due to a non-disjunction event in gamete formation, has allowed a factor VIII level within the normal range, providing protection from symptomatic haemophilia. This indicates that there has not been significant skewing of X inactivation directed against the X chromosome containing the normal F8 gene.

Protection from the impact of mutations in X linked genes in males with Klinefelter syndrome is a well-established concept, particularly in conditions which are usually considered to be lethal in hemizygous males. For example, small numbers of cases have been reported of males affected by Aicardi syndrome,[2] incontinenti pigmenti,[3] X-linked chondrodysplasia punctata,[4] and Rett syndrome,[5] who have later been identified to also be affected by Klinefelter syndrome. Other X-linked conditions reported in males with Klinefelter syndrome with potentially ameliorated symptoms dependent on X inactivation status include Becker muscular dystrophy,[6] fragile X syndrome,[7] X-linked Alport syndrome,[8] X-linked chronic granulomatous disorder,[9] and properdin deficiency.[10]

While neither haemophilia A nor Klinefelter syndrome are rare in themselves, to our knowledge this is only the third case recorded in the literature of an association of haemophilia with Klinefelter syndrome.

Interestingly, the previously two reported cases indicated the child was phenotypically a haemophiliac. Chipail *et al.*[11] in 1965 described a case of Klinefelter syndrome with an incidental finding of haemophilia A. The expression of the haemophilia was presumed to be associated with the inactivation of the normal X chromosome. Venceslá *et al.*[12] reported the case of a Klinefelter patient inheriting both X chromosomes from the mother with the appearance of a *de novo* mutation resulting in a deletion of exons 1–12 in one of these chromosomes. The unfortunate outcome for this patient was skewed X inactivation of the normal F8 allele resulting in the expression of severe haemophilia A.

In this present case the fact that one of the X chromosomes was carrying a mutation in the F8 gene may have been masked had the child not been the son of a known haemophilia carrier. While unlikely, it is possible that the 'carrier' status in this child could be found in other Klinefelter boys.

The diagnosis of Klinefelter syndrome in this patient at such a young age, although challenging for the family, is potentially fortuitous. It allows the potential for issues related to Klinefelter syndrome to be monitored for in childhood, and preventive management arranged such as hormone treatment to help initiate puberty. In fact, there is an increasing call for instituting newborn screening programs for this condition given the potential advantages of an early diagnosis and targeted therapies.

Until relatively recently, the vast majority of males with Klinefelter syndrome were considered infertile due to azoospermia, with sperm donation being the only opportunity for parenting. However, with current assisted reproductive technology, testicular biopsy may identify viable sperm in up to 50% of affected males which in conjunction with intracytoplasmic sperm injection (ICSI) may allow males to father their own biological children. The risk to offspring of inheriting an extra copy of the X chromosome appears to be low (about 1%).

Should our present patient be fertile, unlike the usual scenario where the daughter of a haemophilia A male is an obligate carrier, in this case there is a 50% chance of a daughter being a carrier. Thus, molecular testing should be offered to any daughters of reproductive age to allow appropriate reproductive risks to be discussed.

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Is it feasible for patients to estimate their own 24 hour urine volume?

Sir,
Twenty-four hour urine collections are considered to be the 'gold standard' for many assays including urinary albumin, catecholamines, and for the evaluation of proteinuria.[1–4] This was advocated as a 24 h urine collection overcame the diurnal

variation in the various analytes measured.[5] Yet, although the volume of urine produced in the period of 24 h needs to be known to determine the excretion rate of a given analyte, the laboratories only need approximately 10 mL of urine to complete the assays.[6] Previous authors have examined the difficulty in the collection of 24 h urine samples; however, none of these authors have studied the possibility of estimation of urine volume at home.[5,7,8] This study examined the feasibility of the measurement of urine volume in the patient's home by comparing self-assessed urine volume with laboratory assessed urine volume. The study included two parts: a preliminary survey and the actual experiment.

The study was approved by the Bond University Human Research Ethics Committee.

A preliminary survey of 104 adults was conducted which involved the subject estimating an unknown volume of water in a 24 h urine bottle. Subjects included 32 hospital and laboratory staff members, 48 consecutive hospital ward patients and 24 consecutive collection centre patients at Sullivan Nicolaides Pathology in September 2012. The 24 h urine bottle contained a set volume of water with yellow food colouring mimicking urine and had the same measurement scale on the bottle as the one included in the study (Fig. 1).

Between 1 December 2012 and 1 December 2013, adult patients presenting to collection centres on the Gold Coast and Coffs Harbour with a request from their doctor for a 24 h urine assay for management of their clinical condition were asked to participate in the study. Participants were invited to complete a questionnaire regarding participant demographics and perceived difficulties in addition to the 24 h urine collection and were also asked to estimate the volume of urine collected by using a measurement scale on the side of the bottle (Fig. 1). The measurement scale included three markings: one for each litre, up to a volume of three litres (Fig. 1). A written explanatory statement was given to all participants and consent was obtained. The collected sample was then processed as per routine protocol in the laboratory. The final volume was obtained using standard laboratory practice of weighing on a calibrated balance. At the end of the study, data in the questionnaires was collated and patient estimated urine volume was compared with the laboratory measured volume. All questionnaires were de-identified by a random nine digit number and participants remained anonymous throughout the study.

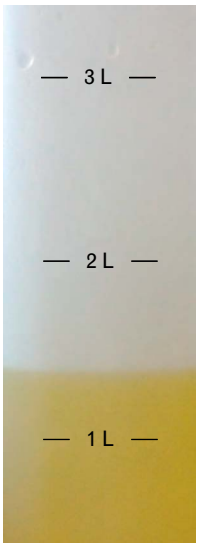

Fig. 1 Measurement scale on side of 24 h urine bottle.

A total of 22 urine samples were collected from the study. Twenty of the collected samples had completed consent forms and were included in our results (Table 1). Of the 20 participants, 17 had previously collected a 24 h urine collection prior to this study.

Analysis of the study questionnaires revealed that 17 participants found the collection easy, including two whom had not previously performed the collection. There were mixed participants' views in terms of how easy it was to miss a sample; eight found it easy to miss a sample, six found it difficult to miss a sample and five did not report ease or difficulty. Ten participants believed it would be easier to measure the 24 h urine volume at home and only bring a small sample to the collection centre whilst eight did not, one was undecided and one did not answer the question. Of particular interest was the fact that 16 of the 20 participants found it easy to transport the 24-h urine sample to the collection centre.

In our preliminary survey, the laboratory measured volume was 1.25 L and the mean volume estimated was 1.33 L [standard deviation (SD) 0.230, coefficient of variation (CV) 0.172]. Thirty-nine participants' estimates were within 2% of the actual volume and 86 participants had an error margin of less than 10% (Fig. 2A). It is unclear why only five participants had estimates which were within 3–5% of the actual volume whilst there were 39 within 2% and 42 within 5–10% (Fig. 2A). There were two participants whose error margin was more than 50% of the actual volume. Of the 86 participants whose estimates were within 10% of the actual volume, 65 were female and 21 were male. Twenty-six were less than 40 years of age, 34 were between 40 and 60 years old and 26 were more than 60 years old.

Seventeen of the 22 participants estimated the volume of urine collected. Paired t test for patient estimation of urine volume was 2.12 ($p = 0.878$). Six participants' estimations were within 2% of the actual laboratory measured volume, and 12 were within 10% of the actual volume. Fig. 2B shows the estimated volume compared with the actual laboratory measured volume. Of the 12 participants whose estimates were within 10% of the actual volume, eight were male and four were female. Eight of the 12 participants were older than 60 years of age and seven had received a tertiary education, two had secondary education and three participants' highest education level was primary school. The two participants whose estimated volume was more than 25% of the actual volume were both male and were more than 50 years of age with secondary and tertiary qualifications, respectively.

Table 1 Participant demographics in preliminary survey and 24 h urine study

	Preliminary survey	Study
Gender		
Male	53	11
Female	51	9
Age, years		
<40	32	4
41–50	23	2
51–60	14	1
61–70	12	4
>71	23	9
Total participants	104	20