# Sensitivity of PRO's in evaluating adverse events in people receiving influenza vaccination

Wade AG[1], Crawford GM[1], Pumford N[1], McConnachie A[2]

Patients Direct, Glasgow, UK

The Robertson Centre Biostatistics, University of Glasgow, UK

## Aim:

To investigate whether patient reported outcomes could detect differences between H1N1 and seasonal influenza vaccinations (SFV) on adverse events over a 26 week follow up period.

## Method:

***PROBE*** methodology consisting of a web-based system supplemented by telephone reporting was used to collect naturalistic data from people who had received an influenza vaccination during 2009-2010 season. People were recruited through media advertising and awareness campaigns in public places and work.

Data collection on day of immunisation, after 3 days, 8 days, 6 weeks, 12 weeks and 26 weeks.

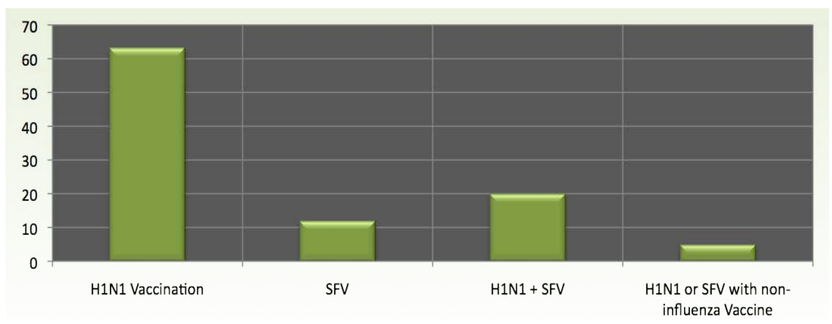
Data included:

- baseline demographics
- presence or absence of chronic illness
- flu vaccination history
- any side effects

## Results:

**Participations:** A total of 1103 vaccine recipients including 134 young children (< 5 years) participated.

### Vaccine received:




694 (63%) received H1N1 vaccine only, 135 (12%) seasonal only, 224 (20%) both H1N1 and seasonal vaccines and 50 (5%) received H1N1 or seasonal vaccine with a non-influenza vaccine (e.g. travel or pneumococcal).

### Side effects:

Overall, 70% of respondents reported experiencing a side effect after vaccination – this includes pain/discomfort at the injection site and any other side effects. Of the 964 recipients of an H1N1 vaccine, significantly more (511, 74%) experienced a side effect compared with those who received only the seasonal flu vaccine (45%, $X^2$-test p <0.001).

Multivariate regression analysis revealed that female sex and the H1N1 vaccination were more likely to report any side effect (OR 2.10, p<0.001 and OR 4.47, p<0.001 respectively) and age > 70 less likely to report (OR 0.29, p<0.001).

Number (%) of respondents with local side effects of discomfort and/or pain and their duration following baseline influenza vaccination

| Discomfort/pain | H1N1 total | Not H1N1 total | Overall | p-value[b] |
|---|---|---|---|---|
| **Presence** | | | | |
| N (NMISSING) | 960 (0) | 143 (0) | 1103 (0) | |
| Discomfort | 377 (39.3%) | 26 (18.2%) | 403 (36.5%) | <0.001 |
| Pain | 212 (22.1%) | 11 (7.7%) | 223 (20.2%) | <0.001 |
| Discomfort/pain | 589 (61.4%) | 37 (25.9%) | 626 (56.8%) | <0.001 |
| **Duration** | | | | |
| N (NMISSING) | 901 (59) | 138 (5) | 1039 (64) | |
| None | 371 (41.2%) | 106 (76.8%) | 477 (45.9%) | |
| <5 min | 32 (3.6%) | 2 (1.4%) | 34 (3.3%) | |
| >5 min, <1 h | 18 (2.0%) | 1 (0.7%) | 19 (1.8%) | p<0.001 |
| >1 h, <1 day | 47 (5.2%) | 5 (3.6%) | 52 (5.0%) | |
| >1 day, <3 days | 278 (30.9%) | 16 (11.6%) | 294 (28.3%) | |
| >3 days | 155 (17.2%) | 8 (5.8%) | 163 (15.7%) | |

Number (%) of respondents recording any side effects following baseline influenza vaccination

| Side effects | H1N1 only | Seasonal only | H1N1 and seasonal | H1N1/seasonal and other | Overall | p-valued | H1N1 total | Not H1N1 total | p-value |
|---|---|---|---|---|---|---|---|---|---|
| N (NMISSING) | 694 (0) | 135 (0) | 224 (0) | 50 (0) | 1103 (0) | | 960 (0) | 143 (0) | |
| Any | 314 (45.2%) | 35 (25.9%) | 94 (42.0%) | 20 (40.0%) | 463 (42.0%) | 0.001 | 425 (44.3%) | 38 (26.6%) | <0.001 |
| Any (including pain/discomfort) | 511 (73.6%) | 61 (45.2%) | 167 (74.6%) | 33 (66.0%) | 772 (70.0%) | <0.001 | 708 (73.8%) | 64 (44.8%) | <0.001 |
| N side effects (including pain /discomfort) /respondent | 2.0 (2.8) | 0.9 (2.0) | 2.4 (3.7) | 2.5 (4.5) | 2.0 (3.0) | <0.001 | 2.1 (3.1) | 1.0 (2.1) | <0.001 |

Number (%) of respondents recording action taken due to a side effect following baseline vaccination, with type of side effect requiring hospital use

| Action taken due to a side effect | H1N1 total | Not H1N1 total | Overall |
|---|---|---|---|
| N (NMISSING) | 949 (11) | 139 (4) | 1088 (15) |
| No event | 535 (56.4%) | 105 (75.5%) | 640 (58.8%) |
| Nothing | 165 (17.4%) | 14 (10.1%) | 179 (16.5%) |
| Self treated | 199 (21.0%) | 16 (11.5%) | 215 (19.8%) |
| Doctor advice | 27 (2.8%) | 1 (0.7%) | 28 (2.6%) |
| Doctor treatment | 17 (1.8%) | 2 (1.4%) | 19 (1.7%) |
| Hospital | 6 (0.6%) | 1 (0.7%) | 7 (0.6%) |
| p-value | | 0.002 | |
| Health service use | 50 (5.3%) | 4 (2.9%) | 54 (5.0%) |
| p-value | | 0.296 | |

Multivariate regression analyses for vaccine recipients having pain or discomfort following baseline vaccination

| Predictor | Level | Odds Ratio (95% CI), p-value | Overall p-value |
|---|---|---|---|
| Pain or discomfort | | | |
| Age | 0-4<br>5-29<br>30-49<br>50-69<br>70+ | -<br>1.06 (0.55, 2.06), p=0.862<br>1.21 (0.71, 2.07), p=0.481<br>0.59 (0.35, 1.00), p=0.049<br>0.24 (0.13, 0.43), p<0.001 | p<0.001 |
| Sex | Female | 2.12 (1.62, 2.77), p<0.001 | |
| Chronic Illness Special Group | Yes | 1.21 (0.90, 1.62), p=0.203 | |
| H1N1p flu vaccination | Yes | 4.69 (2.85, 7.71), p<0.001 | |
| Seasonal flu vaccination | Yes | 1.06 (0.68, 1.66), p=0.794 | |
| Previous H1N1p vaccination | Yes | 1.34 (0.63,2.85), p=0.447 | |
| Previous Seasonal flu vaccination | Yes | 1.28 (0.82,1.98), p=0.276 | |

### Conclusions:

- People receiving the H1N1 vaccination were more likely to experience side effects than seasonal influenza vaccination alone.
- This evaluation shows that the ***PROBE*** methodology captured patient reported outcome information in a vaccinated population including children.
- The ***PROBE*** methodology was sensitive enough to detect differences in outcomes between recipients of H1N1 and SFV.