

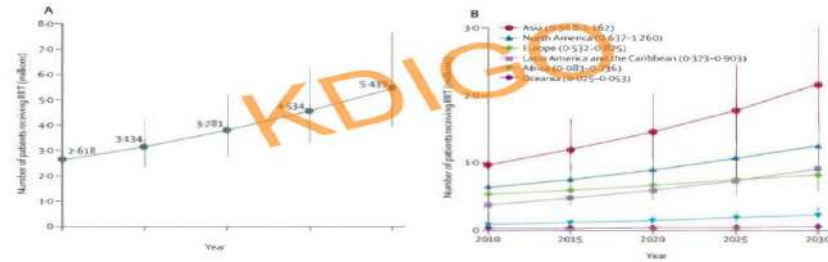


*Διάλυμα «κυτρεκτών», μία «ωράβευση» εναλλακτική λύση
έναντι της ηπαρίτιδας*

*Ioannis Griveas, MD, PhD
Nephrologist*

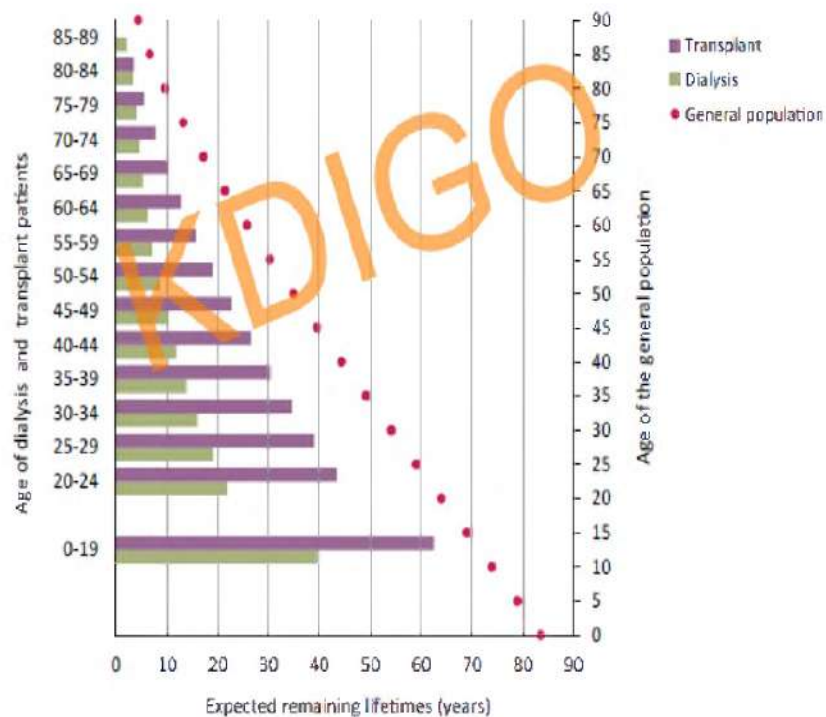
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Estimated number of patients undergoing RRT from 2010 to 2030 worldwide (A) and by region (B)



Liyanage T, et al. Lancet 2015

Expected remaining lifetime (years) of the general population (cohort 2011-2015) and of prevalent dialysis and transplant patients (cohort 2011-2015)



Adequacy Dialysis Dose

“From an **idealistic** clinical perspective,
an **adequately** treated **dialysis patient** is
physically active, well **nourished**, **euvolemic** and
normotensive, with a maintained good **quality of life**
and a **life expectancy** that is **not inferior**
to that of **healthy patients**”¹

1. Floege J et al. Comprehensive Clinical Nephrology, 2015





KDOQI[®]
Kidney Disease
Outcomes Quality Initiative

KDOQI CLINICAL PRACTICE GUIDELINE FOR
HEMODIALYSIS ADEQUACY: 2015 UPDATE

***“It is important to distinguish
adequacy of the dialysis from
adequacy of patient care”.¹***

**We should focus on the patient, and focus on
other dialysis parameters, if we want to increase dialysis
adequacy and improve our patients' outcomes**



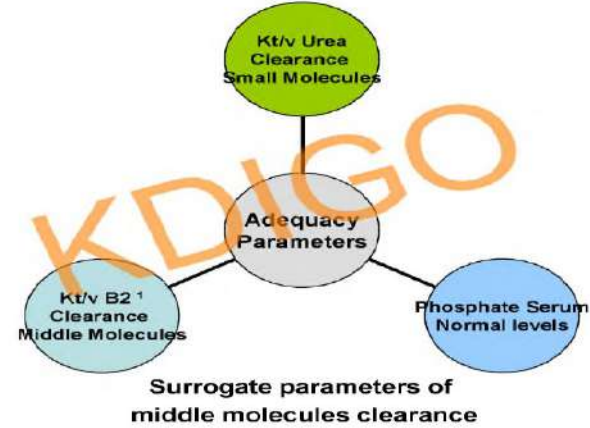
1. KDOQI. Am J Kidney Dis. 2015

VALUE 1

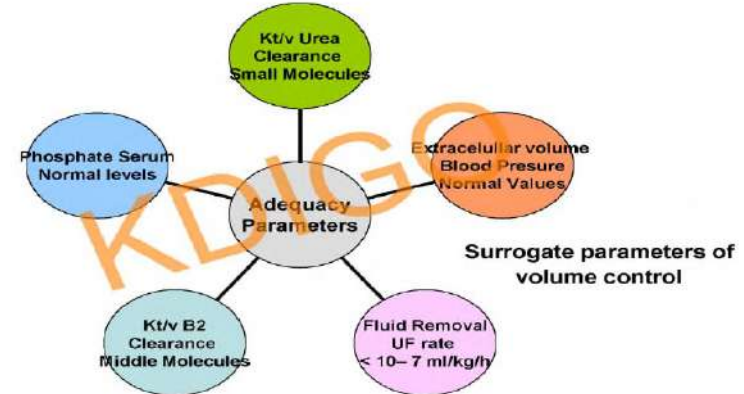
Which other parameters
could be important
to measure dialysis adequacy
in order to improve
our patients' outcomes?

Modifiable risk factors for Sudden Cardiac Death in dialysis patients, related to dialysis procedure

Recommendations	References
1. Dietary counseling for potassium and fluid gain	Beyer et al ¹⁸
2. Individualize and adjust potassium bath at least monthly for each patient; consider point-of-care devices to measure potassium on a more regular basis	Kumar et al. ¹⁵ Sun et al. ¹⁴
3. Do not use dialysate potassium concentrations < 2 mEq/L, particularly if predialysis potassium = 5 mEq/L; if patients present with hypokalemia, serum levels consider extending the dialysis time, but do not lower dialysate potassium concentration to < 2 mEq/L	Kovacs et al. ¹³ Jandou et al. ¹⁹
4. Consider the use of dialysate potassium presorting (ie, start with dialysate concentration of 4 mEq/L and gradually reduce it during the treatment) to 2 mEq/L when predialysis potassium level is > 6 mEq/L	Reisoli et al. ²⁰
5. Adjust dialysate bicarbonate concentration to achieve a target predialysis bicarbonate of 30–32 mEq/L and reduce the risk of severe intradialytic alkalosis	Heggen et al. ²¹
6. Reduce the risk of high intradialytic urea (> 10 mEq/L) by sustaining dialysis time > 4 h	Flythe et al. ²² McIntyre et al. ²³
7. Measure magnesium monthly and supplement magnesium if needed	Burton et al. ²⁴
8. Do not use dialysate calcium concentration < 2.5 mEq/L (and possibly maintain at 2.5 mEq/L), particularly in combination with a low potassium bath in patients at high risk of arrhythmias	Sakaguchi et al. ²⁵
9. Avoid the use of digoxin for heart failure or control of atrial fibrillation in hemodialysis patients, and if unavoidable, consider using a higher potassium bath	Geraud et al. ²⁶ Pun et al. ²⁷
10. Be aware of medications that prolong QTc interval, which may be prolonged further by rapid shift in potassium, calcium, and magnesium concentrations	Chae ²⁸
	Data from the general population ^{29–32}



HIGH VALUE 1



Modifiable risk factors for Sudden Cardiac Death in dialysis patients, related to dialysis procedure

Summary of Procedures and Techniques to Reduce Risk of Sudden Cardiac Death in the Hemodialysis Population

- 1 Dietary counsel
- 2 Individualize and
- 3 Do not use dialy
- 4 Consider the use
- 5 Adjust dialysate
- 6 Reduce the risk
- 7 Measure magne
- 8 Do not use dialy
- 9 Avoid the use of
- 10 Be aware of medication

Avoid rapid electrolyte and volume shifts during dialysis sessions

1. **Adjust** dialysate composition
2. **Adjust** ultrafiltration rate

et al.¹²

et al.³⁰

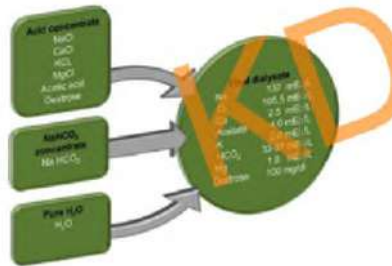
et al.²⁹

Data from the general population³⁴⁻³⁶

Dialysate Composition

Dialysate composition is a **critical aspect** of the **dialysis prescription**, if we want to **avoid rapid electrolyte shifts** ¹

Often, the concentrations of **key components** may be determined **by default**, based on **dialysate manufacturer specifications** or **hemodialysis facility practices**. ²



Composition of Dialysates for Bicarbonate Dialysis		
Component	Concentration	
	Range	Typical
Electrolytes (mmol/l)		
Sodium	135-145	140
Potassium	0-4.0	2.0
Calcium	0-2.0	1.25
Magnesium	0.5-1.0	0.75
Chloride	87-124	105
Buffers (mmol/l)		
Acetate	2-4	3
Bicarbonate	20-40	35
pH	7.1-7.3	7.2
Pco ₂ (mm Hg)	40-100	
Glucose	0-11 (0-200 mg/dl)	5.5 (100 mg/dl)

Dialysate **should be** considered “**as a drug to be adjusted**” to the individual **patient’s needs**

Roadmap

Effect of citrate based dialysate on anticoagulation in maintenance haemodialysis patients.



1

THE EFFICACY OF ASCORBATE-RICH DIALYSATE TO ATTENUATE ANAEMIA IN MAINTENANCE HEMODIALYSIS PATIENTS



3



5

USE OF ASCORBATE-RICH DIALYSATE IN HEMODIALYSIS PATIENTS

Η ΕΠΙΔΡΑΣΗ ΟΞΙΝΟΥ ΚΙΤΡΙΚΟΥ ΔΙΑΛΥΜΑΤΟΣ ΑΙΜΟΚΑΘΑΡΣΗΣ ΣΤΗΝ ΑΝΤΙΠΗΚΤΙΚΗ ΑΓΩΓΗ ΑΣΘΕΝΩΝ ΜΕ ΧΡΟΝΙΑ ΝΕΦΡΙΚΗ ΝΟΣΟ ΤΕΛΙΚΟΥ ΣΤΑΔΙΟΥ ΥΠΟ ΑΙΜΟΚΑΘΑΡΣΗ
19ο Πανελλήνιο Συνέδριο Νεφρολογίας

2

Effect of citrate based dialysate on intradialytic heparin dose in maintenance haemodialysis patients.



4



6

Future Projects

ΑΣΘΕΝΕΙΣ-ΜΕΘΟΔΟΙ

10 ασθενείς με Χρόνια Νεφρική Ανεπάρκεια τελικού σταδίου υπό αιμοκάθαρση (ΧΝΑ-TN) που ελάμβαναν διάλυμα AD, άρχισαν να λαμβάνουν διάλυμα CD για μια περίοδο 9 μηνών. 9 ασθενείς λάμβαναν κλασική ηπαρίνη, ένας ηπαρίνη χαμηλού μοριακού βάρους.

Ασβέστιο ορού, φώσφορος ορού, αλβουμίνη, αιμοσφαιρίνη, αιματοκρίτης, kt/V , pH , διττανθρακικά και CRP μετρήθηκαν στην αρχή της μελέτης, μετά από 4 μήνες και στο τέλος του πρωτοκόλλου.

Κατά τη διάρκεια της μελέτης καταγράφησαν όλες οι αλλαγές στην χρησιμοποιούμενη δόση της ηπαρίνης και αξιολογήθηκαν τυχόν θρομβωτικά επεισόδια (visual clotting score) ή αιμορραγική διάθεση

Κατά τη διάρκεια της περιόδου της μελέτης οι 10 ασθενείς (μέση ηλικία 74 ετών, εύρος: 54-93 ετών και μέσος χρόνος αιμοκάθαρσης 38 μήνες, εύρος: 9-86 μήνες) υποβλήθηκαν σε 647 συνεδρίες AMK με διάλυμα CD.

Το 100% των ασθενών μας ανέχθηκαν την AMK με CD καλά χωρίς προβλήματα. Η αθροιστική δόση κλασικής ηπαρίνης με διάλυμα CD μειώθηκε σταδιακά στο 40,5% (από μέση τιμή 4100 iu με το κλασικό διάλυμα AD σε 1660 iu χρησιμοποιώντας το διάλυμα με CD) της δόσης που χρησιμοποιούνταν με διάλυμα με AD. Στην ασθενή που έπαιρνε ηπαρίνη χαμηλού μοριακού βάρους, όταν χρησιμοποιήθηκε διάλυμα με CD διεκόπει εντελώς.

Κατά τη διάρκεια της μελέτης δεν παρατηρήθηκαν επιπλοκές από αιμορραγική διάθεση. 1/10 ασθενείς εμφάνισε ασυμπτωματική υπασβεστιαμία. Θρομβωτικά επεισόδια στο εξωσωματικό σύστημα κυκλοφορίας που να οδήγησαν σε πρόωρη τερματισμό της συνεδρίας δεν παρατηρήθηκαν. Το μεταβολικό προφίλ (μέσο p H εξόδου 7,47, μέση τιμή διττανθρακικών HCO_3 εξόδου 27,22) και η επάρκεια κάθαρσης των ασθενών παρέμειναν σταθερά ($\text{KT/V} > 1,2$) κατά τη διάρκεια της μελέτης.



Οι περισσότερες μελέτες είναι μικρές μελέτες παρατήρησης που επικεντρώνονται στην επάρκεια της αιμοκάθαρσης, στις θρομβώσεις φίλτρων και σε μεταβολικές, φλεγμονώδεις και αιμοδυναμικές παραμέτρους.

Daimon S, Dan K, Kawano M. Comparison of acetate-free citrate hemodialysis and bicarbonate hemodialysis regarding the effect of intra-dialysis hypotension and post-dialysis malaise. *Ther Apher Dial.* 2011;15(5):460–5.

Kuragano T, Kida A, Furuta M, Yahiro M, Kitamura R, Otaki Y, et al. Effects of acetate-free citrate-containing dialysate on metabolic acidosis, anemia, and malnutrition in hemodialysis patients. *Artif Organs.* 2012;36(3):282–90.

Kuragano T, Furuta M, Yahiro M, Kida A, Otaki Y, Hasuike Y, et al. Acetate free citrate-containing dialysate increase intact-PTH and BAP levels in the patients with low intact-PTH. *BMC Nephrol.* 2013;14:18-2369–14-18.

Σε τυχαιοποιημένη μελέτη ενός κέντρου με 23 ασθενείς υπό AMK, κατά τη διάρκεια των συνεδριών με CD, το 50% των ασθενών δεν χρειάστηκε κάποιας μορφής αντιπηκτική αγωγή, το 32% λειτούργησε με μειωμένη δόση ενώ το 18% των ασθενών χρειάστηκε να διακόψει τη συνεδρία πρώιμα λόγω θρόμβωσης του συστήματος της εξωσωματικής κυκλοφορίας. Η επάρκεια κάθαρσης παρέμεινε ίδια και στις δύο ομάδες των ασθενών.

Stegmayr BG, Jonsson P, Mahmood D. A significant proportion of patients

treated with citrate containing dialysate need additional anticoagulation. *Int J Artif Organs.* 2013;36(1):1–6.

Σε τυχαιοποιημένη μελέτη που μελετήθηκε η χρήση του CD σε ασθενείς υπό on-line αιμοδιαδιήθηση η δόση ηπαρίνης μειώθηκε στο μισό, χωρίς αλλαγές στη επάρκεια και με ένα επεισόδιο θρόμβωσης σε 120 συνεδρίες που χρησιμοποιήθηκε .

Δύο ακόμα μελέτες παρατήρησης σε 20 και 31 χρόνιους ασθενείς υπό AMK με προβλήματα αιμορραγικής διάθεσης στα σημεία παρακέντησης χρησιμοποιήθηκαν διαλύματα CD. Οι δόσεις ηπαρίνης μειώθηκαν κατά 30% μετά από δύο μήνες και κατά 55% μετά τέσσερις μήνες, αντίστοιχα.

Και στις δύο μελέτες, η μείωση της ηπαρίνης επιτεύχθηκε χωρίς μείωση στην επάρκεια αιμοκάθαρσης.

Anion J, Petitclerc T, Creput C. Safe use of citric acid-based dialysate and heparin removal in postdilution online hemodiafiltration.

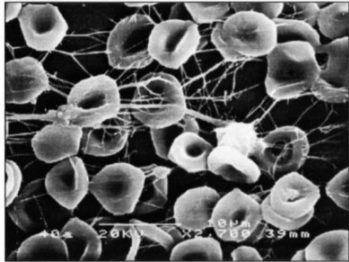
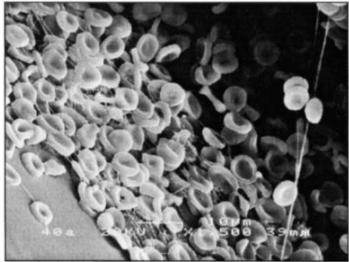
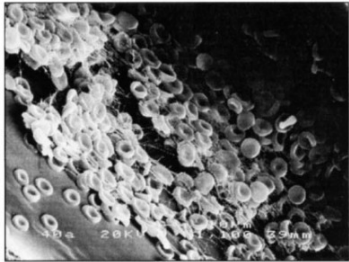
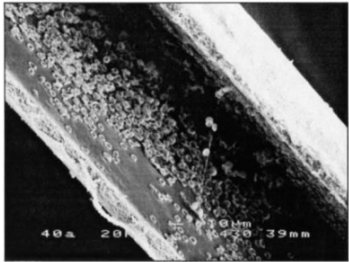
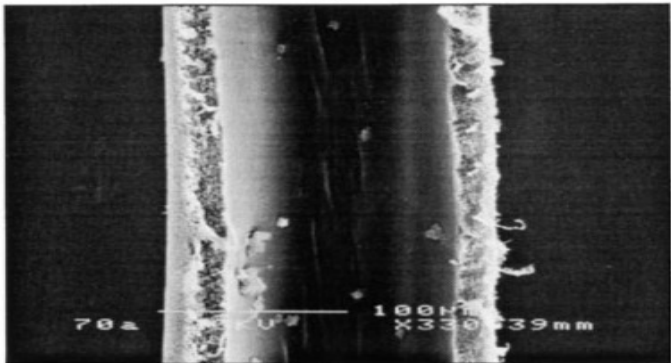
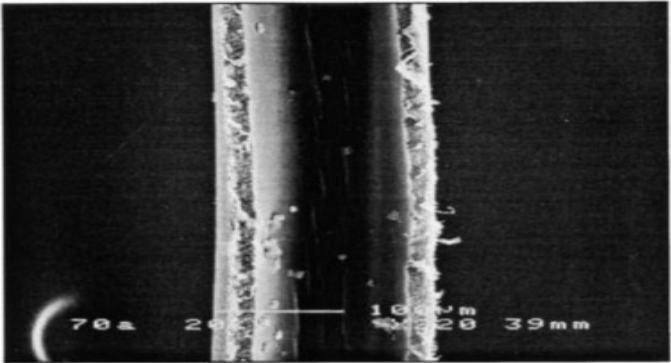
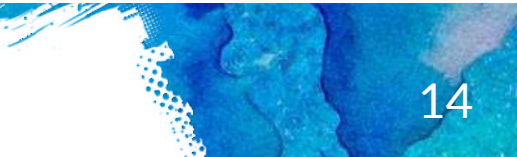
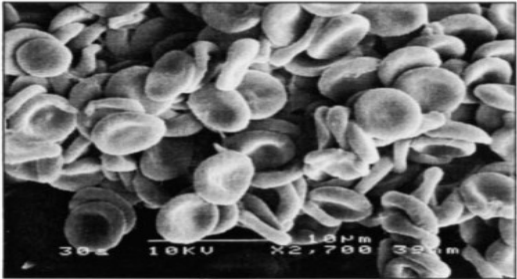
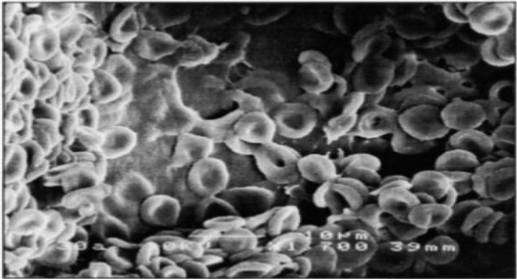
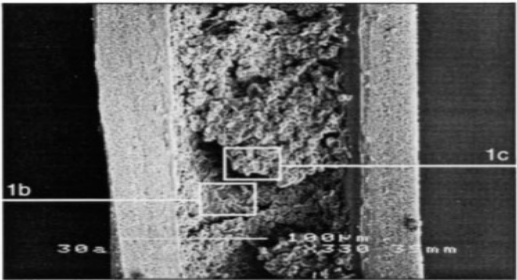
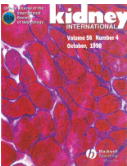
Blood Purif. 2012;34(3-4):336-43.

Kossman RJ, Callan R, Ahmad S. Fifty-five percent heparin reduction is safe with citrate dialysate in chronic dialysis patients [abstract]. American Society of Nephrology Annual Meeting 2006.

Effect of anticoagulation on blood membrane interactions during hemodialysis

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Department of Medical and Chemical Laboratory Diagnostics, Department of Oral and Maxillofacial Surgery, Department of Internal Medicine I (MICU), and Department of Internal Medicine III, Nephrology and Dialysis, University of Vienna, Austria, and Department of Anesthesiology and Intensive Care Medicine, Texas Tech University, Health Science Center, Lubbock, Texas, USA



Κατά τη διάρκεια της διαδικασίας της αιμοκάθαρσης (ΑΜΚ), το αίμα εκτίθεται σε ένα εξωσωματικό κύκλωμα κυκλοφορίας το οποίο ενεργοποιεί διαδικασίες θρομβογένεσης.

Η δημιουργία θρόμβων στο εξωσυστηματικό σύστημα κυκλοφορίας μειώνει την απόδοση της ΑΜΚ και αυξάνει το φόρτο εργασίας του νοσηλευτή και τα κόστη.

Ακόμη και επεισόδια «υποκλινικής» πήξης του κυκλώματος μπορεί να μειώσουν την δραστική επιφάνεια της μεμβράνης και το μέγεθος των πόρων, περιορίζοντας την κάθαρση μικρού και μεσαίου μεγέθους ουσιών.

Επιπλέον, η ενεργοποίηση της οδού της πήξης στους ασθενείς υπό ΑΜΚ μπορεί να σχετίζεται με το φαινόμενο της «χρόνιας φλεγμονής» και της «επιταχυνόμενης» αθηροσκλήρωσης .

Στον Δυτικό κόσμο η «κλασική» ηπαρίνη είναι το πιο δημοφιλές αντιπηκτικό που χρησιμοποιείται για την πρόληψη της πήξης κατά τη διάρκεια της συνεδρίας ΑΜΚ.

Αν και αποτελεσματική και φθηνή, έχει στενό

θεραπευτικό παράθυρο χωρίς επεισόδια ανεπιθύμητων αιμορραγιών. Η ηπαρίνη παρέχει συστηματική αντιπηκτική αγωγή, αντενδείκνυται όμως σε περιπτώσεις ενεργού αιμορραγίας, περικαρδίτιδας, ενδοεγκεφαλικής αιμορραγίας, θρομβοπενίας, και άμεσης μετεγχειρητικής περιόδου. Παράλληλα, η χρήση ηπαρίνης μπορεί να οδηγήσει σε οστεοπόρωση, δυσλιπιδαιμία, υπερκαλιαιμία και την εμφάνιση του συνδρόμου HIT

1. Fischer KG. Essentials of anticoagulation in hemodialysis. *Hemodial Int.* 2007;11(2):178-89.
2. Shen JJ, Winkelmayer WC. Use and safety of unfractionated heparin for anticoagulation during maintenance hemodialysis. *Am J Kidney Dis.* 2012;60(3):473-86.
3. Pawlak K, Naumnik B, Brzosko S, Pawlak D, Mysliwiec M. Oxidative stress - a link between endothelial injury, coagulation activation, and atherosclerosis in haemodialysis patients. *Am J Nephrol.* 2004;24(1):154-61.
4. Cronin RE, Reilly RF. Unfractionated heparin for hemodialysis: still the best option. *Semin Dial.* 2010;23(5):510-5.
5. Brunet P, Simón N, Opris A, Faure V, Lorec-Penet AM, Portugal H, et al. Pharmacodynamics of unfractionated heparin during and after a hemodialysis session. *Am J Kidney Dis.* 2008;51(5):789-95.
6. Wasse H, Gillen DL, Ball AM, Kestenbaum BR, Seliger SL, Sherrard D, et al. Risk factors for upper gastrointestinal bleeding among end-stage renal disease patients. *Kidney Int.* 2003;64(4):1455-61.
7. Chachafi A, Godon JP. Effect of haemodialysis on upper gastrointestinal tract pathology in patients with chronic renal failure. *Nephrol Dial Transplant.* 1987;1(4):233-7.
8. Yang JY, Lee TC, Montez-Rath ME, Paik J, Chertow GM, Desai M, et al. Trends in acute nonvariceal upper gastrointestinal bleeding in dialysis patients. *J Am Soc Nephrol.* 2012;23(3):495-506.
9. Seliger SL, Gillen DL, Longstreth Jr WT, Kestenbaum B, Stehman-Breen CO. Elevated risk of stroke among patients with end-stage renal disease. *Kidney Int.* 2003;64(2):603-9.

Μια εναλλακτική λύση στα παραπάνω προβλήματα αποτελεί η χρήση διαλύματος αιμοκάθαρσης με άνυδρο κιτρικό οξύ (Anhydrous citric acid, CD) σε αντικατάσταση του παραδοσιακού οξικού οξέος (Acetic acid, AD) το οποίο προσφέρει αντιπηξία κατά τη διάρκεια της συνεδρίας AMK.

Υπάρχουν μελέτες παρατήρησης και τυχαιοποιημένες μελέτες που χρησιμοποιούν CD σε ασθενείς υπό AMK.

Η χρήση των CD σχετίζεται με
περιορισμένα επεισόδια θρομβώσεων κατά την συνεδρία AMK
μειωμένες ανάγκες σε ηπαρίνη ,
και αυξημένη κάθαρση μικρού και μεσαίου μοριακού βάρους ουσιών.

Αυτά τα οφέλη προέρχονται από αντιθρομβωτική δράση που περιορίζεται στο εξωσωματικό κύκλωμα χωρίς συστηματική ενεργοποίηση του μηχανισμού πήξης.
Άλλα αναφερόμενα οφέλη από τη χρήση του CD περιλαμβάνουν
μειωμένη οξέωση , μειωμένη φλεγμονή, μειωμένο οξειδωτικό στρες ,
βελτιωμένη αναμία , βελτιωμένη θρέψη , και
αιμοδυναμική σταθερότητα .

Το CD είναι καλά ανεκτό χωρίς ασταθείς μεταβολικές παραμέτρους και χωρίς τεκμηριωμένες ανεπιθύμητες ενέργειες , ακόμη και σε παιδιά,
σε ασθενείς με οξεία νεφρική βλάβη , σε ασθενείς στην μονάδα εντατικής
θεραπείας και σε ασθενείς με προχωρημένη ηπατική ανεπάρκεια.

Ahmad S, Callan R, Cole JJ, Blagg CR. Dialysate made from dry chemicals using citric acid increases dialysis dose. Am J Kidney Dis. 2000;35(3):493-9.
Ahmad S, Callan R, Cole J, Blagg C. Increased dialyzer reuse with citrate dialysate. Hemodial Int. 2005;9(3):264-7.
Kossmann RJ, Gonzales A, Callan R, Ahmad S. Increased efficiency of hemodialysis with citrate dialysate: a prospective controlled study. Clin J Am Soc Nephrol. 2009;4(9):1459-64.
Daimon S, Dan K, Kawano M. Comparison of acetate-free citrate hemodialysis and bicarbonate hemodialysis regarding the effect of intra-dialysis hypotension and post-dialysis malaise. Ther Apher Dial. 2011;15(5):460-5.
Kuragano T, Kida A, Furuta M, Yahiro M, Kitamura R, Otaki Y, et al. Effects of acetate-free citrate-containing dialysate on metabolic acidosis, anemia, and malnutrition in hemodialysis patients. Artif Organs. 2012;36(3):282-90.
Kuragano T, Furuta M, Yahiro M, Kida A, Otaki Y, Hasuiki Y, et al. Acetate-free citrate-containing dialysate increase intact-PTH and BAP levels in the patients with low intact-PTH. BMC Nephrol. 2013;14:18-2369-14-18.
Aniort J, Petitclerc T, Creput C. Safe use of citric acid-based dialysate and heparin removal in postdilution online hemodiafiltration. Blood Purif. 2012;34(3-4):336-43.
Masuda A, Hagiwara S, Tanimoto M, Kodama F, Okumura K, Nohara N, et al. Effects of acetate-free citrate dialysate on glycoxidation and lipid peroxidation products in hemodialysis patients. Nephron Extra. 2012;2(1):256-260

Effect of citrate based dialysate on intradialytic heparin dose in maintenance haemodialysis patients.

I. Griveas, Consultant Nephrologist

Background: During haemodialysis (HD), blood is exposed to an

extracorporeal circuit which activates thrombogenic pathways and clotting and may be associated with increased inflammation and acceleration of atherosclerosis. Even subclinical clotting of the dialysis circuit may reduce effective dialyser surface area and pore size, decreasing both small and middle solute clearance. An alternative to systemic heparin anticoagulation for HD is citrate dialysate (CD) which contains a small amount of citric acid. Aim of our study was to investigate whether CD results in reduced cumulative heparin dose (CHD) compared to acetate dialysate (AD) in HD patients.

Methods: 111 patients receiving HD with AD were recruited in our study. The above study population HD prescription converted to session with CD for a 3 month period. Serum total calcium, albumin, haemoglobin, haematocrit and kt/V were collected at the beginning of the first HD session of the study and in the end of the protocol. After enrolment, data regarding each patient's dose of intradialytic heparin were collected and were evaluated according to a visual clotting score. We compared behavior of our patients on the basis of vascular access type (fistula, graft and central venous catheter), dialysis mode (classic and on-line hemodiafiltration) and age (patients over 65 years old and below 65 years old).





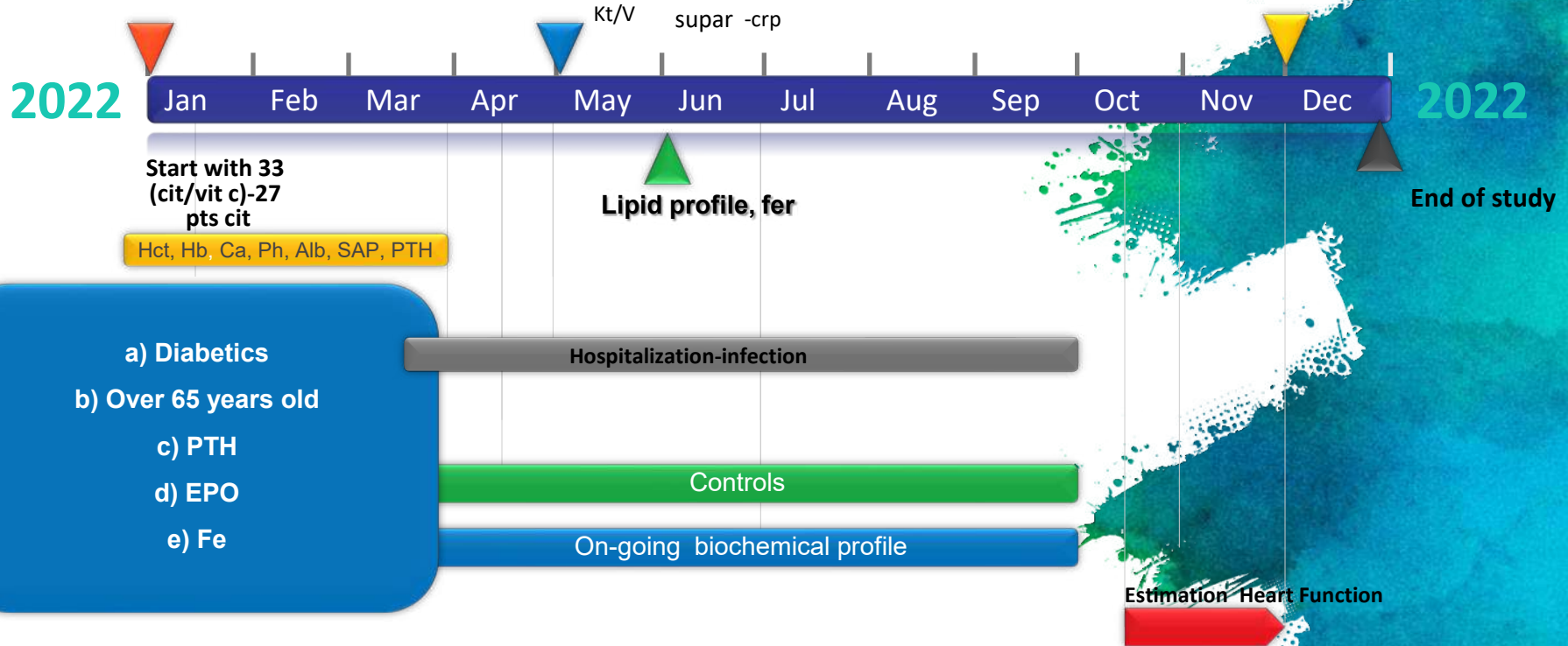
Results: During study period 4329 HD sessions were under notice. 100% of our patients tolerated the procedure with CD well without issues. CHD reduced gradually to 46,57% of the initial dose (from 4429.24 ± 1531.32 to $2080.18 \pm 1.259.51$). None of our patients suffered from bleeding complications. We did not have any HD treatment that had to be abandoned because of clotting in the extracorporeal circuit. Ca levels remained stable through the study period (8.66 ± 0.63 vs 8.57 ± 0.72). Nutrition (albumin 4.19 ± 0.65 vs 4.20 ± 0.63), dialysis adequacy parameters (kt/v 1.25 ± 0.21 vs 1.25 ± 0.24) along with hemoglobin levels (12.36 ± 1.16 vs 12.09 ± 1.06) were stable during the study period. Type of vascular access, dialysis mode and age do not seem to significantly impact the reduction of heparin dose in any way.

Conclusions: Our findings suggested that it is feasible to use CD to dialyse patients safely and effectively, no matter age of patients, dialysis mode or vascular access type. With the contribution of CD, it was possible to anticoagulate the extracorporeal circuit with significant less CHD in a safe and simple manner without minor or major adverse reactions for the patients' clinical condition.



Protocol citrate/ascorbic acid

Estimation heparin dose/restrospective



- × TH-PO262 Poster Thursday
- × Hemodialysis: Volume, Metabolic Complications, Clinical Outcomes
- ×
- × **Experience Comparing the Use of Citric Acid Solution (CD) with L-Ascorbic Acid (Vitamin C) to Simple Citric Solution in Patients with ESRD Under Hemodialysis (HD)**
- × **Ioannis Griveas, et al**
- × Army Share Fund Hospital of Athens, Greece, Dialysis Unit “Polyxenia-Renal” Greece.
- × **The purpose of the study is to record the experience of comparing the use of CD solution with Vitamin-C in relation to the use of pure CD solution in patients with ESRD under HD.**



× **Methods:** 45 patients with ESRD under HD (40 new entrants) receiving CD solution with vitamin-C (2g/lt) for a period of 12 months were compared with 26 patients (18 newentrants) of the same weight who received plain CD solution. Changes in heparin dose as well as the anemia profile of the patients were recorded.

×

× **Results:** In the vitamin C solution the initial cumulative dose of heparin 1818 ± 659.28 iu (24 iu/kgBW) to 3323.52 ± 1467.79 iu (44 iu/kgBW) at 12 months.

× With no observed thrombotic events or bleeding tendency, the heparin dose was significantly reduced from classically recommended doses (loading dose 30-50 IU/kgBW and then 10 IU/kgBW/hour).

× A corresponding observation was also noted in pure CD (29 iu/kgBW beginning-39 iu/kgBW end).

- × Hb and Hct increased significantly (10.63 ± 1.55 start- 11.79 ± 0.91 end, $p < 0.05$, 32.25 ± 4.45 start- 36.5 ± 2.92 end, $p < 0.05$) with constant weekly dose of erythropoietin (14000 ± 9500 iu start- 14000 ± 10000 iu end, $p = \text{NS}$) and constant ferritin levels (526.73 ± 498.72 iu start- 690.44 ± 470.32 in end, $p = \text{NS}$).
- × The above notice was combined with a significant reduction in monthly iron administration (200 mg monthly final dose).
- × In CD without Vitamin-C we had corresponding observations with a consistently significantly higher dose of monthly iron administration (400-500 mg final dose).
- ×

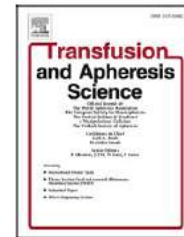
- × **Conclusions:** Our findings suggest that the use of both solutions provides anticoagulation with a significant decrease in heparin while simultaneously increasing hemoglobin with a fixed dose of erythropoietin.
- × The addition of vitamin C is associated with reduced monthly iron intake.



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Transfusion and Apheresis Science

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Citrate, a green alternative to heparin

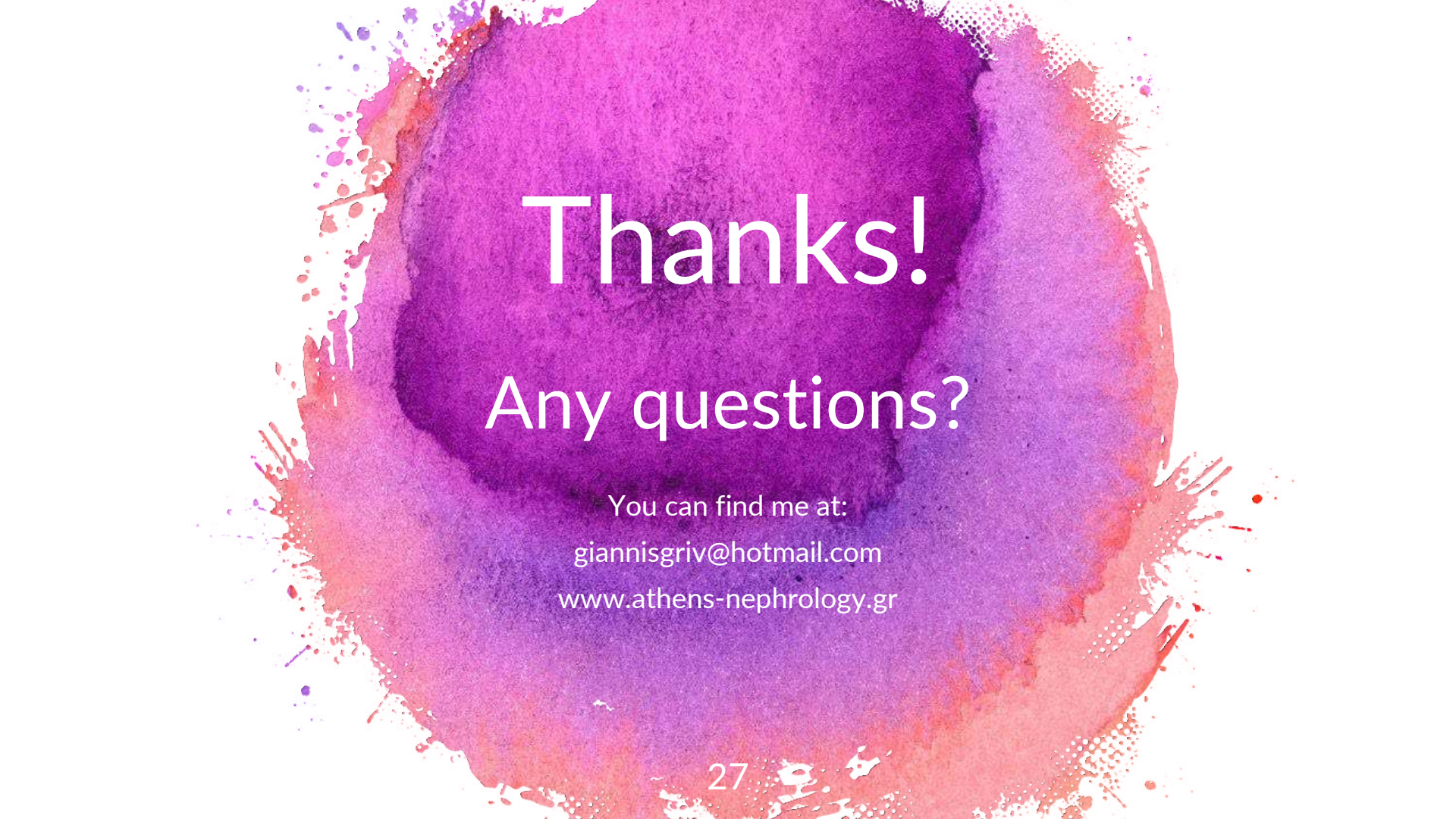
Ioannis Griveas^{*}

Nephrology Department, Army Share Fund Hospital of Athens, 417 NIMTS, Greece, Private Dialysis Unit "Polyxenia-Renal", Athens, Greece

The issue regarding heparin is the external and the internal environment. The raw material for heparin is the intestinal mucosa of pigs. The waste, nearly equal to the weight of the raw material, is the greatest source of pollution. Solvents and detergents can cause air and water pollution [5]. Based on the usual heparin dose of 5000 IU of unfractionated heparin or 5000 IU of dalteparin, a low molecular weight heparin, 1 pig has to be slaughtered per 13 dialysis sessions. The carbon footprint of raising 1 pig is about 670 kg CO₂ equivalent, which poses a serious threat to the external environment [6]. As is mentioned in the introduction, heparin also has a significant impact on the internal environment. Activated monocytes release proinflammatory cytokines associated with arteriosclerosis [7].

The use of citrate is safe, effective and may be a good alternative for patients with blood disorders that have to receive therapy under an extrarenal circuit.





Thanks!

Any questions?

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KIDNEY DISEASE OUTCOMES
QUALITY INITIATIVE

National Kidney Foundation



Academy of Nutrition
and Dietetics

KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CKD: 2020 UPDATE

T. Alp Ikizler, Jerrilynn D. Burrowes, Laura D. Byham-Gray, Katrina L. Campbell, Juan-Jesus Carrero, Winnie Chan, Denis Fouque, Allon N. Friedman, Sana Ghaddar, D. Jordi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple, Daniel Teta, Angela Yee-Moon Wang, and Lilian Cuppari

5.2 Statement on Vitamin C

Vitamin C Supplementation

5.2.1 In adults with CKD 1-5D or posttransplantation who are at risk of vitamin C deficiency, it is reasonable to consider supplementation to meet the recommended intake of at least 90 mg/d for men and 75 mg/d for women (*OPINION*).

**KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN
CKD: 2020 UPDATE**

T. Ali Azizi, Jennifer D. Burrows, Laura D. Bryham-Gray, Katrina L. Campbell, Juan Jesus Camero, Winnie Chan,
Dana Figueira, Allan H. Friedman, Sara Ghaderi, D. Jodi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple,
Daniel Teis, Angela Yee-Moon Wang, and Lilian Cuppatt

Rationale/Background

There are currently limited studies identifying daily vitamin C requirements for individuals with CKD at all stages of the disease. Amount of daily intake and optimal serum level of vitamin C required to maintain nutritional health, reverse deficiency, and avoid toxicity are unclear. Studies included for this current review evaluated the effect of vitamin C supplementation on nutritional status, inflammation, anthropometrics, micronutrient levels, electrolyte levels, fluid status, serum uric acid levels, lipid levels, morbidity events, QoL, mortality, and hospitalizations. Limited data from a very small number of studies prohibit definitive evidence-based conclusions for all these surrogate and hard outcomes. Therefore, we suggest that individualized decision making is the best clinical approach to determine whether vitamin C supplementation, or termination of supplementation, is required for adults with CKD stages 1-5D and posttransplant.

**KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN
CKD: 2020 UPDATE**

T. Ali Azizi, Jennifer D. Burrows, Laura D. Byham-Gray, Katrina L. Campbell, Juan Jesus Camero, Winnie Chan,
Dana Figueira, Allan H. Friedman, Sara Ghaderi, D. Jodi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple,
Daniel Teis, Angela Yee-Moon Wang, and Lilian Cuppatt

Special Discussions

Current nutritional requirements or Recommended Dietary Intake of vitamin C for individuals with CKD stages 1-5D and posttransplant are not known and are based on those from the general population. The prevalence of vitamin C deficiency may vary according to CKD stage and dialysis modality. Toxicity is a possible concern for excessive vitamin C supplementation.

However, these findings do not preclude the importance of assessing for vitamin C supplementation or when to discontinue supplementation. Ongoing monitoring of overall food intake and nutrition status is required to assess for vitamin C deficiency. An individualized approach to evaluation and monitoring of vitamin C status is ideally accomplished by a multidisciplinary care team that includes nephrologist, nurse practitioner, physician assistant, and RDN.

**KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN
CKD: 2020 UPDATE**

*T. Ali Azizi, Jemilyn D. Burrows, Laura D. Byham-Gray, Katrina L. Campbell, Juan Jesus Camero, Winnie Chan,
Dana Fougere, Allan H. Friedman, Sara Ghaddar, D. Jodi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple,
Daniel Teta, Angela Yee-Moon Wang, and Lilian Cuppatt*

Implementation Considerations

- Initiation and cessation of vitamin C supplementation, as well as supplementation dose, should take into account the individual's nutritional status, dietary intake, comorbid conditions, and dialysis modality.
- Suggested vitamin intake should be based on recommendations for the general population (eg, RDA) unless there are specific considerations requiring modification.

**KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN
CKD: 2020 UPDATE**

T. Ali Ruzic, Jemilyn D. Burrows, Laura D. Byham-Gray, Katrina L. Campbell, Juan Jesus Camero, Winnie Chan,
Dana Figue, Allan H. Friedman, Sara Ghaderi, D. Jodi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple,
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Monitoring and Evaluation

Higher doses of vitamin C supplementation (500 mg daily) have been shown to increase serum oxalate levels. Vitamin C is a potent physiologic antioxidant. Lipid metabolism may be affected by vitamin C supplementation and patients receiving vitamin C supplementation should have lipid fractions monitored. Vitamin C also affects immune function and carnitine metabolism. Patients with any malabsorption or diseases of an inflammatory nature may be more prone to having lower plasma vitamin C levels than the general population. Therefore, supplementation dose should take into consideration medical history, comorbid conditions, and concomitant medications. Measurement of serum oxalate may be considered in patients prescribed high doses of vitamin C and/or who are susceptible to calcium oxalate stone formation.

Future Research

- Identify methods to assess vitamin C status. Current methods use serum levels of vitamin C, but reliability is unclear.
- Ascertain the optimal vitamin C status of the CKD population, including CKD stages 1-5D and those with a kidney transplant.
- Confirm the RDA for vitamin C in various CKD populations and the supplemental vitamin C dose that will prevent vitamin C deficiency without increasing risk for toxicity.
- If feasible, evaluate the effect of vitamin C supplementation on hard outcomes, including survival, hospitalization, cardiovascular events, and QoL measures with RCTs in CKD populations.

Ascorbic Acid Depletion in Patients Undergoing Chronic Hemodialysis¹

JOHN F. SULLIVAN,² M.D., AND ALBERT B. EISENSTEIN,³ M.D.

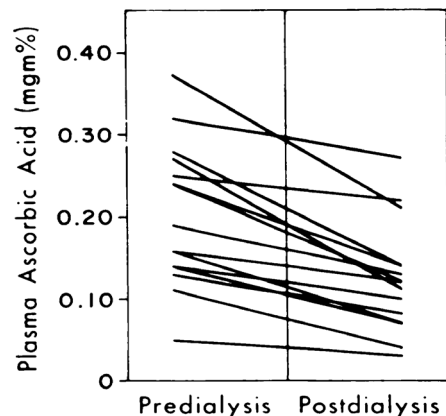


FIG. 1. Effect of hemodialysis on plasma ascorbic acid levels in patients not receiving vitamin C supplements. Each line represents the dialysis of one patient and plasma ascorbic acid levels immediately before and after dialysis.

Ascorbic acid is removed from the plasma of patients undergoing hemodialysis. Patients with chronic renal disease who were not receiving vitamin C supplementation demonstrated a mean decline in plasma ascorbic acid of $40 \pm 4\%$ during hemodialysis, whereas the mean decline in patients receiving vitamin C supplements was $68 \pm 4\%$. Removal of

Summary and conclusions

Dietary restriction, concerns about oxalosis, losses during dialysis and accelerated catabolism have created a situation where a large portion (10–25%) of dialysis patients have plasma vitamin C levels $<10\text{ }\mu\text{M}$, and some patients have plasma vitamin C $<2\text{ }\mu\text{M}$ [6] (Handelman, in preparation).

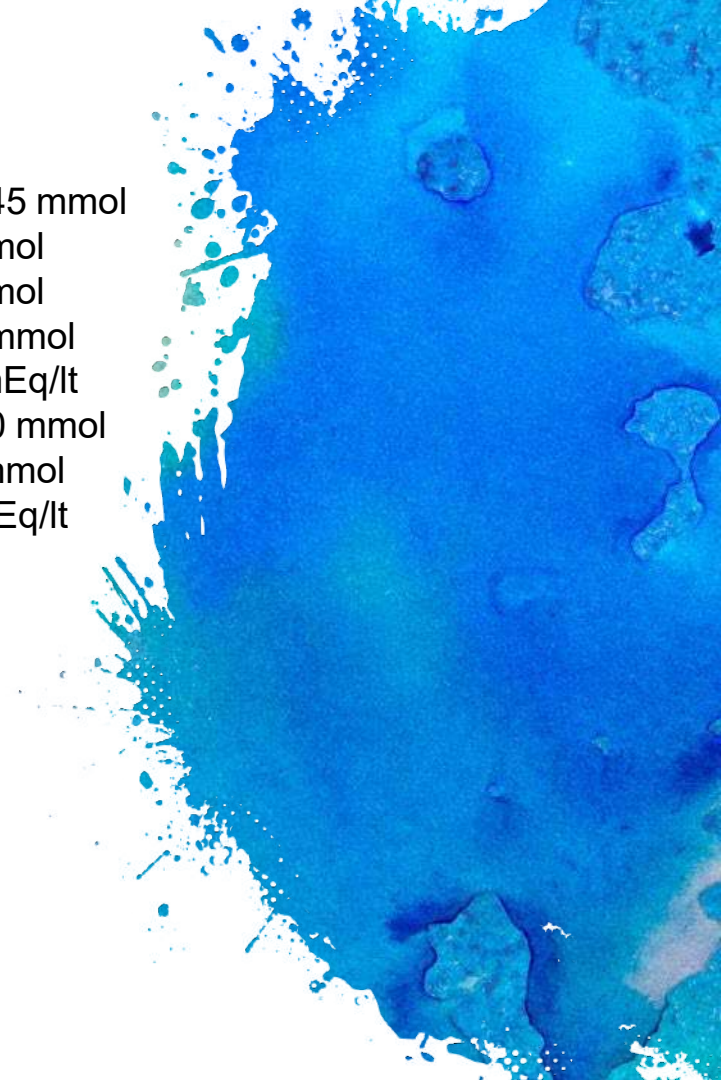
Epidemiological data suggest that these low plasma vitamin C levels are associated with increased mortality [41]. Although a 60–100 mg daily vitamin C supplement is generally recommended, prescriptions are provided only to 10–70% of patients, depending on nationality [42]. Lack of compliance may lead to even lower levels of actual vitamin C usage. Standardized clinical methods for measuring plasma vitamin C are needed, since the instability of vitamin C leads to problems in laboratory analysis [43,44], and vitamin C is not routinely measured in dialysis

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Advance Access publication 14 November 2006

Vitamin C deficiency in dialysis patients—are we perceiving the tip of an iceberg?

Garry J. Handelman

α.	Νατρίου (Sodium)	130-145 mmol
β.	Καλίου (Potassium)	0-3 mmol
γ.	Ασβεστίου (Calcium)	0-2 mmol
δ.	Μαγνησίου (Magnesium)	0-1,2 mmol
ε.	Οξικών (Acetate)	0,30 mEq/lt
στ.	Χλωριούχων (Chloride)	90-120 mmol
ζ.	Γλυκόζης (Glucose)	0-12 mmol
η.	Κιτρικών (Citrate)	0,8 mEq/lt



ΟΞΙΝΟ ΔΙΑΛΥΜΑ ΑΙΜΟΚΑΘΑΡΣΗΣ ΜΕ L-ΑΣΚΟΡΒΙΚΟ ΟΞΥ (ΒΙΤΑΜΙΝΗ C)

1. Όξινο διάλυμα Αιμοκάθαρσης εμπλουτισμένο με 2g/l L-Ασκορβικό οξύ (Βιταμίνη-C) προσφέρει αποτελεσματική αντιμετώπιση του **οξειδωτικού** stress (ελεύθερες ρίζες), διατήρηση-αύξηση επιπέδων αιματοκρίτη και αιμοσφαιρίνης των ασθενών.

2. Όξινο διάλυμα αιμοκάθαρσης εμπλουτισμένο με 2g/l L-Ασκορβικό οξύ (Βιταμίνη-C) προσφέρει προστασία από τις ελεύθερες ρίζες στο σημείο επαφής της μεμβράνης του φίλτρου με το αίμα χωρίς να εισέλθει **στο** διαμέρισμα του αίματος.

3. Διάλυμα αιμοκάθαρσης σύμφωνα με τις αξιώσεις 1 & 2 το οποίο περιέχει

χλωριούχο νάτριο, χλωριούχο κάλιο, χλωριούχο ασβέστιο διυδρικό, χλωριούχο μαγνήσιο εξαυδρικό, δεξτρόζη και οξικό οξύ.

1. Αραιωμένο διάλυμα αιμοκάθαρσης σύμφωνα με τις αξιώσεις 1,2 & 3 όπου οι τελικές συγκεντρώσεις κυμαίνονται εντός των κάτωθι ορίων σε mmol/l

α)	Νάτριο (Sodium)	130-145 mmol
β)	Κάλιο (Potassium)	0-3mmol
γ)	Ασβέστιο (Calcium)	0-2 mmol
δ)	Μαγνήσιο (Magnesium)	0-1,2mmol
ε)	Χλωριούχων (Chloride)	90-120 mmol
στ)	Οξικών (Acetate)	2,5-10 mmol
ζ)	Γλυκόζης (Glucose)	0-12 mmol
η)	L Ασκορβικό οξύ (Βιταμίνη-C)	0,32 mmol

1. Διάλυμα αιμοκάθαρσης σύμφωνα με τις αξιώσεις 1,2 & 3 το οποίο

αναμιγνύεται σε συσκευή τεχνητού νεφρού με φύσιγγα ή σάκο όξινου ανθρακικού νατρίου.

THE EFFICACY OF ASCORBATE-RICH DIALYSATE TO ATTENUATE ANAEMIA IN MAINTENANCE HEMODIALYSIS PATIENTS

Ioannis Griveas, MD, PhD

Nephrology Department 417 Army Share Fund Hospital (NIMTS), Athens, Greece

Hemodialysis (HD) patients with functional iron deficiency (FID) often develop resistance to recombinant human erythropoietin (Epo). The contributory role of chronic inflammation and oxidative stress in its pathogenesis is poorly understood. Recent studies have shown that intravenous ascorbic acid (IVAA) administration could override rhEPO resistance in HD patients. Yet little is known about whether supplementation of ascorbic acid (vitamin C) via extracorporeal circuit has

substantial effects on minimizing oxidative impairment and thus improving Hb levels. This study was undertaken to test the efficacy of Ascorbate-Rich Dialysate to Attenuate anaemia in Maintenance HD Patients.

Νάτριο (Sodium)	130-145 mmol
β) Κάλιο (Potassium)	0-3 mmol
γ) Ασβέστιο (Calcium)	0-2 mmol
δ) Μαγνήσιο (Magnesium)	0-1,2 mmol
ε) Χλωριούχων (Chloride)	90-120 mmol
στ) Οξικών (Acetate)	2,5-10 mmol
ζ) Γλυκόζης (Glucose)	0-12 mmol
η) L Ασκορβικό οξύ (Βιταμίνη-C)	0,32 mmol

Roadmap

Effect of citrate based dialysate on anticoagulation in maintenance haemodialysis patients.



THE EFFICACY OF ASCORBATE-RICH DIALYSATE TO ATTENUATE ANAEMIA IN MAINTENANCE HEMODIALYSIS PATIENTS



USE OF ASCORBATE-RICH DIALYSATE IN HEMODIALYSIS PATIENTS

Η ΕΠΙΔΡΑΣΗ ΟΞΙΝΟΥ ΚΙΤΡΙΚΟΥ ΔΙΑΛΥΜΑΤΟΣ ΑΙΜΟΚΑΘΑΡΣΗΣ ΣΤΗΝ ΑΝΤΙΠΗΚΤΙΚΗ ΑΓΩΓΗ ΑΣΘΕΝΩΝ ΜΕ ΧΡΟΝΙΑ ΝΕΦΡΙΚΗ ΝΟΣΟ ΤΕΛΙΚΟΥ ΣΤΑΔΙΟΥ ΥΠΟ ΑΙΜΟΚΑΘΑΡΣΗ
19ο Πανελλήνιο Συνέδριο Νεφρολόγας

Effect of citrate based dialysate on intradialytic heparin dose in maintenance haemodialysis patients.



Future Projects

Roadmap



1

Red is the colour of
danger and courage

3

Black is the color of
ebony and of outer space

5

2

Yellow is the color of
gold, butter and ripe
lemons

4

White is the color of milk
and fresh snow

6

Blue is the colour of the
clear sky and the deep
sea

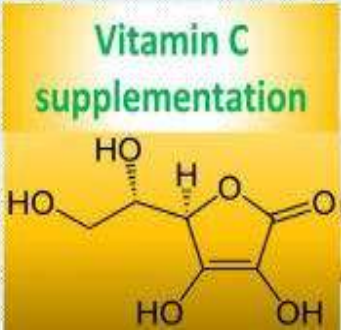
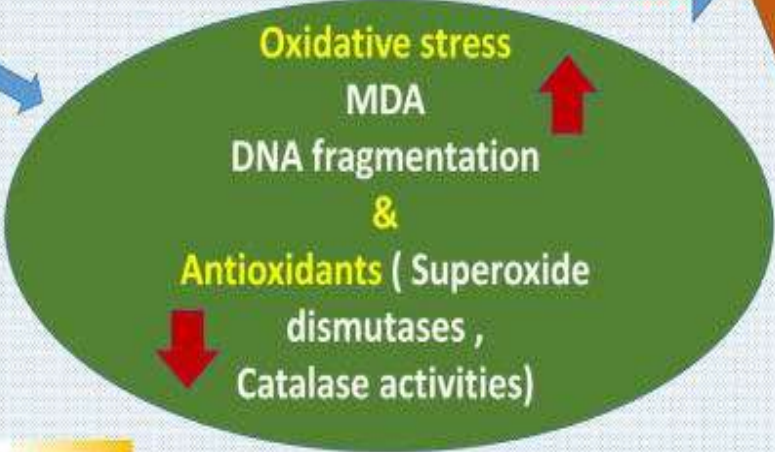
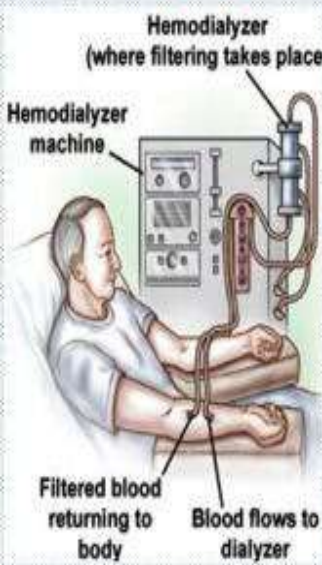
13 HD patients (mean age: 71.3 ± 14.6 years) were recruited for the study. For a period of 8 months they were receiving Ascorbate-Rich Dialysate (2g/L) and we compared their anaemia profile (Hb, Hct, ferritin, TSAT, rhEPO dose) during this period with the previous 8 months that they were receiving conventional dialysate. Additionally we evaluated their "chronic inflammation status" estimating CRP and Soluble Urokinase Plasminogen Receptor (Supar) levels over the study period and also lipids and nutritional profile.



CRP levels declined with the use of ascorbate-rich dialysate from 12.28 to 3.86 mg/L while supar levels remained stable over the whole study period (15 mg/ml). Mean Hct levels increased significantly from $35.56 \pm 2.37\%$ with conventional dialysate to $39.98 \pm 3.64\%$ with 8 months usage of ascorbate-rich dialysate ($p < 0.05$). The above notice started to appear even after 3 months under vitamin C-rich dialysate (35.56 ± 2.37 vs 37.96 ± 3.06 , $p < 0.05$). The same conclusion was noticed with Hb levels (11.23 ± 0.94 vs 12.10 ± 1.04 , $p < 0.05$ after 3 months under vit c, 11.23 ± 0.94 vs 12.59 ± 1.38 , $p < 0.05$ after 8 months under vitamin C). Mean rhEPO dose (darbepoetin alfa) decreased from 48.63 to 33.46 mcg/mL per week with usage of ascorbate-rich dialysate. Ferritin (>500), albumin, TSAT (>20) and PTH levels remained stable over the whole study period. Cholesterol, triglycerides and albumin levels did not change significantly with the change of the conventional dialysate to ascorbic-rich one.

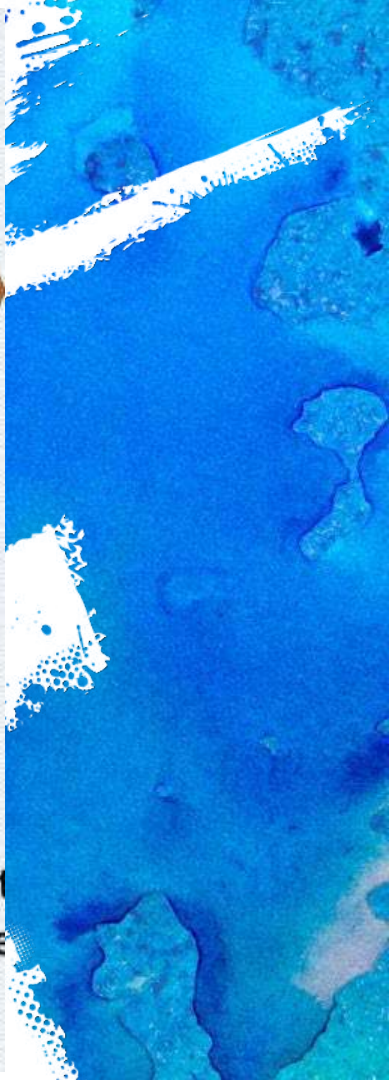
Although our study is limited by small numbers of subjects, short durations of follow-up, these results suggest that compared with standard care, ascorbic acid in dialysate bath may result in an increase in hemoglobin concentration and decrease in rHuEPO requirements. Longer term studies are required to confirm these results, provide information about adverse events, and determine whether these changes translate into improved patient outcomes and cost-effectiveness.

Hemodialysis process



↑ **Mortality**
Morbidity
Hospitalization

↓ **Patient outcome**



Because of the nonspecific nature of many of the symptoms of vitamin C deficiency (fatigue, weakness, poor connective tissue, mental disturbances, anemia), it is possible that subclinical or unrecognized vitamin C deficiency contributes to the disturbances as part of the uremic syndrome in people with low GFR or people on dialysis.

(145). Many vitamin-C-rich foods are also high in potassium, which may lead to their restriction in patients with advanced renal failure and in those on dialysis. Another cross-sectional study estimated dietary intake from dietary records at 94 mg/day in patients with low GFR and 66 mg/day in patients

2 mg/l (149). In addition to low dietary intake, the dialysis procedure also contributes to deficiency: removal of this water-soluble nonprotein-bound small molecule has been estimated at mean 66 mg per HD session (150) and 29 mg per PD exchange

Absorption and Bioavailability

Vitamin C is absorbed actively and passively, and is highly bioavailable, with 75–90% absorbed in a typical diet. Absorption may fall to as low as 16% in people who are vitamin C-replete who have high intakes (139).

Vitamin C (ascorbic acid) is a water-soluble vitamin produced from metabolism of glucose. Only the

A number of critical roles for vitamin C have been identified: it is a cofactor in pathways for collagen synthesis, explaining many of the clinical manifestations of scurvy. It is a potent antioxidant, perhaps the most quantitatively important free radical scavenger in blood (135).

Original Article

Convective and diffusive losses of vitamin C during haemodiafiltration session: a contributive factor to oxidative stress in haemodialysis patients

Marion Morena¹, Jean-Paul Cristol¹, Jean-Yves Bosc², Ciro Tetta³, Gilles Forret¹, Claude-Louis Leger¹, Cécile Delcourt⁴, Laure Papoz⁴, Bernard Descomps¹ and Bernard Canaud²

plasma vit C concentration was significantly reduced at the end of HDF session. Moreover, the higher plasma vit C concentration at the start of session, the more important was the vit C loss during the HDF process leading in all cases to a drastic vit C depletion at the

**Nephrology
Dialysis
Transplantation**

increased rate of vit C oxidation during dialysis session has been recently confirmed by Clermont *et al.* [35]. According to the data, it is essential to accurately estimate the vit C requirement for HD population: a daily dose of 100–200 mg is recommended in some reports [19,20,36]. Costello *et al.* [33] reported that oral supplementation not exceeding 150 mg/day (1050 mg weekly) was still considered a safe dose. This supplementation overwhelms our estimation of 200 mg weekly of vit C losses which does not take into account the potential contribution of dietary restriction or intestinal malabsorption. However, it is interesting to note that vit C losses are directly linked to plasma levels. Thus, an important supplementation at the end of dialysis session could lead to a transient increase in vit C which could be abolished during the next HD session. Thus, it would be better to supply vit C by dialysate during HD session. Among different vit C

USE OF ASCORBATE-RICH DIALYSATE IN HEMODIALYSIS PATIENTS

Ioannis Griveas, MD, PhD

Nephrology Department 417 Army Share Fund Hospital (NIMTS), Athens, Greece

Background and Aims: Increments of oxidative stress have been addressed as one potential cause for the accelerated atherosclerosis of chronic kidney disease patients. Ascorbate (vitamin-C) represents one of the most prominent antioxidants both in plasma and intracellularly. Unsupplemented dialysis patients have reportedly lower plasma levels of ascorbate in comparison to healthy controls, mostly due to a loss into the dialysate. Purpose of our study was the recording of the experience of the use of Ascorbate-Rich Dialysate in patients under hemodialysis (HD).

Method: 11 HD patients were recruited for the study. During a period of 8 weeks they were receiving Ascorbate-Rich Dialysate (2g/l). Ascorbic acid levels were estimated before and at the end of the study period. We also monitored patients' anemia profile (Hb, Hct, ferritin, TSAT, rhEPO dose), lipid and nutrition status.

Results: Ascorbic acid values were towards the lower accepted levels in our patients (3.25 ± 1.01 mg/l) at the beginning of the study period. After 8 weeks receiving Ascorbate-Rich Dialysate, ascorbic-acid levels were significantly increased (6.87 ± 1.50 mg/l) without transcending the upper accepted limit. During the notice period, our patients were behaved normally without any sort of adverse events. Mean Hct levels remained stable ($39.10 \pm 3.70\%$ with conventional dialysate vs $39.67 \pm 1.59\%$ with usage of ascorbate-rich dialysate). The same conclusion was noticed with Hb levels (12.85 ± 1.20 vs 13.15 ± 0.49). Mean rhEPO dose per week (epoetin- alfa) decreased (9000 ± 5200 iu vs 6250 ± 4300 iu, $p=NS$) and administration of Fe stopped to all of our patients. Ferritin (>700), TSAT (>35) remained stable over the whole study period. Cholesterol, triglycerides and albumin levels did not change significantly with the change of the conventional dialysate to ascorbic-rich one.





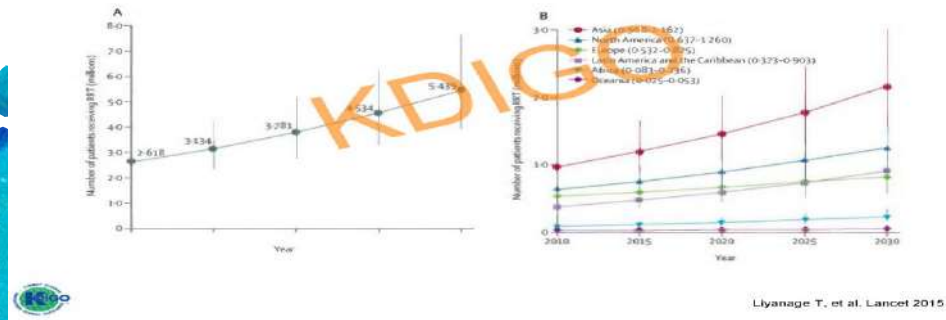
Big concept

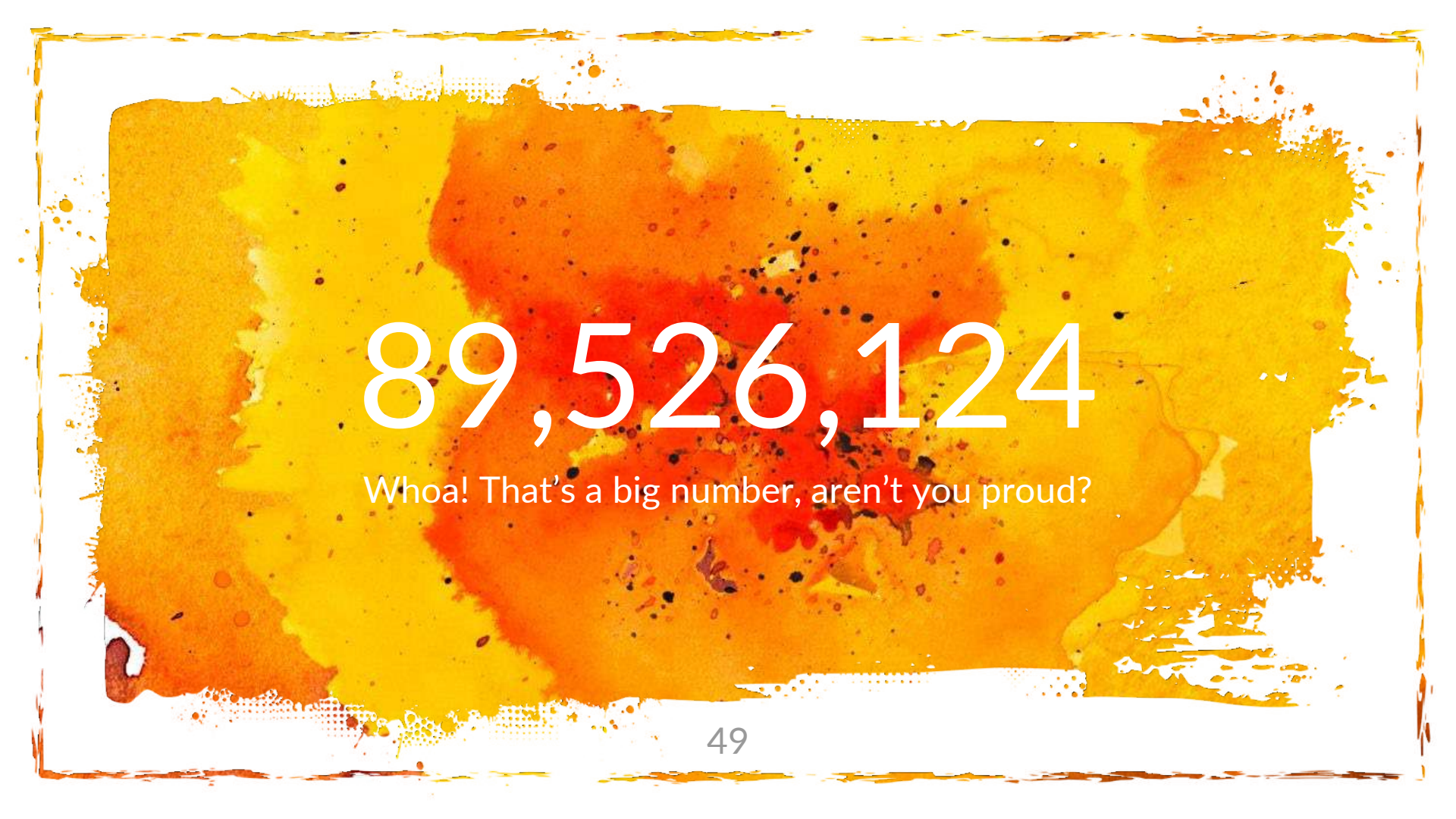
Bring the attention of your audience over a key
concept using icons or illustrations

And tables to compare data

	A	B	C
Yellow	10	20	7
Blue	30	15	10
Orange	5	24	16

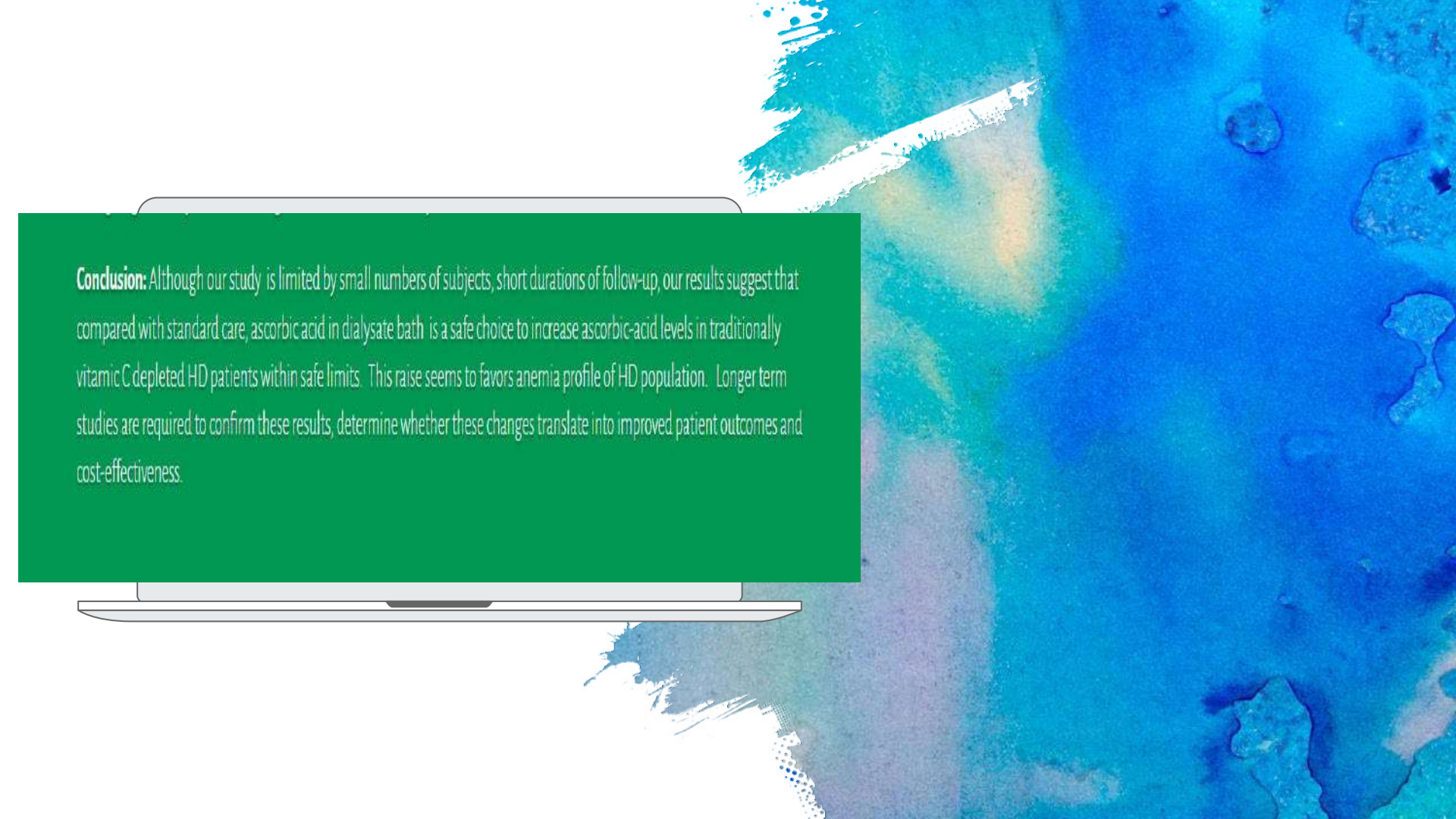
Estimated number of patients undergoing RRT from 2010 to 2030 worldwide (A) and by region (B)



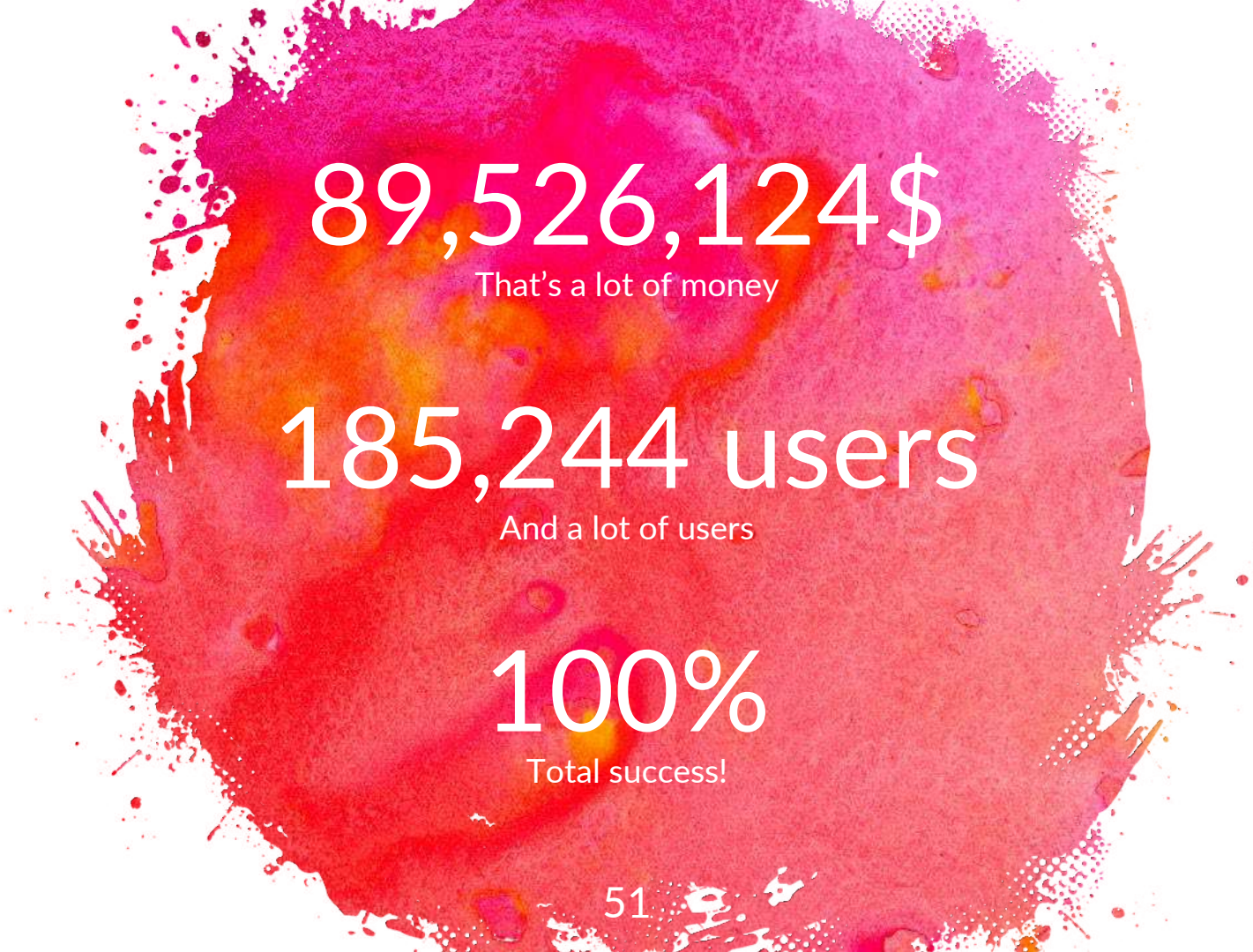


89,526,124

Whoa! That's a big number, aren't you proud?



Conclusion: Although our study is limited by small numbers of subjects, short durations of follow-up, our results suggest that compared with standard care, ascorbic acid in dialysate bath is a safe choice to increase ascorbic-acid levels in traditionally vitamin C depleted HD patients within safe limits. This raise seems to favors anemia profile of HD population. Longer term studies are required to confirm these results, determine whether these changes translate into improved patient outcomes and cost-effectiveness.



89,526,124\$

That's a lot of money

185,244 users

And a lot of users

100%

Total success!

Future Research

- Identify methods to assess vitamin C status. Current methods use serum levels of vitamin C, but reliability is unclear.
- Ascertain the optimal vitamin C status of the CKD population, including CKD stages 1-5D and those with a kidney transplant.
- Confirm the RDA for vitamin C in various CKD populations and the supplemental vitamin C dose that will prevent vitamin C deficiency without increasing risk for toxicity.
- If feasible, evaluate the effect of vitamin C supplementation on hard outcomes, including survival, hospitalization, cardiovascular events, and QoL measures with RCTs in CKD populations.

Our process is easy



Let's review some concepts

Yellow

Is the color of gold, butter and ripe lemons. In the spectrum of visible light, yellow is found between green and orange.

Blue

Is the colour of the clear sky and the deep sea. It is located between violet and green on the optical spectrum.

Red

Is the color of blood, and because of this it has historically been associated with sacrifice, danger and courage.

Yellow

Is the color of gold, butter and ripe lemons. In the spectrum of visible light, yellow is found between green and orange.

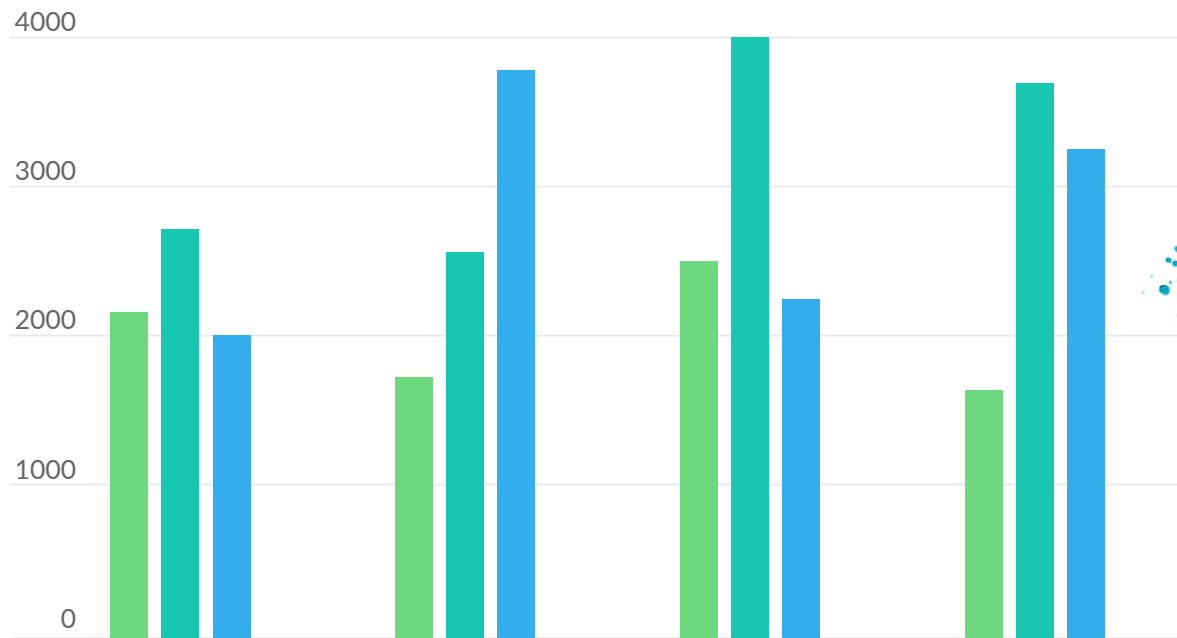
Blue

Is the colour of the clear sky and the deep sea. It is located between violet and green on the optical spectrum.

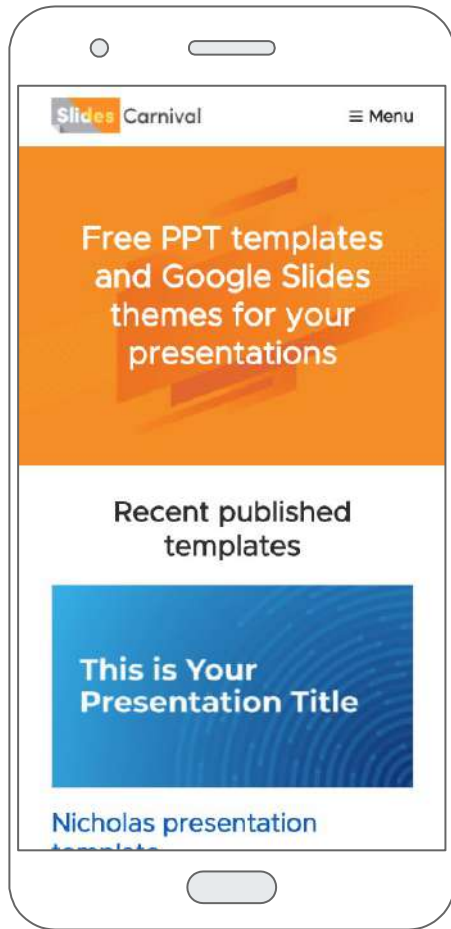
Red

Is the color of blood, and because of this it has historically been associated with sacrifice, danger and courage.





You can insert graphs from Excel or Google Sheets



Mobile project

Show and explain your web, app or software projects using these gadget templates.

Future Research

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Tablet project

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Special thanks to all the people who made and released these awesome resources for free:

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- × Photographs by [Unsplash](#)
- × Watercolor textures by [GraphicBurguer](#)

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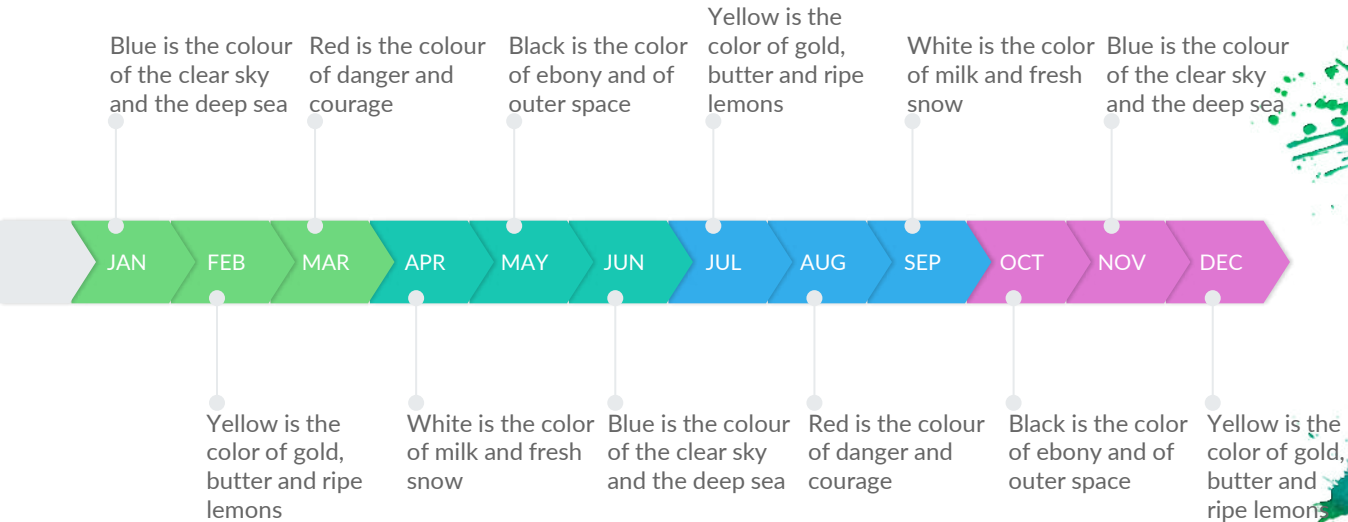
- × Titles: Lato Thin
- × Body copy: Lato Light

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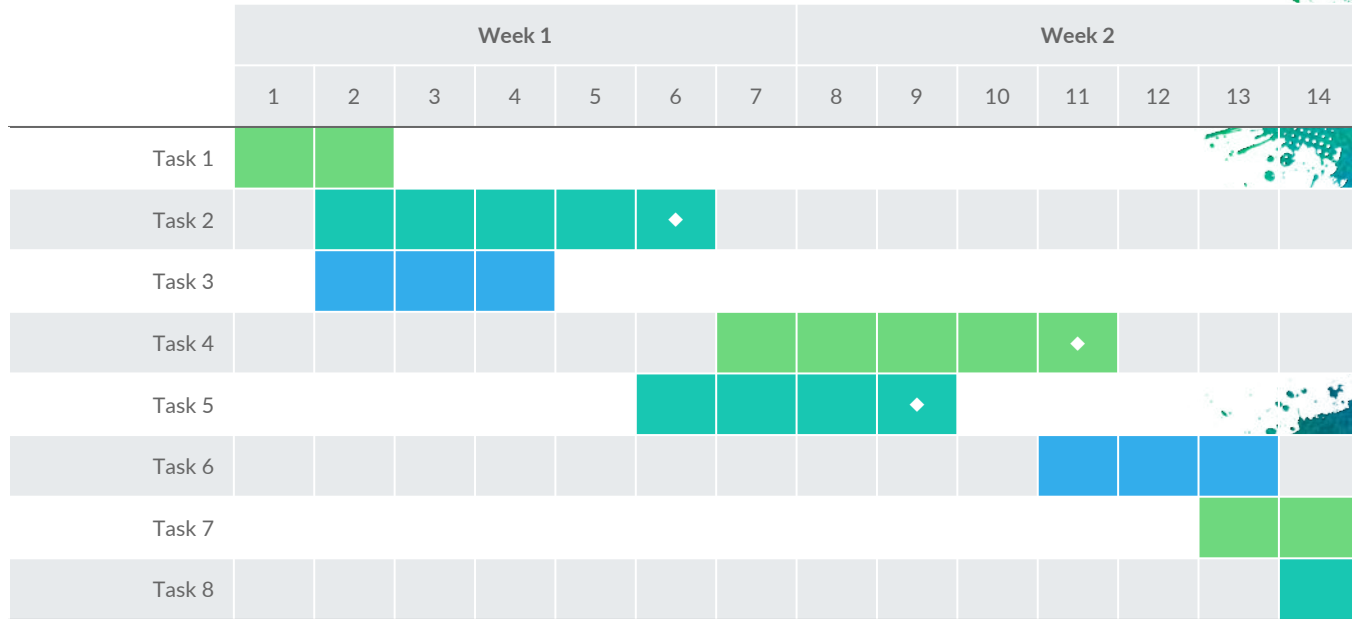
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Timeline



Gantt chart



SWOT Analysis

STRENGTHS

Blue is the colour of the clear sky and the deep sea

S

W

WEAKNESSES

Yellow is the color of gold, butter and ripe lemons

O

T

Black is the color of ebony and of outer space

White is the color of milk and fresh snow

OPPORTUNITIES

THREATS

Business Model Canvas

Key Partners



Insert your content

Key Activities



Insert your content

Value Propositions



Insert your content

Customer Relationships



Insert your content

Customer Segments



Insert your content

Key Resources



Insert your content

Channels



Insert your content

Cost Structure



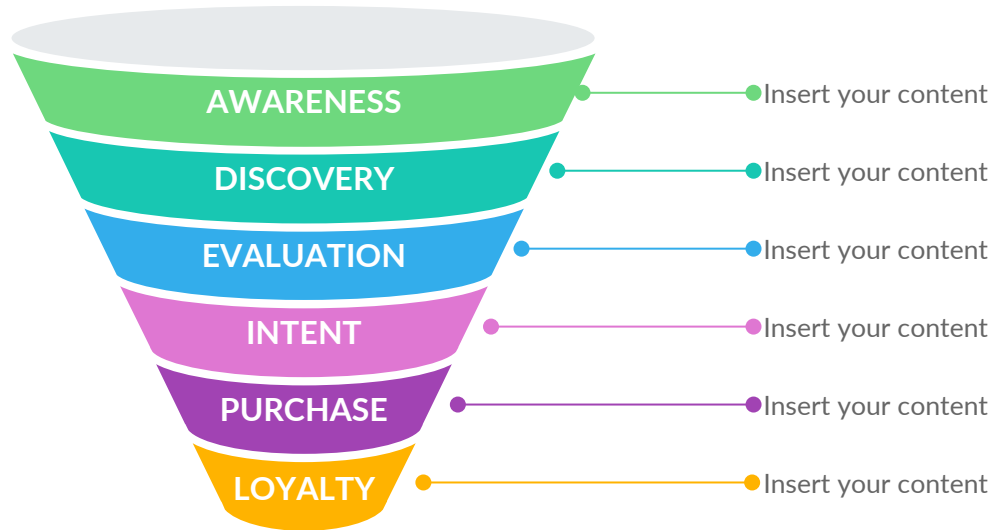
Insert your content

Revenue Streams



Insert your content

Funnel



Team Presentation



Imani Jackson

JOB TITLE

Blue is the colour of the
clear sky and the deep
sea



Marcos Galán

JOB TITLE

Blue is the colour of the
clear sky and the deep
sea



Ixchel Valdía

JOB TITLE

Blue is the colour of the
clear sky and the deep
sea



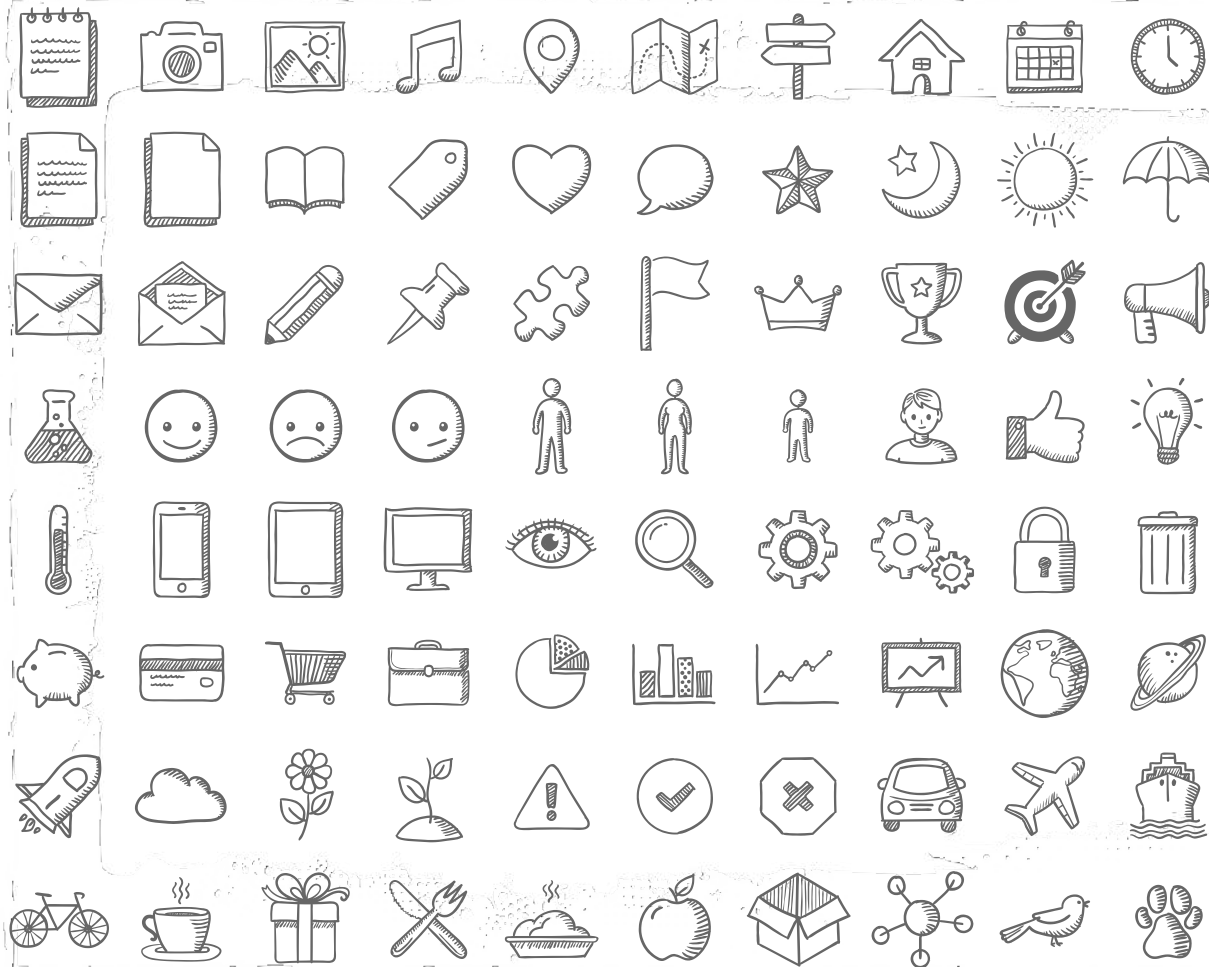
Nils Årud

JOB TITLE

Blue is the colour of the
clear sky and the deep
sea

Weekly Planner

	SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
09:00 - 09:45	Task	Task	Task	Task	Task	Task	Task
10:00 - 10:45	Task	Task	Task	Task	Task	Task	Task
11:00 - 11:45	Task	Task	Task	Task	Task	Task	Task
12:00 - 13:15	✓ Free time	✓ Free time	✓ Free time	✓ Free time	✓ Free time	✓ Free time	✓ Free time
13:30 - 14:15	Task	Task	Task	Task	Task	Task	Task
14:30 - 15:15	Task	Task	Task	Task	Task	Task	Task
15:30 - 16:15	Task	Task	Task	Task	Task	Task	Task



SlidesCarnival icons are editable shapes.

This means that you can:

- Resize them without losing quality.
- Change fill color and opacity.

Isn't that nice? :)

Examples:



Diagrams and infographics



You can also use any emoji as an icon!

And of course it resizes without losing quality.

How? Follow Google instructions <https://twitter.com/googledocs/status/73008724015664332>



and many more...



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Google Slides



100% free for personal
or commercial use



Ready to use,
professional and
customizable



Blow your audience
away with attractive
visuals