



GP Research Review™

Making Education Easy

Issue 140 – 2018

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Abbreviations used in this issue

AF = atrial fibrillation
aOR = adjusted OR
BMI = body mass index
BP = blood pressure
CRP = C-reactive protein
DOAC = direct oral anticoagulant
HR = hazard ratio
IVF = in vitro fertilisation
OR = odds ratio
POC = point-of-care
RR = relative risk
SCFE = slipped capital femoral epiphysis
VAS = visual analogue scale

Welcome to issue 140 of GP Research Review.

One of the papers in this issue reports that preschool children who spend >1 hour daily on electronic screen time are at increasing risk for psychosocial problems with every additional hour of screen time. The study is huge – it involved more than 20,000 preschool children in Shanghai, China. Of all mediators accounting for the effect of screen time on psychosocial well-being, the most significant was parent-child interaction. These are important findings to bring to the attention of parents and caregivers.

In our Natural Health section, one of the papers describes how twice-daily supplementation with a multistrain synbiotic provided meaningful relief for 320 children with atopic dermatitis, a third of whom had severe disease at baseline. After 8 weeks of the supplement, disease symptoms were greatly improved both in children with persistent disease and in atopic dermatitis with flares, as well as in those with and without concomitant atopies, and <5% were considered to still have severe disease. The treatment was well tolerated.

I hope you enjoy this issue and I welcome your comments and feedback.

Kind regards,

Jim

Assoc Professor Jim Reid

jimreid@researchreview.co.nz

Goodfellow Gems

No antibiotics for asymptomatic bacteriuria in non-pregnant women

Bacteria in the bladder is common and may show up as a positive dipstick. But if the patient is asymptomatic then it is not a urinary tract infection (UTI).

Asymptomatic bacteriuria occurs commonly in:

- over 65-year-olds
- catheterised or institutionalised patients
- sexually active women
- diabetics.

Do not treat asymptomatic bacteriuria with antibiotics in non-pregnant women of any age. Pregnancy is different so seek local guidance.

Symptoms that are highly suggestive of UTI can be treated without doing any further tests. A urine culture is useful when the choice of antibiotic is not clear or there is diagnostic uncertainty. Symptoms of UTI with persistent negative midstream urine warrants further exploration for conditions such as interstitial cystitis or malignancy.

In patients unable to report symptoms a urinalysis may be helpful. The dipstick testing is very sensitive but not very specific for detecting a UTI. If positive for either nitrites or leukocytes, the probability of a UTI increases to about 80%.¹

This Gem has been checked by Dr Chris Cameron, Geriatrician.

Reference: Health Pathways Auckland Region: accessed UTI in Adults, 25/9/018. (outside Auckland region please access local regional pathways) [Click here](#)

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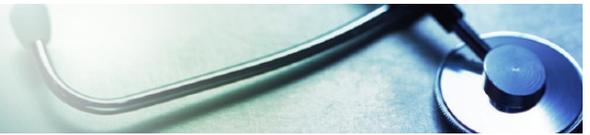


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Measuring and managing blood pressure in a primary care setting: a pragmatic implementation study

Authors: Doane J et al.

Summary: These researchers report outcomes from a US-based automated office blood pressure (AOBP) and home blood pressure management (HBPM) programme that was conducted by a primary care clinic between 2015 and 2016. Results are reported for 183 patients enrolled into the HBPM programme after undergoing guideline-quality, observed, AOBP measurements: 53 patients entered the programme with a single observed AOBP $\geq 140/90$ mm Hg; 40 had an average of 3 observed AOBP measurements $\geq 140/90$ mm Hg; and 90 had an AOBP $\geq 135/85$ mm Hg. Twenty-nine patients (89%) with elevated AOBP and not on antihypertensive treatment at enrolment were found to have white-coat hypertension with average home BP measurements of $< 135/85$ mm Hg. Of patients on BP-lowering treatment at enrolment, 37 (37%) were found to have white-coat BP elevation with an average home BP $< 135/85$ mm Hg. The prevalence of white-coat BP elevation did not differ according to whether patients were enrolled by observed BP or AOBP. Of 37 patients newly diagnosed with hypertension during the study period and who provided additional serial HBPM results to facilitate initiation and adjustment of antihypertensive medications, 19 (51%) achieved average home BP $< 135/85$ mm Hg. Of 39 patients with uncontrolled hypertension who provided serial HBPM results, 18 (46%) achieved average home BP $< 135/85$ mm Hg. Responses to satisfaction questionnaires completed by clinic staff, providers and patients indicated that most considered that the programme was acceptable. Barriers to the implementation of the HBPM programme included incorrect AOBP or HBPM technique, and patients failing to send HBPM results to the clinic.

Comment: This study reinforces my long-held belief that a single normal clinic-based BP is highly significant, whereas mild elevation should be treated with suspicion. The diagnosis of hypertension is a very important one, as frequently, to gain control, we are imposing lifetime medication-taking. How many times do you take a BP reading to find it mildly elevated, leave the cuff on, talk about an upcoming holiday, the weather, the children or grandchildren, or whatever and then take it again. Often, in my experience, the systolic pressure will drop 10 mm Hg! This study demonstrates that by use of home BP, a significant number of patients may not be hypertensive at all and those on treatment may also not be hypertensive or are over-treated. Another way, of course, is to do a 24-hour BP and look at the average over the 24 hours.

Reference: *J Am Board Fam Med.* 2018;**31(3):375-88**

[Abstract](#)



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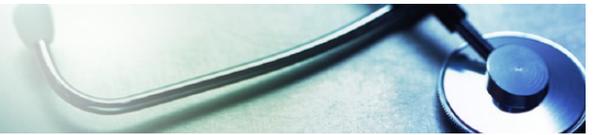
Independent commentary by Associate Professor Jim Reid.



Jim Reid graduated in medicine at the University of Otago Medical School in Dunedin New Zealand. He had previously trained as a pharmacist. He undertook his postgraduate work at the University of Miami in Florida. Currently he is Deputy Dean of the Dunedin School of Medicine. He has a private family medicine practice at the Caversham Medical Centre, Dunedin, New Zealand. He is a Distinguished Fellow of the Royal New Zealand College of General Practitioners and is also a Fellow of the American College of Chest Physicians.

He has a special interest in Respiratory Medicine and has published widely in Asthma and COPD. He is active in research in respiratory medicine and has had wide international lecturing experience.

References: 1. Kendall, M.J., et al. A pharmacokinetic comparison of ibuprofen sustained-release tablets given to young and elderly patients. *J Clin Pharm Ther.* 1990; 15(1): p. 35-40. 2. Brufen SR New Zealand Data Sheet, 2017, 1-13. Available from: <http://medsafe.govt.nz/profs/Datasheet/b/brufenrelatrdtab.pdf>. Accessed February 2018. **Brufen[®] SR (ibuprofen) 800mg modified release tablets.** **Indications:** Rheumatoid arthritis, Osteoarthritis, Juvenile rheumatoid arthritis, Primary dysmenorrhoea, Pyrexia. **Relief of acute and/or chronic pain states in which there is an inflammatory component.** **Contraindications:** Known hypersensitivity to ibuprofen, aspirin or other NSAIDs; history of active gastrointestinal bleeding or perforation related to previous NSAID therapy; active, or a history of, ulcerative colitis, Crohn's disease, recurrent peptic ulceration or gastrointestinal haemorrhage, increased tendency or active bleeding, severe heart failure, severe liver failure, severe renal failure, third trimester of pregnancy. **Precautions:** Prolonged use, cardiovascular disease, cardiovascular risk factors, hypertension, heart failure, history of GI bleeding, ulcer, severe skin reactions, bronchial asthma, respiratory disorders, bleeding tendencies, dehydration, renal, hepatic and cardiac impairment, monitor haematological and ophthalmological function, skin infections and infestations, mask infection, withdrawal of concomitant steroids (reduce gradually), elderly, first and second trimesters of pregnancy, lactation. **Interactions:** Anti-coagulants such as warfarin; anti-platelet agents; SSRIs; aminoglycosides; lithium; cardiac glycosides; cholestyramine; corticosteroids; ginkgo biloba; other analgesics (concomitant use of two or more NSAIDs, COX-2 selective inhibitors); cyclosporine or tacrolimus; methotrexate; quinolone antibiotics; sulfonyleureas; zidovudine; ACE inhibitors; diuretics; CYP2C9. **Adverse Effects:** Gastrointestinal disorders including dyspepsia, diarrhoea, nausea, vomiting, abdominal pain, flatulence, heartburn, constipation, melana, haematemesis, gastrointestinal haemorrhage, exacerbation of colitis and Crohn's disease; headache, dizziness, oedema; rash, fatigue, asthma. **Dosage & administration:** Adults: 2 tablets daily as a single dose or up to 3 tablets taken as two tablets in the early evening and an additional tablet in the morning. The lowest effective dose for the shortest duration should be used. Take with plenty of fluid. Brufen SR is not recommended for children under 12 years. **Brufen SR is a fully funded prescription medicine.** Before prescribing please refer to the full datasheet, available from: www.medsafe.govt.nz. Brufen[®] SR is a registered trademark of Mylan Healthcare GmbH. Mylan NZ Ltd., Auckland. TAFS DA1826FR-164.



Excessive screen time and psychosocial well-being: the mediating role of body mass index, sleep duration, and parent-child interaction

Authors: Zhao J et al.

Summary: This survey recruited 20,324 children aged 3–4 years attending kindergarten in Shanghai, China. Their psychosocial well-being status was assessed by parents' responses on the Strengths and Difficulties Questionnaire. The parents also recorded the times their child spent on screen exposure and duration of sleep, their child's BMI, and parent-child interactive activities. These children had on average 2.8 hours/day of screen time; 78.6% of them had >1 hour/day and 53% had >2 hours/day. Every additional hour of screen time increased the risk for poor psychosocial well-being. Of the 3 factors found to mediate the effect of excessive screen time on children's psychosocial well-being – BMI, sleep duration and parent-child interaction – the most important was parent-child interaction. Parent-child interaction explained 28.1% of the effect of screen time on total difficulties and 58.6% on prosocial behavioural problems.

Comment: There is no reason to think that these findings on outcomes from the time that children in China spend in front of a screen cannot be extrapolated elsewhere. In general, there is a steady rise in risk of excessive body weight, psychological maldevelopment, reduction in sleep duration, and parent-child interaction with increasing screen time. Good advice to give parents.

Reference: *J Pediatr.* 2018;202:157-62

[Abstract](#)

Association between alcohol consumption and nocturnal leg cramps in patients over 60 years old: a case-control study

Authors: Delacour C et al.

Summary: This investigation included ambulatory patients aged ≥ 60 years presenting to their family doctor in the Alsace region, France. Cases (patients complaining of cramps) were matched by age, sex, medical history, and medications known to trigger cramps with patients free from cramps (controls). All participants completed a standardized food frequency questionnaire that assessed alcohol consumption. In a Bayesian sensitivity analysis, consumption of alcoholic beverages was strongly associated with nocturnal leg cramps (OR 6.5; 95% credibility interval, 1.68 to 38.05; posterior probability 99.82%).

Comment: In short – if you want to reduce nocturnal leg cramps, advise reducing the alcoholic drinks! Worth a try? – and a lot less toxic than other “remedies”, all of which are pretty useless – including quinine!

Reference: *Ann Fam Med.* 2018;16(4):296-301

[Abstract](#)

Point-of-care CRP matters: normal CRP levels reduce immediate antibiotic prescribing for acutely ill children in primary care: a cluster randomized controlled trial

Authors: Lemiengre MB et al.

Summary: This Belgium study describes the effect of a point-of-care (POC) CRP test upon antibiotic prescribing rates for acutely ill children consulting their family physician between 15 February 2013 and 28 February 2014. The analysis involved 2,844 infectious episodes and 133 family physicians. The practices were randomly assigned to perform POC CRP or not; testing was performed in half of the children with non-severe acute infections and in all those at risk for serious infection. Compared with infectious episodes not tested by POC CRP, testing reduced immediate antibiotic prescribing in episodes deemed appropriate for antibiotics by evidence-based medicine practice guidelines (aOR 0.54; 95% CI, 0.33 to 0.90). Antibiotic prescribing was reduced when CRP levels were normal, regardless of whether the guidelines advised prescribing (aOR 0.24; 95% CI, 0.11 to 0.50) or not (aOR 0.31; 95% CI, 0.17 to 0.57). Antibiotic prescribing was not increased in those cases where testing revealed elevated CRP levels.

Comment: We should all be engaged in antibiotic stewardship. In many studies, POC has failed because doctors have followed their gut instincts rather than POC outcomes. These have included POC for influenza, Strep group A, and CRP for viral infections. If the individual (adult or child) was toxic – it mattered little what the POC result was to prescribing outcome, and in general, antibiotics were prescribed. In The Netherlands and Scandinavia, doctors seem to be much more trusting of POC and they have published extensively on this. Maybe the concept is spreading and I hope it is catching on in NZ.

Reference: *Scand J Prim Health Care.* 2018;36(4):423-36

[Abstract](#)

Diastolic hypotension may attenuate benefits from intensive systolic targets: secondary analysis of a randomized controlled trial

Authors: Lee TC et al.

Summary: This secondary analysis of data from the Systolic Blood Pressure Intervention Trial (SPRINT) included 8,046 study participants aged ≥ 50 years with a baseline diastolic BP ≥ 65 mm Hg treated under the intensive (≤ 120 mm Hg; $n=4,041$) or standard systolic target (≤ 140 mm Hg; $n=4,005$). All participants had ≥ 1 additional cardiovascular risk factor. In multivariable Cox proportional hazards modelling, patients who developed diastolic hypotension (defined as ≤ 55 mm Hg) were at greater risk for the primary outcome of cardiovascular morbidity (myocardial infarction, other acute coronary syndromes, stroke, heart failure) and all-cause death (HR 1.67; 95% CI, 1.24 to 2.26). This was true regardless of whether they were in the intensive or standard treatment arms (HR 1.53; 95% CI, 1.04 to 2.26 and HR 2.23; 95% CI, 1.40 to 3.54, respectively; $p=0.09$).

Comment: This study looked at the importance of diastolic hypotension, which as doctors we often create by treating marginal systolic hypertension. But the question in this study is just how important is this? Those in the study who developed diastolic hypotension had a 1.7 hazard ratio of developing a myocardial infarct, other acute coronary syndrome, stroke, heart failure or suffering from all-cause death than those who were diastolic normotensive. Worthy of consideration!

Reference: *Am J Med.* 2018;131(10):1228-33

[Abstract](#)

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Association of dairy consumption and 24-hour blood pressure in older adults with hypertension

Authors: Lana A et al.

Summary: This Spanish investigation included 715 community-living adults aged ≥ 60 years with hypertension who were questioned about their habitual dairy consumption. BP was recorded by 24-hour ambulatory BP monitoring; controlled BP was defined as 24-hour BP $< 130/80$ mm Hg in those receiving antihypertensive medication. In analyses adjusted for confounders (diet, duration of hypertension, and antihypertensive medication), those who consumed ≥ 7 servings/week of whole-fat milk/yogurt had a diastolic BP 1.40 mm Hg higher than consumers of < 1 serving/week. Conversely, those consuming ≥ 7 servings/week of low-fat milk/yogurt had a diastolic BP 1.74 mm Hg lower than those who consumed < 1 serving/week; the likelihood of having controlled BP was 83% higher in those consuming ≥ 7 servings/week of low-fat milk/yogurt, when compared with consumers of < 1 serving/week (OR 1.83; 95% CI, 1.05 to 3.08). No association was seen between cheese consumption and BP.

Comment: As the conclusion states, consumption of low-fat milk/yogurt was associated with lower diastolic BP. The question, which is not answered in this study, is whether a difference of 1.4 mm increase in pressure in those regularly consuming more whole-fat product as compared to those “depriving” themselves is clinically important. And equally important for the low-fat group – did the 1.74 mm lower diastolic value make any difference to morbidity or mortality. That is the important issue.

Reference: *Am J Med.* 2018;131(10):1238-49

[Abstract](#)

Effectiveness and safety of anticoagulants in adults with non-valvular atrial fibrillation and concomitant coronary/peripheral artery disease

Authors: Lopes RD et al.

Summary: This analysis of US Medicare data included patients aged ≥ 65 years with nonvalvular atrial fibrillation diagnosed with coronary/peripheral artery disease who were newly initiating direct oral anticoagulants (DOACs; apixaban, rivaroxaban, dabigatran) or warfarin between 1 January 2013 and 30 September 2015. Propensity score matching that controlled for potential confounders between DOACs and warfarin resulted in 15,527 apixaban-warfarin, 6,962 dabigatran-warfarin and 25,903 rivaroxaban-warfarin-matched pairs, with a mean follow-up of 5–6 months. In Cox proportional hazards modelling, apixaban was associated with a 52% lower rate of stroke/systemic embolism (HR 0.48; 95% CI, 0.37 to 0.62), a 34% lower rate of major bleeding (HR 0.66; 95% CI, 0.58 to 0.75), and a 37% lower rate of stroke/myocardial infarction/all-cause mortality (HR 0.63; 95% CI, 0.58 to 0.69) compared with warfarin. Dabigatran and rivaroxaban were associated with lower rates of stroke/myocardial infarction/all-cause mortality (HR 0.79; 95% CI, 0.70 to 0.90 and HR 0.87; 95% CI, 0.81 to 0.92, respectively) compared with warfarin. Rivaroxaban was also associated with a lower rate of stroke/systemic embolism (HR 0.72; 95% CI, 0.60 to 0.89) and a higher rate of major bleeding (HR 1.14; 95% CI, 1.05 to 1.23) compared with warfarin.

Comment: Another paper confirming the effectiveness of all three DOACs currently being marketed, although only two are funded (dabigatran and rivaroxaban) in this country. All were winners in the stroke/myocardial infarction/all-cause mortality stakes in reduction of strokes, myocardial infarction and all-cause mortality over warfarin in patients suffering coronary or peripheral artery disease.

Reference: *Am J Med.* 2018;131(9):1075-85

[Abstract](#)

Childhood obesity and slipped capital femoral epiphysis

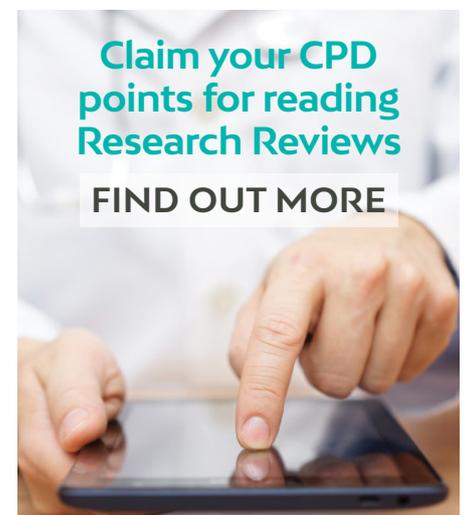
Authors: Perry DC et al.

Summary: This analysis examined BMI data obtained from routine health screening examinations for 597,017 children aged 5–6 years entering primary school in Scotland. Data were also available from 39,468 of those children when they underwent a further screening examination at primary school exit (11–12 years of age). Both cohorts were linked to a nationwide hospital admissions database. The analysis sought to determine whether there is evidence for a causal relationship between obesity and slipped capital femoral epiphysis (SCFE). The total follow-up for these two cohorts was 4.26 million child-years. Of children who were obese at ages 5 and 6 years, 75% of them were still obese at ages 11 and 12 years. A strong biological gradient was observed between childhood BMI at 5 and 6 years of age and SCFE; the risk of disease increased by a factor of 1.7 for each integer increase in BMI z score. Children with the lowest BMI had almost no risk of SCFE, whereas those who were severely obese at ages 5 and 6 years had a 5.9-fold higher risk of SCFE compared with those with a normal BMI; this risk was 17.0-fold higher among those with severe obesity at ages 11 and 12 years.

Comment: This study confirms the very strong association between childhood obesity and SCFE. I think I have seen five in my career, so it is not common, but certainly not a diagnosis to be missed. All five were overweight, and all were girls. The authors say the risk of SCFE is almost negligible among children with low BMI. The condition is a high risk among really heavy 5- to 6-year-olds, who have a 6-fold increase as compared with those of normal BMI. It is our role, as doctors, to inform parents of such at-risk children.

Reference: *Pediatrics.* 2018;142(5):pii:e20181067

[Abstract](#)



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EVIDENCE-BASED NATURAL HEALTH by Dr Chris Tofield

Effect of synbiotic supplementation on children with atopic dermatitis: an observational prospective study

Authors: Ibáñez MD et al.

Summary: In this study, 320 children aged <12 years with atopic dermatitis who had active eczema at the time of initial consultation were prescribed a multistrain synbiotic supplementation containing *Lactobacillus casei*, *L. rhamnosus*, *L. plantarum*, *Bifidobacterium lactis*, fructooligosaccharide, galactooligosaccharide, and biotin as a dose of 1 g twice daily, administered orally or dissolved in liquids, or mixed with food. Around half (52.1%) of the children were on concomitant treatments, mostly topical corticosteroids (21.3%) and antihistamines (19.7%), or were being treated for other diseases. At baseline, over half of the children had moderate disease, as assessed by scores of 25–50 on the Scoring Atopic Dermatitis (SCORAD) index. At 8 weeks, the mean SCORAD index score had fallen from 45.5 at baseline to 19.4 ($p<0.001$), the mean VAS pruritus score had fallen from 5.7 to 2.3 ($p<0.001$) and the mean VAS sleep score had fallen from 3.1 to 1.1 ($p<0.001$). Multiple linear regression analysis identified that both a higher baseline SCORAD index (OR 0.51; 95% CI, 0.41 to 0.61) and higher treatment adherence (OR 7.29; 95% CI, 1.85 to 12.73) were significantly associated with greater declines from baseline in SCORAD index scores.

Comment: Eczema in young children can be heartbreaking to watch – relentless itching resulting in constant scratching with subsequent scarring. While none of us feel good about regularly prescribing strong steroid creams, there is often no choice in those more severely affected. Many natural remedies have been trialled, but to my knowledge none with convincing benefit. This Spanish study had a go at using an oral synbiotic mixture, i.e. a combination of probiotics and prebiotics. They included the B vitamin biotin as well as some commonly used lactobacilli. Results were impressive, with a reduction in the number of kids with moderate-to-severe eczema from 92% to 28% after 8 weeks. While this was an observational cohort study with no randomisation or placebo group, therefore lending itself to observational bias, this synbiotic mixture nonetheless deserves further attention.

Reference: *Eur J Pediatr.* 2018;177(12):1851-8

[Abstract](#)

Effect of acupuncture vs sham acupuncture on live births among women undergoing in vitro fertilization

Authors: Smith CA et al.

Summary: These researchers sought to determine whether acupuncture affects live birth rates in women undergoing IVF. Live birth outcomes are reported from 809 women undergoing a fresh IVF cycle who were recruited from 16 IVF centres throughout Australasia between June 2011 and October 2015. They received either verum acupuncture (n=405) or sham acupuncture using noninvasive needles placed away from the true acupoints (controls; n=404). The women were followed-up until August 2016. The first treatment was administered between days 6 and 8 of ovarian stimulation; 2 treatments were given on the day of embryo transfer. Live birth was defined as the delivery of ≥ 1 living infant at >20 weeks' gestation or birth weight of ≥ 400 g. A total of 371 women had undergone ≥ 2 previous IVF cycles. Live births were registered for 74 women given verum acupuncture compared with 72 controls (18.3% vs 17.8%; RR 1.02 [95% CI, 0.76 to 1.38]).

Comment: It is tempting to think that acupuncture might somehow be able to affect fertility, yet here we learn this may not be so. The pregnancy success rate of around 18% in these women undergoing IVF was almost identical in the acupuncture and sham acupuncture groups. While this was a joint Australian/New Zealand study, it would be interesting to know whether acupuncturists in countries such as China might be seeing different results.

Reference: *JAMA.* 2018;319(19):1990-8

[Abstract](#)

Dr Christopher Tofield

Dr Tofield completed his medical training at St Bartholomew's and the Royal London Hospital in London. He now works part time in general practice in Tauranga, is involved with clinical research, has published several medical papers and a textbook on pharmacology, and is clinical advisor to Bay of Plenty District Health Board.



For full bio [CLICK HERE](#).



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