Information and Communication Technologies

EPIWORK

Developing the Framework for an Epidemic Forecast Infrastructure

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D6.5 Academic papers on the validity of the PBS and on the concordance between results from IMS, PBA, sentinel system and laboratories

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1. Background

1.1. Overall objective of WP6

The overall objective of the work produced within Work Package 6 (WP6) was to provide a comparative analysis of the new Internet monitoring system (IMS/Influenzanet or Influensakoll) that was implemented within the framework of Work Package 5 (WP5) and a population-based approach (PBA, Sjukrapport), recently developed at the Swedish Institute for Communicable Disease Control (Smittskyddsinstitutet, SMI). Comparisons were also to be made with other existing systems for influenza surveillance in Sweden: (1) laboratory reports of influenza diagnosis, and (2) the general practice-based sentinel system of influenza surveillance. Deliverable 6.5 is the last deliverable from WP6 and consists of academic papers on the validity of PBA surveillance and concordance between results from the IMS, PBA and sentinel and laboratory surveillance.

1.2. Overview of activities related to Deliverable 6.5

1.2.1. Population based approach (PBA)

Sjukrapport was developed by epidemiologists at SMI and the Karolinska Institute (KI) and has been in use since 2007 (1). For the past five influenza seasons, SMI has invited between 12,000 and 15,000 people living in Stockholm to be a part of Sjukrapport. The methodology was described in Deliverable 6.1. The weekly cumulative incidence generated by Sjukrapport is used in real-time surveillance, age-standardized and adjusted for misclassification according to Merk, *et al*. (2), which was described in deliverable 6.4.

In the 2011-2012 season, we invited 14,022 people in a random sample of Stockholm's population between the ages of 3 months and 95 years to participate. The methodology was described in Deliverable 6.1 and the recruitment was described in Deliverable 6.4. The invitations resulted in 2,556 participants. Participants were recruited in week 35-37, 2011, and data began to be used in surveillance starting week 40. The system ran until week 20, 2012.

In the 2012-2013 season, the random sample was extended to the national level. We invited 14,558 people in a random sample of Sweden's population between the ages of 3 months and 95 years to participate. The majority of the sample was invited during week 44 of 2012, while about a third was invited in week 50. The invitations resulted in 2,234 participants and data began to be used in surveillance starting week 2, 2013. The system ran until week 20, 2013.

1.2.2. Internet monitoring system (IMS)

The Influenzanet platform was developed in the Netherlands in 2003 (3) and is now used in several European countries, including Sweden since 2011. The Swedish platform is called Influensakoll. Influensakoll is a web-based reporting system engaging the general population to report weekly if they have had any symptoms of colds or influenza-like illness or not in the preceding week. The participants are self-recruited after broad invitations through media campaigns and other communication efforts. See below under method for season-specific recruitment information.

2. Academic Paper on Validity of self-reports in the PBA surveillance system

As part of the development of the PBA system (Sjukrapport), we conducted a validation study to determine how well the system captures ongoing disease status in the population. This analysis was described in deliverable 6.4 and published in PLoS One in April 2013(2). Please see Appendix 1 for the published article.

3. Academic paper on representativeness and concordance between results from IMS, PBA, sentinel system and laboratories

Data from the Swedish IMS system (Influensakoll) collected during the 2011-2012 and 2012-2013 influenza seasons have been analyzed in terms of acceptability, timeliness, representativeness of participants and concordance of epidemic (disease occurrence) curves generated by the IMS system and by three other influenza surveillance systems in Sweden.

The extension of the EPIWORK project to July 2013 enabled inclusion of the 2012/2013 season in our analysis, which strengthens the analysis. This deliverable report is also being condensed into a manuscript for submission to a suitable scientific journal before the review meeting in September 2013.

3.1. Method

All analyses are based on data collected during the influenza seasons 2011-2012 and 2012-2013. In both seasons, information about Influensakoll was spread via regular media, social media and word of mouth, and the website was open for anyone who wished to participate. Additionally, in the 2012-2013 season, participants from the 2011-2012 season were re-contacted via e-mail with a new invitation to participate.

Influensakoll 2012-2013 started recruitment and data collection in week 48, 2012 and ran up to and including week 20, 2013.

Further, to investigate if it would be possible to mount a population-based variant of Influensakoll, a random sample (n=2511) of the Swedish population (aged 3 months to 95 years) was drawn from the essentially complete and continuously updated population register by Statistics Sweden (SCB) for the 2012-2013 season. Selected individuals were personally invited by post (followed by one postal reminder) to participate in Influensakoll. These invited individuals were asked to give an identification code when starting an account at influensakoll.se and thereafter they participated on the same terms as the self-recruited participants.

We analyzed the personally invited population-based participants and the other, self-recruited participants separately in terms of representativeness, reporting activity level, and timeliness of reports. Because of a low participation rate (7.5%), the population-based, invited group consisted of only 166 participants. Therefore, a separate analysis of disease occurrence for this group was not possible.

3.1.1. Active participation

Since it could be suspected that the self-selection into Influensakoll is biased, favouring people with symptoms to join Influensakoll and to respond to the weekly reminders in comparison to the general population, we defined a report as active only if it was preceded by at least one report in the previous three weeks (below referred to as *active*). Further, we also applied a more strict definition in a supplementary analysis to explore the differences in disease patterns generated by participants at different levels of reporting activity. The stricter criteria defined a report as active only if it was preceded by two consecutive reports the previous two weeks (below referred to as *strict active*). Furthermore, participants that filled in unreasonable information, such as a birth date in the future, and participants with missing information on post code, age or sex were excluded from our analyses.

3.1.2. Representativeness

To measure to what extent the Influensakoll participants represented the Swedish population, we compared distributions of age, sex, level of education, and county of residence between Influensakoll participants and the general Swedish population by chi-square tests. For the small, invited group from the 2012-2013 season, we used region of residence instead of county. A p-value of less than 0.05 was interpreted as a significant difference between the participants and the target population. Participants who created an account in the system but never submitted a report were excluded from the analysis of representativeness. Additionally, we performed a supplementary analysis of representativeness including only participants who had contributed at least one *active* report according to the definition described above.

3.1.3. Acceptability

Acceptability reflects the willingness of persons to participate in a surveillance system. To assess acceptability, we calculated the participation rate among actively invited individuals, the weekly response rate among enrolled participants, and the total, mean and median number of reports per participant. The weekly response rate was defined as the number of received reports divided by the accumulated number of participants up through the week in question.

3.1.4. Timeliness

Timeliness reflects the speed between steps in a surveillance system. To assess timeliness in Influensakoll, we analysed the time between the reported date of symptom onset and the date of report.

3.1.5. Comparison of epidemic curves

A report was defined as influenza-like illness (ILI) according to the following case definitions:

2011-2012: Sudden onset of symptoms AND at least one of the following three systemic symptoms; fever or feverishness, headache, or myalgia AND at least one of the following four respiratory symptoms; cough, sore throat, shortness of breath, or coryza (stuffed or runny nose).

2012-2013: Sudden onset of symptoms AND at least one of the following three systemic symptoms; fever or feverishness, headache, or myalgia AND at least one of the following three respiratory symptoms; cough, sore throat, shortness of breath.

Only complete reports were considered for the analysis. The weekly incidence proportions (%) among Influensakoll participants were calculated by dividing the number of active reports of ILI by the number of active reports in total that week. For ILI reports, the week of fever onset or symptom onset was used for analysis. If this information was missing, the date of report was used. Influensakoll allows participants to report episodes of illness from the past. However, in order to evaluate the surveillance system as the data are available in real-time, this analysis excludes reports of symptom onset more than 7 days before the report date. In addition, when an Influensakoll participant reported symptoms fitting the same case definition in two consecutive weekly reports, the two reports were considered the same episode of illness and only the first report was included in the data analysis.

To increase comparability with Sjukrapport 2011-2012, comparison of epidemic curves for this season was based on Influensakoll and laboratory data from Stockholm County only. General practitioner (GP) based sentinel data at the Stockholm level generated small numbers, so comparison to the IMS and PBA systems was not possible. For 2012-2013 data, all comparisons were made on the national level and included all four surveillance systems. The weekly incidence proportions, generated by Influensakoll and Sjukrapport, were smoothed using a two week moving average. For a visual comparison, we plotted the smoothed incidence proportions (Influensakoll and Sjukrapport), the ILI per 100 000 listed patients (GP sentinel reports), and number of laboratory-confirmed influenza cases (laboratory reports from routine diagnosis). We then performed cross-correlation analyses between 1) Influensakoll and Sjukrapport, 2) Influensakoll and laboratory data, 3) Sjukrapport and laboratory data, 4) Influensakoll and GP-sentinel data, and 5) Sjukrapport and GP sentinel data. Correlation coefficients (r) were calculated for different lags using Spearman's correlation on ranked data. The significance cut off was set to $p=0.05$.

Please note that the raw data from sentinel surveillance, laboratory reporting, and community-based reporting systems represent different aspects of an influenza epidemic: the sentinel data denote the activity of ILI among patients visiting GPs; laboratory reports represent the influenza activity in the hospitals; while the Sjukrapport and Influensakoll data refers to the ILI activity in the community.

In order to address the question of if and how Influensakoll incidence data could be calibrated through mathematical transformation, we examined the frequency distribution and temporal pattern of week-wise differences in incidence proportions between Influensakoll and Sjukrapport, which – after correction for previously studied misrepresentation of demographic substrata (1) and remarkably constant under-reporting (2) – was considered to be the validated gold standard. This was done separately for each season. After examination of the appearance of the frequency distributions, the most suitable central tendency and variability measures were chosen. We then plotted the weekly differences, with 95% confidence intervals, against calendar time. Of particular interest was possible systematic drift over time and systematic deviations during the influenza peaks.

3.2. Results

3.2.1. Representativeness

In the 2011-2012 season, 2,554 self-selected Influensakoll participants submitted at least one report, while the corresponding number for the 2012-2013 season was 2,488. In the latter season, another 166 participants, constituting the 7.5% who received and accepted the active invitation, also submitted at least one report.

In Tables 1 through 3, the socio-demographic characteristics of Influensakoll participants are compared with corresponding data from the entire Swedish population, obtained from Statistics Sweden. Table 1 shows data from the 2011-2012 season, Table 2 for the 2012-2013 season among the self-selected Influensakoll participants, and Table 3 for the 2012-2013 season among invited participants. In all of the tables below, participants were defined in two ways: (1) participants who had submitted at least one report; and (2) participants who had submitted at least one *active* report, as elaborated in the Methods section.

In both seasons, and irrespective of how participation was defined, the distributions of age groups, gender, level of education, and county of residence among the self-recruited Influensakoll participants were markedly and statistically significantly different from the distributions in the general Swedish population. Women, highly educated people, those aged 40-64 years, and people living in Stockholm County were the most overrepresented groups. The youngest and oldest age groups (0-17 and 65+), and participants with a low level of formal education, were the most underrepresented groups.

Despite the low participation rate, the age and gender distributions in the actively invited Influensakoll participant group were much more similar to those in the Swedish population. In particular, the under-representation of the 0-17 year and 65+ age groups was less marked and gender was more balanced. With reservation for the small numbers, the geographical distribution by county was similar to that in the Swedish population. One county (Gotland) did not have any participants from the invited group. The regional distribution of participants was also similar to the population. In terms of statistical significance, the distributions in age and education level were significantly different from the population, while the distributions in gender and geography (based on region) were not.

Table 1: Distribution of socio-demographic characteristics among the Influensakoll participants 2011-2012 and the general Swedish population 2011

	Reported at least once N (%)	P-value	At least one active report N (%)	P-value	Sweden N (%)
Age group					
0-17 yrs	294 (12)		199 (11)		1 901 291 (20)
18-39 yrs	934 (37)		589 (33)		2 711 405 (29)
40-64 yrs	1135 (44)		828 (46)		3 065 375 (32)
65+	184 (7)		160 (9)		1 798 034 (19)
Missing	7 (0)		6 (0)		0 (0)
		<0.0001		<0.0001	
Gender					
Men	898 (35)		609 (34)		4 723 159 (50)
Women	1656 (65)		1173 (66)		4 752 946 (50)
Missing					
		<0.0001		<0.0001	
Education yrs**					
< 9 yrs	101 (4)		67 (4)		1 862 355 (20)
10-12 yrs	420 (16)		264 (15)		3 348 458 (35)
13-15 yrs	475 (19)		331 (19)		1 000 336 (11)
>15yrs	1223 (48)		896 (50)		1 426 598 (15)
Missing***	335 (13)		224 (13)		1 838 358 (19)
		<0.0001		<0.0001	
County					
Stockholms län	867 (34)		612 (34)		2 087 902 (22)
Uppsala län	126 (5)		92 (5)		338 466 (4)
Södermanlands län	88 (3)		74 (4)		272 255 (3)
Östergötlands län	94 (4)		55 (3)		431 061 (5)
Jönköpings län	91 (4)		74 (4)		337 861 (4)
Kronobergs län	44 (2)		30 (2)		184 564 (2)
Kalmar län	40 (2)		24 (1)		233 076 (2)
Gotlands län	10 (0)		7 (0)		57 327 (1)
Blekinge län	10 (0)		10 (1)		153 199 (2)
Skåne län	274 (11)		185 (10)		1 251 986 (13)
Hallands län	62 (2)		46 (3)		301 307 (3)
Västra Götalands län	277 (11)		184 (10)		1 589 619 (17)
Värmlands län	31 (1)		19 (1)		272 883 (3)
Örebro län	55 (2)		34 (2)		281 339 (3)
Västmanlands län	43 (2)		32 (2)		253 881 (3)
Dalarnas län	64 (3)		45 (3)		276 730 (3)
Gävleborgs län	48 (2)		34 (2)		276 145 (3)
Västernorrlands län	146 (6)		98 (5)		242 148 (3)
Jämtlands län	20 (1)		16 (1)		126 317 (3)
Västerbottens län	76 (3)		58 (3)		259 602 (3)
Norrbottens län	63 (2)		33 (2)		248 437 (3)
Missing	25 (1)		20 (1)		-
		<0.0001		<0.0001	
Total	2554 (100)		1782 (100)		9 476 105 (100)

**16-95+ year old
*** including children in age group 0-15 yrs

Table 2: Distribution of socio-demographic characteristics among the self-recruited Influensakoll participants 2012-2013 and the general Swedish population 2012

	Reported at least once N (%)	P-value	At least one active report N (%)	P-value	Sweden N (%)
Age group					
0-17 yrs	76 (3)		57 (3)		1 860 527 (19)
18-39 yrs	876 (35)		698 (33)		2 777 239 (29)
40-64 yrs	1337 (54)		1154 (55)		3 087 669 (32)
65+	183 (7)		178 (8)		1 793 463 (19)
Missing	16 (1)		13 (1)		33 477 (0)
		<0.0001		<0.0001	
Gender					
Men	793 (32)		673 (32)		4 760 835 (50)
Women	1695 (68)		1427 (68)		4 785 613 (50)
Missing	-		-		5 927 (0)
		<0.0001		<0.0001	
Education yrs**					
< 9 yrs	124 (5)		98 (5)		1 810 813 (23)
10-12 yrs	473 (19)		394 (19)		3 378 533 (43)
13-15 yrs	502 (20)		407 (19)		1 020 584 (13)
>15yrs	1324 (53)		1145 (55)		1 476 228 (19)
Missing***	65 (3)		56 (3)		158 891 (2)
		<0.0001		<0.0001	
County					
Stockholms län	733 (29)		620 (30)		2 123 337 (22)
Uppsala län	160 (6)		134 (6)		341 465 (4)
Södermanlands län	66 (3)		54 (3)		274 331 (3)
Östergötlands län	74 (3)		63 (3)		433 462 (5)
Jönköpings län	77 (3)		66 (3)		338 907 (4)
Kronobergs län	48 (2)		38 (2)		185 695 (2)
Kalmar län	31 (1)		23 (1)		233 341 (2)
Gotlands län	9 (0)		9 (0)		57 296 (1)
Blekinge län	29 (1)		26 (1)		152 452 (2)
Skåne län	279 (11)		228 (11)		1 262 068 (13)
Hallands län	66 (3)		58 (3)		303 850 (3)
Västra Götalands län	381 (15)		313 (15)		1 598 700 (17)
Värmlands län	33 (1)		25 (1)		273 113 (3)
Örebro län	70 (3)		59 (3)		282 868 (3)
Västmanlands län	47 (2)		38 (2)		256 059 (3)
Dalarnas län	68 (3)		62 (3)		276 379 (3)
Gävleborgs län	43 (2)		40 (2)		276 425 (3)
Västernorrlands län	57 (2)		52 (2)		241 961 (3)
Jämtlands län	36 (1)		35 (2)		126 147 (1)
Västerbottens län	74 (3)		64 (3)		260 044 (3)
Norrbottens län	82 (3)		70 (3)		248 548 (3)
Missing	25 (1)		23 (1)		5 927 (0)
		<0.0001		<0.0001	
Total	2488 (100)		2100 (100)		9 552 375 (100)

**16-95+ year old
*** including children in age group 0-15 yrs

Table 3: Distribution of socio-demographic characteristics among the invited Influensakoll participants 2012-2013 and the general Swedish population 2012

	Reported at least once N (%)	P-value	At least one active report N (%)	P-value	Sweden N (%)
Age group					
0-17 yrs	20 (12)		19 (12)		1 860 527 (19)
18-39 yrs	60 (36)		52 (34)		2 777 239 (29)
40-64 yrs	66 (40)		62 (41)		3 087 669 (32)
65+	19 (11)		19 (12)		1 793 463 (19)
Missing	1 (1)		1 (1)		33 477 (0)
		0.0016		0.0082	
Gender					
Men	76 (46)		68 (44)		4 760 835 (50)
Women	90 (54)		85 (56)		4 785 613 (50)
Missing	-		-		
		0.2944		0.1809	
Education yrs**					
< 9 yrs	16 (10)		15 (10)		1 810 813 (23)
10-12 yrs	45 (27)		41 (27)		3 378 533 (43)
13-15 yrs	30 (18)		27 (18)		1 020 584 (13)
>15yrs	65 (39)		60 (39)		1 476 228 (19)
Missing***	10 (6)		10 (7)		158 891 (2)
		<0.0001		<0.0001	
County					
Stockholms län	40 (24)		38 (25)		2 123 337 (22)
Uppsala län	6 (4)		6 (4)		341 465 (4)
Södermanlands län	7 (4)		6 (4)		274 331 (3)
Värmlands län	2 (1)		2 (1)		273 113 (3)
Örebro län	1 (1)		1 (1)		282 868 (3)
Västmanlands län	2 (1)		2 (1)		256 059 (3)
Dalarnas län	10 (6)		10 (7)		276 379 (3)
Svealand region	68 (41)		65 (43)		3 827 552 (40)
Östergötlands län	6 (4)		5 (3)		433 462 (5)
Jönköpings län	6 (4)		5 (3)		338 907 (4)
Kronobergs län	3 (2)		3 (2)		185 695 (2)
Kalmar län	3 (2)		3 (2)		233 341 (2)
Gotlands län	-		-		57 296 (1)
Blekinge län	2 (1)		2 (1)		152 452 (2)
Skåne län	20 (12)		18 (12)		1 262 068 (13)
Hallands län	8 (5)		8 (5)		303 850 (3)
Västra Götalands län	33 (20)		28 (18)		1 598 700 (17)
Götaland region	81 (49)		72 (47)		4 565 771 (48)
Gävleborgs län	3 (2)		3 (2)		276 425 (3)
Västernorrlands län	4 (2)		4 (3)		241 961 (3)
Jämtlands län	2 (1)		2 (1)		126 147 (1)
Västerbottens län	5 (3)		4 (3)		260 044 (3)
Norrbottens län	3 (2)		3 (2)		248 548 (3)
Norrland region	17 (10)		16 (11)		1 153 125 (12)
Missing	-		-		5 927 (0)
		0.7492*		0. 7492*	
Total	166 (100)		153 (100)		9 552 375 (100)

* p-value regarding the regional distribution (*Svealand, Götaland, Norrland*)
** 16-95+ year old
*** including children in age group 0-15 yrs

3.2.2. Acceptability

As already mentioned, the readiness to participate in Influensakoll among randomly selected, actively invited Swedish residents was low. Less than one out of thirteen participated. The mean and median number of reports by Influensakoll participants is presented in Table 4. Reporting compliance was higher in 2012-2013 than in the preceding season. Actively invited participants were more compliant than those who were self-recruited. The invited participant group had a higher mean and median number of reports than the self-recruited participant group. This difference was statistically significant at the <0.001 level.

Table 4. Activity level of the Influensakoll participant groups 2011-2012 and 2012-2013

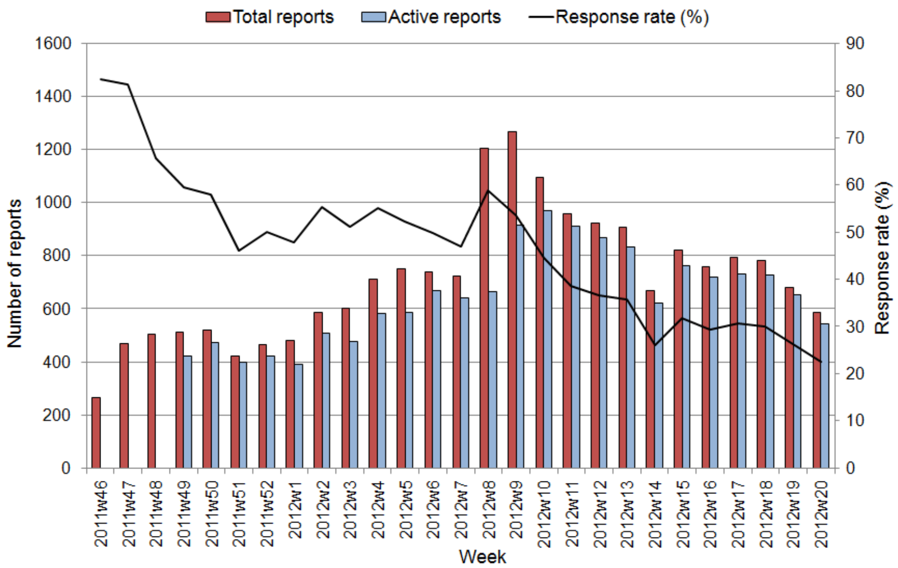
	Number of reports Total	Mean	Median	Min	Max
2011-2012					
Self-recruited participants (n=2554)	19,353	7.58	4	1	27
2012-2013					
Invited participants (n=166)	3,146	18.95	21	1	26
Self-recruited participants (n=2488)	30,744	12.36	13	1	26

Figures 1 and 2 show the total number of reports and number of active reports per week and the weekly response rate among all enrolled self-recruited participants during the 2011-2012 and 2012-2013 seasons. As the accumulated number of enrolled participants, some apparently no longer active, increased over each season, the weekly response rate (black line) decreased. As expected, the lowest point was in the last week of the surveillance season for 2011-2012. For 2012-2013, a deep dip was seen during week 12, which was due to a technical malfunction of the website. Besides this dip, an overall downward trend was observed as in the previous season.

The 2011-2012 season showed a gradual increase in terms of number of reports per week until the end of March, whereupon the trend reversed and the numbers fell somewhat. By and large, the number of reports per week was on a fairly stable level of around 800 throughout the peak of the influenza season. Interestingly, apart from the first three weeks, where no reports could be defined as active (see Methods), the difference between the total number of reports and the total number of *active* reports was generally small, implying that the overwhelming number of reports came from faithful participants who reported regularly. A notable exception was the period from February through March, during which the 2011-2012 season's influenza peaked. In particular during the highest peak (weeks 8-9 2012) the active to total report ratio fell noticeably, suggesting that many new participants entered (or less faithful old participants re-entered) into the surveillance, possibly prompted by their own influenza.

The 2012-2013 season showed a fairly steady number of active reports per week during the period of week 3 to week 11, 2013, of around 1200 reports. This was followed by the aforementioned technical malfunction in week 12, which had a significant impact on reporting. Following this, the number of active reports and response rate fluctuated more, but hovered around 1100 and 45%, respectively. As was seen in the previous season, the difference between the total number of reports and the total number of *active* reports was generally fairly small, although larger than the previous season, implying that the overwhelming number of reports came from faithful participants who reported regularly.

Figure 1: Participation activity of Influensakoll participants during the 2011-2012 influenza season, Sweden. [1]



[1] In figures 1 through 3, the weekly response rate was defined as the number of received reports divided by the accumulated number of participants up through the week in question. For definition of *active* reports, please see Methods.

Figure 2: Participation activity of self-recruited Influensakoll participants during the 2012-2013 influenza season, Sweden.

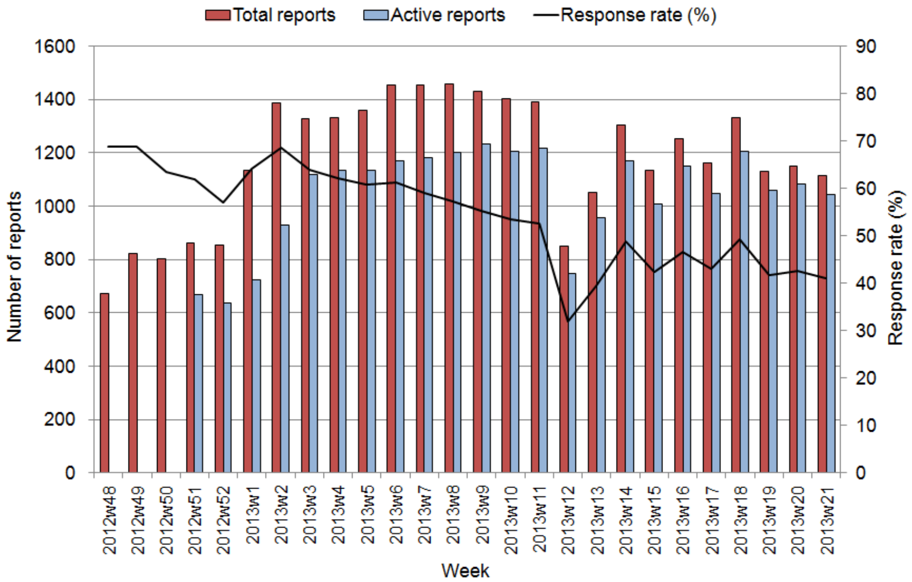


Figure 3 shows, as above, the total number of reports and number of active reports per week and the weekly response rate among the actively invited participants during the 2012-2013 season. As shown, the weekly response rate was steadier in this group (except the aforementioned dip week 12) at somewhere between just under 70% and up to 84% or so. In addition, the number of active reports per week was fairly steady at between 100 and 120 (from 166 participants).

Figure 3: Participation activity of invited Influensakoll participants during the 2012-2013 influenza season, Sweden.

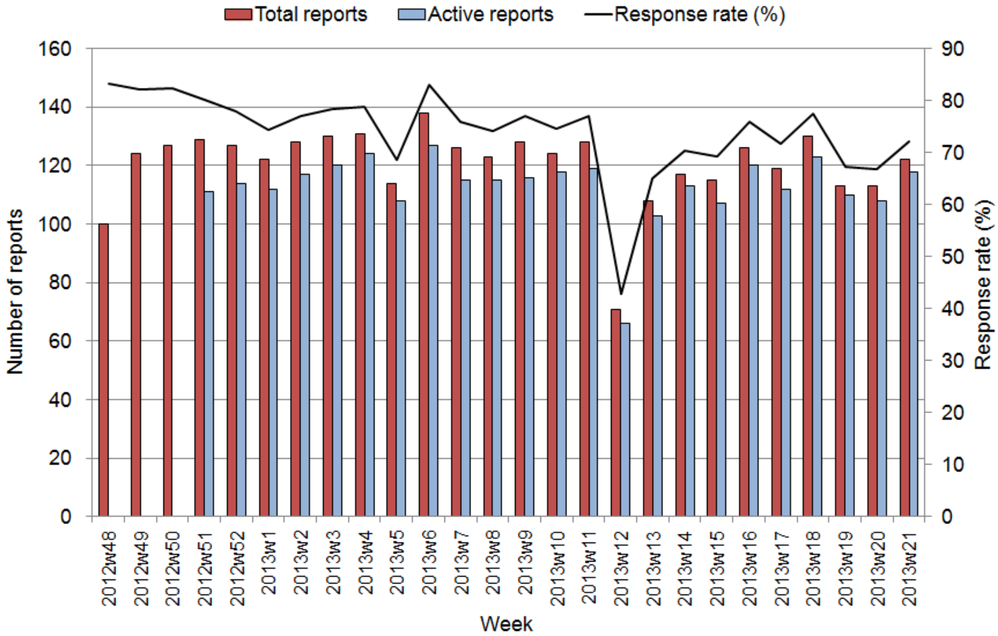
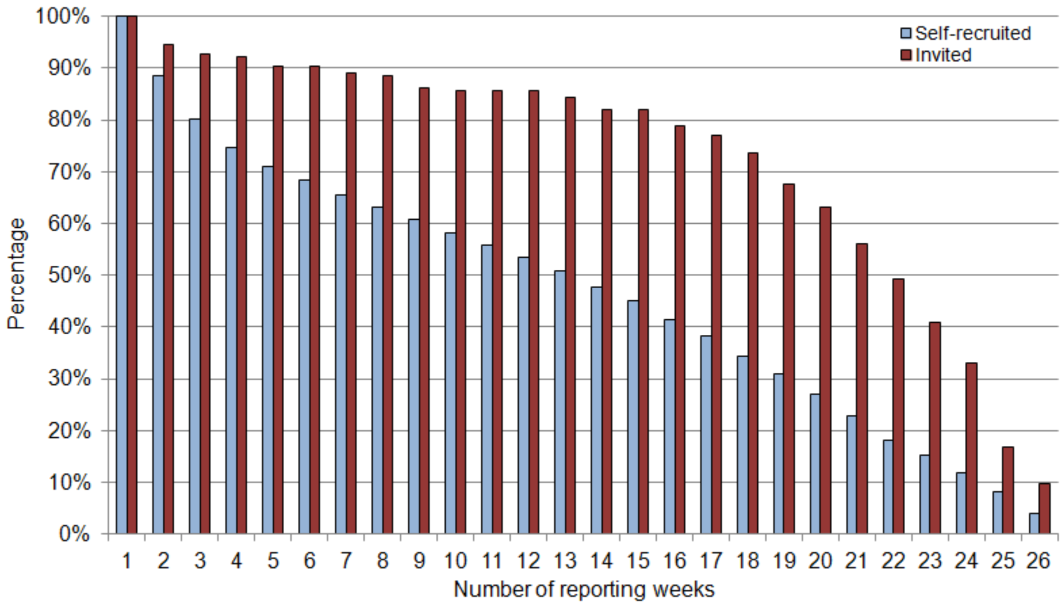


Figure 4 shows percentages of, respectively, all self-recruited and all actively invited participants who submitted 1, 2, 3, … 26 reports during the 2012-2013 season. Of all participants in the actively invited group, more than 80 percent submitted reports for at least 15 of the total 26 weeks of surveillance. In the self-recruited group, the corresponding percentage was approximately 45 percent. As shown, the invited participants had more active weeks than the self-recruited group.

A preliminary analysis of individual accrued person-time among the 2012-2013 participants shows that approximately 24 percent of the invited participants and 15 percent of the self-recruited participants reported once for each week they participated in the project. Two-thirds of invited participants and just over one third (39%) of self-recruited invitees reported at least 80 percent of the time.

Figure 4: Percentage of participants who continued reporting over time (self-recruited vs. invited), 2012-2013



3.2.3. Timeliness

Delays between reporting date and date of symptom onset are presented in Table 5. The patterns are similar across seasons and between self-recruited and invited participants.

Table 5. Delay (in days) between reporting date and date of symptom onset among Influensakoll participants 2011-2012 and 2012-2013

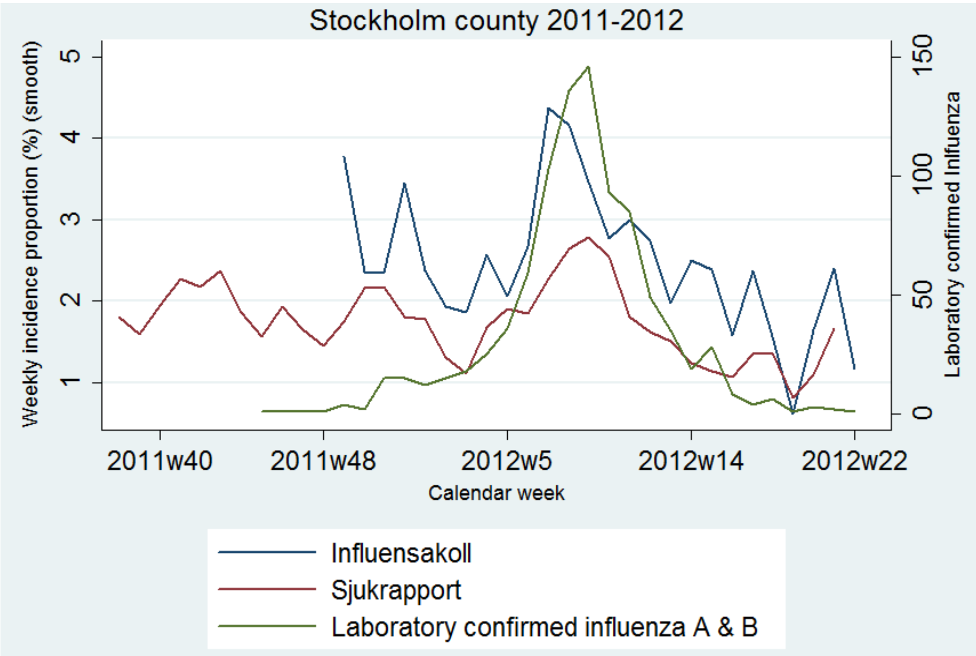
	Number of illness reports	Number of illness reports with missing onset	Delay from symptom onset			
			Mean	Median	Min	Max
2011-2012						
Self-recruited participants (n=2554)	5223	1513	17.31	6	0	4051
2012-2013						
Invited participants (n=166)	462	235	25.7	6	0	3868
Self-recruited participants (n=2488)	6379	1769	20.8	5	0	5208

3.2.4. Concordance of surveillance data

2011-2012 Stockholm County

The smoothed weekly incidence proportions of ILI from Influensakoll (based on active reports) and Sjukrapport (corrected for demographic misrepresentation and underreporting) and the number of laboratory confirmed influenza cases during the 2011-2012 influenza season for Stockholm county are shown in Figure 5. The smoothed weekly incidence proportion of ILI ranged between 0.6-4.6% in Influensakoll and 0.8-2.8% in Sjukrapport. The corresponding ranges for unsmoothed data were 0.4-4.9% and 0.5-3%. Influensakoll reached its peak in week 7, whereas Sjukrapport and laboratory reports of influenza diagnoses reached their peaks in week 9. Cross-correlation analysis showed a maximum correlation of r=0.70 between Influensakoll and Sjukrapport when no lag was applied. Both systems correlated to the same extent with laboratory report data (Influensakoll r=0.66, no lag; Sjukrapport r=0.63, no lag). All correlations were significant at the 0.05 level.

Figure 5: Smoothed weekly ILI incidence proportions generated by Influensakoll and Sjukrapport (the latter corrected for estimated demographic misrepresentation and underreporting) and number of influenza laboratory confirmed cases, Stockholm 2011-2012



2012-2013 Sweden

The smoothed weekly incidence proportions of ILI from Influensakoll and Sjukrapport, the number of laboratory confirmed influenza cases, and the number of ILI among listed patients reported from GPs from the 2012-2013 influenza season in Sweden are shown in Figures 6 and 7. The smoothed weekly incidence proportion of ILI ranged between 1.1-2.8% in Influensakoll and 0.9-3% in Sjukrapport. The corresponding ranges for unsmoothed data were 1-2.9% and 0.7-3.1%.

Cross-correlation analysis showed a maximum correlation of r=0.68 between Influensakoll and Sjukrapport when no lag was applied. This season, Influensakoll correlated better with both laboratory data and GP-sentinel data than did Sjukrapport. However, Sjukrapport's data correlated better when applying lags. Influensakoll correlated best with laboratory data without a lag (r=0.71) and Sjukrapport's when three weeks lag for laboratory data was applied (r=0.50). A maximum correlation between Influensakoll and GP-sentinel reports was found when a one week lag for Influensakoll was applied (r=0.73). Sjukrapport correlated best with GP-sentinel data at three weeks lag for sentinel data (r=0.51). All correlations were significant at the 0.05 level.

Figure 6: Smoothed weekly ILI incidence proportions generated by Influensakoll and Sjukrapport (the latter corrected for estimated demographic misrepresentation and underreporting) and number of influenza laboratory confirmed cases, Sweden 2012-2013

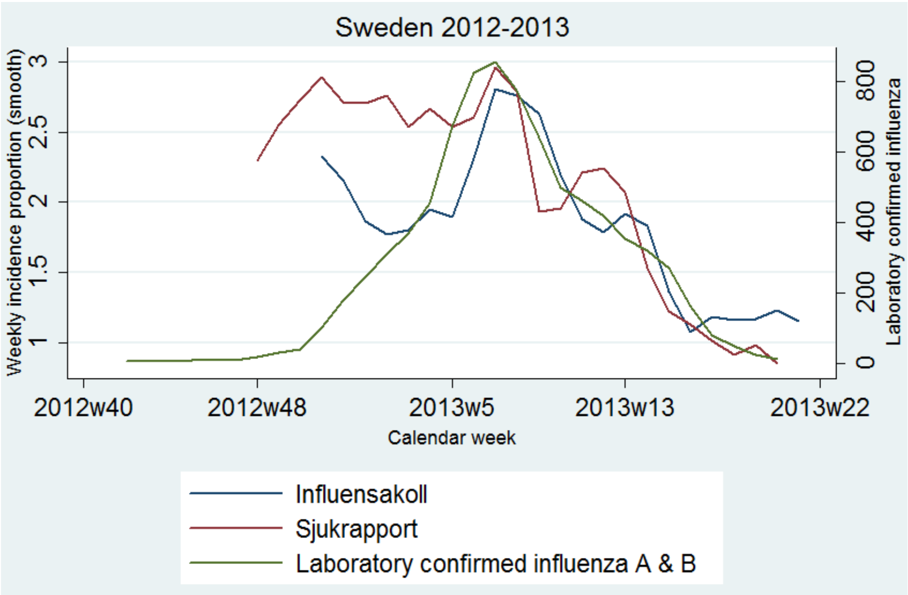
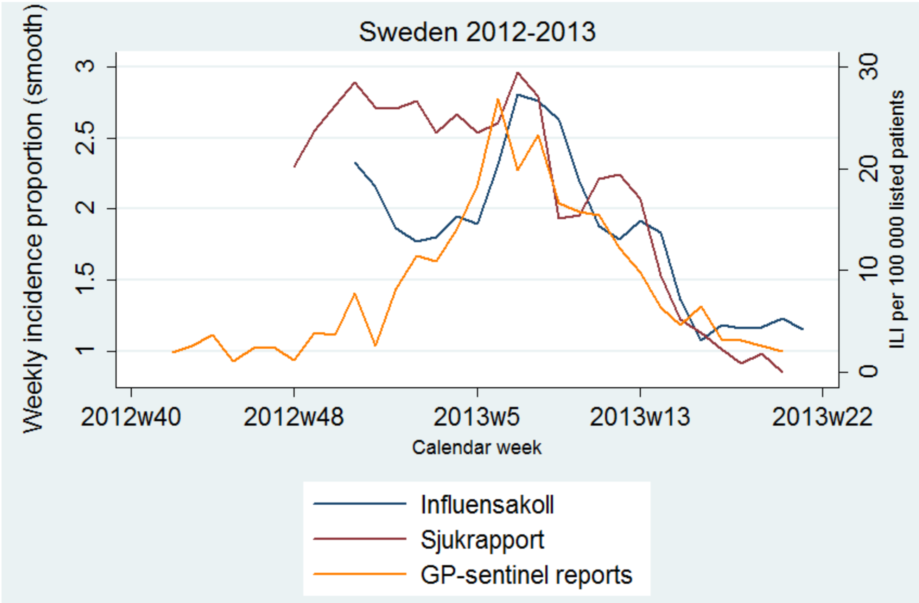


Figure 7: Smoothed weekly ILI incidence proportions generated by Influensakoll and Sjukrapport (the latter corrected for estimated demographic misrepresentation and underreporting) and proportion of ILI among listed patients in GP-sentinel reports, Sweden 2012-2013



3.2.5. Differences in weekly incidence proportions

Figure 8 exhibits the frequency distribution of differences in estimated week-wise incidence proportions between Sjukrapport (corrected for previously estimated demographic misrepresentation and underreporting) and Influensakoll (based on active reports), for the 2011-2012 season. The differences are grouped into brackets of one incidence percentage point (shown as decimal proportions). Where there are negative differences, the incidence proportions generated by Influensakoll are higher than those generated by Sjukrapport. Correspondingly, positive differences indicate Sjukrapport's incidence proportions are higher.

The differences for the season ranged from -3.5 to +1.5 percentage points. The mode of the distribution was the category -1 to -2 percentage points (meaning higher values for Influensakoll), and the distribution was skewed towards less extreme differences and negative differences. The median difference was -0.96 percentage points and the interquartile range was from -1.62 percentage points to +0.01 percentage points. Thus, in the 2011-2012 season, Influensakoll tended to yield higher incidence proportions.

Figure 8: Distribution of grouped differences in weekly incidence proportion between Sjukrapport and Influensakoll 2011-2012. The red line indicates zero difference between Sjukrapport and Influensakoll.

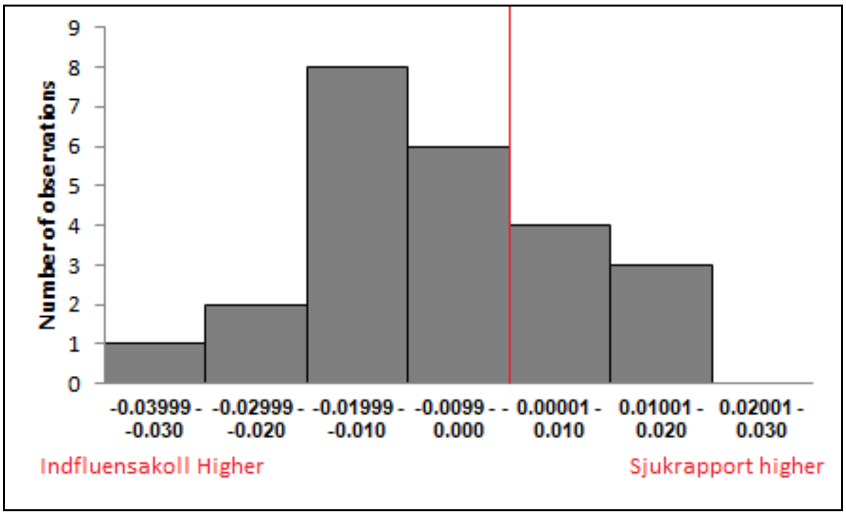
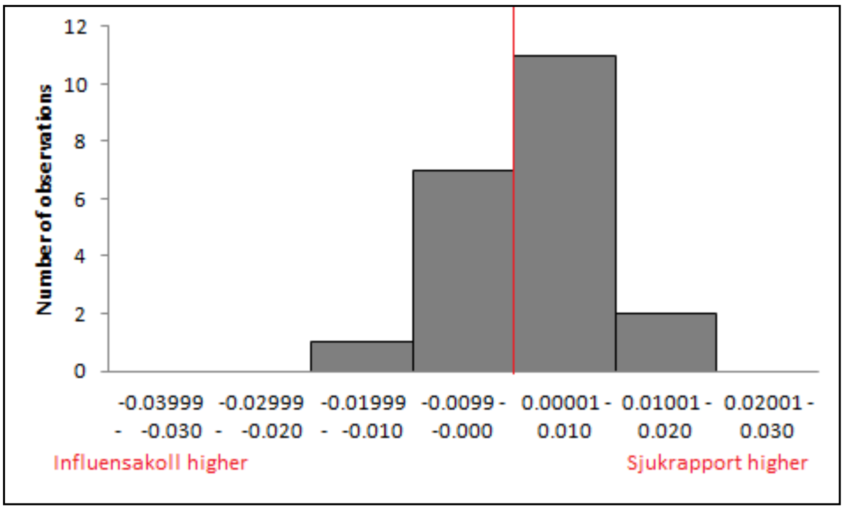


Figure 9 shows corresponding data for the 2012-2013 season. The differences ranged from -1.4 to +1.2 percentage points. Although the distribution in this season was less skewed, the median was +0.10 percentage points (meaning higher values for Sjukrapport), and the interquartile range was from -0.17 percentage points to +0.70 percentage points. Thus, in the 2012-2013 season, the differences were generally smaller, and if anything, Sjukrapport tended to yield higher incidence proportions.

Figure 9: Distribution of grouped differences in weekly incidence proportion between Sjukrapport and Influensakoll 2012-2013. The red line indicates zero difference between Sjukrapport and Influensakoll.



In Figures 10 and 11, the week-wise differences (with 95% confidence intervals) are displayed week by week across the entire surveillance season of 2011-2012 (Figure 10) and 2012-2013 (Figure 11). In order to relate these differences to the influenza activity in the community, data on laboratory-confirmed influenza cases are also shown in the figures (in grey). For most weeks during both seasons, the week-wise differences were not statistically significant (confidence intervals included zero). In the 2011-2012 data, the largest difference was found in the initial, rising phase of the influenza epidemic, during which Influensakoll generated higher incidence proportions. Interestingly, the largest difference in 2012-2013 was observed in the declining phase, two weeks after the influenza peak, also with a higher incidence proportion from Influensakoll.

Figure 10: Differences, with 95% confidence intervals, in weekly incidence proportions between Sjukrapport and Influensakoll, Stockholm 2011-2012

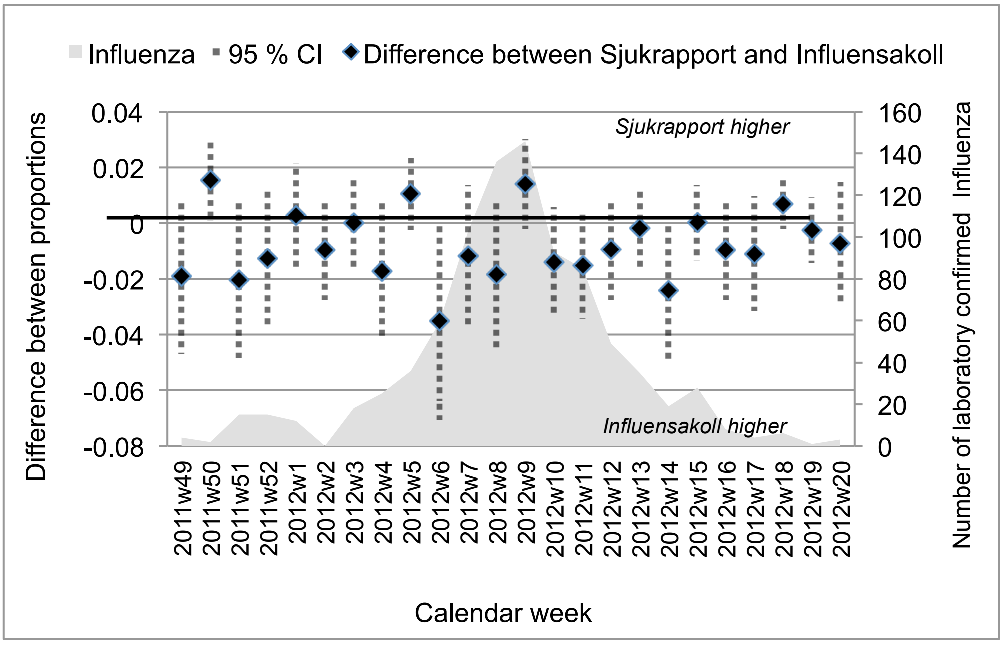
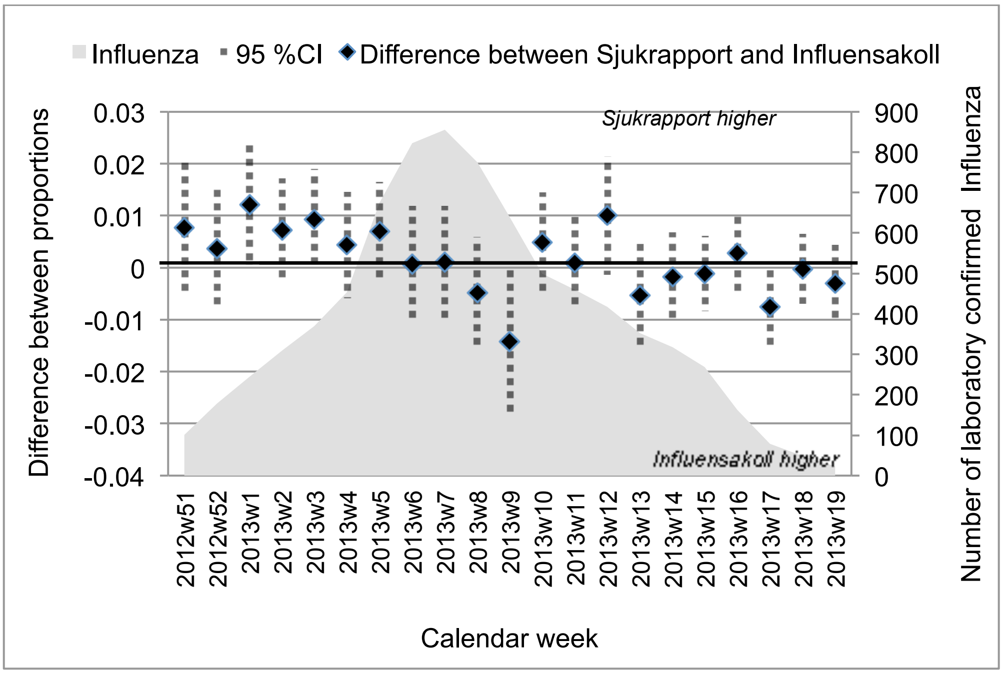


Figure 11: Differences, with 95% confidence intervals, in weekly incidence proportions between Sjukrapport and Influensakoll, Sweden 2012-2013



3.2.6. Comparison of epidemic curves based on two definitions of activity

When applying stricter criteria to define an Influensakoll report as *strict active* (two consecutive reports before valid report), as opposed to the definition used above (*active – that is, at least one report in the previous three weeks before valid reports*), the weekly incidence proportions were slightly lower in both seasons, but the differences were generally small (Figures 12 and 13). The difference was larger in the beginning of the 2011-2012 season than during the rest of the season, but this pattern was not seen in the 2012-2013 season.

Figure 12: Smoothed weekly incidence proportions of ILI generated by Influensakoll, Sweden 2011-2012.

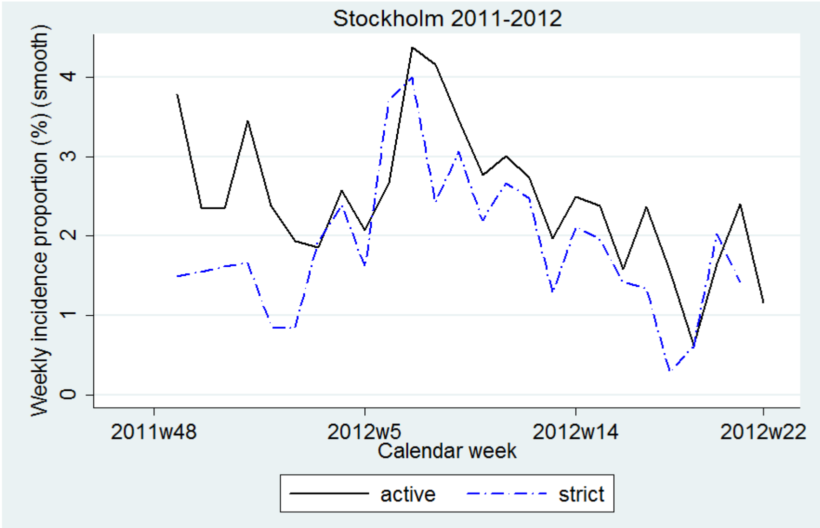
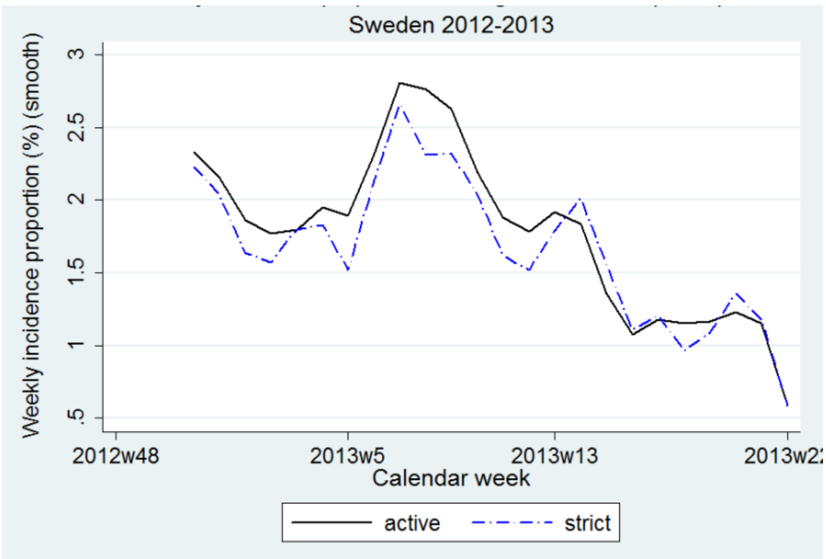


Figure 13: Smoothed weekly incidence proportions of ILI generated by Influensakoll, Sweden 2012-2013. The solid line represents reports defined as active (at least on report in the previous three weeks before valid reports) and the dashed line represents reports defined as *strict active* (two consecutive reports before valid report).



3.3. Discussion

This evaluation showed that in terms of socio-demographic profile, the self-selected Influensakoll participants represented the source population poorly. Moreover, their compliance with the requirement to submit one report per week in response to the prompting e-mail, regardless of health status, was generally limited. All this notwithstanding, the number of reports was fairly stable across each season, and although we suspect that the ILI incidence proportions might have been somewhat inflated due to preferential re-entry of passive participants with ongoing ILI, Influensakoll offered a reasonable representation of the temporal ILI pattern in the community. In particular, Influensakoll appeared to be at least as sensitive in detecting influenza outbreaks as the population-based alternative, Sjukrapport.

In essence, this evaluation confirms previous assessments of Influenzanet showing that this community-based, voluntary influenza surveillance system is able to detect changes in influenza incidence on the population level, and thus to pinpoint the start and culmination of influenza epidemics with reasonable accuracy (3, 4). What this study adds is the comparison with a well-validated population-based surveillance system, Sjukrapport, which generated incidence data in real-time for Influensakoll's target population. After correction for previously quantified demographic misrepresentation (1) and underreporting (2), Sjukrapport could be viewed as the gold standard. In addition, comparisons with regular surveillance systems in routine use, namely laboratory reporting of influenza diagnoses and GP-based sentinel surveillance, although not with optimal functionality in Sweden, offered opportunities to triangulate and narrow in on the true incidence with greater confidence.

With regard to the validity of Influensakoll/Influenzanet data, selection bias has been the most obvious concern. Our evaluation clearly demonstrates that the participants were far from representative of the target population. Yet, the epidemic curves were surprisingly similar to those generated by Sjukrapport. While the general pattern of misrepresentation is similar in Sjukrapport (1), the deviations are considerably smaller in Sjukrapport. The limited impact of the misrepresentation in Influensakoll suggests that neither the misrepresented socio-demographic factors that were measured (female gender, high education, middle age, and residence in Stockholm County), nor unmeasured determinants of participation, were strongly linked to the risk of catching the flu or experiencing ILI.

Preferential initial entry or re-entry of people with ongoing influenza has been another concern. To limit the impact of such selection bias, eligible reports have to be preceded by at least one report in the previous three weeks (*active* reports).

Interestingly, the overwhelming majority of all reports were active reports. Although the requirement does not entirely rule out some preferential re-entry of sick participants, our data show that such re-entry is likely to be a minor problem. This conclusion is additionally supported by the fact that a more stringent requirement (two reports in the previous two weeks), which practically rules out preferential re-entry of sick participants, generated epidemic curves that were very similar to those obtained with the more relaxed requirement.

No more than half of the Influensakoll participants submitted half or more of the required reports. Yet, the overwhelming majority of reports were active reports, and the total number of reports was fairly stable across the entire surveillance season. This suggests that many participants reported continuously during limited periods that did not necessarily start at the beginning of the surveillance season, and that these periods were fairly evenly distributed across the surveillance period. Since only a subset of all participants reported each week, it is conceivable that further selection forces were in operation. Ideally, our analysis of the representativeness of Influensakoll's participants should have been done for each week separately. Age and gender standardization of weekly incidence proportions might be considered.

The reporting activity level among participants improved greatly in the 2012-2013 season. This is most likely an effect of inclusion of motivated participants from the previous season willing to participate again and a concentration of recruitment efforts to the beginning of the season rather than continuously. The higher reporting frequency among Influensakoll's actively invited participants indicates that this group was even more motivated to report regularly. Although a 92.5% non-participation rate likely enriched particularly motivated people, the detailed information in the paper invitation may have contributed to their improved reporting behaviour. Furthermore, the step from receiving the paper invitation to registering online is likely to demand more motivation to participate than reading about Influensakoll online, where registration is only "a mouse click away".

Epidemic curves based on reporting from health care, whether it is laboratory reports or reports from general practitioners, tend to be rather distinct. This is because influenza, particularly cases of influenza that lead to health care contacts, typically is more severe and thus distinguishable from most other viral upper respiratory tract infections. In community-based surveillance with lay people as the reporters, the distinction between influenza and other viral respiratory tract infections is more uncertain. The symptomatology and case definitions are of limited help. In a recent population-based investigation with self-sampling for viral diagnosis of 14 common viruses, influenza accounted for no more than 30% of all upper respiratory tract infections even during the peak of a rather intense influenza epidemic, and other viruses were circulating unabatedly both before and after the influenza high season (unpublished). Therefore, the influenza peaks appear to be less distinct in population-based surveillance with lay informants. Selection bias during the peak influenza season in Influensakoll, however weak, might nevertheless amplify the signal and improve the signal to noise ratio, thus making the peak more distinct in Influensakoll than in Sjukrapport. Our analysis of differences in incidence proportions over time suggested that Influensakoll deviated most from Sjukrapport during the influenza peaks.

The size and direction of the differences in weekly incidence proportions between Influensakoll and Sjukrapport varied across and between seasons to the extent that a simple algorithm for calibration of Influensakoll data seems difficult to create. While Influensakoll appears to be suitable for detection of the start and the peak of influenza epidemics, the continuous monitoring of absolute incidence rates in various substrata of the population may be better accomplished with the Sjukrapport surveillance system.

Age group-specific data is of particular interest in societal disease surveillance but is problematic in Influensakoll since some ages of particular interest, notably infants and elderly, are poorly represented. These age groups are at greater risk for influenza complications. The fact that Sjukrapport offers reporting also over the telephone is likely to appeal to older age groups, where Internet availability and computer literacy may be limited. When a randomly selected population sample was personally invited to Influensakoll, the representativeness improved despite a poor response rate. Availability of alternative modes of communication and active, personal invitations of representative samples might further improve the performance of the Influensakoll surveillance system. Another limitation of Influensakoll, not shared by Sjukrapport, is the unavoidable delay before interpretable data can be derived. First, participants report about disease occurrences in the previous week (or since their last visit to the website) upon prompting once a week. Second, the denominator of the disease rates is constituted by the total number of reports during the reporting week, and this number is not available until this week has passed. Thus in practice, the delay amounts to 1-2 weeks.

As opposed to Sjukrapport, Influensakoll had no time limit for reports of episodes from the past. Evidently, this resulted in Influensakoll reports of episodes up to 14 years back in time. The instructions to participants on what to report might need some clarification. Even if reports of episodes in the distant past can be easily excluded when analysing the data, a technical solution that refuses reports of episodes from the past could contribute to better quality of the surveillance system.

When comparing weekly incidence proportions visually and in cross-correlation analysis, the data was smoothed. This tuned the week-to-week variation, mainly seen in Influensakoll. Smoothing of data increased the correlation between the systems as well as with laboratory and sentinel data. Using smoothed data in real time surveillance might therefore make interpretation of weekly estimates easier.

The surveillance data generated by Sjukrapport during the 2012-2013 season was harder to interpret than data from previous seasons, with similar levels of ILI proportions from November until the peak in March. The reasons for this apparent malfunction in terms of ILI surveillance of the Sjukrapport system remain conjectural. After having been run as a research project for several years, Sjukrapport was more tightly incorporated in the routine surveillance program at the Swedish Institute for Communicable Disease Control. Moreover, after having been confined to Stockholm County, the Sjukrapport surveillance cohort was, for the first time, drawn from the whole Swedish population. Subtle changes in the information material or decreased geographical resolution may possibly explain the deviating findings. It is also conceivable that local outbreaks in different parts of Sweden succeeded each other and that a variety of ILI-causing viruses circulated, thus creating a noisy background.

3.4. Conclusion

Despite the self-recruited sample, resulting in poor reflection of the Swedish populations' demography, Influensakoll offered a reasonable representation of the temporal ILI pattern in the community during the 2011-2012 and 2012-2013 influenza seasons and could be a suitable tool for following ILI trends in the community. However, comparison of self-recruited participants and randomly sampled invitees shows that invited participants represent the target population better and complete a larger number of reports than the self-recruited participants. These findings suggest that a personal invitation to a random sample of the population improves the quality and usability of community-based surveillance data.

4. References

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