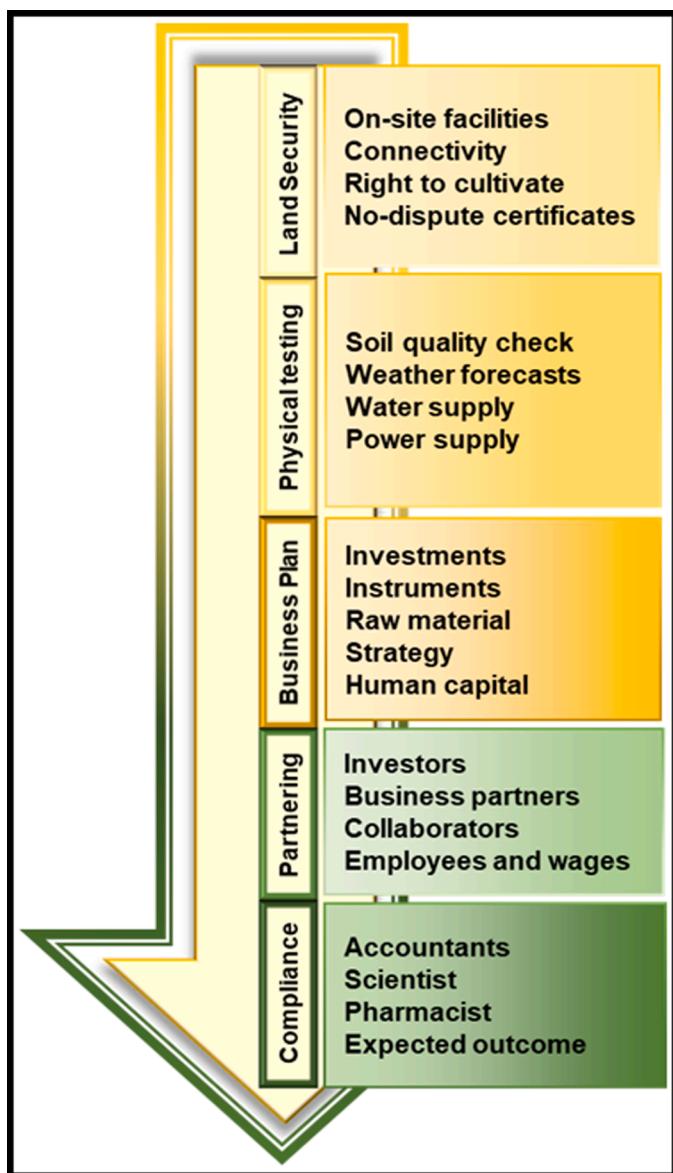


Fig. 4. Five essential preliminary stages in establishing a compliant Cannabis farm in South Africa as an example.

opioid abuse and fatalities<sup>31</sup>. The burgeoning opioid crisis in the USA and Canada has become one of the most concerning public health issues, and attention has turned toward *Cannabis* preparation in light of promising pre-clinical and observational study data.(Schwartz, 2019, [110,115,5](#))

The constituents active pharmaceutical ingredients found within medical *Cannabis* act upon a multitude of receptors that make up the endocannabinoid system and the broader endocannabinidome<sup>23</sup>. The endocannabinidome has been heavily implicated in the transmission of pain signals in response to noxious stimuli, central sensitization of the spinal cord, and the cognitive and emotional manifestations of pain<sup>56</sup>. The major cannabinoids, (–)-trans-Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), have been shown to act upon the constituent parts of the endocannabinidome present in the peripheral and central nervous system to attenuate pain in individuals with chronic pain<sup>110,117,5,56</sup>.

Cannabinoids may be delivered via topical, oral or inhalation routes. Inhalational routes can be controlled (vaporizer) or uncontrolled; Oral ingestion has a slower onset, but has a prolonged length of action, with bioavailability affected by stomach contents. THC and CBD are highly lipophilic, difficult to dissolve in aqueous environment and are absorbed

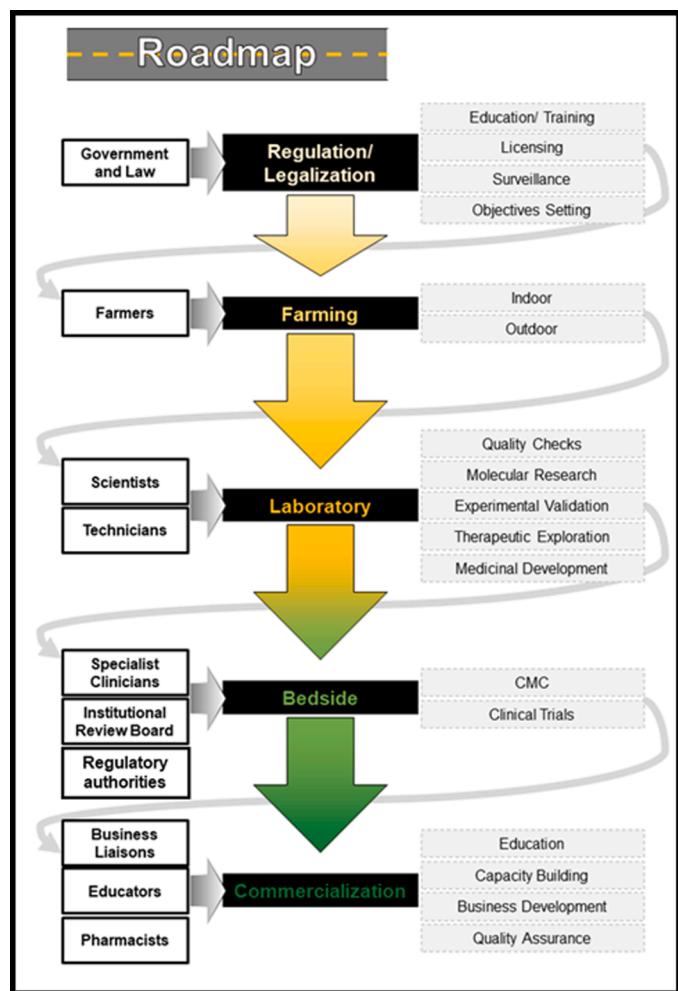
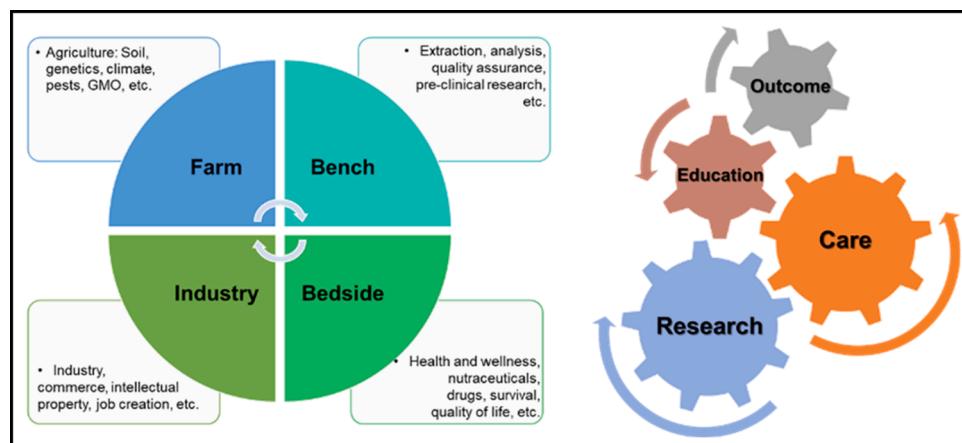


Fig. 5. Roadmap from farm to bedside with recommended steps for consideration.

by gut epithelia, resulting in poor bioavailability (as low as 6%)<sup>69</sup>. Cannabinoids are also found to accumulate in adipose tissue with chronic use and are released slowly<sup>51</sup>. Cannabinoids were shown to be effective analgesics in models of neuropathic, chronic pain from chronic constriction nerve injury, chemically-induced diabetes and chemotherapy-induced peripheral neuropathy and inflammatory arthritis<sup>29,54,70,73</sup>. The efficacy of cannabinoids for chronic pain has been examined using plant-derived formulations: nabiximols (1:1 blend of THC and CBD), smoked or vaporized Cannabis, oromucosal THC spray, and oral THC, as well as synthetic compounds. These studies showed favorable outcomes for patients with chronic pain conditions, including neuropathic pain (Petzke et al., 2022), cancer-related pain<sup>67</sup>, peripheral neuropathies<sup>71</sup>, fibromyalgia<sup>123</sup>, pain due to multiple sclerosis<sup>66</sup>, rheumatoid arthritis<sup>100</sup>, musculoskeletal problems(D.<sup>30</sup>), and chemotherapy-induced pain<sup>55</sup>. However, various studies reported low-quality evidence for improvements in chemotherapy-associated nausea and vomiting,<sup>119</sup>, no convincing or high-quality evidence for fibromyalgia<sup>115</sup>, insufficient evidence for rheumatic diseases<sup>27</sup>, limited evidence for chronic non-cancer pain<sup>106</sup>, and low-quality evidence for mental disorders<sup>17</sup>. As for the treatment of chronic pain, several systematic reviews and meta-analyses have concluded that medical Cannabis is effective<sup>105,117,119,52,74</sup>. However, there is a lack of consensus as to which formulations of *Cannabis* this evidence applies and the associated strength of this evidence. Whilst there have been several randomized controlled trials, several of these have investigated licensed products, such as nabiximols<sup>117</sup>, in a setting outside their



**Fig. 6.** International Phytomedicine and Medical Cannabis Institute model.

licensed application. Whilst other studies are affected by small sample sizes, limited follow-up, heterogeneity of studied product or a combination of the above<sup>14</sup>. Additional work is needed to investigate cannabinoid analgesic effects further and identify mechanisms of action to optimize potential treatment strategies. Future studies could focus on a specific type/etiology of chronic pain, comparing product type, constituent profile, dose, and route of administration, as each mode of use is associated with a unique rate of onset and duration of effects. Research to identify side effect profiles and the impact of drug-drug interactions to address safety concerning the use of Cannabis for pain is essential. In addition to these, the long-term risks and effects of Cannabis also needs to be investigated thoroughly. Utilization of real-world evidence to inform ideal drug candidates for assessment in randomized controlled trials will be essential<sup>14</sup>.

The recent passage of the Cannabis act in the USA now provides support for doctors to discuss Cannabis use with their patients. Educating clinicians and healthcare providers to guide patients about the use of Cannabis is a first step in effecting use. Evidence suggests that many medical Cannabis patients still perceive themselves to be subject to societal stigma, which may adversely affect other aspects of their healthcare<sup>112</sup>. Public education on cannabinoid the public will be an important determinant in the adoption of Cannabis use, globally.

#### 4.2. Outreach

The GHC summits have provided one of the major opportunities for continuous outreach and engagement with different stakeholders including policymakers involved in developing legislation and policy, industry, academic institutions, farmers, and others. One outcome of this outreach has been the launch of the International Phytomedicine and Medical Cannabis Institute (IPI). The IPI provides a platform for collaboration, connecting local/regional credentialed sites globally with faculty and health leaders at world-leading academic institutions,

organizations, and industry<sup>108</sup>. The IPI focuses on integrating phytomedicines, including medical Cannabis, for global health and development to serve as a collaborative platform providing independent verification to establish which formulations of *Cannabis* have the associated strength of evidence. **Box 3** summarizes some of the outcomes of this outreach.

#### 4.3. Research

New regulations facilitating *Cannabis* research have opened significant opportunities for research towards clinical translation of evidence-based *Cannabis* products, from farm to bedside that are expected to impact global health and development. Research is crucial for developing evidence-based *Cannabis* products and enhancing understanding of its varied effects depending on sex<sup>80</sup>, age<sup>93</sup>, ethnicity<sup>61</sup>, and duration of exposure<sup>120</sup>. Products must meet standardized criteria to ensure the availability of safe and effective products for medical use<sup>35</sup>. There are now growing research collaborations between academic institutions and industry. One such collaboration<sup>72</sup> has recently resulted in a clinical trial on *Cannabis* for pancreatic cancer (**Box 3**). This example highlights the importance of these growing research collaborations and their potential impact. Ongoing collaborations for simultaneously targeting cancer and pain represent an exciting frontier.

Other examples of ongoing *Cannabis* research collaborations include The Penn State Medical Marijuana Academic Clinical Research Center (ACRC). The center supports pre-clinical and clinical research and provides scientific evidence on the utility of medical *Cannabis*. The center has more than 30 researchers engaged in *Cannabis* research within two divisions: a basic science division and a clinical science division (*Medical Marijuana Research*). Another example is the Medicinal Cannabis Research Collaboration (MCRC), which is a group of researchers from Swinburne University of Technology, La Trobe University, and the University of Melbourne. The MCRC conducts high-quality research on

#### Box 3

Examples of outreach outcomes.

- Sponsored research collaborations for evidence-based products emerging between industry and healthcare institutions e.g. Harvard-affiliated hospitals (Brigham and Women's Hospital and Dana-Farber Cancer Institute), and the Council for Scientific and Industrial Research (CSIR) in South Africa<sup>77, 1, 78</sup>.
- Collaborations in a new field of phytoradiotherapy<sup>3</sup>.
- A medical Cannabis Awareness Education Initiative led by former National Football League players<sup>39</sup>.
- Outreach collaborations with LMIC government/policy makers<sup>94</sup>.
- First-in-human Food and Drug Administration (FDA)-approved clinical trial of a *Cannabis* product to treat pancreatic cancer.

medical *Cannabis* products for various indications, such as chronic pain, epilepsy, multiple sclerosis, anxiety, depression, and post-traumatic stress disorder. The MCRC also provides education and training for students, clinicians, and industry partners (*Medicinal Cannabis Research Collaboration (MCRC)*). The Marijuana Research program at the University of Mississippi (UM), which is the only entity in the United States that is federally licensed to cultivate marijuana for research purposes has an ongoing research program. The program collaborates with various academic and industry partners to research the chemistry, pharmacology, toxicology, and therapeutic potential of cannabinoids and *Cannabis*. One example of a successful collaboration is UM's ongoing partnership with Nemus Bioscience Inc. in the development and commercialization of cannabinoid-based pharmaceutical products (*Marijuana Research*). The Medical Cannabis Research Group at Imperial College London is also engaged in collaborative, translational research performing pre-clinical research focusing on pain, inflammation and cancer, in addition to working with real-world evidence derived from the UK Medical Cannabis Registry, the largest global patient registry on *Cannabis* prescribing outcomes (<sup>14,15,25,26,57,79,80</sup>; Rifkin-Zybutz et al., 2023;<sup>110,116</sup>).

#### 4.4. Education

Education is critical in the emerging global health of medical *Cannabis* for many reasons including the following<sup>121</sup>. Therapeutics using *Cannabis* is a complex and evolving field that requires up-to-date knowledge and skills to provide safe and effective care to patients. Healthcare professionals need to understand the science, pharmacology, clinical evidence, and legal aspects of *Cannabis* to make informed decisions and recommendations<sup>111</sup>. Medical *Cannabis* is not a one-size-fits-all solution. Different strains, formulations, dosages, and delivery methods may have different effects and interactions depending on the patient's condition, symptoms, genetics, metabolism, and other factors. Education and training can help healthcare professionals tailor medical *Cannabis* therapy to each patient's individual needs and preferences<sup>111</sup>.

*Cannabis* is still a controversial and stigmatized topic in many parts of the world<sup>112</sup>. Education and training or awareness can help healthcare professionals and the public overcome the myths, misconceptions, and biases that may hinder their acceptance and adoption of *Cannabis* as a legitimate treatment option. Education and training can also help healthcare professionals communicate effectively with patients, colleagues, regulators, and the public about the benefits and risks of *Cannabis*. Healthcare professionals with proper training and knowledge can stay abreast of the latest developments and trends in *Cannabis* science, technology, policy, and practice, allowing networking and collaborations with other experts and stakeholders in the *Cannabis* field and contributing to the advancement of *Cannabis* knowledge and practice<sup>33</sup>.

#### 5. Conclusions

There is an emerging opportunity to develop the field of Medical *Cannabis* in global health. New regulations at the UN, USA and many countries have generated global excitement for *Cannabis* stakeholders, especially in facilitating research and development of evidence-based products. The emerging consensus from conferences is that *Cannabis* for medicinal use has significant global health and development potential. Areas, where strategic regulation, quality assurance, and investment of *Cannabis*, could have a substantial impact, include closing the pain divide, addressing the opioid crises, and increasing its access for managing symptoms where there is already substantial scientific evidence. As the African saying goes, collaborations go further than individual efforts. The IPI represents the need for the establishment of collaborative centers that can facilitate the translation of evidence-based products for global health and wealth generation, incorporating care, outreach, research, and education. It is recommended that each country

establish a center of excellence on *Cannabis* or integrate research and education activities with other phytomedicines programs.

#### Ethics approval and consent to participate

Not applicable

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#### Authors' contributions

All authors contributed to the discussions and content of this manuscript. Conceptualization, W.N.; methodology, W.N.; resources, W.N; data curation, G.S, W.N.; writing—original draft preparation, M.B.T, T.A, B.C, B.O, S.E, G.S, W.N; writing—review and editing, M.B.T, T.A., W.N.; supervision, project administration, funding acquisition, W.N. All authors have read and agreed to the published version of the manuscript.

#### Consent for publication

Not applicable.

#### Declaration of Competing Interest

Simon Erridge is Head of Research at Sapphire Medical Clinics; Mikael H Sodergren is Chief Medical Officer at Curaleaf International; Ngeh Toyang is CEO at Flavocure Biotech, Inc.; Henry Lowe is Executive Chairman at Flavocure Biotech, Inc.; Gary Strichartz is a consultant for Flavocure Biotech, Inc; Eric Tanifum owns stock at Alzecca Biosciences, Inc.; Luc Richner is the CEO & Founder of Vigia AG / Cannavigia.

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#### Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ctim.2025.103205.

#### Data availability

The data associated with the research paper, "Farm to Bedside: Potential of Medical Cannabis in Global Health", is available upon request.

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