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RCE-ESMO-ESO Training Course for Rare Cancer Patient Advocates 2022

Perspectives from the rare cancer community

The Research Community's Perspective

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EORTC

AGENDA

- Impact on conducting clinical research during the pandemic
- Impact on researchers
- Lasting changes for clinical research

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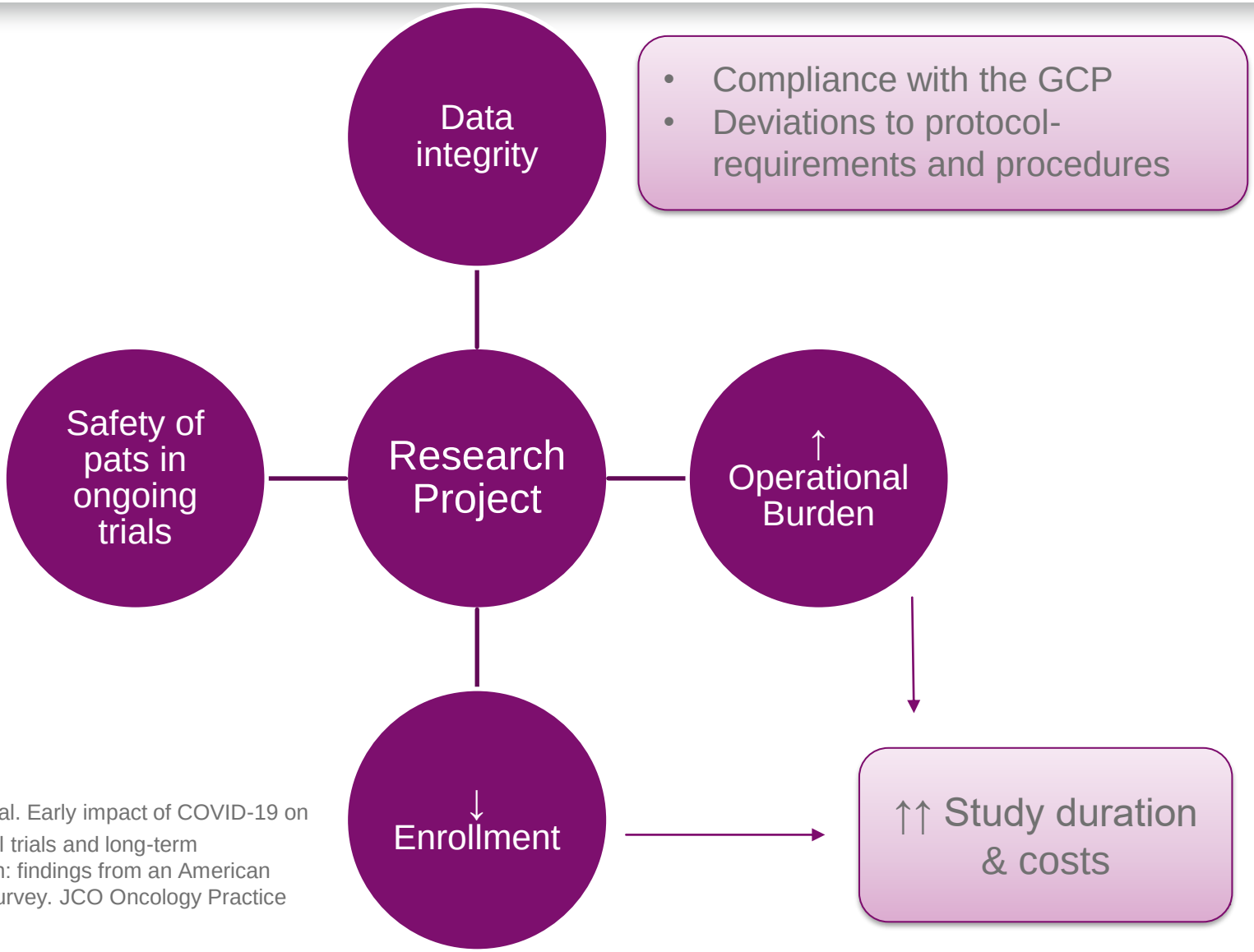
Impact on Conducting Clinical Research during the Pandemic

Impact on Research Projects



Reference: Waterhouse DM et al. Early impact of COVID-19 on the conduct of oncology clinical trials and long-term opportunities for transformation: findings from an American Society of Clinical Oncology Survey. JCO Oncology Practice 2020; 16(7):417–21

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Impact on Enrollment

Clinical Research-Impact on enrollment

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- Drop in cancer diagnosis
- Reorganization of health services
- Change in trial programs
- Consent process
- ↓ Screening activities

Enrollment paused

Drop in Cancer Diagnosis

In Spain* with the comparison of new diagnoses in 2019 and 2020 over 400,000 patients:

» The observed ratio of new diagnoses between 2019 and 2020 was an average decline of 31.1% in new diagnoses. Cancers experience the largest decline (49.7%):

Cancer type	Decline (%)
Breast	17.9
Bowel	31.7
Sarcomas and mesotheliomas	50.2

Large screening programs

In The Netherlands**

» The Cancer Registry has seen a 40% decline in weekly cancer incidence,

In the United Kingdom**

» UK has experienced a 75% decline in referrals for suspected cancer

*Reference: Héctor Pifarré i Arolas & al. Missing Diagnoses during the COVID-19 Pandemic: A Year in Review. Int J Environ Res Public Health. 2021 May: 18(10): 5335.

**Reference: IJzerman M, Emery J. Is a delayed cancer diagnosis a consequence of COVID-19? Published April 30, 2020. Accessed May 1, 2020

Organization-Redeployment in UK

- Period from May to October 2020 → **prioritizing COVID-19 research & redeploying research staff**
- On 16th March 2020 a directive ordered:
  - The suspension of all non-COVID-19-related research
    - **EXCEPT** the studies where research was the standard of care, for example, with experimental cancer treatments.
  - The reorientation of research capacity towards the effort to develop COVID-19 treatments and vaccines

Redeployment to Front line care	Redeployment to non clinical roles
165 clinical research staff reduced by 79% → 131	52 non clinical research staff

Clinical research staff redeployed to clinical roles			Non-clinical research staff redeployed to non-clinical roles		
Role	Destination	No.	Role	Destination	No.
Adult Research Nurse	ICU, COVID wards, NHS Nightingale London Hospital	50	Non-clinical R&D Staff	Ward clerks	31
Paediatric Research Nurse	Evelina clinical activity, NHS Nightingale London Hospital	27	Project Managers	Tactical sub-groups	2
Research Midwife	Routine clinics, maternity helpline	24	Research Technicians	Viapath	7
Clinical Research Practitioner	ICU turning team	14	Research staff	Data entry	6
Unassigned		16	Research staff	Bereavement centre	2
			Research staff	Cancer centre outpatient clinics	4
TOTAL		131	TOTAL		52

Reference: National Institute for Health Research. DHSC issues guidance on the impact of COVID-19 on research funded or supported by NIHR 2020 [01/05/2020]

Change in Trial Programs

To provide access to experimental treatment potentially beneficial to patients but keeping them safe, Academia modified their clinical trial programs:

» Centers kept continuing trials for up to 20% of participants, based on participants' needs, safety, and disease severity. In this case, measures were taken to minimize exposure to the staff and participants.

» Centers stratified trials based on their chance of success with interruption of those in absence of clear benefit.

» Centers continued ongoing trials but limited the activation of new ones.

Decisions from Pharmaceutical companies

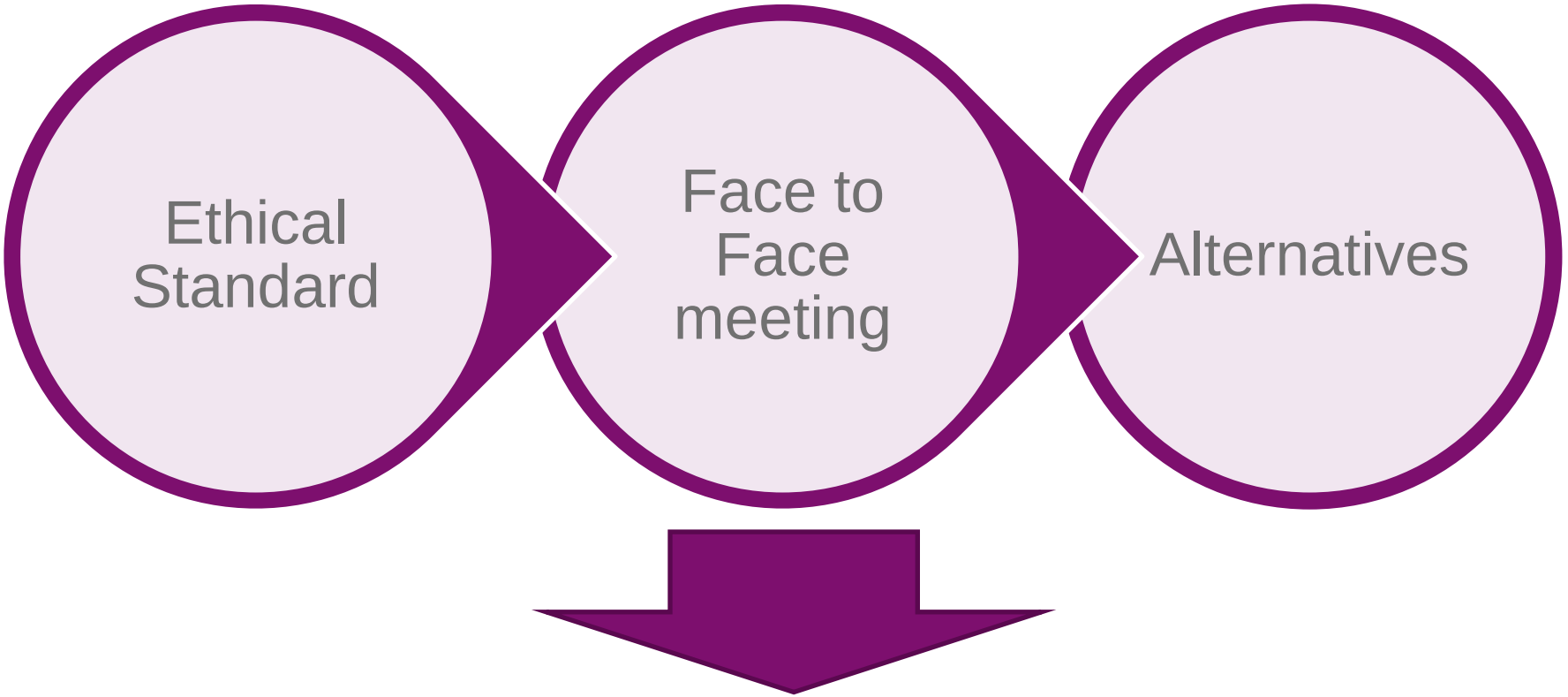
» Lilly delayed the start of most new trials and paused enrollment in most ongoing trials

» Pfizer released a similar plan.

» Bristol-Myers Squibb did continue enrollment in existing trials but postponed activation of new trial sites and new trials

Reference AACR Clinical research slows as COVID-19 surges. Cancer Discov. 2020;10(5):630

Consent Process



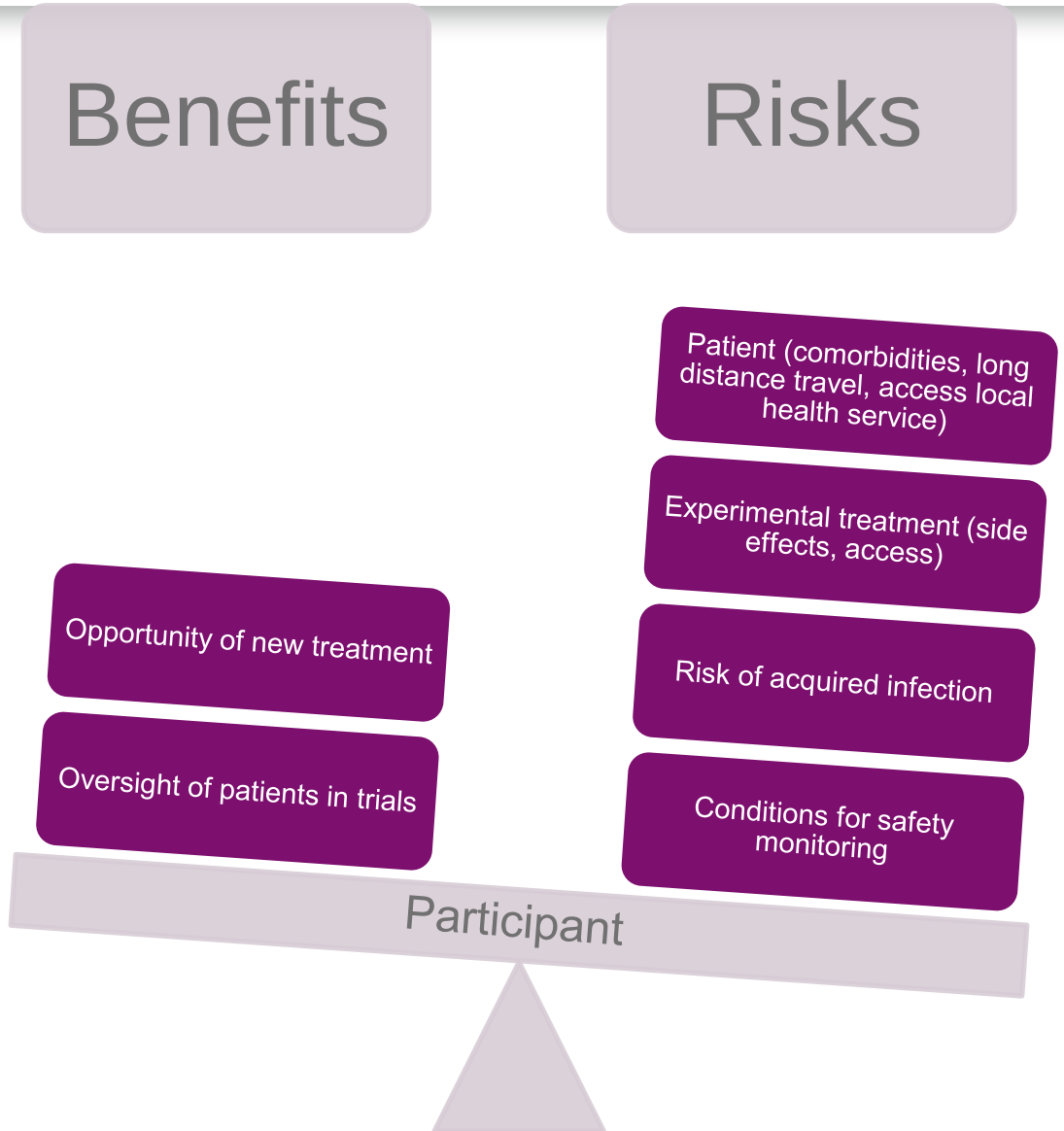
To protect patients

To explain the study & expected benefits/risks

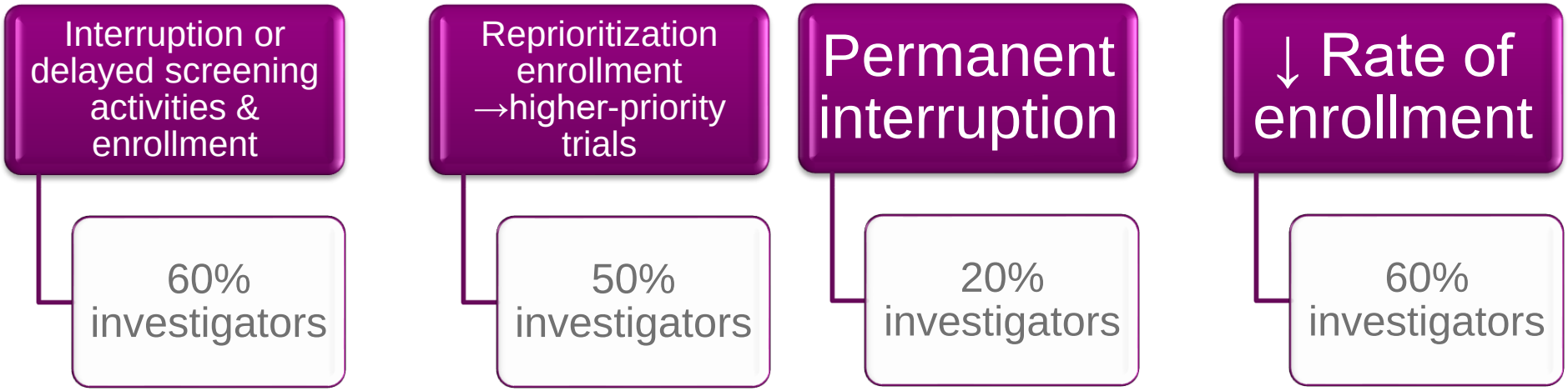
- Telephone
- Video-conference

Screening Activities

- Reorganisation of health care resources
  - Redeployment and repurposing (staff, activities related to clinical research) → affect capacity
  - Increased workload for medical and research staff
- Change in clinical trial programs
- Suspension of medical/surgical procedures
  - Impact on screening activities (imaging procedures, biopsies…)
  - Impact on collection of biomaterial (tumor tissue, blood samples) → impact of biomedical research
- Exposure risk to consider before participating


Benefits
Risks
Patient (comorbidities, long distance travel, access local health service)
Experimental treatment (side effects, access)
Opportunity of new treatment
Risk of acquired infection
Oversight of patients in trials
Conditions for safety monitoring
Participant

- Implementation of preventive measures (lock downs, social distancing, limited access to beds)
- Change of practice by investigators:



Reference: Waterhouse DM, Harvey RD, Hurley P, et al. Early impact of COVID-19 on the conduct of oncology clinical trials and longterm opportunities for transformation: findings from an American Society of Clinical Oncology survey. JCO Oncol Pract. 2020;16(7):417–21.

Reference: Upadhaya S, Yu JX, Oliva C, Hooton M, Hodge J, Hubbard-Lucey VM. Impact of COVID-19 on oncology clinical trials. NatRev Drug Discov. 2020;19(6):376–7.

Impact on Enrollment

Variables	Variables	YoYD* March 2020 Vs March 2019	YoYD* April 2020 Vs April 2019	YoYD* May 2020 Vs May 2019
All countries, All Therapeutic areas		-65%	-79%	-74%
Asia	China	-68%	-33%	-49%
	India	-84%	-97%	-95%
	Japan	-44%	-69%	-72%
	South Korea	-61%	-42%	-54%
Europe	France	-68%	-81%	-76%
	Germany	-33%	-77%	-81%
	Italy	-53%	-49%	-65%
	Spain	-68%	-82%	-68%
	United States	-66%	-83%	-73%
	United Kingdom	-80%	-95%	-100%
Therapeutic areas	Cardiovascular	-69%	-95%	-91%
	CNS**	-68%	-76%	-75%
	Endocrine	-64%	-91%	-89%
	ID/ Anti infectives	-47%	-66%	-52%
	Oncology	-48%	-60%	-58%
	Respiratory	-34%	-86%	-81%

* **YoYD** = year-on-year difference ; ** **CNS** = central nervous system

Reference: Brijesh Sathian and al. Impact of COVID-19 on clinical trials and clinical research: A systematic review. Nepal J Epidemiol. 2021 Mar; 11(1): 959–982

Reference: Medidata. COVID-19 and Clinical Trials: The Medidata Perspective. Release 5.0. Accessed June 10, 2020. https://www.medidata.com/wp content/uploads/2020/05/ COVID19-Response5.0_Clinical-Trials_20200518_v2.2.pdf

Clinical Research-Challenges for the Ongoing Trials

Pandemic markedly affected the ability to conduct trials in safe and effective ways:

- Participant ability or willingness to come to hospitals
- Disruption to supply chains (drug, equipment) due to closed borders
- Limited resources (reorganization/redeployment) and time spent to implement alternatives for participants
- Significant disruption to study protocols
  - Major impact: social distancing impacting tests, investigations, in-person visits.
- Forced adaptation of research protocol (consent process remotely, telemedicine, treatment at home) with emergency amendments

Reference: Louis Fox & Al. Impact of the COVID-19 Pandemic on Cancer Researchers in 2020: A Qualitative Study of Events to Inform Mitigation Strategies. Front. Public Health, 24 November 2021

» Treatment delayed or omitted doses

- Participant with long distance travel (↑risk of acquired infection, national limitations to travel, quarantine)

» Change in the risk and benefit ratio for the participant

- Presence of high-risk comorbidities
- Investigations and tests imposing in-person visits vs possibility of using local facilities
- Access to experimental treatment (hospital vs home (oral treatment))

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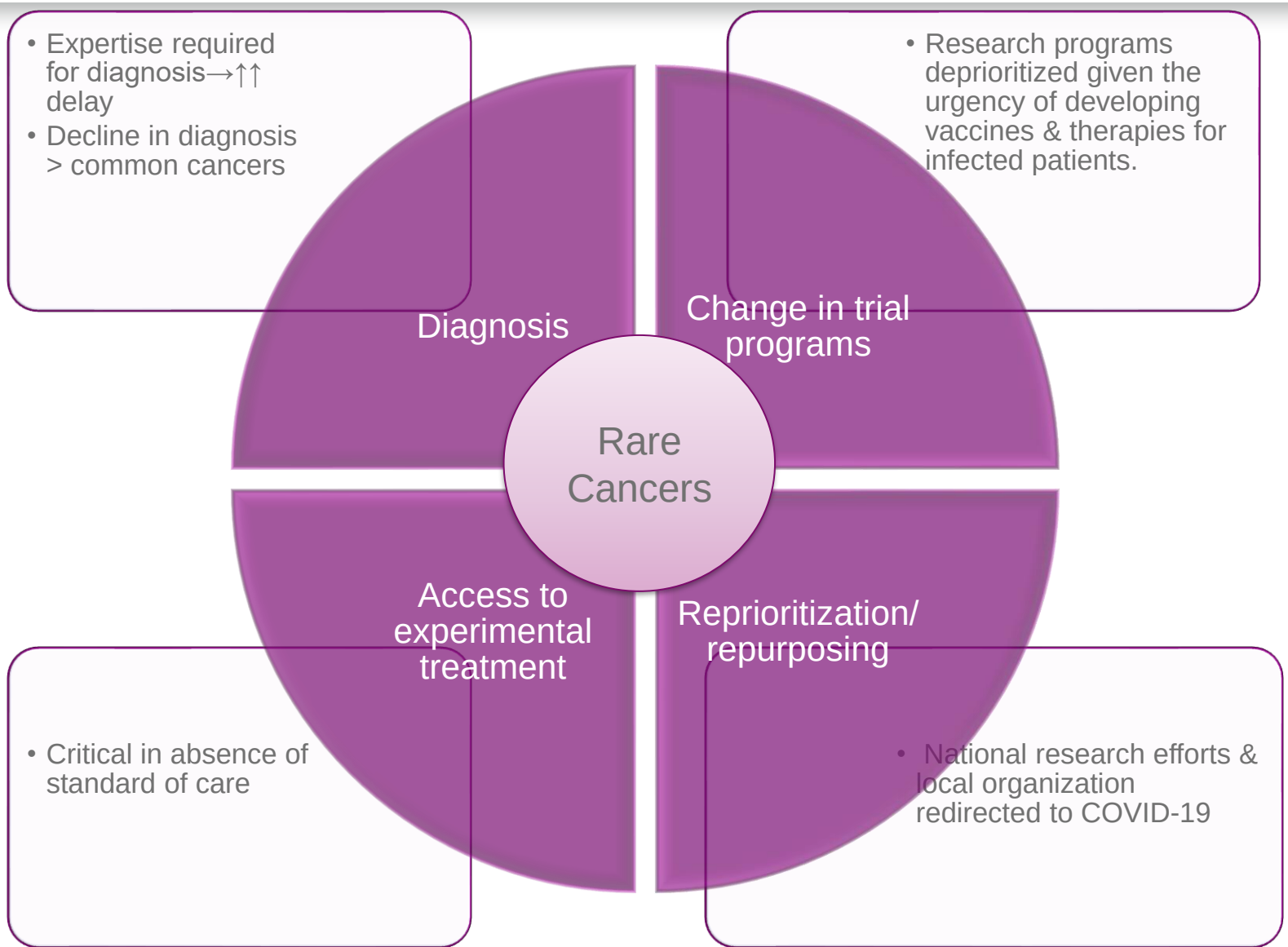
Factors Worsening the Situation for Rare Cancers


• Expertise required for diagnosis→↑↑ delay
• Decline in diagnosis > common cancers
• Research programs deprioritized given the urgency of developing vaccines & therapies for infected patients.
Diagnosis
Change in trial programs
Rare Cancers
Access to experimental treatment
Reprioritization/ repurposing
• Critical in absence of standard of care
• National research efforts & local organization redirected to COVID-19

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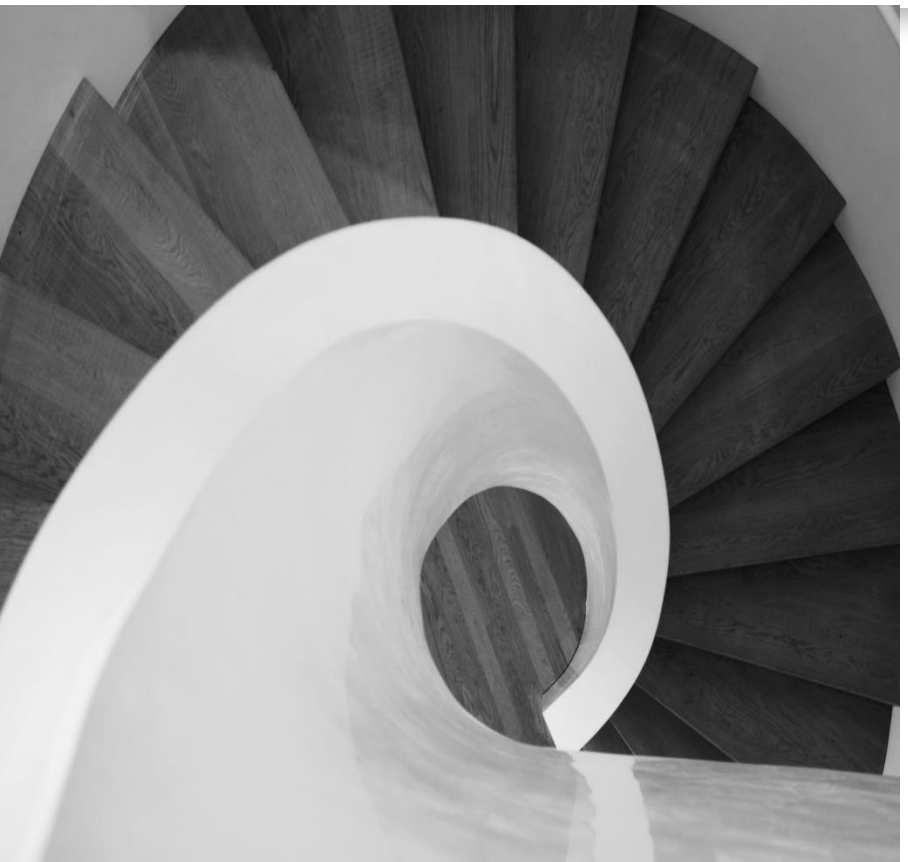
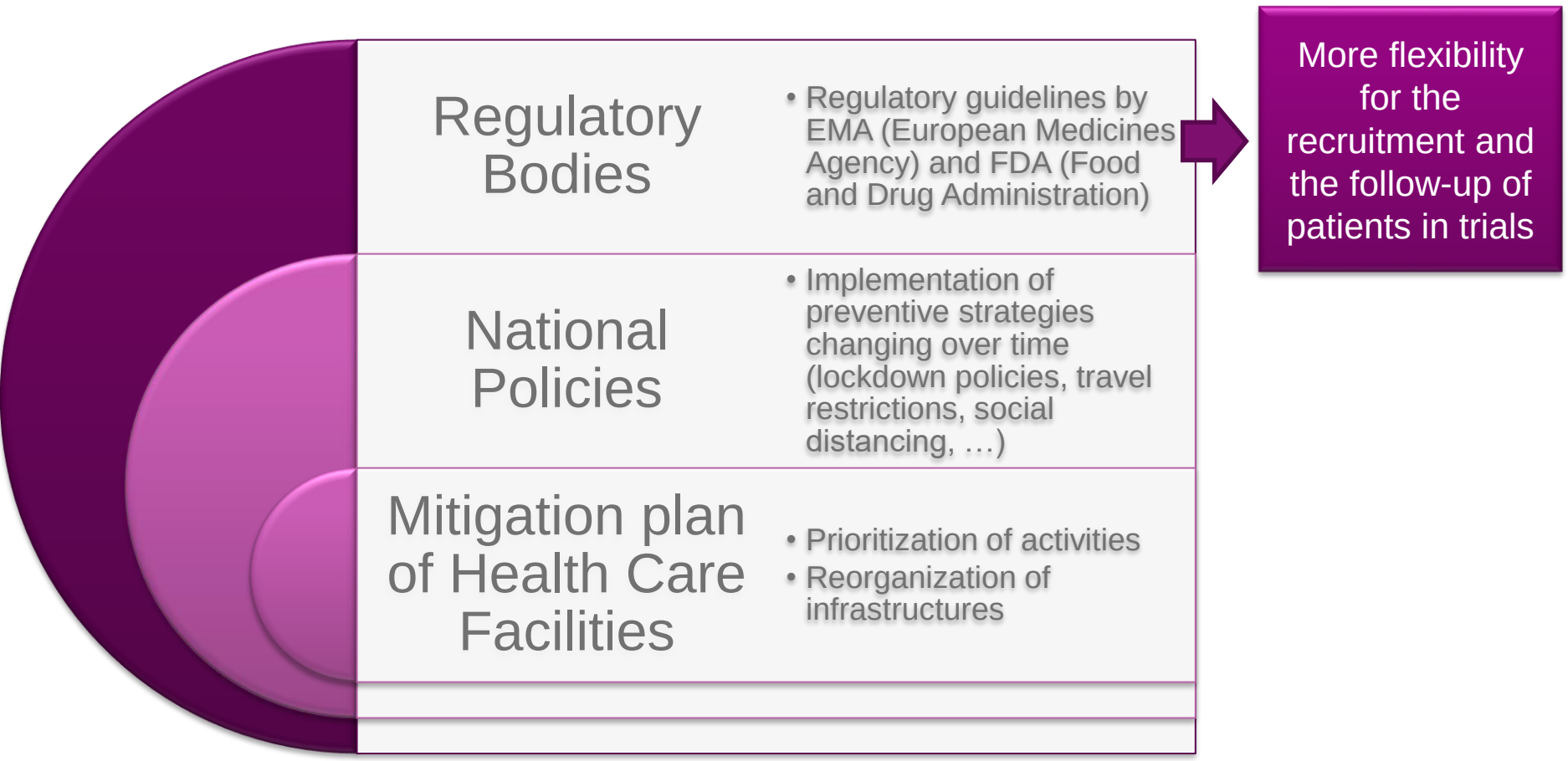


Adapting Clinical Research

European and National Policies



During the Crisis: Flexible arrangements !

Resources : when possible homeworking

Scientific

- Realtime Guidance (study procedures, treatment, reporting of serious toxicities) provided to participating sites
- Collect of information from National and European Regulators
- Adaptation of the ongoing trials → amendments approved by the Competent Authorities and Ethical Committees
- Collect of deviations related to the pandemic , flagging relationship with COVID-19.

Operational

- For study procedures (tolerance to experimental treatment, well being), involvement of local facilities (laboratory, imaging procedures), window of assessments extended.
- Physical visits → virtual visits
- e-consent process
- Ship oral drugs directly to patients
- Remote on site visits from the Sponsor

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Impact on Researchers

Impact on Researchers

The UK Research and Innovation's survey on researchers, conducted between February and March 2021, shows that the pandemic did affect:

- Research
- Mental health
- Future career prospects.

Survey Findings

Researchers (%)	Negative impact	Positive impact
61	Research time	
58	Research planning	
50	Work activities (teaching, administrative tasks)	
27		Unexpected opportunities

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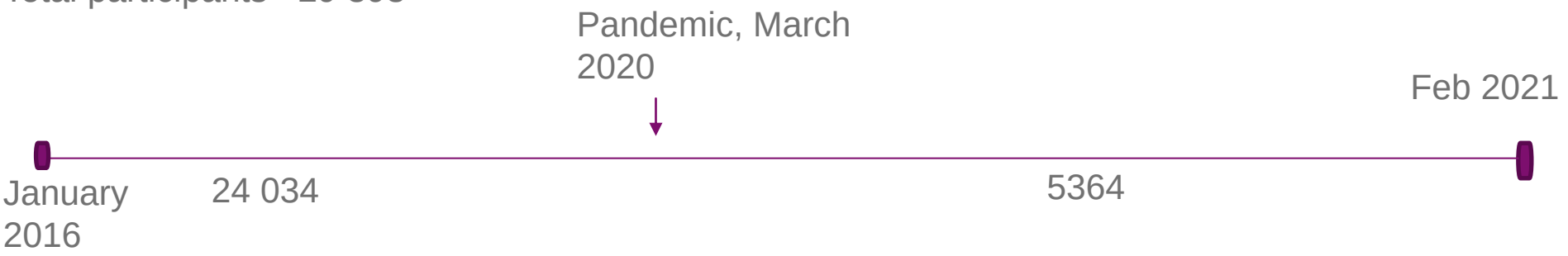
Lasting Changes for Clinical Research

Status of Enrollment …. Recovering!

Given the pandemic and the multiple waves in 2020 and 2021, did the enrollment remain low ?

Used data: Initial enrollments to clinical trials conducted by the SWOG Cancer Research Network (important academic research group in USA) extracted from research program conducted between January 1, 2016, and February 28, 2021.

Total participants= 29 398



- During the pandemic, actual enrollments were 77.3% of expected enrollments.
- With marked reduction for trials focusing on prevention
- Regarding trials focusing on treatment they were less affected

Reference: Unger JM et al. Cancer Clinical Trial Participation at the 1-Year Anniversary of the Outbreak of the COVID-19 Pandemic JAMA Netw Open. 2021 Jul 1;4(7):e2118433

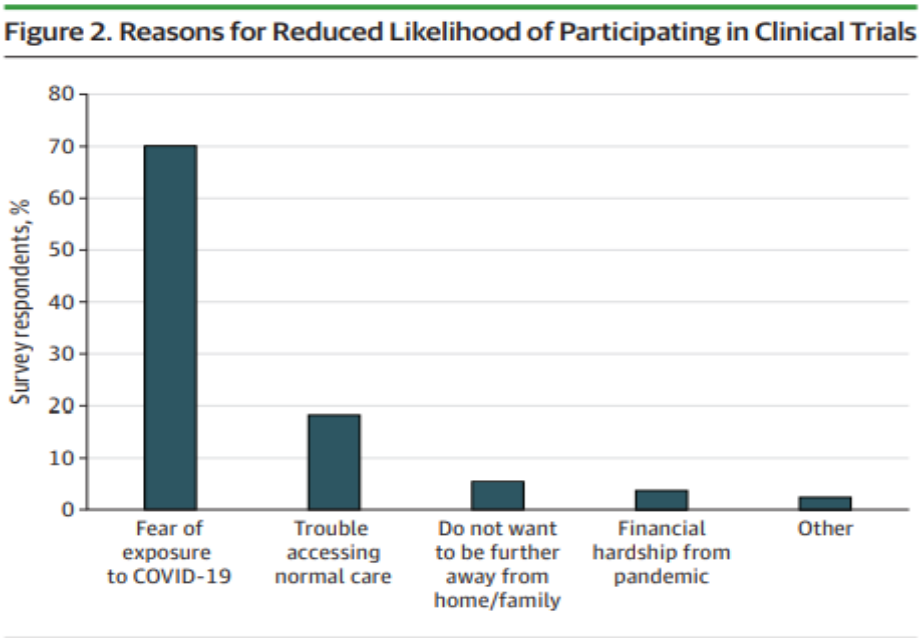
Participation in Clinical Trials

Will patients be as willing to participate in clinical research as before the outbreak ?

» In the USA, a survey has been conducted with 3054 participants between May 27, 2020 and June 17, 2020. A total of 933 responses (30.6%) were received.

» Among respondents, the majority (79.5%) indicated no difference. However nearly one-fifth of patients with cancer reported that they would be less likely to participate in a trial :

High rates of COVID-19 infection → ↓ willingness



Reference: Fleury, M. E et Al. Association of the COVID-19 Outbreak With Patient Willingness to Enroll in Cancer Clinical Trials. JAMA Oncol. 7, 131–132 (2021).

With the rapid development and implementation of clinical trials designed to research COVID-19 → room for improving clinical research in the interest of the community.

Post Crisis: New Model of Collaboration

» Get inspired by the model of collaboration between competitors, regulators and academia used for the accelerated development of vaccines and therapies for COVID-19

Post Crisis: Adopting New Practices

Flexible and creative adaptation

» **Adopting new working practices < lessons about modifications of trials during the crisis**

- The adaptation of existing processes particularly for facilitating the continuation of research:
  - Streamlining data collection (essential ones) and operational processes related to trial management
  - Flexibility for drug delivery
  - Homeworking for research staff (productivity, satisfaction, retention)

» **Reducing patient visits**

- The use of telemedicine (patient's safety, remote management)
  - such as phone calls, video calls

» **Digitalising research processes**

- Increased involvement of technologies to ease data capture
- Implementation of
  - e-consent process
  - e-signatures for trial documents
  - Electronic submission for regulatory process if not already in place

Reference: Waterhouse DM et al. Early impact of COVID-19 on the conduct of oncology clinical trials and long-term opportunities for transformation: findings from an American Society of Clinical Oncology Survey. JCO Oncology Practice 2020; 16(7):417–21

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Thank you!