

# Driving performance and neurocognition of patients with long-term medicinal drug treatment

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# VALORISATION ADDENDUM

## Valorisation Addendum

The valorisation addendum addresses the translation of research output to societal relevance and impact for the general public. The five cornerstones of valorisation are discussed: 1) Relevance for society, 2) Target group, 3) Activities and Products following from the mentioned research output, 4) Innovation within the area of research expertise, and last, 5) Implementation of knowledge. For each of the five cornerstones, the central question (Q) and answer (A) is displayed.

### **Relevance**

*Q: What is the social relevance of these research results?*

A: The goal is to inform the general public about potential drug induced driving impairment, given that the latter is of increasing public and governmental concern (Compton and Berning 2015). Within modern day society, many individuals will at some point in their lifetime experience an affective- (e.g. anxiety, depression) or sleep/wake disorder. Given that one of the treatment options is a pharmacological intervention, it is of importance to correctly inform individuals about the potential driving hazards associated with medication usage (Food Drug Administration 2015; Kay and Logan 2011). Graded level warning systems for medicinal drug usage have been developed to inform individuals about the initial side-effects of medication and how it affects operating a vehicle. Although pharmacological interventions are not meant to be used for a prolonged period of time, a proportion of individuals will develop persistent symptomatology that requires long-term pharmacological treatment. For this group of individuals, it is important to expand the current knowledge of acute- and short-term medicinal drug effects. With long-term usage, ideally, the components of underlying symptomatology and pharmacological intervention should both be examined.

From chapter 2, it can be concluded that treated patients develop forms of tolerance for benzodiazepine induced impairment, but, that a general re-classification for the risk of benzodiazepine-induced driving impairment could not be given. Chapter 4 provides evidence that depressive symptomatology plays a role in driving related impairment and that pharmacological interventions can possibly reduce its severity. Chapter 3 and 5 show that duration of treatment in individuals receiving long-term antidepressant and benzodiazepine treatment is associated with the degree of driving related impairment. In chapter 6, results show individuals diagnosed with central forms of hypersomnolence receiving long-term pharmacological treatment show an absence of driving related impairment, although individual differences exist. Societal relevance from the above-mentioned results comes from expanding

the currently knowledge beyond acute drug effects and by including long-term treatment effects into drug classification systems. In such systems, the impact of disorder and prolonged pharmacological treatment can lead to new recommendations with regard to operating a vehicle safely.

### **Target group**

*Q: To whom are the research results interesting and why?*

A: The results of the various studies mentioned in this dissertation are interesting for patients receiving medicinal drug treatment, health professionals, and regulatory authorities. In a general sense, the investigation of prolonged pharmacological treatment and its effects on measures of driving performance gives patients information about traffic accident related risk. It also gives patients insight to what extend their underlying symptomatology may play a role in driving related impairment. For health professionals, it is important to be informed about the newest research developments and to share this information first-hand with treated patients. Finally, regulatory authorities benefit by expanding existing guidelines for operating a vehicle when taking psychoactive substances by incorporating information about treatment duration and symptomatology severity.

### **Activities**

*Q: Into which concrete products, services, processes or (commercial) activities can these results be translated and shaped?*

A: The mentioned studies in this dissertation should contribute to the general perspective of lowering drug-related traffic accidents. A suitable option for achieving this goal is to prevent traffic accidents from happening by informing or screening the corresponding target populations. One of the products that can be derived from the research results is an information leaflet that can be added to new and ongoing drug subscriptions to ensure successful communication with patients. Via this method, practitioners remain updated about the current regulations about driving under the influence of psychoactive substances. Possible services arise from providing the scientific information as a public accessible self-service application. One of these applications are websites that provide the general public with information about driving under the influence with psychoactive medication and its possible consequences. Such a website is already openly available in the Netherlands ([rijveiligmetmedicijnen.nl](http://rijveiligmetmedicijnen.nl)) and provides patients and practitioners with information about responsible medication use when

operating a vehicle. Results mentioned in this dissertation could be communicated via such a channel and incorporated as an add-on service. Finally, activities include the organisation of trainings for healthcare professionals or patient education programs. Via different communication channels, such as lectures, target groups stay informed about the developments in the field of long-term medication use and the consequences for participating in traffic. In summary, the above mentioned activities will lead to successful knowledge communication to the designated target groups.

## **Innovation**

*Q: To what degree are the obtained results innovative?*

A: The work described in the current dissertation differs from previous research in several ways. While most studies within the field of drugs and driving focus on epidemiological data or more acute drug effects, the research presented in this dissertation expands this knowledge by investigating neurocognitive and real-world driving performance in patients who take medication for a prolonged time. The research findings of the various chapters presented in this dissertation contribute to expanding the knowledge in the field of drugs and driving in the following way:

First, the review presented in chapter 2 provides an up-to-date overview of the long-term benzodiazepine literature and solely describes objective measures of driving related performance obtained in a controlled environment. Previous research has mainly focussed on assessing acute effects of benzodiazepine impairment or benzodiazepine related epidemiological crash risk. The review is one of the first to conclude that, within a controlled environment, forms of tolerance develop for benzodiazepine impairment in patient populations.

Second, the studies mentioned in chapter 4 and 6 provide new insights in how prolonged pharmacological treatment can stabilize or improve driving related performance. The research in chapter 4 shows that depression severity is related to driving impairment and that a pharmacological intervention with antidepressants can reduce the severity of driving impairment. This gives the notion that besides estimating the risk of the potential influence of pharmacological treatment on driving performance, the type of clinical disorder seems to share similar impact. Moreover, it contributes to the understanding that pharmacological interventions in depressed patients can be beneficial in reducing driving related impairment. In chapter 6, prolonged pharmacological treatment in patients diagnosed with a sleep/wake

disorder (i.e. narcolepsy) shows that performance parameters were not impaired when compared to a group of normative controls. This study differentiates from earlier work given that the included tests have proven sensitive for the impairment effects of sleep loss and drugs. In addition, the tests show moderate to high validity with actual driving skills. This is also one of the first studies to include patients with minimal practical restrictions (e.g. patients may take a nap, smoke or have co-medication). Combined with controlled assessment through observational research, the study outcomes have high external validity and reflect the performance of patients during their everyday lives.

Third, the research mentioned in chapter 3 and 5 implemented a large test battery of various neurocognitive measures in combination with the on-the-road highway driving for assessing long-term drug-effects. The inclusion of a normative control group, different facets of driving related skills and a measure of actual driving makes these experiments stand out from previously conducted research. In addition, both studies are one of the first to assess the influence of treatment duration and provide evidence that the duration of pharmacological treatment plays a role in the amount of measurable driving related impairment in patient populations. This may lead to the establishment of an experimentally supported criteria cut-off for treatment duration and being able to safely operate a vehicle.

## **Implementation**

*Q: How will the above mentioned information be communicated with a broad audience?*

A: To ensure successful knowledge dissemination, the current research findings have been communicated in various ways with a broad audience. Researchers within the research field (i.e. drugs & driving) have been kept up-to-date with our ongoing research projects with several oral presentations at international congresses organised by the International Council of Alcohol Drugs and Traffic Safety (ICADTS). The research projects in chapter 3, 5 (and partially in chapter 6) have been summarized in a report for the Dutch Ministry of Infrastructure and the Environment and was made accessible for the general public. Furthermore, the work presented in chapter 2 and 4 have been published in the international journal “Pharmacopsychiatry” that target practitioners as a key audience. To make the general public aware of the drugs and driving research conducted at the department of Psychopharmacology, we have collaborated with national television, a regional newspaper, the national magazine for driving instructors and we released a press release about the research described in chapter 3 and 5 in collaboration with the University of Maastricht, Utrecht and Groningen. In addition, the results of chapter 2, 3 and

## Valorisation Addendum

6 have been incorporated in a report of the Dutch Health Council (Gezondheidsraad 2019), which forms an independent scientific advisory body for the Dutch government and parliament. In the future, we continue to promote our research findings via the above mentioned channels to spread awareness and gain recognition within the international research community and general public.

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