# ACTIVE PHARMACOVIGILANCE IN COVID-19: INTENSIVE SURVEILLANCE STRATEGIES FROM PORTO PHARMACOVIGILANCE CENTRE

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## INTRODUCTION

Several investigational agents and drugs approved for other indications are currently being studied in clinical trials to prevent or treat COVID-19 and associated complications. However, observational pharmacoepidemiologic methods should be applied to obtain reliable information on the benefits and harms of those medicines in real life. The beneficial and adverse effects of pharmacotherapy can be studied in outpatient and hospital settings, linking both exposure and outcome data from several sources.

The most common pharmacovigilance approaches are passive and largely spontaneous in nature. However, during situations requiring a fast-track of detection, processing and reporting of safety issues – like the COVID-19 pandemic, robust and responsive active drug monitoring pharmacovigilance programs are crucial to collect data on suspected drug incidents in near real-time. Active monitoring program approaches include collecting ADRs by direct contact with health professionals (e.g. scheduled visits and regular call meetings), adapting reporting systems to the needs of the institutions and respective units/services (e.g. simplifed forms, adapted reporting flowchart and consensus meetings) and engage social media as a potential promoter of patient reporting. Nevertheless, the COVID-19 pandemic presents several challenges to the organisation and workflow of pharmacovigilance centres as a result of the massive increase in adverse drug reactions (ADRs) reports, the need for quick detection, processing and reporting of safety issues and the management of these within the context of lack of complete information on the disease.

## AIM

The aim of this communication is to propose an active pharmacovigilance approach for monitoring drugs used in the context of COVID-19 in hospitals in the Porto district.

## METHODOLOGICAL ISSUES

### SETTINGS & STUDY DESIGN

This active monitoring project is common to hospitals in the Porto district - with the capacity to include new health institutions - in order to increase the probability of detecting suspected drug incidents and accelerate the assessment of causality of the events reported in COVID-19 patients. This multicenter drug monitoring project takes two different but complementary approaches:

1. **Retrospective approach:** intensive tracking the electronic health records of COVID-19 patients;

2. **Prospective approach:** active monitoring of all drugs administered to COVID-19 patients (including supportive medication).

### ADR ENCODING & CAUSALITY ASSESSMENT

We use the terminology to code ADRs based on the Medical Dictionary for Regulatory Activities (**MedDRA®**), used by INFARMED, I.P.. In this terminology, medical terms are coded according to the Systems Organ Classes (**SOC**) affected. If, in the same report, there is more than one adverse reaction belonging to the same SOC, that SOC will be counted only once. Medical terms are coded by Lower Level Term (**LLT**), which are associated with a primary SOC. Regarding seriousness, ADR reports will be characterise based on the definition of Good Pharmacovigilance Practices, Module VI (**ICH-E2A**). The GVP criteria, in turn, are based on the Council for International Organizations of Medical Sciences (**CIOMS**) criteria. According to this definition, a **serious adverse reaction** corresponds to any untoward medical occurrence that at any dose (1) results in death or is life-threatening; (2) requires hospitalisation or prolongation of existing hospitalisation; (3) results in persistent or significant disability or incapacity; and/or (4) results in a congenital anomaly (birth defect). The seriousness criterion "other" includes many conditions that were considered by the reporter as "medically important", i.e., that it does not meet preceding criteria but is considered serious because treatment/ intervention would be required to prevent one of the preceding criteria.

### ABOUT PORTO PHARMACOVIGILANCE CENTRE

The Porto Pharmacovigilance Centre (UFPorto) is one of the regional units of the Portuguese National Pharmacovigilance System. It was created in July 2000 and is positioned in MEDCIDS – Department of Community Medicine, Health Information and Decision of the Faculty of Medicine of the University of Porto. The UFPorto has technical and administrative autonomy and works in collaboration with the Medication Risk Management Department of the INFARMED, I.P.

## RESULTS

We propose a multidimensional strategy that, together with the traditional pharmacovigilance methods - namely, spontaneous reports (passive pharmacovigilance) - can promote active pharmacovigilance and accelerate the process while optimising resources (**Fig. 1 & 2**).

It is expected that the results found will meet a satisfactory safety profile of drugs based on previous data published by internationals pharmacovigilance systems, mostly non-serious and transitory ADRs. Therefore, we hope that the profile of ADRs that we will find is representative of the Portuguese population.

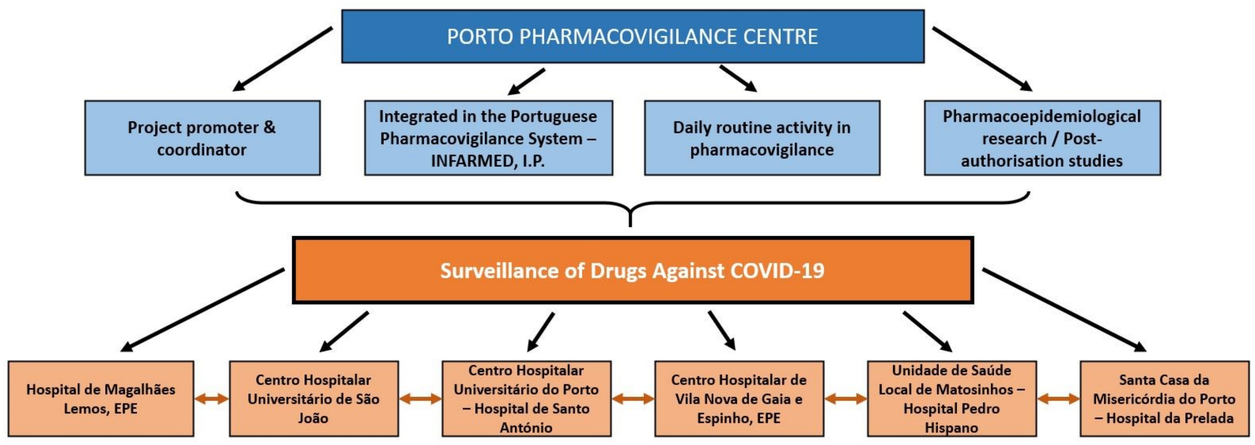


**Fig. 1** Competences of UFPorto and overview of the active surveillance project.

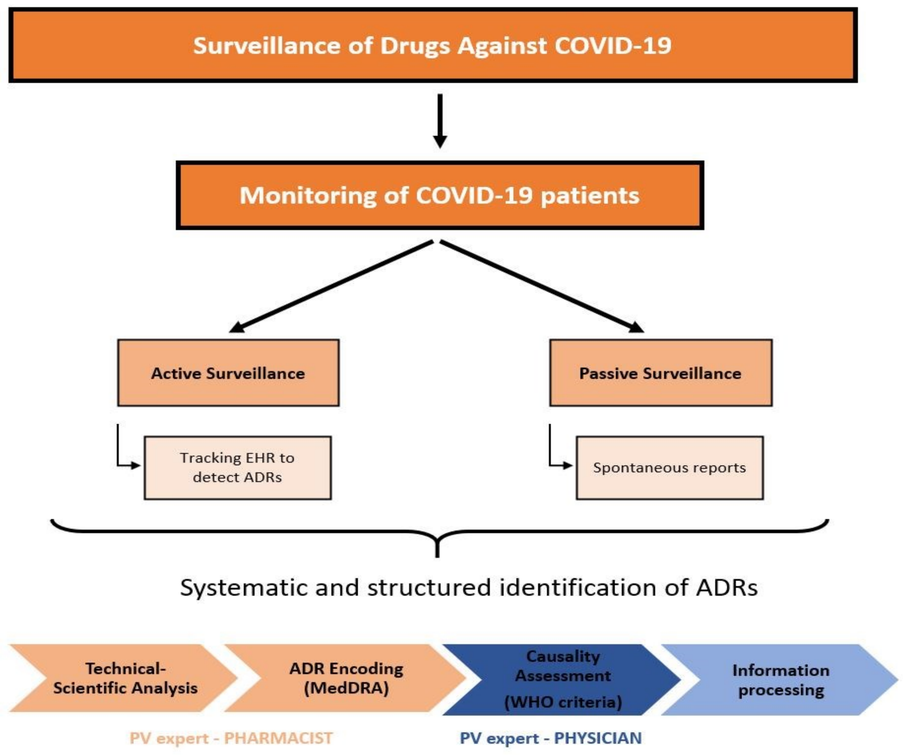


**Fig. 2** Active surveillance project workflow.

## DISCUSSION / CONCLUSION

In contrast to passive surveillance (spontaneous report), active surveillance seeks to ascertain more completely the number of adverse events in a given population via a continuous organised process. Also, intensive monitoring is a system of record collection in designated areas, e.g. hospital units or by specific healthcare professionals in community practice. Thus, the importance of implementing active monitoring systems prevails, particularly by the exhaustive search for suspected ADR in the electronic health records of patients diagnosed with SARS-CoV-2 infection. Accessing clinical records is of uttermost relevance since they include specific parameters crucial for causality analysis, like demographics, clinical history, suspected drug(s), date and time of onset of the ADR, temporal relationship, description of the reaction, dechallenge, rechallenge, previous knowledge about the ADR, management, and outcome of the ADR.

In general, it is more feasible to get comprehensive data on individual adverse event reports through an active surveillance system than through a passive reporting system.

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