Remote digital urinalysis with smartphone technology as part of remote management of glomerular disease during the SARS-CoV-2 virus pandemic: Single centre experience in 25 patients

Madelena Stauss 1,2, Ajay Dhaygude 2, Arvind Ponnusamy 2, Martin Myers 3, Alexander Woywodt 2

1 Department of Nephrology, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK
2 Division of Medical Education, School of Medical Sciences, University of Manchester
3 Department of Clinical Biochemistry, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK

Correspondence to: Alexander Woywodt; E-mail: Alex_Woywodt@lthtr.nhs.uk
ABSTRACT

Background. The COVID-19 pandemic has necessitated the provision of healthcare through remote and increasingly digitalised means. The management of glomerular pathology, for which urinalysis is crucial, has been notably affected. Here, we describe our single-centre experience of using remote digital urinalysis in the management of patients with glomerular disease during the COVID-19 pandemic.

Method. All patients with native kidney glomerular disease who consented to participate in digital smartphone urinalysis monitoring between March, 2020 and July, 2021 were included. Electronic health records were contemporaneously reviewed for outcome data. Patient feedback was obtained through the testing portal.

Results. Twenty-five patient utilised the digital urinalysis application. A total of 105 digital urinalysis tests were performed for a wide variety of indications. Four patients experienced a relapse (detected remotely), and two patients underwent three successful pregnancies. The majority of patients were managed virtually (60%) or virtually and face to face (F2F) combined (32%). The average number of clinic reviews and urine tests performed during the pandemic either virtually and/or F2F was comparable to levels pre-pandemic and the ratio of reviews to urinalysis (R:U) was stable (pre-pandemic 1:0.9 vs during pandemic 1:0.8). Patients seen exclusively F2F with supplementary home monitoring had the highest R:U ratio at 1:2.1. 95% of users provided feedback, all positive.

Conclusion. Remote urinalysis proved a safe and convenient tool to facilitate decision making where traditional urinalysis was difficult, impractical, or impossible. Our approach allowed us to continue care in this vulnerable group of patients despite lack of access to traditional urinalysis.
Keywords: glomerular disease, smartphone technology, telemedicine, urinalysis

INTRODUCTION

The COVID-19 pandemic has caused widespread disruption in healthcare. One key issue is the lack of access to face-to-face (F2F) interaction due to infection control policies, workload pressures, and patient preference. These factors are unlikely to disappear in the near future. One area that has become particularly difficult is the care of patients with glomerular disease (1). In our institution much of their care is now carried out through telephone or video appointments. However, while blood pressure and weight can be obtained during such consultations, urinalysis is now largely impossible to obtain in primary care and difficult to carry out in other ways. Dipstick kits have on occasion been provided to patients, however results may be difficult to interpret by them and this can cause anxiety for patients. Bringing patients back to outpatient facilities solely for the purpose of a urine dipstick is equally impractical. We were keen to address this gap in service provision for this vulnerable cohort of patients. Healthy.io™ digital urinalysis (Dip.io™) has been used previously for the diagnosis of urinary tract infections (2) and for population screening (3) (4). Here, we report a novel use of the technology namely for remote monitoring of patients with glomerular disease. We describe single centre experience with an emphasis on clinical utility and integration into new patterns of virtual outpatient care.
MATERIALS AND METHODS

Study setting

The study was carried out in a regional centre with a catchment area of 1.7 million people in Lancashire and South Cumbria. The centre serves a heterogeneous area with urban conurbations and thinly populated rural countryside in the North West of the United Kingdom. Care is provided in a hub at Preston, with satellite clinics in a further 10 locations across the area. All outpatient renal clinics within our centre were automatically converted to virtual (telephone or video) in March 2020, with F2F reviews carried out only if required.

Patients, inclusion and exclusion criteria and consent

Twenty-five adult patients with a variety of glomerular disease (Figure 1) who agreed to participate in smartphone urinalysis technology from May, 2020 to July, 2021 were included in the study. Renal transplant recipients were not included. Written information was provided and consent obtained initially in writing from May, 2020 to March, 2021. At this point our institution felt that verbal consent was sufficient since participation was part of usual clinical care.

Remote urinalysis with Healthy.io technology

Frequency of remote urinalysis was agreed on an individual basis and patients could either be prompted to perform additional urinalysis (via smartphone notification) by their clinician or do so of their own volition. The kit and analytic and reporting pathway are shown in Figures 2 and 3. In brief, the clinician takes verbal consent, uploads patient data onto the web portal, then triggers kits to be sent out. On receipt, patients test their urine and take a photo with their smartphone using the company app against a background contained in the kit. The clinician is prompted via email to access the result online.
Validation studies performed by Dip.io™ had demonstrated repeatability, reproducibility, linearity, limit of detection, method comparison, usability, interference, stability, multiple phones and biocompatibility; with correlation to physical urinalysis confirmed by our internal laboratory.

Data was obtained from patients’ hospital records. Patient feedback was obtained through the company app which is open to patients on completion of each urinalysis test. In order to evaluate for provision of comparable clinical care, data on the number of clinic attendances and physical in-clinic urine tests performed was also obtained for the 12 months prior to virtual clinic delivery (March 2019 - March 2020), when all reviews were performed F2F.

Ethical approval was not required as our institution viewed this work as provision of clinical care and associated service evaluation.

RESULTS

Demographics and clinical information
Twenty-five patients (14 female, 11 male) used the smartphone urinalysis application between March, 2020 and July, 2021. Their average age was 49.2 years (range 20-80). Women using the application were slightly younger than men, with an average age of 46.9 (median 45.5) years vs 52.1 (median 59) years respectively. The patients’ median estimated glomerular filtration rate (eGFR), calculated according to the CKD-EPI Creatinine (2009) equation, was 72.0 ml/min/1.73m² (range 18-138 ml/min/1.73m²) at the point of starting digital smartphone urinalysis.
Uptake of digital urinalysis and indications for use

A total of 105 digital urine tests were performed, averaging at 4.2 per patient (median number 3 per patient, range 1-20). The most common reason for urinalysis was monitoring of stable disease (9/25 patients, 36%). Other reasons included monitoring during changes in the immunosuppressive regime (4/25 patients, 16%), detection and early treatment of relapse (4/25 patients, 16%), suspicion of impending relapse (3/25 patients, 12%), monitoring during pregnancy (2/25 patients, 8%), new referral to renal services (1/25 patients, 4%) and facilitating discharge from routine nephrology follow-up with regular self-monitoring thereafter (1/25 patients, 4%).

Clinical outcomes

No deaths were observed and no patient required renal replacement therapy during the study period. A summary of clinical data is shown in Table 1. The mean eGFR (CKD-EPI) was 61.5 ml/min/1.73m² (range 24-129 ml/min/1.73m²) at the end of the data collection period. Twelve out of 25 patients (48%) experienced a fall in eGFR (average 10.9 ml/min/1.73m²), 11/25 patients (44%) experienced an improvement in eGFR (average 4.7 ml/min/1.73m²), and two patients either did not have their results repeated or experienced no change in eGFR respectively.

Interventions triggered by digital urinalysis results

Results of testing prompted therapeutic interventions in eight patients (asterixed in Table 1). Four patients (patients 1, 3, 10 and 11) experienced a relapse which was detected remotely: two patients experienced two relapses each of minimal change disease (MCD), one patient had a flare of lupus nephritis and one patient experienced a relapse of FSGS during steroid
taper. Besides the final patient, all relapses were managed with up-titration of treatment almost exclusively virtually; with 16 virtual and 1 F2F, 5 virtual and 1 F2F and 5 virtual and 1 F2F reviews respectively. The patient with relapsed FSGS was switched to alternating virtual and F2F reviews, with 11 and 6 reviews respectively. Three patients remained clinically asymptomatic but were able to perform increased frequency of urinalysis for monitoring of possible disease relapse: two patients (one with MCD, patient 18, and one with membranous nephropathy, patient 4 had increasing proteinuria, the final patient had a newly equivocal ANCA however urinalysis remained negative. The patient with MCD was only seen in F2F clinic but supplemented frequent in-person reviews with home urinalysis; the remaining two patients were reviewed exclusively virtually. The final patient (patient 16) was a new referral to services in whom the remote detection of substantial proteinuria (subsequently confirmed via urine protein:creatinine ratio) prompted a decision to biopsy. Furthermore, two patients (patients 9 and 13), one with lupus nephritis and one with IgA vasculitis, had three successful pregnancies (2 singleton, 1 twin) and were managed exclusively in virtual renal clinics (albeit seen F2F in obstetric clinic).

**Comparison to service delivery pre-pandemic**

In the 12 months pre-pandemic, 21/25 patients were known to services and all were seen exclusively F2F. Pre-pandemic a total of 84 clinic reviews were performed (average 4/patient, range 1-10) with 78 physical in-clinic urine tests performed (average 3.7/patient, range 1-10). The review to urinalysis (R:U) ratio was therefore 1:0.9. During the pandemic study period (16.5 months) 15/25 patients (60%) were seen exclusively in virtual clinics, 2/25 patients (8%) exclusively in F2F clinics and the remaining 8/25 patients (32%) were seen in a combination of virtual and F2F clinics. The number of reviews (either virtual, F2F or combined), urinalysis tests performed (either remote smartphone or physical) and the
subsequent review to urinalysis (R:U) ratio during this time are shown in Table 2. For those seen exclusively F2F, in addition to physical in-clinic urinalysis these patients also performed 9 supplementary remote urine tests at home, giving a combined total of 17 urinalyses (average 8.5/patient) and an overall F2F R:U ratio of 1:2.1. For those seen in a combination of virtual and F2F clinics, there was an average number of 9.5 reviews/patient and 7.6 urine tests/patient. The R:U ratio was 1:0.7 virtually and 1:1 F2F, resulting in overall 1:0.8 when combined.

**Clinical vignette**

An example of our approach for one individual patient is depicted in Figure 4. This particular patient lives 35km (40 minutes) away from the nearest satellite renal clinic, and 115km (95 minutes) from the renal centre. The patient experienced two relapses of MCD, and had their reviews remained F2F in order to guarantee a urine dipstick this would have resulted in a total travel distance of at best 1,190km (approximately 23 hours travelling) to the satellite clinic and at worst 3,910km (approximately 54 hours travelling) to the hub.

**Patient feedback**

95% of smartphone urinalysis application users provided feedback on the service, with 100% reporting the app ‘easy’ or ‘very easy’ to use. No problems were reported by patients or relatives in using the technique. Only one patient, a man in his eighties with significant comorbidity, lost the ability to carry out digital urinalysis temporarily during an inter-current illness (peripheral vascular disease with below knee amputation). 100% of users would recommend the application to family or friends and 100% of patients preferred home urinalysis testing to physical urine testing in-clinic.
DISCUSSION

The care of patients with glomerular disease has been a particular challenge during the COVID-19 pandemic (1). Firstly, these patients are more vulnerable to COVID-19 particularly during periods of active disease and immunosuppression. In addition, data from the International Registry of COVID infection in glomerulonephritis (IRoc-GN) confirm that such patients have higher mortality and more frequent episodes of acute kidney injury (5). The timing of immunosuppressive treatment in patients with recent COVID-19 infection is equally difficult. Furthermore, immunosuppressive treatment affects the efficacy of COVID-19 vaccines (6) and assessing immunity is not straightforward (7). Finally, patients with glomerular disease themselves have become much more reluctant to attend clinics or undergo treatment that will render them vulnerable to COVID-19 or compromise vaccination. In the difficult decision whether or not to initiate or change immunosuppressive therapy, urinalysis is a salient factor, yet one that proved increasingly difficult or impossible to obtain at the start of the pandemic.

Smartphones have been used to monitor a variety of medical parameters (8). These include heart rate and rhythm, sleep, skin and eye health (9) amongst others (10). Remote urinalysis as a concept is not new, although previous approaches were cumbersome (11), unreliable (12) or used for niche indications such as drug titration in renal stone disease (13). In this study we used more straightforward technology which is already well established for the early detection of urinary tract infection during pregnancy (14) and in renal transplant recipients (2). Others have also used this approach for screening in primary care (4) (3). Here, we describe a novel use of this technology, namely the monitoring of disease activity and response to treatment in glomerular disease in the context of the SARS-19-CoV virus pandemic.
We describe the use of remote urinalysis beyond its established use in urinary tract infection and for population screening and describe a novel application in the care of patients with glomerular disease. Our experience with this new approach has been very positive. All patients were able to learn the technology and use it throughout the study period, the only exception being an octogenarian who struggled with the technology during a period of intercurrent illness. There was a wide age range within our cohort, with a mean age just under 50 years. Women were on average younger than men, which may reflect the different underlying aetiologies and reasons for monitoring such as lupus nephritis and pregnancy. Patients were satisfied with the application and found it easy to use, and amongst those who responded all preferred using the home testing method. Although there was an overall fall in average eGFR of just over 10 ml/min/1.73m$^2$ during the period of data collection, meaningful conclusions are difficult to draw from this due to the large variability in patients, underlying disease and treatment although some mild decline in renal function is not surprising in this cohort.

Within our cohort, almost all patients were reviewed exclusively virtually (60%) or in combination with occasional F2F reviews (32%). Our approach allowed us to make clinical decisions involving urinalysis without relying on seeing the patient F2F or asking primary care for help. Knowing the urinalysis result during virtual consultations has provided us with invaluable help in decision making in a variety of different clinical situations, but especially in terms of initiating and changing immunosuppression. Of particular note are the cases of disease relapse (Figure 4), which were detected and treated almost exclusively remotely. We also feel that our approach has helped patients engage with their health issues and may therefore be advantageous for patient empowerment. Another advantage of our approach is a reduction in inter-observer variability that is often reported with physical urinalysis (15) (16). Finally, in our experience patients develop more of an interest in their health issues after they have tested their own urine prior to the appointment.
Over the course of the pandemic, through virtual means, we were able to continue to provide comparable renal care to our patients in the sense that the average number of both reviews and urine tests performed remained similar to pre-pandemic levels. The ratio of number of reviews to urine tests performed remained relatively constant. The exception to this is for patients who were reviewed exclusively F2F during the pandemic, who had a much higher average number of urine tests performed (R:U ratio 1:2.1 compared to 1:0.7-0.9 for others). This is due to urinalysis being done both in-clinic and supplemented by further home monitoring. Furthermore, those who were seen in a combined virtual and F2F capacity had a higher average number of reviews and urine tests performed, being almost double that of both pre-pandemic levels and for those seen exclusively either virtually or F2F. This may be because patients had a need for more frequent follow-up and monitoring due to their clinical situation, and therefore benefited from the different advantages that using both remote and F2F reviews contemporaneously may provide. It is worth noting there was a lag of a few months between when virtual reviews began and smartphone technology became available, therefore as the service matures the R:U is likely to increase further.

We view the approach described here as an ideal adjunct to video consultations with implications beyond the pandemic. With an increasing emphasis on providing patient-centred, accessible, digitalised care it is tempting to think that at some stage in the future clinicians may use a portfolio of remote technologies, such as remote monitoring of peripheral oedema (17), blood pressure (18) or even calcium and pH values (19). We also highlight the benefit of remote urinalysis in monitoring two patients during three successful pregnancies, including one twin pregnancy in a woman with lupus nephritis. The technology allowed us to monitor the patients extremely closely, whilst not contributing to the burden of multiple hospital attendances. The environmental aspect of our approach also warrants brief consideration as illustrated in our case vignette. A substantial amount of time, travel expense
and fuel was saved by remote management. We speculate that those considerations will become progressively more relevant and should be taken into account in service provision i.e. when virtual models of care are considered.

Our approach has limitations and pitfalls. Firstly, connection to the internet is required and may not be easily available everywhere. Secondly, our approach requires access to a smartphone which is also not universally available. Thirdly, some patients who are otherwise able to use the technology may struggle for example during inter-current illness. We remain mindful of the “digital divide” (20) and acknowledge that in this study we lacked specific resources to bridge it i.e. to support less IT literate patients or those with a language barrier.

The issue of cost also deserves consideration. At approximately $11.00 USD each kit contains four digital urinalysis tests which is substantially higher than the cost of a physical urine dipstick test at approximately $0.30 USD. Cost-effectiveness is beyond the focus of this study but we estimated the cost of a traditional urine dipstick when bringing patients in for this purpose (i.e. including urine container, staff time and protective equipment) at approximately $5.17 USD which is more expensive (21). When compared to handing patients traditional urine dipsticks the main advantage of our approach is to give a semi-quantitative and unequivocal result that takes many patient factors, such as colour blindness, out of the equation. Finally, we emphasise that for any more widespread use of our approach an interface to the electronic health record is desirable and needs to be including in costing.

We acknowledge the fact that our patients are highly selected insomuch as they have chosen to use the smartphone technology and are more likely to report favourably on it (22). We did not record whether and for what reason patients declined to use the smartphone application. Finally, we need to acknowledge the remote possibility that patients could
manipulate the test result as described in other settings (23) (24). We have no evidence to suggest that patients manipulated their tests in our study but remain mindful of this scenario.

CONCLUSION

We report positive single-centre experience with remote urinalysis to facilitate the care of patients with glomerular disease during the pandemic. In our institution this approach is now a routine part of the care of such patients and our experience is a good example of how technology can be used to overcome the constraints imposed by the ongoing COVID-19 pandemic (25). Other institutions, in particular those with a large geographical catchment area, should consider this approach. We speculate that rather than being part of a temporary response this approach could become standard of care for patients with glomerular disease due to its reliability combined with low cost, its advantages in terms of patient empowerment, and the ease of use and convenience to patients.

ACKNOWLEDGEMENTS

We are grateful to colleagues in our department for using the technology and to our patients for their cooperation. We thank the manufacturer of the kit, Healhy.io (Tel Aviv, Israel) for providing patient satisfaction data obtained through their app. We are grateful to current and previous staff of Healthy.io for their help in setting this up during a time of high clinical workload overall. In particular we would like to thank Katherine Ward, Shabbir Lorgat, Michelle Burdett, Chuk Anyaegbuna, Thariea Whisker and Samantha Scully.
CONFLICT OF INTEREST STATEMENT

None declared. The manufacturer of the kit Healthy.io had no role in analysis of data or writing of this manuscript. The results presented in this paper have not been published previously in whole or part.

REFERENCES

1. Kronbichler A, Gauckler P, Windpessl M, et al.; COVID-19: implications for immunosuppression in kidney disease and transplantation. *Nature Reviews Nephrology* 2020; 16(7):365-367

2. Middleton RJ, Bailey A, Griffiths L, et al. Remote urine dipstick analysis for faster treatment of urinary tract infections using smartphone technology. https://lp.healthy.io/wp-content/uploads/2020/05/Salford_UTI-in-post-transplant-patients-1.pdf Last accessed: July 30 2021

3. Leddy J, Green JA, Yule C, Molecavage J, Coresh J, Chang AR; Improving proteinuria screening with mailed smartphone urinalysis testing in previously unscreened patients with hypertension: a randomized controlled trial. *BMC Nephrol* 2019; 20(1):132

4. Shore J, Green M, Hardy A, Livesey D; The compliance and cost-effectiveness of smartphone urinalysis albumin screening for people with diabetes in England. *Expert Review of Pharmacoeconomics & Outcomes Research* 2020; 20(4):387-395
5. Waldman M, Soler MJ, García-Carro C, et al.; Results from the IRoc-GN international registry of patients with COVID-19 and glomerular disease suggest close monitoring. *Kidney Int* 2021; 99(1):227-237

6. Carr EJ, Kronbichler A, Graham-Brown M, et al.; Systematic Review of Early Immune Response to SARS-CoV-2 Vaccination Among Patients with Chronic Kidney Disease. *Kidney Int Rep* 2021

7. Phipps WS, SoRelle JA, Li QZ, et al.; SARS-CoV-2 Antibody Responses Do Not Predict COVID-19 Disease Severity. *Am J Clin Pathol* 2020; 154(4):459-465

8. Perkel JM; Pocket laboratories. *Nature* 2017; 545(7652):119-121

9. Majumder S, Deen MJ; Smartphone Sensors for Health Monitoring and Diagnosis. *Sensors (Basel, Switzerland)* 2019; 19(9):2164

10. Ong DSY, Poljak M; Smartphones as mobile microbiological laboratories. *Clin Microbiol Infect* 2020; 26(4):421-424

11. Coskun AF, Nagi R, Sadeghi K, Phillips S, Ozcan A; Albumin testing in urine using a smart-phone. *Lab Chip* 2013; 13(21):4231-8

12. Adams JD, Capitan-Jimenez C, Burchfield JM, Jansen LT, Kavouras SA; Smartphone-Based Analysis of Urine Reagent Strips Is Inaccurate for Assessing Underhydration. *Telemed J E Health* 2020; 26(5):683-686

13. Prosiannikov MY, Shaderkin IA, Konstantinova OV, Anokhin NV, Voytko DA, Nikushina AA; [Remote monitoring of urinalysis parameters during treatment of patients with uric acid stones by citrate-containing compounds]. *Urologiya* 2019(3):60-65
14. Burke AE, Thaler KM, Geva M, Adiri Y; Feasibility and acceptability of home use of a smartphone-based urine testing application among women in prenatal care. *Am J Obstet Gynecol* 2019; 221(5):527-528

15. Bell SC, Halligan AW, Martin A, et al.; The role of observer error in antenatal dipstick proteinuria analysis. *Br J Obstet Gynaecol* 1999; 106(11):1177-80

16. Waugh JJ, Bell SC, Kilby MD, et al.; Optimal bedside urinalysis for the detection of proteinuria in hypertensive pregnancy: a study of diagnostic accuracy. *Br J Obstet Gynaecol* 2005; 112(4):412-7

17. Fallahzadeh R, Pedram M, Ghasemzadeh H; SmartSock: a wearable platform for context-aware assessment of ankle edema. *Conf Proc IEEE Eng Med Biol Soc* 2016; 2016:6302-6306

18. Sana F, Isselbacher EM, Singh JP, Heist EK, Pathik B, Armoundas AA; Wearable Devices for Ambulatory Cardiac Monitoring: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020; 75(13):1582-1592

19. Nyein HYY, Gao W, Shahpar Z, et al.; A Wearable Electrochemical Platform for Noninvasive Simultaneous Monitoring of Ca2+ and pH. *ACS Nano* 2016; 10(7):7216-7224

20. Chesser A, Burke A, Reyes J, Rohrberg T; Navigating the digital divide: A systematic review of eHealth literacy in underserved populations in the United States. *Inform Health Soc Care* 2016; 41(1):1-19

21. (NICE) NCGC. Preoperative tests. Appendix M: Economic considerations (draft for consultation). https://www.nice.org.uk/guidance/ng45/documents/guideline-appendices-13

Last accessed: Nov 8 2021
22. Rygh E, Arild E, Johnsen E, Rumpsfeld M; Choosing to live with home dialysis-patients' experiences and potential for telemedicine support: a qualitative study. *BMC Nephrology* 2012; 13(1):13

23. Kuljis J, Money AG, Perry M, Barnett J, Young T; Technology-assisted self-testing and management of oral anticoagulation therapy: a qualitative patient-focused study. *Scand J Caring Sci* 2017; 31(3):603-617

24. Fries H, Norlén BJ, Danielson BG; Self-inflicted haematuria and the syndrome of hospital addiction. *Scand J Urol Nephrol* 1977; 11(3):309-13

25. Stauss M, Floyd L, Becker S, Ponnusamy A, Woywodt A; Opportunities in the cloud or pie in the sky? Current status and future perspectives of telemedicine in nephrology. *Clin Kidney J* 2021; 14(2):492-506
Figures

Figure 1: Underlying kidney diseases in our cohort of patients (n=25)
Figure 2: Digital smartphone urinalysis testing kit comprising a collection beaker, single urine dipstick and colour chart. The Dip.io urinalysis dipstick measures 10 different parameters (range of values in brackets) – leukocytes (negative or 15/70/125/500 leu/µL), nitrates (negative or positive), glucose (negative or 100/250/500/1000 mg/dL), ketones (negative or 5/15/40/80 mg/dL), protein (negative or 15/30/100/300 mg/dL), blood (negative or 10/25/80/200 ery/µL), pH (5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5 or 9.0), urobilinogen (negative or 1/2/4/8 mg/dL), bilirubin (negative or 1/2/4 mg/dL), and specific gravity (1.000, 1.005, 1.010, 1.015, 1.020, 1.025 or 1.030). The dipstick result is analysed and processed via the smartphone camera using the company app (versions for apple™ and android™ are available). The results are then uploaded onto a secure portal, and the overseeing clinician notified of the new result. Currently one pack contains four tests, which can be re-ordered prior to the last test being used. Illustration courtesy of Health.io™ (Dip.io™ Tel Aviv, Israel) reproduced with permission.
Figure 3: Clinical pathway of digital urinalysis from test delivery to online result. Pictures courtesy of Health.io™ (Dip.io™ Tel Aviv, Israel) reproduced with permission. SMS denotes short message service (text message).
Figure 4: Timeline of a patient with relapsing minimal change disease (MCD) with proteinuria (as determined by smartphone technology and confirmed by formal urine protein creatinine ratio [uPCR]), appointments and key interventions. Changes in the steroid dose are not shown. The patient experienced two relapses of MCD during the study period with increased proteinuria detected via digital smartphone urinalysis and subsequently confirmed by uPCR. During the first relapse the immunosuppression was up-titrated before the onset of symptoms and the patient achieved clinical remission and normalisation of proteinuria. This was followed by a second relapse with clinical symptoms confirmed on immediate testing via smartphone technology. Remission was eventually achieved following treatment with rituximab. Note that the patient was reviewed almost exclusively virtually (16 reviews) during the pandemic.
Table 1: Individual patient circumstances and outcomes. Information is shown for underlying diagnosis, change in eGFR, urinalysis result, treatment and clinical outcome. Change in eGFR was calculated from change in numerical value between the last available result before digital urinalysis testing began (all between January 2020 and the date of their first digital test) and the last result prior to the end of the study period in July 2021; blood samples were taken via differing pathways depending on patient location and mobility, such as attending GP surgeries, phlebotomy clinics or home visits from home therapy and redeployed renal specialist nurses. Patients with an accompanying asterisk are further elaborated on in the body of the text regarding specific interventions that were triggered following a digital urinalysis result.

FSGS denotes focal segmental glomerulosclerosis, MCD minimal change disease, MN membranous nephropathy, ANCA antineutrophil cytoplasmic antibody associated vasculitis, IgAN IgA nephropathy, SLE systemic lupus erythematosus with renal involvement, CKD chronic kidney disease with haematuria or proteinuria (no biopsy), MCGN mesangiocapillary glomerulonephritis, C1qN C1q nephropathy, F2F face-to-face, RTX rituximab, AZA azathioprine, ACEi angiotensin converting enzyme inhibitor

| Patient | Diagnosis | Change in eGFR (ml/min/1.73 m²) | Overall remote urinalysis result | Treatment | Clinical course |
|---------|-----------|----------------------------------|----------------------------------|-----------|----------------|
| 1*      | FSGS      | -12                              | Ongoing proteinuria              | Steroids: initially weaned due to covid-19 infection Subsequent up-titration of steroids | Monitoring during steroid reduction Relapse subsequently detected and converted to alternate F2F/virtual review |
|   | Condition | Stage | Acute Symptoms | Steroids | Management Notes |
|---|-----------|-------|----------------|----------|------------------|
| 2 | MCD       | Unknown | Nil acute      |Steroids: being weaned| Continued successful steroid wean without relapse |
| 3*| MCD       | -13    | Increased proteinuria|Steroids: up-titrated during each relapse, subsequently tapered|x2 relapses Treated with steroids almost exclusively virtually |
| 4*| MN        | +3     | Increased proteinuria|No change|Increased frequency of monitoring for suspected impending relapse, exclusively virtual review |
| 5 | ANCA      | +6     | Nil acute      |RTX held due to pandemic, started AZA in lieu|Monitoring of disease activity, stable |
| 6*| ANCA      | -7     | Nil acute      |No change|Newly equivocal ANCA (previously negative), no other features of active disease, increased monitoring with exclusively virtual review |
| 7 | ANCA      | -7     | Nil acute      |Started RTX|Monitoring of disease activity, stable |
| 8 | IgAV      | -10    | Nil acute      |No change|Monitoring of disease activity, stable |
| 9 | SLE       | -6     | Nil acute      |No change|Increased monitoring during x2 successful pregnancies (1 singleton, 1 twin) |
| 10*| SLE      | +2     | Increased haematuria|Steroids: initially being weaned Mycophenolate mofetil and|Monitoring during steroid reduction Relapse |
|   |   |   | steroids up-titrated during flare | detected, confirmed serologically | Treated almost exclusively virtually |
|---|---|---|-------------------------------|-----------------------------------|-------------------------------------|
| 11* | MCD | + 3 | Increased proteinuria | Steroids: up-titrated during each relapse, subsequently tapered | x2 relapses Treated with steroids almost exclusively virtually |
| 12 | ANCA | - 2 | Nil acute | No change | Monitoring of disease activity, stable |
| 13 | IgAV | 0 | Increased proteinuria | No change | Increased monitoring during x1 successful pregnancy (singleton) |
| 14 | ANCA | + 2 | Nil acute | No change | Monitoring of disease activity, stable |
| 15 | MN | - 31 | Ongoing proteinuria | Ongoing heavy nephrosis despite up-titrating of immunosuppression | Progressive clinical deterioration: Required inpatient admission followed by frequent F2F review |
| 16* | CKD | - 31 | Ongoing proteinuria | ACEi up-titrated | New referral Ongoing proteinuria therefore ACEi up-titrated and decision made to biopsy |
| 17 | ANCA | + 1 | Nil acute | AZA stopped | Monitoring of disease activity, stable |
| 18* | MCD | + 3 | Increased proteinuria | No change | New diagnosis of MCD Increased frequency of monitoring for suspected impending |
|   | Disease | Change | Status | Action                                                                 | Comments                                                                 |
|---|---------|--------|--------|------------------------------------------------------------------------|--------------------------------------------------------------------------|
| 19| MCD     | + 12   | Nil acute | Discharged from routine nephrology follow-up | To re-contact department if recurrence of haematoproteinuria |
| 20| MCGN    | + 1    | Nil acute | No change | Monitoring of disease activity, stable                                   |
| 21| C1qN    | - 4    | Nil acute | Ciclosporin weaned | Monitoring of disease activity, stable                                   |
| 22| MN      | + 7    | Nil acute | No change | Monitoring of disease activity, stable                                   |
| 23| ANCA    | + 12   | Nil acute | Continued RTX | Monitoring of disease activity, stable                                   |
| 24| CKD     | - 1    | Nil acute | No change | Monitoring of disease activity, stable                                   |
| 25| SLE     | - 7    | Nil acute | No change | Monitoring of disease activity, stable                                   |
Table 2: Comparison of the number of clinic reviews and urine tests performed pre-pandemic (exclusively F2F) and during the pandemic (combination of virtual and/or F2F).

|                              | Pre-Pandemic |          | During Pandemic |          |
|------------------------------|--------------|----------|----------------|----------|
|                              |              |          |                |          |
| **Timeframe**                | 12 months    | 16.5 months |                |          |
| **Type of clinic follow up** |              | **Exclusively** |          | **Exclusively** |          |
|                              |              | **F2F**  |          | **F2F**  |          |
|                              |              | **Virtual** |          | **Virtual** |          |
| **No. patients**             | 21/21 (100%) | 15/25 (60%) | 2/25 (8%)   | 8/25 (32%) |
| **No. clinic r/v**           |              | **Total** |          | **Total** |          |
|                              |              | 84       | 70          | 8         | 55       |
|                              |              | 4        | 4.7         | 4         | 6.9      |
|                              |              | 1 – 10   | 2 – 8       | 2 – 6     | 3 – 16   |
| **No. urinalysis**           |              | **Total** |          | **Total** |          |
|                              |              | 78       | 56          | 8         | 40       |
|                              |              | 3.7      | 3.7         | 4         | 5        |
|                              |              | 1 – 10   | 1 – 20      | 2 – 6     | 1 – 15   |
|                              |              |          | With additional remote added: |          |
|                              |              |          | 1 : 2.1     |          |
| **Review:urinalysis (R:U) ratio** | 1 : 0.9    | 1 : 0.8  | 1 : 1       | 1 : 0.7  |
|                              |              |          | With additional remote added: |          |
|                              |              |          | 1 : 2.1     |          |
|                              |              |          | Total combined: | 1 : 0.8  |
|                              |              |          |              |          |