

DISCUSSION PAPER SERIES

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Prescription Drugs**

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ABSTRACT

Do-It-Yourself Medicine? The Impact of Light Cannabis Liberalization on Prescription Drugs

Governments worldwide are increasingly concerned about the booming CBD (cannabidiol) products. However, little is known about the impact of their liberalization. We study a unique case of unintended liberalization of a CBD-based product (light cannabis) that occurred in Italy in 2017. Using unique and high-frequency data on prescription drug sales and by exploiting the staggered local availability of the new product in each Italian province, we document a significant substitution effect between light cannabis and anxiolytics, sedatives, opioids, anti-depressants, and antipsychotics. Such medical non-adherence is consistent with a self-medication interpretation. Results are informative for regulators and suggest that policies contrasting this “green oil” boom risk to disregard the effective need of patients to seek effective reliefs of their symptoms.

JEL Classification: H51, H75, I18, K32, K42

Keywords: light cannabis, self-medication, marijuana, difference-in-difference, prescription drugs, CBD

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1 Introduction

The cannabis market has gained momentum worldwide. Ranging from recreational and medical marijuana to cannabis-derived products- such as CBD (cannabidiol), a relaxant compound of cannabis- its consumption is booming around the World. In Europe, marijuana is the most used illicit drug, with approximately 20% of individuals aged 15-24 having used it in 2018 (ECCMDA, 2019).¹ More recently, low-strength versions of cannabis such as hemp (or industrial hemp), rich in CBD, have also become widely popular and sold in the form of herbal cannabis (light cannabis, hereafter), lotions, extracts, and candies. A major case interested Italy, a country with a conservative view on cannabis, in which “light cannabis shops” unexpectedly blossomed due to a loophole in the legislation and received massive media and political attention.² With the 2018’s *Farm Bill*, hemp was removed from the definition of marijuana of the *Controlled Substances Act* and similar products have become available in the US as well, where this industry is expected to hit \$20 billion by 2024 (BDS Analytics).

Despite the considerable interest that these products received, little is known about the impact of this CBD market and several concerns have regarded the health effects of their use. While, as pointed out by the National Academies of Sciences, Engineering, and Medicine (2017), CBD might not present itself a risk for human health, this is certainly the case of its misuse to treat serious disorders. In May 2019, just before launching a public hearing with experts on CBD, the Food and Drug Administration (FDA) issued a warning that “*misleading and false claims associated with CBD products may lead consumers to put off getting important medical care, such as proper diagnosis, treatment, and supportive care*” (FDA, 2019).³ Likewise, due to a high uncertainty, in 2019 New York City banned CBD-derived food and drinks, whereas several states (i.e., Kansas, Indiana, Louisiana, Texas, and more recently North Carolina) announced or enforced a ban on light cannabis (New York Times, 2019). A similar hard stance on light cannabis was proposed by the Italian National Health Council (CSS), which in 2018 expressed its concern for the safety of products based on cannabis inflorescence and suggested a ban on the commercialization of the product. In their statement, the CSS was

¹ In the US, ten states and the District of Columbia allowed for recreational use of cannabis and many others approved medical marijuana laws. As of 2018, Canada passed a law to remove restrictions on production, possession, and consumption of marijuana. In Europe, instead, most states have a strong stance against both versions of cannabis (ECCMDA, 2019).

² In May 2019, the industry received massive media and political attention when the Italian Ministry of Interior, Matteo Salvini, started a crusade against local retailers. Local retailers were accused of being “places of mass miseducation” and helping the transition to real drugs (Reuters, 2019).

³ In 2019, the US FDA issued FAQs regarding hemp and the recently approved Farm Bill (2018). Responding to the question n. 4 “*Aside from Epidiolex, are there other CBD drug products that are FDA-approved? What about the products I’ve seen in stores or online?*”, FDA stated that “*We are aware that some firms are marketing CBD products to treat diseases or for other therapeutic uses, and we have issued several warning letters to such firms.*”

concerned about the impossibility to monitor individual users and their effects in the short- and long-run as well as about the risk linked to other conditions (e.g., age, pregnancy, other pathologies).

This paper aims to go deeper into the understanding of the “hidden” use of light cannabis and tries to investigate how people reacted to the introduction of this new and potentially risky product in the market. On the one hand, as already pointed out by previous studies (i.e., Carrieri *et al.* 2019), light cannabis can be a substitute for *street marijuana* and thus generate spillovers on the illegal market. On the other hand, for its relaxant effects, this product can be regarded as a substitute for existing drugs and induce self-medication.

To explore this second channel, we exploit a unique case of unintended liberalization that occurred in Italy in 2017 when light cannabis was unexpectedly allowed to circulate in the market.⁴ Moreover, we use a unique dataset that combines the local availability of this light cannabis across Italian provinces and monthly sales of a large set of prescription drugs for which CBD is often *advertised* to be effective by producers. These include opioids, anxiolytics, sedatives, anti-migraines, anti-epileptics, antipsychotics, and anti-depressants.

Several features of the Italian case of liberalization make it an ideal setting to explore the *causal substitution effect* between light cannabis and prescription drug consumption. In December 2016, the Italian government passed a law (Law 242/16) to facilitate the cultivation of industrial hemp in Italy. Due to a loophole in the legislation, the law rendered “not illegal” the large-scale commercialization of the cannabis flower (light cannabis) in the absence of psychotropic effects (0.2-0.6% THC). Given the unintended scope of the liberalization, the product was sold as a collector’s item and not suitable for human consumption since May 2017. Critically, due to lack of anticipation effects, this policy shock provides a plausibly exogenous variation in the policy setting. Indeed, this allows us to test the substitution between existing drugs and light cannabis in the absence of institutional adaptation and potential confounding factors (such as changes in national or local health policies).

A second critical aspect is that the liberalization was accompanied by territorial heterogeneity in the market availability of the product. The presence of light cannabis shops was primarily driven by the morphological and geographical conditions of the territory that made the cultivation of cannabis crops more suitable (see e.g., Carrieri *et al.*, 2019). The first retailers of light cannabis were existing *grow*

⁴ Another interesting case, which dealt with indoor prostitution, is studied by Cunningham and Shah (2018). The authors study the effects of a Rhode Island District Court ruling, which unexpectedly decriminalized indoor prostitution, on several outcomes such as sexual infections and violence, amongst others.

shops that before the law were selling products related to the cultivation of industrial hemp and, after the change in the legislation, began selling light cannabis exploiting large economies of scope. Subsequently, the commercialization of light cannabis flourished at a different pace across provinces. As the market availability of the product was not linked to the demand for illegal or medical marijuana as well as of pharmaceuticals, the market entry of these retailers can be regarded as plausibly exogenous in our setting.

To identify the effect of interest, we exploit the idiosyncratic availability of light cannabis in the 106 NUTS-3 Italian provinces in a staggered difference-in-differences (DiD) framework in the period of time surrounding the approval of the law. We find that the local availability of light cannabis led to a significant decrease in the number of dispensed boxes of anxiolytics by approximately 11.5%, a reduction of dispensed sedatives by 10%, and a reduction of dispensed antipsychotics by 4.8%. More nuanced but still significant effects are found for anti-epileptics (-1.5%), anti-depressants (-1.2%), opioids (-1.2%), anti-migraines (-1%). An event-study specification shows that the substitution between these pharmaceuticals had a larger effect starting from the third month after the introduction of the product in the local market and remains statistically significant also after six months post-liberalization. This is consistent with a learning process and the dynamics of self-medication, which may stem from the need to be aware of the local market availability of the product, experimentation, and finally more substantial partial or full self-medication. This interpretation is further corroborated by anecdotal evidence from Google Trends, which shows an increasing number of queries on the potential clinical effects of light cannabis after the policy. The figure indicates that patients might have searched for information regarding the new product and their potential relaxant effects when this became available. Finally, we find that drug prescriptions across provinces did not trend differently for up to six months prior to the light cannabis seller entry in the province, thus reinforcing our identification strategy. These results are robust in a number of checks, including alternative model specifications, randomization tests based on fake treatments and placebo regressions using drugs for which an *a priori* case of substitution with light cannabis cannot be made.

Our findings contribute to several streams of literature. First, they are related to studies on the substitution effects induced by marijuana legalization. Dinardo and Lemieux (2001) and Crost and Guerrero (2012) used minimum drinking age regulations to show clear substitution patterns between alcohol and marijuana. Powell *et al.* (2018) show that medical marijuana laws, and in particular the number of marijuana dispensaries, are associated with fewer opioid overdoses. Similar patterns were already documented by Shy (2017), Liang *et al.* (2018), Chan *et al.* (2019), Smith (2019), and

McMicheal *et al.* (2019). Bradford and Bradford (2016; 2017; 2018) studied how the availability of medical marijuana impacted on Medicare and Medicaid drug prescriptions in the US, with a significant reduction for those related to pain relief, anxiety, nausea, depression, psychosis, and sleep disorders. Our contribution to this stream of the literature is threefold. First, this represents the first-ever evidence from Europe on the substitution effects induced by a compound of cannabis, the CBD. As the product is increasingly available in other European countries (e.g., Belgium, Germany), our results provide relevant implications for policymakers. Second, while there is a high degree of variation in medical and recreational marijuana laws in the US - where some states adopted a more liberal (almost recreational marijuana) approach, and others a stricter one (where people need a terminal diagnosis to get a prescription) - the Italian experience has been both liberal and strict at the same time. More importantly, the loophole in the legislation was homogenous in the entire country, although the local availability of the product was initially heterogeneous between local areas. Arguably, this represents a suitable setting to explore medical substitution between light cannabis and several different types of prescription drugs by exploiting territorial heterogeneity in product availability. Third, while substitution effects arising from medical marijuana laws in the US are consistent with a supply-side driven substitution (i.e. induced by doctors' decision)⁵, ours is a form of consumer-driven substitution which does not involve any medical decision. This is because light cannabis is sold as a technical and collector's item and, hence, virtually not suitable for human consumption.

Secondly, our paper is related to the literature on the economics of risky, or potentially risky, behaviors (for a review, see *e.g.*, Cawley and Ruhm, 2012). Traditionally, these behaviors, and in particular addictive ones (such as heavy drinking, smoking, and drug abuse), have mostly been considered as a consequence of imperfectly rational individual's choices, time-inconsistent preferences or triggered by incomplete information regarding possible risks.⁶ More recently, risky behaviors have been associated with the so-called "death of despair" (Case and Deaton, 2015). However, these may also emerge as a form of rational self-medication for symptoms not effectively treated by currently available drugs. This is the new perspective highlighted by Darden and Papageorge (2018) who recently proposed a novel rational interpretation which is consistent with a utility-maximizing framework and tested it empirically. They find that the availability of new and

⁵ In the US, physicians in states where there is cannabis liberalization can sign a state form certifying that the patient has a qualifying medical condition to buy cannabis at dispensaries.

⁶ Starting with seminal contributions of Becker and Murphy (1988), the literature on rational addiction has evolved further including time-inconsistent preferences (Gruber and Koszegi, 2001) and has been tested with respect to alcohol (Baltagi and Griffin, 2002; Dragone, 2009), caffeine (Olekanls and Bardsley, 1996) cigarettes (Chaloupka, 1991; Becker *et al.*, 1994), cocaine (Grossman and Chaloupka, 1998), among other goods.

better drugs for depression has led to a reduction of forms of self-medication, such as alcohol, in the US. Our study contributes to this literature from a novel angle by testing the effect of the availability of a new product suitable for self-medication on existing drugs consumption. The unintended nature of our liberalization offers the *unique* opportunity to test for the presence of self-medication by exploiting an exogenous variation in the availability of the product.

Lastly, our analysis also relates to the stream of the literature on partial or non- medical adherence, that is, the patient's decision to abandon individual therapy (Egan and Philipson, 2014). In fact, self-medication may be a potential cause of lack of adherence to prescribed care. Previous research identified in the non-adherence a major problem in the US health care, with an annual cost of approximately 2.3% of GDP (New England Healthcare Institute. 2009), while, to the best of our knowledge, there is no evidence from Europe on this issue. By the same token, our analysis also complements the literature concerned with the effect of marijuana liberalization. This has already shown effects on other outcomes, i.e., crime (Carrieri *et al.*, 2019; Shephard and Blackely, 2016; Brinkman and Mok-Lamme, 2017; Chang and Jacobson, 2017; Gavrilova *et al.*, 2017; Chu and Townsend, 2018; Dragone *et al.*, 2019), the labor supply of older adults (Nicholas and Maclean, 2019), migration (Zambiasi and Stillman, 2019), traffic fatalities (Anderson *et al.*, 2013; Hansen *et al.*, 2018), teenager use (Červený *et al.* 2017; Lynne-Landsman *et al.*, 2013), fertility (Baggio *et al.*, 2020), body weight and obesity (Sabia *et al.*, 2017) but it lacks of studies on drug consumption.

The rest of the paper is structured as follows. In Section 2, we present the policy reform that occurred in Italy. In Section 3, we discuss our data and the identification strategy. In Section 4, we present our main results, followed by some sensitivity analyses and robustness checks of these results in Section 5. In the final section, we present some concluding remarks.

2 Institutional setting

Italy has a long historical tradition of the cultivation of cannabis. One of the earliest large cultivation dates back to the 1st century A.D. (Mercuri *et al.*, 2002). In the 1940s, Italy was the second-largest producer of industrial cannabis worldwide. Despite this fact, marijuana cultivation, possession, and sale remain illegal, except for its industrial and medical use.

However, in 2016, the government passed Law 242/2016, which was intended to remove some restrictions on cultivation, transformation, and commercialization of industrial hemp, a strain of *Cannabis sativa*, widely used for textiles, clothing, and food. For its use, hemp is not classified as a drug as it is (almost) free of the cannabis psychoactive compound (THC). The latter should be kept below 0.6, and it is rich in CBD, a relaxant compound. Failing to account for this limit would imply narcotic effects and hence be subject to confiscation, closure, and risk of being convicted for drug dealing. In 2018, as demand for CBD products grew, Italy had approximately 4,000 hectares of land dedicated to hemp cultivation, that is, 10 times more than in 2013.

The law, however, did not explicitly intervene on the commercialization of the cannabis flower leaving a loophole in the legislation. As a result, as not explicitly forbidden, herbal cannabis was essentially liberalized. From May 2017 onwards, once the inflorescence phase was over, several startups exploited this grey and completely unregulated market and started selling light cannabis as a “technical product”, that is, as a collector’s item not meant to be smoked or consumed. The same retailers started selling also other CBD-based products such as oil, leaves, extracts, food, and beverage.

Interestingly, the local market availability of light cannabis did not arise simultaneously in all geographical areas of the national territory. Due to the unannounced liberalization, local availability in the first months after the policy mainly affected those areas previously served by grow shops, that is, shops selling seeds and cannabis-related products. As documented elsewhere (*e.g.*, Carrieri *et al.*, 2019), these grow shops were mainly concentrated in those areas in which industrial cannabis cultivation was more likely due to the geographical and morphological conditions of the territory. As a result, the first retailers selling the product were those grow shops that, before the policy shock, were already supplying industrial hemp and items for its cultivation and that could exploit existing supply chain and network.

[Figure 1 around here]

Figure 1 depicts this staggered entry into the market during the period covered by this study. In May 2017, 22 out of 106 provinces were served by at least one light cannabis retailer. After a first introductory phase, light cannabis shops blossomed becoming a “social phenomenon”. Tobacco and herbalist shops, para-pharmacists, and automatic machines began selling this product as well and expanded their local coverage. As shown by Figure 1, by February 2018, the number of provinces

reached 87 and the entire country was gradually covered by retailers throughout 2018. In 2019, more than 1,000 shops were open.

Interestingly, in May 2019, the situation in the market changed dramatically. The former Minister of the Interior, Matteo Salvini, announced a crackdown on this herbal cannabis and several retailers had their products precautionary confiscated. The reason was that, in several cases, the flowers was containing more THC than what allowed by the law for not being considered as an intoxicating substance triggering intervention from the police.⁷ In the same month, the Court of Cassation, Italy's Supreme Court, aimed to close the loophole in the legislation by deciding for a ban on the sales of cannabis derivatives such as "oil, leaves, inflorescences, and resin". However, the Court's ruling left a backdoor open for a mild interpretation of the law for those CBD-derived products free of narcotic effects, creating more uncertainty in the market. Precautionary, many business and shops shut down in June 2019. Our study thus exploited the possibility of study this phenomenon in the time in which the market was entirely left unregulated. Figure 2 provides a time framework regarding our study, which covers market entry data from May 2017 to February 2018.

[Figure 2 around here]

3 Data and Methods

We use a unique longitudinal dataset recording monthly drug sales and mapping the local market availability of retailers selling light cannabis at the province level (106 NUTS-3 provinces) over the period from January 2016 to February 2018.⁸ Data on these dispensaries were collected using the *Archive Internet Wayback Machine* on the websites of the four main producers of light cannabis in 2017. These were then matched with data on prescription drug sales obtained by *Federfarma*, the Italian association of pharmacy owners. Our data tracks the pharmaceutical expenditure of the Italian NHS for each Local Health Authority (ASL) and covers more than 95% of Italian pharmacies. As

⁷ This was not the case, instead, of CBD, for which no limitation in its quantity per milligram existed.

⁸ We collected monthly information on the entry in a market in each Italian province by having access to archived copies of their early pages of the four main producers in 2017 (Easyjoint, Marymoonlight, RealHemp, XXXJoint) using the Internet Archive Wayback Machine <https://archive.org/web/>. Data were collected monthly from May 2017 (first entry in the market) and using the last accessible page for each month. When data were not available, the average number of retailers between the months with missing information was imputed.

provinces can be served by one or more ASLs, data were aggregated at the province level (106 provinces).

A key feature of our dataset is that of tracking all “Class A” drugs dispensed by the Italian NHS containing active ingredients often used to treat symptoms for which marijuana can also provide relief or, at least, relaxant effect. We consider the following categories: opioids, anxiolytics, sedatives, anti-migraines, anti-epileptics, antipsychotics and anti-depressives. These pharmaceuticals have shown patterns of substitutability with medical marijuana (Bradford and Bradford 2016; 2017; 2018), which however presents some differences with respect to the light one. For instance, medical marijuana, rich in THC, is largely used to deal with chronic pain, glaucoma, insomnia, and anxiety. Instead, for its clinical effects, CBD is often associated with antipsychotic, analgesic, anti-inflammatory, anti-arthritic, and anti-neoplastic properties and is used to treat inflammations, migraines, depression, and anxiety (Blessing *et al.*, 2015; CIBG, 2018). However, CBD-based products have come under scrutiny in the US for misleading claims made by some CBD producers relative to effectiveness in treating the above pathologies. Apart from Epidiolex, a drug recently approved by the FDA to treat rare forms of epilepsy, no other drug contains CBD. Opioids were also included as, according to recent anecdotal evidence, Canadian veterans started substituting opioids (along with benzodiazepines) with marijuana after their introduction of medical marijuana in Canada to treat anxiety, insomnia and for pain relief. Similar patterns of substitutability with medical marijuana were documented by several scholars (*e.g.*, Bradford and Bradford, 2016, 2018; Shi, 2017; Bachuuber *et al.*, 2014).

These drugs refer to the group “N - Nervous System” according to the WHO Centre for Drug Statistics Methodology. Note that the latter require a doctor’s prescription and are available either free of charge or with a very small patient co-payment, which depends on the regional co-payment settings and individuals’ equivalent income.⁹ Our dataset tracks all prescriptions that translated into a final sale in each province.

[Table 1 around here]

Table 1 provides a description of the main variables we use and shows a large heterogeneity across drug categories in the number of dispensed drug packets. On a monthly average, the Italian NHS

⁹ According to Federfarma (2018), “Classe A “drugs are the most consumed drugs in Italy, accounting for approximately 52% of all market for pharmaceutical products (which also include dietary products, herbs, para-pharmaceuticals, and products for health and beauty care). Co-payments range from 1 euro per box to 4 euro per the entire prescription.

provides reimbursement for 28 packets of sedatives and 72 boxes of anxiolytics per province. Much higher numbers are documented for anti-epileptics (18,460 packets), antipsychotics (4,802 packets) and anti-migraines (2,504 boxes). With 27,198 packets sold on average, anti-depressants represent the drug with the largest sales in our sample. ISTAT, the Italian National Institute of Statistics, estimates that more than 2,4 million Italians suffered from mental health problems in 2015, and approximately 1,3 million presented symptoms of depression (ISTAT, 2018).

Interestingly, opioids, which are widely used in the US and Canada for acute and chronic pain relief but have severe side effects such as dependence and sedation, show lower numbers, accounting for an average monthly sale at the province level of 12,610 packets. Although the number of prescriptions increased in recent years, these numbers depict the general skepticism of Italians with respect to this drug.

Finally, by matching this information with those available from light cannabis local retailers, we obtained a balanced panel with a total of 2,756 province-month observations.

3.1 Identification Strategy

In order to identify the causal effect of light cannabis on the prescriptions of drugs, we employ a staggered DiD, which exploits the idiosyncratic availability of light cannabis in a given province. Thus, our identification relies both on the staggered timing of the product availability and the provinces without any retailer as the control group.¹⁰ More formally, we estimate the following equation:

$$Y_{it} = \alpha + \sum_k \beta_k Entry_{ik} + \delta X_{it} + \gamma_i + \mu_t + \varepsilon_{it}$$

where Y_{it} is the number of packets of dispensed drugs (i.e., opioids, anxiolytics, sedatives, anti-migraines, anti-epileptics, anti-depressants and antipsychotics) reimbursed by NHS at the time t in the province i , $Entry$ is an indicator that takes value 1 if at least a cannabis retailer has entered in all periods $k < t$ in province i . γ and μ are province and time (month and year) fixed effects, ε represents

¹⁰ In our identification strategy we cannot rule out cross-province movements to buy light cannabis, as recently shown by Hansen *et al.* (2017). However, in the period of time we consider, it is very unlikely that people managed to know about the local availability of light cannabis in a different province and *systematically* move to that province accordingly to buy the product. As a result, in our setting, cross-province shopping does not represent a concrete issue.

the error term. X_{it} is a vector of controls for province population size and density and a dummy for post-May period to take into account eventual changes which occurred at national level after the unintended liberalization. Our coefficient of interest is β , which captures the monthly change in the demand for dispensed drugs due to the local availability of light cannabis.

The credibility of our identification strategy relies on the natural experiment which characterized the policy. As discussed, the policy was unannounced and concerned hemp, a product that, when sold as light herbal cannabis, differs in its composition from both recreational and medical marijuana. Thus, the entry of light cannabis retailers in a local market can be regarded as plausibly exogenous as it was not linked to the demand for illegal or medical marijuana as well as pharmaceuticals. Moreover, the possibility of endogenous entry is essentially ruled out for several reasons. First, the particular nature of the unintended liberalization process rendered any anticipatory effect to be implausible. The law was approved in December 2016 and the product was first marketed in May 2017, after an early cultivation phase. Second, the local availability during the period under investigation mainly depended on the geographical presence of grow-shops before the policy. The latter are retailers specialized in industrial hemp, which were the first to sell light cannabis after the liberalization by exploiting large economies of scope and their existing supply chain (see for instance Carrieri *et al.*, 2019). Finally, we make use of high-frequency data to focus on a narrow window around the time during which the policy took effect (May 2017 – February 2018). This allows us to rule out potential changes in national and local health policies concerning prescribed drugs and systematic changes in the prescription choices of medical doctors. This is because any change requires time to be fully operational and extensively included in medical guidelines and protocols.

More formally, our empirical analysis relies on the classical DiD's identifying assumptions in the pre-liberalization periods, that is, the existence of a common trend in drugs prescriptions. In our setting, it implies assuming that those provinces experiencing different timings in the local availability of light cannabis (treatment group) and those provinces never served by cannabis retailers in the period we consider (control group) should have observed the same pre-policy trends for all drug categories. In Section 5, we find strong support for this hypothesis by performing a visual inspection of common trends and more formal tests such as placebo regressions and falsification tests based on alternative approaches to statistical inference.

4 Results

Our results are reported in Table 2 for all pharmaceuticals for which medical marijuana can be considered as a substitute or adjuvant therapy. For ease of interpretation, the dependent variable is expressed in logs. This allows us to interpret the DID-coefficient as the average percentage change in the monthly number of dispensed drugs resulting from local availability of light cannabis.

[Table 2 around here]

For all drugs categories, we document a significant and negative effect. Specifically, as the market availability of light cannabis became possible due to the entry of at least one retailer in a given province, the number of dispensed drugs sales decreased by approximately 1.6%, on average. The extent of this reduction reveals a considerable degree of heterogeneity. The boxes of anxiolytics prescribed by doctors and sold by pharmacies significantly decreased by 11.4%, the sedatives consumption decreased by approximately 10%, whereas the number of antipsychotics decreased by 4.8%. These drugs account for the largest reduction. Interestingly, these are also the type of drugs for which CBD – but not *light cannabis* itself - is recognized or advertised as having a clinical effect, that is, to treat anxiety and psychosis (Blessing *et al.* 2015; CIBG, 2018). This is intuitively explained by the relaxant properties of CBD, which is often used to treat sleep disorders. Moreover, the large coefficients that we observe for sedatives and anxiolytics can be explained by the marketing strategies for cannabis and CBD-related products sold which are typically advertised for its relaxant effects. These marketing strategies fueled a government investigation in the US. Hence, it is largely plausible that individuals decided to (partially) abandon a conventional medical treatment and switched to these products to treat symptoms such as anxiety and sleep disorders.

More relatively nuanced yet significant reductions are found for other pharmaceuticals, which appear to offer a more chronic therapy. These findings are consistent with a self-medication interpretation also for these drugs. There is a mild average monthly reduction in the number of packets for anti-epileptics (-1.5%), anti-depressants (-1.2%), opioids (-1.2%) and anti-migraines (approximately -1%). These are all drugs requiring a constant and consistent therapy, often prescribed by specialists, and for which the switching to an “alternative therapy” based on self-medication may be more problematic, especially for risk-averse individuals. Still, despite the short time window, local market availability of light cannabis and other cannabis-derived products led to a reduction in prescription drugs but with a lower intensity.

Moreover, it is noteworthy that opioids, anti-depressants, and anti-epileptics are all pharmaceuticals that show severe side effects and can be associated with a social stigma. In Italy, opioids are also generally less prescribed than in the US, where unregulated prescription led to an opioid crisis (Case and Deaton, 2015). Indeed, some patients may have seen in this new product the possibility to seek (partial) relief or improve their quality of life. For instance, by recurring to a largely accessible product without the need for a medical prescription and which can be perceived of common use (*e.g.*, oils, essences, or even similar to recreational yet illegal cannabis).

An interpretation consistent with the self-medication hypothesis is also anecdotally supported by looking at online information seeking. Figure 3 provides further support for the use of light cannabis as a form of self-medication using Google Trends statistics. It shows that both the general interest in the product and its use to treat anxiety disorders peaked in the month of the introduction of the product on the Italian market (May 2017) and remained at a higher level in the subsequent period. This supports the idea that people were seeking information online for treating their symptoms before actually switching to the new product.

[Figure 3 around here]

5 Robustness Checks

To assess the robustness of our results, we present several checks. First, we restrict the time before the policy. This renders the time windows before and after the policy more symmetric (May 2016 - February 2018). Despite reducing the number of observations (2,332), our main results and intuitions remain unaltered. Estimates of the DID coefficients are reported in the first row of Table 3 for all drug categories we consider. Specifically, the local availability of light cannabis leads to a reduction in the number of dispensed boxes of sedatives by 11.5%, anxiolytics by 12.3% and antipsychotics by 4.3%. Consistently with the baseline specification, we find a more nuanced but significant effect on other prescribed drugs: the selling of anti-epileptics decreases by 1.5%, whereas those of anti-depressants, opioids, and anti-migraines by approximately 1%.

Second, we include a linear time trend to capture any time-varying confounding factor which might affect our estimates. Estimates of the DID coefficient are reported in the second row of Table 3 and are very similar to those reported in the main model specification. Moreover, we include province-specific time trends. This allows us to allay any remaining concerns regarding province-specific changes in prescriptions and drugs sale. Results are reported in the last row of Table 3 and are qualitatively similar to those presented in Table 2. However, we observe a reduction in the coefficient of antipsychotics sales, which loses significance but remains negative. We thus suggest a more cautious interpretation of this effect.

[Table 3 around here]

Third, we test whether the common trend assumption can be credibly maintained. In fact, a typical concern arising when adopting a DID approach is the presence of pre-policy trends which may drive the main results. To allay this concern, we make a graphical inspection of the trends for provinces experiencing early (May – September 2017) and late (October 2017 – February 2018) local availability in the market and for those provinces never having local access to light cannabis during the period we consider. This allows us to verify whether provinces experiencing different timing in the entry of light cannabis retailers followed similar trends in drug sales before the actual liberalization (May 2017). As highlighted in Figure 4, pre-policy trends are parallel and the post-policy drop in dispensed drugs is consistent with the timing of the local availability in treated provinces, compared to the controls. This supports the credibility of the common trend hypothesis in our setting.

[Figure 4 around here]

Fourth, we perform a placebo test using as dependent variables prescription drugs for which there is no medical evidence of possible substitution patterns with light cannabis. Indeed, we consider insulin, anti-hypertensives, and genito-urinary system drugs (sex hormones and urologicals), which do not belong to the category “N – Nervous System” of the WHO Collaborating Centre for Drug Statistics Methodology. As a result, these prescription drugs should not be affected at all by light cannabis availability. Estimates are reported in Table 4. All the DID coefficients are not statistically significant and very close to zero in magnitude. This provides further support to our main results in terms of causality.

[Table 4 around here]

Finally, to reduce any residual concern about possible violations of common trend assumptions, we also perform a permutation test based on a Monte Carlo simulation. The permutation test also allows us to explore the robustness of the results to assumptions about the structure of the error distribution. This is a strategy that is increasingly used in many empirical applications (i.e., Wing and Marier, 2014). Hence, we simulate the effect of local accessibility to light cannabis by randomly assigning the treatment to provinces at different points in time, in place of the real one. We repeat this procedure 5,000 times to generate a distribution of placebo treatment effects. Figure 5 presents the non-parametric distributions of these placebo estimates for all prescribed drugs included in our study, separately.

[Figure 5 around here]

Figure 5 shows that the average of the placebo treatments is zero and the actual coefficient, which is depicted by the red vertical line, falls far from the left tail of the distribution. As a result, this indicates that the negative and significant effect we find on drug prescriptions is very unlikely to have occurred by chance.

5.1 Event Study

To shed some further light on the observed substitution, we also explore the dynamic of patient's responses to local market availability of the new cannabis-light product. By exploiting a rather rare policy set-up with heterogeneous and staggered effects at a local level, our setting is ideal to study patients' responses and to verify the self-medication hypothesis above discussed. We thus perform an event-study analysis conceived as follows. We include in equation (1) a series of dummies coding the month of in which entry in the market occurred and one to six months pre-entry and post-entry. One-month pre-entry is the excluded dummy for each dimension and is set equal to zero in our presentation of the results.

Results of the event-study specification are reported graphically in Figure 6. We find that reductions in the number of dispensed drugs occur since the second month after the entry of local retailers and it is more pronounced from the third month onwards. The figure also shows non-linearity in the substitution pattern but proves a statistically significant effect also in the six months following the

local product availability. Importantly, Figure 6 also shows that there is little evidence of systematic pre-trends affecting the results and this provides further support for the hypothesis of exogeneity in the cannabis light seller entry in each province.

[Figure 6 around here]

6 Discussion

Many countries worldwide have legalized or decriminalized marijuana for recreational and medical purposes. Others have recently legalized the cultivation of commercialization of hemp, an industrial strain of cannabis rich in CBD and almost free of psychoactive components. While on one hand, this market is gaining momentum and is often described as the new “green oil”, on the other hand, uncertainty is fueling among regulators and authorities about potential misuse. Given the uncertainty on how to govern this phenomenon and exploiting the difficulties in distinguishing light cannabis from illegal marijuana, several states such as Kansas, Louisiana, Texas, and North Carolina opted for a tough stance by banning smokable hemp. Yet, this largely unregulated market kept booming.

This paper provides a self-medication argument for such popularity by exploiting a unique opportunity offered by a loophole in the Italian legislation regarding the commercialization of a new CBD-based product. Indeed, we look at whether the availability of a new product suitable for self-medication impacted on dispensed drugs sales to treat anxiety, psychosis, chronic pain, insomnia, migraine and epilepsy.

Using a staggered DiD model and considering monthly data for 106 Italian provinces during the period between January 2016 and February 2018, we find that the local availability of light cannabis led to a significant and large reduction of dispensed boxes of anxiolytics and sedatives, which amounted to approximately 10%. These drugs usually treat symptoms for which CBD is often effective and for which symptoms can be easily detected by a non-specialist. We also find that the entry of a light cannabis retailer in a given province led a 1-1.5% reduction in the number of anti-epileptic, anti-depressant, opioid and anti-migraine prescriptions, whereas prescriptions for psychotic patients decreased by approximately 4-5%. Much higher coefficients are more likely to emerge when considering a longer time window. Indeed, our coefficient indicates a *lower bound* for the effect of light cannabis on prescription drugs. On the contrary, no substitution effect was found for prescription

drugs not having relaxant effects, such as insulin, anti-hypertensives, as well as sex hormones and urologicals.

Our results are compatible with a self-medication hypothesis, that is, the adoption of risky behaviors to seek quality of life improvements and relief. Indeed, the large-scale accessibility to the new product, which was widely advertised as a relaxant one, induced some patients to abandon traditional medicine to seek relief. Self-medication arises as the product was neither suitable for medical purposes nor was allowed to be consumed. This renders less likely that the substitutional patterns we observed were driven by medical advice. As discussed, light cannabis liberalization was due to a legislative void and, for this reason, unannounced and not capable of creating an anticipatory effect, therefore reducing the likelihood of “off the record” medical advices. Our estimates assume more relevance when considering the relatively short time window we consider, that is 10 months after the policy was implemented, the lack of clinical support, and the unusual way in which light cannabis was made available as well as our focus on a short period after the introduction of the product. Patient response to new drugs and therapies is usually heterogeneous and sluggish because of typical risk aversion. Nonetheless, we find a significant and negative effect on several drugs treating pathologies for which medical cannabis (and not light cannabis) has demonstrated some degree of effectiveness.

The event study also provides additional insights into patients’ response. We observe that substitutional patterns are more accentuated starting from the third month after the entry of the first light cannabis retailer in the local area and significant also after six months post entry. This result may indicate that individuals started substituting therapy after some weeks of experimentation or just after realizing that the new product had become locally available, thereby reinforcing the “rational” characterization of self-medication. In this sense, the paper provides a self-medication explanation, different from “hype-seeking” for the explosive success of cannabis-derived products, even in the absence of the psychoactive compound (THC), in the US and Europe.

Our results are partly similar to those found by Bradford and Bradford (2016; 2017). However, there are some interesting and relevant differences. They showed a larger reduction in drug prescriptions (up to 10-20%) than ours. These differences can be attributed to a number of causes. First, they focus on some population samples restricted to those eligible for either Medicare Part D or Medicaid, whereas our data refers to the overall number of drug sales (and indeed) prescriptions without age limitation and eligibility constraints. Hence, our results may indicate that substitution effects are

lower when estimated on a general population. Second, we focus on a non-medical treatment (i.e. light cannabis) that can be bought without a physician indication. Indeed, we estimate a demand-driven substitution and not a doctor-driven substitution. With these lenses, our results suggest that a substitution driven by self-medication may be lower than the one induced by the physician.

Finally, our estimates present a series of important public policy implications which go beyond Italy's case. First, a clear regulation for the light cannabis market may be required alongside the larger availability of medical marijuana. The substitution we identify may stem from a poorly designed distribution channel of medical marijuana and the need for patients for more effective relief. In this sense, our results suggest that consumers may have found in light cannabis a more effective alternative than traditional medicine. This suggests that policies such as a ban on light cannabis, as suggested by several US states and by Italian policymakers in 2019, might eventually decrease patients' welfare as disregarding their needs for more effective relief.

Second, forms of self-medication should ring the alarm bells of policy makers as individuals may not follow expert advice even when taking care of their health. Whereas any substitution may be rational from a consumer perspective, as resulting from a utility-maximizing behavior, forms of partial or non-medical adherence can be risky in the long terms. In this respect, our results suggest that regulatory authorities should be cautious and vigilant as the large-scale availability of light cannabis may induce substitution patterns not clinically indicated. In this respect, instructing doctors and providing labels and certification alongside with information regarding doses to these products may be a first attempt to make light cannabis, and in general CBD-derived product consumption, much controlled.

Third, from a public policy perspective, we observe that the shift in consumption from traditional drugs to light cannabis came from a non-negligible cost for a patient. This is because, unlike the drugs we consider, which are either fully reimbursed by the NHS or subject to a small co-payment from a patient, light cannabis is often sold at 8-10 euro per gram. This suggests that the unintended policy liberalization had an unexpected effect on pharmaceutical expenditure. Pharmaceutical expenditure worldwide has rapidly increased in recent years and this is equally true in Italy (Federfarma, 2018). However, even if CBD products are generally considered by the World Health Organization (WHO) as not-intoxicating, in the absence of any clinical validation of light cannabis, these short-term financial benefits may be outweighed by long-term public health costs.

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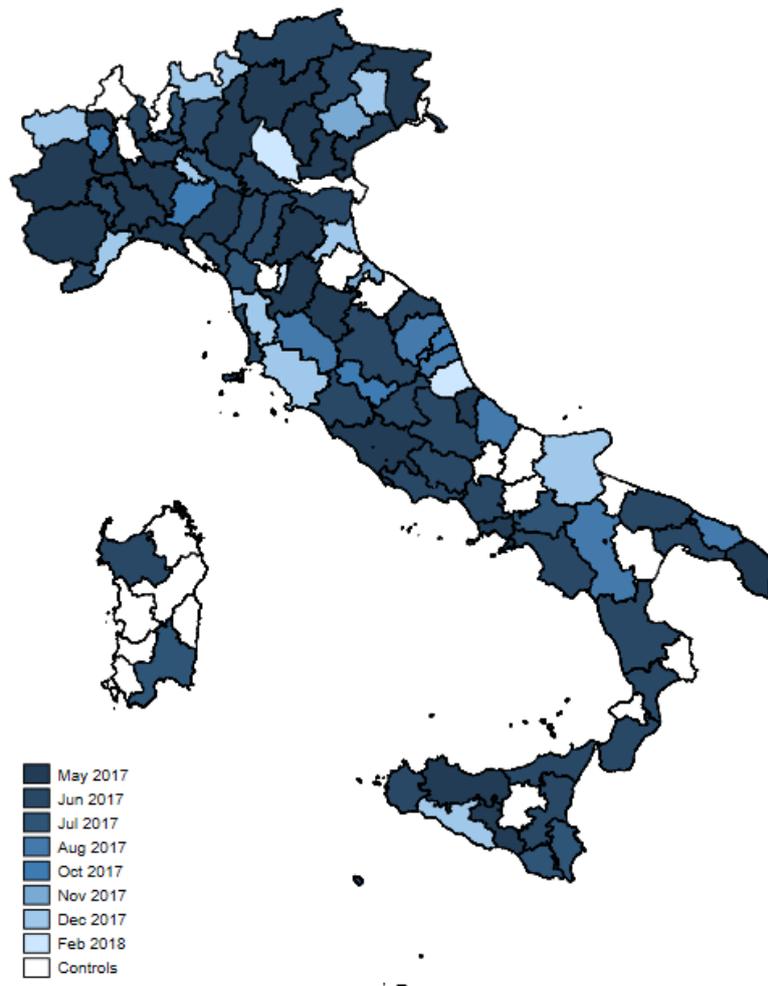
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Figures and Tables

Figure 1. Timing of Local Availability of Light Cannabis



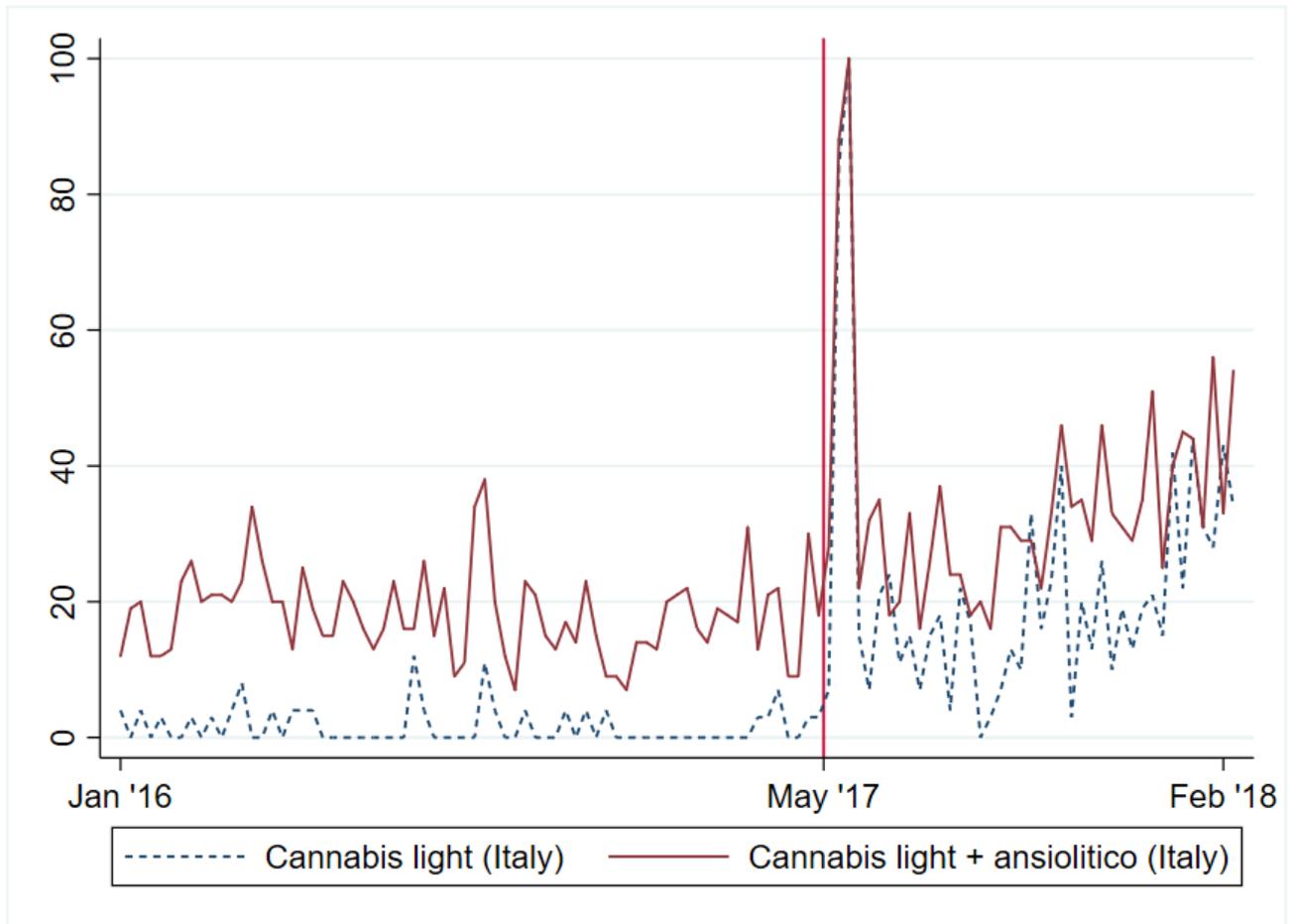
The map reports the different timing of local availability of light cannabis in the 106 provinces we consider starting from May 2017. Data are retrieved from the Internet Wayback Machine Archive.

Figure 2. Timeline



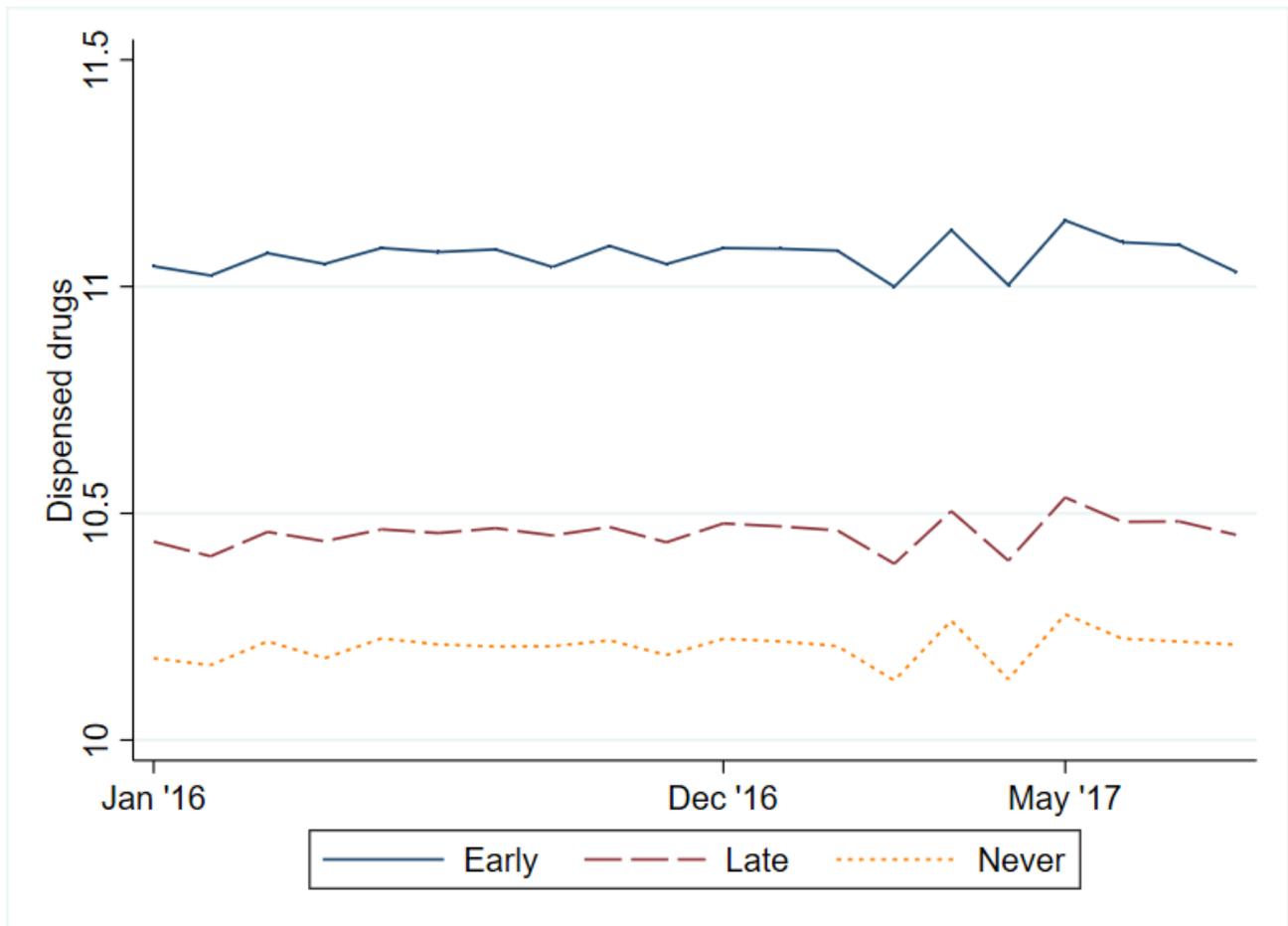
Our study covers monthly data from January 2016 to February 2018. The Law (242/2016) was approved on December 2016. In May 2017, the first entry in the market occurred (see Figure 2). In May 2019, Italy’s High Court decided about the possibility to commercialize the product.

Figure 3. Google Trends Queries on “cannabis light” and “cannabis light + anxiolytics” in Italy



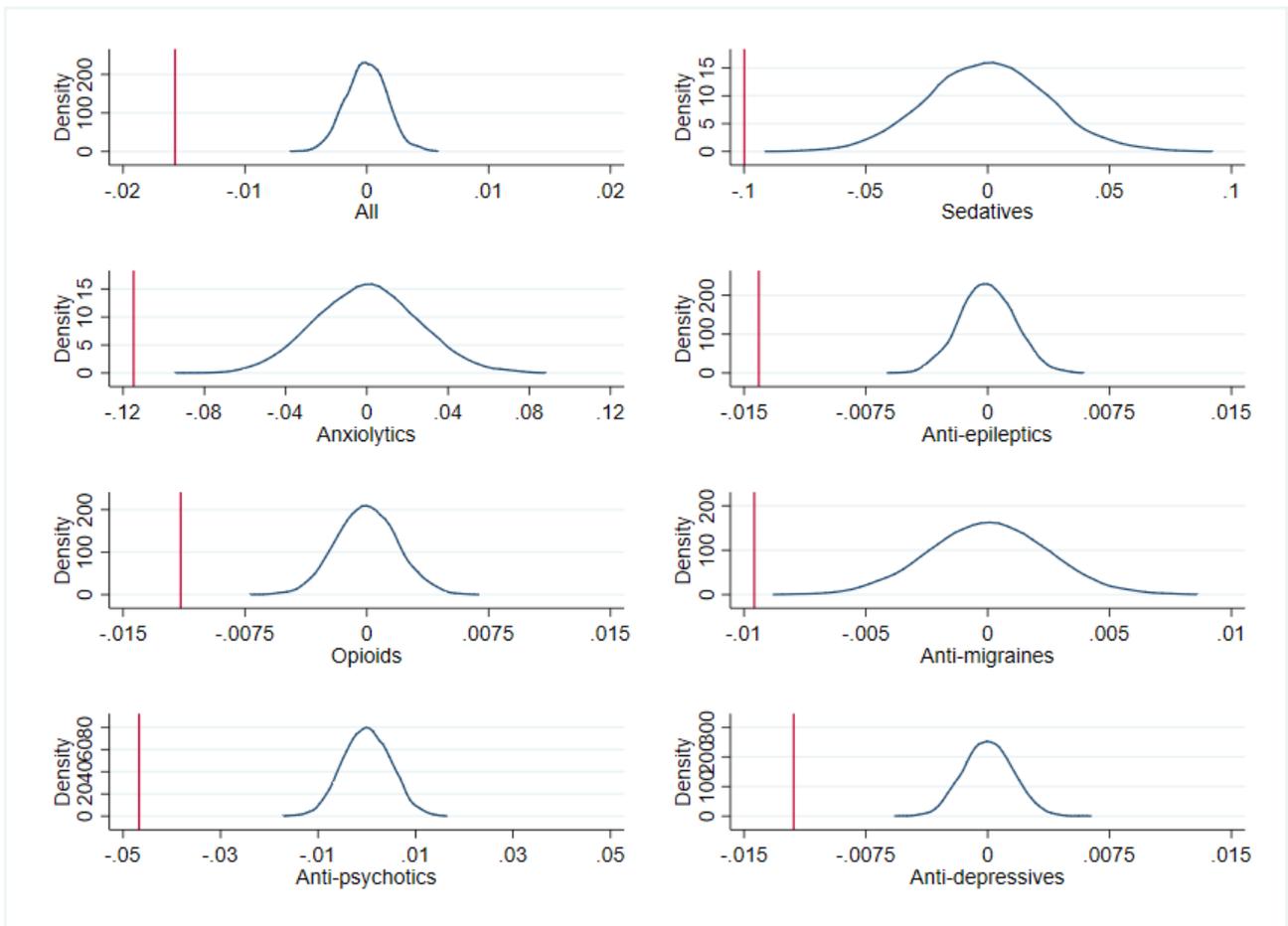
The figure presents the number of Google Search queries on “cannabis light” and “cannabis light + ansiolitico (anxiolytics)” in Italy during the period we considered. In May 2017, when the product was announced, the number of queries had a spike and the number of queries remained at a higher level in the subsequent period.

Figure 4. Common Trend



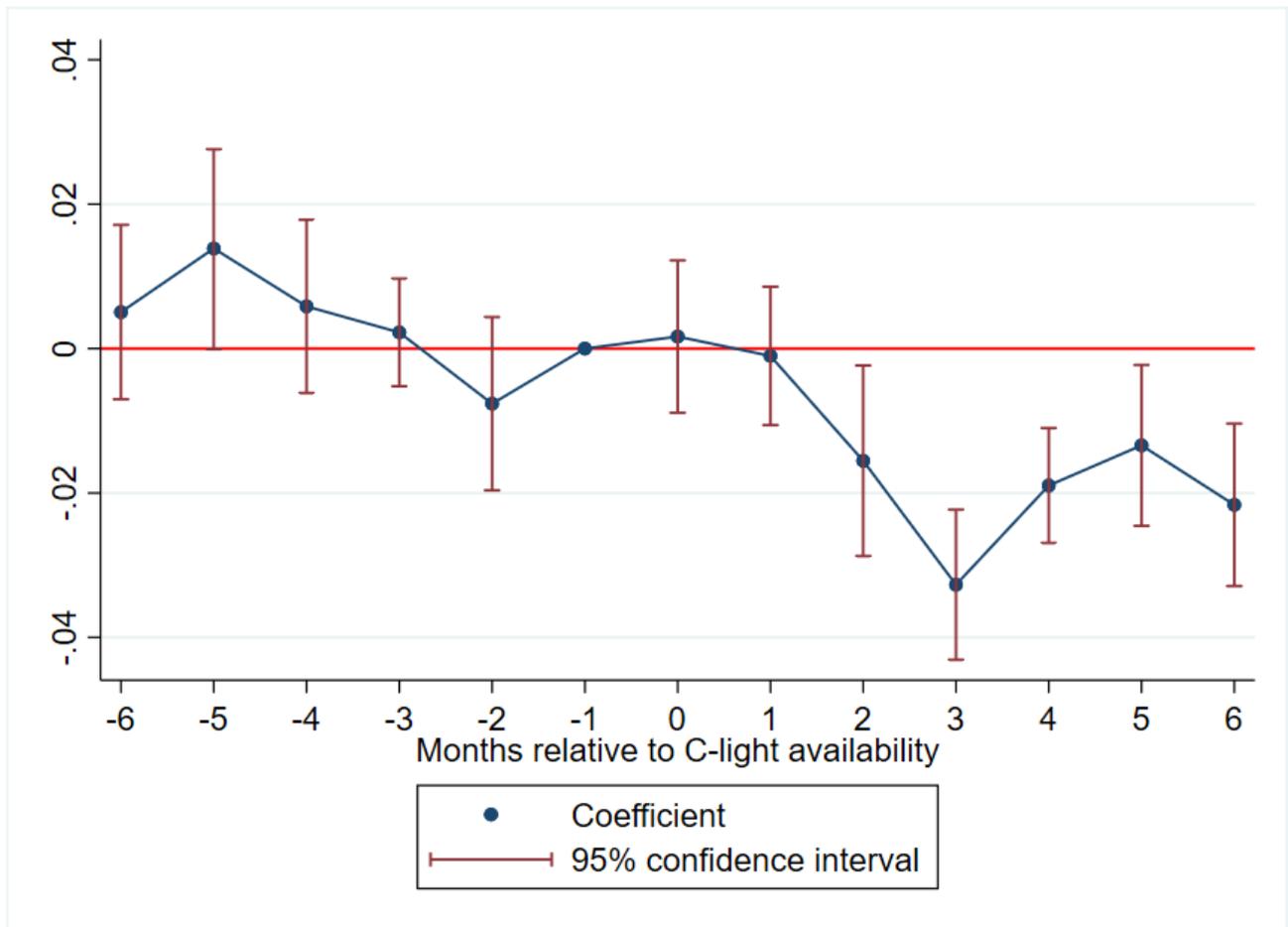
The figure presents the trends in all dispensed drugs in our dataset (opioids, anxiolytics, sedatives, anti-migraines, anti-epileptics, antipsychotics and anti-depressives) for provinces exposed to early, late and no local accessibility to light cannabis. Early entry refers to local availability during the first 5 months after the first entry (between May and September 2017). Late entry refers to local availability during the last 5 months we observe, that is between October 2017 and February 2018.

Figure 5. Randomization Inference



The figures show the distributions of the placebo estimates based on 5,000 permutations for all out outcomes, separately. The vertical red lines represent the estimated coefficients in our baseline specification in Table 2.

Figure 6. Event Study



The figure presents an event study of the effects of local availability (represented by the red vertical line) on all dispensed drugs. One-month pre-entry is the excluded dummy for each dimension and is set equal to zero.

Table 1. Descriptive Statistics

<i>Variable</i>	<i>Description</i>	<i>Mean</i>	<i>Std. Dev.</i>
Sedatives	Monthly number of dispensed sedatives and hypnotic drugs per province (boxes)	28.20	109.73
Anxiolytics	Monthly number of dispensed anxiolytics per province (boxes)	72.52	359.45
Anti-epileptics	Monthly number of dispensed anti-epileptics per province (boxes)	18,459.67	21,474.39
Opioids	Monthly number of dispensed opioids per province (boxes)	12,610.91	13,065.20
Anti-migraines	Monthly number of dispensed anti-migraines per province (boxes)	2,504.26	2,626.09
Antipsychotics	Monthly number of dispensed anti- psychotics per province (boxes)	4,802.44	5,903.55
Anti-depressives	Monthly number of dispensed anti-depressives per province (boxes)	27,198.25	26,290.68
Nr. Observations	106 provinces X 26 months	2,756	

Note: data are made available by Federfarma for all “Classe A”, category “N – Nervous System” drugs dispensed by the Italian NHS.

Table 2. Difference-in-Differences regression

	(1) All	(2) Sedatives	(3) Anxiolytics	(4) Anti- epileptics	(5) Opioids	(6) Anti- migraines	(7) Antipsychotics	(8) Anti- depressives
DiD	-0.016*** <i>0.004</i>	-0.095* <i>0.053</i>	-0.114** <i>0.055</i>	-0.015*** <i>0.004</i>	-0.012** <i>0.005</i>	-0.009* <i>0.005</i>	-0.048** <i>0.018</i>	-0.012*** <i>0.003</i>
Controls	yes	yes	yes	yes	yes	yes	yes	yes
Year FE	yes	yes	yes	yes	yes	yes	yes	yes
Month FE	yes	yes	yes	yes	yes	yes	yes	yes
Province FE	yes	yes	yes	yes	yes	yes	yes	yes
<i>N</i>	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756

Log transformation of the dependent variable. S.E. clustered at the province-level in italics. ***, **, * indicate statistical significance at 1%, 5%, and 10% respectively.

Table 3. Robustness checks: parameter estimates

	(1) All	(2) Sedatives	(3) Anxiolytics	(4) Anti- epileptics	(5) Opioids	(6) Anti- migraines	(7) Antipsychotics	(8) Anti- depressives
Shorter time window	-0.016*** <i>0.003</i>	-0.115** <i>0.054</i>	-0.123** <i>0.058</i>	-0.015*** <i>0.004</i>	-0.011** <i>0.004</i>	-0.010** <i>0.005</i>	-0.043** <i>0.018</i>	-0.012*** <i>0.003</i>
Linear trend	-0.016*** <i>0.004</i>	-0.100* <i>0.052</i>	-0.115** <i>0.055</i>	-0.014*** <i>0.004</i>	-0.011** <i>0.005</i>	-0.010* <i>0.005</i>	-0.047** <i>0.018</i>	-0.012*** <i>0.003</i>
Province-trend	-0.017*** <i>0.003</i>	-0.186** <i>0.076</i>	-0.157* <i>0.093</i>	-0.018*** <i>0.003</i>	-0.019*** <i>0.004</i>	-0.012** <i>0.005</i>	-0.020 <i>0.013</i>	-0.011*** <i>0.003</i>

Log transformation of the dependent variable. S.E. clustered at the province-level in italics. ***, **, * indicate statistical significance at 1%, 5% and 10%, respectively. The first row reports the estimates of the DID coefficient considering a shorter time window (May 2016 – February 2018). The second row reports the estimates of the DID coefficient in presence of a linear trend. The third row reports the estimates of the DID coefficient in presence of a province-specific trend.

Table 4. Robustness checks: placebo regressions

	(1) Insulin	(2) Anti-hypertensives	(3) Sex Hormones and Urologicals
DiD	0.015 <i>0.034</i>	-0.002 <i>0.005</i>	0.006 <i>0.006</i>
Controls	yes	yes	yes
Year FE	yes	yes	yes
Month FE	yes	yes	yes
Province FE	yes	yes	yes
<i>N</i>	2756	2756	2756

The drugs considered refer to the following ATC/DDD classification of the WHO Collaborating Centre for Drug Statistics Methodology: A10A (Insulin), C02 (Anti-hypertensive), G03 and G04 (Sex hormones, modulators of the genital system and Urologicals) Log transformation of the dependent variable. S.E. clustered at the province-level in italics.