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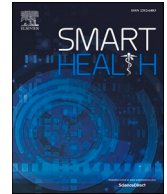
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## Telemedicine: A cornerstone of healthcare assistance during the SARS-Cov2 pandemic outbreak but also a great opportunity for the near future

Edoardo Tartaglia<sup>a,f,\*</sup>, Emilia Anna Vozzella<sup>b</sup>, Anna Iervolino<sup>c</sup>, Rosanna Egidio<sup>b</sup>, Gaetano Buonocore<sup>a</sup>, Antonietta Perrone<sup>d</sup>, Guglielmo Toscano<sup>d</sup>, Raffaele Tremante<sup>d</sup>, Francesca Cesaro<sup>e</sup>, Vincenzo Sommella<sup>b</sup>, Paola Magri<sup>c</sup>, Lanfranco Iodice<sup>b,g</sup>

<sup>a</sup> Department of Public Health, University "Federico II" via Pansini, 5, Naples, Italy, Zipcode 80131

<sup>b</sup> Health Management - University Hospital "Federico II" via Pansini, 5, Naples, Zipcode 80131, Italy

<sup>c</sup> General Management - University Hospital "Federico II" via Pansini, 5, Naples, Zipcode 80131, Italy

<sup>d</sup> Unit of Informative System, ICT and New Information Technology - University Hospital "Federico II" via Pansini, 5, Naples, Zipcode 80131, Italy

<sup>e</sup> Engineering S.p.A. c/o University Hospital "Federico II" via Pansini, 5, Naples, Zipcode 80131, Italy

<sup>f</sup> Health Management - University Hospital "Saint John of God and Ruggi d'Aragona" - Salerno, Largo Città di Ippocrate, Salerno, Zipcode 84131, Italy

<sup>g</sup> Italian Health Ministry c/o USMAF Campania via Immacolatella Vecchia Napoli, Naples, Zipcode 80133, Italy

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## ABSTRACT

**Background:** At the end of 2019, Wuhan, China, experienced an outbreak of a novel coronavirus. The SARS-CoV2 epidemiologic burden was constantly evolving, with numbers of infected persons, hospital admissions and deaths growing near exponentially. The pandemic outbreak of COVID-19 worldwide caught the health care systems in every country by storm and without a proper defense mechanism to cope and control such a pandemic, causing an overwhelming burden of illnesses that stressed the Health System capacity. In this context, telemedicine has been promoted and scaled up to reduce the risk of transmission. During the "lockdown", the AOU "Federico II" was forced to create peculiar pathways to ensure the safety of the patients and medical staff, and to keep an appropriate medical assistance, therefore it was introduced the telemedicine, wherever possible, by modifying the Information Technology (IT) related to the waiting times, rescheduling all booked visits and identifying several outpatient clinics suitable for telemedicine activities. In this paper the Authors reports their own experience with Telemedicine.

**Abbreviations:** WHO, World Health Organization; SARS, Severe Acute Respiratory Syndrome; MERS, Middle East Respiratory Syndrome; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19, CoronaVirus Disease 19; ACE2, Angiotensin-converting enzyme; CRS, Cytokine release syndrome; ARDS, Acute respiratory distress syndrome; AOU, Azienda Ospedaliera Universitaria (Teaching Hospital); IT, Information Technology; HM, Health Management; TM, Telemedicine.

\* Corresponding author. Department of Public Health, University "Federico II" via Pansini, 5, Naples, Zipcode 80131, Italy.

E-mail address: [edo.tartaglia@libero.it](mailto:edo.tartaglia@libero.it) (E. Tartaglia).

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## 1. Background

Coronaviruses are a group of related RNA viruses, phylogenetically belonged to Nidovirales order, that cause diseases in mammals and birds. They are minute in size (about 65–125 nm) and contain a single-stranded RNA as nucleic material, size ranging from 26 to 32 kbs in length, and categorized in four subgroups (alpha  $\alpha$ , beta  $\beta$ , gamma  $\gamma$  and delta  $\delta$ ). Recently, at the end of 2019, Wuhan, an emerging business hub of China, experienced an outbreak of a novel coronavirus that killed more than 3000 and infected about 81,000 individuals within the first fifty days of the epidemic (WHO, 2022). This new virus, responsible for a new severe respiratory syndrome, was reported to be a member of the  $\beta$  group of coronaviruses (Shereen et al., 2020) and it was defined as “Severe Acute Respiratory Syndrome Coronavirus 2” (SARS-CoV-2) by the International Committee on Taxonomy of Viruses ( ).

As remarked by Lippi et al., the novel coronavirus disease (COVID-19) “is the third coronavirus outbreak to have emerged in the past twenty years, after Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS)” ( ).

Generally the human-to-human transmission occurs with close contact; in fact, the transmission primarily happen through the respiratory droplets production, just as influenza and other respiratory pathogens (Shereen et al., 2020); however transmission may also occur through fomites in the immediate environment by touching an infected surface or object ( ).

Airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed. Other routes of transmission, such as fecal-oral and blood borne transmission, may be possible too. Usually, SARS-CoV-2, like other respiratory viruses, is considered to be more contagious when people are symptomatic. But, it was also reported some cases in literature, in which several people were infected from asymptomatic subjects during the “prodrome period” (Kong et al., 2020). The estimated incubation period between infection and onset of symptoms is approximately 5 days (range: 2–14 days) but with a high variability (Possible outliers: 0–27 days). The last Situation Report of the WHO attests that COVID-19 has already infected as many as 489,060,735 people up to Apr 05, 2022, from 222 countries and territories, causing 6,150,333 deaths (WHO, 2022).

Initially, the case fatality rate was calculated at approximately 6,5%; currently it is about 1,25%. The advent of vaccination and the frequent appearance of new variants led to a rapid and significant evolution of the epidemiological and clinical situation there so, the symptomatology of the new variants is milder and shorter than that of the old variants (Malika, 2022; Mendiola-Pastrana, 2022; Sarabadani et al., 2022; Wise, 2022). The changes in these variants demonstrate how ongoing evolution in SARS-CoV-2 can drive changes in how the virus interacts with host cells (Rando et al., 2021) and how the illness could change quickly. However, initially, at beginning of 2020, the clinical picture was dramatic and all Health Systems were unprepared to withstand the pandemic wave (Sahin et al., 2020); as reported by Columbus et al., approximately 25% of patients required intensive care, reporting a clinical deterioration at roughly day 8 of illness; besides, 10% of them required intubation and mechanical ventilation and approximately 3% required extracorporeal membrane oxygenation (Columbus, 2020). Clinically, the immune responses induced by SARS-CoV-2 infection was two phased:

- The first phase occurred during the incubation period and it represented a “non-severe stage”; in this phase, a specific adaptive immune response was required to eliminate the virus and preclude the disease progression toward more severe stages (Shi et al., 2020).
- The second phase occurred later, when the protective immune response was almost impaired; in this phase, the virus propagated in host’s cells resulting in a massive destruction of the affected tissues, especially in organs that had high ACE2 expression. (Shi et al., 2020). A cytokine release syndrome seemed to affect patients with severe conditions associated to a genetic susceptibility (Shi et al., 2020).

As reported by Shi et al. in this phase, “the innate immune response to tissue damage caused by the virus could lead to acute respiratory distress syndrome (ARDS), in which respiratory failure is characterized by the rapid onset of widespread inflammation in the lungs and subsequent fatality” (Shi et al., 2020). Hence, the clinical features of COVID-19 were varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction (Singhal, 2020).

Due to the incontrovertible evidence demonstrating worldwide diffusion of SARS-CoV-2, COVID-19 had been declared a global pandemic disease by the World Health Organization (WHO) (Lippi et al., 2020); in that occasion, T.A. Ghebreyesus, the General Director of the Agency, warned the entire World on “the alarming levels of spread and severity, and by the alarming levels of inaction” (Lippi et al., 2020). From then, the epidemiologic burden of COVID-19 was constantly evolving, with numbers of infected persons, hospital admissions and deaths growing near exponentially (Lippi et al., 2020). The pandemic outbreak of COVID-19 worldwide caught the health care systems in every country around the world by storm and without a proper defense mechanism to cope and control such a pandemic (Kong, 2020). In fact, this outbreak was causing an overwhelming burden of illnesses that stresses health system capacity and adverse effects on healthcare workers including the risk of infection. The confinement of population and the outbreak impact on health care systems was disrupting routine care for non COVID-19 patients (Ohannessian et al., 2020).

The health care had undergone a progressive significant worsening for these patients over the last pandemic weeks. In this dramatic context, every Healthcare Company in the World had to take measures to tackle effectively the SARS-CoV2 pandemic. During the “lockdown”, in order to ensure adequate medical assistance at COVID patients, also the AOU “Federico II” had to cancel or delay the usual medical assistance to non COVID patients, securing the latter just the essential services, such as urgencies, emergencies, time-related conditions (such as pregnancy, onco-haematologic diseases, dialysis) and other rare conditions, exclusively followed by our facility, but not other medical services, resulting in a remarkable reduction of workloads. These stronger criteria were dictated by National and Regional Guidelines in order to reduce the viral spread among people. In this context, telemedicine, particularly video

consultations, has been promoted and scaled up to reduce the risk of transmission (Ohannessian et al., 2020); in fact, it is a versatile tool with a wide range of applications. The framework included tele-expertise, remote patient monitoring of contact cases, and teleconsultation for triage and isolated cases (Ohannessian et al., 2020).

Telemedicine permits to non COVID-19 patients to get the necessary health care they need, while minimizing exposition to infection of themselves and medical staff. It is very important to remark that medical staff might become a potential and powerful vehicle for viral spread (Anelli et al., 2020).

### 1.1. Aims

In this paper the Authors reports their own experience with Telemedicine; the aim of this observational study is to describe the role and the possible positive effects of telemedicine on activity volume of outpatient clinics during the recent covid-19 pandemic and the further developments in the near future.

### 1.2. Healthcare setting

The AOU “Federico II” is a high specialization hospital center and the largest teaching hospital in Southern Italy. It is a health company with legal, financial and organizational autonomy, located in the city of Naples, a metropolis with over 1,500,000 inhabitants and with one of the highest density of population (more than 2616.8 inhabitants per square kilometer) in Italy and probably in the whole Europe. The facility covers all fields of medicine and surgery and has a very strong commitment in research and technology, hosting one of biggest and the eldest school of medicine in the World. It includes 11 Departments and 61 Operational Units. Its outpatient activity ranges average from 180,000 to 200,000 visits per year, reaching peaks of 250,000, with an average of 875 patients seen every day, but during the “lockdown” it was reported a remarkable reduction of workloads.

## 2. Material and methods

To counter the negative trends, the AOU “Federico II” was forced to create peculiar routes to ensure, by one hand, the safety of the patients and medical staff working in presence by means of personal protective device utilization, social distancing and protective behaviors, and, by other hand, to keep an appropriate medical assistance and ensure an adequate activity volume. To reach these goals and to serve the highest possible number of people at the same time, considering the mandatory limitations enforced by national and regional government, we first decided to introduce telemedicine, wherever possible. Whenever there was no possibility to introducing telemedicine, the patients were booked for a medical consult in person. In this last case, safe pathways were properly studied to screening them before their admission to outpatient clinic; all the patients were screened by mean of a pre-triage via phone (Phone-survey) in the day before the consult and a triage in person (body temperature measurement, rapid test SARS-COV2) in the consult day. The decision about the type of visit (telemedicine vs face to face consult) was made by clinicians based on specific rules and protocols established by every outpatient clinic based on type of patient, type of diagnosis and type of health service to be provided.

The Strategic Management developed new strategies to implement the care services and minimize the risk factors for all stakeholders (patients and medical staff), diversifying the access mode to health services, and Telemedicine played an important role in this strategy implementation.

Initially, usual platforms such as zoom or skype or others (including IM apps on mobile devices, such as Whatsapp or Viber, that showed to be more user-friendly, especially if the user were older than 35–44 y.o.) were used; Each of these technologies have pros/cons but they were relative because they were related to needs of each outpatient clinic which chose the platform that it considered most appropriate for its purposes. However, because the telemedicine is one of objectives of the National Recovery and Resilience Plan (PNRR), at present a single platform, Sinfonia-telemedicine, managed by the Campania Region is being tested.

A group of outpatient clinics (16), representing 24.61% of all active outpatient clinics in AOU “Federico II”, were firstly identified to take part in a pilot project (Table 1) and secondly the Health Management (HM) established a common protocol to define different patient pathways in which each patient is directed towards a consult via telemedicine or a medical consult in presence on based of clinician indications.

In the first case, the patients are booked, via phone or e-mail, for a teleconsultation; afterwards they can pay the copayment, if due, and send the receipt via e-mail to the booking center that will shortly contact them to set a date for a video or phone appointment. The Medical staff will call the patient at the meeting date for the teleconsultation. Otherwise, in case of consult in presence, the patient is

**Table 1**  
Outpatient Clinics that took part in the Telemedicine project of AOU “Federico II”.

1	<i>Diabetology</i>	9	<i>Gastroenterology and Hepatology</i>
2	<i>Clinical Nutrition</i>	10	<i>Medical Genetics</i>
3	<i>Internal Medicine and Emo-Coagulation</i>	11	<i>Clinical Dermatology</i>
4	<i>Internal Medicine and Emergency medicine</i>	12	<i>Child Neuropsychiatry</i>
5	<i>Rheumatology</i>	13	<i>Pediatrics</i>
6	<i>Endocrinology</i>	14	<i>Hygiene and Preventive Medicine</i>
7	<i>Hypertension</i>	15	<i>Motor Rehabilitation</i>
8	<i>Allergology and Clinical Immunology</i>	16	<i>Neurology</i>

called the day before the consult for a pre-triage and then, the day of consult, the patient is screened to check their coronavirus free condition before to be admitted to the outpatient clinics by mean of medical history collection, epidemiological survey, body temperature measurement and COVID rapid test. If negative, the patient goes to the booking center for the payment, when due, and, subsequently, the patient is admitted to outpatient clinic for consult (Fig. 1).

Since the main target of Telemedicine is the outpatient clinical activity and especially for follow up activities, we monitored the volume of outpatient clinics, using it as an output indicator, to value what were the effective positive effects of telemedicine on activity volume, firstly comparing the activities during two consecutive years (2019 vs 2020), month by month, and considering that the second bimester of 2020 coincided in Italy with lockdown (March 9, 2020–May 4, 2020); secondly considering three areas of activity (Ordinary, Day Hospital/Day Surgery and Outpatient Clinical Activity), reporting percent variation in both groups within the referential periods. Furthermore, to valuing the Health System resilience, we have considered the overall weight of telemedicine on whole volume of activities throughout the year 2020 (from January 01, 2020 to December 31, 2020), considering the global response of Health System at the first (March–May) and second (October–December) infection wave. The percentage changes in revenues and related losses were also calculated. The data relating to 2021 were not taken into consideration since the introduction of vaccine could have constituted a confounding selection bias for the subsequent data analysis as the vaccine has changed the access modalities; in fact, the Italian Health Ministry reopened all medical activities and health services on march 2021 there so many people preferred to have a visit face to face rather than in Telemedicine. This preference also emerged from our survey in which just 48% of interviewees believed that Telemedicine is better than visit in presence. The data were collected by means our digital archives (data warehouse) and the statistical analysis was performed using Stata15. To analyze the data was used T-test as parametric statistic. To achieve all these objectives, we had to modify the Information Technology (IT) related to the waiting times, rescheduling all booked visits and identifying several outpatient clinics suitable for telemedicine activities. The payment methods had to be adapted to the new requirements, too, by encouraging electronic payment systems (e-payment) and on line booking systems; for these reasons, it was strengthened the staff belonging to the booking center hiring new units to be used mainly for phone and on-line reception and, at the last, it was activated a dedicated new online payment system. We used online medical consulting platforms to perform teleconsults, adopting privacy protection mechanisms (documents' cryptography, use of strong passwords, sending of documents and password per different way) to share sensitive personal information according with It-GDPR. New strategies were also developed for visiting the patients in telemedicine such as sending patient's home some tools for self-diagnosis (self-diagnosis kits such as pulse oximeter, glucometer, fast allergy self-tests and many other tools).

### 3. Results

At pandemic outbreak there was a drastic drop of admissions to outpatient clinics compared to admissions in the same period of previous year. This drop has been rated to be from 875 to 200 patients seen daily (−76,28%). As a consequence, in that period, the reduction also affected the activities of AOU “Federico II” with a dramatic abatement of hospitalizations (−47,59%) both in ordinary (−38,96%) and in Day Hospital/Surgery (−57,54%), inasmuch it was ensured just emergencies/urgencies and time-related or rare conditions (Fig. 2).

The outpatient clinical activity throughout 2020, compared with 2019, was certainly reduced (Fig. 3) and this reduction was

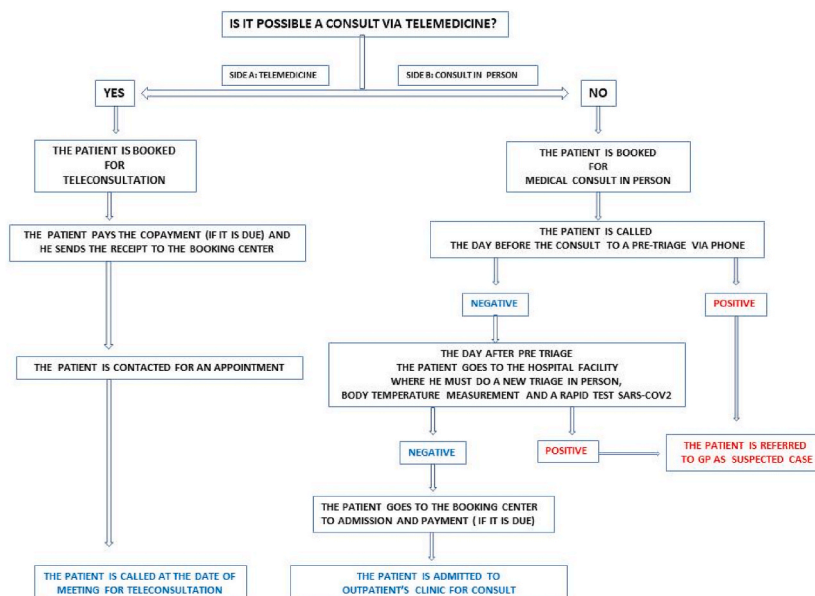


Fig. 1. Different patient pathways: Consult via telemedicine vs Medical Consult in presence.

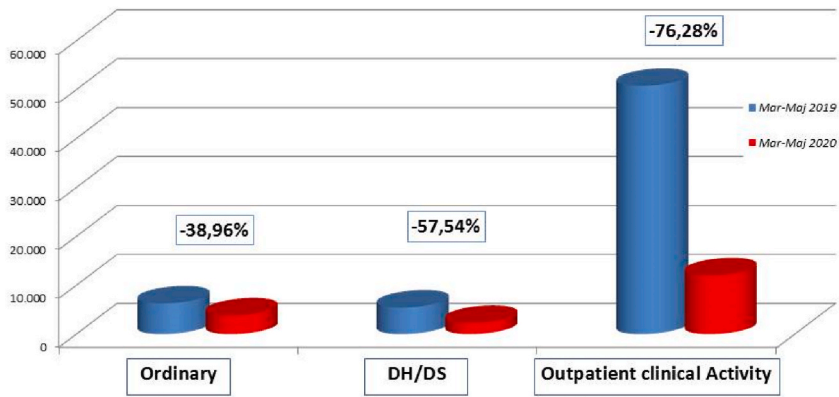


Fig. 2. Activity Volumes of AOU “Federico II” at pandemic outbreak compared with the same period of 2019.

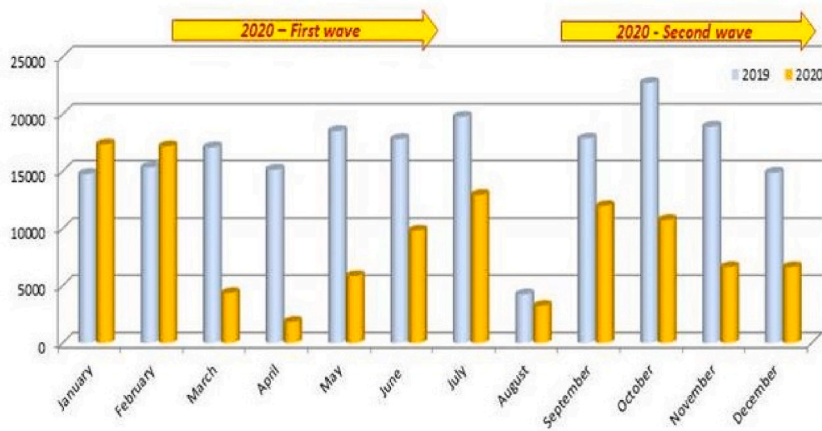


Fig. 3. The outpatient clinical activity throughout 2020, compared with 2019.

statistically significant ( $p = 0,0005$ ): the reduction of outpatient clinical activity throughout the 2020 was globally about  $-44,92\%$  with a consequential reduction of hospitalizations ( $-20,59\%$ ) both in ordinary ( $-16,99\%$ ) and in Day Hospital/Day Surgery ( $-23,02\%$ ) activity (Fig. 4), and a consequent reduction of relative rescues (with a global loss of 24,5 million €) ( $p = 0,0005$ ). We have to underline that in August there was a physiological annual reduction of volumes due to summer holidays and not related to pandemic

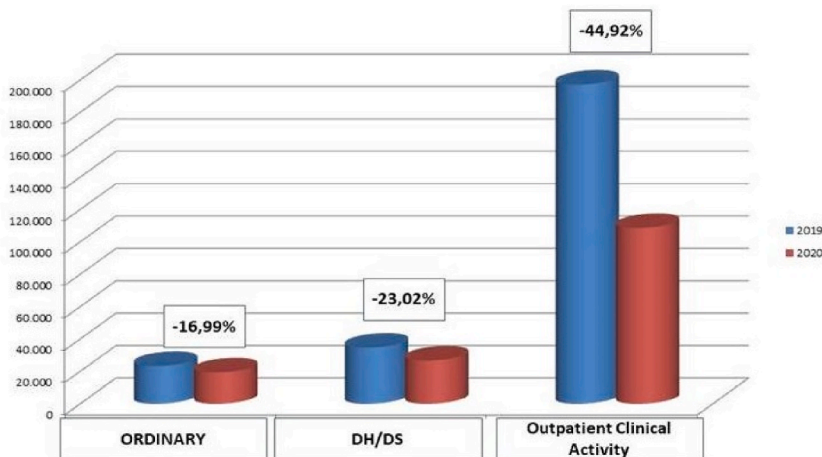


Fig. 4. Activity Volumes of AOU “Federico II” throughout 2020, compared with 2019.

situation.

However, since the introduction of telemedicine service, about 15% of all medical consults delivered by AOU “Federico II” during the lockdown were provided in this way, (going from 4.03% of all consults in April to 15.51% in May), of which 97,38% of them were follow-up visits, that would otherwise have been missed during the current pandemic, so an economic loss has been avoided. In addition, considering that the direct costs for a consult in person are to be attributed mainly to medical staff and secondly to triage, medical supplies and consumables, it has been calculated that, using Telemedicine visits vs a face-to-face consultation, about 65–70% of direct costs were spared by our Healthcare Company.

Besides, there was also a reduction in the average consultation/waiting time which, despite being remarkably variable from clinic to clinic, it account approximately –30%, due to more direct approach of telemedicine to patient (no waiting time, no downtime, no travelling time that could result in delays); in fact, telemedicine procedures totally remove the waiting times at the entrance due to “triage” (swab tests, interview and so on). The “time of visit” should not substantially change but the agenda could be more flexible in terms of start-end time every day, potentially increasing the number of visits that eventually could reflect a reduction of waiting time lists.

To value the customer satisfaction, an anonymous satisfaction questionnaire was administered at the end of the visit; nine items were questioned. Only 60% of patients returned the completed questionnaire by which 84% of patients was fully satisfied of Telemedicine and 78% of them find telemedicine an acceptable way to receive health care services. Nevertheless only 68% of them declare that they will use telemedicine again and only 48% believe that Telemedicine is really better than visit in presence.

Our telemedicine experience was also continued after the lockdown (Fig. 5) and, currently, the telemedicine represents, with 40 (61,5%) active outpatient clinics, about 12% of whole outpatient activity and about 10% of all revenue derived from outpatient activities, although the most people still prefer a face to face consultation.

Most telemedicine consultations (98,51%) continue to be follow-up visits but a positive trend is observed for the first medical examinations too.

Many first visits were performed in this way in medical specialties that did not necessarily required an instrumental or physical approach to the patient, such as pediatric, allergology, dermatology, diabetology, endocrinology, neuropsychiatry and many others and, after some “emergency” experience with this new approach, we started planning an official, structured outpatient telemedicine offer in collaboration with the health service department of the Campania Region, which is the institutional partner providing financing and coordination for all the local health trusts. This new special offer started in 2021 included outpatient first visits and follow-up visits for the disciplines: endocrinology, dermatology and child neuropsychiatry, with dedicated hardware and software; so overall it is possible to state that there was a good Health System resilience already starting from the second infection wave with a positive trend observed from the second semester of 2020.

#### 4. Discussion

The pandemic has brought about a dramatic and statistical significant reduction of Outpatient Clinics activity both in terms of volume and revenues, especially during the first phases, and telemedicine has been promoted and scaled up to reduce the risk of transmission and to ensure an adequate outpatient health care for non COVID patients. Telemedicine, known also as “remote medical care”, refers to providing clinical healthcare through electronic communication technologies rather than in presence. The initial form of telemedicine involved the use of a telephone but the use of video-calls and other telecommunication applications more recently has improved the service greatly (Hau, 2020), though a phone call may be yet necessary as not all patients have the required device for a video consult (Gadzinski, 2020). It was the first time that telemedicine was experienced on such a large scale not only at AOU “Federico II”, but probably in the whole Southern Italy, also taking into account that traditionally such an approach is lacking, mainly due to poor

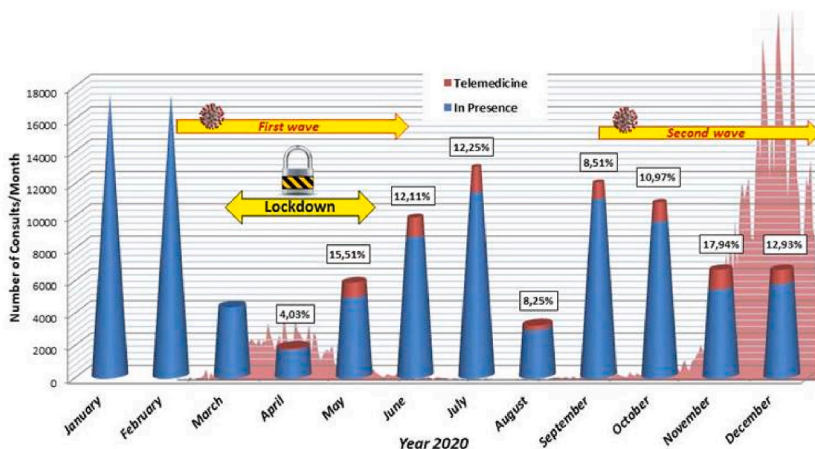


Fig. 5. Telemedicine experience in AOU “Federico II” throughout 2020.

compliance of end users. However, Telemedicine is particularly advantageous for densely populated areas, such as Naples, or for several specific subtypes of population such as geriatric patients, inhabitants located in areas far away from the outpatient clinics, patients who have to be submitted to follow-up visits but, mostly, TM has showed all its potential to help in special situation such as the current Pandemic by permitting mildly ill patients to get the supportive care they need while minimizing their exposure to other acutely ill patients, in fact, as reported by Portnoy et al., “... after all, the only infection that one can catch while use TM is a computer virus” (Portnoy, 2020).

Certainly, Telemedicine include limitations with performing comprehensive physical examinations and possibilities for technical difficulties; besides, the quality of the signal is linked to the speed and quality of the internet transmission and to the ability of healthcare providers and patients to use the programs; last but not least, telemedicine encounters, compared with face-to-face encounters, are more vulnerable to privacy and security risks (i.e., an issues, in terms of privacy, was the delivery of the medical report; it has been solved by sending a double e-mail, the first including the pdf file encrypted, the second including the password to open the file attached to the first email). In any case, the benefits of telemedicine outweigh the risks and the disadvantages, such as reducing healthcare costs, increasing efficiency and revenue, providing easier and better access to healthcare services, and, particularly during pandemic, allowing to visit patients in safety; indeed, during the “Day after” lockdown, National and Local Regional Governments boosted new strategies to implement the care services and minimize the risk factors for all stakeholders (patients and medical staff), diversifying the access mode to Healthcare services and Telemedicine played an important role in this strategy implementation. The AOU “Federico II” of Naples adopted this solution to cope with healthcare needs of population; in fact Telemedicine allowed to recover a part of medical check-ups that had been put on standby, reducing the waiting times, and minimized drastically direct and indirect healthcare costs; indeed, telemedicine reduced consultation times, medical supplies and consumables, triage costs, and all indirect costs of health care (Patient and caregiver absenteeism, transport costs and risks ...). We are aware that our results could suffer from a misclassification due to an initial misalignment of copayment data vs booking data so that the real proportion of volume of telemedicine may be underestimated. There is also a group of patients “free of charge” that could balance this misalignment, though. Least but not last, as remarked by Moazzamia et al., “the Telemedicine has the ability to reinforce those health care workers that have been quarantined at home after exposure to COVID-19 and employ quarantined physicians to communicate with patients remotely via computer” (Moazzamia et al., 2020).

To achieve these goals our facility had to modify Information Technology (IT) related to the waiting times and rescheduled all booked visits, organize spaces and modality of video calling, using the smart work too, and readapt the terms of payment to the new needs, although some limitations including payment, credentialing, privacy, ethical consideration, loss of the patient medical relationship and staffing of specialists are exist too, and necessarily, they needs to be taken into account. Specially IT has been a cornerstone of organizational response to coordinating operational and clinical needs and must rapidly rearrange infrastructure, policies, and priorities to remain responsive (Grange, 2020). The Unit of “Informative System and New Information Technology” and Engineering made possible the technical realization of project; the General Management and the Health Management of University Hospital Federico II of Naples played an organizational and managerial role as well as a role in verifying the results and efficiency of the System.

Certainly, telemedicine cannot replace in person patient care, and not all clinical situations are appropriate for video consultations (Greenhalgh, 2020), but could benefit other frontline physicians by reducing their workload and optimizing their time to attending to patients being in a critically-ill condition (Moazzamia et al., 2020). However, as reported by Moazzamia et al., “creating telemedicine program takes time and does not happen overnight but it requires sources, funding and precise guidelines” (Moazzamia et al., 2020). Besides, telemedicine requires a new dynamic approach to the patient, using a distinctive standard of care dedicate for telemedicine including the use of self-diagnosis kits and new rules about the physician-patient relationship, electronic prescribing and in-person follow-up. The AOU “Federico II” had made stringent protocols and dedicate pathways to ensure safety and healthcare assistance to their patients. As reported by Ohannessian et al., “all stakeholders are encouraged to address the challenges and collaborate to promote the safe and evidence-based use of telemedicine during the current pandemic and future outbreaks, and the COVID-19 pandemic is a call to adopt the necessary regulatory changes supporting wide adoption of telemedicine” (Ohannessian et al., 2020). Our study is a descriptive observational study, and merely tried to describe the healthcare needs of users and the reaction capacity of System but surely our preliminary data needs further investigation by means of analytics studies and a deeper economical evaluation. The data of 2021 were not reported because the introduction of vaccine on large scale, the appearance of new variants, that led to a rapid and significant evolution of the epidemiological and clinical situation, as well as reopening of all medical activities and health services in presence could have been a confounding bias in the assessment of real role played by telemedicine in the resilience of Health System to the pandemic attack.

## 5. Conclusions

Telemedicine has been the keystone that has allowed a rapid, appropriate response of whole overloaded healthcare systems to current Pandemic. Indeed, this crisis has presented dramatic events that have harshly stressed the health system capacity but also unprecedented opportunities that should not be ignored without making progress. TM has showed all its potential to relieve the work’s burden of healthcare systems, though it will be necessary planning appropriate studies to clarify what telemedicine is best for as well as inappropriate; probably it will be necessary to improve the methodology and the approach to patients, proving them with opportune medical devices that allow an actual interaction between medical staff and patient. This will require heightened engagement to ensure that regulatory and policy gains are not rescinded. Telemedicine is central to care going forward, not just through this crisis. This way, future generations will derive benefits from our bitter experience (Bashshur, 2020).



## Ethics approval and consent to participate

“Not applicable”.

## Consent for publication

“Not applicable”.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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The Authors declare that they not receive any funding for this work.

## Author contributions

**Tartaglia E.** Data curation; Formal analysis; Investigation; Methodology; Writing - original draft; Writing - review & editing. **Vozzella E.A.** Conceptualization; Supervision; Validation; **Iervolino A.** Conceptualization; Funding acquisition; Supervision; Validation; **Egidio R.** Data curation; **Buonocore G.** Data curation; **Perrone A.** Software; **Toscano G.** Software; **Tremante R.** Software; **Cesaro F.** Data curation; Software; **Sommella V.** Data curation; **Magri P.** Resources; **Iodice L.** Methodology; Project administration; Writing - review & editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

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