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Editorial Comment

EDITORIAL COMMENT

# Acute peritoneal dialysis in the treatment of COVID-19-related acute kidney injury

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## ABSTRACT

The kidney is not typically the main target of severe acute respiratory syndrome coronavirus 2, but surprisingly, acute kidney injury (AKI) may occur in 4–23% of cases, whereas the dialysis management of AKI from coronavirus 2019 has not gained much attention. The severity of the pandemic has resulted in significant shortages in medical supplies, including respirators, ventilators and personal protective equipment. Peritoneal dialysis (PD) remains available and has been used in clinical practice for AKI for >70 years; however, it has been used on only a limited basis and therefore experience and knowledge of its use has gradually vanished, leaving a considerable gap. The turning point came in 2007, with a series of sequential publications providing solid evidence that PD is a viable option. As there was an availability constraint and a capacity limit of equipment/supplies in many countries, hemodialysis and convective therapies became alternatives. However, even these therapies are not available in many countries and their capacity is being pushed to the limit in many cities. Evidence-based PD experience lends support for the use of PD now.

**Keywords:** acute kidney injury, COVID-19, cytokines, mortality, peritoneal dialysis

## INTRODUCTION

Since December 2019, the world has been facing a new challenge with a novel pandemic virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), known as coronavirus 2019 (COVID-19). The global healthcare system has been severely impacted due to the rapidly increasing number of patients. The kidneys are not typically the main target of SARS-CoV-2, but surprisingly, acute kidney injury (AKI) occurs in 4–23% of cases [1–5]. However, dialysis management of AKI from COVID-19 has not gained much attention.

The key question is whether peritoneal dialysis (PD) can be used in COVID-19 AKI, as it often severely affects the respiratory system. Around 5% of the cases are critically ill patients who develop pneumonia, eventually leading to acute respiratory distress syndrome (ARDS) [6]. A few cases require renal replacement therapy (RRT), mainly from acute tubular necrosis due to multiorgan failure. Extracorporeal dialysis, either

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continuous renal replacement therapy (CRRT) or hemodialysis (HD)/hemodiafiltration (HDF), has been the main AKI treatment modality. The severe hypoxic COVID-19 patients usually need extracorporeal membrane oxygenation (ECMO) therapy [6, 7], which may aggravate AKI, thereby associating CRRT to the main ECMO circuit. As there is an availability constraint and a capacity limit of CRRT, HD and HDF equipment, supplies and replacement solutions worldwide, PD, which has been used in clinical practice for both AKI as well as end-stage renal disease (ESRD) for >70 years [8], becomes an option. The experience and knowledge acquired and reported in the application of PD in the AKI setting from the 1950s through the early 1980s gradually vanished during the late 1980s to the early 2000s, leaving a considerable gap of knowledge and experience for several generations of nephrologists. The turning point for going back to the future in PD utilization for AKI was a 2007 publications by a group of nephrologists from Botucatu, a university city in Brazil, interested and experienced in PD [9]. Their series of publications provide solid evidence that PD can be considered as an alternative form of RRT in AKI, and more new evidence is being gathered worldwide in recent years [9–13]. Current published studies do not support significant differences in outcomes between PD and the other dialysis alternatives (CRRT and intermittent HD) [10, 14–17].

## CONSIDERATION OF OFFERING PD IN COVID-19

PD is a home therapy option for ESRD patients. Home therapies are considered ideal when pandemics occur, keeping patients away from hospitals. PD patients usually attend the clinic once a month, whereas HD patients must go to the HD clinic usually three times a week. However, precautionary measures such as education, clinical management and specific arrangements in case the home PD patient needs hospitalization during an outbreak must still be taken. Yank and Dong [18] describe thoroughly their positive experience by applying these operational measures for PD patients and healthcare staff during the height of the COVID-19 pandemic.

Alfano and Mussini [19] present a different PD perspective during the COVID-19 pandemic, endorsing PD as the preferred RRT modality for ESRD patients. Among the advantages, they mention the minimized risk of viral transmission through interpersonal contacts, as well as the use of telemedicine to deliver renal care without exposure of the patient to the risks of contacts.

If the pathogenesis and natural history of AKI from COVID-19 patients are similar to those of sepsis resulting from other infectious causes, then the indication of PD using high-volume PD (HVPD) may well be one rational therapy option. Sepsis-associated AKI mortality rates have not changed throughout the years, and PD is comparable to that of extracorporeal dialysis in AKI [10–13]. Nonetheless, there are specific issues of concern regarding dialysis modalities for COVID-19-related AKI treatment.

First, as pneumonia often develops in COVID-19 infection, which, in some critical cases, turns into ARDS (partial pressure of oxygen/fraction of inspired oxygen <200), PD can be used early before patients develop ARDS. When ARDS occurs, PD should not be used as the first dialysis choice, but certainly as the last resort, if any technical or clinical scenario presents impeding the execution of CRRT, HD or HDF. It should also be used with caution, especially in acute lung injury. When a patient needs prone ventilation to help improve oxygenation, PD with a lower infusion volume (20–25 ml/kg) can be used without mechanical problem or hemodynamic disturbance, according to a case report [20]. A Brazilian study found that ventilated AKI patients with a 2-L PD dwell exchange presented a slightly increased intra-abdominal pressure on the first dwell. However, this did not interfere with the patients' ventilation and oxygenation. Moreover, after the first three HVPD sessions, the entire lung mechanic parameters improved as a result of the removal of excess fluid accumulated in the body [21].

Second, SARS-CoV-2 is a highly contagious airborne disease. Ideally the patients should be kept in an isolation room, should not be transported and should be minimally exposed to healthcare providers [22]. When applying this concept to dialysis for COVID-19 patients, automated PD (APD) works well because APD can be moved and installed anywhere, does not require a large space and is easy to set up. Moreover, the PD fluid exchanges occur automatically and the used PD bags need to be changed once daily; typically only the nurse needs to enter the room to connect and disconnect the patient from the PD cycler. Such minimum contact with the patient reduces not only the risk of contagion, but also the need for personal protective equipment (PPE) use, especially in times when resources are very limited. Moreover, in extreme situations where nephrology nurses are not available, intensive care unit (ICU) nursing staff can easily learn how to manage a cycler [HVPD or tidal PD (TPD)] or manual exchanges [continuous ambulatory peritoneal dialysis (CAPD)] and any troubleshooting can be managed by phone or virtual communication. It is much easier to learn how to manage PD, whether it's HVPD, TPD or CAPD, than to learn how to handle CCRT or HD equipment and techniques. Confirming our personal experience with PD in different settings, El Shamy *et al.* [23] reported that a major advantage of PD during this crisis has been the ability to train non-nursing staff in the PD procedure, which is not technically challenging.

As SARS-CoV-2 is mainly detected in respiratory tract secretiond, and some in feces and blood [24], there is so far no evidence of the virus spreading from PD effluent. The data from the previous SARS outbreak in 2013 show that SARS-CoV was not detected in PD effluent of infected cases [25, 26].

Lastly, resource allocation in healthcare, including dialysis, is an option that should be taken into consideration in scarce resource settings (clinics/hospitals) during the pandemic. PD is simple and efficient, there is no need for heparin, it provides continuous steady fluid removal, it requires less equipment and infrastructure when compared with extracorporeal dialysis and it offers lower work intensity, with a nurse being able to manage at least four PD cyclers simultaneously. PD catheter insertion can be made bedside by a nephrologist or other physician with local anesthesia. PD is also an easy method for nurses to learn, as it only involves connection of the flexible catheter and its transfer set to the disposable sets and PD fluid bags in the PD cycler, which performs the exchanges (or cycles) automatically. Such an efficient resource management method helps address the shortage of medical equipment and reduce exposure of the healthcare staff, which are critical issues amidst the pandemic.

Because of the above-mentioned benefits, PD should be considered as one of the options to treat COVID-19-related AKI, and APD is the preferred form to minimize the risk of exposure. Wherever APD is not available, CAPD could be used. Initially, using several (10–12) exchanges per day, and depending on the clinical evolution, it could be decreased after 3–4 days to four to five exchanges per day.

Another important option is the use of icodextrin, even though not much experience has been published on its use in AKI. However, it is important to understand that the use of icodextrin for a long dwell in AKI may be a good option, especially using a mix of icodextrin and glucose-based PD fluids for the long dwell (15 h), as reported early for seven anuric APD patients [27]. A solution containing both crystalloid (glucose 2.61%) and colloid (icodextrin 6.8%) osmotic agents enhanced fluid removal by 2-fold and sodium removal by 3-fold when compared with 7.5% icodextrin solution during a dwell of 15 h, indicating that such a combination solution could represent a new treatment option for anuric PD patients. The preparation and composition of the combined PD fluid as well as some of the results are described in the Supplementary data. Since much of the daily need for fluid and sodium removal can be achieved during a long dwell with combination fluid, this strategy also provides the advantage of reducing exposure of the peritoneal membrane to high-tonicity glucose-based dialysate during the remainder of a 24-h CAPD/APD treatment cycle.

To effectively and efficiently fight against COVID-19, as many methods of dialysis as possible should be considered. PD should be regarded as one of the options, where neither diffusive (HD) nor convective (HDF or HF) therapies are technically, logistically or realistically possible. In order to substantiate the possible indication of PD, it is important to look back to the 1960s when Scribner made an observation that patients maintained on intermittent PD did remarkably well clinically, even though PD was much less efficient than HD at removing the commonly considered uremic toxins of small molecular weight, such as urea [26]. The longer treatment time (24 h or longer) presumably permitted the slowly diffusing middle molecular weight solutes to be adequately removed. This ‘speculation’ gave birth to the idea by Henderson and Bluemle that convection would provide a superb tool to test the importance of the ‘middle molecule’ hypothesis and possibly might offer a new treatment modality for uremia. It is interesting to note that these observations from PD patients would be the basis for the development of the convection concept in dialysis. The identification of convective solute transport in conjunction with water removal was achieved in an experiment with PD patients using the peritoneal membrane by Henderson in 1966 [27]. In the first phase of the experiment, the amount of urea removed by a 1.5% dextrose exchange was measured in the effluent dialysate of PD patients treated with conventional solutions and techniques, then it was compared in the same patients when using 7.0% dextrose exchange. The measured urea clearance showed that 7% dextrose exchanges removed 38% more than 1.5% dextrose exchanges. The second and crucial phase of the experiment involved using the same patients, but placing urea in the hypertonic dialysate at values equal to or slightly higher than its concentration in the patient’s plasma just prior to the exchange. The urea present in the drained dialysate was measured as before and its clearance was calculated. Examination of the urea content of the diffusion-blocked hypertonic dialysate showed a significant net transport of urea into the dialysate from the blood, in spite of the lack of a driving gradient for diffusion. The 38% enhanced clearance noted with hypertonic dialysate in the first phase of the experiment was amply explained by the amount of urea retrieved from the diffusion-blocked second phase of the experiment. This nondiffusional transport was ascribed to ‘solvent drag’ or the frictional forces exerted on the urea molecule by the stream of water moving through the porous peritoneal membrane from blood to dialysate. Solvent drag as the relevant force for this nondiffusional transport had already been identified by physiologists [28]. Henderson’s experiment was, however, the first experiment of maintenance dialysis to identify this force, in operation, as an integral part of blood cleansing by dialysis [26, 29].

## PRACTICAL ASPECTS OF PRESCRIBING, DELIVERING AND MONITORING PD IN COVID-19

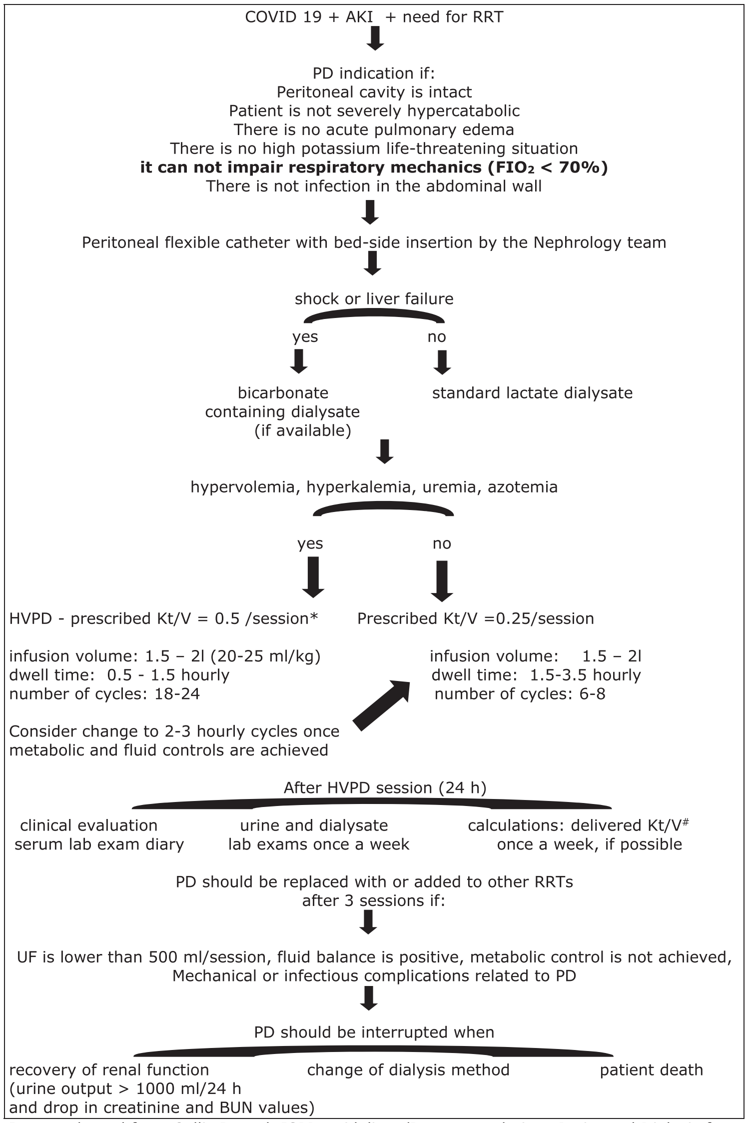
Please see the Supplementary data. We have prepared a flowchart of the practical aspects of prescribing, delivering and monitoring PD in AKI patients (Figure 1).

## PD IN THE TREATMENT OF COVID-19-RELATED AKI: RECENT EXPERIENCES TREATING COVID-19-RELATED AKI WITH PD

The first experiences were preliminarily communicated to the nephrology community on 23 April 2020 during an International Society for Peritoneal Dialysis (ISPD)/International Society of Nephrology (ISN) webminar ‘Use of PD for COVID-19-associated AKI: clinical experience and updated 2020 ISPD guidelines’ [30]. Hugh Cairns and Senior Nurse Elaine Bowes presented their clinical experience in the ICUs at Kings College Hospital, London, UK. The background to this experience is based on the high rate of AKI requiring dialysis associated with a potential shortage of continuous veno-venous haemofiltration (CVVHDF) machines. As a renal unit, they have a history of PD catheter insertion and PD use. PD catheter insertion at the ICU was done either by a senior nurse or by the consultant nephrologist; 27 of 32 attempts were successful. The reported patient outcomes were as follows: 7 recovered renal function, 3 held PD as they are passing urine, 3 died of COVID, 14 remained on PD and 5 failures (not successful catheter insertion), and those patients are still on HDF or intermittent HD. There were no complications (leaks, exit-site infections, peritonitis, catheter migration), relatively few PD cycler alarms and no patients required proning. All patients were treated with APD. Their main conclusions were that PD works and is safe, there were no leaks/wound breakdowns/peritonitis, it reduced the use of CVVHDF and, last but not the least, it reduced the workload for the whole PD team.

The second experience in the same webminar [30] was preliminarily presented by Dr Mihran Naljayan from the Louisiana State University School of Medicine (New Orleans, LA, USA). Staffing and PPE shortages were reasons for considering PD in their department. Peritoneal catheters were inserted by a surgeon or an interventional radiologist/nephrologist. They used APD, low dwell volumes and rapid exchanges for 24 h (ICU) or 12 h (ward). They have so far treated 18 patients with the following outcomes: 12 on AKI-PD, 2 discharged to an outpatient PD unit, 1 recovered renal function and 3 died (nondialysis related).

The third experience was preliminarily communicated to the Latin America nephrology community on 23 April 2020 during the web meeting ‘COVID 19-associated AKI protocol and Latin America experiences’ [31], by Dr Bazarra Durand from Clínica Ricardo Palma, Lima, Peru. So far three patients admitted to the ICU have been treated using HVPD (lower infusion volumes: 20 mL/kg; rapid exchanges: dwell time from 35 to 60 min, lasting 24 h), with the following outcomes: two




It was adapted from Cullis B et al. ISPD guidelines/Recommendations Peritoneal Dialysis for Acute Kidney Injury [13]
*prescribed Kt/V
K = volume of dialysis solution prescribed in 24 hours (mL) × 0.60 (considering the D/P relationship for dwell time between 30 and 60 min); t = 1 (day) and V = patient urea distribution volume (mL).
The number of exchanges was obtained by dividing the K value by 1.5 or 2 L (volume infused in the peritoneal cavity per exchange).
[#] all effluent is collected to calculated delivered Kt/V, cell counts and culture are collected to diagnose peritonitis every third day
[#] Delivered Kt/V
Kt/V = mean dialysate urea nitrogen (mg/dL) / mean serum urea nitrogen pre and post dialysis (mg/dL) × drained 24 h volume (mL) / patient urea distribution volume (mL).

**FIGURE 1:** Flowchart of the practical aspects of prescribing, delivering and monitoring PD in AKI patients.

are on AKI-PD and one died (nondialysis related). There were no mechanical or infectious complications related to PD.

Clinical experiences and studies leveraged on worldwide nephrology practice, especially in developing countries, support the use of PD in AKI situations; the outcomes are not different from the ones reported with other dialytic techniques such as CRRT, sustained low-efficiency dialysis and intermittent hemodialysis. A shortage of CRRT and HD machines and supplies, as well as of staff and PPEs, has brought PD to the forefront. Preliminary experience reported here provides evidence that PD can contribute to confront the kidney impact of this pandemic. The time has come for PD to be included as an option in the critical care of COVID-19 patients.

## SUPPLEMENTARY DATA

Supplementary data are available at ckj online.

## CONFLICT OF INTEREST STATEMENT

None declared.

## REFERENCES


1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323: 1239
2. Guan W-J, Ni Z-Y, Hu Y *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382: 1708–1720
3. Arentz M, Yim E, Klaff L *et al*. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA* 2020; 323: 1612
4. Shi Q, Zhao K, Yu J *et al*. Clinical characteristics of 101 non-surviving hospitalized patients with COVID-19: a single center, retrospective study. *medRxiv* 2020; doi: 10.1101/2020.03.04.20031039
5. Ronco C, Navalesi P, Vincent JL. Coronavirus epidemic: preparing for extracorporeal organ support in intensive care. *Lancet Respir Med* 2020; 8: 240–241
6. Naicker S, Yang C-W, Hwang S-J *et al*. The novel coronavirus 2019 epidemic and kidneys. *Kidney Int* 2020; 97: 824–828
7. Villa G, Katz N, Ronco C. Extracorporeal membrane oxygenation and the kidney. *Cardiorenal Med* 2015; 6: 50–60
8. Boen ST. Peritoneal dialysis: a clinical study of factors governing its effectiveness. *Kidney Int Suppl* 2008; 108: S5–S17
9. Gabriel DP, Nascimento GV, Caramori JT *et al*. High volume peritoneal dialysis for acute renal failure. *Perit Dial Int* 2007; 27: 277–282
10. Chionh CY, Soni SS, Finkelstein FO *et al*. Use of peritoneal dialysis in AKI: a systematic review. *Clin J Am Sov Nephrol* 2013; 8: 1649–1660
11. Cullis B, Abdelraheem M, Abrahams G *et al*. Peritoneal dialysis for acute kidney injury. *Perit Dial Int* 2014; 34: 494–517
12. Gabriel DP, Caramori JT, Martim LC *et al*. High volume peritoneal dialysis vs daily hemodialysis: a randomized, controlled trial in patients with acute kidney injury. *Kidney Int Suppl* 2008; 73: S87–S93
13. Ponce D, Berbel MN, Abrão JMG *et al*. A randomized clinical trial of high volume peritoneal dialysis versus extended daily hemodialysis for acute kidney injury patients. *Int Urol Nephrol* 2013; 45: 869–878
14. Vinsonneau C, Camus C, Combes A *et al*. Continuous venovenous hemodiafiltration versus intermittent hemodialysis for acute renal failure in patients with multiple organ dysfunction syndrome: a multicenter randomized trial. *Lancet* 2006; 368: 379–385
15. Pedersen KR, Hjortdal VE, Christensen S *et al*. Clinical outcome in children with acute renal failure treated with peritoneal dialysis after surgery for congenital heart disease. *Kidney Int Suppl* 2008; 73: S81–S86
16. Al-Hwiesh A, Abdul-Rahman IS, Finkelstein FO *et al*. Acute kidney injury in critically ill patients: a prospective randomized study of tidal peritoneal dialysis vs. continuous renal replacement therapy. *Ther Apher Dial* 2018; 22: 371–379
17. Parapiboon W, Jamratpan T. Intensive versus minimal standard dosage for peritoneal dialysis in acute kidney injury: a randomized pilot study. *Perit Dial Int* 2017; 37: 523–528
18. Yank Z, Dong J. Operational considerations for peritoneal dialysis management during the COVID-19 pandemic. *Clin Kidney J* 2020; 13: 322–327
19. Alfano G, Fontana F, Ferrari A *et al*. Peritoneal dialysis in the time of coronavirus disease 2019. *Clin Kidney J* 2020; 13: 265–268
20. Klisnick A, Souweine B, Filaire M *et al*. Peritoneal dialysis in a patient receiving mechanical ventilation in prone position. *Perit Dial Int* 1998; 18: 536–538
21. Almeida CP, Ponce D, de Marchi AC *et al*. Effect of peritoneal dialysis on respiratory mechanics in acute kidney injury patients. *Perit Dial Int* 2014; 34: 544–549
22. Wang W, Xu Y, Gao R *et al*. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* 2020; 323: 1843–1844
23. El Shamy O, Sharma S, Winston J *et al*. Peritoneal dialysis during the coronavirus 2019 (COVID-19) pandemic: acute inpatient and maintenance outpatient experiences. Kidney Med 2020; 10.1016/j.xkme.2020.04.001
24. Kwan B-H, Leung C-B, Szeto C-C *et al*. Severe acute respiratory syndrome in dialysis patients. *J Am Soc Nephrol* 2004; 15: 1883–1888
25. Freida P, Issad B, Dratwa Max Lobbedez T *et al*. Glucose-sparing advantage and improved ultrafiltration and sodium removal efficiency in PD using a combined crystalloid (glucose) and colloid (icodextrin) PD fluid (bimodal ultrafiltration): a prospective multicenter study in APD. *Perit Dial Int* 2009; 29: 433–442
26. Scribner BH. In discussion. *Trans Am Soc Artif Intern Organs* 1965; 11: 29
27. Henderson LW. Peritoneal ultrafiltration dialysis: enhanced urea transfer using hypertonic peritoneal dialysis fluid. *J Clin Invest* 1966; 45: 950–955
28. Ussing HH, Andersen B. The relation between solvent drag and active transport of ions. *Proceedings of the Third International Congress of Biochemistry*, Brussels 1955, 434
29. Henderson LW. Discovering the presence of convective transport: an artiphysiological moment in time. *Artif Organs* 2015; 39: 985–988
30. Cairns H, Bowes E, Naljayan M. *Use of PD for COVID-19-Associated AKI: Clinical Experience and Updated 2020 ISPD Guidelines*. https://academy.theisn.org/isn/2020/covid-/293275/edwina.brown.brett.cullis.hugh.cairns.elaine.bowes.mihran.naljayan.simon.html? f=menu%3D13*browseby%3D8*sortby%3D2*label%3D19791 (23 April 2020, date last accessed)
31. Duran BJ. *COVID 19-Associated AKI Protocol and Latin America Experiences*. https://zoom.us/u/and5oTx1 (23 April 2020, date last accessed)