York Central Hospital

Caring to make a difference™

Care of the geriatric population with CKD

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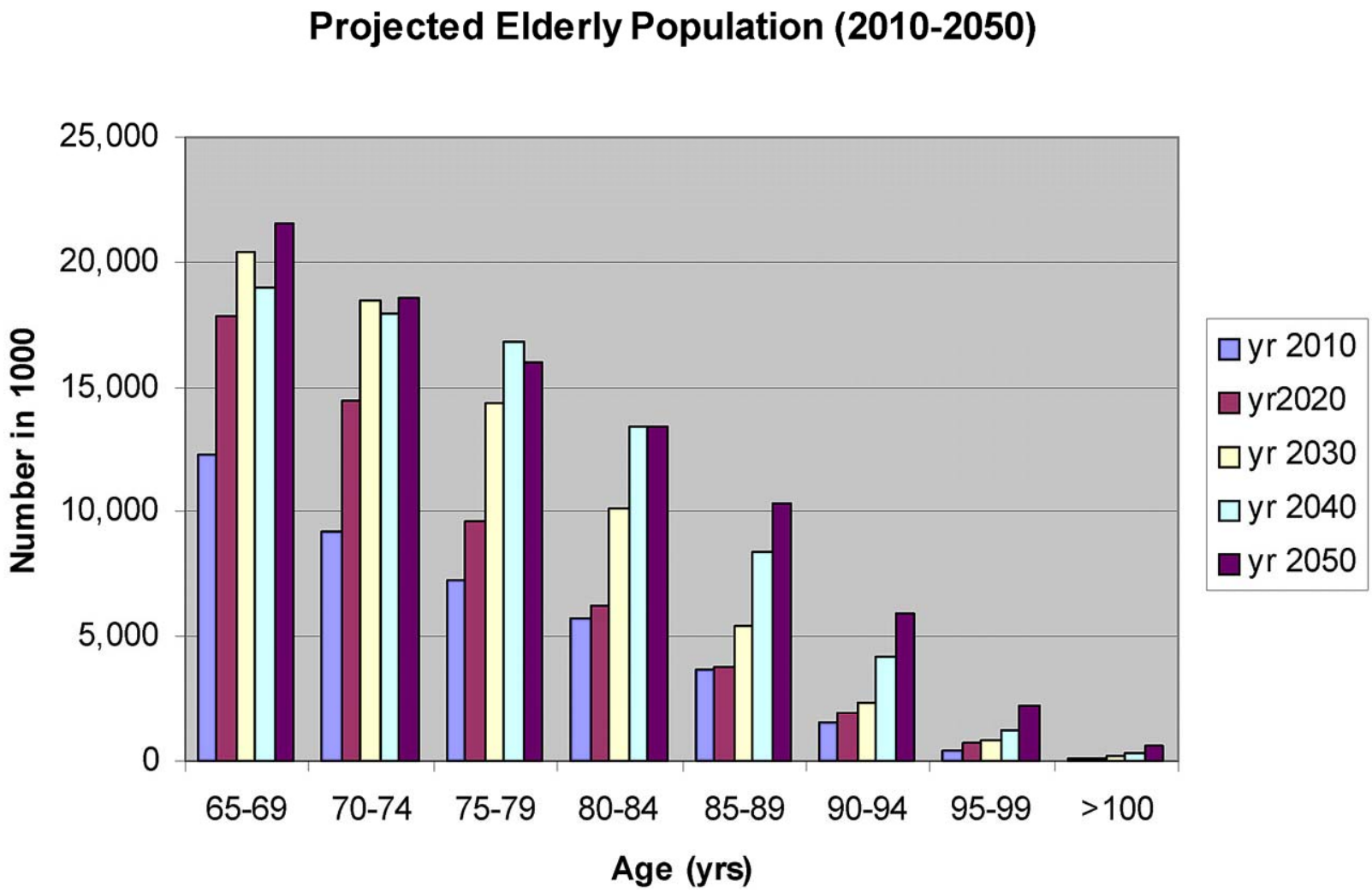
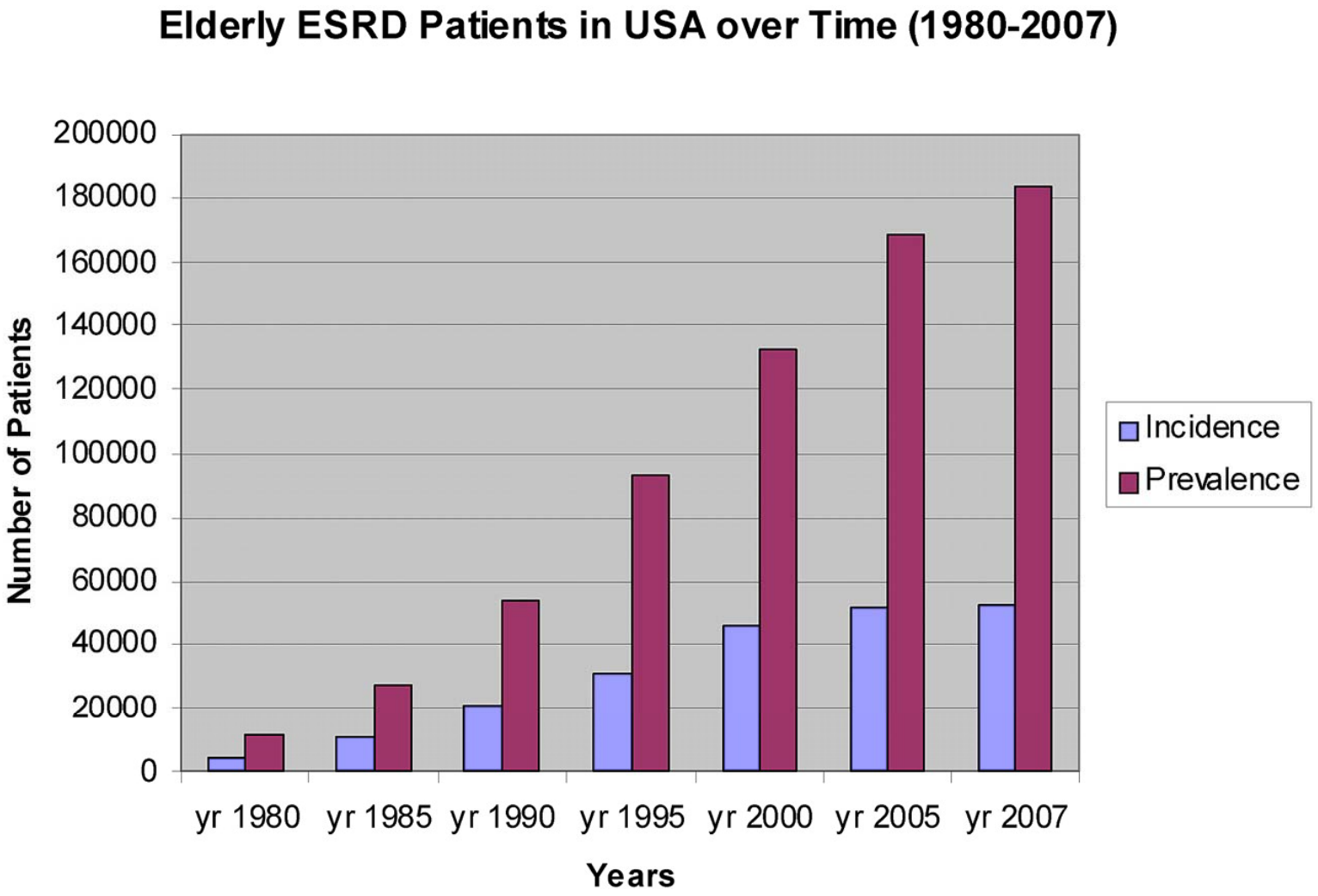
Projected elderly population, 2010 to 2050.



Rosner M et al. CJASN 2010;5:936-942

Clinical Journal of the American Society of Nephrology CJASN

Growth over time of elderly (age >65 years) treated ESKD patients.



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Histologic changes associated with aging

- Expansion of the mesangium and obliteration of the mesangial loop with capillary tuft collapse and fibrosis
- Fibrosis of the glomerulus primarily in the superficial cortex associated with cortical atrophy (5% at 40y 10% at 80y)
- Hypertrophy of the remaining glomeruli due to decreasing total number of glomeruli

Histologic changes in the tubulointerstitium

- Increase of tubular dilatation with intratubular cast formation
- Medullar fibrosis with increased influx of monocytes
- Distal tubules develop diverticuli that promotes infection

Histologic changes in the blood vessels

- Hyalin deposition in the blood vessels leads to obliteration of the lumen and sclerosis of the glomerulus
- Small arteries show elastic duplication, fibrous intimal thickening destructive changes in the media and thus obliteration of the lumen
- Loss of vascular structures plays a role in the loss of the renal mass

Summary

- Glomerulus
  - Thickening of BM,increased masangial matrix,focal global sclerosis, hypertrophy
- Podocytes
  - Fusion, detachment,intermittent vacuoles
- Interstitium
  - Tubular atrophy,tubular cast, monocyte infilitrate,intestitial fibrosis
- Vessels
  - Atrophy of afferent and efferent vessels, hyalinosis, “aglomerulus” vessels

Functional changes

- Decrease of renal blood flow and GFR at 40y
- Increase of FF and RVR
- Decrease of renal blood flow due to imbalance of vasoactive agents
- Attenuation to nitric oxide, endothelial vasoactive factor, prostaglandins and enhanced response to all endothelins
- The renal functional reserve on a normal diet is preserved until age 80

Functional changes in the tubules

- Under normal circumstances the elderly person is able to maintain homeostasis
- Concentrating and diluting capacity decreases
- Potassium excreting capacity decreases
- Decreased ammonium excreting capacity
- Blunted renal response to salt deprivation and load

Functional changes

- Decrease in plasma renin,and aldosterone levels
- Increased in ADH secretion, with blunted response to water load and no diurnal diurnal variation
- Increase of ANP
- Elderly are more prone to hyper and hyponatremia, concentrating and diluting capacity decreases

Summary of functional changes

- Decrease of renal blood flow by 10% yearly after age 40
- GFR decrease is 0.87 cc/min/1.73m2/year
- Increase of RVR
- Decrease of diluting and concentrating capacity
- Normal renal functional reserve

Biologic mechanism

- The exact molecular basis of aging is not clear
- Oxidative processes, senescence genes, replicative genes, cyclin dependent kinase inhibitors, caloric restriction, and sex dimorphism play parts

Cellular processes that change with age

- Epigenetics
  - Regulatory genes determine the active and inactive domain of the DNA and as such cell replication
- MicroRNA-s
  - Single stranded non-coding, non translated RNA – act to repress mRNA and prevent translation
- Mitochondria
  - Intracell organelles, produce energy in the form of ATP vie oxidative phosphorilation – imp. role in the apoptosis pathway

Individual aging genes

- IGF-1
- TOR signaling
- Sirtuins
- Klotho

- Insulin receptor pathway gene – inhibition of it increases the lifaspan
- Pathway senses availibity of nutrients and controls growth and development – TOR inhibition increases the lifespan
- Broadly conserved family of enzymes – important in adaptation of low nutrient conditions, mitochondrial function, DNA repair
- Gene that is chanracterized with close connection of accelerated aging phenomenon and phosphate homeostasis

Dietary restriction

- Aging is slower in animal models when dietary restriction is maintained
- 30-40% caloric restriction reduces the oxidative stress leading to aging
- Modulation of apoptosis, pro inflammatory processes, fibrosis and renal lipid accumulation

Molecular mechanisms of the kidney senescense

- Oxidative stress
- Autophagy
- Telomeres
- DNA damage

- Advances glycation end products – lead to reactive O2 species and inflammation
- Defective autophagy is associated with cell dysfunction and aging
- Specialized repetitive structure at the end of the chromosomes –the length of those dictates the cell's lifespan
- Mutation of the genes responsible for DNA repair,replication,trascription – can lead to accelerated aging

The kidney senescence

- Reflects the structural and functional phenotype associated with the aging kidney
- The challenge is to decipher the normal structural and physiologic changes from the changes associated with systemic diseases accompanying aging
- The molecular mechanism is unclear

Decrease of glomerular filtration rate

	GFR 80-20y	Method	Authors
1	-46%	Inulin	Davies et al 1950
2	-68%	Creatinine	Cockroft Gault 1976
3	-40%	Creatinine	Lindeman 1985
4	-55%	Creatinine	Friedman 1989
5	-30%	Creatinine	Sokoll 1994
6	-15%	Inulin	Fliser 1997
7	-14%	EDTA	Peters 2000
8	-40%	Inulin	Fuiano 2001
9	-13%	Inulin	Fliser 2001

Structural changes

- Renal mass increases from 50 g at birth to 400g at age 40 then declines to 300g with age
- The loss mostly involves the cortical region and is related mostly to vascular changes

Gestational growth

- The total number of glomeruli are predetermined at 32-36 weeks gestation (247652-18525380)
- The number of glomeruli are determined by gestational age, race and gender and birthweight
- The number of glomeruli are decreasing in by 6752 yearly after age 18 years

Prevalence of chronic kidney disease

- Increases dramatically with age
- Estimates of prevalence of CKD in older adults are remarkably consistent across wide range of populations average 0.75ml/min/year loss of GFR
- Caucasian men 18-14y 100ml/min/1.73m2 to 62ml/min/1.73m2 at age 80y
- Caucasian women 18-24 91ml/min/1.73m2 to 59ml/min/1.73m2 at age 80y

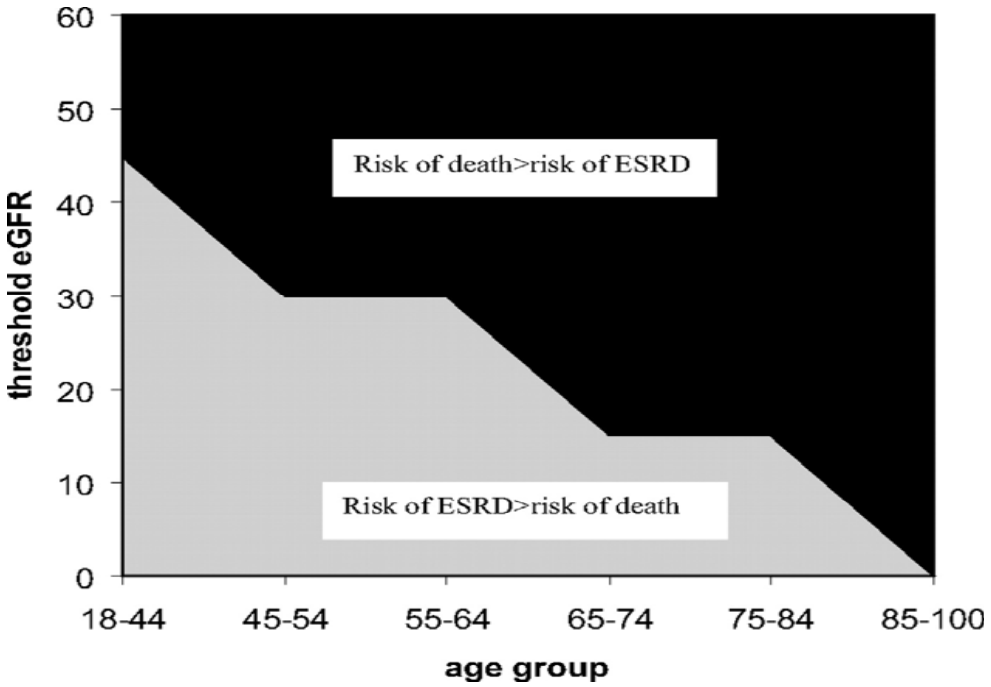
Low eGFR is associated with poor outcome

- Cardiovascular events
- Cardiac survival
- Overall survival
- Postoperative survival
- Frailty
- Renal progression

Clinical aim of interpreting eGFR for the individual

- Preparation for ESRD and slowing progression
- Reducing morbidity – drug management
- Improving death

Competing risks of ESRD and risk of death



O'Hare A M et al. JASN 2007;18:2758-2765

Risk factors for progression to ESRD in the elderly

- Importance of individual risk factors vary with age
- In the older age group (>65years) risk factors for renal replacement therapy include lower eGFR, greater eGFR slope, proteinuria and anemia

Acute kidney injury

- Age related yearly incidence of AKI is 17 per million adults at age<50 vs 949 per million when age >80
- Average age of ARF/CRF is 80.5 years and this group has much higher risk of adverse outcomes
- Incidence of AKI increased – especially in older adults (>80y) 1996 2867.5/100000 person-years vs 2003 4884.3 /100000 person-years

Older than 70 years population is at the highest risk for the development of AKI

- Frequent prerenal and obstructive causes
- More invasive investigations, frequent medication exposures
- Changes in drug metabolism and disposition at advances age
- Associated comorbid conditions
- Higher probability of underlying chronic renal impairment

Cellular and molecular changes increasing the aging kidney's susceptibility to AKI

- Increased rate of apoptosis
- Telomere length shortening
- Increased oxidative stress and decreased defense
- Mitochondrial abnormalities and ATP depletion
- Decreased rate of cellular proliferation
- Increased mRNA and proteins associated with candidate genes of senescence
- Increased expression of genes inhibiting cellular proliferation
- Age related decline in Klotho expression
- Increased AGEs and decreased renal growth factors

Diagnosis of AKI in the elderly

- Rate and magnitude of serum creatinine rise may be blunted in the elderly due to the decreased muscle mass
- Biomarkers CystatinC, Neutrophil gelatinase associated lipocalin (NGAL) and IL-18 could perform differently in older adult and need to be further evaluated

Impact of AKI on the elderly

- Short term mortality can be as high as 40% dependent on the setting, and AKI is associated with increased risk of long term mortality
- Elderly patients who suffer AKI have x13 higher risk of ESRD
- Quality of life studies show that 94.5% believe that the treatment was worthwhile and would undergo the same treatment if needed again

General approaches to the prevention of AKI

- Recognition of the risk
- Avoidance of nephrotoxic exposure
- Avoidance of nosocomial infections
- Extracellular fluid expansion
- Avoid agents that impair renal blood flow autoregulation
- Use of computer surveillance system

Given limited therapeutic options for AKI and the significant impact of AKI on outcomes, it is imperative that preventive strategies be used whenever possible

Therapeutic options for older individuals with CKD

Older patients with advanced stages of CKD should have a baseline comprehensive geriatric assessment done as part of their predialysis care. Predialysis education should include detailed information about non dialysis care particularly for vulnerable seniors

Most important aspects of geriatric assessment

- Frailty (unintentional weight loss,self reported exhaustion,slow gait speed,weakness,low physical activity
- Falls
- Dementia
- Functional impairment and disability

Home based therapies HHD,PD

- Only 22% of our elderly patients have absolute medical or social contraindication to PD
- Most commonly appreciated barriers are decreased strength and mobility, manual dexterity, and decreased vision
- Family support can alleviate some of the barriers even if present
- Assisted home therapy may help to overcome those barriers

Hospital or center based therapy

- Higher rate of tunneled catheter use, more frequent difficulties with poorly maturing AV fistulas
- High rate of hospitalizations
- Higher rate of malnutrion
- Increased risk of depression and adynamic bone disease
- Nocturnal dialysis is a new prospect to consider in NH setting

Nondialysis care as active treatment strategy

- Long term dialysis therapy is a burdensome treatment with significant impact on the QoL
- Many of the non ESRD related symptoms persist even after dialysis therapy is established,reducing the overall QoL
- Interventions and medications could be sued to minimize the symptoms and to promote good living rather than lengthy living

Transplantation

- Patients older than 65 are the least likely to undergo kidney transplantation
- Underuse of transplantation could be attributable to subtle physician and patient biases
- Older patients are the least likely placed on the waiting and the most likely offered kidneys of extended donor criteria
- Functional renal transplant offers improved QoL at lower cost (5 years survival rate is 65%)

Palliative care

Is a form of treatment that strive to match medical care to patient’s goals relieve pain and improve QoL for people with chronic or life threatening illnesses regardless of prognosis

The simultaneous care model of palliative care is an appropriate template for the evaluation and treatment of dialysis patients who undergo targeted medical therapies to address their myriad needs

Palliative care in advanced CKD and dialysis

- Mutually agreed management plan to optimize QoL and relieve suffering offered simultaneously with all the appropriate medical therapies
- A process of ongoing communication to update prognosis/goals or care/preferences as the trajectory of decline progresses
- Pain and symptom management
- Patient and Family support

Geriatric medical decision making

- Documented survival of older patients in dialysis is poor (>80years 1year mortality is 46%)
- Related to advanced age, serum albumin concentration, non ambulatory status, congestive heart failure, co-morbid conditions, underweight status and smoking

Functional age and frailty are necessary factors to assess in the dialysis decision process

- Get up and go test
- Rapid chair rise
- VES-13 (staging the aging classification)

To Healthy, Vulnerable or Frail

Four Topics Method Adapted to Dialysis Decisions

Medical Indication for intervention

- What is the functional age of the patient
- Is this patient “healthy, vulnerable or frail”
- What are the survival data
- What are the geriatric susceptibility factors
- Are nursing home patients different?

Is this patient dialysis candidate or not?

Quality of life

- No universal metric
- Personal value judgment
- Some objective criteria (dementia, cachexia, advanced cancer)
- Significant symptom burden
- Time limited trial to assess if QoL is acceptable

Patient preferences

- Establish “big picture goal”
- Explore patient’s personal narrative
- Engage the family
- Be prepared
  - Preferences may change
  - Patient is unable to express wishes or want only limited or no information

Contextual features

- Is the family supportive of the patient's decision
- Are there conflicts between family members
- Are the patient's wishes consistent
- What is the cultural,ethnic and religious background
- Is there conflict among the healthcare providers

Conclusions

- Care should focus on the need of the elderly patient and their families as they perceive them

Relief,practical help, support, hope, comfort