What’s New in Heart Failure

Dr Nigel Rowell
GP, Endeavour Practice Middlesbrough
GPSI, James Cook University Hospital
Conflict of Interests

Nigel has received payments from Pfizer and Servier, Bayer and Boehringer-Ingelheim
Commission

Definition- Oxford Concise Dictionary
V.t., To empower command of a ship
Part-time women GPs blamed for NHS failings

Chris Smyth Health Correspondent

A health minister sparked a row with doctors yesterday after suggesting that women GPs who work part-time while looking after their children are placing a huge burden on the NHS.

Anna Soubry told MPs that there were "unintended consequences" to the rise in the number of female doctors. Well over half of medical students are women, and GP leaders have said that the shift in the gender balance means that the NHS needs to train more doctors in order to provide the same level of service.

In a Westminster Hall debate on the NHS II helpline yesterday, Anne McIntosh, a Tory MP, said: "It's a controversial thing to say, but perhaps as a woman I can say this 70 per cent of medical students currently are women and they are very well educated and very well qualified.

"When they go into practice, and then in the normal course of events, will they marry and have children, they often want to go part-time and it is obviously a tremendous burden training what
What’s in this Talk..
Chronic Heart Failure since 2010

1. Telehealth – does it work in HF?
2. The National Heart Failure Audit
3. Eplerenone – the EMPHASIS trial
4. Cardiac Resynchronisation Therapy – new indications
5. Ivabradine – SHIfT trial
6. A postscript on Beta-Blockers
7. Palliative Care
Telehealth
Telemonitoring
Telemedicine
WHAT DO WE WANT?
EVIDENCE-BASED CHANGE
WHEN DO WE WANT IT?
AFTER PEER REVIEW
The Whole System Demonstrator

..To assess the effect of home-based telehealth intervention on the use of secondary care and mortality....

- 179 general practices across Cornwall, Kent and Newham
- 3230 patients with COPD/HF and Diabetes
- – 12 month trial period
- End points Mortality, length of stay emergency admissions and A+E attendances
Kit

Oximeter for COPD

And a Glucose meter for diabetics

Scales for Heart Failure
Data

• Clinical readings at same time each day
• 5 days/ wk
• Symptom questionnaire and educational material via a set top box next to their TV
Not Forgetting the other end of the phone...
WSD Results

• 42.9 % admitted vs. 48.2% controls (p<.017)
• 4.6% in trial arm vs. 8.3% controls died (p<.001)

• Secondary Endpoints
  • Intervention arm 0.54 emergency admissions vs 0.68 for controls –NS when adjusted
  • Hospital Activity Costs to the commissioner GBP 188 lower per intervention patient
Whole System Demonstrator

- Was not designed or powered to detect differences between different devices or monitoring schemes
- Excluded regular ward attendances
- No costing for Mental health/ Critical Care/ High cost drugs/Outpatient Physiotherapy
The WSD

- Not all details published
- Some benefits
- Costs not disclosed
- Wholesale roll out
- “3 million Lives” → 3 million sets of data
- (Why 3 million?)
WSD - Flaws

• Intervention and control groups could have accessed primary care, social care and community services in different ways
• Increase in emergency admissions in control groups – newly discovered conditions (Oops)
• Community teams diverted to Trial Patients
• Telemonitoring and education were combined – which one worked
Meta-analysis of trials of Telemedicine in HF - 2007

Clark & Inglis and others
BMJ 2007 April 10
14 RCTs (4264 patients)
4 evaluated Telemonitoring

- Remote monitoring reduced admission by 21% and all cause mortality by 20%
- How do you meta-analyse such disparate trials?
Telemonitoring in Patients with Heart Failure (Tele-HF)

Chaudhry SI et al NEJM 2010 363 ;2301-2309

1653 patients recently hospitalised patients randomised to usual care or tele-health: daily phoning in of weight and symptoms reviewed by clinician
Tele-HF Trial

- 826 HF patients randomly assigned to Telemonitoring – Interactive Voice Response around symptoms and weight
- Reminder if unused for 2 days
- Data reviewed daily by clinician

- 827 on usual care
826 daily wt/
symptoms by
phone

Readmission 49.3%

Death 11.1%

827
Usual care

Readmission 47.4%

Death 11.4%
Tele-HF results

• 180 days
• No reduction in risk of readmission
• No reductions in risk of admission for heart failure
• No change in number of days in hospital
• No difference in time to readmission or death
TIM-HF study 2010

The Telemedicine Interventional Monitoring in Heart Failure Study

- 354 Telemonitoring
- 356 usual care
- 24 months
- No effect on primary end point of death
- No effect on secondary endpoint of CV or HF admission
- Monitored group improved physical function, and less depression
TIM-HF

- 14% never used the kit
- Only 55% using it at 6 months
- May be better if “embedded in practice”
Points

- Usually co-morbid
- But in most trials only 1 Long Term Condition seemed to be monitored
- Yet HF patients often readmitted with a co-morbidity
- Drop-Off of usage of kit over time
Kings Fund Report

“Previous claims of success based on small populations of patients and methodological weaknesses are not supported by the results of a large Multicentre Trial”
What would I spend my money on as a commissioner

- Weighing scales & telephones
- Another troop of HFSNs
- Hot line or e-mail line to HF cardiologist
- Good communication
- Direct e-booking of appointments for patients to Primary care and GPs to Hospital
Using the latest Technology in Middlesbrough
The National Heart Failure Audit
The National Heart Failure Audit

• 59% of all Acute HF admissions England & Wales
• Length of stay :13.1 d 1\textsuperscript{st} admission
• LoS: 13.4d on re-admission
• 7.8% mortality on Cardiology wards
• 13.2% mortality on General Medical wards
• 17.4% mortality on Other Wards
Treatment as In-Patients

- 86% echo during admission
- 84% ACEI
- 78% Beta-Blocker (up on 65% last year)
- 45% MRA (increase from 36%)
- 54% referred to HF Liaison Service
- 52% followed up by cardiology
Usage of Beta-Blockers on Discharge

- OPTIMIZE – HF trial: 87.2% deemed eligible though given in 49% at discharge
- EMPHASIS trial (Eplerenone): 87%
- National HF Audit: 78%

Rowell’s Rule of Beta-Blockade

“ You can put a lot of people on a Beta-Blocker but you can’t put a LOT of people on a LOT of Beta-Blocker”
USA comparator : ADHERE registry

• After hospitalisation for HF
• 69% ACEI  (UK 84%)
• 59% BB     (UK 78%)

JCAHO indicators ( a bit like OFSTED)
• Echo 82% (UK 86%)
• 63% acei
QOF 2011-12

- ACEI/ARB thresholds - no payment till 40% patients on them; max payment once 80% on ACEI or ARB
- Beta-blockers – 40% min threshold; max 60%
- GPs achieved 97.7% of points for ACEI and 96.6% for BB
- Therefore 78% of patients are on ACEI and 57% on betablockers
- (exclusions are around 5%)
Eplerenone
Kidneys sense falling Cardiac Output

*But respond in entirely the wrong way!!*

*And it only makes matters worse!!!*

1. Activated Renin-Angiotensin system makes arteries tighten up to increase pressure in system

2. Release Aldosterone to retain salt and water and increase circulating Volume

3. Release Adrenaline to flog the heart harder and faster
What the kidneys did next..
Aldosterone – What is it?

- A steroid like compound released from the adrenal cortex
- Acts on DCT – opposes BNP
- Conserves sodium
- Retains water
- Puts up BP
- Secretes potassium
Mineralocorticoid Receptor Antagonists (MRAs) Studies in Heart Failure

• Spironolactone – (intr. 1959)
  RALES Study  NIH – USA (1998)

• Eplerenone
  EPHESUS (post-MI HF)
  EMPHASIS (Chronic HF) (2012)
Nigel’s Heart Failure Classification

- NHA1 (= NYHA I)
- NHA2 (=NYHA II)
- NHA3 ( =NYHA III)
- NHA4 (=NYHA IV)
### Differences in the 2 MRA studies

<table>
<thead>
<tr>
<th></th>
<th>RALES (Spiro)</th>
<th>EMPHASIS (Eple)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>822</td>
<td>1364</td>
</tr>
<tr>
<td>NYHA II - nil</td>
<td>nil</td>
<td>100%</td>
</tr>
<tr>
<td>NYHA III 70.5%</td>
<td>100%</td>
<td>Nil</td>
</tr>
<tr>
<td>NYHA IV 25%</td>
<td>Nil</td>
<td>27%</td>
</tr>
<tr>
<td>Digoxin 73%</td>
<td>Nil</td>
<td>87%</td>
</tr>
<tr>
<td>B-Blockers 10.5%</td>
<td>27%</td>
<td>87%</td>
</tr>
</tbody>
</table>
EMPHASIS-HF Study

PRIMARY ENDPOINT RESULTS
CV DEATH OR HOSPITALIZATION FOR HF

HR* [95% CI] = 0.63 [0.54, 0.74], p < 0.0001, RRR = 37%

*Unadjusted HR 0.66; 0.56, 0.78; p<0.0001, HR = Hazard Ratio, CI = Confidence Interval, RRR = Relative Risk Reduction

# EMPHASIS-HF Study

## SECONDARY ENDPOINT RESULTS

### CAUSES AND MODES OF DEATH

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Eplerenone (N=1364)</th>
<th>Placebo (N=1373)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause (%)</td>
<td>171 (12.5)</td>
<td>213 (15.5)</td>
<td>0.76 (0.62, 0.93)</td>
<td>0.008</td>
</tr>
<tr>
<td>Cardiovascular death (%)</td>
<td>147 (10.8)</td>
<td>185 (13.5)</td>
<td>0.76 (0.61, 0.94)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death from worsening heart failure (%)</td>
<td>45 (3.3)</td>
<td>61 (4.4)</td>
<td>0.68 (0.46, 1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>Sudden cardiac death (%)</td>
<td>60 (4.4)</td>
<td>76 (5.5)</td>
<td>0.76 (0.54, 1.07)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

All results are adjusted for prespecified baseline characteristics. Unadjusted analyses revealed similar results.
Summary

• Both work
• Spironolactone 11.3% absolute risk reduction
• In a group of sicker patients without the benefit of betablockers
• Eplerenone absolute 7.6% risk reduction on a lower risk and optimally treated group with milder symptoms
"But I don't want water tablets, Doctor!"

Not a diuretic – they just stop your body retaining fluid in the first place!
Cardiac Re-Synchronisation Therapy
CRT – Cardiac Resynchronisation Therapy

- This occurs in HF with LBBB
- 10% of HF patients per annum develop LBBB
- It results in the septum contracting long before the Posterior wall
- Putting in a pacemaker to make both walls contract at the same time greatly improves SOME HF patients and
- Improves cardiac output, reduces Mortality and reduces Mitral Regurgitation
- If you see HF and the ecg shows LBBB - - broad QRS –
- REFER THEM!
CRT – New Indications

Santangeli P
Meta-analysis and systematic review

• 4 Trials - : MIRACLE ICD-II ; REVERSE;MADIT-CRT & RAFT
• Decreased mortality (OR 0.78 p<0.024)
• HF events (OR 0.63 p< 0.001)
• Prevention of progression(OR 0.54 p<0.026)
• Improved reverse remodelling (p<0.015)
CRT Now indicated in...

- AHA : NYHA II – Class 1 recommendation (QRS >150)
- ESC : NYHA III/IV Class 1 recommendation (QRS >120)
Ivabradine
Ivabradine

• A Rate slowing agent that acts on the Sinus Node
• That Means you have to have a working sinus node – lie be in Sinus Rhythm
• In AF you don’t have a functional sinus node

SO IT WILL NOT WORK IN AF!!
Heart rate in CHF

Heart rate and mortality in CHF

- Change in mortality (%)
- Change in heart rate (bpm)

- XAMOTEROL
- VHeFT (prazosin)
- PROFILE
- PROMISE
- CIBIS
- NOR TIMOLOL
- GESICA
- BHAT
- ANZ
- US CARVEDILOL
- MOCHA
- SOLVD
- CONSENSUS
- VHeFT (HDZ/ISDN)
Kaplan-Meier curves showing the effects of beta blocker (BB) dose measured at visit 2 on survival and adjusted for heart rate, left ventricular impairment, loop diuretic use, creatinine, and age.
Increasing evidence suggesting that HR achieved not beta blocker dose predicts outcome\textsuperscript{1,2,3}

Kaplan–Meier curves showing the effects of heart rate measured at visit 2 on survival and adjusted for beta blocker use, left ventricular impairment, loop diuretic use, creatinine, and age.

<table>
<thead>
<tr>
<th>Heart Rate Quartiles</th>
<th>( \leq 57 \text{ bpm} )</th>
<th>58-64 bpm</th>
<th>65-74 bpm</th>
<th>&gt;74 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pair-wise p-values</td>
<td>0.46</td>
<td>0.11</td>
<td>0.023</td>
<td>0.05</td>
</tr>
<tr>
<td>( 58-64 \text{ bpm} )</td>
<td>-</td>
<td>0.023</td>
<td>-</td>
<td>0.011</td>
</tr>
<tr>
<td>( 65-74 \text{ bpm} )</td>
<td>0.023</td>
<td>-</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>&gt;74 bpm</td>
<td>0.011</td>
<td>0.023</td>
<td>0.69</td>
<td></td>
</tr>
</tbody>
</table>
Risk of hospitalisation or death at six months according to baseline heart rate

6 month event rates for the primary composite endpoint in patients on standard background therapy* according to quintiles of HR at baseline

*Placebo group background therapy:
- BB 88%
- ACEi/ARB 90%
- Diuretics 83%
- MRA** 61%
- Cardiac glycosides 24%

**Mineralocorticoid receptor antagonist

n=3,264
And it seems good!- for Beta-blocker intolerance and extra slowing
Key facts on Ivabradine

- Push Beta-blocker as much as possible first
- NY II – IV
- Stable
- Licensed if EF < 35% AND pulse > 75 BPM
- **AND HAVE TO BE IN SINUS RHYTHM**
Beta Blockers
A post script
EVEREST trial (tolvaptan)

Not being on a beta-blocker imparts a major risk of death in HF
Beta-Blockers in COPD

Lipworth B 2011 BMJ
Visits to A+E for asthma and COPD patients given beta-blockers

Brooks TW., Pharmacotherapy 2007

• Retrospective Observational cohort study
• 11,592 patients

Asthma +/- COPD

• + Cardioselective BB 0.89 risk of admission; 1.40 for A+E visits
• Non-selective BB - 2.47 Hosp Adm. 1.21 A+E
And in COPD...

• Cardiode selective BB 0.64 for admission and relative risk of 1.19 for A+E visits
• Non-selective BB 1.02 and 0.51

Conclusions

1. Be cautious in Asthma
2. Cardiode selective BB slight risk
3. Nonselective betablockers REDUCED visits and admissions
Rowell's Rule of Beta-Blockade

You can put a lot of people on a beta-blocker but you can’t put a lot of people on a lot of beta-blocker!!
The End

Thank you for Listening

If you didn’t, I hope you managed a good deal!

No Meerkats were harmed in the making of this presentation