Patient self-management of oral anticoagulation

Professor DA Fitzmaurice
Department of Primary Care & General Practice
University of Birmingham
GPs and Anticoagulation

• Massive increase in pt numbers
• Non-rheumatic AF
• Pressure on hospital clinics
The Birmingham Experience

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Objective

- To develop a model to effect the transfer of warfarin management from secondary to primary care
  - Safely
  - Effectively, clinically and financially
  - Minimal organisational disruption
# Results - INR point prevalence

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Back data</th>
<th>Study data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients in range (%)</td>
<td>Patients in range (%)</td>
</tr>
<tr>
<td><strong>Intervention</strong> n=98</td>
<td>65</td>
<td>77*</td>
</tr>
<tr>
<td><strong>Intra control</strong> n=84</td>
<td>61</td>
<td>63*</td>
</tr>
<tr>
<td><strong>Inter control</strong> n=131</td>
<td>55</td>
<td>70</td>
</tr>
<tr>
<td><strong>Total control</strong> n=215</td>
<td>57</td>
<td>67*</td>
</tr>
</tbody>
</table>

* McNemar p < 0.05
## Results - INR time in range

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Back data (%)</th>
<th>Study data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention n=112</td>
<td>56</td>
<td>70*</td>
</tr>
<tr>
<td>Intra-control n=92</td>
<td>53</td>
<td>55</td>
</tr>
<tr>
<td>Inter-control n=138</td>
<td>62</td>
<td>65</td>
</tr>
<tr>
<td>Total control n=230</td>
<td>59</td>
<td>61</td>
</tr>
</tbody>
</table>

*Wilcoxon p < 0.01
# Results - Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>CVA</th>
<th>TIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>1*</td>
<td>0</td>
</tr>
<tr>
<td>Intra-control</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Inter-control</td>
<td>4**</td>
<td>3</td>
</tr>
</tbody>
</table>

* fatal
** Includes 1 fatality
Cost-effectiveness

• Strokes/charges
  – Intervention cheaper with fewer strokes

• Strokes/costs
  – Intervention costs $1500 per stroke averted
Summary

• **Intervention**
  – Improved clinical outcomes
  – Improved INR point prevalence
  – Improved INR time in range
  – Cost effective in terms of charges
  – Similar QoL measures
The current debate


“GPs shouldn’t do this”
The current debate

Fitzmaurice DA, Hobbs FDR, Murray ET


“Should Haematologists be allowed to do it?”
The current debate

ESCAT study
Bernando A. Patient self-management of oral anticoagulation
J Thrombosis Thrombolysis 1996;2:1886

“Patients should do it”
Patient self-management (PSM)

- Alternative model of care similar to glucose monitoring
- Widespread in Germany, also USA
- Routine care not comparable to UK standards
- NPT used (Coaguchek S) shown to be reliable in previous studies
Pilot Study

Fitzmaurice DA, Murray ET, Gee KM, Allan TF, Hobbs FDR.


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## Results - Pilot

<table>
<thead>
<tr>
<th></th>
<th>Percent time in range (95%CI)</th>
<th>Proportion of tests in range (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self management</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=23</td>
<td>74 (67-81)</td>
<td>66 (61-71)</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=26</td>
<td>77 (67-86)</td>
<td>72 (65-80)</td>
</tr>
</tbody>
</table>

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Aim of SMART

To evaluate clinical and cost effectiveness of PSM compared to routine care
Outcome measures

• INR control (ITT and on-treatment)
  Percentage time in range
  Number of tests in range
• Bleeding/thrombotic complications
• Associated costs
Method

• 49 general practices recruited
• All patients aged 18 or over with long term indication having taken warfarin for at least 6 months
• Randomly allocated into intervention (PSM) or control (routine care)
Training

- 2 workshops of 2 hours one week apart
- Theoretical and practical aspects
  - Performing blood test using NPT
  - Quality control
  - Managing the result
- Assessment
Management

• 12 month intervention
• NPT device for INR estimation
• Simple algorithm for dosage adjustment
Coaguchek S

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<table>
<thead>
<tr>
<th>Blood Test Result</th>
<th>Action</th>
<th>Next Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 5</td>
<td>Warning icon</td>
<td>As advised</td>
</tr>
<tr>
<td>3.1 – 4.9</td>
<td>Decrease dose by $\frac{1}{2}$ mg</td>
<td>1 week</td>
</tr>
<tr>
<td>2 – 3</td>
<td>Remain on same dose</td>
<td>2 weeks</td>
</tr>
<tr>
<td>1.6 – 1.9</td>
<td>Increase dose $\frac{1}{2}$ mg</td>
<td>1 week</td>
</tr>
<tr>
<td>Under 1.5</td>
<td>Warning icon</td>
<td>As advised</td>
</tr>
</tbody>
</table>

- **Brown tablet** = 1 mg
- **Blue tablet** = 3 mg
- **Pink tablet** = 5 mg

Contact the research team
Before you contact the research team:
Carry out an internal quality control test and note down your result to tell the research team
Think
Have you taken too many or missed any warfarin tablets?
Have you started any new medications recently?
Management

• 2 weekly tests unless dosage change then 1 weekly

• IQC and EQA

• Support from hospital, practice and research staff
Control patients

• Continued with routine care (mainly hospital)
Results

- 2530 eligible
- 60 excluded by GP
- 2470 invited
- 617 (25%) recruited
  - 337 PSM, 280 control
Results

337 patients randomised to PSM

95 (28%) did not complete training
242 (72%) commenced PSM
193 (57%) completed 12 months PSM
Results

Main reasons for drop out of training:
  Concerns over frequency of testing, difficulty obtaining sufficient blood sample or correct placing onto test strip

Main reasons for drop out during intervention:
  Concerns over accuracy of NPT, serious adverse events, hospitalisation, protocol violation
Results - Demographic

Significantly more men than women invited and consented to enter the study
55% male, 45% female (p<0.001)

Mean age 64 years PSM arm v 66 years control arm

Significantly more patients recruited were educated above GCSE 47% v 39% (p=0.03)
Results INR control

No difference in pre study versus study INR control within both groups

Study INR control equivalent between PSM and control arms (70% versus 68%)
### Results - INR % percentage time in range

<table>
<thead>
<tr>
<th></th>
<th>Pre study</th>
<th>study</th>
<th>Patient years</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSM total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 337</td>
<td>68</td>
<td>70</td>
<td>318</td>
</tr>
<tr>
<td>On treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 242</td>
<td>69</td>
<td>72</td>
<td>216</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 280</td>
<td>69</td>
<td>68</td>
<td>264</td>
</tr>
</tbody>
</table>

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# Results - Number of tests in range

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<th>Patient years</th>
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Adverse events

PSM 9 events, (5 off treatment*)
1 Cerebral haemorrhage (fatal)*, 2 thrombotic strokes,  
2 GI bleeds* (1 fatal), 1 femoral artery graft thrombosis*,  
1 TIA, 1 epistaxis* and 1 rectal bleed*  
Control 7 events  
1 cerebral haemorrhage, 2 PE,  2 GI bleeds,  
1 haematuria, 1 thrombotic stroke
Results - Costs

• PSM total costs
  £381.53 for 12 month study period

• Control total costs
  £89.89 for 12 month study period
Patient self-management of warfarin

- SMART trial

- Economic evaluation
  - Cost data
  - Effectiveness data

- Patient preferences
  - focus groups
  - willingness to pay
Economic evaluation - methods

• Stochastic cost analysis
  – Mean costs (95% CI)
  – Bootstrapping for skewed data

• Complete case analysis

• Intention to treat

• Incremental cost effectiveness analysis
  – no difference in utility/time in range
  – cost minimisation analysis
Economic evaluation - results

Control arm total costs

PSM arm total costs

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## Economic evaluation - results

<table>
<thead>
<tr>
<th></th>
<th>Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n=265)</td>
</tr>
<tr>
<td>Anticoagulation costs (£)*</td>
<td>89.89 (82.90-96.87)</td>
</tr>
<tr>
<td>Additional NHS costs (£)</td>
<td>32.43 (12.39-52.47)</td>
</tr>
<tr>
<td>Total costs (bootstrapped) (£)*</td>
<td>122.32 (103.47-143.69)</td>
</tr>
<tr>
<td>Costs incurred by the patient (£)*</td>
<td>57.48 (53.71-61.24)</td>
</tr>
<tr>
<td>QALYs after one year</td>
<td>0.725 (0.686-0.764)</td>
</tr>
</tbody>
</table>

* p<0.001

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Willingness to pay

“A method of measuring the value an individual places on a good, service or reduction in the risk of death and illness by estimating the maximum monetary amount an individual would pay in order to obtain the good, service, or risk reduction”

Willingness to pay - methods

- Questionnaire mailed to all study participants
- Explanation of PSM
- Payment “ladder” approach
  - Cost per month (£0 to £100+)
  - Choose maximum WTP value
  - Reason for response
- Mean WTP
- Preferred model of care
Preferred model of care

![Graph showing preferred model of care for different trial arms. The graph compares PSM and Routine care for All, Control, and PSM groups, with percentages ranging from 42.8 to 53.6.](image)

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Willingness to pay results (1)

- 512 mailed (230 control, 282 PSM)
- Completed replies 395 (77.1%)
- Did not state WTP value 28 (7.1%)
- Not willing to pay 184 (50.4%)
- “Protest” responses 74 (40.0%)
Willingness to pay results (2)

Frequency distribution of WTP values

Mean WTP (sd) £5.28 (9.92)
## Willingness to pay results (3)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean WTP (sd) (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control arm (n=157)</td>
<td>3.61 (5.60)</td>
</tr>
<tr>
<td>PSM arm (n=182)</td>
<td>6.98 (12.74)</td>
</tr>
<tr>
<td>&lt;65 years old (n=112)</td>
<td>8.86 (14.84)</td>
</tr>
<tr>
<td>65+ years old (n=227)</td>
<td>3.72 (6.25)</td>
</tr>
<tr>
<td>Prefer routine care (n=175)</td>
<td>1.79 (3.51)</td>
</tr>
<tr>
<td>Prefer PSM (n=164)</td>
<td>9.32 (13.09)</td>
</tr>
<tr>
<td>No preference (n=23)</td>
<td>4.26 (6.73)</td>
</tr>
<tr>
<td>No qualifications (n=86)</td>
<td>3.20 (4.95)</td>
</tr>
<tr>
<td>GCSE/O’Level (n=110)</td>
<td>4.43 (6.80)</td>
</tr>
<tr>
<td>A Level (n=73)</td>
<td>7.48 (14.53)</td>
</tr>
<tr>
<td>Degree level (n=46)</td>
<td>10.28 (15.15)</td>
</tr>
</tbody>
</table>
Issues raised

• PSM equally effective…but more expensive

• Patient benefits not measured by QoL

• Preferences for PSM explored
  – Personal benefits
  – Willingness to pay

• Do these benefits to patients matter?

• Should public money be used to fund PSM?
Discussion

• 25% of patients willing and able to self-manage
• INR control/Adverse event rates equivalent
• Follow-up?
• Who pays?
• Ximelagatran?
Recent meta-analysis

- Heneghan C, et al

“significant reduction in thromboembolic events (odds ratio 0.45), major hemorrhagic events (odds ratio 0.65), and all-cause mortality (odds ratio 0.61) for those in a SM or self-test strategy”
Conclusion

• PSM is clinically effective and may be useful for a significant minority of patients
• SMART training model is simple and effective
• PSM will have a role in oral anticoagulation management for the foreseeable future