

PROFESSOR GEORGE NICHOLSON

Memorial Lecture



Nephrology Challenges in the Caribbean - 2018

Presenter

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Nephrology Challenges in the Caribbean 2018

• OUTLINE OF PRESENTATION-

- 1. Introduction & summary of Disparate Demographics & History of Regional Nation- States.**
- 2. Challenges related to providing Renal Replacement Therapy (Haemodialysis & Kidney Transplantation).**
- 3. Disease –Specific Challenges Relevant to the Region.**
- 4. Potential Areas for Research.**
- 5. Proposals for Addressing above –noted Challenges.**

Nephrology Challenges in the Caribbean



Nephrology Challenges in the Caribbean

2018

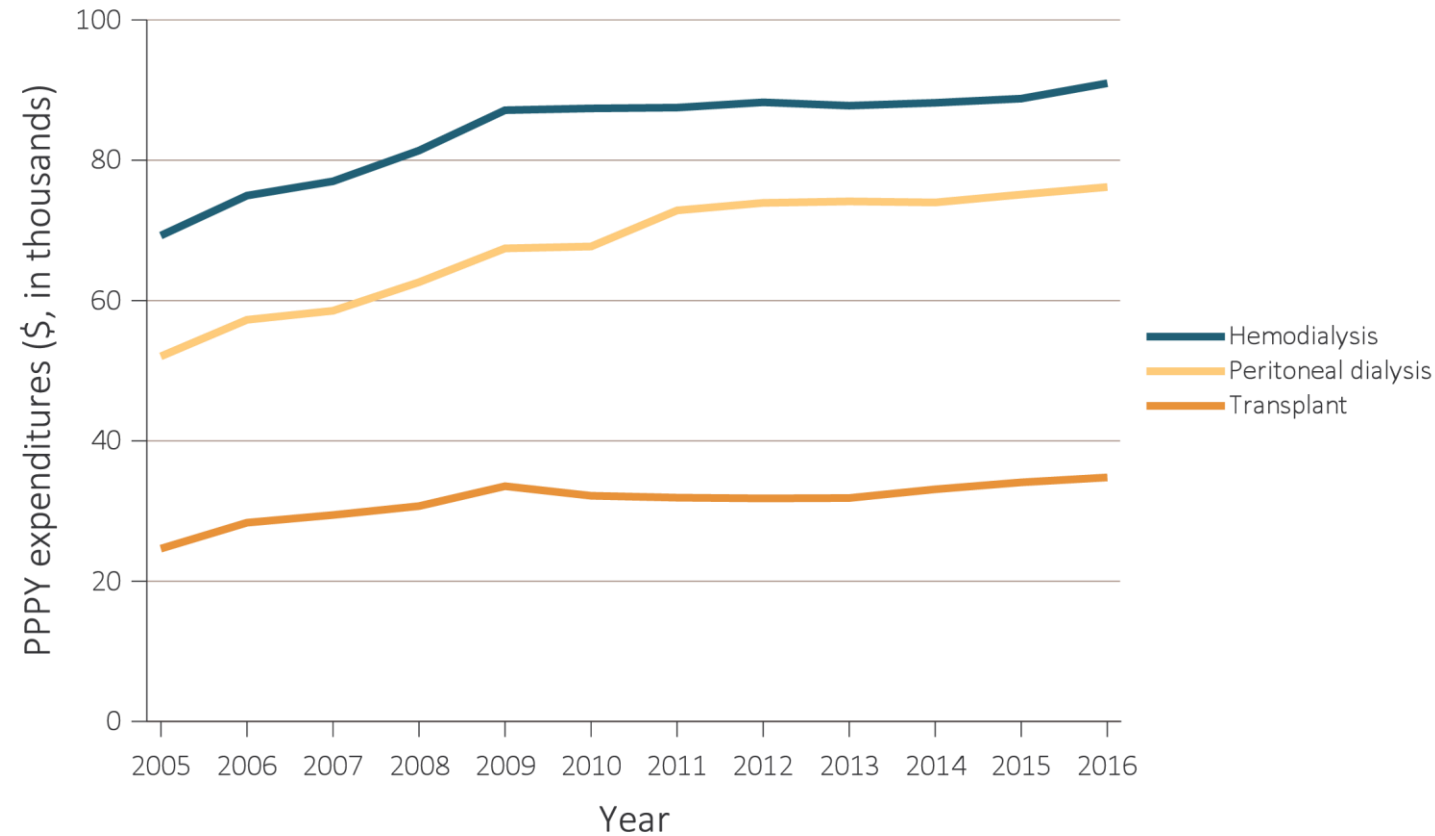
- 1. Geography- The Archipelagic distribution of the component Nation states as evidenced from the regional map.
- 2. Language communication Disparities as evidenced by:
 - The English- speaking Caribbean;
 - Spanish- speaking Nations; Cuba ; Honduras, & others;
 - Dutch-Speaking Nations; Curacao, Aruba & The Dutch Antilles;
 - Francophone Nations: Haiti, Guadeloupe & Martinique;
 - Others.
 -



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- The ISN has 10 regional boards for the 10 world regions.
 - Group 3 is listed: Latin America & the Caribbean;
 - Group 6 is listed: North America & the Caribbean.
 - Most individual Caribbean states not individually listed.
- 
- A silhouette of a tree with a thick trunk and a wide, spreading canopy, set against a vibrant sunset background. The sky transitions from a deep orange near the horizon to a darker purple at the top. The tree's shadow is cast onto the ground in the foreground.

vol 2 Figure 9.8 Total Medicare ESRD expenditures per person per year, by modality, 2004-2016



Data Source: USRDS ESRD Database; Reference Tables K.7, K.8, & K.9. Period prevalent ESRD patients; includes all claims with Medicare as primary payer only. Abbreviations: ESRD, end-stage renal disease; PPPY, per person per year.

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- Milliman Research Report

- 2017 U.S. organ and tissue transplant cost estimates and discussion
- Number of Renal Transplants (2017)..... 16,804
- Most Common Primary Diagnoses:
- Diabetes..... (27%);
- Hypertension..... (20%);
- Glomerulonephritis..... (19%).
- Living Donor Transplants..... 5, 627.
- African Americans account for 27% of Kidney Transplants

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- Milliman Research Report

- 2017 U.S. organ and tissue transplant cost estimates and discussion.- Kidney Transplant:

• 30 Days Pre-Transplant.....	\$ 30,100.00;
• Procurement.....	\$ 96,800.00;
• Hospital Transplant Admission.....	\$159,400.00;
• Physician During Transplant Admission.....	\$ 24,900.00;
• 180 Days Post Transplant Discharge.....	\$ 75,000.00;
• OP Immunosuppressants & Other Rx.....	\$ 28,600.00;
• <u>Total</u>	<u>\$ 414 ,800.00.</u>

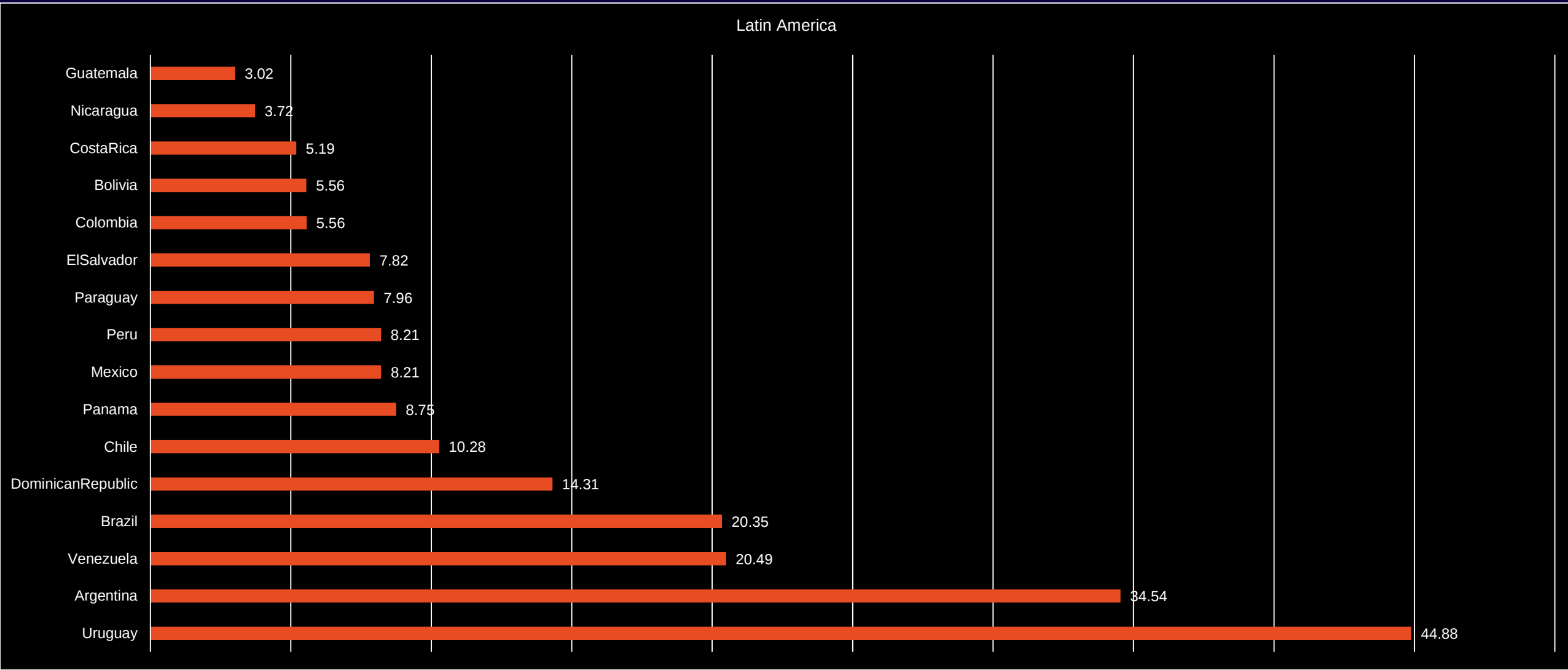
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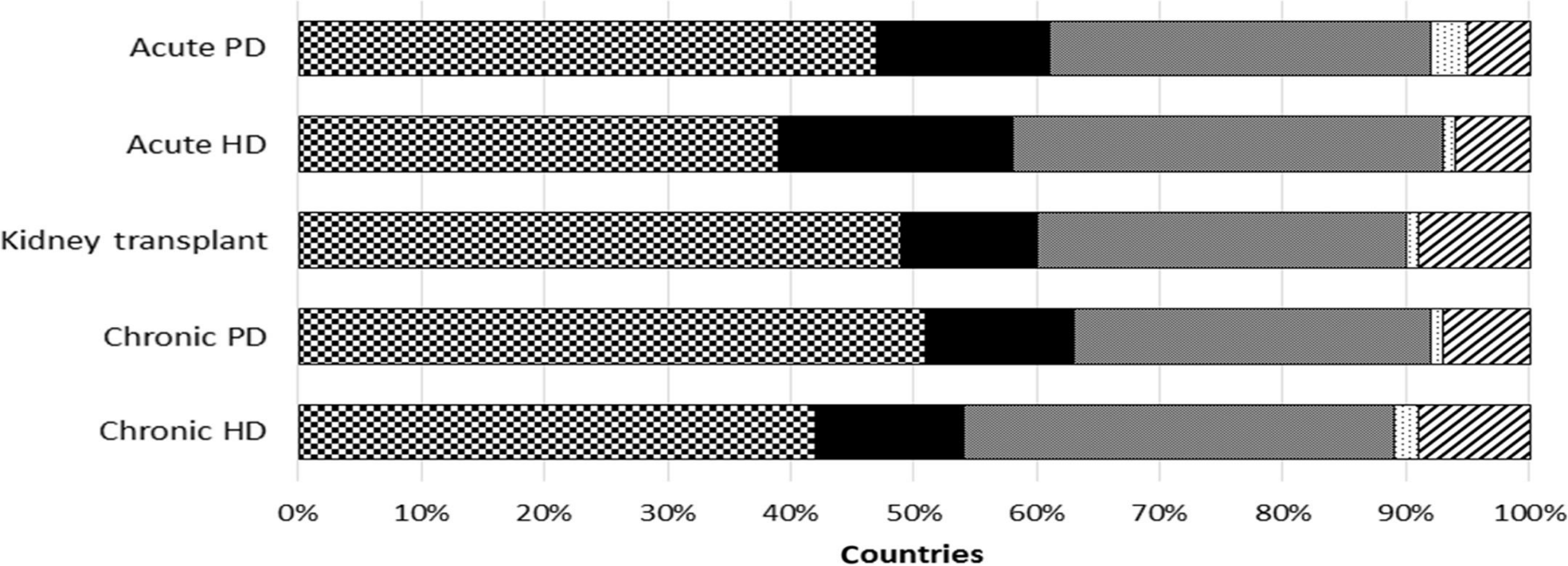
• Global Kidney Health Atlas

- Kidney International Supplement February 2018 Volume 8, Issue 2.
- First ever global survey/report on the availability, delivery, funding, health systems, kidney care provider gaps and research undertaken by the ISN.
- 125 U.N.-recognized nations, representing 93% of world population.

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Publicly funded by govt; free at the point of delivery

Publicly funded by govt but with some fees at the point of delivery

Mix of public and private funding systems

Solely private and out-of-pocket

Solely private through health insurance providers

Mixed systems programs provided by govt, organizations (NGOs), and communities



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Terms and conditions

Kidney transplant patients

Dialysis patients

CKD patients

0%

20%

40%

60%

80%

100%

Countries

Publicly funded by govt; free at the point of delivery

Publicly funded by govt but with some fees at the point of delivery

Mix of public and private funding systems

Multiple systems programs provided by govt, organizations (NGOs), and communities

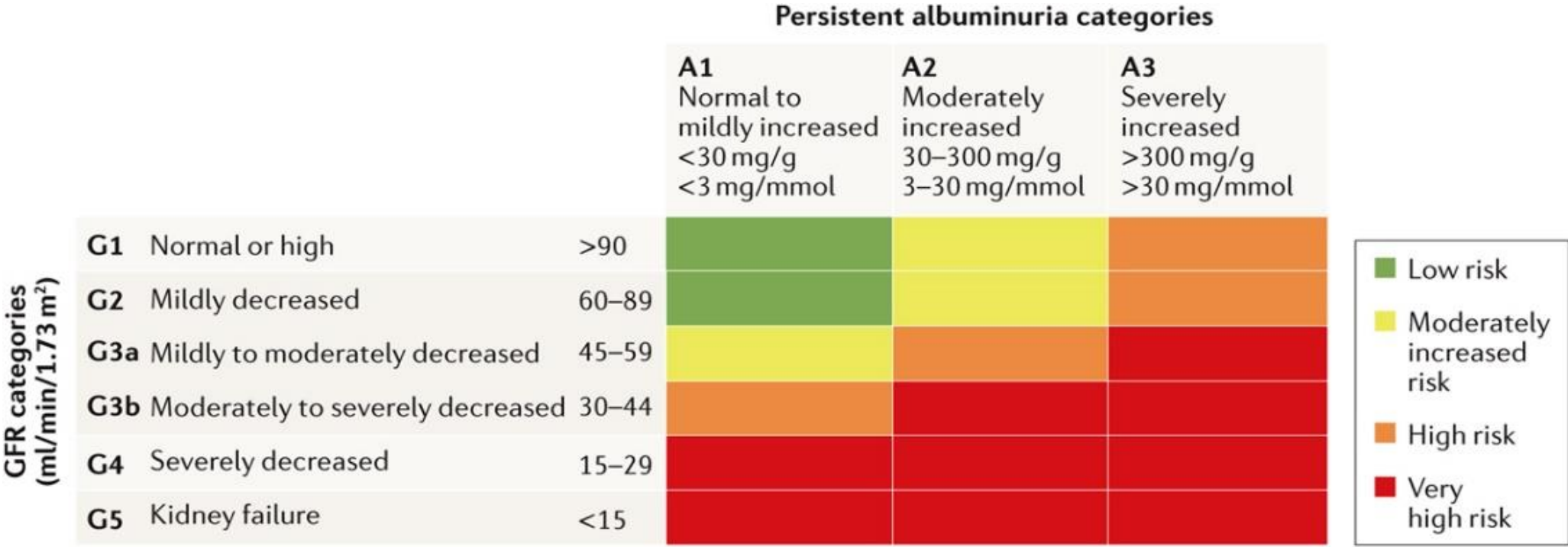
Solely private and out-of-pocket

Solely through health insurance providers



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Figure 1 The KDIGO classification of CKD



Reproduced with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int. Suppl.* 3, 1–150 (2013), Elsevier

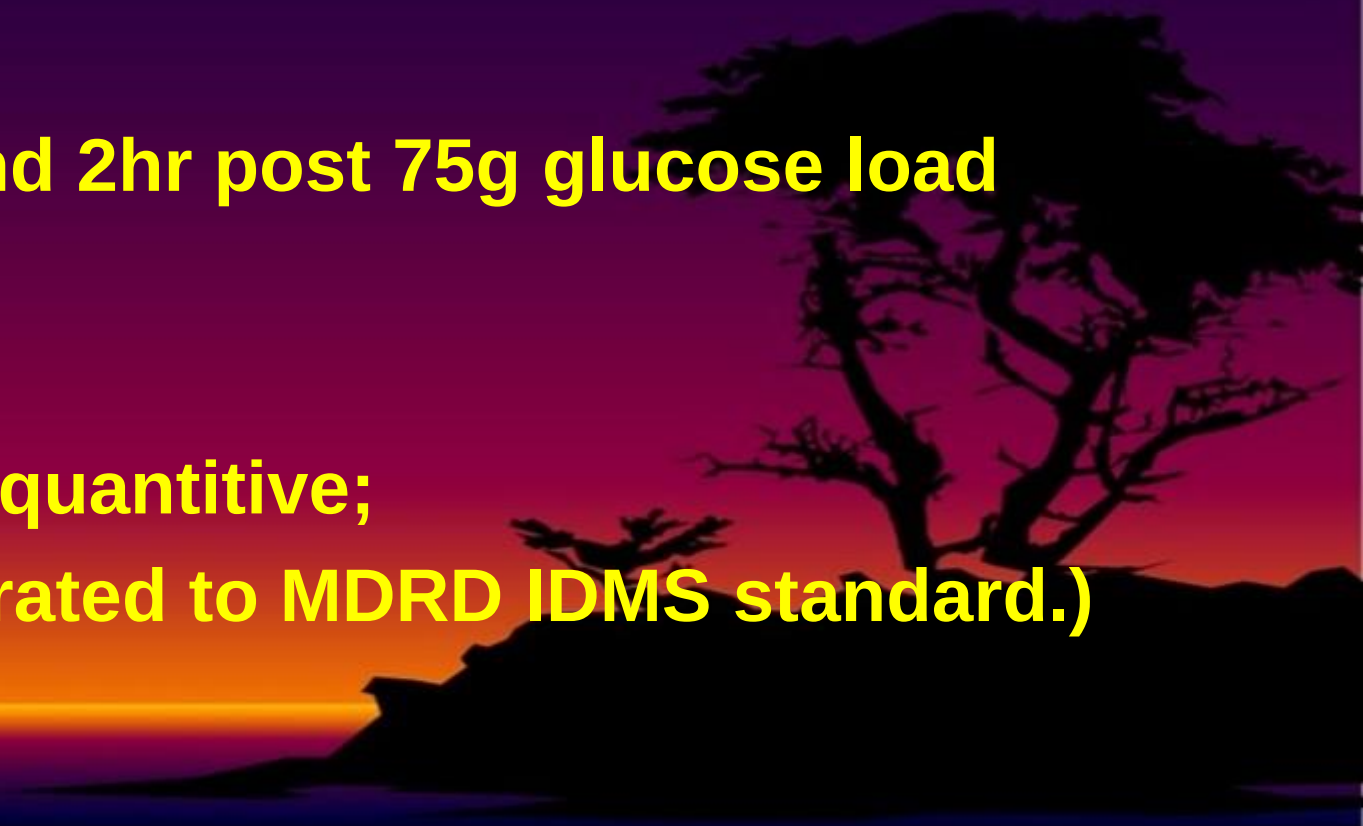
GFR Stages, Description and Range (mL/min/1.73m ²)				optimal and high-normal		high	very high and nephrotic	
				<10	10-29	30-299	300-1999	≥2000
GFR Stages, Description and Range (mL/min/1.73m ²)	G1	high and optimal	>105					
			90-104					
	G2	mild	75-89					
			60-74					
	G3a	mild-moderate	45-59					
	G3b	moderate-severe	30-44					
	G4	severe	15-29					
	G5	kidney failure	<15					

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- Ascertainment of Disease Burden

- Metrics for Primary Care:

- 1. Weight & Height;
- 2. Blood Pressure;
- 3. Fasting Glucose/ FBS and 2hr post 75g glucose load
- glucose;
- 4. Lipid Profile;
- 5. Urinalysis- qualitative & quantitative;
- 6. Serum Creatinine (calibrated to MDRD IDMS standard.)



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- Metrics for Secondary & Tertiary Care
- 7. Creatinine & e-GFR (MDRD-IDMS- standardized method);
- 8. Urine Albumin: Creatinine Ratio (UACR)/ or Urine Protein : Creatinine Ratio (UPCR).
- 9. Renal Imaging Studies: U.S.; CT; MRI; Radiology.
- 10: Nephro-pathology.

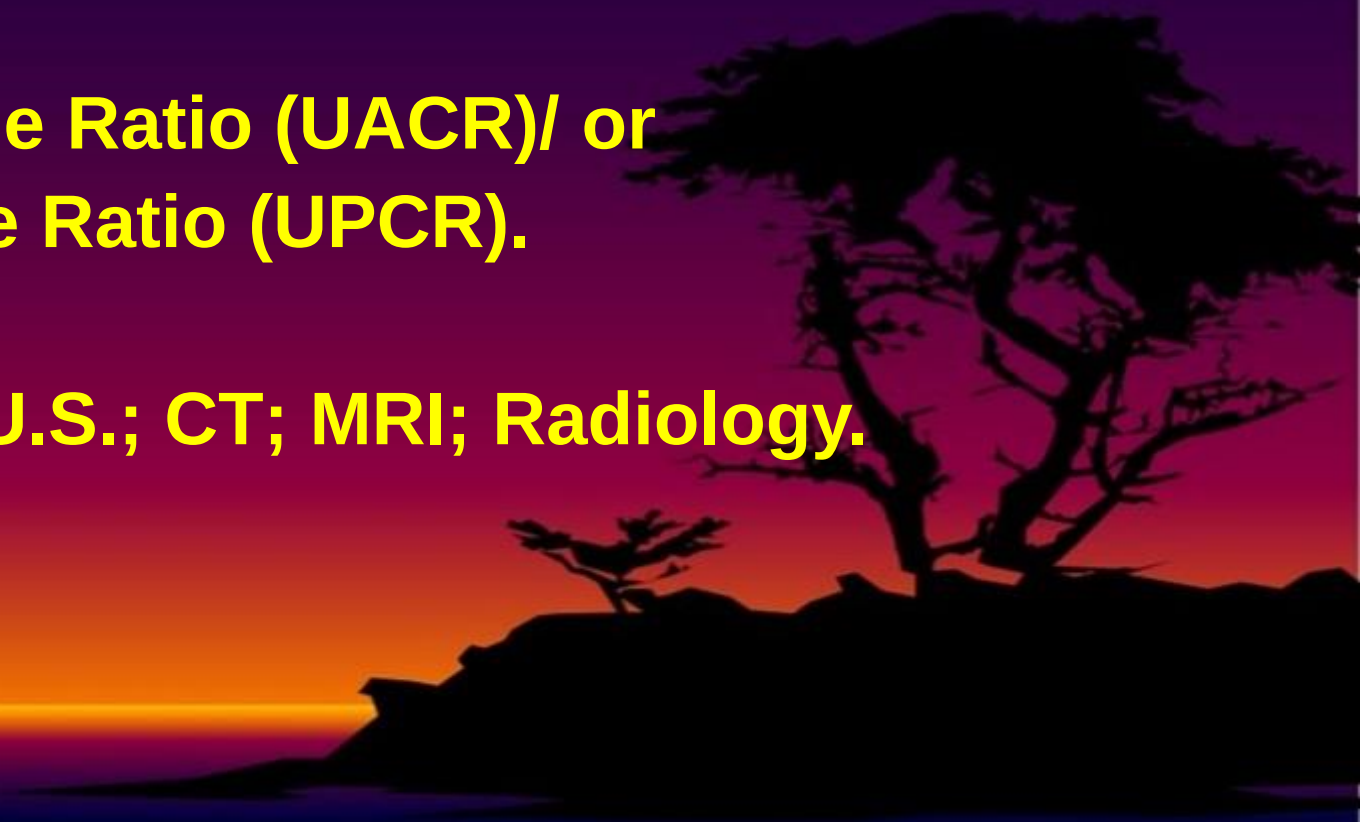
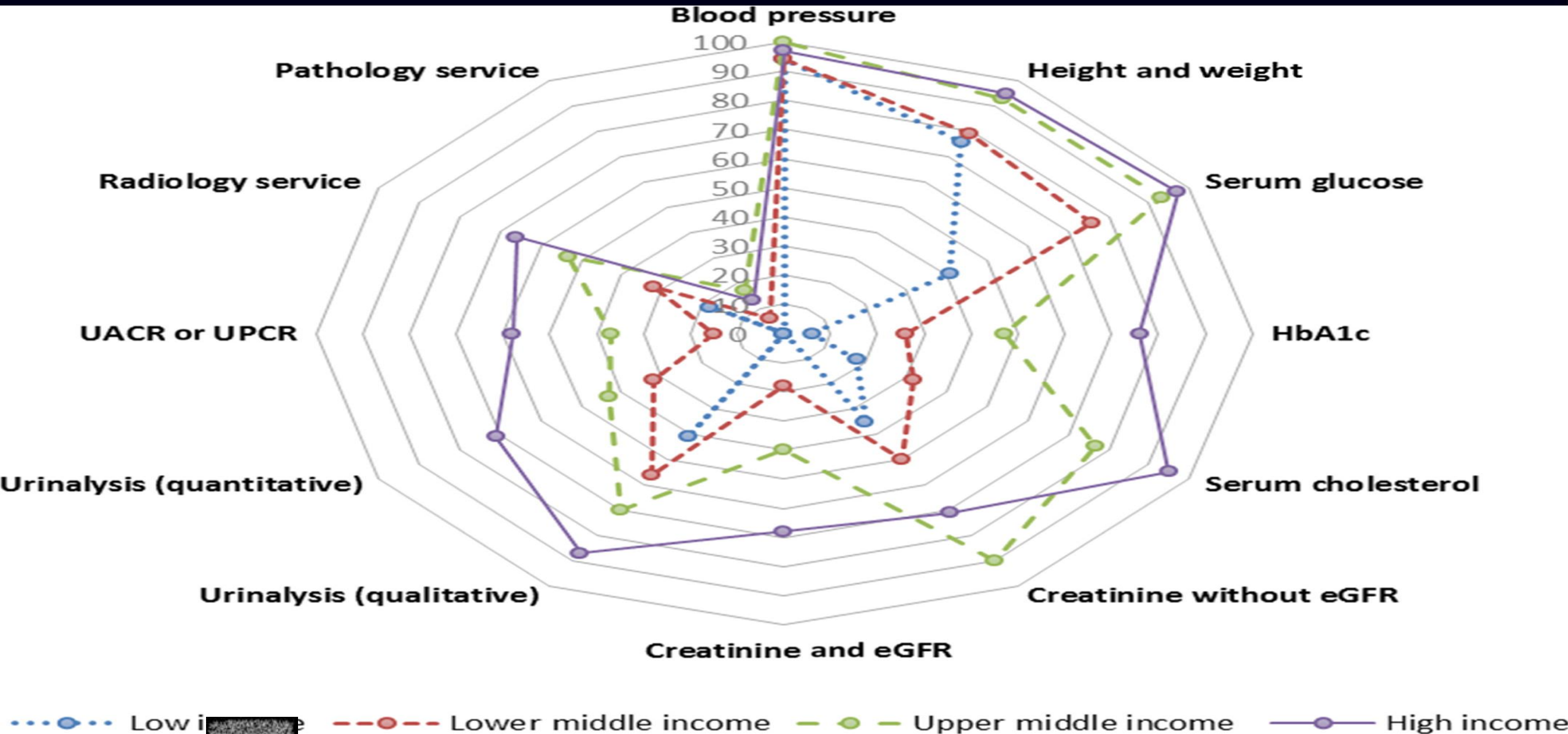


Figure 1



Nephrology Challenges in the Caribbean 2018

- Diabetic Kidney Disease

- Evidence for a non-proteinuric phenotype emerged in observational studies in 2003 & 2004:
- Kramer & colleagues using NHANES III data found eGFR of
- $< 60 \text{ mL/min per } 1.73 \text{ m}^2$ in 14% of 1197 Type 2 Diabetics;
- 81% of these had normo or microalbuminuria and 19% had overt proteinuria
- MacIsaac & colleagues found prevalences of 39% normoalbuminuria; 35% microalbuminuria & 26% Overt proteinuria in 109 patients with m-GFR $< 60 \text{ mL/min}$
- per 1.73 m^2

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- Diabetic Kidney Disease

- Non-Proteinuric Phenotype:
- Females are at greater risk;
- Obesity;
- Increased Systolic and Pulse pressures;
- Elevated HbA1c & triglycerides;
- Reduced retinopathy;
- Advanced Tubulointerstitial and arteriolar lesions;
- ? Increased cardiovascular mortality.

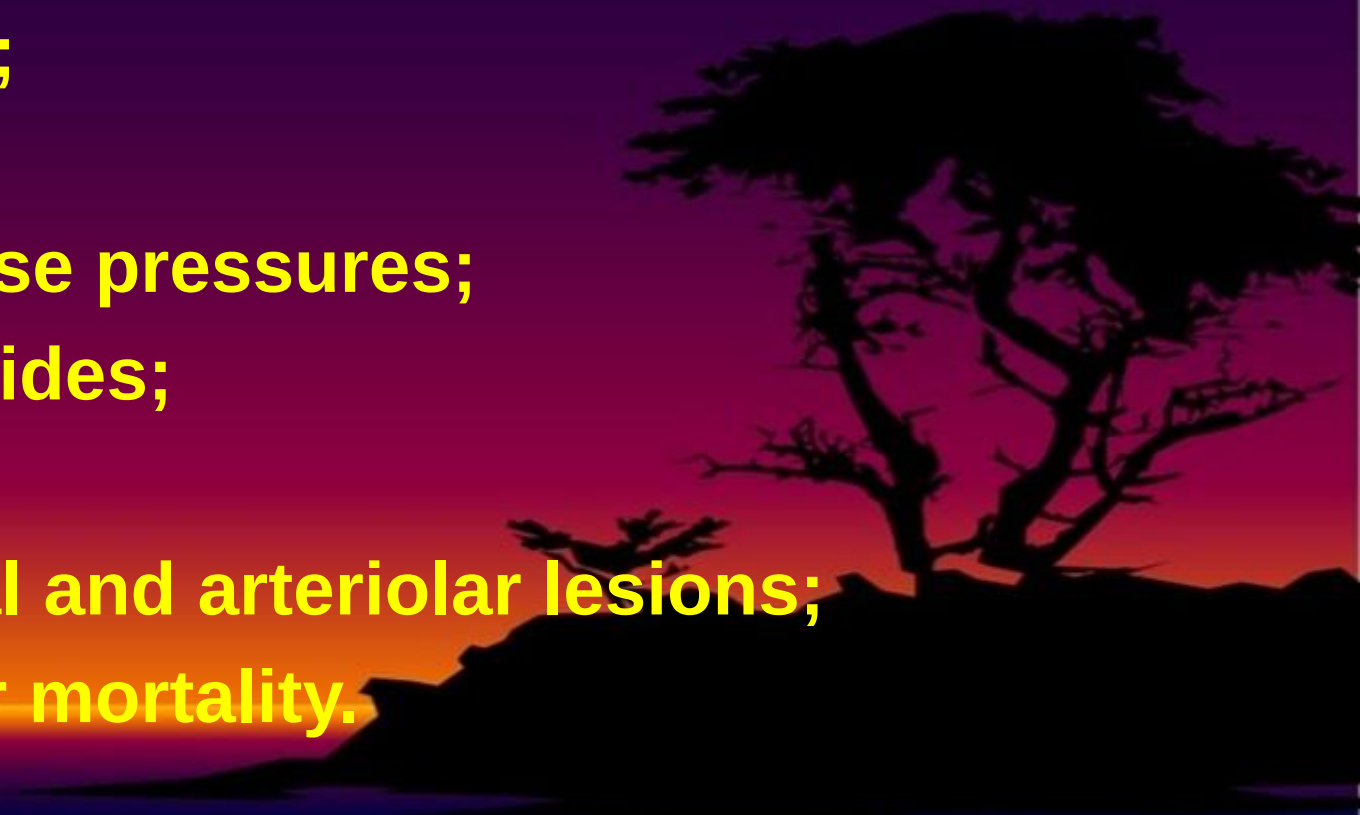
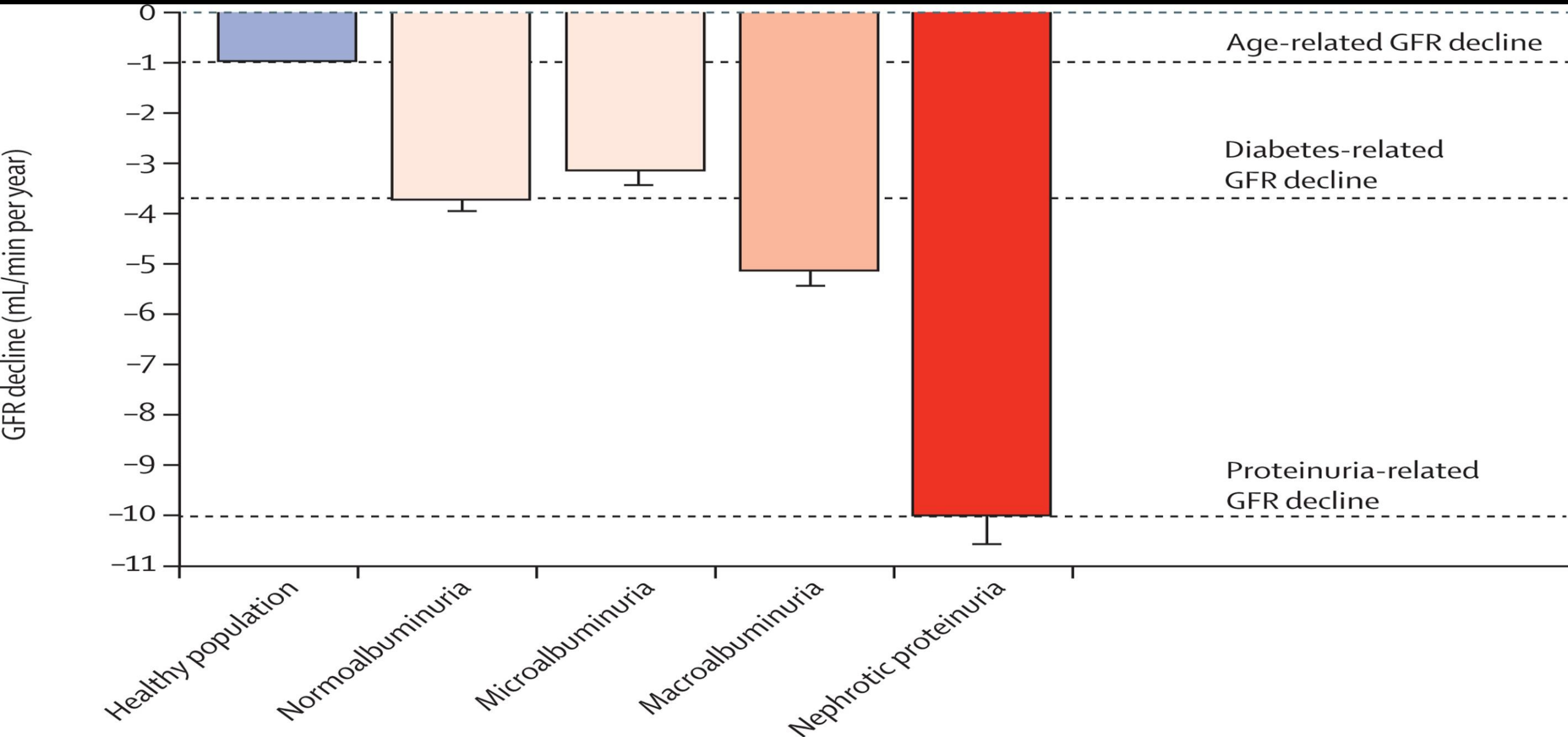


Figure 1



Nephrology Challenges in the Caribbean 2018

- The Modern Spectrum of Renal Biopsy findings in Patients With Diabetes
- Sharma, S.G. ,Bomback, A.S. et al. CJASN October 2013,8 (10) 1718-1724.
- N -611 of 620 renal biopsies from Jan. – Dec. 2011.
- 37% of patients had Diabetic Nephropathy(DN) alone;
- 39% had Non Diabetic Renal disease(NDRD) alone;
- 27% had DN & NDRD.
- Conclusion: 25% of Biopsies performed in Diabetics
- NDRD alone or superimposed on DM in Majority. ATN is emerging.

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Diabetic Kidney Disease

The impact of novel therapies in Diabetes:

SGLT 2 Inhibitors: Empagliflozin- EMPA-REG OUTCOME Trial: reduced relative risk of CV and all-cause mortality

**By 35% and composite secondary microvascular end points
By 38% (mainly reno-protective.).**

GLP-1 receptor agonists- Liraglutide- LEADER Trial: disclosed that when added to usual care, the rates of development and progression of Renal disease was lowered.

Costs are the issue with these medications.

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- Hypertension & Chronic Kidney Disease
- ACC/AHA 2017 BP guidelines- class 1 recommendation for a BP goal of $< 130/80$ mm hg in adults with CKD, regardless of albuminuria.
- Recommendations driven by the SPRINT trial:
 - 9,361 non-diabetic adults with HTN and elevated CVD risk;
 - Targeted SBP of < 120 mm hg versus < 140 mm hg.
 - Intensive BP group reduced risk of CVD by 25% and all cause mortality by 27%. 28% were > 75 years of age, 33 % were Black, 10% Hispanic and almost one third (2,646) had CKD.
 - New definition of hypertension ($130/80$ mm hg.).

Recent guidelines have different target blood pressure recommendations for patients with CKD.
ACC, American College of Cardiology; AHA, American Heart Association; JNC-8, Eighth Joint National Committee; KDIGO, Kidney Disease Improving Global Outcome.

	ACC/AHA 2017	JNC-8 2014	KDIGO 2012
Stage 3–5 CKD without albuminuria*	< 130/80 mmHg	< 140/90 mmHg	< 140/90 mmHg
Stage 1–5 CKD with albuminuria*	< 130/80 mmHg	< 140/90 mmHg	< 130/80 mmHg

*albuminuria is defined as albumin excretion rate ≥ 30 mg/24 h, approximately equivalent to urine albumin/creatinine ratio ≥ 30 mg/g.

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• Infectious Disease Challenges

- **1. HIV Disease: Tenofovir-based combination anti-retroviral**
 - induce proximal tubular dysfunction with mitochondrial
 - damage along with long term irreversible GFR decline.
 - Monitoring of renal parameters required.
- **2. HCV Disease: in the U.S. 5-10 % prevalence in Dialysis**
 - Patients; now treatable and curable in CKD & ESRD.
 - Grazoprevir + Elbasvir achieved a SVR 12 of 94%
 - C-SURFER ; cost for 12 weeks of treatment
 - \$ U.S. 54,600.00/ 12 weeks.

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• LUPUS RENAL DISEASE

- Disproportionately more frequent and severe in African-origin diaspora with significant progression to ESRD. It has been studied in Jamaica and Barbados.
- Apolipoprotein L1 gene alleles (APOL1), G1 & G2 are strongly associated with several progressive non-diabetic nephropathies in African Americans-
- Focal Segmental Glomerulosclerosis (FSGS);
- HIV-Collapsing Glomerulonephropathy (HIVAN);
- Hypertension related ESRD;
- Sickle Cell Nephropathy

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- Lupus Renal Disease

- Approximately 12% of African Americans carry both G1 & G2 alleles.

- End-Stage Renal Disease in African Americans with Lupus Nephritis is Associated With APOL1. Arthritis Rheumatol, 2014 Feb; 66 (2); 390-396), Freedman, B. et al.

855 patients with LN-ESRD; 534 without nephropathy:

25% of LN-ESRD cases & 12 % of controls had 2 alleles (OR 2.57);

Mean time to ESRD from SLE diagnosis was 2 years earlier;

Age at SLE diagnosis was 27.3 years versus 39.5 years.

Challenges in Nephrology in the Caribbean 2018

- The Kidney in Sickle cell anaemia
- G.A.O. Alleyne , L.W. Statius Van Eps , S.K. Addae ,
• G.D. Nicholson , H. Schouten.
• Kidney International, June 1975, Volume 7, Issue 6, Pages
371-379.



Nephrology Challenges in the Caribbean 2018

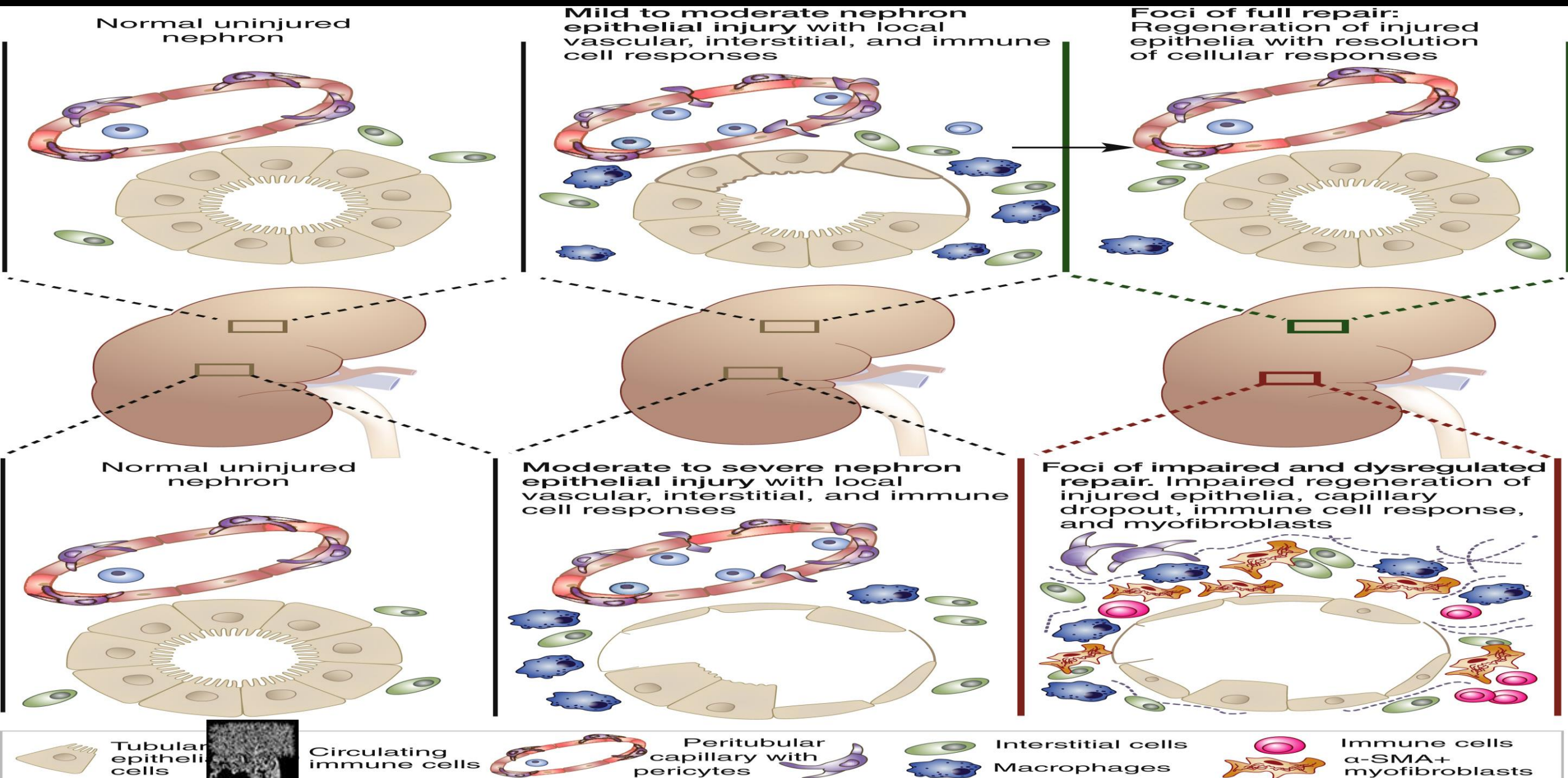
- Sickle Cell Kidney-Disease

- Kidney failure is not uncommon; Multiple transfusions and other organ comorbidities e.g. pulmonary hypertension contribute to limited kidney transplantation access mostly related to development of transfusion-induced allo-antibody development. Risk of antibody –related rejection is increased.
- The role of APOL1 nephropathy risk alleles , G1 & G2, have recently emerged as risk factors for progressive kidney disease in Sickle Cell Anaemia.
- The contribution of regional experts in the past , related to
- Kidney disease in Sickle Cell Anaemia has been noted -

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- Acute Kidney Injury (AKI) & Chronic Kidney Disease (CKD)
- Acute Kidney Injury is an independent predictor of in-hospital mortality (50 %-70 %).
- Acute Kidney Injury leading to Chronic Kidney Disease is
- Responsible for 9 fold, 3 fold and 2 fold risk of progression to CKD, ESRD and mortality, respectively, compared to patients without AKI.
- Some centres now have special follow-up clinics to track these patients.

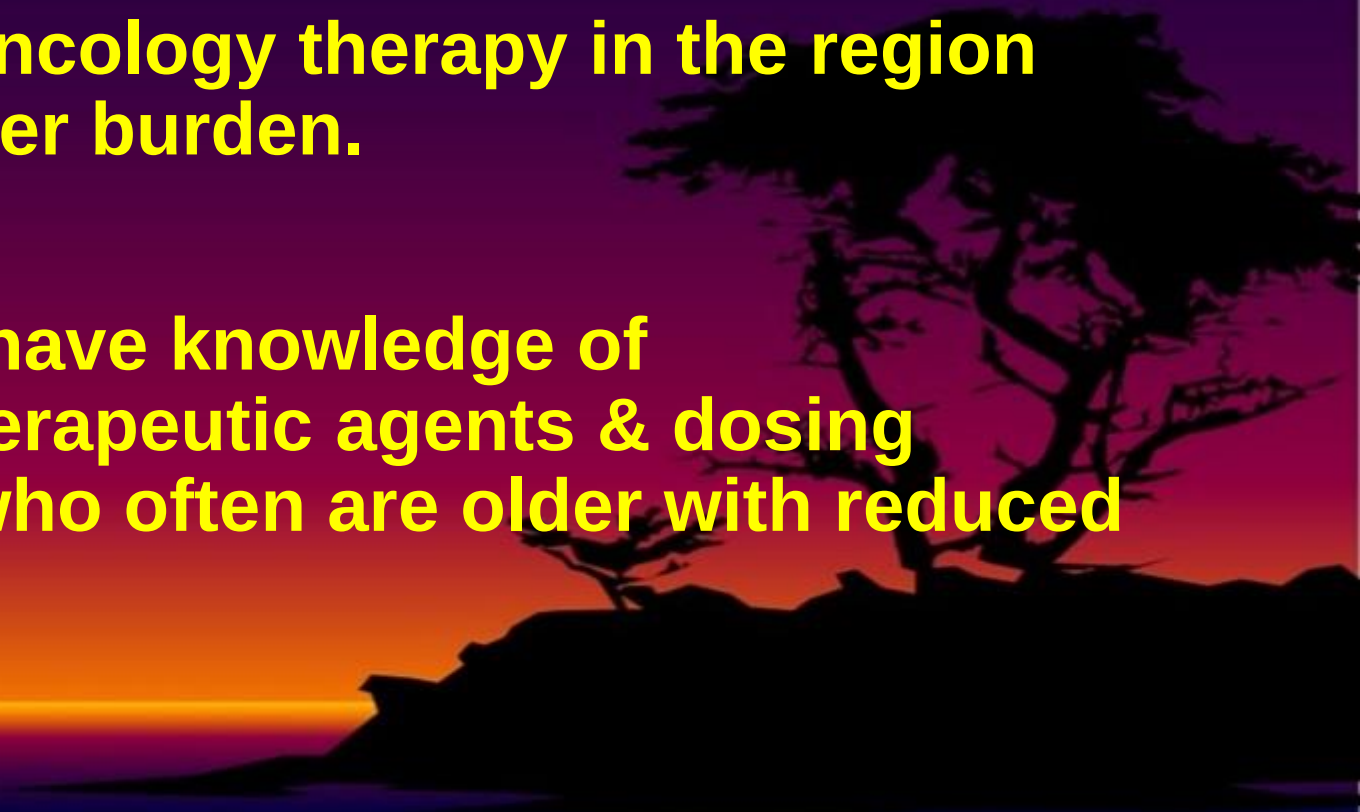
Figure 1



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- ONCO-NEPHROLOGY

- Emerging sub-specialty over last decade.
- Increasing availability of Oncology therapy in the region along with increasing cancer burden.
- Nephrologists required to have knowledge of nephrotoxicities of chemotherapeutic agents & dosing adjustments for patients, who often are older with reduced GFR / CKD.



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• ONCONEPHROLOGY

- Electrolyte disturbances caused by cancer or chemotherapeutic agents.
- Patterns/sites of nephrotoxic injury associated with agents:
- Cisplatin/ Ifosphamide- Proximal Tubule injury-AKI/ATN;
- Bevacizumab-Proteinuria, hypertension, nephrosis; TMA;
- Cituximab-Mg⁺⁺ wasting;
- Bisphosphonates- AKI;
- Glomerular disease associated with malignancy.
- Tumour Lysis Syndrome

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- Proposed Means of Addressing Challenges
- Encourage & recommend laboratory standards for creatinine measurement (IDMS –based calibration) with e-GFR print out and use of CKD-epi equation.
- Educate primary care physicians-
- BP ; BMI; Office Urinalysis; Urine Alb/Creat.; early Nephrology referral for tertiary level evaluation.
- National & Regional Electronic data systems data bank for
- Documenting CKD burden, and Acute Kidney Injury.

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- Proposed Means of Addressing Challenges-
- Education of public and patients of risks of CKD drivers such as diabetes & hypertension & promote healthy life styles adoption.
- Advise & inform government/Health Ministries of need to address expanded funding for data collection and treatments of patients requiring dialysis & transplantation.
- Encourage Private- sector participation in funding research activities.
- Establishment of a Regional Nephrology Professional Group that includes the non-English speaking nations.

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- Proposed Means of Addressing Challenges
 - Co-operation & engagement with Centres of Excellence with Interest & expertise in advanced molecular medicine
 - Technological investigations
- Increased Funding & Training for Regional Students with a view to enhancing Regional potential in these areas.

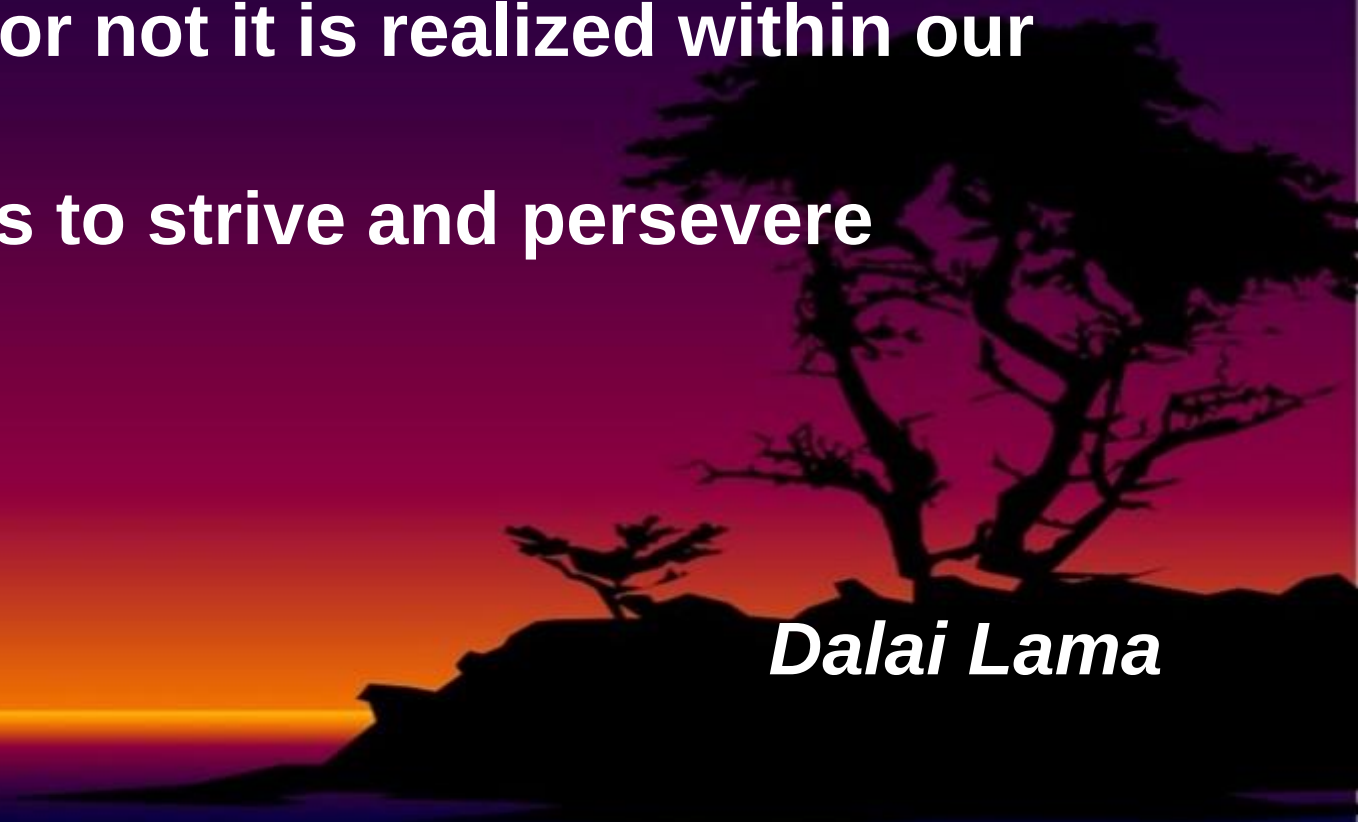
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“To remain indifferent to the challenges we face is indefensible

If the goal is noble, whether or not it is realized within our lifetime is largely irrelevant.

What we must do therefore is to strive and persevere and never give up “

Dalai Lama

A silhouette of a tree with a thick trunk and several branches, set against a vibrant sunset background. The sky transitions from a deep orange near the horizon to a darker purple at the top. The tree is positioned on the right side of the frame, with its branches reaching out towards the center.