

A vertical decorative bar on the left side of the slide. It features a dark blue background with a greenish-yellow, abstract, circular pattern that resembles a microscopic view of a virus or cellular structure.

New insights through cross portfolio risk analysis

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Pictured left: The structure of HIV

Cross portfolio risk analysis

- Cross portfolio analysis was performed to identify possible impact of systemic issues affecting several countries and TAs at same time
- Analysis focused on identify the impact of pandemic situation on Adverse Events (AE) reporting and Major Protocol deviations (MPDs) operational processes
- Impact assessment was done using Key risk indicators (KRI).

AEs Analysis (timeline analysis)

Cross portfolio risk analysis

3 Key Risk indicators (KRI) were analyzed in 73 clinical trials with at least 6 months of data in 2019 and 2020:

- AEs reported by patient treatment week (PW) cumulative
- AEs data entry time (days from next patient visit since AE onset date to AE data entry)
- AEs Opened for more than 6 months
- MPDs reported in last 5 weeks

3 different periods were compared based on operational actions:

- Pre-Covid: 1/Jan/2019 to 31/Dec/2019
- Covid: 1/Jan/2020* to 30/Jun/2020, No specific actions implemented
- Covid Response: 1/Jul/2020** to 1/Jul/2021, specific actions implemented

* January 2020 was selected as starting date of “Covid” period based on operational feedback, AEs data entry time and time between visits.

** Jul 2020 was selected as response start date as it was the month in which specific action plans were implemented related AE reporting trend detected.

AE process KRI analysis

Input_pa_open_6m:

Input_padet_avg: avg.

Input_pacnt_cum_by_pw:

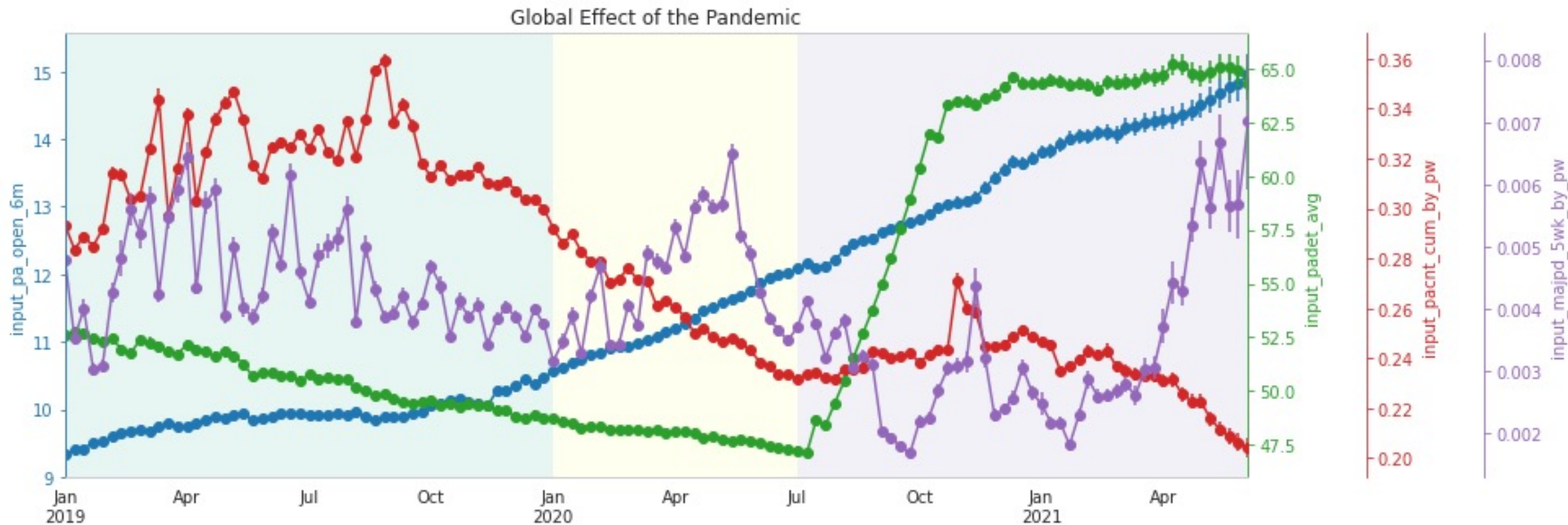
Input_majpd_5w_by_pw:

AEs opened > 6 months

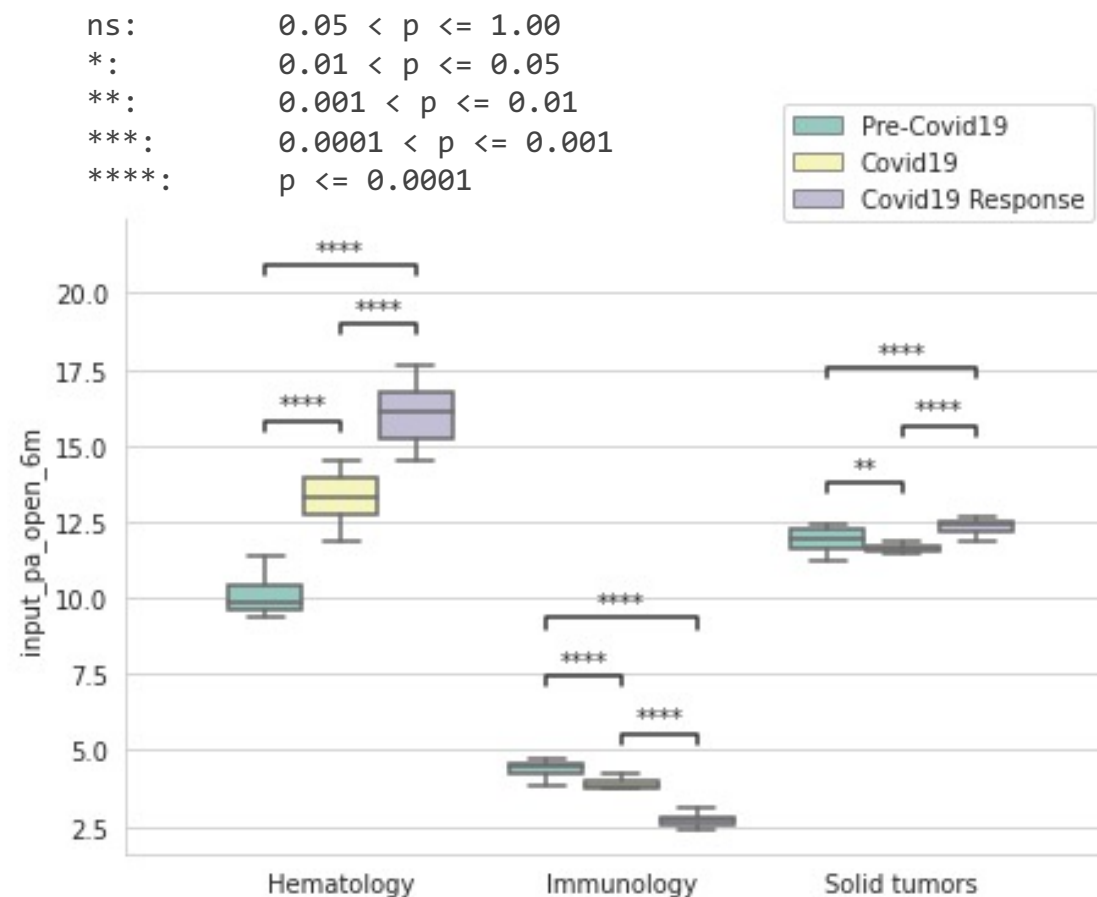
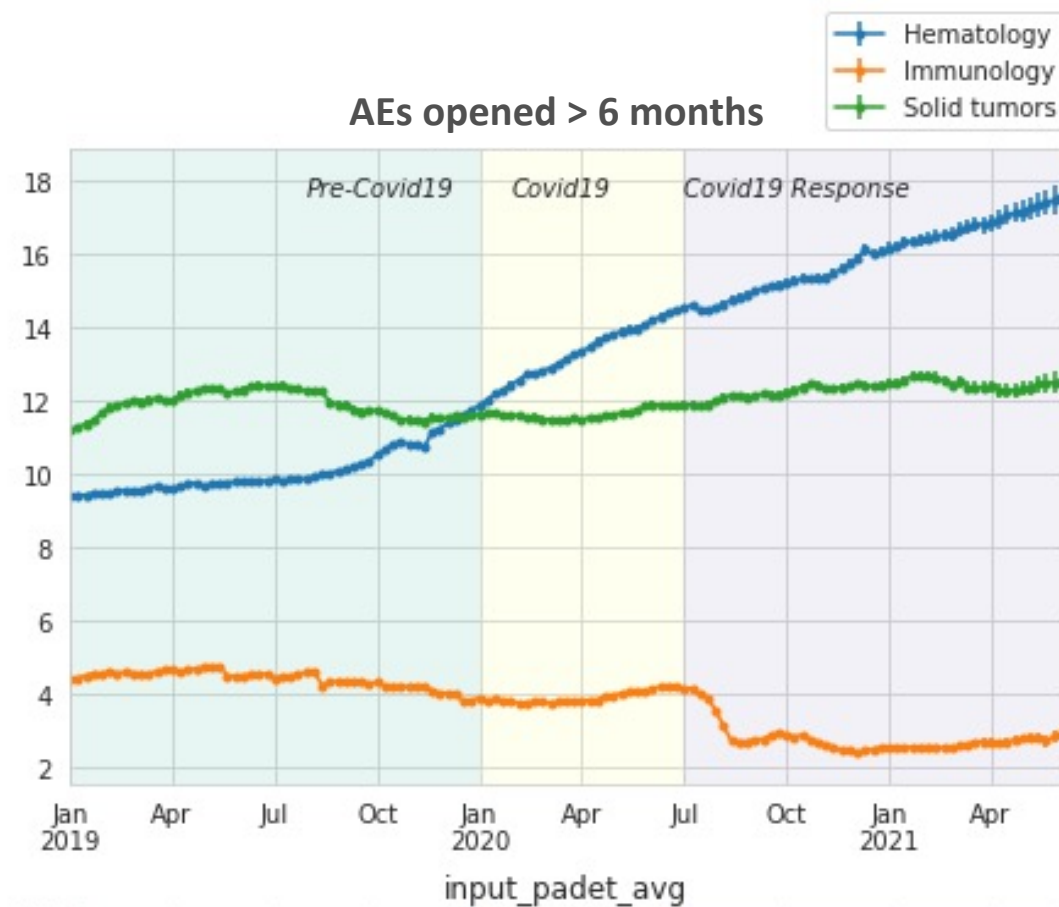
AEs data entry time

#AEs per PW cumulative

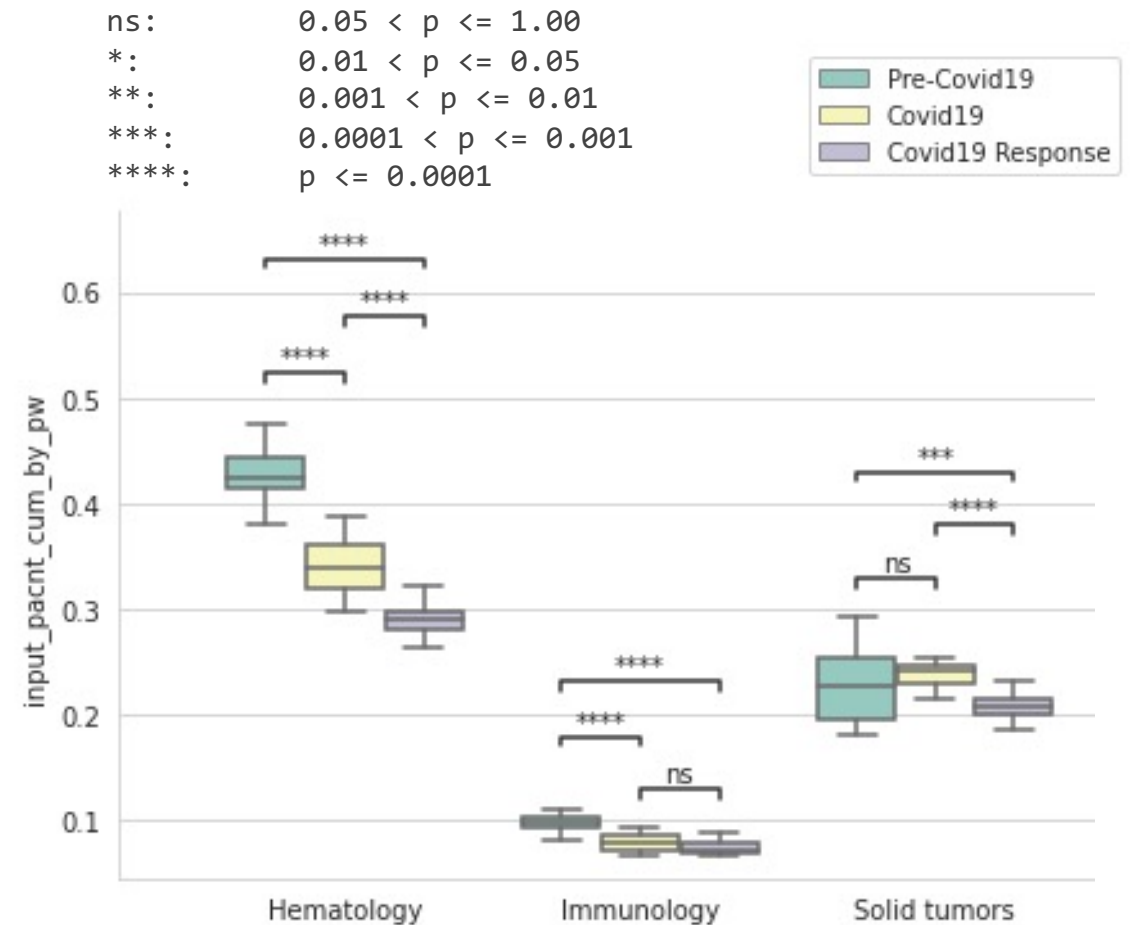
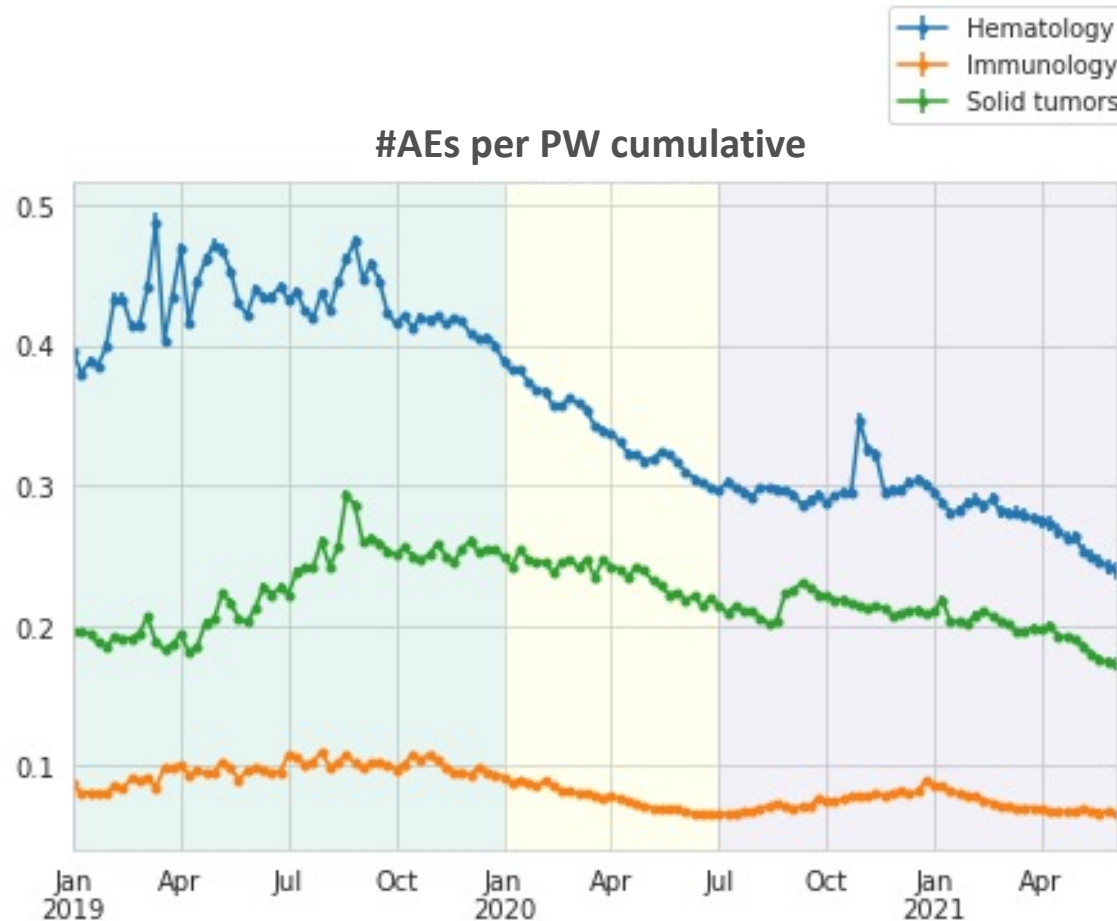
Major Protocol Deviations per PW



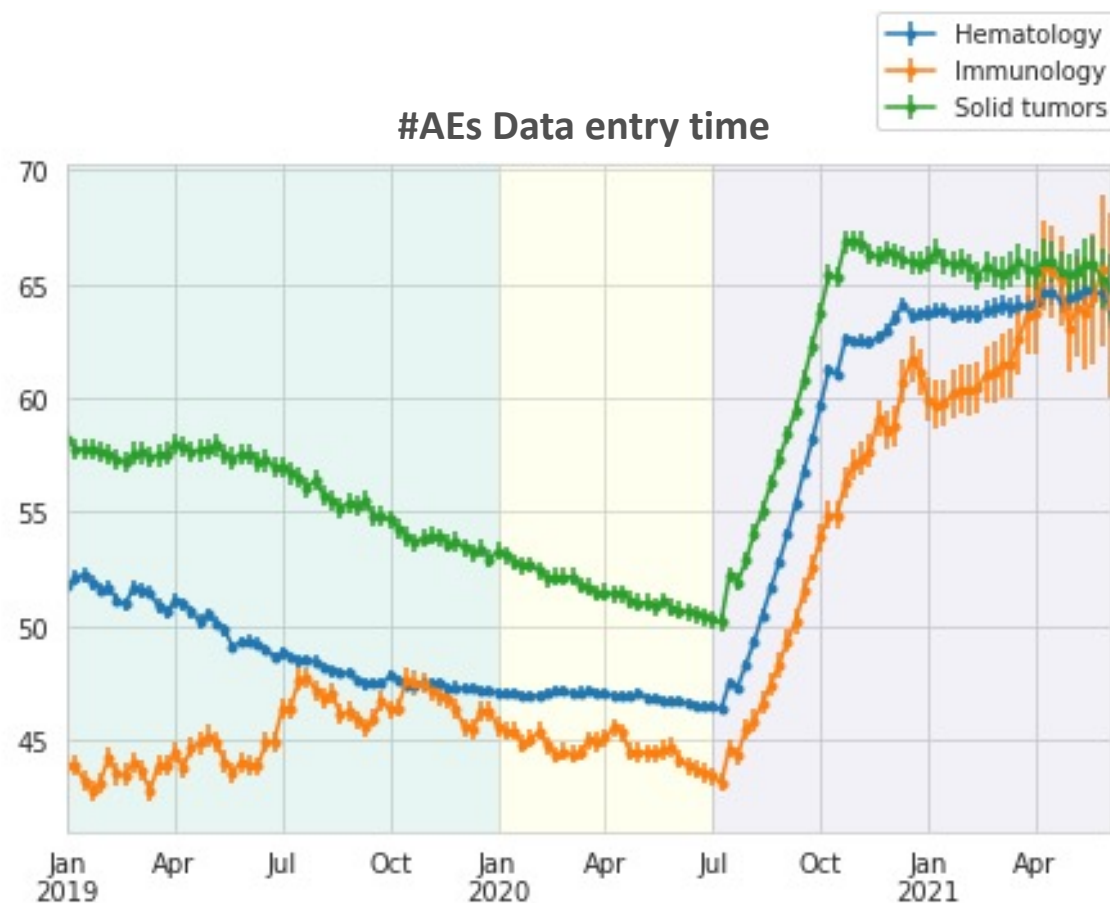
Avg. AEs Open for more than 6 months analysis



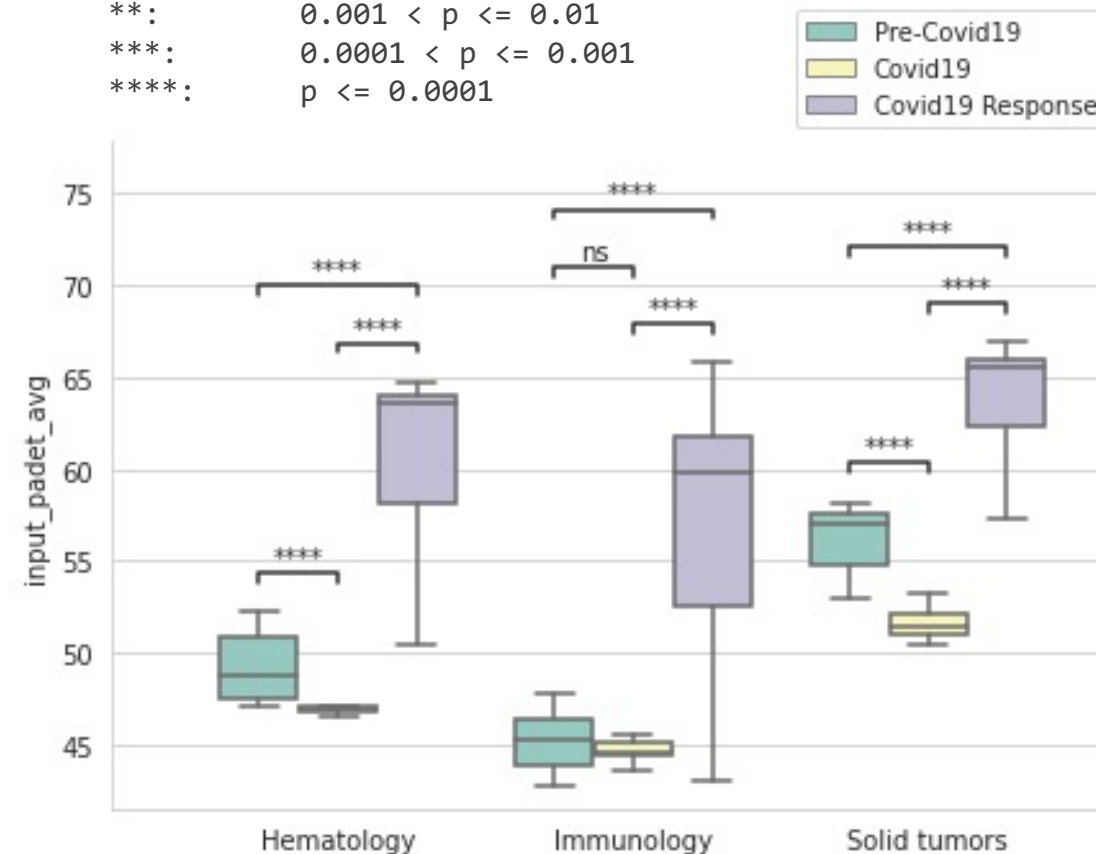
AEs rate (avg. AEs per Patient treatment Week cumulative)



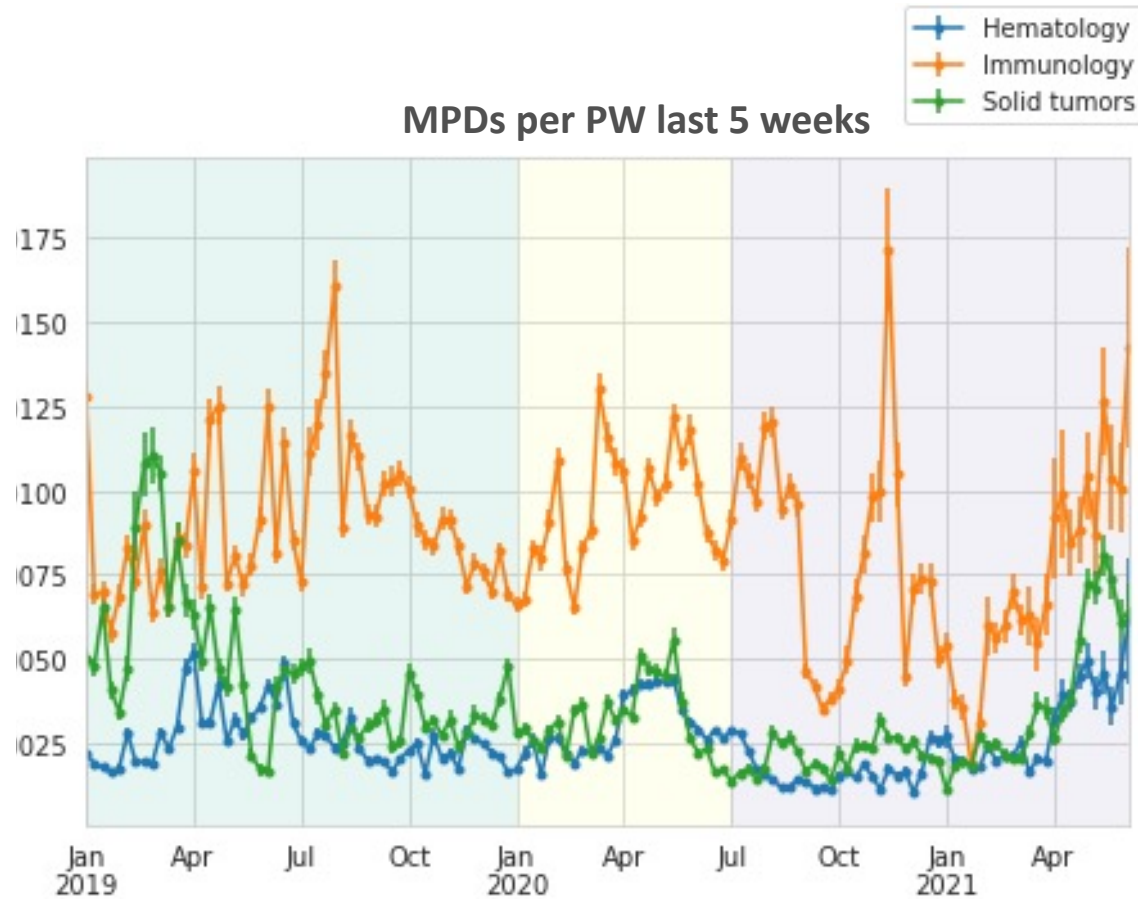
AEs Data entry time in days (AE DET)



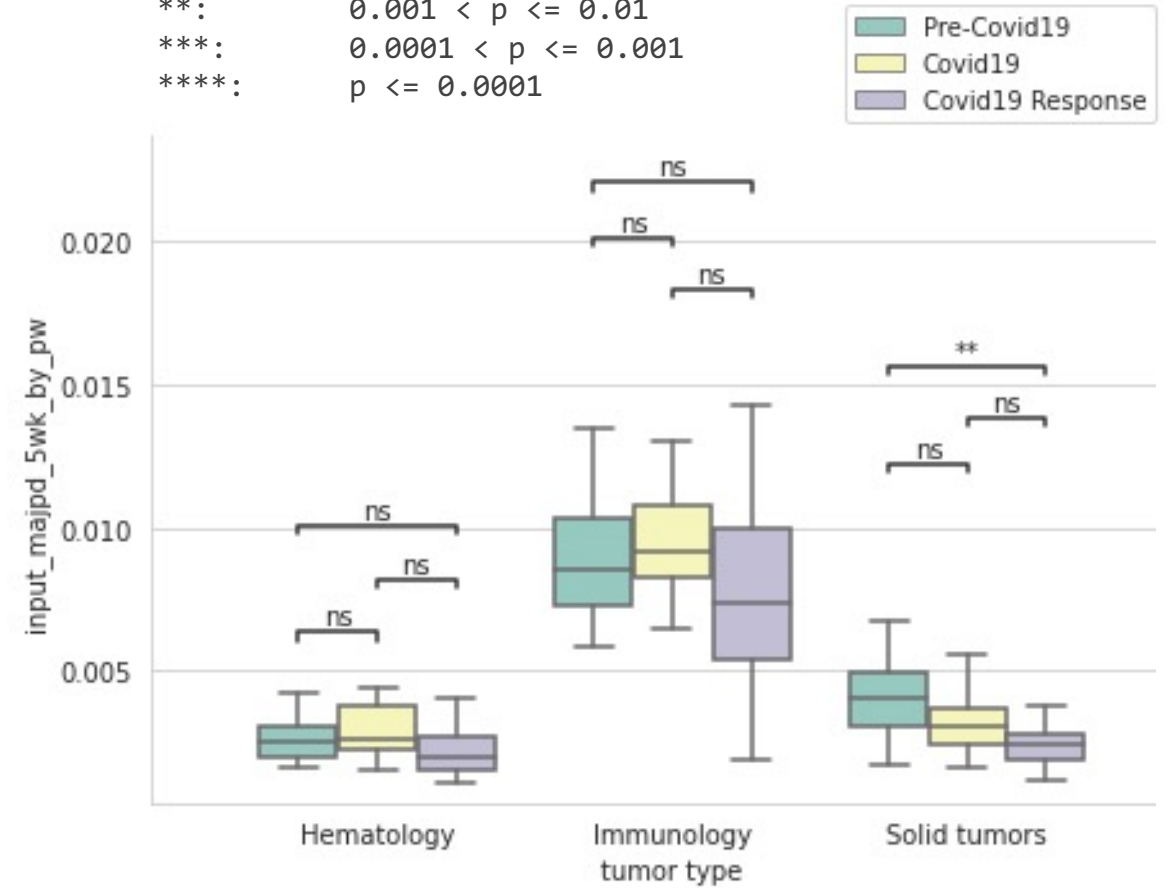
ns: $0.05 < p \leq 1.00$
 *: $0.01 < p \leq 0.05$
 **: $0.001 < p \leq 0.01$
 ***: $0.0001 < p \leq 0.001$
 ****: $p \leq 0.0001$



MPDs per PW last 5 weeks



ns: $0.05 < p \leq 1.00$
 *: $0.01 < p \leq 0.05$
 **: $0.001 < p \leq 0.01$
 ***: $0.0001 < p \leq 0.001$
 ****: $p \leq 0.0001$



Conclusion of AE analysis

- Covid pandemic impacted the AEs reporting process, reducing AE rate reported, increasing the number of AEs opened for more than 6 months and impacting the AEs DET.
- Covid impact on AEs reporting is heterogeneous and depend on Therapeutic Area (TA) specificities as per example probability of AEs of long duration.
- Actions implemented halted the trend detected but were not sufficient to revert it.
- MPDs Pandemic impact was not identified using timeline analysis, additional analysis needed and performed using MPDs classification algorithm.

Major Protocol deviations (MPD) Analysis

Cross portfolio risk analysis

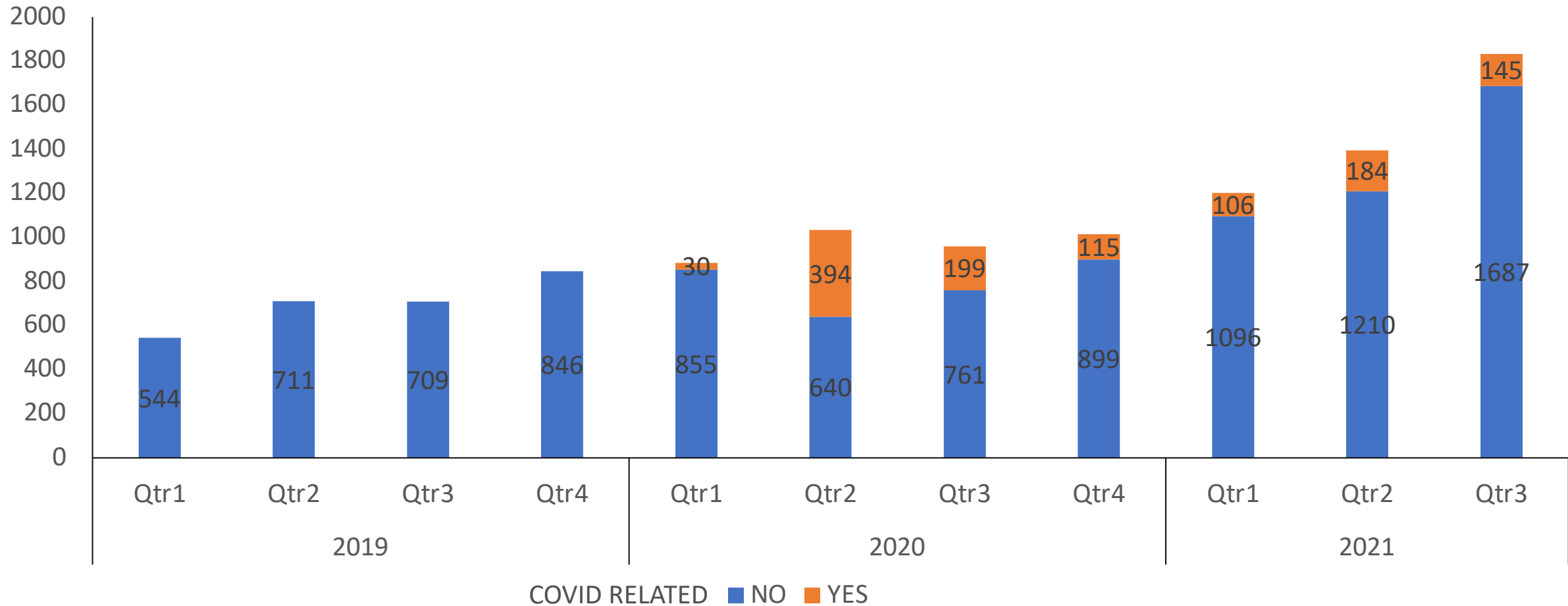
Two Key Risk indicators (KRI) were analyzed using algorithm to classify MPDs using description text, including COVID related.

Analysis was performed in 222 trials on-going in 2019:

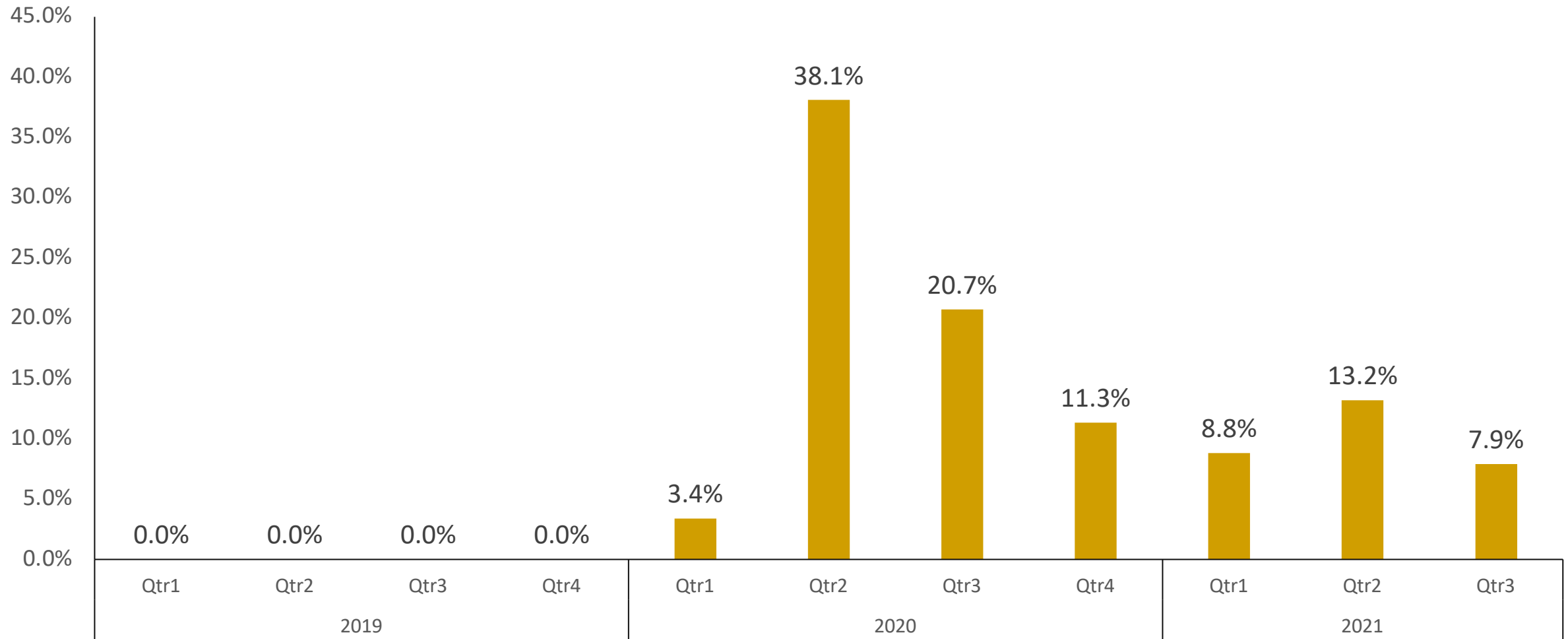
- MPDs reported per month related to COVID
- MPDs per category predicted

No periods defined as the Covid related category was included in the analysis

MPDs COVID related (# MPDs per Quarter)



MPDs COVID related as percentage of total MPDs



COVID impact per PD category (2020 -2021)

MPD category	PD No Covid related	PD Covid related	Total PD	Percentage COVID related
Exam/procedure not done	592	426	1018	41,8%
Visit out of window	711	186	897	20,7%
Sample not collected	994	113	1107	10,2%
Concomitant medication	498	103	601	17,1%
Visit missed	238	103	341	30,2%
Exam/Procedure incorrect/out of order	468	63	531	11,9%
Dose out of window/missed	69	46	115	40,0%
Informed Consent Form	560	32	592	5,4%
Did not satisfy inclusion/exclusion	709	28	737	3,8%
Patient not compliant with Investigational Product	247	21	268	7,8%
Questionnaire not done	221	18	239	7,5%
Incorrect dose/wrong IP	652	13	665	2,0%
Serious AE not reported on time	130	5	135	3,7%
IP procedure not correct	188	5	193	2,6%
Questionnaire out of window	52	4	56	7,1%
Sample other	302	3	305	1,0%
Patient not taken off study drug	174	2	176	1,1%
Exclusion criteria met and not withdraw	141	2	143	1,4%

Conclusion of MPD analysis

- Covid pandemic impacted the number of MPDs reported, showing percentage of Covid related MPDs ranging from 8% to 39%. Higher impact noticed in 2Q2020
- Covid impact is heterogeneous and depend on MPD category, impacting mainly:
 - Protocol procedures compliance
 - Visits compliance
 - Dosing compliance
 - High impacts detected also in concomitant medications and samples collection
- Actions implemented halted the trend detected but were not sufficient to revert it.

Conclusion

- Cross-portfolio analysis in bringing added value to risk management and central monitoring activities.
- Cross-portfolio analysis can be use as a tool to identify systemic issues impacting several different TAs/countries and should be included as a core analysis within Analytical Risk Based Monitoring.
- Additional discussions are needed to define the best approach to analyze cross-portfolio data within ARBM methodology.