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François-Olivier Baudot

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François-Olivier Baudot

**BENZODIAZEPINE USE: A TWO-WAY
RELATIONSHIP WITH WORK ACCIDENTS AND
IMPACT OF COVID-19 PANDEMIC**

Sous la direction de

Thomas Barnay, Professeur à l'Université Paris-Est Créteil

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The chapters in this thesis are scientific papers in progress that can be read independently of each other. As a result, some redundancies in concepts, context, and literature may appear from one chapter to another.

The numbering of the sub-sections and the appendices are specific to each chapter.

Résumé

Les benzodiazépines sont des médicaments psychotropes qui font l'objet d'une forte attention des pouvoirs publics en raison de leur consommation élevée en France et du risque d'effets indésirables, notamment de dépendance. Cette thèse s'intéresse à la fois aux déterminants et aux conséquences de cette consommation. Les deux premiers chapitres ont pour objectif d'étudier les liens de causalité entre consommation de benzodiazépines et accidents du travail. Le troisième chapitre a pour objectif de comprendre les mécanismes qui ont été à l'œuvre au cours de la pandémie de Covid-19 et qui expliquent la hausse de consommation qui a été observée. Les données utilisées proviennent du Système national des données de santé (SNDS), qui contient les données de remboursement de l'Assurance maladie en France.

Le premier chapitre utilise un modèle de sélection en deux étapes, qui permet d'estimer les modifications de consommation et de surconsommation de benzodiazépines suite à la survenue d'un accident du travail. La population d'étude comprend plus de 350 000 personnes ayant été victimes d'accidents du travail et plus de 1,1 million de personnes n'en ayant pas subis. La survenue d'un accident du travail entraîne une augmentation de la probabilité de consommer et de surconsommer des benzodiazépines l'année qui suit. Le modèle de sélection montre un net effet sur la probabilité de consommer (+39 %), mais faible sur la probabilité de surconsommer (+1.7 %). Ces résultats appellent à cibler la primo-prescription de benzodiazépines pour limiter le risque de surconsommation après un accident du travail.

Le deuxième chapitre utilise les données du SNDS en panel et un modèle à effets fixes pour estimer le risque d'accident du travail en fonction de la consommation de benzodiazépines dans les mois qui précèdent. La population d'étude est composée de personnes ayant subi un accident du travail de 2017 à 2019 (environ 2,5 millions de personnes). Une consommation récente est associée à une baisse du risque d'accident, en revanche le dépassement des durées de traitement recommandées et l'intensité du traitement sont associés à une augmentation du risque (une augmentation de 1 % de la consommation entraîne une augmentation de 4,4 % du risque d'accident du travail). Par ailleurs, l'arrêt du traitement est également associé à une augmentation du risque. Ces résultats appellent au respect des recommandations et à une vigilance particulière à l'arrêt du traitement.

Le troisième chapitre utilise les données de ventes de benzodiazépines en France agrégées à la commune et complétées par des données administratives de l'Insee. La forte augmentation de la consommation de benzodiazépines observée en 2020 et 2021 pourrait avoir des conséquences néfastes en termes de santé publique. Des modèles linéaires sont utilisées pour comparer les

déterminants de cette évolution au niveau communal, de 2018 à 2021. Les résultats montrent que la sévérité de la pandémie dans le département de résidence a joué un rôle modeste dans l'évolution constatée. En revanche, l'augmentation est associée à des facteurs socioéconomiques (vulnérabilité sur le marché du travail et isolement social), et pas aux facteurs de risque de Covid-19 grave. Ces résultats invitent à mieux prendre en compte les risques pour la santé mentale lié aux mesures de contrôle de la pandémie.

Mots-clés : benzodiazépines ; psychotropes ; médicaments ; accidents du travail ; Covid-19 ; SNDS ; données administratives ; France.

Abstract

Benzodiazepines are psychotropic drugs widely used in France. Public authorities are monitoring their use because of the high consumption in France and the potential adverse effects, especially dependence. This dissertation focuses on both the determinants and consequences of this consumption. The first two chapters aim to study the two-way relationship between benzodiazepine use and accidents at work. The third chapter aims to understand the mechanisms of the steep rise in benzodiazepine sales that occurred during the COVID-19 pandemic. This dissertation relies on the National Health Data System (SNDS), which is the reimbursement database of French National Health Insurance.

The first chapter uses a two-step selection method that allows for estimating the changes in benzodiazepine use and overuse after a work accident. The study population is composed of more than 350,000 people who had a work accident and more than 1.1 million people who had not. The occurrence of a work accident leads to an increase in benzodiazepine use and overuse the following year. The selection model shows a clear influence of the accident on the use probability (+39%), but a very slight impact on the risk of overuse (+1.7%). Results call for targeting the first-time benzodiazepine prescription to limit the risk of overuse after a work accident.

The second chapter relies on panel data from SNDS and a fixed effects model to estimate the risk of work accidents according to benzodiazepine consumption in the preceding months. The study population is composed of people who had at least one work accident from 2017 to 2019 (approximately 2.5 million people). The results show a decrease in work accident risk after a short use of benzodiazepines (one month). However, the risk increases with the intensity of use (a 1% increase in use leads to a 4.4% increase in the risk of work accidents) and when the treatment time exceeds guidelines. These results call for adherence to guidelines and special caution when discontinuing treatment.

The third chapter relies on the benzodiazepine sales data in France aggregated to the municipality and completed by administrative data from the National Institute of Statistics (INSEE). Increased benzodiazepine use in 2020 and 2021 may harm public health. I use linear models to compare the determinants of these changes at the municipality level from 2018 to 2021. The results show a small effect of the severity of the pandemic in the area of residence. The increase is associated with socioeconomic factors (employment vulnerability and social isolation) and not with the risk factors of severe Covid-19. These findings suggest that the mental health risks associated with pandemic control measures should be better considered.

Keywords: benzodiazepines; psychotropic drugs; drugs; work accidents; accidents at work; occupational accidents; Covid-19; SNDS; administrative data; France.

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General introduction

1. Context and motivations

Benzodiazepines (BZDs) are psychotropic drugs widely used in northern countries for their anxiolytic, hypnotic, antiepileptic, and muscle relaxant properties. They are sometimes used in other indications, such as before anesthesia, to obtain a rapid tranquilization for patients with agitation or severe psychotic symptoms, or to manage withdrawal from alcohol. Although a slight but weak efficacy of BZDs is shown to reduce anxiety and sleeping troubles, their therapeutic effect quickly declines after the first weeks of treatment (van Hecke, 2010; Vorspan et al., 2018).

One of the main risks of BZDs is the induction of dependence. To avoid it, doctors should prescribe them at the lowest effective dose and give them intermittently (Baldwin et al., 2013). The dependence is characterized by a withdrawal syndrome, which typically comprises severe sleep disturbance, anxiety, irritability, muscular pain and stiffness, panic attack, sweating, etc., and usually lasts 10-14 days. To avoid these symptoms after long-term use, treatments should be stopped gradually. Withdrawal syndrome is sometimes hard to distinguish from rebound insomnia or anxiety and the reappearance of the symptoms of the treated disease (Baldwin et al., 2013; Pétursson, 1994). Other adverse effects of BZDs are mainly cognitive effects (sedation and drowsiness, mental slowing and anterograde amnesia) and psychomotor effects (increased risk of falls and accidents while driving) (Baldwin et al., 2013; Brandt & Leong, 2017). To limit the risk of adverse effects, the French High Authority for Health (HAS) defined guidelines that include starting the treatment with the smallest useful dose, limiting the duration of treatment (twelve weeks for anxiolytic BZDs and four weeks for hypnotic BZDs), do not prescribe multiple BZDs at the same time, and be very careful when prescribing in the elderly (who are more sensitive to BZDs effects).

BZD consumption is a concern regarding high levels of consumption, especially in France (ANSM, 2017). It is extremely difficult to estimate the share of dependence among patients following these treatments because dependence is hard to define and withdrawal syndrome can go unnoticed (because symptoms are mild, or they are seen as a reappearance of previous symptoms). In this dissertation, dependence cannot be estimated due to the nature of the data. I will use the term *overuse*, which refers to exceeding the recommended treatment duration.

Non-compliance with guidelines can be a source of treatment inefficiency. Due to the high level of non-compliance in France, it is essential to understand the nature of determinants of BZD use and overuse, and the adverse consequences for public health and the economy that consumption may imply. The use of BZDs is closely related to mental health problems, some of which stem from the labor market and worsen during the COVID-19 pandemic. In return, BZD use may affect work health through work accidents (WAs). This dissertation focuses on the interrelationship between BZD use and WAs, and aims to shed light on the mechanisms at work during the pandemic that affected BZD consumption.

In the introduction, I provide general information about the drug market in France in section 2: how the drug circuit works, prescription practices, the insurance which solves the demand, and drug expenses, with a particular focus on mental health and psychotropic drugs. In section 3, I provide more specific information about BZDs: what they are, the difference between use and abuse, some consumption figures, and factors associated with greater use. In section 4, I discuss interactions between health and work, issues for occupational health and the specific case of WAs, and how insurance cover this risk. In section 4.3, I analyze how the onset of COVID-19 affected work and health, and thus mental health and BZD consumption. Last, in section 6, I provide the theoretical framework, empirical basis, and research outline of this dissertation.

2. Drug consumption

2.1. Drug circuit in France

City pharmacies assured the drug selling (and hospital pharmacies in rare cases). They obtain their supplies from wholesale distributors (80% of cases) or directly from the producer (mainly for generics and over-the-counter drugs) (Pilorge, 2016).

Reimbursed medicines (such as BZDs) are subject to prescription. Prescriptions are mostly made by physicians but also by midwives, dental surgeons, or directors (or assistant directors) of analysis laboratories within the limits of their profession. The demand for them is inelastic because the buying decision is made by the prescriber, while the payment is made by the patient or the insurer (which solves the demand). The prescription and the selling are separated (between prescribers, mainly doctors, and pharmacists) to avoid them being influenced by a profit motive. The price elasticity varies according to the portion of the drug that is reimbursed, that is, the ex-post moral hazard: the drug demand is related to insurance coverage (Pilorge, 2016).

In France, compulsory health insurance reimburses drugs at four different rates, 100%, 65%, 30%, and 15%, according to the medical benefit, and applies a deductible of €0.5 per box. The

unreimbursed share (minus the deductible) can be reimbursed by complementary health insurance (which insures 95% of the population). A specific system called ALD (*Affections de longue durée*) is designed for patients with chronic disease and allows full coverage by compulsory health insurance for care related to the disease.

The market is more regular for non-reimbursed medicines. The demand is elastic to price. Patients and pharmacists are the only agents involved and interact in a commercial relationship.

2.2. Prescription practices

In the case of a reimbursed drug, the buying decision relies on the prescriber. There is variability in medical practices, which can rely on patients' features, prescribers' features, and the characteristics of the health care system. The patient's health condition is of course a major determinant of a prescription, but other nonmedical characteristics are involved, such as social characteristics (Bradley, 1992; Fleishman & Cohen, 2010; Mousquès et al., 2003). Prescribers' characteristics are also related to prescription practices: younger doctors prescribe less frequently (Lancry & Paris, 1997), and information is fundamental. Doctors prescribe more antibiotics as they receive more medical visitors and less as they do more continuing medical education (Mousquès et al., 2003). Other motivations influencing misprescribing have been mentioned: demand pressure for prescriptions from patients (Schwartz et al., 1989) and the desire to preserve the doctor-patient relationship (Bradley, 1992). A very high demand pressure in the specific case of psychotropic drug prescriptions among elderly individuals has been shown (Collin et al., 1999), where a psychotropic prescription is a means to alleviate pain and suffering related to aging, and nonprescription would be ineffective because of competition with other doctors.

Characteristics of the health care system play on prescription behavior. Competition between doctors seems to be central. Indeed, in France, doctors are free to settle wherever they want, which leads to unequal distribution on the territory (Delattre & Samson, 2012). Delattre and Dormont (2003) have shown a physician-induced demand. French physicians are paid on a fee-for-service basis. When the number of physicians increases for a given population, they face a decrease in consultation numbers and counterbalance it by increasing the volume of care delivered during a consultation. In lower-density areas, the number of patients per doctor is higher and may lead to shorter consultations and more frequent prescriptions (Mousquès et al., 2003; Ventelou et al., 2010). Other studies have shown a positive effect of competition on prescription volumes (Kann et al., 2010; Schaumans, 2015) and of activity level on prescription volumes (Lancry & Paris, 1997).

In addition, public policies have been implemented to influence prescribers' practices. Payment-for-performance (P4P) consists of relating the doctor's remuneration to the achievement of objectives, such as complying with prescribing good practices. In particular, doctors are encouraged to reduce their BZD prescriptions (Michel-Lepage & Ventelou, 2016).

2.3. Insurance mechanism

Health insurance solves the healthcare demand, by covering the financial risk related to health problems. This includes expenses related to care provided and compensation for wage loss during work interruption. The French insurance system is founded on a Bismarck model: mandatory insurance for all salaried workers (later extended to the entire population), independent of the state, managed by social partners, and financed by employer and employee contributions. Employers' role is essential in the health insurance system: through contributions to public insurance and by offering private insurance contracts (negotiated with private insurance companies) (Barnay & Jusot, 2018).

The French national public health insurance (*l'Assurance Maladie*) covers a selected basket of care. Private insurers can extend the basket of care covered and improve the reimbursement of care covered by public insurance. Affiliation with public insurance is mandatory for all people living in France. Since 2016, employers have been required to provide complementary health insurance to employees (who cannot refuse, with some exceptions), and employees stay insured for one year in case of job loss. However, the affiliation with complementary health insurance for nonsalaried individuals remains voluntary. In 2017, 96% of the French population was covered by complementary health insurance (Fouquet, 2020).

Public health insurance plays a major role in the reduction of social inequalities in France. For the poorest 20% of people, its benefits represent approximately 40% of disposable income. To a lesser extent, progressive contributions also contribute to reducing health inequalities (Fouquet & Pollak, 2022).

2.4. Drug expenses in France

National public health insurance provides the majority of health care expenses. In 2019, the consumption of medical care and goods (CSBM: *Consommation de soins et de biens médicaux*) in France was €208 billion (8.6% of GDP): 47% for inpatient expenses and 53% for outpatient expenses (DREES, 2020). This expense was financed by compulsory health insurance at 78%, by complementary health insurance at 13%, and by patients at 7% (OOP: out-of-pocket). Among ambulatory care, the drug consumption was €32.6 billion, 92.5% of which was reimbursable.

Expenditure on reimbursable drugs has been fairly stable over the years, combining a trend decrease in price and an increase in volume. The specific financing for drugs is 74% by compulsory health insurance, 12% by complementary health insurance, and 12% by patients (and the share left by the State).

The total health expenditure (which has an internationally harmonized definition and is broader than the CSBM) is 11.3% of GDP (€3,970 per inhabitant in purchasing power parity). That is the second-largest share of health expenses in the EU-28, behind Germany.

In France, mental diseases were the first item of expenditure in 2019: €22.7 billion (14% of total health expenditure), compared to €20.1 billion for cancers and €17.7 billion for cardiovascular diseases (CNAM, 2021). A closer look at mental health expenses shows a twofold breakdown: psychiatric illnesses, which affect relatively few people but with a high expense (€6,413 on average per patient, due to high frequency of hospitalization), and chronic psychotropic treatment (without identified disease), which includes many people but is less expensive (€1,187 on average per patient).

In 2019, among 66.3 million people (97% of the French population), 2.5 million were affected by psychiatric diseases, and 5.6 million used psychotropic reimbursed drugs without identified disease. Between 2015 and 2019, the total expense related to chronic psychotropic treatments increased by 4.1% (a 6.6% decrease in the number of people treated and an 11.4% increase in mean expense). The increase between 2018 and 2019 was more dynamic than in previous years. The decrease in the number of treated people mainly came from a decrease in the number of people treated by anxiolytics and hypnotics. The average increase in expenses showed that the decrease in the number of treated people was related to patients being potentially less burdensome, which shows a slight success of the actions of control of these treatments.

Among psychotropic drugs, BZDs accounted for 84% and 81% of anxiolytics and hypnotics sales in 2015, respectively (ANSM, 2017). They represented 111.6 million boxes sold in 2015 (117 million including hospitals), i.e., 4% of the total drug consumption this year. In value, it was €118 million for city pharmacies, i.e., 0.6% of total sales. The difference between quantities and values comes from the low price of BZDs.

3. Benzodiazepines

3.1. What are they?

BZDs were developed in the 1950s. The first introduced on the market was chlordiazepoxide, at the very beginning of the 1960s, quickly followed by many others, starting with diazepam. The use of BZDs increased quickly in the 1960s and 1970s, mainly in the replacement of other psychotropic drugs, in particular barbiturates. Barbiturates are known to lead to dependence and to be dangerous in overdose, so they were replaced by BZDs, deemed safer (M. Lader, 1991).

BZDs act on the GABA (gamma-aminobutyric acid) system. The GABA is an inhibitory neurotransmitter that is widely distributed in the nervous system. BZDs bind a specific site of the GABA_A receptor (distinct from the GABA binding site), which increases the affinity of the receptor for the GABA. This results in neuronal hyperpolarization and reduced excitability of the target cell (Baldwin et al., 2013).

BZDs can be divided into different groups according to their chemical structure and pharmacokinetic properties, but they all share the same mechanism of action and similar effects. Long-acting BZDs are used as anxiolytics, and short-acting BZDs are used as hypnotics. Other drugs are frequently assimilated to BZDs: they are Z-drugs (zaleplon (not sold in France), zolpidem, and zopiclone). They are not BZDs, as their chemical structure differs, but they bind on the same site as BZDs, on the GABA_A receptor, and share some of their properties (Baldwin et al., 2013). They are used only as hypnotics. In this dissertation, they are included with the BZDs unless otherwise noted.

In France, twenty medicines belonging to the BZDs are marketed: eleven anxiolytics, seven hypnotics (including two Z-drugs), and two anticonvulsants. BZDs are cheap drugs: the best-selling drug is alprazolam (€1.23 for 0.25 mg, reimbursable at 65% by compulsory health insurance, the share left by complementary health insurance). The best-selling drug for hypnotics is zolpidem (€1.64, reimbursable at 15%).

3.2. Use and abuse of benzodiazepines

The efficacy of BZDs to treat anxiety disorders is debated. In a meta-analysis including 23 trials, BZDs showed a better efficacy to reduce the risk of treatment discontinuation due to lack of efficacy for BZDs (compared to placebo), but not to reduce the risk of all-cause discontinuation. Authors mention publication bias as an explanation, as the more recent the study, the smaller the positive effect of the drug (M. Lader, 2008; Martin et al., 2007). In a meta-analysis of 58 trials,

BZDs were more effective than placebo in studies with higher baseline anxiety and in studies with shorter treatment duration (Gale et al., 2019).

The British National Institute for Health and Care Excellence (NICE) and the HAS recommend psychotherapy and cognitive behavioral therapy for anxiety treatment in the first instance, and drug treatment (including BZDs) only in the second.

The adverse effects of BZDs, in particular dependence, and their wide availability have led to fears of overuse for a long time (WHO Review Group, 1983). Misuse can be defined as the non-respect of recommendations and the use of BZDs without prescription. Overuse refers to exceeding the recommendations, such as high doses, long-term treatment, or use of multiple BZDs.

The risk of fatal overdose with BZDs is relatively low (Buckley et al., 1995), especially when compared to barbiturates (Buckley & McManus, 2004). However, it significantly increases when BZDs are used with other sedatives (Charlson et al., 2009). Misuse is associated with many poor outcomes, including mortality and poor self-reported quality of life (Votaw et al., 2019).

BZDs are implied in the current opioid crisis in the US and contribute to increased overall mortality (Compton et al., 2021). In the US, from 2019 to 2020, BZD overdoses emergency visits greatly increased, both with and without opioid involvement (Liu et al., 2021). From 2002 to 2014, the annual proportion of people with prescribed BZDs and opioids concomitantly increased from 6.8% to 9.6% (Hwang et al., 2016). The situation regarding opioids is very different in Europe (although heterogeneous), where the prescribed opioid rates and fatal overdose rates are far lower than in the US (while increasing) (Pierce et al., 2021).

In September 2020, the US Food and Drug Administration (FDA) announced an update on the boxed warning on all BZDs to “address the serious risks of abuse, addiction, physical dependence, and withdrawal reactions” (Center for Drug Evaluation and Research, 2020; Hirschtritt et al., 2021).

3.3. Consumption figures

There are few studies about the BZD use in the general population and data are scarce to compare evolutions between different countries (Tournier et al., 2018). The general trend in northern countries seems to be decreasing in recent years, although still high. From prescription billing data in the region of Lleida, Spain, Torres-Bondia et al. (2020) found a decrease in the annual prevalence of BZDs dispensing from 15.3% in 2002 to 14.2% in 2015 (18.8% in women and 9.6% in men). In Finland, from a prescription register relative to the Finns aged 18-25 years, Tähkäpää et al. (2018) found a decreasing trend in the population with prescribed BZDs from 2.4% in 2006 to 1.9% in 2014. In Ireland, an analysis of a national pharmacy claims database between 2005 and 2015 showed

a decrease in the share of the population (aged 16 and over) treated by BZDs, with opposite trends for BZDs without Z-drugs (from 22.6% in 2005 to 16.6% in 2015) and Z-drugs (from 9.5% in 2005 to 10.9% in 2015), with an increase of the share of people receiving a BZD and a Z-drug at the same time, but a decrease of quantity of defined daily doses (DDDs) (Cadogan et al., 2018).

In Israel, for the period 2005 to 2013, from data of pharmaceutical companies about the quantity of active substances dispensed each year, Berman et al. (2017) showed an increase in BZD use. In Canada, for 18 years and over people living in the province of Manitoba, the share of people with a prescription for BZDs (including Z-drugs) increased slightly between 2001 and 2016 (from 9.2% to 11.7%) (Brandt et al., 2019). In the US, the prescription for BZDs among Medicaid beneficiaries raise from 8 million in 1991 to 17 million in 2009 (Gorevski et al., 2012), and the use is still increasing between 1999 and 2014 in a cohort of 82,000 individuals (Kaufmann et al., 2018). In more recent years, Milani et al. (2021) showed from a US commercial health insurance database a decrease from January 2018 to March 2021, with a slight increase in April 2020 among women. The trend of Z-drugs is shown apart and increases from January 2020 (for women) and February 2020 (for men) to October 2020. These increases in 2020 are related to the COVID-19 pandemic. In a cross-sectional survey in the US conducted in 2015-2016, 12.6% of adults reported past-year BZD use, 10.4% as prescribed, and 2.2% misuse (i.e. without a doctor's prescription) (Maust et al., 2019).

Some studies are related to specific subpopulations, especially the elderly, for whom BZDs are not recommended. In a cohort of nursing home residents (aged 65 and over) in 7 European countries and Israel, the prevalence of BZDs differed widely, from 14.5% in Germany to 44.1% in Israel (Lukačičinová et al., 2021).

The French agency for the safety of drugs and health products (ANSM) monitors BZD consumption in France. According to its latest report (ANSM, 2017) and despite a decreasing trend since the beginning of the 2000s, BZD consumption in France is still high compared to that in other European countries. It is also higher than the consumption reported by Maust et al. in the US. However, consumption has decreased more rapidly in France than in Europe on average (-10% and -5.1% between 2012 and 2015, respectively). In 2015, French pharmacies delivered 64.6 million boxes of anxiolytic BZDs and 46.1 million boxes of hypnotic BZDs.

In 2015, 13.4% of French people consumed a BZD at least once: mainly anxiolytic (10.3%) and hypnotic (5.6%). The share of users decreased by 5.7% between 2012 and 2015, faster for hypnotic BZDs (-12.8%) than for anxiolytic BZDs (-3.8%). Concomitant use of hypnotic BZDs and anxiolytic BZDs is also decreasing. The share of French people starting a new BZD treatment in

2015 was 5.4%. Women are more frequent users (65%), and the prevalence of treatment increases with age. This prevalence is maximal among women aged 80 and over (38.3%). The first prescription of BZDs is mainly done by GPs (82%), doctors employed in healthcare facilities (specialty unknown, 12%), liberal psychiatrists (2%), and other liberal specialists (4%) (ANSM, 2017).

The most commonly used BZDs in 2015 were alprazolam (3.8%), zolpidem (3.1%), and bromazepam (2.7%). We observed a diminution of zolpidem and zopiclone use, in line with the observed decrease in hypnotic BZD consumption, and the substitution of long-acting BZDs for short-acting BZDs. In 2014, 76.2% of new treatment episodes consisted of a single delivery. In 13.5% of cases, the duration of treatment was noncompliant with the maximal recommended durations (four weeks for hypnotic BZDs and twelve weeks for anxiolytic BZDs); in 6% of new treatments, the duration exceeded 12 weeks; and in 1.7%, it exceeded 12 months (ANSM 2017).

The observed decrease in BZD consumption in France is the result of a series of measures taken to improve their use (ANSM, 2017). These measures include improvement of information for health workers and patients (such as distribution of information letters and pictograms to discourage driving), incentive measures for prescribers (prescription indicators used for P4P (payment for performance)), and control of prescriptions (some medicines need to be prescribed by a specialist doctor, or in a special kind of prescription).

3.4. Factors associated with benzodiazepines use

The main factors associated with BZD use are old age, being female (ANSM, 2017), health status (especially psychiatric diseases, such as anxiety, depression, and neurotic disorders) (Demyttenaere et al., 2008; Lagnaoui et al., 2004; Sidorchuk et al., 2018; Takano et al., 2019), concomitant use of psychotropic drugs (Johnell & Fastbom, 2009; Sidorchuk et al., 2018) and other chronic diseases, such as cancer (Takano et al., 2019). Other characteristics associated with higher use include being jobless (Lagnaoui et al., 2004), being less educated (Demyttenaere et al., 2008), and living in an urban area (Johnell & Fastbom, 2009).

There are no studies that specifically address the impact of work on BZD use, but many studies stressed the impact of work characteristics on psychotropic drug use, in the case of psychosocial work factors (Lassalle et al., 2015; Lavigne & Bourbonnais, 2010) and low job satisfaction (Baumann et al., 2001). Other job-related factors play a role on psychotropic drug use such as organizational downsizing (Blomqvist et al., 2018; Kivimäki et al., 2007) and mass layoffs (effect on remaining employees) (Le Clainche & Lengagne, 2019).

Factors associated with exceeding recommended treatment times are advanced age, comorbidities (in particular history of depression and sleep disorders), other drugs used (in particular antidepressants and psychotropic drugs), and socio-professional characteristics (low educational level, low household income, and not having a job) (Baumann et al., 2001; Fride Tvetet et al., 2015; Tanguay Bernard et al., 2018).

While literature suggests a relationship between work environment and BZD consumption, most studies do not address reverse causality. Indeed, there is a vast literature on health and work interactions, which shows a deep entanglement.

4. Occupational risks and occupational health

4.1. Work and health

4.1.1. Work effects on health

Work and health are linked by a two-way relationship: work affects health status, and health status affects work (Barnay, 2016). Two aspects of work can be distinguished: intensive margin (working hours, job quality) and extensive margin (employment status). Being employed is related to better health. Employment increases income and thus improves socioeconomic conditions. Poor socioeconomic conditions lead to deteriorated health through risky behaviors (Peretti-Watel et al., 2009), while work can increase the use of complementary health insurance (directly via company-provided insurance or indirectly via an increase in income). Moreover, favorable socioeconomic conditions result in better access to health care and higher investment in health (e.g., sport, diet, and housing) (Barnay, 2016).

Consequently, the loss of work can be detrimental. Browning and Heinesen (2012) have shown from panel data in Denmark that job loss due to plant closing increased overall mortality and deteriorated health (by increasing circulatory diseases and road traffic accidents) and mental health in particular (by increasing suicides, alcohol-related diseases, and mental illnesses). Other studies found fewer effects on health from job loss: a transitory effect on psychological distress (Østhus, 2012) and an increase in health expenditure for antidepressants and related drugs, and hospitalizations due to mental health problems among men (Kuhn et al., 2009). Retirement seems to have a positive effect on physical health (Barnay, 2016; Bound & Waidmann, 2007; Coe & Zamorro, 2011), especially on workers who are more exposed to detrimental working conditions (Barnay & Defebvre, 2021), but it harms mental health (Mazzonna & Peracchi, 2012).

Regarding intensive margin, working conditions can have harmful effects on health. There is strong evidence that job strain (association of high psychological demand and low decision latitude) is a risk factor for depression and suicide ideation (Bonde, 2008; Choi, 2018; Theorell et al., 2015). The role of job insecurity has been stressed for a limited subgroup of health outcomes (Caroli & Godard, 2016) or on self-assessed health but only in some European countries (László et al., 2010). Bassanini and Caroli (2015) assert, in a literature review, that most of the negative impact of work on health relies on the role of constraints (both in intensive and extensive margins), i.e., the gap between the desired and effective working situations.

While bad working conditions can deteriorate health, many qualities of work-life indicators have deteriorated in recent years. In France, we have observed an increase in the pace of work and a decrease in workers' autonomy since 1994 (Algava et al., 2014; Arnaudo et al., 2012). During the financial crisis in 2008, psychosocial risks increased (Fontaine et al., 2016). From 2005 to 2015, the European working conditions surveys showed a decreasing trend in the quality of work across the European Union (EU). Working conditions have deteriorated, while work has become more intense and more complex (Greenan et al., 2014).

An accident occurring at work may impair mental health and lead to depression, anxiety, sleep disorders, and post-traumatic stress disorders (PTSD) (Ghisi et al., 2013; J. Kim, 2013). The degradation of mental health is related to the degree of impairment (Larsson & Björnstig, 1995; O'Hagan et al., 2012). Indirectly, all these work-related events are likely to increase psychotropic drug use, at the forefront of which are BZDs (which are used to treat anxiety, sleep disorders, and PTSD).

4.1.2. *Health effects on work*

On the other way, health affects work. The *healthy worker effect* refers to the selection of workers in good health. Becoming disabled decreases the probability of being employed (Lechner & Vazquez-Alvarez, 2011), and people who experience health shocks are more likely to leave employment and transition into disability (García-Gómez, 2011). Jones et al. (2020) have shown that acute health shocks (cancer, stroke, or heart attack) increase the probability of labor market exit and reduce work hours and earnings. The impact is stronger for women, older workers, and people with more severe limitations and impairments. Mental health disorders are also detrimental to job retention (Barnay & Defebvre, 2019). Moreover, Duguet and Le Clainche (2014) show that chronic illnesses and injuries have negative effects on career outcomes (participation and wages). The results differ according to sex: for men, accidents are followed by short-term effects and chronic illnesses by long-term effects, while for women, both health events are followed by long-term effects.

Diseases may also increase the risk of WAs. For instance, insomnia is related to impaired work performance and a higher risk of WAs (Daley et al., 2009). More widely, chronic health problems (Palmer et al., 2008) and mental health problems (Palmer et al., 2014) are associated with a higher risk of WAs. The potential effects of treatment used for these diseases complicate the case. In particular, psychotropic drug use (antidepressants, anxiolytics, and hypnotics) may increase the risk of WAs (Palmer et al., 2014). In the case of BZDs, Garbarino et al. (2021) point out that published studies do not provide consistent results and are prone to various biases. In a meta-analysis, they do not show an increased risk of WAs among BZD users but call for additional work to fill gaps in existing studies.

As we can see, selection effect and reverse causation are inherent to the relationship between health and work and must be considered to estimate causal effects. It is a great challenge and will be central to this dissertation.

Employers are responsible for their employees' safety at work; and public policies aim to improve health at work and reduce WAs. In the same way as for health insurance, the risk is covered by national public insurance, which also has a prevention role.

4.2. Occupational health

4.2.1. Governments commitment

Occupational safety and health (OSH) is a public authority priority. This is one of the areas where the EU has had the biggest impact (guaranteed by Article 153 of the Treaty on the Functioning of the EU, which gives the EU the right to adopt legislation in the field of OSH). The European Pillar of Social Rights (proclaimed in 2017) provides that every worker in the EU has the right to a healthy, safe, and well-adapted work environment. Two community agencies are devoted to gathering, producing, analyzing, and sharing information about safety at work: the EU-OSHA (European Agency for Safety and Health at Work) and Eurofound (European Foundation for the Improvement of Living and Working Conditions).

Improving the prevention of work-related diseases was one of the axes of the EU strategic framework on health and safety at work from 2014-2020 (European Commission, 2014). The new 2021-2027 OSH framework sets out the key priorities to improve the health and safety of workers. Several challenges must be considered: the consequences of the COVID-19 pandemic, green and digital transitions, the aging of the population, and changing notions of the workplace environment. This new framework focuses on three crosscutting key objectives, including the need to improve the prevention of workplace accidents and illnesses (European Commission, 2021). Improving the

prevention of work-related illnesses and deaths is possible by identifying and addressing the causes of the accidents and by increasing awareness of the risks related to WAs and occupational diseases. Research and data collection (at the national and EU levels) are a precondition for the prevention of work-related accidents and diseases.

At the French level, the government's objectives are presented in the *Plans Santé au Travail* (PSTs). Since 2005, four successive PSTs have aimed to improve health and safety at work. Since PST3 (2016-2020), prevention has been privileged over compensation, but it does not provide enforcement action (Barnay & Jusot, 2018). The results of PST3 showed a contrast. Physical constraints were increasing for blue-collar workers, but other indicators were stable between 2016 and 2019 (intensity, autonomy, social support) (Beatriz et al., 2021). The frequency of work-related accidents is between two and three times the average during the first month of employment, the number of accidents due to falls is increasing, the isostrain is slightly decreasing, physical activity during work is decreasing, and health-at-work data remain underutilized (in terms of analysis and sharing of results) (Ministère du Travail, de l'Emploi et de l'Insertion, 2021b). The government's objectives for the 2021-2025 period are presented in PST4. The focus is on prevention and workers' mental health protection (Ministère du Travail, de l'Emploi et de l'Insertion, 2021a). Other plans are used for specific objectives in health at work. For instance, the *Plan pour la prévention des accidents du travail graves et mortels 2022-2025* aims to prevent serious and fatal work-related accidents (Ministère du Travail, de l'Emploi et de l'Insertion, 2022).

Whether the government wants to improve the prevention of WAs (which requires understanding the causes), the current system is rather based on compensation and therefore insurance.

4.2.2. Occupational risk insurance

In France, occupational risk insurance is provided by the national public insurance (*l'Assurance ATMP (accidents du travail et maladies professionnelles)*) for workers affiliated with the general scheme of social security. The affiliation is mandatory for salaried workers and voluntary for self-employed workers. Farmers are covered by a specific scheme (MSA: *Mutualité Sociale Agricole*), and public officers are covered by various insurance plans depending on their jurisdiction. Employers come into play by financing the insurance and because they are required to ensure the safety of workers (Articles L4121-1 and L4121-5 of Labor Code).

Employers are free to take out a supplementary insurance policy with a private organization to insure risks related to disability, incapacity, work absence, or death. The coverage is highly variable according to the type of contract, with a variation from 19% to 84% of salaried employees covered

according to the kind of guarantee (Perronin, 2019). In 2013, approximately 60% of employers took preventive measures against occupational risks, and only 46% developed or updated a single document of occupational risk evaluation, even though it has been mandatory since 2001 (Amira, 2016).

The benefits provided by the ATMP branch of social security are twofold: benefits in kind (all kinds of medical expenses) and cash benefits (wage replacement). In 2019, 944 million euros were paid in benefits in kind, 3,446 million euros for temporary disability (daily allowance), and 4,354 million euros for permanent disability (lump sum or rent), for a total of 8.7 billion euros. This figure increases each year (+2.6% compared to 2018). It came from the strong increase in daily allowances (+8% compared to 2018).

4.2.3. *History of the compensation system*

The organization and functioning of this insurance stem from its history, which predates the creation of social security. In France, the first law regarding work accidents was implemented in 1898. It provides a legal basis for the presumption of employer liability in the case of a WA, the employee's compensation, and the possibility for the employer to insure himself against this risk. In the beginning, only industry worker sectors were covered, but the coverage gradually extended until 1938, when all employees were covered. In 1905, all employers needed to be insured against WA risk, but these insurances were provided by the private sector until 1946 (Irdes, 2019).

In 1945, after World War II, French social security was set up by the orders of 4 and 19 October. Occupational risk insurance was integrated into social security by the law of 30 October 1946, which repealed the 1898 law. This law gave birth to the current system of compensation for occupational risks. In 1967, the general scheme (i.e., for private sector employees) was reorganized into three financially autonomous branches: disease, family, and retirement. Three national funds were created to manage them: the *Caisse nationale de l'assurance maladie des travailleurs salariés* (CNAMTS), the *Caisse nationale des allocations familiales* (CNAF), and the *Caisse nationale de l'assurance vieillesse des travailleurs salariés* (CNAVTS). The CNAMTS also managed occupational risk insurance. In 1994, occupational risks became the fourth branch of social security (ATMP) and acquired financial autonomy while remaining managed under the CNAMTS. Since then, several reforms have extended the scope of health coverage beyond salaried workers (in 1996, 2000, and 2016) and extended the scope of the general scheme (in 2018, especially when CNAMTS became CNAM by extending the general scheme to self-employed workers). These reforms did not change the scope of occupational risk coverage, except for some specific situations, such as temporary workers or

childcare at home. In contrast, several changes in the compensation rules have been made since 1986, especially related to the calculation of allowances (Irdes, 2019).

4.2.4. Organization of occupational risk insurance

The ATMP branch is based on three principles: occupational risk prevention in companies, financial compensation for victims, and the pricing system (taxation of companies to allow the financial balance of the branch). The branch is managed under the CNAM (which also manages the health insurance branch). It is placed under the supervision of both the health and labor ministries. At the local level, file management is entrusted to CPAM (health insurance primary funds), CARSAT (retirement insurance and health at work funds), and medical services (Jeantet & Thiebeauld, 2017).

The recognition of a WA depends on the existence of an accidental fact date and a subordinate relationship when the accident occurs. The employer, according to the employee's declaration, makes the declaration. The employer declares the accident via the DAT form (work accident report). A doctor fills out and sends a CMI form (initial medical certificate) that describes the injuries. The WA recognition entitles insured people to better payments than regular public health insurance. While care reimbursement with regular disease insurance is subject to copayments, care related to a recognized WA is fully reimbursed. The compensation payment of wages is also better than for a work interruption in the case of a disease unrelated to work (Jeantet & Thiebeauld, 2017).

Beyond the compensation of victims, the ATMP branch has a prevention role and is coordinated by the CNAM. Regional funds have specific means to improve occupational risk prevention, such as getting into companies, asking for all justified preventive measures, granting contribution reductions or increases, and granting financial aid to support investments in OSH (Jeantet & Thiebeauld, 2017).

The funding of this assurance system is based on firms' contributions. All firms belonging to the general scheme are insured (regardless of the risk), and all their salaries are covered (even in the event of employer insolvency). In addition to insuring employees, this system allows pooling the risk for employers and has a preventive role (because the contribution level varies according to the risk level of the enterprise). A firm's contribution depends on the number and gravity of WAs (risk cost) and payroll expenditures, both being calculated over the three previous years (Jeantet & Thiebeauld, 2017).

4.3. Occupational accidents

All information in this section comes from the annual report of the ATMP branch for 2019 and 2020 (L'Assurance maladie - Risques professionnels, 2020, 2021). Occupational risks are the risks of work to impair health and include WAs and occupational diseases. In this dissertation, I distinguish between workplace accidents and commuting accidents among WAs. Workplace accidents are accidents occurring at the place or in the course of a job. Commuting accidents are accidents occurring between the place of residence and the job, or between a dining destination and the job. In France, commuting accidents are considered regular WAs, and the declaration procedure and compensation are identical. Occupational diseases are due to exposure to a work-related factor. In the case of an accident, the event leading to the disease is sudden, whereas in the case of a disease, the cause is prolonged exposure and often difficult to estimate precisely.

In 2019, the CNAM received 937,642 full claims of workplace accidents; 880,885 were recognized (94% positive decisions), and 655,715 led to work interruption or disability (74%). From 2013 to 2019, the number of recognized WAs slightly increased each year. However, due to the increasing number of employed people, the frequency index (i.e., the number of WAs per 100,000 employees) remained stable overall through this period. They led to 733 deaths in 2019, a significant increase over the previous year.

The major causes of workplace accidents are manual handling (50%), falls at the floor level (17%) and from height (11%), accidents due to hand tool use (8%), and aggression (4%). From a business line perspective, the group (CTN are groups of business sectors) with the highest frequency index of WA is composed of companies belonging to the CTN I (service activities: temporary employment, social action, health, cleaning...): 53 WA for 100,000 employees; followed by CTN B (construction): 51; CTN C (transport): 45; CTN D (grocery): 43; and CTN F (wood, furniture): 42. The severity index (sum of disability rate by millions of hours worked) is the highest in companies belonging to CTNs B, C, and F.

Regarding commuting accidents, the CNAM received 144,369 full claims; 137,846 were recognized (96% positive decisions), and 98,899 led to work interruption or disability (72%). They led to 283 deaths in 2019 (a slight increase over the previous year). The evolution is jagged (increasing from 2014 to 2019) and highly dependent on weather conditions. The severity of commuting accidents has decreased over time (a decrease in the share of commuting accidents leading to disability).

The causes of commuting accidents are loss of vehicle control (mostly cars, then motorbikes, bikes, and scooters) in 60% of cases and falls in 30% of cases.

The average duration of the work interruption is 103 days for workplace accidents and 111 days for commuting accidents. The average recognition period was 21 days for workplace accidents and 24 days for commuting accidents.

5. Impact of the COVID-19 pandemic

5.1. Disruption of work

The outbreak of COVID-19 in 2020 had a strong impact on people's lives and their work in particular. The first cases of COVID-19 were detected in France in January 2020. The epidemic quickly spread and led to the first lockdown from 17 March to 10 May (1 month and 25 days); the second lockdown from 30 October to 14 December (1 month and 15 days); a curfew period until 2 April 2021; and then the third phase of restrictive measures from 3 to 25 April 2021 (22 days).

The first wave of the pandemic led to a major disruption, and most of the global population was subject to lockdown policies and had to stay at home. Except for "essential workers", i.e., those who were considered essential to the functioning of society, workers interrupted their in-place work: they worked from home if possible or not at all.

According to the report of the ATMP insurance (*L'Assurance maladie - Risques professionnels*, 2021), on a monthly average in 2020, 3.35 million employees were in partial unemployment (up to 8.39 million in April 2020), compared to an average of 40,000 in a normal year. Partial unemployment was used during confinements for "unessential workers" unable to work from home and for companies whose activity had been impacted by the pandemic. In this case, the employee's remuneration was at least 84% of the net salary (up to 100% if the employer made up the difference) until 30 June 2021 (72% of the net salary after). Eighty-four percent of net salary was copaid by the state and public unemployment insurance, and the employer could compensate the remaining share.

Beyond stay-at-home orders during confinement, other work interruptions can be related to COVID-19: because of the infection itself (regular sick leave); contact case with a person positive for COVID-19; people at high risk of severe COVID-19 or cohabiting with a high-risk person; child care (during school closures); and people isolated when coming back from another country. In these situations, the national health insurance paid sick pay, without an unpaid day. The

compensation equaled 50% of gross salary, and the employer paid 40% (up to 50% depending on the collective agreement) during the first 30 days.

These factors combined (partial unemployment and work interruption) led to a strong decrease in work hours in 2020 and thus a lower exposure to occupational risks. This lower exposure resulted in a decrease in the total number of accidents at work in 2020. Of course, variations were strongly related to the companies' sector, according to the share of essential workers, exposure to COVID-19, and the business shock.

We saw a decrease of 20% in claim flow (WAs and professional diseases), correlated with the confinements and activity restriction periods. The number of workplace accidents with work interruption decreased by 18% (539,833). New permanent disabilities decreased by 21%, deaths by 25%, and the number of days of temporary disability by only 0.4% (45.7 million days of work interruption). While the number of new permanent disabilities strongly decreased, the severity of accidents seemed to remain constant: the disability rate and share of new workplace accidents leading to disability were also roughly the same as in 2019.

The strongest declines were in arts and entertainment, accommodation and food services, and education. Conversely, the decrease was small in mining and carrying, and the water supply industry. In some specific subsectors, workplace accidents increased, such as distance selling, food purchasing centers, and ambulances.

Similarly, commuting accidents decreased by 20% in 2020 due to confinement and homeworking. Permanent disabilities and deaths also strongly declined, while the decrease was small for temporary disabilities. The severity of commuting accidents seemed to decrease, as the number of new permanent disabilities by commuting accidents declined. We noted an increase in the share of accidents involving bikes and scooters, particularly in the Île-de-France area.

The benefits paid increased by 62 million euros. Compensation in kind and permanent disabilities decreased, but expenses for temporary disability strongly increased. This increase came from expenses incurred in previous years and an increase in the mean length of work interruptions.

5.2. Increase in psychotropic drug use

Beyond work, the pandemic affected our habits and everyday lives through the direct effect of the COVID-19 disease and the indirect effect of mitigation measures (such as travel restrictions, social distancing, and curfews). Mental health has deteriorated during the pandemic. The CoviPrev survey (from Santé Publique France, the French agency of epidemiology) shows, since the beginning of the first confinement, that levels of anxiety, trouble sleeping, and depression are higher than before

the pandemic, and remain at high levels, at least until May 2022 (last wave of the survey). Alongside this deterioration, we have seen a steep increase in psychotropic drug use.

EPI-PHARE is a scientific interest group formed by the CNAM and the ANSM to monitor drug consumption in France and conduct studies on these drugs. Since the first confinement in France (March 2020), following the beginning of the COVID-19 pandemic, EPI-PHARE has regularly published a report related to drugs delivered in pharmacies by prescription. All figures in this section come from these reports.

The first confinement was unique because of the speed and strength of the measures taken and the surprise they generated. They observed a storage phenomenon for treatments of chronic diseases (such as antihypertensive drugs, antidiabetics, and to a lesser extent treatments of mental illnesses). Sales of these drugs increased greatly at the beginning of the confinement and then fell below the normal numbers. After 3-4 weeks of confinement, consumption returned gradually to normal. On the other hand, treatments that require administration by a doctor (such as vaccines) collapsed immediately, and the consumption stayed far below normal during all confinements (Weill, Drouin, Desplas, Cuenot, et al., 2020a; Weill, Drouin, Desplas, Dray-Spira, et al., 2020). The storage phenomenon of treatments for chronic diseases hid a decrease in the initiation of new treatments (Weill, Drouin, Desplas, Cuenot, et al., 2020b). It has been observed elsewhere, in Portugal (Romano et al., 2020) and Germany (Kostev & Lauterbach, 2020) for instance.

However, EPI-PHARE observed a specific trend for anxiolytics and hypnotics (mostly composed of BZDs). After an initial period of storage (first week) and slight underconsumption (second week), the consumption quickly went to an above-normal level (even before the end of the confinement). The week following the end of the confinement, anxiolytic and hypnotic consumption was 6.9% and 1.2% higher, respectively, than expected. At this point, antidepressants were not overconsumed, compared to the previous year (Weill, Drouin, Desplas, Cuenot, et al., 2020b). Over the 6 months since the beginning of the confinement, sales of anxiolytics and hypnotics were higher by 1.1 million and 480,000, respectively, than expected. Sales of BZDs remained constantly above normal until the end of the summer. We observed a decrease in new treatment with anxiolytic and hypnotic drugs (respectively -0.5% and -10.1%) during the first confinement, but the start of new treatments resumed after the confinement. Over the 6 months since the beginning of the confinement, new treatments were higher by 4.6% and 2.6% from the equivalent period in 2019 for anxiolytic and hypnotic drugs, respectively (Weill, Drouin, Desplas, Cuenot, et al., 2020c).

Unlike during the first confinement, we did not observe a storage phenomenon for the second and third periods of restrictions. The consumption of anxiolytics and hypnotics stayed at a level well above normal. During the first four months of 2021, we observed increases of 1.3 million and 580,000 in anxiolytic and hypnotic treatments, respectively. Over the same period, the new treatments were 15.2% (190,000 new patients) and 26.4% (80,000 new patients) higher than expected (Weill, Drouin, Desplas, Cuenot, et al., 2020d; Weill et al., 2021).

Although the struggle of the health authorities for years to decrease BZD consumption had been successful, the COVID-19 pandemic led to a clear increase in consumption both in people already treated and by increasing the number of new people treated. This increase probably came from the psychological impact of the pandemic and its consequences (such as loss of job, decrease in social activities and hobbies, and financial loss).

To return to the previous consumption trajectory, the CNAM made a set of proposals, which include measures to improve the use of anxiolytics and hypnotics (whose misuse is historically important in France) and promote access to nonmedicinal care (such as psychotherapy). In particular, a major plan to evaluate the relevance of BZD prescriptions will be launched, in partnership with the HAS and the ANSM (CNAM, 2021).

6. Research questions

6.1. Conceptual framework

We saw in section 4.1 that work and health are linked by a two-way relationship. Work affects health, and health affects work. There is extensive literature dedicated to the study of these relations at the interface between health economics, labor economics, and insurance economics. Identifying causal relations between health and work is a challenge due to their intertwining. In the first two chapters of this dissertation, I study the interaction between a WA (which is a shock on health capital) and BZD use (care consumption). BZDs, like psychotropic drugs more widely, are used to improve health (the stock of health capital), but like all medicines, they have adverse effects and can impair health capital. BZD use is a concern in France, and as such, it is important to understand both its determinants and its consequences. Likewise, the CNAM is engaged in a struggle against WAs (requiring knowledge of their determinants) and covers their consequences. This is therefore a complex and interesting case study of health and work interaction but also a significant contribution to scientific knowledge, as no previous study deals with these research questions, to my knowledge, and thus to the fight against BZD overuse and occupational accidents.

The conceptual framework of health and work interaction refers to health capital theory (Grossman, 1972). This theory is built on Becker's human capital theory (Becker, 1964), which is itself in line with Smith's capital stock theory (Smith, 1776). According to Grossman's health capital theory, each individual inherits a certain stock of health that depreciates with age and increases with investment. The health state is endogenous; health is both demanded (healthcare consumption) and produced (investment) by consumers. Health determines the time available for market and nonmarket activities. Each individual determines his desired level of health capital (via health care consumption and health investment), which maximizes his utility.

The studies on health and work relationships are prone to various biases (Defebvre, 2017), which are very common in the health and work literature and which I will try to address in this dissertation. First, selection bias is commonly observed, as the initial stock of health capital influences the choice to work. Healthier workers tend to prefer (self-selection) or be preferred (discrimination) for more demanding jobs ("healthy-worker effect") (Barnay, 2016). WAs can occur only in a working population (subject to the healthy-worker effect) and are not evenly distributed in the working population. The second is reverse causality bias: while health affects work, work affects health (by working conditions, insurance mechanisms, wage effects, etc.), and it is difficult to identify the direction of causality. This is clear in our case, as medicines can be used to ease a health problem but can produce adverse effects. Third, the omission of variables increases unobserved heterogeneity. The probabilities of working and consuming care depend on individual preferences (such as time preference), are interlinked, and may lead to biased estimates. The population more exposed to the risk of WAs could use more BZDs as a result of an omitted variable. Fourth, depending on the data source, measurement and declaration bias are commonly present. In particular, misdeclaration may be present when talking about health-related behaviors and risky behaviors. Psychotropic drug consumption is a concern (Parry et al., 1970), and working with administrative databases is especially welcome to address that bias. However, declaration bias may also be present in the administrative database, as WAs are notably underreported (while they are mainly less severe) (Askenazy, 2006), and the BZD black market is not considered.

6.2. Empirical evidence

BZDs are useful to treat anxiety and sleep disorders, among other problems, but their therapeutic effect quickly declines over time, and the longer the treatment, the higher the risk of dependence. Public authorities defined guidelines to limit the risk of adverse effects, and compliance is a public health issue. An accident (at work or not) is a shock on health and can lead to injury and consumption of care. The health impairment can be temporary or permanent, according to the

injury. In particular, a WA can impair mental health and increase the risks of depression, anxiety and sleep disorders (Ghisi et al., 2013; J. Kim, 2013). These diseases may be treated by drugs, BZDs in the case of anxiety and sleep disorders. Because of the risk of dependence, BZD use may be absorbent state, lead to adverse effects, and finally result in inefficiency of treatment. This dissertation adds to the literature by analyzing how a shock on health, namely a WA, which is likely to lead to BZD use, could lead to BZD overuse.

The literature highlights the very strong association between age and sex (female) and BZD use, as well as with mental and physical illnesses (see e.g. Demyttenaere et al., 2008; Lagnaoui et al., 2004). Other studies are interested in factors related to overuse. Results vary according to the definition of overuse, but this literature shows, in particular, the role of comorbidities and socioeconomic characteristics (see e.g. Fride Tvette et al., 2015; Takano et al., 2019). To my knowledge, this dissertation is the first work that clearly distinguishes between risk factors for use and overuse, and considers the selection effect for people who overuse. Moreover, the specific impact of a WA has not been studied, despite the psychological consequences of a WA.

It is a challenge to consider the two-way relationship between WAs and BZDs, as the adverse effect of BZDs could increase the risk of WAs. From an insurance perspective, French law is clear: all accidents occurring at the time or place of work are presumed to be of occupational origin. Nevertheless, from a prevention perspective, the knowledge of WA determinants is crucial, whether they are professional or not. The literature is rather extensive on this topic and stresses the role of individual characteristics (such as age, sex, education, and income (Askenazy, 2006; Dembe et al., 2004; Ghosh et al., 2004; Guadalupe, 2003; Krause et al., 2001; Piha et al., 2013)), job characteristics (such as kind of occupation, work environment, work schedule, kind of contract (Amuedo-Dorantes, 2002; Ghosh et al., 2004; Hernanz & Toharia, 2006; Khlal et al., 2008; H.-C. Kim et al., 2009; Wagstaff & Sigstad Lie, 2011)), employer characteristics (such as size (Ruser, 1985)), and insurance (Krueger, 1990).

Workers' health is also involved in the risk of WAs through different channels. A disease can increase the risk of accidents by itself, such as insomnia or mental health problems (Daley et al., 2009; Palmer et al., 2014), but medical treatments can also increase the risk of WAs, such as psychotropic medication (Palmer et al., 2016). Moreover, health condition plays a role in risk exposure in the short term, by increasing sickness absences, and in the long term, by decreasing employability and the probability of staying employed (Barnay et al., 2015; Barnay & Defebvre, 2019). We see that the influence of the state of health is very ambiguous. For example, in the case of insomnia, the disease could increase the risk of WAs (if the worker is tired or inattentive), but

the treatment (classically with a BZD) could lead to adverse effects, such as cognitive impairment (Brandt & Leong, 2017), that might increase the risk of WAs. Moreover, the worker can stay at home if he or she feels unable to work. How will the risk of WAs evolve? Unfortunately, some preexisting studies on the influence of BZD consumption on the risk of WAs are subject to the risk of reverse causality, declarative bias, selection effects, or confounders (Garbarino et al., 2021; Palmer et al., 2014).

We see that answering this question is not trivial because several mechanisms are involved. Moreover, reverse causality prevents us from using statistics to estimate the impact of BZD use on the risk of WAs or the impact of WAs on BZD use. These two processes are intertwined, and we need to study both together to better understand the mechanisms at work. This dissertation draws on the literature on the interaction between health and work, and attempts to estimate causal effects in both directions of the relationship.

In France, public authorities have taken steps since the late 1990s to reduce consumption, which was one of the highest in Europe (Alonso et al., 2004; ANSM, 2017). These measures were effective, as the BZDs sales continuously decreased from the beginning of the 2000s. However, the Covid-19 pandemic, which occurred in 2020, led to a rebound in sales (see section 5.2). The pandemic strongly impaired the mental health of the population and thwarted years of efforts to combat overconsumption. Understanding what led to the increase in BZD use during the Covid-19 pandemic is critical to improving mental health policy and trying to improve the management of future pandemics.

6.3. *Research outline*

This dissertation relies on data from the SNDS (national health data system), which is used by French health insurance to reimburse care to the whole population. It contains information about the people insured, the care provided, and the accidents at work.

This dissertation is interested in challenges and problems with the use of BZDs. BZD consumption is closely linked to occupational outcomes, and, in return, BZD use may result in consequences on work, especially around the issue of WAs. Moreover, determinants of BZD use have been affected (including those related to work) during the pandemic and it is crucial to understand how in order to contain it and consider the possible consequences.

The first two chapters of this dissertation aim to explain the impact of the occurrence of a WA on BZD consumption (for the first) and the influence of BZD consumption on the risk

of WAs (for the second). In these two chapters, I distinguish BZD use, i.e., consumption under the maximal duration recommended, and overuse, i.e., consumption beyond the recommendations.

The objective of the first chapter is to determine the extent to which WAs lead to BZD use and overuse. Our study sample includes all members of the general scheme of social security who experienced a single work accident in 2016 (and not since 2007). This sample includes 350,000 individuals and more than 1.1 million people who are randomly drawn from the population of members who did not experience work accidents from 2007 to 2017. The occurrence of a WA is followed by an increase in both BZD use and overuse the following year. Once considered the selection effect, the WA leads to an increase in BZD use the following year (+39%), but a slight increase in the risk of overuse (+1.7%) among people who already consumed. The effect on overuse is higher for more severe WAs and among women. Results call for targeting the first-time BZD prescription to limit the risk of overuse after a WA.

The objective of the second chapter is to estimate the effect of BZD use on the risk of WAs by differentiating between recommended use and overuse. I use a fixed-effect model to deal with time-constant heterogeneity. The results show a decreased risk of WAs following a short use of BZDs (one month), but the risk of WAs increases when treatment exceeds the guidelines. The intensity of use results in a greater risk of WA: a 1% increase in BZD use leads to a 4.4% increase in the monthly risk of WAs. Moreover, we see an increase in risk in the month following the treatment cessation. Health professionals and BZD users should be made aware of the WA risk induced by BZD use, not only at the beginning of treatment but also following extended use and after treatment stops. This study provides more evidence for the need to limit the duration of BZD treatment.

The objective of the third chapter is to study the impact of the COVID-19 pandemic on the determinants of BZD consumption. The year 2020 was very specific due to the COVID-19 pandemic. Our health systems, as well as the labor market, were deeply affected. Under these conditions, it seems complicated to study weak interactions between care consumption and labor in 2020 without considering the pandemic. Moreover, while public policies to reduce BZD consumption were slowly bearing fruit, consumption rose sharply in 2020 and remained at a high level due to anxiety, depression, and sleep disorders.

The year 2020 interrupted a 20-year decreasing trend in BZD use in France. Although public health was strongly affected by the COVID-19 pandemic that year, it is crucial to understand how the pandemic affected BZD use to improve the struggle against BZD overuse. In particular, the

objective of this chapter is to disentangle the effect of the direct effect of the pandemic from the effect of mitigation measures.

In this last chapter, the SNDS data have been aggregated at the French municipality level and completed by census data from the National Institute of Statistics (Insee) and excess mortality in 2020 at the French department level. Using linear models, I compare the influence of variables related to the severity of the pandemic and variables related to some vulnerability factors (on the labor market, in housing, and health). The results show that the increase in BZD use in 2020 and 2021 was related to deprivation and fragility in the labor market (unemployment rate and share of people without a diploma) and poor social connection (share of single-person households). The severity of the pandemic in the area of residence positively affected the trend of BZD use in a small way. Conversely, the risk factors for severe COVID-19 did not increase BZD use in 2020 and 2021. These results show a greater impact of mitigation measures and their economic consequences on BZD use variation than the direct effect of the pandemic. It stresses the role of socioeconomic vulnerability factors in the increased use of psychotropic drugs during the pandemic and should be considered in the struggle against BZD overuse.

**Chapter 1. Work accident effect on the use
of psychotropic drugs: the case
of benzodiazepines**

With Thomas Barnay

1. Introduction

In 2016, in France, 715,130 work accidents (WAs) (including 13% of commuting accidents) were recorded, resulting in 768 deaths, more than 40,000 permanent disabilities, and €5.6 billion of daily allowances (CNAM, 2017). In total, nearly 4% of employees insured under the general scheme were victims of WAs during that year (authors' calculation based on SNDS data). These WAs have countless effects on health, related to the great variety of jobs, people, and circumstances. In particular, they may impair mental health and lead to depression, anxiety, sleep disorders, and post-traumatic stress disorders (PTSD) (Ghisi et al., 2013; J. Kim, 2013). The degradation of mental health is related to the degree of impairment (Larsson & Björnstig, 1995; O'Hagan et al., 2012). Moreover, some studies show persistence during years after the accident of these psychiatric symptoms (Chin et al., 2017; Cohidon et al., 2009), including road accidents (which represent a particular case of occupational accidents) (Arnberg et al., 2011; Barth et al., 2005).

These psychiatric symptoms can be treated with various medications. Among them, benzodiazepines (BZDs) are especially useful, because they are indicated to treat anxiety, trouble sleeping, and PTSD. They are also often used along with antidepressant drugs at the beginning of antidepressant treatment. Like other drugs, they have several adverse effects, like psychomotor impairment, resulting in motor vehicle accidents and falls (Brandt & Leong, 2017). Moreover, extended use is associated with a loss of treatment efficacy and can lead to dependence, with an increased risk of withdrawal symptoms at standstill (Ashton, 2005; Gudex, 1991; Vorspan et al., 2018), so it is a source of inefficiency of treatment. To limit this risk, the French National Authority for Health (HAS) recommends limiting the duration of prescriptions to four weeks for hypnotic BZDs and twelve weeks for anxiolytic BZDs (HAS, 2017, 2018). Yet, in 2014 in France, 14% of new BZD users consumed the drug beyond the recommended treatment time (ANSM, 2017).

The frequency of WAs raises the question of their impact on BZD overuse. Because a WA may lead to deteriorating mental health, BZDs are indicated in short-term treatment and so likely to be prescribed. However, prolonged use could result in inefficiency of treatment and be counterproductive.

Sex and age appear as the main drivers of BZD use. Sixty-five percent of consumers in France in 2015 were women and usage increased with age (ANSM, 2017). The use of psychotropic drugs (including BZDs) was also related to the socioeconomic group, with executives and higher intellectual professions consuming less than those in intermediate professions, employees, and workers (Beck et al., 2014). Nearly 90% of BZD prescriptions are made by general practitioners (GPs), and 82% of new BZDs treatments are initiated by GPs (ANSM, 2017).

Concerning overuse, the risk factors vary according to the criteria retained (duration of treatment or several BZDs taken simultaneously). In studies using duration of treatment as criteria of BZD overuse, the main drivers are advanced age, comorbidities (in particular history of depression and sleep disorders), other drugs used (in particular antidepressants and psychotropic drugs), and socio-professional characteristics (low educational level, low household income, and not having a job) (Baumann et al., 2001; Fride Tvette et al., 2015; Tanguay Bernard et al., 2018). The impact of sex on BZD overuse is not consensual: in some studies, BZD overuse is associated with being a man (Baumann et al., 2001; Fride Tvette et al., 2015), but sometimes the association is not significant (Tanguay Bernard et al., 2018).

In addition, the role of prescriber characteristics on inappropriate prescriptions (not focused on psychotropic drugs) is not well established in the literature. Having several prescribers seems to be a risk factor (Dhalla et al., 2002; Holmes et al., 2013). Dhalla et al. (2002) show an effect of prescriber characteristics (other predictors were male sex, age 50 and over, in general practice, and practice in a rural area), while others do not (Avery et al., 2013; Cahir et al., 2014; Hansen et al., 2004).

Work characteristics may also impact BZD consumption. In most cases, employment protects health status (Barnay, 2016); however, it can sometimes be pathogenic (Caroli & Bassanini, 2015; Caroli & Godard, 2016; Defebvre, 2018). There are no studies that specifically address the impact of work on BZD use, but many studies stressed the impact of work characteristics on psychotropic drug use, in the case of psychosocial work factors (Lassalle et al., 2015; Lavigne & Bourbonnais, 2010) and low job satisfaction (Baumann et al., 2001). Other job-related factors play a role in psychotropic drug use such as organizational downsizing (Blomqvist et al., 2018; Kivimäki et al., 2007) and mass layoffs (effect on remaining employees) (Le Clainche & Lengagne, 2019). However, as far as we know, there is no published study on the impact of WA on psychotropic drug use.

Our objective is to measure the change in consumption of BZDs following the occurrence of a WA. The question is twofold: because WAs affect mental health, they could indirectly result in higher psychotropic drug consumption, and, in the case of BZD, extended use could be especially harmful because of the risk of dependence and this process feeds on itself.

To answer this question, we use the French National Health Data System (SNDS), which is an administrative database that contains all information related to reimbursed care in France, for the whole population. We distinguish between the use and overuse of BZDs, overuse being defined as non-compliance with the maximum recommended duration of treatment. We proceed in two steps: first, we use a two-step selection model to estimate the probability of BZD use and overuse after

a WA; second, we focus on the population with WA to estimate the impact of severity of accident on BZD use and overuse.

Considering both the incidence of WAs and the important use of BZDs in France (and associated adverse events), the consequences of WAs on BZD use is a major question that has not been answered, to our knowledge. We provide here the first consistent analysis of the impact of a WA on BZD use and overuse. Moreover, previous studies analyzing risk factors of BZD overuse did not consider the selection effect in overuse (the need to be a user before overusing) and therefore confused factors associated with use and overuse. Our study shows that WAs increase the risk of BZD use and overuse. However, the increase in overuse comes from an increase in the likelihood of using after the WA, not from a large increase in the likelihood of overusing among those who use. Nevertheless, among people with WAs, the longer the subsequent work interruption, the higher the probability of overusing BZDs.

2. Material and methods

2.1. Data

The data come from the French National Health Data System (SNDS), which is a nationwide administrative database produced and managed by statutory health insurance (CNAM). It contains all information relating to reimbursements made by the CNAM (outpatient care, hospitalization, and cash benefits) (Tuppin et al., 2017). It also contains data related to WAs and occupational diseases (ATMP in French), and it is used by the eponymous branch to reimburse insured persons, adjust firm pricing, and prevent occupational risks.

The information system makes it possible to know the exact dates of drug dispensation. It contains the following information on patients: year of birth, sex, department of residence, recipient of universal complementary health insurance (called CMU-C), and registration in a long-term disease scheme (called ALD), which allows exemption from user fees for care relating to registered diseases. It also contains information about prescribers (such as medical specialty, sex, and age). The exact dates and circumstances of WAs are also known. Finally, ATMP data were available from 2006 to 2017. Information on non-ATMP care was available from 2015 to 2017. Statistical analyses were performed using SAS 9.4 on Red Hat Enterprise Linux Server 7.4.

Using SNDS data, the CNAM produces the *Healthcare Expenditures and Conditions Mapping*, which allows patients to be classified into 58 nonexclusive groups according to their health status and treatments. This classification is based on reimbursements specific to some diseases, medical

diagnosis during hospitalization, and registration as an ALD if applicable, according to the methodology described by Rachas et al. (2022). We use the year 2015.

2.2. Scope of the study

The study covers the entire French population insured under the general scheme of the welfare system, i.e., employees in the private sector (except farmers) and civil servants. It covers the period from 2015 to 2017.

The inclusion criteria are as follows: having at least one treatment reimbursed by the general scheme in 2015 and 2016, and being between 18 and 65 years of age in 2016 (selection of a working-age population). We exclude persons who died before January 1, 2018, with an occupational injury (WA or professional disease) from 2007 to 2015 or in 2017 and with more than one occupational injury in 2016.

Our study population is composed of both people who have had a single WA in 2016 (and none other since 2007) (WA group) and people who have not had any WA between 2007 and 2017 (non-WA group). We consider only recognized WAs, and relapses are not considered. The selection of the period 2007-2017 for the non-WA group avoids a disruptive effect related to another damage and therefore allows identification of a “pure” effect of WAs occurring in 2016. Finally, because of the volume of data, we make a random selection of one-twentieth of the population that did not experience a WA from 2007 to 2017.

2.3. Definition of use and overuse

In 2016, 19 different BZDs (including two related drugs: zolpidem and zopiclone) were marketed in pharmacies in France. We include all of these in this study. All BZDs have close effects and differ by their kinetics (Griffin et al., 2013), short-acting BZDs are rather used as hypnotics and long-acting are rather used as anxiolytics, but there are possible substitutions. The homogeneity of the drug class in terms of effects justifies considering them all together.

Purchase dates are calculated around the WA date, occurring in 2016. To be able to calculate use in the same way for people with and without WAs, the WAs dates of the WA group are randomly distributed to the non-WA group. A month is assimilated to a 30-day period since prescriptions are often monthly and benzodiazepine boxes have a capacity of 30 tablets. A year corresponds to 12 times 30-day periods.

At least one BZD purchase defines use. Overuse corresponds to at least four months with BZDs issued in five consecutive months. According to the recommendations, the maximum duration of

treatment with BZDs is twelve weeks of treatment for anxiolytics and four weeks for hypnotics (HAS, 2017, 2018). Overuse, therefore, corresponds to noncompliance with the recommended treatment times for anxiolytic BZDs. We apply the same rule to hypnotics for reasons of simplicity and homogeneity. We assume that at least four months with at least one dispensation for five consecutive months can characterize at least twelve weeks of continuous consumption, considering the variability that there may be in dispensation dates.

2.4. *Econometric strategy*

We estimate the causal effect of the occurrence of a WA on BZD use and overuse. Estimating the overuse using a logit or probit may lead to biased results. Indeed, overuse can only exist among people who consume BZDs, and if the factors associated with use and overuse differ, there is a potential selection bias. We use a two-step selection method to consider this bias (Heckman, 1976, 1979). It consists of estimating *via* a probit model the probability of using BZDs ($BZDuse_i^*$) in the first step (selection equation):

$$P(BZDuse_i^* = 1|X') = \Phi(X_i'\beta) \quad (1.1)$$

With $\Phi()$ the probability density function of a normal distribution and

$$\begin{aligned} X_i'\beta = & \beta_0 + WA_i'\beta_1 + age_i'\beta_2 + sex_i'\beta_3 + urbanArea_i'\beta_4 + Xinsurance_i'\beta_5 \\ & + XpastBZD_i'\beta_6 + Xhealth_i'\beta_7 + u_i \end{aligned}$$

Then, we estimate the probability of overusing BZDs ($BZDoveruse_i^*$) in the population using BZDs after the WA date in the second step (outcome equation):

$$P(BZDoveruse_i^* = 1|Z', BZDuse_i^* = 1) = \Phi(Z_i'\delta) \quad (1.2)$$

With

$$\begin{aligned} Z_i'\delta = & \delta_0 + WA_i'\delta_1 + age_i'\delta_2 + sex_i'\delta_3 + urbanArea_i'\delta_4 + Zinsurance_i'\delta_5 \\ & + ZpastBZD_i'\delta_6 + Zhealth_i'\delta_7 + Zprescriber_i'\delta_8 + \rho\lambda_i + \varepsilon_i \end{aligned}$$

Where

$$BZDoveruse_i = BZDoveruse_i^* \text{ if } BZDuse_i^* > 0$$

$$BZDoveruse_i = 0 \text{ if } BZDuse_i^* \leq 0$$

In the first step, we explain the BZD use in the year following the WA by a dummy variable for WA in 2016 (WA); the age in 2016 (age); the sex (sex , ref. = male); a variable describing the urban

area in 2016 by labor market size (Brutel, 2011) (*urbanArea*', 10 modalities); a vector of insurance-related variable ($X_{insurance}'_i$): CMU-C in 2015 (0/1), aid for the payment of supplementary health insurance (called ACS) in 2015 (0/1), and disabled adults' allowance (called AAH) in 2015 (0/1), which are mean-tested benefits and therefore provide information on income levels; a vector ($X_{pastBZD}'_i$) of BZD use during the year preceding the WA (four dummies for at least one BZD use each quarter of the year); and a vector of health-related variables ($X_{health}'_i$) including 15 dummies of health variables in 2015 from the *Healthcare Expenditures and Conditions Mapping*: cancers, cardioneurovascular diseases, treatment of vascular risk, inflammatory or rare disease or HIV/AIDS, neurological or degenerative diseases, psychiatric disorders, chronic end-stage renal disease, chronic respiratory disease diabetes, liver or pancreas disease, addictions, other long-term diseases, maternity, antidepressant dispensation, and dispensation of neuroleptics; u_i is the error term.

In the second step, variables explaining BZD overuse in the year following the WA are close to the first step. The past BZD use ($Z_{pastBZD}'_i$) includes a dummy of BZD overuse in the year preceding the WA in addition to the four dummies for BZD use in the quarters of the year. The vector of insurance ($Z_{insurance}'_i$) is similar to $X_{insurance}'_i$. Health ($Z_{health}'_i$) variables are similar to $X_{health}'_i$, except for *inflammatory or rare disease or HIV/AIDS (0/1)* which is absent. $Z_{prescriber}'_i$ is a vector of characteristics of the prescriber of the first BZD after the WA: medical specialty (GP, psychiatrist, another specialist, non-physician, multiple BZD prescribers the same day, or missing information), age (three modalities), and sex. Other variables are unchanged. Finally, $q\lambda_i$ is the inverse of the Mill ratio and ϵ_i is the error term.

The identification of the model relies on the assumption of nonlinearity of the Mill inverse ratio, but it may be nonrobust due to collinearity (Puhani, 2000). It is recommended to use an identification variable, which would be a good predictor of *BZDuse* and would not be used in equation (1.2). Identifying such a variable (that is a variable influencing BZD use without influencing BZD overuse) is not an easy task, because the two outcomes are closely related, and previous studies did not consider the selection effect in overusing estimation. We used the variable *inflammatory or rare disease or HIV/AIDS (0/1)* as an identification variable because it is positively associated with BZD use, but not with BZD overuse in the estimation without an identification variable. These results are presented in section 3.

As robustness checks, we provide in the Appendix estimations without an identification variable and using sex as an identification variable. Indeed, while being a woman is positively associated with BZD use, overuse is not significantly associated with sex according to some studies.

Conversely, other studies show that substance use disorders are more common among men (Brady & Randall, 1999). Results are available in Appendix. Nevertheless, the results of the main estimation show a significant effect of being a woman in the two steps (positive on BZD use and negative on BZD overuse), which goes against the use of this variable as an identification variable. Its non-significance in previous studies on BZD overuse may come from the non-consideration of selection and the opposite direction of sex effect on use and overuse.

The test for the correlation of the error terms shows that the null hypothesis must be rejected for all the specifications, which means that there is indeed a selection bias that must be corrected and that the ‘naïve’ model is biased. We provide in Table 1.A9 in the Appendix a ‘naïve’ probit estimation: an estimate of the probability of overuse for the population that consumed the year following the WA (which corresponds to the second step of the Heckman model).

2.5. Descriptive statistics

Table 1.1 compares sociodemographic characteristics in WA and non-WA groups. The WA group is younger (78.5% are under 50 compared to 65.7% in the non-WA group), more often male (51% compared to 41%), and less disadvantaged. These differences refer to a selection bias. People with WA are people who worked at least once in 2016, while people without WA are people who used at least one treatment in 2015 and 2016 but whose employment status is unknown. This selection effect clearly appears in terms of health and healthcare expenditure heterogeneity. Thirty-one percent of the sample suffer from at least one disease, with 34% in the non-WA group but only 23% in the WA group. Statistics relative to health status are shown in Table 1.A1 in the Appendix. Whatever the disease, the WA group is healthier than the non-WA one. This group also has less frequent maternity leave and drug treatments. Differences in the typology of the municipality of residence are presented in Table 1.A2 in the Appendix.

Table 1.1: Descriptive statistics

Variables	WA group	Non-WA group
<i>Sociodemographic variables in 2016</i>		
Average age	37.5 years	42.0 years
18–29	33.5%	22.9%
30–39	23.0%	21.1%
40–49	21.9%	21.8%
50–59	18.7%	21.6%
60–65	2.9%	12.7%
Male	51%	41%
CMU–C	9.4%	12.1%
ACS	3.8%	4.1%
AAH	0.9%	3.2%
<i>BZD consumption in the year preceding the WA</i>		
At least one BZD use	12.15%	15.08%
BZD overuse	2.89%	5.30%
<i>BZD consumption in the year following the WA (variation compare to the previous year)</i>		
At least one BZD use	16.79% (+38%)	14.93% (-1%)
BZD overuse calculated on 8 months	3.72% (+29%)	5.36% (+1%)
BZD overuse [§]	4.30%	5.92%
Observations	353,792	1,105,177

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA (N = 1,458,969).

Interpretation: In the study population, the average age of those who experienced a WA in 2016 is 37.5 years.

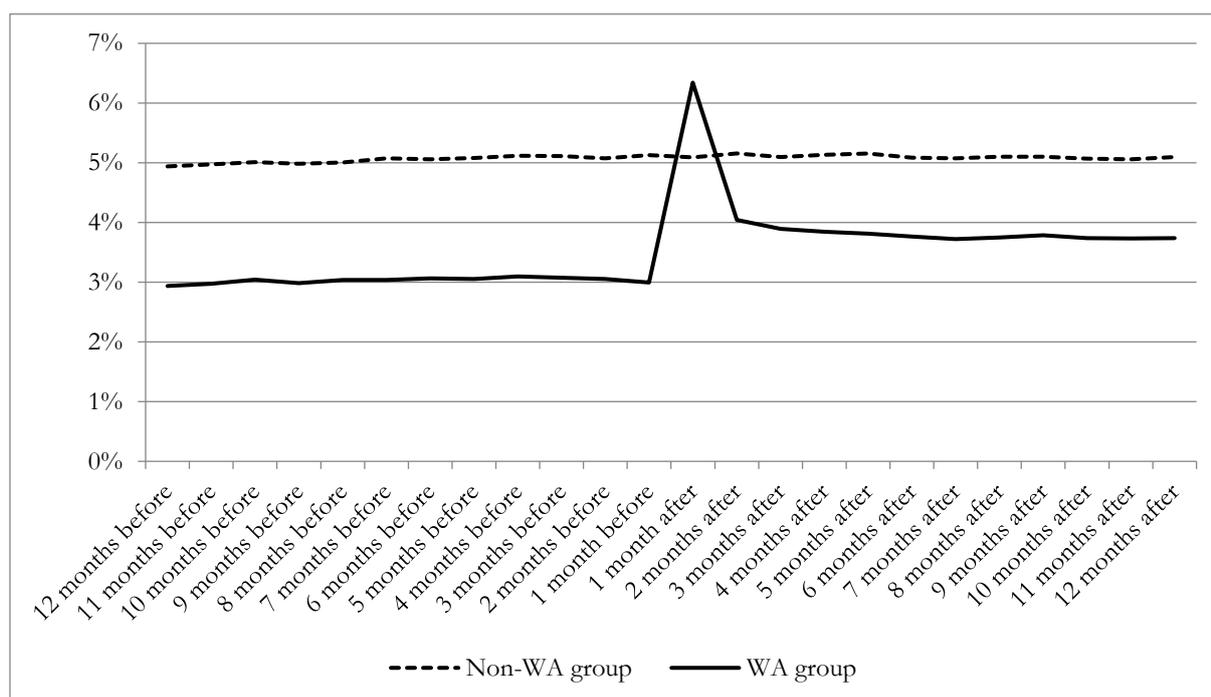
Significance: All figures in this table are significantly different between both groups at the 0.1% threshold.

§: BZD overuse is not comparable between the year before and the year after the WA, because of the four months lagged required.

We see in Table 1.1 statistics relative to BZD use and overuse. People with a WA in 2016 widely increased their use of BZDs during the following year (+38%) and overuse in a slightly smaller proportion (+29%, calculated over eight months after the WA to be comparable to the year before, because of the 4 months lagged required). In the group without WA, BZD use and overuse are higher; the slight decrease in use (-1%) refers to the downward trend in BZD consumption in France during the 2010s (ANSM, 2017), but with a slight increase in overuse (+1%).

Figure 1.1 shows that the proportion of BZD users in the non-WA group is stable during the two-year study period, and higher than the proportion of people with WA, before the WA occurrence. There is a very significant increase in BZD use in the month following the WA, and then it decreases but remains at a higher level than before the WA.

Figure 1.1: Percentage of monthly BZD users in both groups



Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA (N = 1,458,969).

Time refers to months before and after the date of the accident (in the WA group), occurring in 2016.

The majority of the population is made up of individuals who had no BZD dispensation: 85% in the non-WA group and 88% in the WA group during the year before the accident (85% and 83%, respectively, for the following year). For the others, most had a single dispensation: 5.6% of people in the non-WA group and 5.8% of people in the WA group the year before the accident (5.5% and 8%, respectively, for the year after). Among people in the WA group who had a single dispensation in the year following the accident, 27% had a single dispensation in the month following the accident.

During the year following the WA, in the population using a BZD at least one time, a GP prescribed the first BZD in 92% of cases in the WA group, vs. 87% in the non-WA group. After a WA, the ascertainment and declaration of the accident are usually done by a GP, which explains this difference if the GP prescribes the BZD during the same consultation. More statistics about prescribers of the first BZD after the WA are available in Appendix Table 1.A3.

3. Results

3.1. Effect of the occurrence of a WA on BZD use and overuse

The results of the main estimation are presented in Table 1.2. The left-hand column shows the result of the selection equation, that is the estimation of BZD use. A WA occurrence led to an increase by 5.9 percentage points (pp) in the probability of using BZDs the following year, i.e., a 39.3% increase. This is consistent with the statistic of BZD use shown in Table 1.1. The right-hand column shows results regarding BZD overuse, the WA led to an increase of 0.006 pp, i.e., 1.67%. This is far smaller than the increase in BZD overuse presented in Table 1.1. The correlation coefficient of error terms (ρ) is significant at the 0.1% threshold, confirming the selection effect in BZD overuse and leading to reject the probit without selection correction (results are presented in Table 1.A9 in the Appendix). This result means that the strong increase in the risk of overusing BZDs after a WA observed in statistics, comes from the increase in BZD use, but, inside the population using BZDs, the increase of the probability of overuse BZDs is small. In other words, the increase in BZD overuse comes from the increase in the share of people using BZDs once after the WA, which translates into overuse, and not from a strong increase in the probability of overuse among BZD users.

Table 1.2: Estimated impact of WA on the use and overuse of BZDs the following year

Variables	Effect of the WA on BZD use	Effect of the WA on BZD overuse
Population	1,458,969	224,371
Mean of the dependent variable	15% [§]	36% [¶]
Marginal effect of WA (pp)	0.059***	0.006***
Mean effect on the dependent variable	+39.3%***	+1.67%***
Sociodemographic controls	Yes	Yes
Municipality of residence	Yes	Yes
Past BZD use	Yes	Yes
Health status	Yes	Yes
Prescriber characteristics	NA	Yes
ρ (correlation coefficient of error terms)	NA	0.29***

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA (N = 1,458,969).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. NA: not applicable.

Interpretation: Suffering from a WA in 2016 increases the probability of having had at least one BZD use the following year by 39.3%.

§: Percentage of people using BZDs the year following WA in the whole population.

¶: Percentage of people overusing BZDs the year following WA among the population who used it.

Estimates of control variables are consistent with the literature (ANSM, 2017; Beck et al., 2014). BZD use (see Table 1.A5 in the Appendix) increases with past BZD use, age, being a woman, markers of social disadvantage (CMU-C, ACS, and AAH), and bad health (except diabetes). Motherhood has a negative effect on the probability of BZD use (consistent with the

recommendations for use during pregnancy). We see a particularly strong association with psychiatric chronic diseases and antidepressant treatment, which refers to comorbidities and the frequent association between antidepressants and BZDs. The typology of the municipality of residence shows, when significant, that middle hub and isolated municipalities are associated with lower use compared to a large hub, which is consistent with previous literature that shows more use in urban areas (Johnell & Fastbom, 2009).

Regarding overuse (see Table 1.A6 in the Appendix), the effect of age is positive, and being a woman has a protective effect, consistent with findings in the literature on the overuse of BZDs and other substances (Brady & Randall, 1999; Fride Tvetet et al., 2015; Lesén et al., 2010). The insurance variables (proxies of economic deprivation) are strongly related to BZD overuse, in particular for AAH, which refers also to disability. Conversely to results in the selection equation, BZD overuse is associated with the outskirts of large hubs and small municipalities. Past BZD use and overuse, and chronic diseases are positively associated with BZD overuse. The probability of overuse increases when a psychiatrist or multiple prescribers the same day made the first BZD prescription after the WA. This may come from more severe diseases in the case of psychiatrists and misuse in the case of multiple prescribers. Other specialists are associated with less overuse, age and sex of the prescriber are insignificant.

We identify a possible dose-response relationship of WA to BZD use. To do this, we repeat the analyses on the population who were victims of a WA in 2016, using the duration of sick leave following the accident as a proxy for the severity of the accident. We consider only the duration prescribed by GP during the first medical consultation after WA and not any extensions. The variable is divided into quartiles (7, 15, and 45 days). We also add the salary as a control variable in the model, recalculated from the amount of the sickness benefits (which is capped). The sample is therefore composed of individuals who had a WA followed by at least one day off work. The results are summarized in Table 1.3. Full results are available in Tables 1.A7 and 1.A8 in the Appendix.

Table 1.3: Impact of sick leave duration on BZD use and overuse

Sick leave duration	Population	Coefficients (SE)
<i>Estimation of use</i>		
≤ 7 days		Ref.
> 7 days and ≤ 15 days	250,791	0.045*** (0.0094)
> 15 days and ≤ 45 days		0.1073*** (0.0091)
> 45 days		0.3794*** (0.0088)
<i>Estimation of overuse</i>		
≤ 7 days		Ref.
> 7 days and ≤ 15 days	46,280	-0.0031 (0.0278)
> 15 days and ≤ 45 days		0.0276 (0.0266)
> 45 days		0.3945*** (0.0287)

Source: SNDS.

Field: WA group (without missing information about sick leave) (N = 250,791).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

The longer the duration of sick leave, the greater the probability of consuming a BZD in the year following the WA. Similarly, if the effect of the shortest stops is not significant, the longest stops (beyond 45 days) lead to an increased risk of overuse in the year following the WA. This result is substantial, meaning among the population with WA (employed), the risk of both using and overusing BZDs increases with the duration of sick leave, i.e., with the severity of the accident. This result is consistent with the literature showing the harmful effect of occupational accidents on psychological health (Ghisi et al., 2013).

3.2. Robustness checks

The robustness checks aim to account for the selection effect related to employment status and measure and methodological issues. The results are summarized in Table 1.4, the first column being the result of the main estimation, as a reference.

The first two checks are related to the identification variable. The use of the variable *inflammatory or rare disease or HIV/AIDS* (0/1) seems to us the most relevant choice, given its positive association with BZD use but not overuse. Nevertheless, we report the results of two others specifications (see Table 1.A10 in the Appendix): without an identification variable (in this case, the identification relies on the assumption of nonlinearity of the Mill inverse ratio), and using sex as the identification variable. The results are identical to those of the main estimation.

Check 3 is the most important. We focus on the subpopulation of sickness benefits recipients in 2015. As already mentioned and checked using descriptive statistics, we are faced with a serious selection effect related to employment status, the WA group being employed, and the employment status of the non-WA group being unknown (combining employees and non-employees). There is no available variable on employment status in the database. The use of this subpopulation reduces

this selection bias; indeed, it is composed of people with employment in 2015. We assume that this is still the case in 2016. We include in the model the number of days compensated in 2016 and the average daily amount, which is a proxy for salary (for descriptive statistics, see Table 1.A4 in the Appendix). The results are almost identical to those obtained for the selected population. This test greatly increases our confidence in the results, because the employment status does not appear to bias the results. The full results are available in Tables 1.A11 (for the first step) and 1.A12 (for the second step) in the Appendix. The decile of sickness benefits (i.e., wage) is negatively associated with both BZD use and overuse; the decile of sick leave duration in 2015 is only associated with the probability of BZD overuse.

Large differences exist in BZD consumption between both groups. To account accurately for BZD dispensation in the year before WA, we conduct check 4: an exact matching (with replacement). The matching variables are as follows: sociodemographic variables (age, sex, CMU-C, ACS, AAH beneficiary in 2015); BZDs lagged variables (before a WA) (number of BZD dispensation each month (12 variables) and number of different BZDs dispensed each month (12 variables)); and the decile of reimbursable health expenses in 2015. Thanks to the large dataset, 333,347 cases are matched to 300,656 controls, i.e. a matching rate of 94%. The coefficient of the WA variable in the second step is close to the main estimation but non-significant. The slightly higher coefficient in the first step (see Table 1.A11 in the Appendix) and the non-significant coefficient in the second step (see Table 1.A12 in the Appendix) reinforce the finding following the main estimation: when the previous BZD use is accurately controlled in the model, the WA occurrence increases the probability to use BZDs, but not the probability to overuse BZDs among users.

We test two new definitions of overuse in checks 5 and 6: at least five months with at least one BZD dispensation in six consecutive months, and at least six months with BZD dispensation in seven consecutive months, respectively. These two new overuse variables are used as variables explained in the second step of the model. They are also used as control variables in these estimations (for overuse in the year before WA). Results are close to estimates with the previous overuse variable and are available in Table 1.A13 in the Appendix.

Finally, in the baseline model, health status is defined based on 15 diseases. These cover a limited number of individuals since 69% suffer from no disease. Therefore, we test variants using the decile of reimbursable expenditure in 2015 in check 7 (the reimbursable expenditure corresponds to the total amount of care provided and not the amount actually reimbursed by the statutory health insurance). Once again, results are similar to those of the main estimation. Full results of the first and second steps are available in Tables 1.A14 and 1.A15 in the Appendix.

Table 1.4: Robustness checks, results of the outcome equation (estimation of BZD overuse)

	Main model	Check 1	Check 2	Check 3	Check 4	Check 5	Check 6	Check 7
Coefficient of WA variable (SE)	0.1099*** (0.0099)	0.1107*** (0.0099)	0.1176*** (0.0097)	0.0806*** (0.018)	0.0543 (0.0349)	0.1011*** (0.0107)	0.082*** (0.0114)	0.1074*** (0.0097)
Identification variable	Inflammatory or rare disease or HIV/AIDS	None	Sex	Inflammatory or rare disease or HIV/AIDS	None			
Population	Selected population	Selected population	Selected population	Population with sickness benefits	Matched population	Selected population	Selected population	Selected population
Overuse variable	4 out of 5 months with BZDs	4 out of 5 months with BZDs	4 out of 5 months with BZDs	4 out of 5 months with BZDs	4 out of 5 months with BZDs	5 out of 6 months with BZDs	6 out of 7 months with BZDs	4 out of 5 months with BZDs
Health controls	15 health-related variables	15 health-related variables	15 health-related variables	15 health-related variables	15 health-related variables	15 health-related variables	15 health-related variables	Decile of health expenditure
Observations	224,371	224,371	224,371	50,476	70,512	224,371	224,371	224,371

Source: SNDS.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

The results are reinforced by robustness checks. None of the results deviate significantly from the main estimate, particularly for the population with sickness benefits in 2015. This check strongly reduces the possibility that uncontrolled occupational status is a source of bias. In the main estimation, the occurrence of WA increases the BZD overuse by 0.006 pp, which is very small. The nonsignificance of the coefficient in check 4 indicates an even smaller (or null) effect on BZD overuse when past BZD use is properly controlled.

3.3. Heterogeneity

In order to check for heterogeneity, we stratify our sample by sex. The results of estimations are summarized in Table 1.5. Full results are available in Tables 1.A16 and 1.A17 in the Appendix. The occurrence of the WA appears to have a slightly higher effect on benzodiazepine use and overuse in the following year for women.

Table 1.5: Estimation of BZD use and overuse, stratified by sex

Population	Observations	Coefficients (SE)
<i>Estimation of BZD use</i>		
Men	634,786	0.2933*** (0.0052)
Women	824,183	0.3669*** (0.0044)
<i>Estimation of BZD overuse</i>		
Men	79,129	0.0986*** (0.0159)
Women	145,242	0.1181*** (0.013)

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA ($N = 1,458,969$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

4. Discussion

4.1. Discussion of results

The contribution of the two-step selection model is to distinguish between determinants of BZD use and overuse by considering the selection effect in BZD overuse. To our knowledge, this has not been done before in the literature. The occurrence of a WA, which is a shock on health (mental health in particular), increases the probability of BZD use and overuse, as observed in statistics (see Table 1.1 and Figure 1.1). The selection model shows that the increase of BZD overuse comes from the increase in BZD use (+39% after the WA), which translates into overuse (i.e., exceeding the maximum recommended treatment times), and slightly from an increased risk of overuse among users (+1.7%), once corrected from selection bias.

BZDs are prescription drugs, and their use refers both to the patients' health demand and the prescribers' behavior. After years of high consumption in France, public authorities have taken measures to reduce it. Successfully, since BZD consumption has decreased overall since the early 2000s (ANSM, 2017). Prescribing physicians are encouraged to limit the duration of BZD treatments because a portion of their pay depends on the share of their patients overusing BZDs (Michel-Lepage & Ventelou, 2016). Nevertheless, we see that in the WA group, the BZD use translates into overuse for 36% of people in the year following the WA (see Table 1.2).

Results show that public authorities should target primary prescribing to limit the risks associated with BZD overuse after a WA. The risk of overusing BZDs after a WA increases very slightly *when we withdraw the effect on BZD use* compared to the non-WA population, except for WAs resulting in a work interruption of more than 45 days. After a WA, the prescribers (mainly GPs) should question the need for BZDs, knowing the involved risk of overuse. Once prescribed, the focus should be on the more impaired workers to prevent the adverse effects of BZDs from adding to the consequences of the WA. Although being male is associated with more BZD overuse, the WA is associated with a slightly higher increase in the risk of use and overuse among women.

4.2. Limitations

Some limitations come from the information system. We do not know if reimbursed drugs have been used. Regardless of whether the likelihood of unused medicine is significant for a single-box dispensation, we think it is very low for multiple deliveries. Socioeconomic variables are very scarce in the SNDS, which does not provide employment status and profession. That could bias the results if the profession is correlated with both employment and BZD use. Nevertheless, the closeness of results for the population with sickness benefits in 2015 addresses this objection even

if the sample is small. This makes it possible to focus on the employed population in 2015 and to control for recalculated income, which is a strong proxy for the socio-professional category. Moreover, in estimations using the severity of WAs, the population is limited to the employed population, and values of WA benefits are used as a proxy of socioeconomic status (because they are directly related to salary).

The choice of BZD overuse variable can be discussed. Since medical diagnoses are not included in our database, we used a proxy of BZD use for an excessive duration compared to recommendations. Our results are robust to different definitions of the overuse variable. We did not take into account simultaneous use, because of the small case number, or distinguished hypnotic and anxiolytic BZDs, for reasons of simplicity and because of the homogeneity of the BZD class.

As WA could have long-run effects, an interesting extension of this study could be to explore these effects, which was not possible here due to only three years of data available.

5. Conclusion

France is a big consumer of anxiolytic and hypnotic medications, and, in particular, BZDs. Maximum consumption durations are often exceeded, and the non-respect of guidelines can lead to adverse effects, including dependence. Extended use of BZDs is a source of treatment inefficiency and should be avoided regardless of the underlying disease. It is a major concern to identify the factors that could lead to BZD overuse. We provide the first estimation of a WA impact on the risk of BZD overuse.

A WA increases the risk of BZD use and overuse. The selection model makes it possible to show that the effect on BZD overuse comes mainly from an increase in the new BZD consumption and not from an increase in the risk of overusing among BZD users. The risk of overusing BZDs increased among the most impaired workers and women.

In order to limit BZD overuse after a WA, these results call for limiting the first-time BZD prescriptions to those patients for whom it seems most necessary. BZDs showed limited benefits in treating anxiety and insomnia, and it is crucial that their possible adverse effects do not add to the consequences of WAs on health.

6. Appendix

6.1. Additional statistics

Table 1.A1: Health status differences in the WA and the non-WA groups in 2015

Variables	WA group	Non-WA group
Vascular risk treatments (excluding pathologies)	6.81%	10.67%
Psychotropic treatments (excluding pathologies) [§]	6.09%	8.33%
Antidepressant, Lithium, Depakote, and Depamide treatments (excluding pathologies)	3.61%	4.77%
Chronic respiratory diseases	3.47%	4.17%
Maternity (with or without pathologies)	2.45%	4.35%
Psychiatric illnesses	2.28%	4.39%
Diabetes	2.24%	4.08%
Cardioneurovascular diseases	1.66%	3.24%
Inflammatory or rare diseases or HIV or AIDS	1.44%	1.98%
Cancers	1.33%	2.68%
Others long-lasting diseases	1.17%	1.93%
Neurologic or degenerative diseases	0.69%	1.38%
Liver or pancreas diseases	0.58%	0.88%
Addictive disorders	0.51%	0.75%
Neuroleptic treatments	0.26%	0.49%
End-stage renal diseases	0.04%	0.13%
Observations	353,792	1,105,177

Source: SNDS

Field: People with a WA in 2016 in France and randomly selected people without a WA (N = 1,458,969)

Reading guide: In the study population, 6.81% of people with a WA in 2016 are treated for a vascular risk in 2015.

Note: All figures in this table are statistically different between the WA and the non-WA groups at the 0.1% threshold.

§: Not used in the model because this variable includes BZD treatments.

Table 1.A2: Typology of the municipality of residence in the WA and the non-WA groups

Typology of the municipality of residence	WA group	Non-WA group
Municipality belonging to a large hub (10,000 or more jobs)	57.8%	61.69%
Municipality belonging to the outskirts of a large hub	18.62%	17.98%
Multipolarized municipality of large urban areas	5%	4.68%
Municipality belonging to a middle hub (5,000 to less than 10,000 jobs)	2.56%	2.72%
Municipality belonging to the outskirts of a middle hub	0.49%	0.47%
Municipality belonging to a small hub (from 1,500 to less than 5,000 jobs)	3.2%	3.04%
Municipality belonging to the outskirts of a small hub	0.22%	0.21%
Other multipolarized municipality	4.61%	4.21%
Isolated municipality outside a hub influence	3.25%	3.28%
Missing or inconsistent	4.25%	1.71%
Observations	353,792	1,105,177

Source: SNDS

Field: People with a WA in 2016 in France and randomly selected people without a WA (N = 1,458,969)

Reading guide: In the study population, 57.8% of people in the WA group are living in a municipality belonging to a large hub.

Table 1.A3: Characteristics of prescribers of the first BZD after the WA

Variables	Non-WA group	WA group
<i>Prescriber position</i>		
General practitioner	61.62%	65.51%
Psychiatrist	6.64%	3.33%
Non-physician	0.40%	0.24%
Other medical specialties	2.37%	2.35%
Multiple BZD prescribers on the same day	0.15%	0.13%
Missing information	28.82%	28.44%
<i>Prescriber sex</i>		
Man	41.94%	42.61%
Woman	17.04%	17.83%
Missing information	41.01%	39.56%
<i>Prescriber age</i>		
Below 40	5.96%	7.20%
40-59	31.58%	33.38%
60+	21.45%	19.86%
Missing information	41.01%	39.56%

Source: SNDS.

Field: People using at least once a BZD after the WA date (N = 224,371) in the study population.

Reading guide: Among those who used at least once a BZD after the WA date, the first BZD was prescribed by a GP for 61.62% of people in the non-WA group.

Table 1.A4: Descriptive statistics for the population that received sick benefits in 2015

Variables	WA group	Non-WA group
Mean age in 2016	39 years	40 years
% Male	47%	40%
CMU-C in 2015	5.6%	4.5%
Average total expenditure repayable in 2015	€3,189	€5,090
At least one BZD use in the year preceding the WA	19.89%	20.87%
At least one BZD use the year following the WA	22.69%	18.38%
Average daily amount of sick leaves in 2015	€32	€39
Average sick leaves duration in 2015 (days)	34 days	52 days
Observations	97,354	154,448

Source: SNDS.

Field: Population having received at least one daily allowance payment in 2015 for sickness ($N = 251,802$).

Interpretation: In this population, the average age in the WA group in 2016 was 39 years.

Significance: All figures in this table are statistically different between the WA group and the non-WA group at the 0.1% threshold.

6.2. Main results

Table 1.A5: Results of the selection equation (1.1) in the study population

Variables	Coefficients (SE)	Marginal effects
WA	0.3342*** (0.0034)	0.0590
<i>Demographic</i>		
Age in 2016	0.0098*** (0.0001)	0.0016
Sex (ref. = male)	0.2019*** (0.0031)	0.0323
<i>Insurance</i>		
CMU-C	0.1087*** (0.0046)	0.0184
ACS	0.0406*** (0.0076)	0.0067
AAH	0.0843*** (0.0098)	0.0142
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref.	Ref.
Outskirts of a large hub	-0.0057 (0.004)	-0.0009
Multipolarized municipality of large urban areas	-0.0042 (0.007)	-0.0007
Middle hub (5,000 to less than 10,000 jobs)	-0.025** (0.0092)	-0.0041
Outskirts of a middle hub	-0.0093 (0.0214)	-0.0013
Small hub (from 1,500 to less than 5,000 jobs)	0.003 (0.0085)	0.0006
Outskirts of a small hub	-0.0065 (0.0322)	-0.0011
Other multipolarized municipality	-0.0072 (0.0074)	-0.0012
Isolated municipality outside a hub influence	-0.0242** (0.0084)	-0.0038
Missing or inconsistent	-0.1781*** (0.0107)	-0.0263
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	1.1242*** (0.0058)	0.3032
BZD use in the third quarter of the year preceding the WA	0.7407*** (0.0061)	0.1728
BZD use in the second quarter of the year preceding the WA	0.5971*** (0.0063)	0.1306
BZD use in the first quarter of the year preceding the WA	0.589*** (0.0061)	0.1280
<i>Health</i>		
Cancers	0.0301** (0.0092)	0.0050
Cardioneurovascular diseases	0.0278** (0.0088)	0.0046
Vascular risk treatments (excluding pathologies)	0.0223*** (0.0051)	0.0036
Inflammatory or rare diseases or HIV or AIDS	0.0821*** (0.0104)	0.0141
Neurological or degenerative diseases	0.1327*** (0.0129)	0.0229
Psychiatric illnesses	0.4024*** (0.0086)	0.0804
Chronic end-stage renal disease	0.0342 (0.0438)	0.0034
Chronic respiratory diseases	0.1029*** (0.0072)	0.0175
Other long-term conditions	0.0548*** (0.011)	0.0092

Diabetes	-0.0558*** (0.0081)	-0.0088
Diseases of the liver or pancreas	0.0686*** (0.0158)	0.0117
Maternity (with or without pathologies)	-0.0215** (0.0081)	-0.0035
Addictive disorders	0.1027*** (0.0185)	0.0178
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.3726*** (0.0066)	0.0732
Neuroleptic treatments (excluding pathologies)	0.2155*** (0.0218)	0.0407

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA (N = 1,458,969).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 1.A6: Results of the outcome equation (1.2) in the study population

Variables	Coefficients (SE)	Marginal effects
WA	0.1099*** (0.0099)	0.0061
<i>Demographic</i>		
Age in 2016	0.0055*** (0.0004)	0.0002
Sex (ref. = male)	-0.03*** (0.0084)	-0.0016
<i>Insurance</i>		
CMU-C	0.1377*** (0.0106)	0.0080
ACS	0.0569*** (0.016)	0.0031
AAH	0.1947*** (0.0159)	0.0121
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref.	Ref.
Outskirts of a large hub	0.0214* (0.0101)	0.0011
Multipolarized municipality of large urban areas	0.0516** (0.0173)	0.0028
Middle hub (5,000 to less than 10,000 jobs)	0.0411 (0.0221)	0.0022
Outskirts of a middle hub	0.081 (0.0528)	0.0045
Small hub (from 1,500 to less than 5,000 jobs)	0.0841*** (0.0199)	0.0047
Outskirts of a small hub	0.0285 (0.0805)	0.0015
Other multipolarized municipality	0.0769*** (0.0178)	0.0042
Isolated municipality outside a hub influence	0.0425* (0.02)	0.0023
Missing or inconsistent	0.0209 (0.0279)	0.0011
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	0.941*** (0.0163)	0.1053
BZD use in the third quarter of the year preceding the WA	0.3181*** (0.0139)	0.0220
BZD use in the second quarter of the year preceding the WA	0.1069*** (0.0132)	0.0062
BZD use in the first quarter of the year preceding the WA	0.1812*** (0.0123)	0.0111
BZD overuse in the previous year	1.3201*** (0.0128)	0.1771
<i>Health</i>		

Cancers	0.0528** (0.018)	0.0029
Cardioneurovascular diseases	0.1408*** (0.0164)	0.0084
Vascular risk treatments (excluding pathologies)	0.052*** (0.0102)	0.0028
Neurological or degenerative diseases	0.1839*** (0.0224)	0.0114
Psychiatric illnesses	0.4887*** (0.0134)	0.0384
Chronic end-stage renal disease	-0.0382 (0.0801)	-0.0019
Chronic respiratory diseases	0.1408*** (0.0138)	0.0083
Other long-term conditions	0.0442* (0.0205)	0.0024
Diabetes	0.1012*** (0.016)	0.0058
Diseases of the liver or pancreas	0.1286*** (0.0275)	0.0076
Maternity (with or without pathologies)	-0.0053 (0.0266)	-0.0003
Addictive disorders	0.0561* (0.0249)	0.0031
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.297*** (0.011)	0.0200
Neuroleptic treatments (excluding pathologies)	0.3154*** (0.0289)	0.0219
<i>Prescriber position</i>		
GP	Ref.	Ref.
Another specialist	-0.1336*** (0.0239)	-0.0146
Missing information	-0.5639*** (0.0137)	-0.0461
Multiple	0.2088* (0.0953)	0.0281
Non-physician	0.0734 (0.0586)	0.0091
Psychiatrist	0.1917*** (0.0154)	0.0255
<i>Sex and age of the prescriber</i>		
Missing information	0.0943*** (0.0179)	0.0046
Male prescriber	0.0154 (0.0102)	0.0007
Age < 40	Ref.	Ref.
Age 40-59	-0.0166 (0.0153)	-0.0009
Age > 59	0.0157 (0.0163)	0.0008
ρ (correlation coefficient of error terms)	0.2931*** (0.0266)	NA

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA, using at least once a BZD after the WA date (N = 224,371).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.3. Complementary analysis

Table 1.A7: Results of the selection equation (1.1) with the duration of sick leave in the WA group

Variables	Coefficients (SE)
<i>Duration of sick leave following the WA</i>	
Sick leave ≤ 7 days	Ref.
Sick leave > 7 days and ≤ 15 days	0.045*** (0.0094)
Sick leave > 15 days and ≤ 45 days	0.1073*** (0.0091)
Sick leave > 45 days	0.3794*** (0.0088)
<i>Sociodemographic</i>	
Decile of daily wage	0.0077*** (0.0012)
Age in 2016	0.0074*** (0.0003)
Sex (ref. = male)	0.3165*** (0.0067)
<i>Insurance</i>	
CMU-C	0.1173*** (0.0106)
ACS	0.0639*** (0.0157)
AAH	0.0603 (0.0326)
<i>Typology of the municipality</i>	
Large hub (10,000 or more jobs)	Ref.
Outskirts of a large hub	-0.0062 (0.0085)
Multipolarized municipality of large urban areas	-0.0086 (0.0148)
Middle hub (5,000 to less than 10,000 jobs)	-0.0247 (0.0202)
Outskirts of a middle hub	-0.003 (0.046)
Small hub (from 1,500 to less than 5,000 jobs)	-0.0454* (0.0184)
Outskirts of a small hub	0.1503* (0.0642)
Other multipolarized municipality	-0.0055 (0.0154)
Isolated municipality outside a hub influence	-0.0156 (0.0181)
Missing or inconsistent	-0.2069*** (0.022)
<i>Past BZD use</i>	
BZD use in the last quarter of the year preceding the WA	0.9439*** (0.0144)
BZD use in the third quarter of the year preceding the WA	0.6742*** (0.0147)
BZD use in the second quarter of the year preceding the WA	0.5413*** (0.015)
BZD use in the first quarter of the year preceding the WA	0.5189*** (0.0148)
<i>Health</i>	
Cancers	0.0089 (0.0271)
Cardioneurovascular diseases	-0.0166 (0.0244)
Vascular risk treatments (excluding pathologies)	-0.0074 (0.0127)
Inflammatory or rare diseases or HIV or AIDS	0.0191 (0.0259)
Neurological or degenerative diseases	0.1909*** (0.0359)

Psychiatric illnesses	0.401*** (0.0235)
Chronic end-stage renal disease	-0.2134 (0.1671)
Chronic respiratory diseases	0.0655*** (0.0166)
Other long-term conditions	0.0237 (0.029)
Diabetes	-0.1071*** (0.0211)
Diseases of the liver or pancreas	0.0406 (0.0391)
Maternity (with or without pathologies)	0.0043 (0.0203)
Addictive disorders	0.0749 (0.0465)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.3445*** (0.0167)
Neuroleptic treatments (excluding pathologies)	0.2377*** (0.061)

Source: SNDS.

Field: WA group (without missing information about sick leave) (N = 250,791).

*Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.*

Table 1.A8: Results of the outcome equation (1.2) with the duration of sick leave in the WA group

Variables	Coefficients (SE)
<i>Duration of sick leave following the WA</i>	
Sick leave ≤ 7 days	Ref.
Sick leave > 7 days and ≤ 15 days	-0.0031 (0.0278)
Sick leave > 15 days and ≤ 45 days	0.0276 (0.0266)
Sick leave > 45 days	0.3945*** (0.0287)
<i>Sociodemographic variables</i>	
Decile of daily wage	-0.0107*** (0.0032)
Age in 2016	0.0068*** (0.0009)
Sex (ref. = male)	-0.0914*** (0.0234)
<i>Insurance</i>	
CMU-C	0.0661* (0.0268)
ACS	0.0071 (0.0398)
AAH	0.1895** (0.0617)
<i>Typology of the municipality</i>	
Large hub (10,000 or more jobs)	Ref.
Outskirts of a large hub	-0.0015 (0.0227)
Multipolarized municipality of large urban areas	0.0357 (0.0388)
Middle hub (5,000 to less than 10,000 jobs)	-0.0394 (0.054)
Outskirts of a middle hub	0.138 (0.1184)
Small hub (from 1,500 to less than 5,000 jobs)	0.0939* (0.0454)
Outskirts of a small hub	0.0124 (0.1601)
Other multipolarized municipality	-0.0151 (0.0406)
Isolated municipality outside a hub influence	0.0072 (0.047)
Missing or inconsistent	0.1166 (0.0663)
<i>Past BZD use</i>	
BZD use in the last quarter of the year preceding the WA	0.7307*** (0.0473)
BZD use in the third quarter of the year preceding the WA	0.195*** (0.0378)
BZD use in the second quarter of the year preceding the WA	0.0629 (0.034)
BZD use in the first quarter of the year preceding the WA	0.1089*** (0.0318)
BZD overuse in the previous year	1.3188*** (0.0333)
<i>Health</i>	
Cancers	-0.005 (0.0564)
Cardioneurovascular diseases	0.0319 (0.0504)
Vascular risk treatments (excluding pathologies)	0.0697** (0.0265)
Neurological or degenerative diseases	0.1955** (0.0717)
Psychiatric illnesses	0.3549*** (0.0399)

Chronic end-stage renal disease	-0.3081 (0.3368)
Chronic respiratory diseases	0.116*** (0.0349)
Other long-term conditions	0.0146 (0.0619)
Diabetes	0.0722 (0.0464)
Diseases of the liver or pancreas	0.0146 (0.0807)
Maternity (with or without pathologies)	0.0506 (0.0601)
Addictive disorders	0.0576 (0.0699)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.257*** (0.0292)
Neuroleptic treatments (excluding pathologies)	0.4016*** (0.0844)
<i>Prescriber position</i>	
GP	Ref.
Another specialist	-0.1645** (0.0554)
Missing information	-0.4009*** (0.0313)
Multiple	0.3071 (0.1887)
Non-physician	0.1411 (0.1672)
Psychiatrist	0.2729*** (0.0425)
<i>Sex and age of the prescriber</i>	
Missing information	0.0175 (0.0399)
Male prescriber	-0.0214 (0.0232)
Age < 40	Ref.
Age 40-59	0.0158 (0.0333)
Age > 59	0.0982** (0.036)
ρ (correlation coefficient of error terms)	-0.0154 (0.0733)

Source: SNDS.

Field: WA group (without missing information about sick leave), people using BZD at least once after the WA date (N = 46,280)

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.4. Robustness checks

6.4.1. Results of the probit

Table 1.A9: Results of the probit equation among BZD users after the WA

Variables	Coefficients (SE)
WA	0.06*** (0.009)
<i>Demographic</i>	
Age in 2016	0.0039*** (0.0004)
Sex (ref. = male)	-0.0623*** (0.008)
<i>Insurance</i>	
CMU-C	0.1206*** (0.0108)
ACS	0.0532** (0.0162)
AAH	0.186*** (0.0161)
<i>Typology of the municipality</i>	
Large hub (10,000 or more jobs)	Ref.
Outskirts of a large hub	0.0233* (0.0103)
Multipolarized municipality of large urban areas	0.0548** (0.0177)
Middle hub (5,000 to less than 10,000 jobs)	0.0461* (0.0225)
Outskirts of a middle hub	0.1033 (0.0539)
Small hub (from 1,500 to less than 5,000 jobs)	0.087*** (0.0203)
Outskirts of a small hub	0.0394 (0.0821)
Other multipolarized municipality	0.0821*** (0.0181)
Isolated municipality outside a hub influence	0.0473* (0.0204)
Missing or inconsistent	0.0513 (0.0285)
<i>Past BZD use</i>	
BZD use in the last quarter of the year preceding the WA	0.7675*** (0.0094)
BZD use in the third quarter of the year preceding the WA	0.2084*** (0.0106)
BZD use in the second quarter of the year preceding the WA	0.0185 (0.011)
BZD use in the first quarter of the year preceding the WA	0.1017*** (0.0104)
BZD overuse in the previous year	1.3663*** (0.0117)
<i>Health</i>	
Cancers	0.0494** (0.0182)
Cardioneurovascular diseases	0.1384*** (0.0167)
Vascular risk treatments (excluding pathologies)	0.0513*** (0.0104)
Inflammatory or rare diseases or HIV or AIDS	0.0223 (0.0216)
Neurological or degenerative diseases	0.1654*** (0.0226)
Psychiatric illnesses	0.4408*** (0.013)

Chronic end-stage renal disease	-0.0517 (0.0814)
Chronic respiratory diseases	0.1316*** (0.014)
Other long-term conditions	0.0352 (0.0208)
Diabetes	0.1115*** (0.0162)
Diseases of the liver or pancreas	0.1194*** (0.028)
Maternity (with or without pathologies)	-0.002 (0.0275)
Addictive disorders	0.0369 (0.025)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.2491*** (0.0104)
Neuroleptic treatments (excluding pathologies)	0.2972*** (0.029)
<i>Prescriber position</i>	
GP	Ref.
Another specialist	-0.1316*** (0.0244)
Missing information	-0.5779*** (0.0138)
Multiple	0.2515** (0.0975)
Non-physician	0.0891 (0.06)
Psychiatrist	0.1901*** (0.0156)
<i>Sex and age of the prescriber</i>	
Missing information	0.0931*** (0.0183)
Male prescriber	0.016 (0.0105)
Age < 40	Ref.
Age 40-59	-0.0172 (0.0156)
Age > 59	0.0158 (0.0167)

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA, using at least once a BZD after the WA date (N = 224,371).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.4.2. Other identification variables

Table 1.A10: Coefficients (SE) of the outcome equation (1.2) with other identification variables

Variables	Without an identification variable	Sex as the identification variable
WA	0.1107*** (0.0099)	0.1176*** (0.0097)
<i>Demographic</i>		
Age in 2016	0.0055*** (0.0004)	0.0057*** (0.0004)
Sex (ref. = male)	-0.0296*** (0.0084)	NA
<i>Insurance</i>		
CMU-C	0.1388*** (0.0106)	0.14*** (0.0106)
ACS	0.0567*** (0.016)	0.0544*** (0.0159)
AAH	0.1945*** (0.0159)	0.1999*** (0.0158)
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref. 0.0215* (0.0101)	Ref. 0.0212* (0.01)
Outskirts of a large hub	0.052** (0.0173)	0.0538** (0.0172)
Multipolarized municipality of large urban areas	0.0401 (0.0221)	0.0353 (0.022)
Middle hub (5,000 to less than 10,000 jobs)	0.0815 (0.0528)	0.076 (0.0526)
Outskirts of a middle hub	0.0847*** (0.0199)	0.0825*** (0.0198)
Small hub (from 1,500 to less than 5,000 jobs)	0.0267 (0.0805)	0.023 (0.0802)
Outskirts of a small hub	0.0775*** (0.0178)	0.0796*** (0.0177)
Other multipolarized municipality	0.0427* (0.02)	0.0396* (0.0199)
Isolated municipality outside a hub influence	0.0218 (0.0279)	0.0219 (0.0277)
Missing or inconsistent		
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	0.9424*** (0.0163)	0.9592*** (0.0154)
BZD use in the third quarter of the year preceding the WA	0.3198*** (0.0139)	0.3299*** (0.0135)
BZD use in the second quarter of the year preceding the WA	0.1066*** (0.0132)	0.117*** (0.0129)
BZD use in the first quarter of the year preceding the WA	0.1813*** (0.0123)	0.1889*** (0.012)
BZD overuse in the previous year	1.3192*** (0.0128)	1.3128*** (0.0128)
<i>Health</i>		
Cancers	0.0524** (0.018)	0.0498** (0.0179)
Cardioneurovascular diseases	0.1401*** (0.0164)	0.1473*** (0.0162)
Vascular risk treatments (excluding pathologies)	0.0522*** (0.0102)	0.0528*** (0.0102)
Inflammatory or rare diseases or HIV or AIDS	0.0348 (0.0213)	0.0359 (0.0213)
Neurological or degenerative diseases	0.1834*** (0.0224)	0.1837*** (0.0223)
Psychiatric illnesses	0.4903*** (0.0134)	0.4935*** (0.0132)
Chronic end-stage renal disease	-0.0387 (0.0801)	-0.0362 (0.0798)
Chronic respiratory diseases	0.1395*** (0.0138)	0.1429*** (0.0138)

Other long-term conditions	0.0428* (0.0205)	0.0423* (0.0205)
Diabetes	0.1008*** (0.016)	0.1006*** (0.0159)
Diseases of the liver or pancreas	0.1266*** (0.0276)	0.1325*** (0.0274)
Maternity (with or without pathologies)	-0.005 (0.0266)	-0.0135 (0.0262)
Addictive disorders	0.0568* (0.0249)	0.0631* (0.0247)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.2972*** (0.011)	0.2985*** (0.0109)
Neuroleptic treatments (excluding pathologies)	0.3166*** (0.0289)	0.3275*** (0.0287)
<i>Prescriber position</i>		
GP	Ref.	Ref.
Another specialist	-0.1329*** (0.0239)	-0.1284*** (0.0237)
Missing information	-0.5627*** (0.0137)	-0.5613*** (0.0137)
Multiple	0.1978* (0.0951)	0.1726 (0.0944)
Non-physician	0.0707 (0.0586)	0.067 (0.0582)
Psychiatrist	0.1921*** (0.0154)	0.191*** (0.0153)
<i>Sex and age of the prescriber</i>		
Missing information	0.0936*** (0.0179)	0.0967*** (0.0178)
Male prescriber	0.0156 (0.0102)	0.0169 (0.0102)
Age < 40	Ref.	Ref.
Age 40-59	-0.0167 (0.0153)	-0.0165 (0.0152)
Age > 59	0.0158 (0.0163)	0.016 (0.0162)
ρ (correlation coefficient of error terms)	0.2954*** (0.0267)	0.3291*** (0.0255)

Source: *SNDS*.

Field: People with *WA* in 2016 in France and randomly selected people without *WA*, using at least once a BZD after the *WA* date ($N = 224,371$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.4.3. Other populations

Table 1.A11: Coefficients (SE) of the selection equation (1.1) in the population with sickness benefits and the matched population

Variables	Population with sickness benefits in 2015	Matched population
WA	0.2685*** (0.0067)	0.3376*** (0.0044)
Decile of sickness benefits	-0.0062*** (0.0013)	NA
Decile of sick leave duration in 2015	0.0023 (0.0013)	NA
<i>Demographic</i>		
Age in 2016	0.0088*** (0.0003)	0.0104*** (0.0002)
Sex (ref. = male)	0.2385*** (0.0073)	0.2481*** (0.0045)
<i>Insurance</i>		
CMU-C	0.1011*** (0.015)	0.1354*** (0.0074)
ACS	0.0676*** (0.0189)	0.083*** (0.0116)
AAH	0.0156 (0.0295)	-0.0289 (0.0249)
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref.	Ref.
Outskirts of a large hub	-0.0026 (0.0083)	-0.0061 (0.0058)
Multipolarized municipality of large urban areas	-0.0128 (0.0147)	-0.0099 (0.0102)
Middle hub (5,000 to less than 10,000 jobs)	-0.0221 (0.021)	-0.0547*** (0.014)
Outskirts of a middle hub	0.0625 (0.0437)	-0.0162 (0.0313)
Small hub (from 1,500 to less than 5,000 jobs)	0.018 (0.0188)	-0.0264* (0.0128)
Outskirts of a small hub	0.0246 (0.0669)	0.0338 (0.0456)
Other multipolarized municipality	-0.0092 (0.0153)	-0.0156 (0.0107)
Isolated municipality outside a hub influence	-0.0402* (0.0188)	-0.0261* (0.0125)
Missing or inconsistent	-0.0437 (0.0255)	-0.267*** (0.0147)
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	1.0045*** (0.0117)	0.9814*** (0.0119)
BZD use in the third quarter of the year preceding the WA	0.6439*** (0.0118)	0.7521*** (0.0125)
BZD use in the second quarter of the year preceding the WA	0.5026*** (0.0118)	0.6752*** (0.0127)
BZD use in the first quarter of the year preceding the WA	0.4525*** (0.0115)	0.6394*** (0.0123)
<i>Health</i>		
Cancers	-0.0146 (0.0181)	0.0057 (0.017)
Cardioneurovascular diseases	-0.0093 (0.0187)	-0.0064 (0.0164)
Vascular risk treatments (excluding pathologies)	0.0305** (0.0115)	0.0187* (0.0085)
Inflammatory or rare diseases or HIV or AIDS	0.0734*** (0.0206)	0.0657*** (0.017)
Neurological or degenerative diseases	0.1134*** (0.0302)	0.1901*** (0.0235)
Psychiatric illnesses	0.3757*** (0.0185)	0.4757*** (0.0161)

Chronic end-stage renal disease	0.0198 (0.0942)	-0.1119 (0.1008)
Chronic respiratory diseases	0.0642*** (0.0153)	0.101*** (0.0114)
Other long-term conditions	0.0442 (0.024)	0.0325 (0.019)
Diabetes	-0.0433* (0.0194)	-0.0701*** (0.0146)
Diseases of the liver or pancreas	0.0528 (0.0323)	0.1067*** (0.0275)
Maternity (with or without pathologies)	-0.1689*** (0.0134)	-0.0345** (0.0125)
Addictive disorders	0.1394*** (0.0393)	0.1095** (0.034)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.283*** (0.0127)	0.4748*** (0.0113)
Neuroleptic treatments (excluding pathologies)	0.2124*** (0.0508)	0.3109*** (0.0418)

Source: SNDS.

Field: Left: study population with sickness benefits (N = 251,802); Right: WA group and matched non-WA group (N = 666,694).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 1.A12: Coefficients (SE) of the outcome equation (1.2) in the population with sickness benefits and the matched population

Variables	Population with sickness benefits in 2015	Matched population
WA	0.0806*** (0.018)	0.0543 (0.0349)
Decile of sickness benefits	-0.0166*** (0.0031)	NA
Decile of sick leave duration in 2015	0.0081** (0.0029)	NA
<i>Demographic</i>		
Age in 2016	0.0069*** (0.0009)	0.0081*** (0.0013)
Sex (ref. = male)	-0.0271 (0.0196)	-0.0731** (0.0275)
<i>Insurance</i>		
CMU-C	0.0582 (0.033)	0.1392*** (0.0278)
ACS	0.0238 (0.0421)	0.061 (0.0403)
AAH	0.1722** (0.0525)	0.1525* (0.0716)
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref.	Ref.
Outskirts of a large hub	0.0046 (0.0197)	-0.0091 (0.02)
Multipolarized municipality of large urban areas	0.0651 (0.0337)	0.0882** (0.0339)
Middle hub (5,000 to less than 10,000 jobs)	0.0319 (0.0475)	-0.0455 (0.0507)
Outskirts of a middle hub	0.0613 (0.1032)	0.0264 (0.1083)
Small hub (from 1,500 to less than 5,000 jobs)	0.1216** (0.041)	0.0663 (0.0426)
Outskirts of a small hub	0.0749 (0.153)	-0.0642 (0.1596)
Other multipolarized municipality	0.0497 (0.0355)	0.0005 (0.0372)
Isolated municipality outside a hub influence	-0.0135 (0.0437)	0.0753 (0.0411)
Missing or inconsistent	0.1003 (0.0585)	0.1854** (0.0579)
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	0.944*** (0.0335)	0.4066*** (0.0896)
BZD use in the third quarter of the year preceding the WA	0.3198*** (0.0289)	-0.0637 (0.0671)
BZD use in the second quarter of the year preceding the WA	0.0972*** (0.027)	-0.0047 (0.0634)
BZD use in the first quarter of the year preceding the WA	0.1796*** (0.024)	-0.0149 (0.0603)
BZD overuse in the previous year	1.1641*** (0.0276)	2.4115*** (0.1254)
<i>Health</i>		
Cancers	0.0266 (0.0358)	0.0794 (0.0484)
Cardioneurovascular diseases	0.0951** (0.0357)	-0.0112 (0.0494)
Vascular risk treatments (excluding pathologies)	0.0688** (0.0219)	0.0536* (0.0249)
Neurological or degenerative diseases	0.1963*** (0.0546)	0.164* (0.0662)
Psychiatric illnesses	0.3933*** (0.0292)	0.4644*** (0.0595)
Chronic end-stage renal disease	-0.1146 (0.1771)	-0.6273 (0.5198)

Chronic respiratory diseases	0.1078*** (0.0295)	0.1162*** (0.0346)
Other long-term conditions	-0.027 (0.0463)	0.0057 (0.057)
Diabetes	0.0859* (0.0393)	0.1263*** (0.0433)
Diseases of the liver or pancreas	-0.0361 (0.06)	0.0501 (0.0773)
Maternity (with or without pathologies)	-0.0467 (0.0404)	0.0425 (0.0469)
Addictive disorders	0.1034* (0.0512)	0.0226 (0.0755)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.2378*** (0.0219)	0.3238*** (0.051)
Neuroleptic treatments (excluding pathologies)	0.3146*** (0.0674)	0.4192*** (0.0917)
<i>Prescriber position</i>		
GP	Ref.	Ref.
Another specialist	-0.0864 (0.0501)	-0.1971*** (0.05)
Missing information	-0.5783*** (0.0294)	-0.4176*** (0.0266)
Multiple	0.2485 (0.1859)	0.8007*** (0.2066)
Non-physician	0.0353 (0.1453)	-0.027 (0.1328)
Psychiatrist	0.1623*** (0.0301)	0.419*** (0.0393)
<i>Sex and age of the prescriber</i>		
Missing information	0.17*** (0.0367)	0.1182** (0.0369)
Male prescriber	0.0279 (0.0207)	-0.0387 (0.0217)
Age < 40	Ref.	Ref.
Age 40-59	0.025 (0.0305)	0.0165 (0.0315)
Age > 59	0.0495 (0.0328)	0.0988** (0.0339)
ρ (correlation coefficient of error terms)	0.3117*** (0.067)	-0.1036 (0.1155)

Source: SNDS.

Field: Left: people using BZDs at least once among the study population with sickness benefits ($N = 50,476$); Right: people using BZDs at least once among the WA group and the matched non-WA group ($N = 70,512$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.4.4. Other overuse variables

Table 1.A13: Coefficients (SE) of the outcome equation (1.2) with other overuse variables

Variables	Overuse: 5 out of 6 months with BZDs	Overuse: 6 out of 7 months with BZDs
WA	0.1011*** (0.0107)	0.082*** (0.0114)
<i>Demographic</i>		
Age in 2016	0.0046*** (0.0004)	0.0034*** (0.0005)
Sex (ref. = male)	-0.0512*** (0.0089)	-0.0556*** (0.0094)
<i>Insurance</i>		
CMU-C	0.1471*** (0.0113)	0.1391*** (0.0118)
ACS	0.0437** (0.0166)	0.0606*** (0.0171)
AAH	0.2031*** (0.0161)	0.2023*** (0.0162)
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref. 0.0125	Ref. 0.0207
Outskirts of a large hub	(0.0109)	(0.0115)
Multipolarized municipality of large urban areas	0.053** (0.0186)	0.0669*** (0.0196)
Middle hub (5,000 to less than 10,000 jobs)	0.0373 (0.0235)	0.0524* (0.0245)
Outskirts of a middle hub	0.1178* (0.0568)	0.07 (0.0615)
Small hub (from 1,500 to less than 5,000 jobs)	0.075*** (0.0212)	0.1013*** (0.0221)
Outskirts of a small hub	0.0591 (0.0856)	0.0012 (0.0921)
Other multipolarized municipality	0.0703*** (0.0191)	0.068*** (0.0201)
Isolated municipality outside a hub influence	0.0449* (0.0213)	0.0254 (0.0224)
Missing or inconsistent	-0.003 (0.03)	0.0049 (0.0317)
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	0.9331*** (0.0183)	0.9431*** (0.02)
BZD use in the third quarter of the year preceding the WA	0.3848*** (0.0147)	0.4385*** (0.0157)
BZD use in the second quarter of the year preceding the WA	0.0887*** (0.0139)	0.0931*** (0.0146)
BZD use in the first quarter of the year preceding the WA	0.1383*** (0.0131)	0.1567*** (0.0136)
BZD overuse in the previous year	1.4797*** (0.0126)	1.5606*** (0.0127)
<i>Health</i>		
Cancers	0.0344 (0.0189)	0.0328 (0.0195)
Cardioneurovascular diseases	0.1174*** (0.017)	0.1169*** (0.0173)
Vascular risk treatments (excluding pathologies)	0.0468*** (0.0108)	0.055*** (0.0112)
Neurological or degenerative diseases	0.1748*** (0.0229)	0.1807*** (0.0232)
Psychiatric illnesses	0.4606*** (0.0137)	0.4429*** (0.0139)
Chronic end-stage renal disease	-0.0096 (0.0833)	0.045 (0.0851)
Chronic respiratory diseases	0.1246*** (0.0144)	0.1248*** (0.0148)
Other long-term conditions	0.0549** (0.0212)	0.0557* (0.0217)

Diabetes	0.1034*** (0.0166)	0.1277*** (0.017)
Diseases of the liver or pancreas	0.0899** (0.0281)	0.0744** (0.0284)
Maternity (with or without pathologies)	-0.0403 (0.0305)	-0.0472 (0.0339)
Addictive disorders	0.0408 (0.0248)	0.0417 (0.0246)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.2753*** (0.0115)	0.2715*** (0.0118)
Neuroleptic treatments (excluding pathologies)	0.2995*** (0.0287)	0.2728*** (0.0287)
<i>Prescriber position</i>		
GP	Ref.	Ref.
Another specialist	-0.1202*** (0.0258)	-0.1519*** (0.0278)
Missing information	-0.5972*** (0.0149)	-0.6308*** (0.0162)
Multiple	0.2204* (0.0962)	0.2192* (0.0962)
Non-physician	0.0284 (0.0613)	0.0245 (0.0635)
Psychiatrist	0.1791*** (0.0156)	0.1546*** (0.0157)
<i>Sex and age of the prescriber</i>		
Missing information	0.0961*** (0.019)	0.0971*** (0.0198)
Male prescriber	0.0219* (0.0109)	0.0263* (0.0113)
Age < 40	Ref.	Ref.
Age 40-59	-0.0123 (0.0162)	-0.0094 (0.017)
Age > 59	0.0091 (0.0173)	0.007 (0.0181)
ρ (correlation coefficient of error terms)	0.2507*** (0.0298)	0.2437*** (0.0331)

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA, using at least once a BZD after the WA date (N = 224,371).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.4.5. Other health control variable

Table 1.A14: Results of the selection equation (1.1) with other health control variable

Variables	Coefficients (SE)
WA	0.3285*** (0.0034)
<i>Demographic</i>	
Age in 2016	0.0087*** (0.0001)
Sex (ref. = male)	0.1704*** (0.0031)
<i>Insurance</i>	
CMU-C	0.0832*** (0.0046)
ACS	0.044*** (0.0076)
AAH	0.1913*** (0.0091)
<i>Typology of the municipality</i>	
Large hub (10,000 or more jobs)	Ref.
Outskirts of a large hub	-0.0034 (0.004)
Multipolarized municipality of large urban areas	-0.0051 (0.007)
Middle hub (5,000 to less than 10,000 jobs)	-0.0198* (0.0092)
Outskirts of a middle hub	-0.0083 (0.0214)
Small hub (from 1,500 to less than 5,000 jobs)	0.0093 (0.0085)
Outskirts of a small hub	-0.0064 (0.0321)
Other multipolarized municipality	-0.0035 (0.0074)
Isolated municipality outside a hub influence	-0.0152 (0.0084)
Missing or inconsistent	-0.173*** (0.0107)
<i>Past BZD use</i>	
BZD use in the last quarter of the year preceding the WA	1.1381*** (0.0058)
BZD use in the third quarter of the year preceding the WA	0.7568*** (0.0061)
BZD use in the second quarter of the year preceding the WA	0.6211*** (0.0062)
BZD use in the first quarter of the year preceding the WA	0.6223*** (0.0061)
<i>Health</i>	
Decile of health expenditure in 2015	0.0411*** (0.0006)

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA (N = 1,458,969).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 1.A15: Results of the outcome equation (1.2) with other health control variables

Variables	Coefficients (SE)
WA	0.1074*** (0.0097)
<i>Demographic</i>	
Age in 2016	0.006*** (0.0003)
Sex (ref. = male)	-0.0493*** (0.008)
<i>Insurance</i>	
CMU-C	0.1329*** (0.0103)
ACS	0.0825*** (0.0156)
AAH	0.3501*** (0.0149)
<i>Typology of the municipality</i>	
Large hub (10,000 or more jobs)	Ref.
Outskirts of a large hub	0.0199* (0.0098)
Multipolarized municipality of large urban areas	0.0448** (0.017)
Middle hub (5,000 to less than 10,000 jobs)	0.0425* (0.0216)
Outskirts of a middle hub	0.0692 (0.0517)
Small hub (from 1,500 to less than 5,000 jobs)	0.0855*** (0.0195)
Outskirts of a small hub	0.0419 (0.0788)
Other multipolarized municipality	0.0794*** (0.0174)
Isolated municipality outside a hub influence	0.0456* (0.0196)
Missing or inconsistent	0.0145 (0.0272)
<i>Past BZD use</i>	
BZD use in the last quarter of the year preceding the WA	0.9962*** (0.0149)
BZD use in the third quarter of the year preceding the WA	0.3613*** (0.0133)
BZD use in the second quarter of the year preceding the WA	0.1506*** (0.0128)
BZD use in the first quarter of the year preceding the WA	0.2396*** (0.012)
BZD overuse in the previous year	1.3484*** (0.013)
<i>Health</i>	
Decile of health expenditure in 2015	0.0425*** (0.0016)
<i>Prescriber position</i>	
GP	Ref.
Another specialist	-0.158*** (0.0234)
Missing information	-0.583*** (0.0136)
Multiple	0.2837** (0.0931)
Non-physician	0.1127* (0.0567)
Psychiatrist	0.2676*** (0.0147)
<i>Sex and age of the prescriber</i>	
Missing information	0.1293*** (0.0174)
Male prescriber	0.0136 (0.01)

Age < 40	Ref.
Age 40-59	-0.0205 (0.0149)
Age > 59	0.0102 (0.0159)
ρ (correlation coefficient of error terms)	0.3847*** (0.0257)

Source: SNDS.

Field: People with WA in 2016 in France and randomly selected people without WA, using at least once a BZD after the WA date (N = 224,371).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.5. Heterogeneity analysis results

Table 1.A16: Coefficients (SE) of the selection equation (1.1) by sex

Variables	Men	Women
WA	0.2933*** (0.0052)	0.3669*** (0.0044)
<i>Demographic</i>		
Age in 2016	0.0104*** (0.0002)	0.0094*** (0.0002)
<i>Insurance</i>		
CMU-C	0.1194*** (0.0077)	0.1026*** (0.0058)
ACS	0.0541*** (0.0127)	0.0333*** (0.0095)
AAH	0.1214*** (0.0145)	0.0404** (0.0134)
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref.	Ref.
Outskirts of a large hub	-0.0242*** (0.0065)	0.0065 (0.0051)
Multipolarized municipality of large urban areas	-0.0207 (0.0114)	0.0069 (0.0089)
Middle hub (5,000 to less than 10,000 jobs)	-0.0261 (0.015)	-0.0235* (0.0117)
Outskirts of a middle hub	0.012 (0.0343)	-0.02 (0.0273)
Small hub (from 1,500 to less than 5,000 jobs)	-0.0192 (0.014)	0.0194 (0.0108)
Outskirts of a small hub	0.0557 (0.0503)	-0.051 (0.0418)
Other multipolarized municipality	-0.0246* (0.012)	0.0045 (0.0093)
Isolated municipality outside a hub influence	-0.0242 (0.0138)	-0.022* (0.0106)
Missing or inconsistent	-0.2033*** (0.0171)	-0.1613*** (0.0138)
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	1.2186*** (0.01)	1.0727*** (0.0072)
BZD use in the third quarter of the year preceding the WA	0.7691*** (0.0106)	0.7212*** (0.0075)
BZD use in the second quarter of the year preceding the WA	0.6207*** (0.0109)	0.5827*** (0.0077)
BZD use in the first quarter of the year preceding the WA	0.609*** (0.0107)	0.5768*** (0.0075)
<i>Health</i>		
Cancers	0.0236 (0.0169)	0.0368*** (0.011)
Cardiovascular diseases	0.019 (0.0115)	0.0157 (0.014)
Vascular risk treatments (excluding pathologies)	0.0263** (0.0081)	0.0198** (0.0065)

Inflammatory or rare diseases or HIV or AIDS	0.0829*** (0.0169)	0.0825*** (0.0132)
Neurological or degenerative diseases	0.1598*** (0.0193)	0.1091*** (0.0173)
Psychiatric illnesses	0.4001*** (0.0137)	0.4006*** (0.011)
Chronic end-stage renal disease	0.0712 (0.0602)	-0.0149 (0.064)
Chronic respiratory diseases	0.0807*** (0.0119)	0.1157*** (0.0091)
Other long-term conditions	0.0529** (0.0178)	0.0588*** (0.014)
Diabetes	-0.052*** (0.0117)	-0.0624*** (0.0111)
Diseases of the liver or pancreas	0.0823*** (0.0216)	0.0332 (0.0235)
Maternity (with or without pathologies)	NA	-0.0287*** (0.0082)
Addictive disorders	0.0972*** (0.024)	0.063* (0.0315)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.3922*** (0.0126)	0.3701*** (0.0077)
Neuroleptic treatments (excluding pathologies)	0.211*** (0.0306)	0.186*** (0.0315)

Source: SNDS.

Field: Men (N = 634,786) and women (N = 824,183) among the study population.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 1.A17: Coefficients (SE) of the outcome equation (1.2) by sex

Variables	Men	Women
WA	0.0986*** (0.0159)	0.1181*** (0.013)
<i>Demographic</i>		
Age in 2016	0.0061*** (0.0007)	0.0051*** (0.0005)
<i>Insurance</i>		
CMU-C	0.185*** (0.0176)	0.1071*** (0.0134)
ACS	0.059* (0.0262)	0.0548** (0.0201)
AAH	0.2146*** (0.0244)	0.1786*** (0.0213)
<i>Typology of the municipality</i>		
Large hub (10,000 or more jobs)	Ref.	Ref.
Outskirts of a large hub	-0.0126 (0.0171)	0.0409** (0.0124)
Multipolarized municipality of large urban areas	-0.0293 (0.0296)	0.0985*** (0.0214)
Middle hub (5,000 to less than 10,000 jobs)	0.07 (0.0373)	0.0243 (0.0275)
Outskirts of a middle hub	0.0189 (0.0922)	0.1132 (0.0645)
Small hub (from 1,500 to less than 5,000 jobs)	0.0922** (0.0343)	0.0852*** (0.0245)
Outskirts of a small hub	0.0108 (0.1345)	0.0348 (0.1007)
Other multipolarized municipality	0.0685* (0.0307)	0.0863*** (0.0218)
Isolated municipality outside a hub influence	-0.0253 (0.0344)	0.0789** (0.0245)
Missing or inconsistent	0.0151 (0.0467)	0.0235 (0.0349)
<i>Past BZD use</i>		
BZD use in the last quarter of the year preceding the WA	0.9346*** (0.0294)	0.9398*** (0.0201)

BZD use in the third quarter of the year preceding the WA	0.2863*** (0.0239)	0.3335*** (0.0173)
BZD use in the second quarter of the year preceding the WA	0.0916*** (0.0225)	0.1128*** (0.0165)
BZD use in the first quarter of the year preceding the WA	0.1501*** (0.0209)	0.1962*** (0.0153)
BZD overuse in the previous year	1.3453*** (0.0214)	1.3061*** (0.0161)
<i>Health</i>		
Cancers	0.0564 (0.0341)	0.0517* (0.0211)
Cardioneurovascular diseases	0.1256*** (0.0224)	0.1531*** (0.0246)
Vascular risk treatments (excluding pathologies)	0.001 (0.0176)	0.0798*** (0.0126)
Neurological or degenerative diseases	0.1603*** (0.0341)	0.1959*** (0.0298)
Psychiatric illnesses	0.4628*** (0.0226)	0.503*** (0.0167)
Chronic end-stage renal disease	-0.0401 (0.1167)	-0.0396 (0.1106)
Chronic respiratory diseases	0.1423*** (0.0237)	0.1401*** (0.0171)
Other long-term conditions	0.0619 (0.0345)	0.0343 (0.0256)
Diabetes	0.0728** (0.0244)	0.1212*** (0.0212)
Diseases of the liver or pancreas	0.1509*** (0.0371)	0.0989* (0.0414)
Maternity (with or without pathologies)	NA	-0.0034 (0.0268)
Addictive disorders	0.0271 (0.0333)	0.0954* (0.0396)
Antidepressant, lithium, Depakote, and Depamide treatments (excluding pathologies)	0.3006*** (0.0205)	0.2964*** (0.0132)
Neuroleptic treatments (excluding pathologies)	0.3041*** (0.042)	0.3225*** (0.04)
<i>Prescriber position</i>		
GP	Ref.	Ref.
Another specialist	-0.1419*** (0.0391)	-0.1254*** (0.0302)
Missing information	-0.568*** (0.0217)	-0.5605*** (0.0178)
Multiple	0.3195 (0.1677)	0.1412 (0.1156)
Non-physician	0.1045 (0.0885)	0.042 (0.0786)
Psychiatrist	0.1552*** (0.0254)	0.2129*** (0.0193)
<i>Sex and age of the prescriber</i>		
Missing information	0.0625* (0.0305)	0.1044*** (0.0223)
Male prescriber	-0.0112 (0.0185)	0.0281* (0.0123)
Age < 40	Ref.	Ref.
Age 40-59	-0.0432 (0.0267)	-0.0054 (0.0186)
Age > 59	0.0113 (0.0282)	0.0144 (0.02)
ρ (correlation coefficient of error terms)	0.2427*** (0.041)	0.316*** (0.0363)

Source: SNDS.

Field: Men ($N = 79,129$) and women ($N = 145,242$) using BZDs at least once after the WA date in the study population.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

**Chapter 2. Impact of benzodiazepine use
on the risk of occupational
accidents**

1. Introduction

The prevention of work accidents (WAs) and illnesses is a public health priority and one of the key objectives of the EU Strategic framework on health and safety at work for 2021-2027 (European Commission, 2021). In 2016, the global burden of work-related diseases was estimated by a joint report of the World Health Organization (WHO) and the International Labor Organization (ILO) to be 1.9 million deaths (19% from WAs) and 90 million disability-adjusted life years (DALYs) (30% from WAs) (WHO-ILO, 2021). In France, more than one million WAs were identified by the national health insurance fund (*Caisse nationale de l'assurance maladie*, CNAM) in 2018, including commuting accidents. The frequency of WAs has decreased overall since 2000, and the slight increase in the number of WAs from 2013 to 2019 came from the increase in salaried employment (CNAM, 2019). In France, prevention is also a priority of the fourth *Plan santé au travail* (Health at Work Plan, PST4) (Ministère du Travail, de l'Emploi et de l'Insertion, 2021a) and requires increasing our knowledge of the causes of accidents.

WAs can have deleterious consequences for the victim (such as temporary or permanent deterioration of health and loss of job), for the company (such as the cost of hiring and training, increased insurance premiums for occupational hazard, and legal risk in the event of fraud), and for social security (payment of daily allowance, health care reimbursement). The European Agency for Safety and Health at Work (EU-OSHA) estimates (using a DALY methodology) the global cost of work-related accidents and illnesses at €2,680 billion (which is 3.9% of global GDP) and the European cost at €476 billion (which is 3.3% of the European GDP) (EU-OSHA, 2017).

Improving WAs prevention requires understanding their determinants. The economic literature on work absences and the risk of accidents at work is extensive and sheds light on the roles of cost of absence, individual characteristics, and job characteristics (Pouliakas & Theodossiou, 2013). The role of health and health care on WAs has been understudied and may appear ambiguous due to possible mixed intertemporal effects. Poor health is likely to increase the WA risk: effect per se (in case of impairment of vision for instance), and effect of medical treatment (affecting awareness, cognition, and behavior) (Palmer et al., 2016). However, there is a strong two-way causality between health and care use, and WAs. Poor health will decrease the probability of being at work (Barnay et al., 2015) and thus the WA risk. Appropriate access to care requires time off work but may result in improving health and preventing future WAs.

This study is focused on drug consumption. One particular class of drugs deserving attention is benzodiazepines (BZDs), which are used broadly as anxiolytics and hypnotics. In France, despite a slight downward trend since 2000, 13% of the population consumed these drugs at least once in

2015, and the country remains a major consumer of BZDs in Europe (ANSM, 2017). The adverse effects of BZDs may lead to a higher risk of WAs (Brandt & Leong, 2017). However, other mechanisms may also be involved (such as health improvement and reduction of occupational exposure), and the overall effect remains understudied. Evidence for the risk of WAs after using BZDs is scarce, and some previous studies have serious methodological bias, namely, simultaneity (i.e., the effect of a WA on BZD consumption is not assessed) (see section 2.6). The side effects of BZDs are well known, and compensatory mechanisms could exist: workers may attempt to minimize their exposure or take extra precautions because they are aware of the risk.

This study aimed to determine the impact of past BZD use on WA risk. I distinguish different levels of use according to official recommendations. Data come from the French National Health Data System (SDNS), which allows me to use the entire French population salaried in the private sector with at least one reported WA from 2017 to 2019. I use a two-way fixed effects model on the panel data to deal with time-constant heterogeneity. The results show differences according to treatment duration: BZD's recent use is associated with a 0.18 percentage points (pp) decrease in WA risk, while past use and overuse are associated with 0.12 and 0.07 increases, respectively. They encourage paying particular attention to WA risk after treatment ceases and during extended treatment.

The outline of this paper is as follows. Section 2 presents a literature review relative to determinants of WAs. Section 3 presents the methodology, including the source of data, the scope of the study, the econometric strategy, and statistics. Section 4 presents the results, including stratified analyses and robustness checks. Section 5 presents the discussion and section 6 is the conclusion.

2. Determinants of work accidents

2.1. A conceptual framework for absences from work

As a WA can lead to a work interruption, some WA determinants correlate with the determinants of work absences. From a neoclassical perspective, absences from work result from a trade-off between scheduled work periods and leisure. WAs are inversely related to wages, flexibility (having paid time off), and the perceived degree of occupational safety (Allen, 1981). If the number of contractual hours exceeds the desired hours, workers may be encouraged to take time off (Brown & Sessions, 1996). A high unemployment rate decreases the probability of shirking by reducing the probability of being rehired in after job loss (and thus increasing the opportunity cost of shrinking) (Shapiro & Stiglitz, 1984).

The cost of absence is a major determinant of absence from work. The share of the salary compensated is positively associated with absenteeism (Barmby et al., 2001; Chaupain-Guillot & Guillot, 2017; Frick & Malo, 2008). The effect of individual characteristics is higher than the effect of the institutional framework: employment protection legislation does not affect absenteeism (Frick & Malo, 2008), and sick-leave legislation has a minor role in absence behavior (Chaupain-Guillot & Guillot, 2017).

This literature treats absence behavior as a labor supply decision and ignores the influence of health on absences in theoretical models, although empirical works show that disease is correlated with higher absenteeism (Allen, 1981; Brown & Sessions, 1996). Further developments will aim to fill this gap (see, e.g., Barmby et al. (1994) and Case and Deaton (2003), who used health status to explain absences and labor force participation).

From a theoretical point of view, improvements in working conditions reduce the negative health effect on workers and therefore lower absenteeism. However, worker absence is the result of a composition mechanism and a higher participation rate may increase absenteeism: a healthy work environment gives marginal workers the possibility to work and may lead unhealthy workers to extend their working careers, thereby increasing absenteeism. Empirically, work absences are positively related to poor working conditions, meaning that these are not fully compensated by wages (Ose, 2005). Similarly, working an irregular schedule is associated with a higher sickness absence rate (Afsa & Givord, 2014). Overall, factors associated with poor psychological health (such as long hours worked, work overload and pressure, lack of control over work and lack of participation in decision-making, unclear management, and work role) are associated with absences due to illness (Michie & Williams, 2003).

Even if WA occurrence is one of the determinants of work interruption, a high risk of WAs can increase work absences through indirect means. Workers exposed to WA risk will strive to minimize their exposure time to this risk and thus have a greater probability of being absent due to a work-related disease (Johansson & Palme, 1996; Ose, 2005). As I mentioned, the literature on absences due to illness often assumes a share of voluntary absenteeism due to moral hazard (see, for example, Askildsen et al. (2005) or Khan and Rehnberg (2009)). Nevertheless, if we assume the independence of the physician's diagnosis and the employer's statement, the risk of moral hazard in the case of WAs seems to be lower than for sickness absences, although present. Thus, WA determinants should be less dependent on individual preferences than work absence determinants. WA determinants can be grouped under individual (including job characteristics and health-related factors), organizational, and insurance-related factors.

2.2. Individual factors

According to Pouliakas and Theodossiou (2013), many individual determinants are linked to the risk of WAs. Some of the demographic characteristics include being male (Askenazy, 2006; Guadalupe, 2003; Krause et al., 2001), being between 25 and 35 or over 55 (Guadalupe, 2003), and being of older age (Ghosh et al., 2004). The European Commission (2009) finds age to be negatively related to nonlethal accidents and positively related to lethal accidents. Socioeconomic and professional characteristics play an important role, and the risk of WAs increases with a lower income, a lower occupational class, and rural residency (Dembe et al., 2004; Piha et al., 2013).

2.3. Job characteristics

Blue-collar workers are more affected because of their greater exposure to biological, physical, and biomechanical risks. In particular, exposure to noise and manual material handling are associated with the risk of work injury for both genders, while work injuries among men are significantly associated with thermic constraints and vibrations. Psychosocial work factors are also involved, including low social support, job strain, and isostrain (H.-C. Kim et al., 2009; Niedhammer et al., 2018). Manual workers and farmers (and, to a lesser degree, men in intermediate occupations¹, clerks, craftsmen, and tradesmen) have a much higher occurrence of occupational accidents than men in higher-level occupations², while craftsmen and tradesmen have more traffic accidents (Khlat et al., 2008). A poor work environment or perception of it plays a role in occupational injuries (Ghosh et al., 2004), as well as job dissatisfaction (Dembe et al., 2004). Shift work and long working hours also seem to be detrimental to safety (Wagstaff & Sigstad Lie, 2011).

According to Guadalupe (2003), fixed-term contracts increase the WA risk due to the employer's lower investment in human capital and the employee's greater effort to increase the probability of being rehired. However, after controlling for working conditions, these temporary workers exhibit fewer injuries than permanent workers, thus indicating that poorer working conditions are responsible for this increased risk (Amuedo-Dorantes, 2002). Hernanz and Toharia (2006) found similar results by controlling for job characteristics. For Benavides et al. (2006), the differences between temporary and permanent workers could come from job experience and knowledge of workplace hazards because the significance of differences disappears when controlling for length of employment (except for fatal injuries related to work). Accidents are also more severe for temporary workers than for permanent workers, although most of this difference is due to

¹ Intermediate occupations are managerial staff, schoolteachers, skilled technicians, foremen, and medical and social workers.

² High-level occupations are intellectual professionals, upper managerial staff and administrators, medical doctors, independent professionals, and engineers.

underreporting of the least serious accidents among temporary workers (Picchio & van Ours, 2017).

2.4. *Organizational and firm characteristics factors*

Determinants of work accidents can also occur at the organizational level, with the size of the firm appearing to be a particularly important determinant. In France, statistics show an inverted-U curve: the WA frequency is 24 per 1,000 employees in microenterprises (below 10 employees); 42 in small- and medium-sized enterprises (between 10 and 250 employees); and 30 in enterprises with more than 250 employees (author's calculation). This curve profile is reported in other studies and may come from underreporting in small enterprises (Oleinick et al., 1995; Sørensen et al., 2007). Generally, small private enterprises have a more hazardous work environment than large enterprises (Sørensen et al., 2007). This size relation is identical across most industry groups. Small businesses face more challenges to survive, while bigger companies can invest more in occupational safety and health (OSH) and may be more aware of increased monitoring by regulators and insurers. Conversely, social contacts might be better in small companies (Fenn & Ashby, 2004; Pouliakas & Theodossiou, 2013; Ruser, 1985; Sørensen et al., 2007).

2.5. *Insurance-related factors*

From a theoretical point of view, wage and compensation benefits affect the financial cost of sick leave for employees: higher compensation benefits should increase the number and duration of work absences by lowering their cost (compensation of loss of income), while higher wages should lower work absences by increasing their cost (higher loss of income) (Krueger, 1990). The empirical work of Krueger confirms the positive association between benefits and WA claims among men (controlled for the occupation and the industry, among others). The effect of wage is harder to observe because of the potential endogeneity of wage (the wage increases with the risk of WA), as shown by Kaestner and Grossman (1998) and in line with the theory of compensating wage differentials that suggests workers may accept worse working conditions in exchange of higher wages (Ose, 2005).

When businesses pay compensation benefits, they encourage a reduction in WAs. Businesses in France have to pay a social security contribution for the risk of WAs. For each business with over 150 employees, this contribution is calculated directly based on the number of WAs that have occurred over the previous 3 years, while this calculation is mixed for enterprises of between 20 and 150 employees. This contribution system has demonstrated efficacy in reducing the number of WAs (Lengagne, 2018).

2.6. Health-related factors, the role of benzodiazepines, and contribution of this study

The relationship between health and absences from work is highly complex because of the many factors involved. Untreated health problems and medical treatments may increase work absences as well. Ill health is also associated with changes in employment and thus with exposure to occupational risk.

Symptoms of diseases may be directly related to an increased risk of WAs. For instance, insomnia is related to impaired work performance and a higher risk of WAs (Daley et al., 2009). More widely, chronic health problems (Palmer et al., 2008) and mental health problems (Palmer et al., 2014) are associated with a higher risk of WAs. On the other hand, ill health may result in unemployment. Work absences will increase during the year following the occurrence of cancer, and the employability of workers suffering from cancer decreases over time (Barnay et al., 2015). Moreover, men suffering from anxiety and men and women suffering from depression are less likely to remain in their jobs (Barnay & Defebvre, 2019). Absence from work should lead to a decrease in the WA rate.

Beyond the direct effect of diseases, medical treatments may be associated with WAs. Kaestner and Grossman (1998) showed that drug use could increase the WA risk for men. Some psychotropic medications could also increase the WA risk (Palmer et al., 2016). Among them, BZDs are frequently used to treat insomnia and anxiety (ANSM, 2017). We may expect a positive effect on the risk of WAs because of their adverse effects. They can cause cognitive impairment (Buffett-Jerrott & Stewart, 2002), increase the risk of falling in the elderly (Brandt & Leong, 2017; Pariente et al., 2008), and lead to behavioral disorders (Hall & Zisook, 1981). The risk of traffic accidents after consuming BZDs is well known (Dassanayake et al., 2011; Gustavsen et al., 2008; Ravera et al., 2011). In France, 3.4% of traffic accidents may be related to medication intake, and half of them to BZD intake (ANSM, 2013).

In a literature review about the role of health problems and drug treatments in accidental injury at work, Palmer et al. (2016) reported that most of the studies screened suffered important limitations. The two major sources of limitation were a non-independent assessment of exposures and outcomes, and reverse causation. The increase in BZD use after a WA has been shown previously (see Chapter 1). Many of these studies are cross-sectional and prone to both biases: exposures and outcomes being self-reported at the same time and with a lack of clarity about whether exposure preceded injury or followed it.

To assess the role played by the BZDs in accidents, sometimes patients are tested (blood or urine) after an accident without any evidence of BZD use being higher than in the general population (Girre et al., 1988; Kurzthaler et al., 2005; Price, 2014). This approach allows declarative bias to be avoided, which is common in cases of psychotropic drug use (including BZDs) (Fendrich et al., 2004; Rockett et al., 2006).

Some studies have found no effect of BZD intake on WA risk, such as the study by Montastruc et al. (1992), who hypothesized that knowledge of risk might provide an incentive to avoid BZD use. Gilmore et al. (1996) did not find a significant association between hypnotics (in the 30 days before the date of injury) and injuries for the entire population of a health maintenance organization in the US. Other studies show a positive relationship between BZD use and increased WA risk. Voaklander et al. (2006) reported an OR = 3 of injury among farmers who took sedatives within 30 days before the date of injury. Palmer et al. (2016) highlighted that the risk of reverse causation is sometimes huge, e.g., in the study of Wadsworth et al. (2003), where the taking of sleeping pills is reported up to 14 days before questioning, whereas injuries might have occurred up to one year beforehand.

Palmer et al. (2014, 2016) provided a case-control study based on a large cohort in the UK to address some of these biases. They showed that being prescribed psychotropic drugs before the index date is significantly ($p < 0.001$) associated with occupational injury: OR = 1.59 (OR = 1.39 for antidepressants, OR = 1.65 for hypnotics, and OR = 1.76 for anxiolytics). The effect remained significant after controlling for mental health problems (OR = 1.77 overall). The time horizon of the study is very long (22 years); hence, the psychotropic drug use may be far from the injury. The effect of consumption in the 12 months before the injury is significant for antidepressants (OR = 1.26, at the 5% threshold) and hypnotics (OR = 1.72). One substantial bias of the study is the patient's occupation is not known. If the cases of work-related injuries have been selected, by definition, from people in work, controls may be unemployed. Similarly, cases may hold manual jobs more often than controls. Bias could arise if controls over-represent health problems that prevent work (or having manual jobs). Based on a previous study (Palmer et al., 2010) that compared the relative risks of several diseases unemployed vs. employed individuals and in manual vs. non-manual occupations, they assume a very small bias.

In a recent meta-analysis on the relationship between occupational injuries and BZDs, Garbarino et al. (2021) insist on the high risk of bias in numerous studies. In particular, they estimate the risk of confounding factors high in most studies because important potential confounders were not evaluated, and a lack of rigor in the collection of information on drug intake. The positivity rate

for BZDs among injured workers was 2.71% (95% confidence interval: 1.45-4.98), with a lower share for commercial drivers and air pilots. The meta-analysis did not suggest any increased risk of occupational injury among BZD users, and the authors call for more work to better define the association between both.

This study aims to fill gaps in the literature by examining the effect of BZD use and compensatory mechanisms (such as more exposed workers avoiding treatment and treated patients reducing their occupational exposure) on the WA risk. It tries to address biases often encountered in the existing literature: the declarative bias by using an administrative database, omitted variables by using fixed effects to deal with time-constant heterogeneity, and the reverse causality by accounting for past BZD use.

3. Methodology

3.1. Data

I rely on the French National Health Data System (*Système national des données de santé*, SNDS). The SNDS contains individual data used for billing and reimbursement (Tuppin et al., 2017). National Health Insurance is mandatory for all people living in France (French and foreigners). The database includes information related to outpatient health care consumption (such as physician consultation and drug reimbursement); hospital data (private and public); compensated days off work (due to sick leave, maternity, WA or occupational disease); and information related to long-term diseases, which open access to specific health care reimbursement (ALD: *Affections de longue durée*).

More information is available for people whose WA leads to at least four days off work. These data are relative to the employee (such as the contract type), the employer, and the accident.

Continuous variables (expenses, number of consultations, and number of days) are capped at the 99th percentile (of monthly and non-zero values).

3.2. Population and scope of the study

The study population is insured by the general scheme, which covers mainly private-sector employees and their relatives, except for farmers. The relative WA data that were available pertained to almost 76% of the population living in France in 2015 (Tuppin et al., 2017). The inclusion criteria were as follows: having experienced at least one WA from 2017 to 2019 and being between 16 and 79 in 2017. In this age group and during these years, all the WAs that occurred in France are included, except for farmers, civil servants, and self-employed workers.

The period of study was 36 months (i.e., from January 2017 to December 2019). The population studied totaled 2,544,237 at the beginning of 2017 (deceased people were excluded in the month following the death). In France, the National Health Insurance compensates for commuting accidents as regular WA. In this study, WAs included accidents that occurred at work (workplace accidents) and accidents that occurred between residence and work or between work and catering area (commuting accidents).

3.3. *Econometric strategy*

I gathered panel data by calendar month, thus covering 36 periods. I estimated a monthly WA probability with a linear probability model, using the four previous months as a control variable (thus, the first four periods are not used for the estimation). Two-way fixed effects were used to eliminate any time-constant variable (which is especially helpful in this case due to the lack of individual social and economic data) and any time effect independent of individuals (such as seasonal variations).

The econometric model is written as follows:

$$\begin{aligned}
 WA_{it} = & \beta_0 + \beta_1 BZD_{it} + \beta_2 ChronicCond_{it} + \beta_3 \log \left(1 + \sum_{\tau=t-4}^{t-1} DrugExp_{i\tau} \right) \\
 & + \beta_4 Drug_{it} + \beta_5 \sum_{\tau=t-4}^{t-1} Consult_{i\tau} + \beta_6 \sum_{\tau=t-4}^{t-1} DaysAbs_{i\tau} + \alpha_i + \lambda_t \quad (2.1) \\
 & + u_{it}
 \end{aligned}$$

with $t = 5, 6, \dots, 36$ (because of the four-month lag variables).

WA_{it} is a dummy variable indicating whether the individual i had a WA in month t . All control variables refer to the four months before t :

- BZD_{it} is a qualitative variable with four mutually exclusive terms: no BZD use (no BZD reimbursed in the four previous months), recent use (at least one BZD reimbursed in month $t-1$), past use (at least one BZD reimbursed in months $t-4$ to $t-2$ and none in $t-1$), overuse (at least one BZD reimbursed each month from $t-4$ to $t-1$).

- $ChronicCond_{it}$ is a vector of two dummies indicating whether the individual i has been recognized as having a chronic psychiatric disease or any other kind of chronic disease (ALD) during the four preceding months.
- $DrugExp_{it}$ is a vector of three variables indicating the amount reimbursed for psycholeptics (antipsychotics, anxiolytics, and hypnotics, excluding BZDs), antidepressants, and other reimbursed medicines; the amount used in the model is the sum (+1) from $t-4$ to $t-1$, and the log is used to normalize the distribution.
- Because there is a lot of 0 in drug reimbursements, 1 is added to each variable in $DrugExp_{it}$ vector. To correct the bias induced, three dummies indicating whether the sum of drug expenses over four months is 0 are added and noted in the vector $Drugs_{it}$.
- $Consult_{it}$ is a vector of three variables indicating the number of consultations with a GP (including home visits), a psychiatrist, or another specialist, summed over four months.
- $DaysAbs_{it}$ is a vector of two variables indicating the number of days hospitalized and the number of compensated days off work (due to sickness, maternity, WA, or occupational disease), summed over four months.

α_i is the vector of individual fixed effects (i.e., differences between individuals stable over time), λ_t is the vector of time fixed effects (i.e., time variations independent of individuals), and u_{it} contains unobserved time-varying factors dependent on individuals.

Data are relative to reimbursed medications but do not provide information regarding actual drug intake; thus, this study equates *BZD use* to *BZD reimbursement*, i.e., dispensation in a pharmacy. *BZD overuse* means exceeding the treatment duration recommended by the French National Authority for Health (HAS) for anxiolytic BZDs: 12 weeks at most (HAS, 2018).

All variables in the model control for healthcare consumption. They are proxies for health conditions, potential adverse effects of drugs, and absences from work. Mental health-related variables (chronic psychiatric diseases, psychiatrist consultations, antidepressants, and other psycholeptic treatments) allow for controlling confounding factors associated with BZD reimbursements and identifying the proper effect of BZD use, as far as possible. In particular, antidepressants are distinguished because they are frequently co-prescribed with BZDs. Other

drugs variable controls for potential adverse effects of drugs. Chronic conditions and doctor consultations are proxies of poor health. Doctor consultations may also refer to prevention advice and care. Days hospitalized and compensated are proxies of poor health, but above all are nonwork days, without exposition to WA risk.

Control variables are relative to the four months preceding month t . I made this choice for the sake of consistency with the period considered for BZD use. The maximum treatment duration recommended by health authorities for BZDs is 12 weeks, therefore, I consider four months without treatment interruption as overuse and then control for other care consumption during that time. It aims to identify the effect of past care consumption on current WA risk. It allows for avoiding simultaneity by using lagged variables, as the occurrence of a WA probably leads to a strong increase in care consumption.

I made another estimation using a different variable of interest. In the main results, BZD overuse is defined regarding the HAS guidelines for anxiolytics BZDs. Although this recommendation is built on medical evidence, the threshold is debatable, and it may be interesting to look at the effect of an increase in BZD use. For this purpose, I replace the qualitative BZD use variable with two variables: the log of the amount reimbursed for BZDs in the previous four months (+1), which expresses the intensity of treatment, and a dummy variable, which is 1 when there was a least one BZDs reimbursement in the same period. This dummy corrects the bias introduced by adding 1 to the amount reimbursed and expresses the effect of using BZDs with the lowest intensity, i.e., one single use.

The use of fixed effects prevents me from estimating the coefficient of time-constant factors. Analyses were stratified to observe whether BZD use has heterogeneous effects in some specific subpopulations.

Because of the small share of the study population with more than one WA throughout the 3-year study period (14%), the lagged-dependent variable was not included in the model. Nevertheless, a robustness check was made by restricting modeling to the population with a single WA throughout the study period.

The use of individual fixed effects allows for eliminating time-constant heterogeneity. Some of these variables are missing from the database (such as social origin, type of employment, and professional exposure) and could be controlled by a fixed effects model. Employment is considered a fixed effect (because it is known only at the time of WA), but it could change in the study period. I made a robustness check by comparing two subpopulations: with a fixed-term contract (expected

to change jobs more often) and with a permanent contract (expected to change jobs less often) at the time of WA.

3.4. Statistics

Statistics regarding the structure of the population by age, sex, and number of WAs are presented in Table 2.1. The average age of the study population was 37 in January 2017, and 42% were women. This is younger and more masculine than the French population in 2017 when the average age was 41 and 52% were women (source: Institute of Statistics, INSEE) and refers to the double selection of people who are employed and have had an accident at work. Most of the study population was between 20 and 60 years old (92%), and the frequency of age decreased slightly from 20 to 60 years old, with a drop between 36 and 44 years old, which is in line with the literature about the age of WA (European Commission, 2009; Guadalupe, 2003).

In the population, 39% of people experienced at least one WA in 2017, 40% in 2018, and 39% in 2019. Throughout the 3-year study period, 85.6% of the population experienced one single WA, 11.8% experienced two WAs, and only 2.6% experienced three or more WAs. Accidents at the workplace constitute the majority of WAs (gathering workplace and commuting accidents) and affected 87% of the population experiencing a WA in 2017, compared to commuting accidents affecting 14% of the same population.

Table 2.1: Yearly statistics of age, sex, and number of WA

Year	N people (January)	Variable	Minimum	Mean	Maximum	Std Dev
2017	2,544,237	Age	16	37.39	79	12.409
		Women (0/1)	0	0.42	1	0.493
		WA number	0	0.39	17	0.540
2018	2,543,018	Age	17	38.38	80	12.407
		Women (0/1)	0	0.42	1	0.493
		WA number	0	0.40	12	0.540
2019	2,540,810	Age	18	39.38	81	12.405
		Women (0/1)	0	0.42	1	0.493
		WA number	0	0.39	12	0.538

Note: In 2017, the study population was 37 years old on average, 42% of women, and 39% of the population experienced a WA this year.

Field: study population alive in January from 2017 to 2019 (deceased people are excluded from the study population the month following the death).

Statistics of care use related to variables used in the regressions are presented in Table 2.2 (dummy variables) and Table 2.3 (continuous variables). Statistics are given monthly, i.e., for the study population (N=2,544,237) and at 36 months (minus the deceased people after their death) and over the 3-year study period, on average for the whole study population. Every month 3.3% had a WA,

3.4% used BZDs, and 0.9% overused them (i.e., used them for at least four months), on average. Throughout the 3-year study period, 100% had a WA (this is the selection criterion), 27% used BZDs at least once, and 3.7% overused them at least once. Other statistics refer to control variables.

Table 2.2: Frequency of dummies, monthly and over the 3 years

Variables	Monthly (N = 91,502,091)	3-year (N = 2,544,237)
WA (0/1)	3.28%	100%
BZD use (0/1)	3.41%	27.02%
BZD overuse (0/1)	0.87%	3.68%
Chronic psychiatric disease (0/1)	2.68%	3.08%
Other chronic condition (0/1)	8.61%	10.09%

Note: The frequency of WA for a given month is 3.28%. One hundred percent of the population experienced a WA throughout the study period (3 years).

Field: Population having had at least one WA from 2017 to 2019 (N = 2,544,237).

Table 2.3 shows statistics of care use for continuous variables. The dispersion is important, especially for amounts reimbursed. We see that there are many zeros, especially in monthly values. Psycholeptics and antidepressants are little used but they are included in the model because they may be frequently used along BZDs and are confounding factors. The high number of compensated days comes partly from illness absences due to work accidents.

Table 2.3: Statistics of care use, monthly and over the 3 years

Variables	Monthly (N = 91,502,091)				3-year (N = 2,544,237)			
	Mean	Q3	P90	SD	Mean	Q3	P90	SD
Mean amount reimbursed for psycholeptics (except BZDs) (€)	0.29	0	0	6.43	10.54	0	1.84	186.94
Mean amount reimbursed for antidepressants (€)	0.28	0	0	1.98	10.20	0	8.03	50.02
Mean amount reimbursed for other drugs (€)	10.25	6.84	29.09	28.30	368.60	383.38	870.74	666.74
Number of GP consultations	0.34	0	1	0.77	12.36	17	27	11.70
Number of psychiatrist consultations	0.01	0	0	0.22	0.54	0	0	4.68
Number of other consultations	0.08	0	0	0.31	2.75	4	7	3.89
Number of compensated days off work	2.49	0	5	8.64	89.49	99	257	152.97
Number of hospitalized days	0.08	0	0	1.51	3.00	1	5	14.04

Note: The average amount reimbursed for psycholeptics is €0.29 a month.

Field: Population having had at least one WA from 2017 to 2019 (N = 2,544,237).

4. Results

4.1. Estimations

Table 2.4 shows the results of WA risk estimation by a stepwise approach. In the first two models (without control variables, without and with fixed effects), all modalities of BZD use are associated with a decrease in WA risk (reference: no use). To explain this negative association, we can assume a lower probability of working for people with worse health (captured by BZD use), which seems to dominate the potential adverse effects of BZDs. The effect size increases when fixed effects are added. As expected, the effect size decreases when adding control variables. Effects of BZD overuse and past use become positive when I add the number of compensated days off work during the four previous months. It strengthens the hypothesis of a decrease in WA exposure among people treated with BZDs, captured by the working time-related variables.

In the comprehensive model (Model 5), the effect of recent use remains negative (-0.18 pp), and the effects of past use (+0.12 pp) and overuse (+0.07 pp) become positive on the WA risk. Relative to the probability of WA every month in the study population (3.28%), that means a decrease of 5.4% in the risk for recent BZD use, and increases of 3.6% and 2.3% for past use and overuse, respectively.

Chronic diseases (ALDs) are the variables with the largest effect on WA probability: -2.2 pp (-67%) and -1.1 pp (-33%) for chronic psychiatric diseases and other chronic diseases, respectively. This reflects the health deterioration, which probably leads to a decrease in the probability of being exposed (loss of job, decrease in working time, and decrease in exposure during work) (see section 2.6). Regarding drug uses (except BZDs), a 1% increase in other psychotropics use decreases the probability of WA by 0.09 pp (2.7%), and a 1% increase in antidepressant and other drug uses increases the risk of WAs by 0.13 pp (4.1%) and 0.06 pp (1.7%) respectively. Whether psychotropics may be beneficial on the risk of WAs, antidepressants have a detrimental effect, which confirms other studies (Haslam et al., 2005; Palmer et al., 2014). Other drugs use also has a positive effect on the risk of WAs, which could reflect adverse effects of treatments, such as effects on attention, vigilance, and motor coordination. Doctor's consultations are negatively associated with the WA risk (except for psychiatrist, whose effect is not significant): one additional GP consultation within the previous four months decreases by 0.27 pp (8.3%) the probability of WA (by 0.19 pp, 5.8% for other specialist's consultations). They could have a protective effect through prevention and recommendations on the proper use of medication (including BZDs), but also capture a deterioration of health state. Last, days of absence from work (hospitalization and compensated days) are negatively related to the WA risk because they reflect a non-exposition to

occupational risk. One additional day of absence from work within the previous four months leads to a decrease of 0.04 pp (1.1%) and 0.02 pp (0.6%) in the probability of WA for compensated days and hospitalization days, respectively.

Table 2.4: Regressions of WA probability (stepwise model)

Variables	Model 1	Model 2	Model 3	Model 4	Model 5
<i>BZDs</i>					
Overuse	-0.00277*** (0.0002)	-0.01241*** (0.00031)	-0.00181*** (0.00032)	0.00294*** (0.00022)	0.00075* (0.00032)
Recent use	-0.00542*** (0.00013)	-0.01087*** (0.00015)	-0.00326*** (0.00016)	-0.00004 (0.00013)	-0.00178*** (0.00016)
Past use	-0.00322*** (0.0001)	-0.00731*** (0.00012)	-0.00051*** (0.00012)	0.0021*** (0.00011)	0.00118*** (0.00012)
<i>Chronic conditions</i>					
Psychiatric	-	-	-0.02748*** (0.00058)	0.00146*** (0.00013)	-0.02198*** (0.00058)
Other diseases	-	-	-0.01526*** (0.00031)	0.00005 (0.00007)	-0.01091*** (0.00031)
<i>Drugs reimbursed</i>					
No other psycholeptics (1=No)	-	-	-0.00284*** (0.00034)	-0.00207*** (0.00025)	-0.00258*** (0.00034)
Other psycholeptics (log(€))	-	-	-0.00141*** (0.00016)	-0.00053*** (0.00009)	-0.00089*** (0.00016)
No antidepressants (1=No)	-	-	0.00155*** (0.00043)	0.00034 (0.00034)	0.00228*** (0.00043)
Antidepressants (log(€))	-	-	-0.00062*** (0.00016)	0.00069*** (0.00012)	0.00133*** (0.00016)
No other drugs (1=No)	-	-	0.00176*** (0.0001)	0.00197*** (0.00008)	0.00326*** (0.0001)
Other drugs (log(€))	-	-	-0.00009** (0.00003)	0.00084*** (0.00002)	0.00055*** (0.00003)
<i>Doctor consultations</i>					
GP	-	-	-0.00434*** (0.00001)	-0.00115*** (0.00001)	-0.00272*** (0.00001)
Psychiatrist	-	-	-0.00109*** (0.00004)	-0.0001*** (0.00003)	-0.00004 (0.00004)
Other specialists	-	-	-0.00532*** (0.00003)	-0.00151*** (0.00003)	-0.00191*** (0.00003)
<i>Absence from work</i>					
Compensated days off work	-	-	-	-0.00024*** (0.00000)	-0.00037*** (0.00000)
Hospitalization days	-	-	-	-0.00019*** (0.00001)	-0.0002*** (0.00001)
<i>Fixed effects</i>					
Individual	No	Yes	Yes	No	Yes
Time	No	Yes	Yes	No	Yes

Field: Population having had at least one WA from 2017 to 2019 ($N = 2,544,237$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.

-: the variable is not used in this specification.

Interpretation: In model 1, BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is associated with a decrease of 0.277 pp (percentage points) of WA probability in month t .

In the following estimation, instead of using a BZD use variable referring to health authorities' guidelines, I use a variable indicating the intensity of BZD use and a dummy variable of use. Table 2.5 points out findings using these new BZD variables. We see that the dummy's effect is negative: -0.15 pp (-4.6%) in the WA probability; but the effect of the intensity variable is positive: a 1%

increase in BZD use leads to a 0.14 pp (+4.4%) increase in the risk of WAs. The results are unchanged for other variables. Among all drugs used, the effect of an additional 1% of BZD use is the largest, compared to antidepressants +0.1 pp (+3.2%) and other drugs +0.05 pp (+1.7%). These results stress the importance of distinguishing the single use and the intensity of use.

Table 2.5: Regression of WA risk on the intensity of BZD use

Variables	Model 6
<i>BZDs</i>	
BZD use (log(€))	0.00144*** (0.00015)
BZD use (1=Yes)	-0.0015*** (0.00021)
<i>Chronic conditions</i>	
Psychiatric	-0.02225*** (0.00058)
Other diseases	-0.01094*** (0.00031)
<i>Drugs reimbursed</i>	
No other psycholeptics (1=No)	-0.00271*** (0.00034)
Other psycholeptics (log(€))	-0.001*** (0.00016)
No antidepressants (1=No)	0.00189*** (0.00043)
Antidepressants (log(€))	0.00104*** (0.00017)
No other drugs (1=No)	0.00323*** (0.0001)
Other drugs (log(€))	0.00055*** (0.00003)
<i>Doctor consultations</i>	
GP	-0.00272*** (0.00001)
Psychiatrist	-0.00007 (0.00004)
Other specialists	-0.00191*** (0.00003)
<i>Absence from work</i>	
Compensated days off work	-0.00037*** (0)
Hospitalization days	-0.0002*** (0.00001)
<i>Fixed effects</i>	
Individual	Yes
Time	Yes

Field: Population having had at least one WA from 2017 to 2019 (N = 2,544,237).

*Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.*

Interpretation: An increase of 1% in BZD use in the four previous months is associated with an increase of 0.144 pp of WA probability in month t .

4.2. Heterogeneous effects

To test the heterogeneity, I repeated analyses by stratifying the population by gender, age, and duration of work interruption following the WA. The results are presented in the Appendix. Both sex and age are related to WA risk and BZD use (ANSM, 2017; CNAM, 2019). The statistics (cf.

section 3.4) show that the study population is younger and more masculine than the general French population. BZD consumption in the study population is related to sex and age. Over the 3 years, 21% of men consumed at least one BZD vs. 35% of women; 2.8% and 4.9% overused it, respectively. The frequencies of use (overuse) over the same period for people under 30, between 30 and 44, between 45 and 59, and over 60 are 18% (1.1%), 29% (3.7%), 34% (6.3%), and 33% (7.1%), respectively.

Regressions by sex show no difference compared to regressions for the whole population (see Table 2.A1 in the Appendix), except for BZD overuse among women, which is no longer significant. Regarding regressions by age, the effect of overuse is positive on the risk of WAs among people under 60 years of age, but significant only between 30 and 44 (see Table 2.A2 in the Appendix). For people aged 45 to 59 years, the effect size of overuse is smaller than that of past use. For people aged 60 and over, all measures of use are associated with a lower WA risk, which could come from a lower return at work after a shock on health for older workers.

The length of time off work after the WA is an indicator of the accident's severity. When stratifying by the work interruption duration following the WA, I only used the population with a single WA within the three years of the study (2,169,528 people) (see Table 2.A3 in the Appendix). BZD overuse is positively and significantly associated with the risk of WAs leading from 8 days (median) to 26 days (3rd quartile) of work interruption. Below and above, the effect of overuse is not significant. We see that for the most serious accidents, i.e., leading to more than 26 days of work interruption, the effect size of past use is greater than that of recent use: +0.2 pp vs. -0.13 pp, respectively.

4.3. Robustness checks

The model used is not autoregressive, i.e., the lagged-dependent variable is not included in the model. The hypothesis made is that of no effect of past WA on the current risk of WAs (except via days of absence that are controlled). To relax this hypothesis, a new analysis was conducted on the subpopulation with a unique WA throughout the three-year study period. The results are shown in Table 2.A4 in the Appendix and are similar to those for the full population, except for BZD overuse whose effect is no longer significant.

In this study, employment is assimilated into a fixed effect. This hypothesis can be debated because people may change jobs during the study period, and this information is not present in the data. To try to estimate whether it could be a source of bias, estimations were repeated for the populations with fixed-term and permanent contracts. People with permanent contracts are

presumed to change jobs less frequently than people with fixed-term contracts. If changing jobs is a source of bias, estimates may differ between both populations. Information about the type of employment contract is available only at the time of the accident and for a few people (when the WA results in at least four days off work, which is known within two days following the accident, and the variable still includes approximately 40% missing values). The results are similar to those for the whole study population (see Table 2.A5 in the Appendix), except for the effect of recent use, which becomes insignificant for fixed-term contracts (and significant at a 5% threshold for permanent contracts), and the effect of the number of consultations with a psychiatrist, which becomes positive and significant. Most importantly, the results are identical between both contract types, except for the effects of a new psychiatric illness, which is not significant for the population with a fixed-term contract. For both populations, the effect of overuse becomes larger than that of past use: 0.3 pp vs. 0.15 pp and 0.53 pp vs. 0.21 pp for permanent and fixed-term contracts, respectively.

Due to the dichotomous nature of the explained variable, the natural choice for estimates should have been a logit estimation. Because of the large dataset and individual fixed effects, the logit is too computationally intensive. Instead, I used a linear probability model. To test the influence of this estimation choice, another estimate was made for a subpopulation (randomly restricted to one-tenth of the total population) using a logit instead of a linear model. The results are presented in Table 2.A6 in the Appendix. These results are not directly comparable with the main results because odds ratios are provided (vs. marginal effects), but we can see that signs and significance are coherent with the main estimation, even though the effect of two variables becomes insignificant at the 5% threshold (BZD overuse and other psycholeptics use).

5. Discussion

5.1. Discussion of results

Compared to other studies on the impact of psychotropic drug use on the risk of WAs (Kaestner & Grossman, 1998; Palmer et al., 2016), this study is the first, to my knowledge, to specifically examine the influence of the duration and treatment status (active or not) of a particular medication and therefore to allow distinguishing the effects between recommended use and overuse. Moreover, the study relies on an administrative database, which avoids declarative bias that is known to be high in the case of psychotropic drug use (and even more for overuse) and misclassification of drugs (Glintborg et al., 2008; Murray et al., 1981; Rockett et al., 2006).

We observed a decrease in WA risk when people use BZDs in the preceding month. Regarding the adverse effects of BZDs (such as psychomotor impairments that lead to motor vehicle accidents, falls, and fractures (Brandt & Leong, 2017)), the expected consequence of BZD use was instead an increase in WAs the month following use. Some hypotheses can be put forward to explain this result. First, improved health may minimize accident risk. Because BZDs are recommended for treating numerous diseases and when used under medical guidelines, their use is expected to improve patient health, they could thus decrease WA risk (Vorspan et al., 2018). Second, behavioral changes: workers can anticipate the risk of accidents and, if possible, try to minimize their exposure. The prescribing doctor may remind and warn patients about the risks potentially induced by BZDs, especially those whose professions make them highly exposed. While doctors seem to have good knowledge of the adverse effects of BZDs (Neves et al., 2019), the dissemination of information could be flawed (Iliffe et al., 2004) and result in poor knowledge of BZDs risks among patients (Sirdifield et al., 2017). However, information transmission could be better for highly exposed employees. Furthermore, the government and employers conduct prevention campaigns against the use of psychoactive substances in the workplace (France Stratégie, 2019), and a pictogram strongly advising against driving is present on all BZDs packaging. Another hypothesis is put forward by Montastruc et al. (1992), who state that the knowledge of risk may lead to avoiding BZD consumption. In France, doctors are financially incentivized to reduce their BZD prescriptions (Michel-Lepage & Ventelou, 2016), so they could choose to avoid BZD prescriptions for patients who are more exposed to the WA risk. In the same vein, Garbarino et al. (2021) hypothesized that the lower BZD use in some professions (such as commercial drivers) may result in a paradoxical effect: whether these professions suffer from work-related stress and poor sleep quality, they could benefit from appropriate use of BZDs. Last, an omitted variable may act on BZD use and WA probability. For example, a worker exposed to job-related anxiety could want to decrease their time at work and increase their BZD consumption.

The WA risk increases with past BZD use, i.e., in the 4th to 2nd preceding months but not in the last. After an initial period of decrease in exposure when the treatment started, an employee may try to catch up on delayed work. A medical explanation is also possible, as treatment discontinuation is known to lead to a rebound effect (Gudex, 1991), i.e., anxiety or insomnia may become worse than before treatment. After only a few weeks of treatment, withdrawal symptoms may even occur in the form of irritability, increased stress, anxiety, panic attacks, difficulty in concentration, muscular pain, and stiffness, among others (Pétursson, 1994).

The effect of BZD overuse (BZDs reimbursed in the four preceding months) is also positively associated with the risk of WAs. The beneficial effect of BZD use quickly declines after two weeks

of treatment for hypnotic BZDs and after four weeks for anxiolytics (M. H. Lader, 1999). If their effectiveness is proven for short-term treatment, long-term use is controversial (adverse effects could progressively overlap with the therapeutic effect) (Revet et al., 2018). This hypothesis is strengthened by the estimates that include the intensity of BZD use: the use is associated with a decrease in WA risk, while this risk is positively related to the intensity of BZD use. When stratifying the population, the effect of BZD overuse remains significant and positive for people between 30 and 44 and time off work following a WA between 8 and 26 days.

These different tests and stratifications show that the effect of BZD overuse is not stable. It goes from +0.53 pp among people with fixed-term contracts, who are a highly selected sample from the population, to -0.3 pp among people over 60. Mostly, the effect of overuse is insignificant, especially in the logit estimation, and it should be taken with caution. Exceeding the recommendations could reveal specificities of subpopulations. After 60, the overuse of BZDs may reflect a diminution of the probability of working or returning to work after a health deterioration. Conversely, among people between 30 and 44, the positive effect of overuse may show both a higher risk of WAs in this age group and a higher probability of staying at work when health deteriorates. While presenteeism (i.e., going to work when sick) is more often reported among women, it is also associated with high job demand (Schnabel, 2022). If more risky jobs (where men are overrepresented) were associated with presenteeism that may explain why men overusing BZDs remain more often than women in exposed employment.

5.2. Limitations

The database only tells us about reimbursed care, and I assume that one reimbursement is one use. The risk of error exists only for medication reimbursement, if a drug is bought and not used, and mainly for a single box drug delivery.

Measuring WAs is not an obvious task. WAs are significantly underreported in the EU (Jacinto & Aspinwall, 2004) and the USA (Rosenman et al., 2006). Underreporting in France has been estimated at approximately 20% by the French survey *Working Conditions 1998* (Askenazy, 2006). Thus, because of underreporting, working with administrative databases entails incorporating reporting determinants into the WA determinants. One of the major causes of underreporting is job insecurity (Probst et al., 2013). The reporting increases for serious accidents in large companies and qualified people (Askenazy, 2006).

This study was conducted on the population affected by a WA between 2017 and 2019. This population is particular because WAs are not homogeneously distributed in the population (more

men, younger, in better health, employed, and other factors). Consequently, the findings of this study cannot be applied to the whole population. Calculation of the increase of WA likelihood was done from the WA probability each month of the study population, which is higher than in the general population. Therefore, the effect size could be underestimated compared to the entire population. Although non-directly comparable (different temporality and different measurement of BZD use), the effect sizes reported by Palmer et al. (2014, 2016) in a case-control study are higher than in this study.

Some variables highlighted in the literature review are absent from the control variables (such as socioeconomic and professional characteristics) due to data limitations. The fixed-effect model addresses time-constant heterogeneity and seasonal variations. I assume that most of the variables involved in the risk of WAs (and not used in the model) are fixed throughout the study period, such as education, blue/white-collar workers, business line, and urban/rural residence. Nevertheless, time-varying variables acting on both BZD use and WA risk can be sources of bias. In particular, a change in employment during the study period could lead to a change in exposition, enterprise size, work environment, and satisfaction at work. Although not controllable with the study data, I tried to estimate the risk of bias by comparing estimates of people with fixed-term and permanent contracts at the time of the accident, which led to very slight differences. These results increase my confidence that contract type and job change are not a source of bias.

6. Conclusion

BZDs are broadly used to treat various diseases, mainly anxiety and insomnia. They have adverse effects (psychomotor and cognitive) that one may reasonably expect to increase the risk of WAs. This study shows that the resulting effect is not trivial and varies according to the duration of treatment.

The study design does not allow for distinguishing between the direct effect of BZDs and changes in occupational risk exposure. Short-term treatment with BZDs (1 month) is associated with a decreased risk of WAs in the following month. This effect may come from a healing effect or compensatory mechanisms linked to knowledge of risks (avoidance of treatment or taking extra precautions). Treatment discontinuation is associated with an increased risk of WAs that might come from rebound effects and catch-up effects. When the treatment is prolonged over the recommendation, it becomes associated with an increase in the risk of WAs, which may come from adverse effects overriding the beneficial effects of treatment. Moreover, the risk of WAs is directly related to the intensity of treatment.

These results should help to improve medical guidelines and constitute useful information about the therapeutic benefits and adverse effects of BZDs. In particular, prescribers and BZD users should be aware of the increased risks of WA after BZD use, not only at treatment initiation but also after months of use and after treatment stops. This study provides more evidence for the need to limit the duration and intensity of BZD treatments. Prevention related to psychoactive substance use in companies should take better account of the posttreatment period.

7. Appendix

7.1. Results of stratified analyses

Table 2.A1: Regressions of WA risk by sex

Variables	Men	Women
<i>BZDs</i>		
Overuse	0.00097* (0.00048)	0.00053 (0.00042)
Recent use	-0.00147*** (0.00024)	-0.00206*** (0.00021)
Past use	0.00138*** (0.00018)	0.00101*** (0.00016)
<i>Chronic conditions</i>		
Psychiatric	-0.0179*** (0.00085)	-0.02594*** (0.00078)
Other diseases	-0.00739*** (0.00041)	-0.01535*** (0.00047)
<i>Drugs reimbursed</i>		
No other psycholeptics (1=No)	-0.0024*** (0.00051)	-0.00255*** (0.00047)
Other psycholeptics (log(€))	-0.00079*** (0.00023)	-0.0009*** (0.00023)
No antidepressants (1=No)	0.00204** (0.00069)	0.00255*** (0.00054)
Antidepressants (log(€))	0.00096*** (0.00026)	0.00154*** (0.00021)
No other drugs (1=No)	0.0045*** (0.00014)	0.00068*** (0.00016)
Other drugs (log(€))	0.00062*** (0.00004)	0.00045*** (0.00004)
<i>Doctor consultations</i>		
GP	-0.00258*** (0.00002)	-0.0028*** (0.00002)
Psychiatrist	0.00008 (0.00007)	-0.00015** (0.00005)
Other specialists	-0.00204*** (0.00005)	-0.00183*** (0.00004)
<i>Absence from work</i>		
Compensated days off work	-0.00041*** (0)	-0.00035*** (0)
Hospitalization days	-0.0002*** (0.00001)	-0.0002*** (0.00001)
<i>Fixed effects</i>		
Individual	Yes	Yes
Time	Yes	Yes
Observations	1,480,432	1,063,805

Field: Population having had at least one WA from 2017 to 2019 ($N = 2,544,237$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.

Interpretation: For men, BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is associated with a 0.097 pp increase in WA probability at month t .

Table 2.A2: Regressions of WA risk by age

Variables	< 30 years	30-44 years	45-59 years	> 59 years
<i>BZDs</i>				
Overuse	0.00154 (0.00109)	0.00211*** (0.00054)	0.00053 (0.00044)	-0.00304* (0.00138)
Recent use	-0.0027*** (0.00038)	-0.002*** (0.00026)	-0.00122*** (0.00024)	-0.00153 (0.00079)
Past use	0.00135*** (0.00028)	0.00118*** (0.0002)	0.0013*** (0.00019)	-0.00027 (0.00065)
<i>Chronic conditions</i>				
Psychiatric	-0.01641*** (0.00125)	-0.02042*** (0.00094)	-0.02589*** (0.00093)	-0.02785*** (0.00368)
Other diseases	-0.02574*** (0.00082)	-0.00916*** (0.0006)	-0.00613*** (0.00042)	-0.00847*** (0.00118)
<i>Drugs reimbursed</i>				
No other psycholeptics (1=No)	-0.00222** (0.00067)	-0.00175** (0.00055)	-0.00373*** (0.00059)	-0.00732*** (0.00213)
Other psycholeptics (log(€))	-0.00025 (0.00032)	-0.0008** (0.00026)	-0.00163*** (0.00028)	-0.00276* (0.00107)
No antidepressants (1=No)	0.00211* (0.00107)	0.00232*** (0.00069)	0.00191** (0.00065)	0.00443 (0.00227)
Antidepressants (log(€))	0.00175*** (0.00043)	0.0014*** (0.00027)	0.00095*** (0.00025)	0.00202* (0.00086)
No other drugs (1=No)	0.00245*** (0.00018)	0.00412*** (0.00017)	0.00444*** (0.0002)	0.00401*** (0.00074)
Other drugs (log(€))	0.00093*** (0.00006)	0.00058*** (0.00005)	0.00035*** (0.00006)	0.00006 (0.0002)
<i>Doctor consultations</i>				
GP	-0.00231*** (0.00003)	-0.00273*** (0.00002)	-0.00307*** (0.00003)	-0.0029*** (0.00008)
Psychiatrist	0.00013 (0.0001)	-0.00005 (0.00007)	-0.00012 (0.00007)	-0.00029 (0.00025)
Other specialists	-0.00206*** (0.00006)	-0.00189*** (0.00005)	-0.00178*** (0.00005)	-0.00175*** (0.00016)
<i>Absence from work</i>				
Compensated days off work	-0.00042*** (0)	-0.00038*** (0)	-0.00035*** (0)	-0.00028*** (0)
Hospitalization days	-0.00024*** (0.00002)	-0.0002*** (0.00001)	-0.00018*** (0.00001)	-0.00023*** (0.00003)
<i>Fixed effects</i>				
Individual	Yes	Yes	Yes	Yes
Time	Yes	Yes	Yes	Yes
Observations	823,029	895,579	763,944	61,685

Field: Population having had at least one WA from 2017 to 2019 (N = 2,544,237).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.

Interpretation: For people under 30 years old, BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is not significantly (at a 5% threshold) associated with WA probability at month t .

Table 2.A3: Regressions of WA risk by duration of work interruption following the WA

Variables	0 day	1-7 days	8-26 days	> 26 days
<i>BZDs</i>				
Overuse	0.00016 (0.00049)	-0.0005 (0.00092)	0.00172* (0.00075)	0.00045 (0.00059)
Recent use	-0.0005* (0.00025)	-0.00174*** (0.00045)	-0.00167*** (0.00036)	-0.00133*** (0.0003)
Past use	0.00044* (0.00019)	0.00042 (0.00035)	0.00068* (0.00028)	0.00198*** (0.00024)
<i>Chronic conditions</i>				
Psychiatric	-0.00879*** (0.00092)	-0.01768*** (0.00171)	-0.0214*** (0.00138)	-0.03282*** (0.00103)
Other diseases	-0.01766*** (0.00045)	-0.0074*** (0.00092)	-0.00445*** (0.00074)	-0.01129*** (0.00058)
<i>Drugs reimbursed</i>				
No other psycholeptics (1=No)	-0.0014** (0.00052)	0.0005 (0.00094)	-0.00238** (0.00078)	-0.00498*** (0.00069)
Other psycholeptics (log(€))	-0.00067** (0.00025)	-0.00008 (0.00044)	-0.00065 (0.00037)	-0.00188*** (0.00032)
No antidepressants (1=No)	0.00143* (0.00066)	0.00269* (0.00123)	0.00092 (0.00101)	0.00162* (0.0008)
Antidepressants (log(€))	0.00077** (0.00025)	0.00167*** (0.00047)	0.00162*** (0.00039)	-0.00008 (0.00031)
No other drugs (1=No)	0.00383*** (0.00015)	0.00537*** (0.00027)	0.00361*** (0.00023)	-0.00082*** (0.00022)
Other drugs (log(€))	0.00063*** (0.00005)	0.00118*** (0.00009)	0.00089*** (0.00007)	-0.00036*** (0.00006)
<i>Doctor consultations</i>				
GP	-0.00175*** (0.00002)	-0.00311*** (0.00005)	-0.0033*** (0.00003)	-0.00173*** (0.00003)
Psychiatrist	-0.00018** (0.00006)	0.00002 (0.00012)	0.00011 (0.0001)	-0.00025** (0.00008)
Other specialists	-0.00149*** (0.00005)	-0.00155*** (0.0001)	-0.00172*** (0.00008)	-0.00253*** (0.00006)
<i>Absence from work</i>				
Compensated days off work	-0.00005*** (0.00000)	-0.0003*** (0.00000)	-0.00039*** (0.00000)	-0.00043*** (0.00000)
Hospitalization days	-0.00019*** (0.00001)	-0.00027*** (0.00002)	-0.00022*** (0.00002)	-0.0002*** (0.00001)
<i>Fixed effects</i>				
Individual	Yes	Yes	Yes	Yes
Time	Yes	Yes	Yes	Yes
Observations	773,685	351,821	537,581	507,057

Field: Population having had a single WA from 2017 to 2019 (N = 2,170,144).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.

Interpretation: For people whose WA did not lead to a work interruption, BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is not significantly (at a 5% threshold) associated with WA probability at month t .

7.2. Results of robustness checks

Table 2.A4: Regression of WA risk for the population with one single WA throughout the study period

Variables	Marginal effect (SE)
<i>BZDs</i>	
Overuse	0.00056 (0.00032)
Recent use	-0.00114*** (0.00016)
Past use	0.00104*** (0.00012)
<i>Chronic conditions</i>	
Psychiatric	-0.02078*** (0.00058)
Other diseases	-0.01126*** (0.00031)
<i>Drugs reimbursed</i>	
No other psycholeptics (1=No)	-0.00238*** (0.00035)
Other psycholeptics (log(€))	-0.00088*** (0.00016)
No antidepressants (1=No)	0.00181*** (0.00043)
Antidepressants (log(€))	0.00097*** (0.00016)
No other drugs (1=No)	0.00311*** (0.0001)
Other drugs (log(€))	0.00054*** (0.00003)
<i>Doctor consultations</i>	
GP	-0.00233*** (0.00002)
Psychiatrist	-0.00006 (0.00004)
Other specialists	-0.00179*** (0.00003)
<i>Absence from work</i>	
Compensated days off work	-0.00032*** (0)
Hospitalization days	-0.00019*** (0.00001)
<i>Fixed effects</i>	
Individual	Yes
Time	Yes
Observations	2,170,144

Field: Population having had one single WA from 2017 to 2019 ($N = 2,170,144$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.

Interpretation: BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is not significantly (at a 5% threshold) associated with WA probability at month t .

Table 2.A5: Regressions of WA risk by type of employment contract

Variables	Permanent contract	Fixed-term contract
<i>BZDs</i>		
Overuse	0.00302*** (0.00062)	0.00534*** (0.00121)
Recent use	-0.00077* (0.00032)	0.00059 (0.00064)
Past use	0.00151*** (0.00025)	0.00212*** (0.0005)
<i>Chronic conditions</i>		
Psychiatric	-0.00551*** (0.00108)	0.00119 (0.00216)
Other diseases	0.01012*** (0.00061)	0.00916*** (0.00128)
<i>Drugs reimbursed</i>		
No other psycholeptics (1=No)	-0.00268*** (0.00073)	-0.00349** (0.00128)
Other psycholeptics (log(€))	0.00006 (0.00035)	-0.0001 (0.00057)
No antidepressants (1=No)	0.0019* (0.00083)	-0.0019 (0.0017)
Antidepressants (log(€))	0.00335*** (0.00032)	0.0019** (0.00066)
No other drugs (1=No)	0.01107*** (0.00022)	0.01426*** (0.00041)
Other drugs (log(€))	0.00086*** (0.00007)	0.00175*** (0.00012)
<i>Doctor consultations</i>		
GP	-0.0064*** (0.00003)	-0.00643*** (0.00006)
Psychiatrist	0.00049*** (0.00008)	0.00085*** (0.00016)
Other specialists	-0.00152*** (0.00006)	-0.00135*** (0.00013)
<i>Absence from work</i>		
Compensated days off work	-0.00026*** (0)	-0.00035*** (0)
Hospitalization days	-0.00008*** (0.00001)	-0.00012*** (0.00002)
<i>Fixed effects</i>		
Individual	Yes	Yes
Time	Yes	Yes
Observations	312,904	98,615

Field: Population having had a single WA from 2017 to 2019, resulting in at least a 4-day work interruption, and for whom the information is available (N = 411,519).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses.

Interpretation: For people with a permanent contract at the time of WA, BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is associated with a 0.302 pp increase in WA probability at month t .

Table 2.A6: Regression of WA risk using logit among a sample at the 10th

Variables	Coefficient (SE)	Odd ratios (95% Confidence Limits)
<i>BZDs</i>		
Overuse	-0.0026 (0.024)	1.009 (0.944-1.078)
Recent use	-0.0397** (0.0126)	0.972 (0.941-1.004)
Past use	0.0535*** (0.0118)	1.067 (1.041-1.094)
<i>Chronic conditions</i>		
Psychiatric	-0.3264*** (0.0327)	0.521 (0.458-0.592)
Other diseases	-0.1911*** (0.0168)	0.682 (0.639-0.729)
<i>Drugs reimbursed</i>		
No other psycholeptics (1=No)	-0.045* (0.0182)	0.914 (0.851-0.982)
Other psycholeptics (log(€))	-0.033 (0.0178)	0.968 (0.934-1.002)
No antidepressants (1=No)	0.0143 (0.0232)	1.029 (0.940-1.127)
Antidepressants (log(€))	0.0373* (0.0179)	1.038 (1.002-1.075)
No other drugs (1=No)	0.0453*** (0.00512)	1.095 (1.073-1.117)
Other drugs (log(€))	0.0276*** (0.00322)	1.028 (1.022-1.034)
<i>Doctor consultations</i>		
GP	-0.0922*** (0.00176)	0.912 (0.909-0.915)
Psychiatrist	0.00028 (0.00591)	1.000 (0.989-1.012)
Other specialists	-0.0724*** (0.00385)	0.930 (0.923-0.937)
<i>Absence from work</i>		
Compensated days off work	-0.0228*** (0.00019)	0.977 (0.977-0.978)
Hospitalization days	-0.0208*** (0.00161)	0.979 (0.976-0.982)
<i>Fixed effects</i>		
Individual		Yes
Time		Yes
Observations		254,310

Field: Study population randomly selected at the 10th ($\bar{N}=254,310$).

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Interpretation: BZD overuse (compared to no BZD use, calculated for months $t-4$ to $t-1$) is not significantly (at a 5% threshold) associated with WA probability at month t .

Chapter 3. Benzodiazepine consumption in time of pandemic

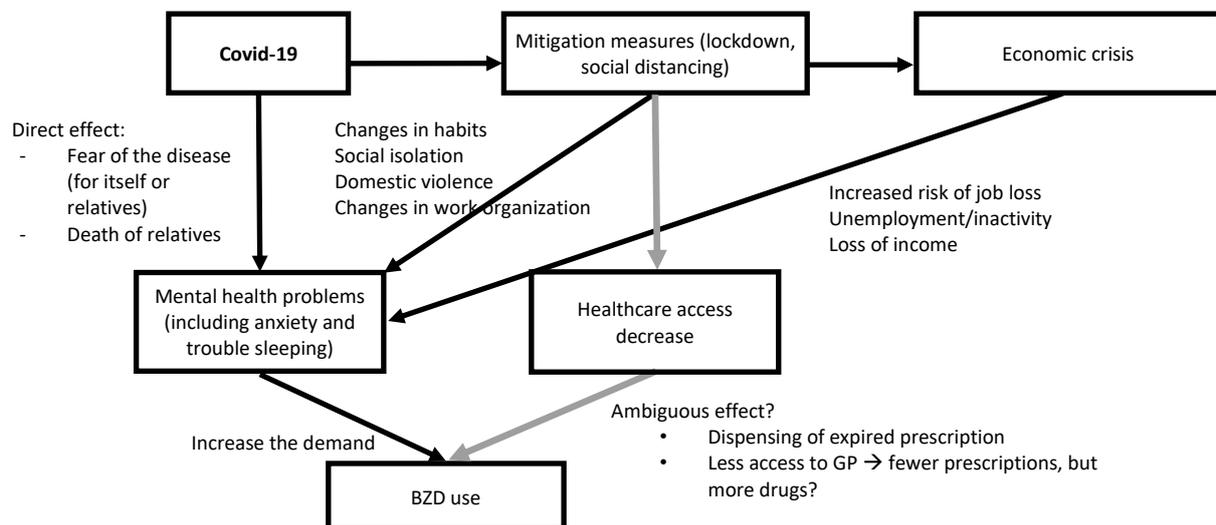
1. Introduction

From the first COVID-19 case detected in France on January 24, 2020, the disease quickly spread and affected millions of people, leading to hospital saturation and 124,000 deaths on January 1, 2022 (source: Santé Publique France). In reaction, public authorities decided on three national lockdowns (from March 17 to May 11, 2020; from October 30 to December 15, 2020; and from April 3 to May 3, 2021). Lockdowns have been associated with restrictive measures on movement and an increase in worrisome communication from the media, which have resulted in a strong economic shock and a deep impact on people's mental health (see e.g. Peretti-Watel et al., 2020). In France, anxiety disorders increased during this time from 13.5% in 2017 to 26.7% at the beginning of the 2nd week of the first lockdown (Chan-Chee et al., 2020). Sales of psychotropic drugs, which are a proxy for mental health, quickly grew after the beginning of the first lockdown and remained at a high level until the first four months of 2021 (Weill et al., 2021). The objective of this study was to disentangle the different effects of the pandemic that may have affected psychotropic drug use at the intensive and extensive margins.

Two main channels may help to explain how the COVID-19 pandemic has increased psychotropic drug use, including the direct effect of the pandemic and the indirect effect of containment measures, such as lockdowns. These channels are presented in Figure 3.1 and empirical evidence is reviewed in section 2. The direct effect of the pandemic is the fear of the virus for self and loved ones, which may be amplified by the severity of the pandemic in a particular area of residence, exposure to media, and deceased relatives. Measures taken to stop the spread of the disease may also have impaired mental health. Habit and work modification (such as travel restriction, work interruption, work at home, and school closures) and social distancing (such as curfews, bans of large gatherings, and stay-at-home orders) may have led to an increase in social isolation and domestic violence. These measures led to an economic shock that may have caused concern about one's financial situation or work disruption. Both of these channels could have contributed to mental health problems, stress, anxiety, and trouble sleeping, which in turn could lead to the consumption of mental health medications. Containment measures also led to difficulties accessing healthcare, especially in the beginning of the first lockdown (Arnault et al., 2021). This could have ambiguous effects with fewer GP consultations, but more prescriptions or the use of expired prescriptions. Indeed, during the two lockdowns in 2020, pharmacists even issued expired prescriptions, which in normal circumstances cannot be refilled and should be renewed by a doctor. At the beginning of the first lockdown, Weill et al. (2020) noticed an increase in anxiolytic and hypnotic sales, but a decrease in the initiation of treatments, which means that there was an increase

in use among people who already had a prescription. During the second lockdown, new treatments also increased, i.e., people started to use these medicines for the first time. For this reason, the effect on the share of users (extensive margin) and the intensity of use among users (intensive margin) is distinguished.

Figure 3.1: Possible transmission channels of the effect of the COVID-19 pandemic on BZD use



The focus of this study is on benzodiazepine (BZD) consumption, which are psychotropic drugs that are mainly used as anxiolytic and hypnotic drugs, and were the main representatives of these drugs, 84% and 81%, respectively, in 2015 (ANSM, 2017). They are only available with a medical prescription, as they have adverse effects that justify strict control of their use, such as psychomotor impairment that can lead to motor vehicle accidents, falls and fractures, and dependence when treatment is prolonged (Brandt & Leong, 2017; Gudex, 1991). This is a source of treatment inefficiency and has economic consequences. Beyond the direct cost of treatment through social security (in 2019, psychiatric diseases and psychotropic drugs accounted for a €22.7 billion expense for the National Health Insurance (CNAM, 2021)), potentially inappropriate prescribing results in greater expenses through hospitalizations and healthcare costs. For example, in Quebec, this cost more than \$3,000 per patient among a community-dwelling population (Dionne et al., 2013), and, in the EU, the total annual hospital costs in 2000 related to fall-related injuries attributable to BZDs were €1.8 billion (Panneman et al., 2003). BZD use also results in a decrease in productivity at work (Sorge et al., 2019) or leisure activities (Bazin et al., 2012). The high level of consumption in France in the 1990s led health authorities to set up measures to reduce it, such as guidelines regarding treatment duration, restriction of prescribing for some molecules, lower reimbursement rates, and pictogram advertising against driving vehicles while using BZDs. Consumption declined from the beginning of the 2000s until the onset of the pandemic, but in 2015, France was still the second highest consumer country among eight European countries, with 13.4% of the population who

used at least one BZD in the year (ANSM, 2017). This figure is also greater than in other northern countries such as in the USA (10.4% of prescribed BZDs reported by Maust et al. (2019) in 2015-2016) or in Manitoba province in Canada (11.7% in 2016 according to Brandt et al. (2019)).

Regardless of the pandemic, the main factors associated with BZD use are old age, being female (ANSM, 2017), health status (especially psychiatric diseases, such as anxiety, depression, and neurotic disorders) (Demyttenaere et al., 2008; Lagnaoui et al., 2004; Sidorchuk et al., 2018; Takano et al., 2019), concomitant use of psychotropic drugs (Johnell & Fastbom, 2009; Sidorchuk et al., 2018) and other chronic diseases, such as cancer (Takano et al., 2019). Other characteristics associated with higher use include being jobless (Lagnaoui et al., 2004), being less educated (Demyttenaere et al., 2008), and living in an urban area (Johnell & Fastbom, 2009).

I used administrative data at the municipality level, from the French National Data Health System (SNDS: *Système national des données de santé*) provided by the National Health Insurance for BZD consumption, and from the National Institute of Statistics (Insee) for information about the economic situation, housing, and severity of the epidemic. This study sought to identify the main contributors to the BZD evolution at the municipality level from 2018 to 2021 to determine the respective contributions of the direct and indirect effects of the pandemic. The results show a significant increase in BZD sales in 2020. The factors associated with the rise were mainly related to employment and housing (namely, the share of unemployed, the share of people without a diploma, and the share of people living alone). The severity of the pandemic in 2020 had a slight impact, while risk factors for severe COVID-19 were negatively associated with BZD use increase.

This study makes a useful contribution to the literature by improving knowledge of the determinants of healthcare consumption changes during the pandemic and provides new evidence about the impact of the pandemic on mental health. It constitutes a lesson for future pandemics and can guide policy responses. In particular, the struggle against psychotropic drug overconsumption should consider the mechanisms by which a new pandemic could influence consumption.

The outline of this study is as follows. In section 2, a literature review explores the impacts of the COVID-19 pandemic on mental health, as well as potential channels influencing psychotropic drug consumption. In section 3, the methodology (data and econometric strategy) is presented. Section 4 includes the results with some complementary analyses. Section 5 includes the discussion, and section 6 is the conclusion.

2. Literature review

2.1. *Impacts of the COVID-19 pandemic on mental health*

In early 2020, researchers attempted to forecast the consequences of lockdowns on people's mental health, in particular social isolation from previous experiences of confinement. Anxiety disorders and depression have been identified as possible consequences (Mengin et al., 2020) and as possible risk factors (Brooks et al., 2020). The COVID-19 pandemic differs from previous epidemics, including confinement situations, the speed of diffusion globally, the high number of deaths, worldwide media coverage, and the high levels of restrictive measures.

The pandemic has had detrimental impacts on mental health, observed in many countries, including France with the survey CoviPrev, from Santé Publique France (Chan-Chee et al., 2020), Spain (Fernández-Abascal & Martín-Díaz, 2021), Italy (Amerio et al., 2021), the USA (Adams-Prassl et al., 2022; Kämpfen et al., 2020), Brazil (Feter et al., 2021), China (Huang & Zhao, 2020), etc. These studies stress the rise of anxiety, trouble sleeping, and depressive symptoms after the beginning of the pandemic. In the European Union (EU), even after the countries had lifted their COVID-19 restriction, the mental well-being measured in spring 2022 was below the level measured at the start of the pandemic, although slightly improved compared to the level of spring 2021 (Eurofound, 2022). Many studies have been conducted among specific populations, such as children (e.g., Monnier et al., 2021; Samji et al., 2022), parents (e.g., Yamamura & Tsustsui, 2021; Zamorro & Prados, 2021), students (e.g., Cao et al., 2020; Husky et al., 2020), workers (e.g., Lesage et al., 2020; Pelly et al., 2021; Perelman et al., 2021), especially health care workers (e.g., Krishnamoorthy et al., 2020; Luo et al., 2020), and psychiatric patients (e.g., Chatterjee et al., 2020; Hao et al., 2020). All of these cited studies rely on surveys (mostly ad hoc) starting during the pandemic or long-term surveys, such as the Understanding America Study (UAS) in the study of Kämpfen et al. (2020).

Millions of deaths worldwide (H. Wang et al., 2022) have been a major source of stress from fear of infection of oneself and relatives. This stress has likely impacted mental health (Usher et al., 2020). The main risk factors for death and hospitalization from COVID-19 are advanced age (≥ 65 years), male sex, and chronic conditions, such as mental health disorders, chronic respiratory diseases, diabetes, cardiovascular diseases, and chronic kidney diseases (Du et al., 2021; Semenzato et al., 2021). In addition, people more affected by psychological impairment during confinement were youth, women, people affected by chronic disease, and people previously receiving mental health treatment (Czeisler, 2020; Findlay et al., 2020; Peretti-Watel et al., 2020; Qiu et al., 2020; Ran et al., 2020; Y. Wang et al., 2020). For youth and women, a lower fear of infection (at least for themselves) can be overcome by other mechanisms, such as a greater decrease in social interaction

(Etheridge & Spantig, 2022; Samji et al., 2022). For people with chronic disease, the fear of death or serious symptoms could be greater than for healthy people, but other mechanisms may be present. Confinement may have generated unmet healthcare needs, especially among people of poorer health (Arnault et al., 2021; Davillas & Jones, 2021b).

Some risk factors can be directly related to the virus: people who have had COVID-19 have a greater risk of needing psychological support (Peretti-Watel et al., 2020), and the severity of COVID-19 in the area of residence negatively affects life satisfaction (Zhang et al., 2020) and is positively associated with anxiety (Y. Wang et al., 2020). Fitzpatrick et al. (2020) showed a spatial diffusion of COVID-19 fear in the US, which appears to be concentrated in the regions with the highest number of reported COVID-19 cases. From a Turkish survey, Bakioglu et al. (2021) showed a correlation between the fear of COVID-19 and stress, anxiety, and depression. In addition, intensive exposure to media is positively related to stress and is detrimental to mental health (Peretti-Watel et al., 2020; Planchuelo-Gómez et al., 2020; Y. Wang et al., 2020).

Measures taken to contain the epidemic have also generated anxiety or depressive symptoms. García-Prado et al. (2022) have shown that lockdown strictness is related to more anxiety, insomnia, and depression in 17 countries (using the SHARE survey). Adams-Prassl et al. (2022) have shown from US data that lockdown measures lowered mental health, but this effect was entirely driven by women. Lockdowns led to various consequences, such as a decrease in social relations, more time spent at home, and work modifications; and their impact on mental health may have been unevenly distributed within the general population. While poor housing is known to impair mental health (Evans et al., 2003), stay-at-home orders could have increased inequality regarding housing: small apartments and collective dwellings were associated with depressive symptoms during lockdown (Akbari et al., 2021; Amerio et al., 2020). In Spain, where no outdoor physical activity was allowed during the first confinement, the intention to go outdoors and practice sports was positively associated with self-reported stress (Planchuelo-Gómez et al., 2020). Among young adults in the US, loneliness was associated with a higher level of mental health symptomatology, and those reporting an increase in feelings of loneliness also (mostly) indicated an increase in anxiety and depression, as well as in drinking and drug use (Horigian et al., 2021).

The school closures negatively affected the mental health of parents. In Japan, Yamamura and Tsustsui (2021) have shown a negative effect only for less-educated mothers who had children attending primary school. From US data, Zamarro and Prados (2021) showed that women carried a heavier load of childcare than men in the provision of childcare during the COVID-19 crisis, with only a limited influence on their working situation. The effect on psychological distress was

driven by mothers of elementary school-age and younger children. In China, Wu et al. (2020) found stronger anxiety among parents of the primary, middle, and high school students than among parents of college students.

The impact of containment measures on work is important to explore. The risk of being affected varies widely according to the employment sector, resulting in a differential impact on mental health (Lesage et al., 2020). Among people affected, changes in work organization were detrimental: people who stopped working were more affected than people working from home (for whom it was a novelty), who were more affected than people working as usual (Lesage et al., 2020; Peretti-Watel et al., 2020; Zhang et al., 2020).

From a COVID-19-focused questionnaire of the UAS implemented between March 10 and 31, 2020, Kämpfen et al. (2020) showed that worsening mental health was more strongly associated with concerns about the economic consequences of the pandemic than with social distancing and the perceived risk of dying from COVID-19.

COVID-19 has not homogeneously affected the population, and the crisis has increased health inequalities. Deprived people were more prone to psychological distress during lockdowns (Gandré et al., 2020), and the decrease in anxiety observed in the general population during the first months of the pandemic was not observed among them (Chan-Chee et al., 2020). They were also more prone to severe forms of COVID-19, as deprived people are more often affected by risk factors, more exposed to the virus, and have a higher probability of foregoing health care (Coutrot et al., 2021; Dubost et al., 2020), with higher mortality in deprived municipalities (Brandily et al., 2021). The lockdown further decreased the prevalence of infections among richer people (Bajos et al., 2021). On the other hand, the lockdown policy primarily affected those people, as they were more exposed to the risk of loss of jobs, have less access to telework, and are more likely to live in overcrowded housing (Amossé et al., 2021; Jauneau & Vidalenc, 2021; Lambert et al., 2020).

From UK data, Davillas and Jones (2021) showed both an increase in psychological distress in the population and an increase in inequality in psychological distress. The decomposition of this inequality shows that during the first wave of COVID-19, age and gender contributed a large share, but after April 2020, this share decreased in favor of chronic health conditions, housing conditions, and neighborhood characteristics.

In a systematic review and meta-analysis, Robinson et al. (2022) highlight the risk of bias among surveys about COVID-19 impact on mental health due to differences in samples' recruitment processes (before and after the onset of the pandemic) and demographic profiles. Their results

show a mental health deterioration during the pandemic but qualify the extent of this effect, with changes in symptoms that became smaller over months. There was a significant increase in symptoms of depression and anxiety, a decrease in symptoms of psychosis, and no significant change in measures of general mental health. It calls for using other data sources, less prone to that kind of bias.

2.2. Demand for mental healthcare and psychotropic drug consumption

It would be expected that the effects of the pandemic on psychotropic drug consumption reflect a negative impact on mental health. However, beyond this effect, psychotropic drug consumption depends on other factors that can interfere, namely, healthcare demand, prescription behaviors, drug availability, and insurance coverage. More information about BZD dispensing and reimbursement is provided in section 3.2.

The lockdown that started in March 2020 led to a sharp decrease in GP activity (Tuppin et al., 2022), but mental health care demand increased for half of GPs, and the increase in consultations for stress, anxiety and depressive disorders was slightly more frequent in the most impacted areas (Monziols et al., 2020). Stress, anxiety, and depressive symptoms associated with COVID-19 have been related, among some people, to an increase in tobacco and alcohol consumption or new substance use (Czeisler, 2020; Guignard et al., 2021; Rodriguez et al., 2020).

During the pandemic, the French scientific interest group EPI-PHARE relied on the SNDS data to accurately monitor medication consumption in France (Weill, Drouin, Desplas, Cuenot, et al., 2020c). They noticed stockpiling behavior at the beginning of the first lockdown, followed by underconsumption. This behavior comes from people who already had a prescription and went to refill. It has been noticed in other countries, such as Germany (Kostev & Lauterbach, 2020) and Portugal (Romano et al., 2020). In the specific case of anxiolytics and hypnotics (among which BZDs are prominent), use quickly became higher than expected (after the first month of lockdown). Over six months since the beginning of the lockdown, sales were higher by 1.1 million and 480,000 than expected, and introductions of new treatments were higher by 4.6% and 2.6% from the equivalent period in 2019. Since then, consumption has remained above the expected level, including during 2021 (Weill et al., 2021). Sanchez et al. (2022) found the same trend in the military population. From the same database, Levallant et al. (2021) showed a significant increase in the share of patients weekly treated from March 2020 compared to the previous period, with a steeper rise for the youngest patients.

Varied trends in psychotropic drug use have been seen worldwide. In an early review, Sarangi et al. (2021) highlighted that some studies showed an increase in the consumption of BZDs while others showed a decrease in prescription refills, which may come from gaps in mental healthcare. The Google Trends score of the most used BZDs has increased in Italy in the four months following the emergence of COVID-19 in the country (Mattiuzzi et al., 2022). Among children and adolescents, incident anxiolytic and hypnotic treatments decreased in the second semester of 2020 (compared to the same period in 2019) in the Manitoba Province, Canada (Leong et al., 2022); and immediately dropped after the beginning of the pandemic in Portugal (Estrela et al., 2022). In the longer term, psychotropic drug use increased after the onset of COVID-19. In Asturias, Spain, consumptions of anxiolytics and hypnotics were 8.7% and 15.3% higher in 2021 than in 2018 (expressed in Defined Daily Doses (DDDs) for 1000 persons per day), respectively (García et al., 2022). In the US, De Dios et al. (2021) showed a significant increase (+2%) in the share of BZDs dispensed in a set of controlled substances, from the declaration of COVID-19 as a pandemic (March 13, 2020). In the Northeast region of Argentina, the DDDs dispensations of anxiolytics and hypnotics increased by 6.62% and 7.85%, respectively, in the semester following the beginning of the lockdown (Fridman, 2021). In Canada, Uthayakumar et al. (2022) did not detect any significant variation in the rate of BZD use after the declaration of a state of emergency. From an insurance database in the US, Milani et al. (2021) showed a downward trend in BZD prescribing from January 2018 to March 2021, except for a slight increase among women in April 2020 (5.32% of the population treated in April 2020); and a decreasing trend of Z-drugs use, interrupted from January 2020 for men and February 2020 for women until October 2020 (1.46% of patients treated in October 2022). In the case of two acute psychiatric inpatient units in Australia, Zaki and Brakoulias (2022) showed an increase in BZD use despite a diminution in admission, which peaked further when restrictions eased and admissions in the hospital raised.

To my knowledge, no study explores mechanisms through which the pandemic affected psychotropic drug use. At the individual level, Davillas and Jones (2021a) used the Shapley-Shorrocks decomposition to measure the contribution of demographics, chronic conditions, housing, household composition, and job status to socioeconomic inequalities in mental health. At the municipality level, Brandily et al. (2021) explore the effects of labor-market exposure and housing conditions on mortality inequalities in France. In England, Albani et al. (2022) show that inequalities in transmission and vulnerability to COVID-19 explain most of the geographical inequality in mortality (among four pathways).

Similarly, different channels can explain the impact of the COVID-19 pandemic on psychotropic drug use. Beyond the literature about mental health (see section 2.1), there is little evidence of direct

or indirect mechanisms by which COVID-19 may change BZD consumption. One possible channel is the negative impact on the economy. In France, the first confinement, which started in March 2020, led to a decrease in economic output of 5% of GDP (Malliet et al., 2020). The use of partial unemployment (up to 25% of the active population during the first confinement) allowed for the avoidance of a sharp rise in unemployment in 2020, although there was a decrease in the number of hours worked. The employment decrease was higher for youths, low-skilled workers, and those with short-term contracts (Jauneau & Vidalenc, 2021). Entire sectors have been at a standstill, and service-oriented activities have been most affected (Fernandes, 2020). However, layoffs tended to spill over to all economic sectors (Alstadsæter et al., 2020; Forsythe et al., 2020).

Evidence of a link between economics and psychotropic drug consumption is scarce, but economic decline might lead to feelings of insecurity, anxiety, and depression and lead people to use more psychotropic drugs to alleviate these feelings (Ketting, 1989). Recent data about the 2008 financial crisis tended to show an increase in psychotropic drug consumption during the time of crisis in Spain (Barceló et al., 2016) and Portugal (Silva et al., 2020), while another study did not find a significant effect (Martínez-Jiménez & Vall Castelló, 2020). For Martin Bassols and Vall Castelló (2016), the great recession had a procyclical effect on alcohol consumption (income effect hypothesis) and a countercyclical effect on tobacco, marijuana, and cocaine consumption (economic stress hypothesis and substitution effect).

The impact of the financial crisis on psychotropic drug use seems closely related to unemployment (Barceló et al., 2016), and job loss and insecurity are related to higher purchases of psychotropic drugs (Kaspersen et al., 2016; Rugulies et al., 2010).

The COVID-19 pandemic had a strong impact on mental health, and this has affected psychotropic drug consumption. While many channels can explain this effect, such as fear of the virus, loss of job, and a decrease in social interaction, the literature does not answer the mechanisms that could explain the relation with an increase in BZD consumption. With two years of hindsight (2020 and 2021), this study provides the factors associated with the increase in BZD use in 2020 and 2021 in France and compares them to preexisting determining factors. Moreover, it distinguished the extensive and intensive margin, which is not done in the literature, to my knowledge, although the increases in frequency and intensity of use have not been strictly concomitant.

3. Methodology

3.1. Data

The main source of data was the French National Data Health System (SNDS), a database that aggregates some nationwide sources of health data and data used for reimbursement of care (at the individual level). In particular, it matched outpatient care (i.e., relative to doctor consultations, drugs reimbursed in pharmacies, and medical laboratories) with inpatient care (relative to hospitalizations). This database provides information on the BZDs reimbursed to each patient from 2017 to 2021, per year.

Enrollment in the National Health Insurance is mandatory for all people living in France (citizen or not), and all BZDs (20 marketed molecules, including two related molecules) are subject to medical prescription and reimbursed by the National Health Insurance. I considered only BZDs sold in city pharmacies (belonging to the municipality or not) and not in the hospitals. The reimbursement rate is 65% for anxiolytic BZDs and 15% for hypnotic BZDs. The share left can be reimbursed by complementary health insurance, which covered 96% of the population in 2017 (Fouquet, 2020). As an indication, the prices in 2022 for the best-selling anxiolytic and hypnotic BZDs are €2.25 (alprazolam 250 mg) and €1.64 (zolpidem 10 mg), respectively.

From SNDS, it is possible to infer some health conditions. This methodology has been described by Rachas et al. (2020). Using reimbursements of medications, medical procedures, and ICD-10 codes (International Classification of Diseases) for long-term diseases and hospitalizations, they can attribute health conditions to each patient. These conditions include diseases, episodes of care, and chronic treatments. Only health conditions in 2019 in this study were used, but care consumption in 2019 and previous years were used to infer these conditions.

Because the SNDS does not provide socioeconomic information, these data were aggregated per municipality. This is the municipality of the primary residence of people, so even if people move to another municipality, the care consumption is related to their primary residence municipality. This methodology avoided the potential confounding factor of people who moved away from large cities during lockdowns. These data were completed with information on the structure of the labor market and housing at the municipality level from the census survey 2017 and 2018 of the French National Institute of Statistics (INSEE). The excess mortality in 2020 (compared to 2019) was available at the department level (which divides the French territory into 101 areas). Finally, access to GP was approached with the indicator APL in 2019 (*Accessibilité potentielle localisée*, localized potential accessibility). It aggregated data about physical proximity to GPs, the activity of GPs, and

the demand for health care regarding the age structure in the municipality of residence (Barlet et al., 2012; Vergier, 2016).

The statistical unit is the French municipality. For Paris, Lyon, and Marseille, I decomposed the municipality into districts (*arrondissements*). The study focuses on metropolitan France (overseas regions are excluded), and I excluded municipalities with fewer than 100 inhabitants in estimations (3,970 municipalities excluded). A total of 30,919 municipalities remain, 16 of which have missing data. The remaining 30,903 municipalities included 57,103,354 inhabitants.

3.2. *Econometric strategy*

The only information that varies over time is BZD consumption; other information is fixed over time (which prevents the use of panel data methods). Each year from 2018 to 2021, the influence of factors fixed over time was estimated on the BZD use variable using ordinary least squares. The model is written as follows:

$$\begin{aligned} \Delta BZD_{ym} = & \beta_1 ExcessMortality_{2020d} + \beta_2 R_{2019m} + \beta_3 Unemployment_{2017m} \\ & + \beta_4 E_{2018m} + \beta_5 H_{2018m} + \beta_6 Density_{2019m} \\ & + \beta_7 \log(1 + BZD)_{y-1m} + \beta_8 APL_{2019m} + \beta_9 Region + u_{ym} \end{aligned} \quad (3.1)$$

With $\Delta BZD_{ym} = \frac{BZD_{ym} - BZD_{y-1m}}{BZD_{y-1m}}$.

The estimated variable ΔBZD_{ym} is the variation rate (in %) of BZD use in each municipality (compared to the previous year). BZD use in the municipality is the number of BZD boxes reimbursed to people living in the municipality divided by the number of people insured in the municipality.

Independent variables were chosen to allow testing the two channels of effect: the effect of the pandemic and the effect of mitigation measures. The severity of the pandemic was captured by the excess mortality rate (%) in the French department during March-April 2020 compared to 2019 (*ExcessMortality*_{2020d}). I used the excess mortality rate at the beginning of the pandemic all years (even before the pandemic) for control reasons. The vulnerability to the pandemic is captured by risk factors for hospitalization or death from COVID-19 (*R*_{2019m}): the share of people over 65 years old in 2019; the share of people with a chronic disease (except psychiatric) in 2019; and the share of people with a chronic psychiatric disease in 2019 (Semenzato et al., 2021).

The second channel, the effect of public policies to fight the outbreak, is captured by employment and housing characteristics. The employment variables should allow controlling for labor market

vulnerability related to the impact of economic shock. They include $Unemployment_{2017m}$, the unemployment rate in the municipality in 2017, and E_{2018m} , a vector of employment-related variables in 2018 in the municipality: the share of people without a diploma in 2018 (proxies of economic vulnerability), and the share of employees in the total jobs in 2018 (kind of protection against job loss, as the French State maintained the wages of employees who stopped working during the lockdown, through the partial activity mechanism). The housing characteristics are related to the stay-at-home orders impact and controlled via H_{2018m} a vector of variables related to housing in the municipality in 2018: the share of apartments in the total housing in 2018 and the share of single-person households in 2018; and $Density_{2019m}$ the density of the municipalities in 2019 (four modalities). These variables aim to capture both the characteristics of housing (such as the possibility of going outdoors or benefit from rural areas) and of social connection (inside the household but also friendships throughout the municipality).

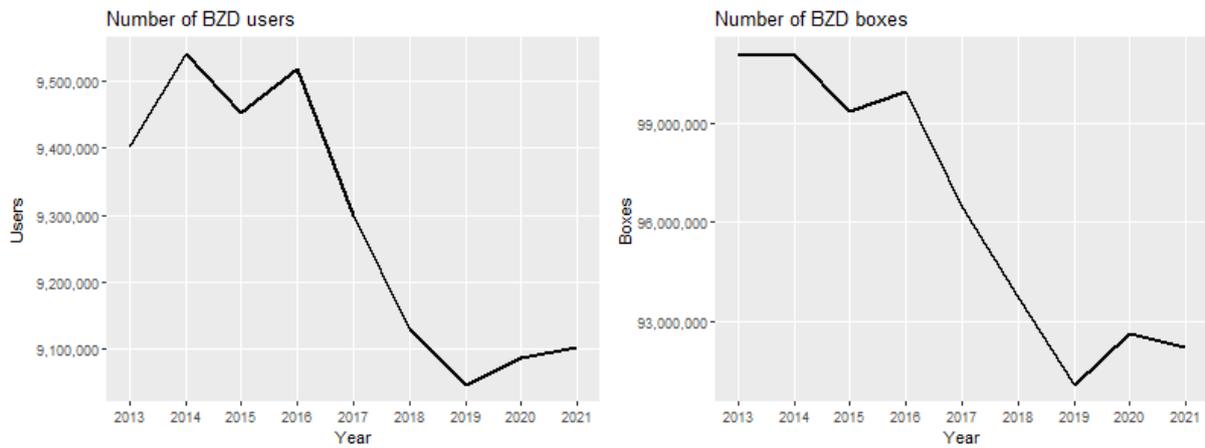
Other control variables are the log (+1) of BZD use in the previous year in the municipality, access to health care (through GP localized potential accessibility: APL_{2019m}), and the region (13 modalities).

I performed statistical analyses using R version 4.1.2. I considered a p-value of less than 0.05 statistically significant.

3.3. Statistics

After years of struggle against overconsumption, the global BZD consumption tendency decreased until 2015 (ANSM, 2017). Statistics of BZDs sales from 2013 to 2021 confirmed that this trend continues until 2019, but it is interrupted in 2020 (Figure 3.2). In 2020, the number of BZD users (i.e., the number of people with at least one BZD reimbursed in the year) was over 9 million (+0.5% vs. 2019), and the number of BZD boxes reimbursed (in pharmacies) was over 92.6 million (+1.7% vs. 2019). This result is in line with other works related to psychotropic medication consumption in France in 2020 (Weill et al., 2021). The total number of BZDs boxes sold in 2021 remained higher than that in 2019, but slightly decreased compared to that in 2020 (Figure 3.2 right panel). The number of BZD users is increasing in 2021 compared to 2020 (Figure 3.2 left panel), which could indicate a greater increase in the intensity of use in 2020 (intensive margin) and a wider diffusion in 2021 (extensive margin).

Figure 3.2: Trends of BZD sales in France from 2013 to 2021



Source: SNDS. Entire France.

Table 3.1 shows the average BZD use at the municipality level and the average variation rate. Although the average use slowly decreased in 2018 and 2019 (compared to the previous year), we see a clear increase in 2020 and a more moderate increase in 2021.

Table 3.1: Evolution of BZD use per municipality from 2018 to 2021

Year	Average BZD use	Average variation rate of BZD use (%)
2018	1.326	-1.949
2019	1.281	-2.228
2020	1.302	3.250
2021	1.304	1.631

Note: BZD use is the mean number of boxes reimbursed per inhabitant. Data from SNDS.

Field: France, municipalities with fewer than 100 inhabitants and overseas departments are excluded.

N obs. = 30,903

These variables are stratified according to the density of municipalities (four modalities from dense to very low dense), in Tables 3.A1 and 3.A2 in the Appendix, for BZD use and the variation rate of BZD use, respectively. The consumption is higher in densely populated municipalities, in line with the previous literature about psychotropic drug use (Johnell & Fastbom, 2009). Before 2020, the use decreased in all kinds of municipalities. The variation rate became positive in 2020, from 2% for dense municipalities to 4% for very-low-density municipalities. In 2021, it returned to a slightly negative level for dense municipalities (-0.5%) but continued to increase for other densities: from +0.5% for intermediate to +3.1% for very-low dense municipalities.

Statistics about independent variables are presented in Table 3.2. On average, the share of people aged 65 and older was 24% in the municipalities. This figure was greater than the share of people aged 65 and older in the entire French population in 2019 (20%, source: Insee) due to the

overrepresentation of small municipalities, where the population was fewer and older. Similarly, the unemployment rate in the municipalities was 10.8% on average, while it was 9.4% at the French level the same year (source: Insee). The apartments are a minority (compared to houses); more than one-third of people suffer from chronic disorders, but only 3.2% suffer from chronic psychiatric diseases. On average, the accessibility to GP was 3.2% for a full-time GP per 100,000 inhabitants. The excess mortality rate in March-April 2020 was 21.5% on average compared to March-April 2019.

Table 3.2: Municipality statistics

Variables	Mean (SD)	Range	N
Share of people aged 65 and more in 2019	23.925 (6.991)	3.648 - 77.333	30,903
The unemployment rate in 2017	10.784 (4.435)	0.000 - 41.670	30,903
Share of people without a diploma in 2018	21.774 (6.879)	3.200 - 63.000	30,903
Share of single-person households	28.930 (7.998)	0.000 - 66.700	30,903
Share of apartments in total housing in 2018	9.369 (14.080)	0.000 - 97.600	30,903
Share of salaried jobs in total jobs in 2018	65.800 (18.822)	0.000 - 100.000	30,903
Share of people with chronic diseases (except psychiatric) in 2019	34.562 (6.441)	8.182 - 64.957	30,903
Share of people with chronic psychiatric diseases in 2019	3.212 (1.574)	0.000 - 30.982	30,903
Excess mortality in March-April 2020	21.521 (23.307)	-10.600 - 117.100	30,903
Accessibility to GP (APL)	3.186 (1.230)	0.000 - 24.448	30,903

Sources: SINDS for age, Drees for APL, Insee for other variables. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded.

Statistics related to the density of municipalities and belonging regions are presented in Table 3.A3 in the Appendix. Low-density and very-low-density municipalities are prominent: 59% and 29%, respectively.

4. Results

4.1. Factors explaining variation in BZD use from 2018 to 2021

Table 3.3 presents the results per year from 2018 to 2021. The COVID-19 pandemic affected years 2020 and 2021, and 2018 and 2019 are used to compare with the pre-pandemic situation. The effect of the severity of the pandemic was negative before 2020, indicating a decreasing trend before the pandemic in the most affected areas. In 2020, the effect was not significant, which indicated a positive effect on the variation in BZD use (compared to the previous situation). The effect of risk factors for severe COVID-19 did not change from 2020, the opposite for psychiatric diseases whose effect seemed to decline from 2020 (and vanished in 2021).

The effect of socioeconomic variables became stronger over time, particularly in 2020 for the unemployment rate, people without a diploma, and single-person households. The effect of the share of apartments was negative in 2021.

The log of the previous-year BZD use in the municipality was the strongest variable in the model. Its negative effect could come from a statistical artifact: municipalities with the highest and lowest BZD use tend to get closer to the mean the following year. This strong negative effect is present in all the specifications of the model.

Table 3.3: Results of estimations of BZD use variation at the municipality level per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.024* (0.0107)	-0.0315** (0.012)	-0.0209 (0.0136)	-0.0339** (0.0125)
Share of elderly people (> 65 years)	0.0082 (0.0394)	-0.0506 (0.0396)	-0.0483 (0.0473)	-0.0163 (0.0387)
Share of people with chronic disease	0.2326*** (0.0414)	0.2361*** (0.0404)	0.2126*** (0.0569)	0.1819*** (0.0473)
Share of people with psychiatric disease	1.4905*** (0.157)	1.4151*** (0.1117)	0.5613*** (0.117)	0.1611 (0.0955)
<i>Socio-economic variables</i>				
Unemployment rate	0.043 (0.0321)	0.1173** (0.042)	0.174*** (0.05)	0.1395*** (0.0336)
Share of people without a diploma	0.0214 (0.0215)	0.0558* (0.0237)	0.0709** (0.0272)	0.0059 (0.0221)
Share of single-person households	-0.01 (0.0229)	0.0574* (0.0285)	0.0759** (0.0256)	0.1163*** (0.027)
Share of apartments in total housing	-0.0036 (0.0107)	-0.002 (0.0123)	-0.0202 (0.0132)	-0.0241* (0.0099)
Share of employee jobs in total jobs	0.0104 (0.008)	-0.0111 (0.01)	0.0107 (0.0094)	0.0015 (0.0095)
<i>Other control variables</i>				
BZD use (log) the previous year	-23.0417*** (1.07)	-24.3838*** (1.7226)	-26.503*** (1.4038)	-23.491*** (1.2021)
Accessibility to GP	0.1822 (0.1025)	0.2834** (0.1073)	0.2804* (0.111)	0.0538 (0.0925)
Densely populated municipality (ref.: intermediate)	0.5203 (0.3926)	-0.3434 (0.4567)	-0.3475 (0.4505)	-0.4217 (0.4234)
Low-density municipality (ref.: intermediate)	-0.6282* (0.2913)	-1.0091** (0.3243)	-0.7853** (0.277)	-0.4121 (0.2376)
Very low-density municipality (ref.: intermediate)	-0.3862 (0.4088)	-1.2262** (0.4435)	-0.5845 (0.4948)	0.1403 (0.4429)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded. N obs. = 30,903.

*Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.*

While BZD use in France clearly increased since the beginning of the pandemic, the results of this first regression are not straightforward to interpret because the drivers in 2020 do not differ much from previous years. However, the factors related to the pandemic do not explain the steep rise in BZD use. The negative effect of pandemic severity was nonsignificant in 2020 (negative in 2018 and 2019, used as references; and in 2021), and the positive effect of chronic diseases (psychiatric and others) clearly decreased from 2020. Conversely, the magnitudes of the effects of housing and employment characteristics increased from 2020.

At the beginning of the lockdown, people with prescriptions were authorized to refill even when their prescriptions expired. EPI-PHARE, which monitored anxiolytic and hypnotic drug use during the pandemic, showed an increase in the intensity of use (among people who already consumed) at the beginning of the pandemic, followed by an increase in the number of people newly treated by BZDs (Weill, Drouin, Desplas, Cuenot, et al., 2020c). This is strengthened by the sales statistics (see Figure 3.2), which show a decrease in the overall number of BZD boxes reimbursed in 2021 compared to 2020, but an increase in the number of people treated that same year. This suggests that the drivers for starting to use BZDs and for increasing consumption might differ. This is the reason why I distinguished the extensive (frequency of users) and intensive (intensity of use among users) margins.

4.2. Intensive and extensive margin

Table 3.4 provides the results of the decomposition into extensive and intensive margins. In the extensive margin, the explained variable becomes the variation rate of the share of people using BZDs (i.e., with a BZD reimbursed) in the municipality compared to the previous year. In this specification, the control for past BZD use is the share of people using BZDs in the municipality the previous year. In the intensive margin, the explained variable becomes the variation rate of the average BZD boxes reimbursed per BZD user in the municipality, and past BZD use, used as a control, is the log of the average number of BZD boxes used per BZD user in the last year (+1).

Table 3.4: Results of estimations of the extensive and intensive margin of BZD use variation per year

Variables	Extensive margin (variation rate of the share of BZD users)				Intensive margin (variation rate of the average number of BZD boxes used)			
	2018	2019	2020	2021	2018	2019	2020	2021
<i>Covid-19-related variables</i>								
Excess mortality in March-April 2020	-0.0271* (0.0112)	-0.0424** (0.0136)	-0.0194 (0.0129)	-0.0363** (0.0134)	-0.0221** (0.0077)	-0.0126 (0.0113)	-0.0312** (0.0111)	-0.0253* (0.0103)
Share of elderly people (> 65 years)	0.0534 (0.032)	0.0167 (0.0372)	0.1211** (0.045)	0.0362 (0.0326)	-0.0669 (0.041)	-0.0775* (0.0369)	-0.1914*** (0.0356)	-0.0571 (0.0415)
Share of people with chronic disease	0.227*** (0.0387)	0.2591*** (0.0414)	0.2356*** (0.055)	0.1798*** (0.0427)	0.2113*** (0.0458)	0.2061*** (0.0465)	0.1989*** (0.0428)	0.2044*** (0.0499)
Share of people with psychiatric disease	0.8223*** (0.0798)	0.9565*** (0.0997)	0.4577*** (0.0888)	0.4007*** (0.0876)	1.4546*** (0.119)	1.2872*** (0.0923)	1.24*** (0.0955)	0.7463*** (0.0908)
<i>Socio-economic variables</i>								
Unemployment rate	0.069* (0.0319)	0.1225*** (0.0304)	0.1522*** (0.0444)	0.0992*** (0.0261)	0.0328 (0.0305)	0.0539 (0.0396)	0.1248** (0.0419)	0.1194** (0.0375)
Share of people without a diploma	-0.0161 (0.0186)	0.0316 (0.0253)	-0.0161 (0.026)	-0.0088 (0.0236)	0.1299*** (0.0206)	0.0838*** (0.0222)	0.1716*** (0.0283)	0.1169*** (0.0227)
Share of single-person households	0.0118 (0.0236)	0.0169 (0.0187)	0.0401 (0.0247)	0.0597** (0.0209)	0.0334 (0.025)	0.0737** (0.0239)	0.1023*** (0.0269)	0.0991*** (0.0256)
Share of apartments in total housing	-0.0033 (0.0125)	-0.0235* (0.0114)	-0.0082 (0.0138)	-0.0235* (0.0113)	-0.0131 (0.0133)	0.0077 (0.0127)	-0.0348** (0.0134)	-0.0116 (0.0135)
Share of employee jobs in total jobs	0.0119 (0.0068)	-0.0025 (0.0071)	0.0247*** (0.0074)	0.0034 (0.0076)	-0.0108 (0.0084)	-0.0035 (0.0081)	-0.0184* (0.0085)	-0.0093 (0.0079)
<i>Other control variables</i>								
Past BZD use [§]	-1.5982*** (0.0674)	-1.7275*** (0.0757)	-1.8721*** (0.0844)	-1.7714*** (0.0764)	-28.8027*** (0.8078)	-28.3395*** (0.8985)	-33.2534*** (1.0412)	-30.0553*** (0.9222)
Accessibility to GP	0.3379*** (0.0921)	0.3602*** (0.0832)	0.4962*** (0.1068)	0.507*** (0.0945)	-0.025 (0.109)	0.0364 (0.0921)	-0.036 (0.1041)	-0.2499* (0.0996)
Densely populated municipality (ref.: intermediate)	-0.3272 (0.4768)	-0.0766 (0.612)	-1.0212 (0.5488)	-1.1134* (0.5128)	1.3193*** (0.3511)	0.294 (0.4605)	1.183** (0.4332)	0.9714* (0.4816)
Low-density municipality (ref.: intermediate)	-0.8311** (0.2806)	-1.4329*** (0.2959)	-0.6566 (0.3501)	-0.8792** (0.2743)	-0.0735 (0.2351)	0.2269 (0.2435)	-0.6047* (0.2726)	-0.0745 (0.238)
Very low-density municipality (ref.: intermediate)	-0.8575 (0.4554)	-2.0716*** (0.4204)	-1.0429 (0.582)	-0.8827* (0.3954)	0.1423 (0.3798)	0.7959* (0.3817)	0.078 (0.4331)	0.358 (0.4139)
Region	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded. N obs. = 30,903

Note: §: the control at the extensive margin is the share of BZD users in the municipality the previous year; the control at the intensive margin is the average number of BZD boxes used the previous year.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.

It is interesting to look at the factors diverging between both specifications. The severity of the pandemic in the department in 2020 has a positive effect on the extensive margin this same year (compared to the previous year) but a negative effect on the intensity of use. The effect of the share of elderly individuals, which was insignificant in the main estimate, is positive and significant in 2020 at the extensive margin, and negative and significant in 2020 at the intensive margin (slightly in 2018 and 2019). An explanation could be a more preventive prescribing from doctors, but less effective psychological impairment, in accordance with previous studies showing that youth were more affected (see, e.g., Y. Wang et al., 2020). The share of people with chronic and psychiatric diseases affects the frequency and intensity of use in the same way as the main estimate (positive but with decreasing amplitude from 2020).

Regarding socioeconomic factors, the trend is to amplify over time. In 2020, the positive effects of unemployment, the absence of a diploma, and single-person households are clear. This reflects the influence of economic vulnerability and lack of social support, which are risk factors for BZD use in normal times, amplified by the occurrence of the outbreak. The share of apartments in total housing has a negative effect at extensive and intensive margins. The share of employees is positive at the extensive margin and slightly negative at the intensive margin in 2020.

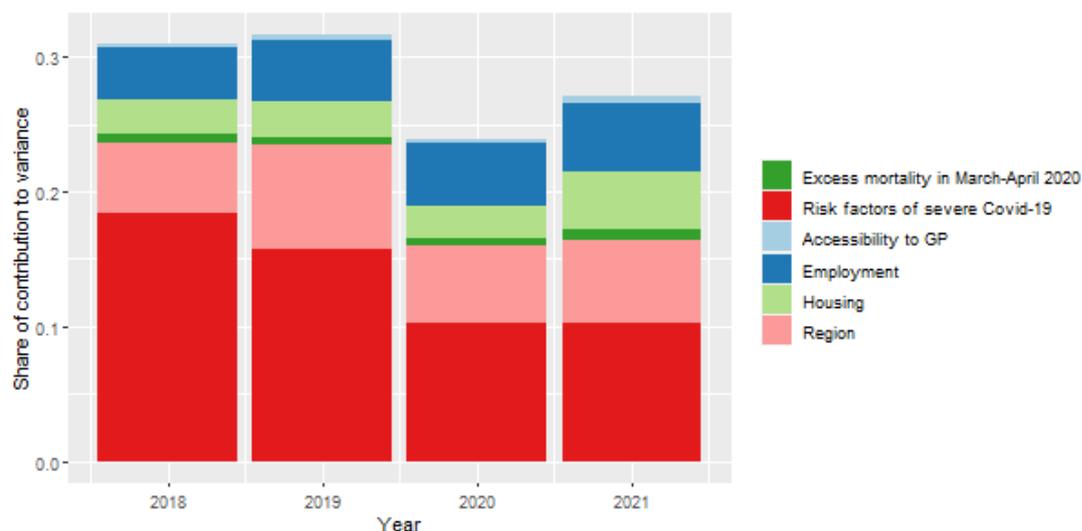
Regarding the other variables, past BZD use is the main factor explaining the variation rate, with an increase (of absolute value) from 2020. The accessibility to GP is associated with an increase in the frequency of use (significant every year) but with a decrease in the intensity of use in 2021. A channel explaining that fact could be better access to drug prescribing in the area with the best physician supply but a higher volume prescribed in the least supplied areas. Ventelou et al. (2010) showed an increase in drug prescriptions (in the case of depression) for doctors with higher consultation rates. The density of municipalities is negatively related to the variation rate but without a large difference between years.

4.3. Decomposition of variance

To ease the comparison between years, I decomposed the variance of the estimations. It was performed using the method proposed by Johnson (2000) through the R package *relaimpo* (Groemping, 2007; Grömping, 2015). Figure 3.3 shows the results of variance decomposition of the variation in BZD use per year. For readability reasons, past BZD use in the municipalities is not represented (it constitutes the gap to 1 on the figure). This is by far the major factor explaining BZD variation, and it is increasing in 2020.

In 2020, the share of variance explained by risk factors for severe COVID-19 fell (from 16% to 10%). The share explained by employment-related and housing-related variables increased in 2021 (5.1% and 4.3%, respectively, compared to 4.6% and 2.4% in 2020).

Figure 3.3: Variance decomposition of the BZD use variation rate, per year



Note: Risk factors for severe COVID-19 are the share of people > 65, the share of people with psychiatric disease, and the share of people with psychiatric disease. Employment includes the unemployment rate, the share of employees in total jobs, and the share of people without a diploma. The housing includes the density of housing, the share of single-person households, and the share of apartments in total housing. For readability reasons, the past use of BZDs is not present in the figure but constitutes the share left to 1.

4.4. Subgroup analysis

The French municipalities include very rural areas, from 100 inhabitants up to more than 500,000 inhabitants in Paris' arrondissements. To address this heterogeneity, the analysis was stratified by the density of municipalities (4 modalities). The results are provided in Tables 3.A4 to 3.A7 in the Appendix.

For dense and intermediate-dense municipalities, few variables have a significant effect. This could result from a lack of statistical power due to the small numbers (cf. Table 3.A3 in the Appendix). For low-dense and very-low-dense municipalities (which are far more numerous), the effects of variables are consistent with the main estimate. In particular, the unemployment rate has a positive effect in 2020. Among the very low-density areas, the share of people without a diploma and the share of single-person households are positive and significant from 2019 to 2021.

4.5. Sensitivity analysis

The weight associated with each municipality is equal to 1. The variance of the smallest ones being far higher than that of the largest could bias the results. The analysis was repeated excluding the

municipalities with fewer than 500 or 1000 inhabitants. The results are shown in Tables 3.A8 and 3.A9, respectively, in the Appendix.

The effect of the share of elderly individuals becomes negative and significant in 2020. Chronic and psychiatric conditions have a positive and large effect but fade out from 2020. The effects of socioeconomic variables are no longer significant, except for a positive effect of the unemployment rate in 2018 and 2020 for municipalities above 500 inhabitants and in 2021 in municipalities above 1,000 inhabitants and a negative effect of the share of people without a diploma in 2018 and 2021 in municipalities above 1,000 inhabitants.

5. Discussion

The deterioration of the mental health of the population during the COVID-19 outbreak is a major concern. An increase in psychotropic drug use could worsen the situation in the case of prolonged use and interrupt the previous decreasing trend. The increase was unevenly distributed in the population, and this study aims to disentangle which of the COVID-19 control measures drive the effect. Many things occurred during this time, which could affect mental health, such as the spread of the disease, work modifications, increased time spent at home, reduction of social connections, and economic issues. All of these factors are interrelated, and it is difficult to disentangle simple effects. They affected the territories in a heterogeneous way.

Before the outbreak of the pandemic, in 2018 and 2019, the main factors associated with the increase in BZD use in the municipalities were the share of people living with chronic disease and the share of people affected by chronic psychiatric illness (apart from past BZD use, which is always the major explanatory factor). From 2020, the importance of these factors decreased (in particular for the share of psychiatric patients). If chronic conditions are expected to increase drug intake, less deterioration in mental health was observed among people with a pre-existing mental health condition (Mengin et al., 2020; E. Robinson et al., 2022). These findings may be explained by a feeling of normalization, a more structured routine, and reduced exposure to external stressors.

In 2020, the consumption of BZDs was stable in the areas most impacted by the pandemic, while they were on a decreasing trend before that. In 2020 and 2021, there was an increase in the importance of socioeconomic variables: factors of fragility in the labor market (the unemployment rate and share of nongraduates) and factors of lower social support (the share of people living alone). Proxy variables of housing are less straightforward to interpret: the share of apartments is not associated with an increase in BZD use, meaning a lesser influence in terms of the kind of

housing. However, after controlling for confounding factors, the density of municipalities is positively associated with changes in BZD use.

The results show that the factors related to the increase in BZD use in 2020 and 2021 are mainly related to the economic situation and lack of social support. The economic shock resulting from containment measures hit the more deprived people harder (the more often unemployed, with more low-quality jobs, and more difficulties in finding a job). Stay-at-home orders and social distancing hit people harder in terms of low levels of social support. This stresses the role of social interactions, which has been noted elsewhere (see, e.g., Etheridge & Spantig, 2022). These people are more concerned or vulnerable to mental health issues and increased use of BZDs. The severity of the pandemic in 2020 was also associated with more BZD use (compared to the preexisting trend), but the share of variance explained is very small. In contrast, the risk factors for severe COVID-19 are not associated with increased use, while they were before 2020.

Working conditions have also been affected and could explain these results. The working class was less able to work from home (half of them stopped working altogether) and less often had a room dedicated to working at home (Lambert et al., 2020). The effect of the share of salaried jobs is ambiguous (positive in 2020 at the extensive margin and negative in 2020 at the intensive margin). Being an employee was a protection against the risk of losing a job (the French State paid the salaries of the employees who stopped working because of the pandemic), but it can be associated with less freedom to adapt (compared to self-employed workers) or more change in work organization (compared to farmers).

While there are studies related to concomitant psychotropic drug use (see, e.g., Lesén et al., 2010), this study clearly distinguished the extensive and intensive margins. The statistics show an increase in the share of people using BZDs, but the results are more striking at intensive margins, i.e., on the increase in BZD consumption.

The study is not free of limitations. The variables used in the model are coarse and can aggregate various situations. The potential collinearity prevents the use of too many variables, those relevant for capturing the effects of pandemic and socioeconomic vulnerabilities are included in the model. Estimations seem robust to stratification by the density of municipalities. The time interval used (year) is also coarse, but decomposition per month did not show any particular results. Moreover, conclusions about the drivers of BZDs during the pandemic are related to municipalities and should not be assimilated to individuals, who are at risk of being subject to ecological fallacy (Freedman, 2015; W. S. Robinson, 1950).

6. Conclusion

After years of struggle against overconsumption of BZDs, the consumption trend has been downward in France since the beginning of the 2000s. However, the COVID-19 pandemic interrupted this trend, with a strong rebound in sales in 2020. The objective of this study was to understand the channels through which the pandemic could have influenced BZD consumption in French municipalities.

In 2020 and 2021, BZD uses increased more in municipalities with a higher unemployment rate, a higher share of people without a diploma, and a higher share of single-person households. These factors tend to show the impact of containment measures (i.e., economic stall, stay-at-home orders, social distancing, and work-at-home and work interruption). The severity of the outbreak in the department of residence was associated with more use in 2020, but this effect was only slight. The risk factors for COVID-19 are not associated with an increase in BZD use.

This study sheds light on the drivers of the increase in psychotropic drug use in France during the COVID-19 pandemic. It should help to improve the struggle against the overconsumption of BZDs, while pandemics may occur more frequently in the future.

7. Appendix

7.1. Others statistics

Table 3.A1: Average (SD) BZD use per year and density of the municipality

Year	Densely populated municipality (N=582)	Intermediate-density municipality (N=3,204)	Low-density municipality (N=18,204)	Very low-density populated municipality (N=8,929)
2018	1.472 (0.541)	1.417 (0.559)	1.314 (0.551)	1.308 (0.616)
2019	1.434 (0.529)	1.381 (0.545)	1.270 (0.536)	1.258 (0.598)
2020	1.461 (0.535)	1.413 (0.551)	1.292 (0.539)	1.272 (0.599)
2021	1.451 (0.525)	1.413 (0.544)	1.294 (0.534)	1.276 (0.594)

Note: BZD use is the average number of BZD boxes reimbursed per inhabitant. The variable is bounded at the 99th percentile. Overseas departments and municipalities with fewer than 100 inhabitants are excluded. N = 30,903.

Table 3.A2: Average (SD) BZD use variation per year and density of the municipality

Year	Densely populated municipality (N=582)	Intermediate-density municipality (N=3,204)	Low-density municipality (N=18,204)	Very low-density populated municipality (N=8,929)
2018	-2.444 (4.328)	-2.259 (8.010)	-2.259 (13.311)	-1.174 (22.547)
2019	-2.434 (3.857)	-2.288 (6.948)	-2.597 (13.374)	-1.440 (27.244)
2020	2.041 (3.854)	2.785 (7.137)	2.915 (14.329)	4.179 (26.276)
2021	-0.487 (3.683)	0.455 (6.797)	1.191 (14.285)	3.087 (25.502)

Note: BZD use variation is the variation rate of BZD use compared to the previous year (%). The variable is bounded at the 95th percentile. Overseas departments and municipalities with fewer than 100 inhabitants are excluded. N = 30,903.

Table 3.A3: Density and region of municipalities

Variables	Mean (SD)
<i>Density of the population in the municipality</i>	
Densely populated municipality	582 (1.9%)
Intermediate-density municipality	3201 (10.4%)
Low-density municipality	18198 (58.9%)
Very low-density populated municipality	8922 (28.9%)
<i>Region</i>	
AUVERGNE RHONE ALPES	3784 (12.2%)
BOURGOGNE FRANCHE COMTE	3015 (9.8%)
BRETAGNE	1205 (3.9%)
CENTRE VAL DE LOIRE	1702 (5.5%)
CORSE	179 (0.6%)
GRAND EST	4281 (13.9%)
HAUTS DE FRANCE	3533 (11.4%)
ILE DE FRANCE	779 (2.5%)
NORMANDIE	2518 (8.1%)
NOUVELLE AQUITAINE	4113 (13.3%)
OCCITANIE	3700 (12.0%)
PAYS DE LA LOIRE	1224 (4.0%)
PROVENCE ALPES COTE D AZUR	870 (2.8%)

Field: France, overseas departments and municipalities with fewer than 100 inhabitants are excluded. N = 30,903.

7.2. Results of subgroup analysis

Table 3.A4: Results of estimations of BZD use variation in dense municipalities per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.0182 (0.011)	-0.0005 (0.0147)	-0.0148 (0.0087)	-0.0047 (0.0151)
Share of elderly people (> 65 years)	-0.1545 (0.1272)	-0.107 (0.0944)	-0.0442 (0.1063)	0.0434 (0.107)
Share of people with chronic disease	0.2074 (0.1956)	0.2202 (0.1285)	0.0898 (0.1379)	-0.0386 (0.1568)
Share of people with psychiatric disease	1.252** (0.4514)	0.891** (0.3392)	0.1922 (0.2192)	0.0295 (0.1641)
<i>Socio-economic variables</i>				
Unemployment rate	-0.0056 (0.1055)	0.0207 (0.0848)	-0.0806 (0.0824)	0.0862 (0.0886)
Share of people without a diploma	-0.0369 (0.0665)	-0.0444 (0.0622)	0.0294 (0.0634)	-0.098 (0.0818)
Share of single-person households	0.0453 (0.0515)	-0.0044 (0.0372)	-0.0459 (0.0369)	0.0043 (0.035)
Share of apartments in total housing	-0.035* (0.0155)	-0.0151 (0.0161)	-0.0047 (0.0114)	-0.0297* (0.0131)
Share of employee jobs in total jobs	-0.0901 (0.0584)	0.022 (0.0454)	-0.022 (0.0607)	0.0559 (0.0424)
<i>Other control variables</i>				
BZD use (log) the previous year	-11.9056*** (2.944)	-8.0981*** (2.1922)	-4.5194* (2.2833)	-3.9923 (2.035)
Accessibility to GP	0.03 (0.1915)	-0.141 (0.1313)	-0.0686 (0.1845)	0.1694 (0.1179)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded. N = 582.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.

Table 3.A5: Results of estimations of BZD use variation in intermediate-dense municipalities per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.0296 (0.0196)	-0.0109 (0.0135)	-0.0187 (0.0117)	-0.0168 (0.0128)
Share of elderly people (> 65 years)	-0.0384 (0.0715)	-0.0576 (0.0616)	-0.0652 (0.0669)	-0.0632 (0.0637)
Share of people with chronic disease	0.2828* (0.1204)	0.1556 (0.0811)	0.1769 (0.0943)	0.18* (0.0761)
Share of people with psychiatric disease	3.2236* (1.5185)	0.6737*** (0.155)	0.316** (0.1113)	0.0898 (0.105)
<i>Socio-economic variables</i>				
Unemployment rate	0.0332 (0.0486)	0.1238* (0.0509)	0.1102* (0.0535)	0.0173 (0.0363)
Share of people without a diploma	-0.087* (0.0428)	-0.0527 (0.0382)	-0.0323 (0.0421)	-0.01 (0.0373)
Share of single-person households	-0.1343 (0.0948)	-0.0124 (0.0441)	0.0419 (0.032)	0.0394 (0.0322)
Share of apartments in total housing	-0.0028 (0.0147)	0.0089 (0.012)	-0.0174 (0.0124)	0.0124 (0.0112)
Share of employee jobs in total jobs	0.0201 (0.0195)	-0.0185 (0.0208)	0.0358 (0.0209)	-0.0143 (0.0229)
<i>Other control variables</i>				
BZD use (log) the previous year	-18.143*** (5.3397)	-9.9054*** (1.5568)	-12.3353*** (1.6564)	-10.574*** (1.3671)
Accessibility to GP	0.1686 (0.132)	0.1102 (0.1417)	0.0081 (0.1485)	0.2128 (0.1547)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded. N = 3,201.

*Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.*

Table 3.A6: Results of estimations of BZD use variation in low-dense municipalities per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.0269** (0.0095)	-0.0229* (0.0106)	-0.0126 (0.0137)	-0.0332** (0.0111)
Share of elderly people (> 65 years)	0.0591 (0.0445)	-0.0066 (0.0405)	-0.0178 (0.0443)	0.0893* (0.0409)
Share of people with chronic disease	0.1477** (0.053)	0.1848*** (0.0461)	0.2268*** (0.0538)	0.0896 (0.0523)
Share of people with psychiatric disease	1.3255*** (0.1385)	1.1429*** (0.1037)	0.503*** (0.1247)	0.0396 (0.1333)
<i>Socio-economic variables</i>				
Unemployment rate	0.1063** (0.037)	0.064 (0.0375)	0.1266*** (0.0367)	0.0758 (0.0448)
Share of people without a diploma	-0.0107 (0.022)	0.0236 (0.0268)	0.0163 (0.0298)	0.0106 (0.0259)
Share of single-person households	0.0188 (0.0264)	0.0192 (0.0296)	0.0462 (0.0274)	0.0732* (0.0347)
Share of apartments in total housing	-0.0181 (0.0116)	0.002 (0.015)	-0.0213 (0.018)	-0.0183 (0.0143)
Share of employee jobs in total jobs	-0.0043 (0.0092)	0.0059 (0.0092)	0.0023 (0.0104)	-0.0117 (0.0087)
<i>Other control variables</i>				
BZD use (log) the previous year	-19.2242*** (1.177)	-18.6608*** (1.1369)	-21.3839*** (1.3468)	-18.6618*** (1.2075)
Accessibility to GP	0.0644 (0.1122)	0.2491 (0.1271)	0.2465* (0.1227)	0.0903 (0.1338)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded. N = 18,198.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.

Table 3.A7: Results of estimations of BZD use variation in very-low-dense municipalities per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.0066 (0.0154)	-0.0432* (0.0185)	-0.0224 (0.0218)	-0.0272 (0.024)
Share of elderly people (> 65 years)	-0.0322 (0.0688)	-0.0984 (0.0654)	-0.0924 (0.0881)	-0.1386 (0.072)
Share of people with chronic disease	0.2999*** (0.0703)	0.2827*** (0.0634)	0.2117* (0.0891)	0.2661*** (0.0707)
Share of people with psychiatric disease	1.3631*** (0.1562)	1.7595*** (0.2083)	0.5925** (0.1926)	0.1729 (0.1678)
<i>Socio-economic variables</i>				
Unemployment rate	-0.0699 (0.0518)	0.1491 (0.0827)	0.1837* (0.0914)	0.1473** (0.0507)
Share of people without a diploma	0.0388 (0.0404)	0.1142* (0.0535)	0.1444** (0.0459)	0.0129 (0.0424)
Share of single-person households	-0.0595 (0.0389)	0.1037* (0.0468)	0.0962* (0.0449)	0.1283** (0.0466)
Share of apartments in total housing	-0.0615 (0.0432)	0.0021 (0.0441)	-0.0624 (0.0487)	-0.1287*** (0.0362)
Share of employee jobs in total jobs	0.0257 (0.0147)	-0.0367 (0.0206)	0.0098 (0.0175)	0.0144 (0.0184)
<i>Other control variables</i>				
BZD use (log) the previous year	-28.9738*** (1.5753)	-32.7135*** (3.4191)	-35.0396*** (2.2323)	-31.4791*** (2.1484)
Accessibility to GP	0.4256* (0.1965)	0.2987 (0.2538)	0.3309 (0.2284)	-0.0231 (0.2118)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 100 inhabitants or belonging to overseas departments are excluded. N = 8,922.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.

7.3. Results of sensitivity analysis

Table 3.A8: Results of estimations of BZD use variation in municipalities above 500 inhabitants per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.0201 (0.0115)	-0.0146 (0.0113)	-0.0145 (0.0104)	-0.0202 (0.0116)
Share of elderly people (> 65 years)	-0.0253 (0.035)	-0.0567 (0.0378)	-0.0887* (0.037)	0.0549 (0.0353)
Share of people with chronic disease	0.187*** (0.0427)	0.2589*** (0.0466)	0.2037*** (0.0439)	0.0746 (0.0472)
Share of people with psychiatric disease	1.3676*** (0.4053)	0.8032*** (0.1066)	0.3707*** (0.088)	-0.0147 (0.0811)
<i>Socio-economic variables</i>				
Unemployment rate	0.1012*** (0.0289)	0.0245 (0.0318)	0.0709* (0.033)	0.0507 (0.0292)
Share of people without a diploma	-0.0577** (0.0184)	0.0066 (0.0202)	-0.019 (0.0246)	-0.0044 (0.0204)
Share of single-person households	-0.035 (0.0256)	-0.0016 (0.0254)	0.0341 (0.022)	0.0555 (0.0344)
Share of apartments in total housing	-0.0066 (0.0079)	0.0186 (0.0101)	-0.0072 (0.0086)	-0.0005 (0.0124)
Share of employee jobs in total jobs	-0.0023 (0.0078)	0.0171* (0.0075)	-0.0009 (0.0084)	0.0006 (0.0089)
<i>Other control variables</i>				
BZD use (log) the previous year	-13.2124*** (1.2959)	-15.065*** (1.1515)	-13.4346*** (0.8862)	-13.2503*** (1.1125)
Accessibility to GP	0.0663 (0.0896)	0.0489 (0.0835)	0.0542 (0.0732)	0.1526 (0.0884)
Densely populated municipality (ref.: intermediate)	0.3102 (0.3044)	-0.1892 (0.3215)	-0.2499 (0.2238)	-0.9533** (0.3027)
Low-density municipality (ref.: intermediate)	-0.5534* (0.2445)	-0.4592* (0.2214)	-0.5838*** (0.1616)	-0.0251 (0.1795)
Very low-density municipality (ref.: intermediate)	-0.6766 (0.6504)	0.8279 (0.6437)	-0.7816 (0.4746)	-0.7238 (0.5866)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 500 inhabitants or belonging to overseas departments are excluded.

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.

Table 3.A9: Results of estimations of BZD variation use in municipalities above 1000 inhabitants per year

Variables	2018	2019	2020	2021
<i>Covid-19-related variables</i>				
Excess mortality in March-April 2020	-0.0115 (0.0107)	-0.0182 (0.0124)	-0.0124 (0.0103)	-0.0117 (0.0122)
Share of elderly people (> 65 years)	-0.0391 (0.0414)	-0.0347 (0.0378)	-0.0925* (0.0412)	-0.0197 (0.0333)
Share of people with chronic disease	0.1731** (0.0594)	0.1976*** (0.0487)	0.2202*** (0.052)	0.1107* (0.0442)
Share of people with psychiatric disease	0.8193*** (0.1127)	0.7992*** (0.136)	0.2722** (0.0986)	-0.0405 (0.0886)
<i>Socio-economic variables</i>				
Unemployment rate	0.0403 (0.0324)	0.035 (0.0315)	0.0534 (0.0325)	0.0666* (0.0271)
Share of people without a diploma	-0.0452* (0.0177)	0.0016 (0.0209)	-0.0326 (0.0251)	-0.0496** (0.019)
Share of single-person households	-0.015 (0.0196)	-0.0151 (0.026)	0.0061 (0.0225)	0.0282 (0.0179)
Share of apartments in total housing	0.0013 (0.007)	0.0176 (0.0119)	-0.0034 (0.0081)	-0.0032 (0.0085)
Share of employee jobs in total jobs	0.0013 (0.0095)	-0.0003 (0.0117)	0.0099 (0.0105)	0.0011 (0.01)
<i>Other control variables</i>				
BZD use (log) the previous year	-9.8382*** (0.9099)	-12.9153*** (1.3902)	-10.4944*** (0.8563)	-8.6046*** (0.9625)
Accessibility to GP	0.0243 (0.0698)	-0.0289 (0.0737)	0.1397 (0.0778)	0.1325 (0.0815)
Densely populated municipality (ref.: intermediate)	0.2612 (0.2286)	-0.0873 (0.3187)	-0.2627 (0.1961)	-0.9544*** (0.2425)
Low-density municipality (ref.: intermediate)	-0.4848** (0.1861)	-0.3858 (0.2203)	-0.2901 (0.1684)	-0.1643 (0.165)
Very low-density municipality (ref.: intermediate)	2.893 (1.6646)	8.009* (4.0581)	-0.6705 (1.1529)	-0.3401 (0.9996)
Region	Yes	Yes	Yes	Yes

Source: SNDS and INSEE. Data relative to municipalities. Field: France, municipalities with fewer than 1000 inhabitants or belonging to overseas departments are excluded.

*Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Standard errors in parentheses are clustered by departments.*

General conclusion

1. Contribution

This dissertation focuses on BZDs. The first objective is to disentangle the interaction between BZD use and WAs (Chapters 1 and 2), which are two specific aspects of health and work. The second objective is to measure and understand the impact of the COVID-19 pandemic on BZD consumption in France (Chapter 3). BZD consumption and WAs are major concerns of public authorities. Public policies aim to reduce overall BZD use, perceived as excessive, and the frequency of WAs.

Defining good prescribing practices is not an easy task because of the uniqueness of each case. The choice of suitable treatment is the role and responsibility of doctors, but public health authorities (the HAS in France) publish guidelines to improve the efficiency of treatments. These guidelines are based on medical evidence and medico-economic studies. Untreated disease can lead to a strong deterioration of health capital and economic consequences (e.g., loss of productivity in case of anxiety or insomnia), but the overuse of medicine is also a source of inefficiency (e.g., due to the loss of efficacy of BZDs and the risk of adverse effects). Prescribers are encouraged to follow these guidelines, especially through financial incentives.

Preventing WAs is also a priority. The impact on public health is strong: there were more than 1 million declared WAs in 2020 and 771 deaths. They represented more than 11 billion euros of expenses in 2020 (including occupational diseases) for the French national health insurance; a loss of productive workforce at the national level (227,553 full-time employees lost in 2020, more than 31,851 permanent disabilities); and a financial burden for companies that must pay according to the number of WAs in the company (from 20 employees) (L'Assurance maladie - Risques professionnels, 2021). The prevention action of health insurance is based on the control and enforcement of prevention measures in companies and on financial incentives.

These politics have been successful, both for BZD consumption (with an overall decreasing trend from 2000 (ANSM, 2017)) and for WAs (with decreasing frequency over time, although there has been a stagnation since 2013 (L'Assurance maladie - Risques professionnels, 2021)).

However, the onset of the COVID-19 pandemic in early 2020 greatly affected these trends. The coronavirus directly affected population health, and the measures taken to fight the pandemic led to deep modifications of habits: changes in work organization (work interruption during lockdowns

and increase in work at home), social distancing, school closures, economic downturn, and travel restrictions. Following the mental health deterioration of the population, BZD use rose in 2020 and has remained at a high level since then. Conversely, the number of WAs fell in 2020, but this is a deceptive statistic, as the number of work hours also fell. This major impact, which occurred during this thesis, led me to explore the drivers of the increase in BZD use in France during the pandemic (Chapter 3).

Chapter 1 is related to the consequence of a WA occurrence on BZD consumption. BZDs are psychotropic drugs used for a therapeutic goal but with potentially adverse effects. This is why we distinguished between simple use and overuse (beyond the maximum recommended duration). The results show clear increases in BZD use and overuse after a WA, but the overuse comes from the increased probability to use (+39%), and not from an increased risk of overuse among people who use BZDs (+1.7%). These results show that public authorities should focus on the first-time BZDs prescription and improve the knowledge of prescribers to fight against BZD overuse and reduce the potential adverse outcomes on health. The risk of overuse increases with the severity of the WA. It makes sense because the stronger the impact on mental health, the higher the need for medication to treat it, but it could add a problem if the BZD use becomes problematic. Moreover, the risk of using and overusing is slightly higher for women.

The research question of Chapter 2 is a mirror of the first: how does BZD consumption affect the risk of WA? In this chapter, I again distinguished BZD use and BZD overuse (according to the duration of treatment). The risk of WAs decreases after the first intake of BZDs. Some explanations can be put forward (beneficial effect of treatment, avoidance of treatment for the more at-risk workers, and precautionary measures at work). The risk of WAs increases when treatment is prolonged and exceeds recommended treatment times and when the treatment is stopped. Overall, the risk of WAs decreases with a single BZD use but is positively correlated with the intensity of BZD use. It provides further evidence of the adverse consequences of long-term BZD use and calls for adherence to recommendations and increased caution when discontinuing treatment.

Chapter 3 focuses on the drivers of BZD use increase during the COVID-19 pandemic (2020 and 2021). This period has been a major disruption in our lives, and the pandemic deeply impacted our health and work. While a major part of the population stayed at home (with interruption of work or working at home), the mental health of the population was strongly impaired. BZD consumption increased because of this degradation. BZD use refers to mental health care but also informs on the most affected populations, on the determinants of health care use, and potentially

on the people who could be concerned by adverse events in case of overuse. This last study is carried out at the French municipality level. It shows a greater BZD use increase where the population is more often unemployed, undergraduate, and living alone. Conversely, the traditional BZD use risk factors, which are higher age and chronic conditions, are not associated with increased use. This stresses the roles of work factors, socioeconomic conditions, and social support in the psychotropic drug increase during the pandemic and provides insight into the population who may be more affected by BZDs adverse effects. It should help to improve the struggle against psychotropic drug overuse, especially in pandemic times.

Many studies about psychotropic drug use rely on survey data. They are prone to the risk of declarative bias. The use of a nationwide administrative database allows for being exhaustive on the French population and avoiding the risk of declarative bias, which is known to be high in the case of psychotropic drug use. This study distinguishes use and overuse in Chapters 1 and 2. BZDs are known to be effective over a short time, and I defined overuse according to the duration of treatment. The objective is to make the difference between the therapeutic effect of treatment and potential adverse effects and loss of efficacy because of overuse. Although there already are studies about determinants of BZD overuse, Chapter 1 is, to my knowledge, the first to study the risk of overuse due to a specific shock on health *after use*, i.e., to consider the selection effect and to identify the factors associated to BZD overuse among users. In Chapter 2, I used a slightly different definition of BZD use to differentiate current use, past use, and overuse. These drugs are widely used. It is fundamental to understand their role in triggering WAs to improve health at work. Finally, the COVID-19 pandemic had countless consequences, particularly on mental health. BZD use is both a proxy for mental health impairment and a sign of future risk if it translates to overuse. It is paramount to understand the drivers of the increase to improve the management of future pandemics and the struggle against BZD overuse. Many studies worldwide showed an increase in BZD use, but Chapter 3 is the first to attempt to understand the mechanisms at work.

2. Public policy recommendations

Public policies that could be affected by the conclusions of this thesis are threefold: BZD overuse prevention, WA prevention, and pandemic management. In the first studied direction of causality (WA effect on BZD use), Chapter 1 shows that we should improve prescribers' information on the risk of BZD overuse that results from the first prescription. It should be efficient to evaluate deeply the need for BZDs at the first prescription rather than trying to reduce the consumption

after people already use BZDs. Moreover, prescribers should pay specific attention to the risk of BZD overuse for the most impaired workers.

In the second direction of causality (BZD use effect on WA risk), the observed effect of a short BZD intake seems associated with a decrease in WA risk, overuse and past use are associated with an increased risk. In the case of past use, this is not an expected result and it should lead to improved worker support after treatment discontinuation. When returning to work, the GP could provide specific information on the risk of WAs. A specific follow-up should be considered for heavy BZD users and more at-risk workers.

The third and last chapter takes place in the very specific situation of the COVID-19 pandemic. The impact on mental health and psychotropic drug consumption was huge. This chapter aims to understand why BZD consumption increased and conclude that socioeconomic determinants related to containment measures were implied. This should be considered in the future in the case of a new pandemic to help protect the more exposed population. The stay-at-home orders could focus on the population at risk of severe disease, and public authorities should consider the risk of mental health impairment and the possible consequences in terms of public health (such as an increase in anxiety and suicide) as well as economic consequences (increase in mental health care use, with an increase in costs, possible congestion, and adverse effects in the long term).

3. Methodological challenges

I have faced many challenges to avoid, as far as possible, the risk of bias. The first one is common in health economics: reverse causality. Health and work influence each other, and BZD use and WAs are interrelated. In the first two chapters, I try to examine a relationship in one direction only. To extract this effect, I use a sequence of events in time: the past influences the future. I aim to examine the “pure” effect by controlling for confounding factors. In the first chapter, I focused on the population with a single WA, so a previous WA cannot influence BZD consumption. The occurrence of a WA is a breaking point from which I observe BZD use. In the second chapter, I use panel data to compute the effect of past BZD use on the current probability of having a WA, controlling by absences and with fixed effects. In the third chapter, the outbreak of COVID-19 is an exogenous event. This is a kind of before/after study, where 2018 and 2019 are used as control years, and 2020 and 2021 are treated years.

The second challenge is to select a counterfactual population, i.e., not affected by a WA but comparable to the population impaired by WAs. In the first chapter, I use as a control a random selection of the French population not affected by WAs. This is a group truly representative of the

French population, but an omitted variable could bias the estimate (the working status) and requires me to use additional robustness checks (on a working subpopulation). In the second chapter, to be certain that the controls are identical to people affected by WAs, I use the full population affected by WA over three years. In period t , I compare people with a WA to people without a WA. It limits the scope of the conclusions, as they apply to a specific population (affected by WAs during the three years). Moreover, the risk of omitted variables is still present (although weaker), as working status can vary over time without being controlled (and then affects the risk of WAs as BZD consumption). Once again, I had to use a robustness check (on the population with long-term contracts). In the third chapter, the severity of the pandemic varied according to the territory, which allowed me to control for this variation. However, the containment measures have been uniform (at least the first time, but they were the strongest) and do not permit the use of counterfactuals. I used past years, unaffected by the disease, as reference years.

The French National Health Data System is at the heart of these three studies. This database is a challenge per se because of the complexity of its organization. It has many advantages: the information is exhaustive on the French population and it contains all information about reimbursed care. The volume of information is a strength, as it allows studying weak effects (such as the change in risk of WAs after BZD consumption), but it is also a difficulty. The data are hard to manipulate, with many datasets to link, many variables, much cleaning work, and computing times can be a problem. Above all, fundamental information is missing from the database. We do not have personal information beyond age, sex, or municipality of residence. Apart from some particular cases, we do not have information about work, marital situation, education, childhood, etc. It constitutes a major issue to control for confounding factors. In the first two chapters, I use specific information about some people (people with illness benefits and people with long-term contracts at the time of the WA) to perform robustness checks. In the third chapter, I aggregate the information at the municipality level to complete it with census data from the National Institute of Statistics. The data are much richer about housing and employment, but the conclusions are about municipalities and not individuals.

The administrative database is an asset because it allows us to avoid, to some extent, reporting bias. In particular, the use of psychotropic drugs is subject to underreporting in surveys, and reimbursement data allow us to avoid this. Moreover, the reporting of WAs is mandatory and should be exhaustive in the database. Nevertheless, we know that WAs underreporting is still present (see Chapter 2), mainly regarding the less severe accidents. Last, the reimbursement data do not allow us to know the reality of drug intake. I assume that the reimbursed BZDs have been

used, but that does not consider the medicines bought but not used. The BZD used without prescription (purchased on the black market, for example) are not considered either.

4. Outlook

The lack of socioeconomic information about individuals is a serious limitation of the database to be used in economic studies. Some extracts of SNDS had been matched to surveys to enrich the survey with detailed care consumption. For instance, the HYGIE survey (*Système d'Information sur les Indemnités Journalières*), from Irdes, and the survey *Conditions de travail* (working conditions), from the French Ministry of Labor, are matched to data extracted from SNDS; and the survey EHIS (*European Health Interview Survey*) will be matched. However, in these cases, SNDS data are aggregated for a specific goal and thus contain only some specific information, such as the number and amount of psychotropic drugs reimbursed in a year (at the individual level). To work on BZD use more accurately, it is required to use the full SNDS, with disaggregated data. For instance, the exact day (or month) of BZD reimbursement is available only in the SNDS and not in the extracted and aggregated data.

There are other information sources linkable to the database (without data extraction), which could allow us to considerably enrich the database. Other French administrations have complementary information, at the forefront of which is the national pension insurance (*L'Assurance retraite*). This is the branch of social security in charge of pensions. Its database contains full information about the career path of people living in France. Although this is not the case currently, the database is theoretically linkable to the database of national health insurance. Another linkable source of data is that of the tax administration, which contains the full income of people. The link is currently used to fight against fraud but not for research goals.

From a closer perspective, the Ministry of Health merged the SNDS with data from the National Institute of Statistics. The permanent demographic sample (EDP: *Echantillon Démographique Permanent*) is a large panel of people, launched in 1967, that is very rich in sociodemographic information. For more than three million people, it contains information about geographical migration, social and professional mobility, relationships, and descent. The information is provided by census data and administrative sources. The DREES (which is the statistical department of the Ministry of Health) has matched the SNDS with the EDP to create the *EDP-Santé*. This new database has been created to evaluate the Health National Strategy 2018-2020, but the research potential is huge and could solve many weaknesses of the SNDS in terms of lacking information.

Whether the SNDS is a mine of information and is commonly used in epidemiology today, its utility for wider economic studies is limited by the lack of socioeconomic information. The possibility of completing it with other data sources may increase the research possibilities tenfold. While access to researchers has grown since the creation of the SNDS in 2016 and should grow even more via the new French *Health Data Hub* (created in 2019, it aims to ease access to these data for researchers), and while the European Commission is working on a new regulation for a *European Health Data Space* (which would aggregate health data across member countries), knowledge and control of these information systems is paramount to improve the potential of future large-scale research.

5. Future research

These new sources of data may overcome many of the limitations present in this thesis. They would provide lots of missing information, allowing for the control of omitted variables at the individual level (like professional history) and the selection of a control population matched on socioeconomic characteristics.

The efficacy of struggle policies against BZD use has been questioned by the COVID-19 pandemic. The impact of the pandemic on mental health was huge and seems to persist. The evolution of BZD use in the coming years (and the evolution of the mental health of the population) should be monitored very closely. Moreover, while the last chapter examines global BZD use in the French population, the evolution of overuse could and should be examined.

Mental health is a big concern worldwide, as well as psychotropic drug consumption, which is closely related. BZDs epitomize psychotropic drugs: they are medications that have proven their effectiveness, but they can have consequences worse than the causes they treat. Understanding the drivers of consumption and the risk it entails is critical to improving global health.

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