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Comparison between self-report of cannabis use and toxicological detection of THC/THCCOOH in blood and THC in oral fluid in drivers in a roadside survey

Trudy Van der Linden,[a,c]* Peter Silverans[b] and Alain G. Verstraete[a]

The objective of this study was to compare the number of drivers who self-reported cannabis use by questionnaires to the results of toxicological analysis.

During roadside surveys, 2957 respondents driving a personal car or van completed a questionnaire to report their use of drugs and medicines during the previous two weeks and to indicate the time of their last intake. Cannabis was analyzed in oral fluid by ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS), in blood by gas chromatography–mass spectrometry (GC-MS).

Frequencies in the time categories were calculated and compared with toxicological results. Diagnostic values were calculated for the time categories in which positive findings were to be expected (<4 h and <2 4h, respectively for tetrahydrocannabinol (THC) and delta9-tetrahydrocannabinol (THCCOOH) in blood, <12 h for THC in oral fluid).

Most self-reported cannabis use was more than 12 h before driving. The sensitivity of the questionnaire was low, while the specificity and accuracy were high. Kappa statistics revealed a fair agreement between self-report and positive findings for THC in oral fluid and blood and moderate agreement with THCCOOH in blood.

Self-report largely underestimates driving under the influence of cannabis, particularly recent cannabis use; therefore analysis of biological samples is necessary. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: cannabis; oral fluid; blood; self-reported use; roadside survey

Introduction

Despite being controlled in many countries, cannabis is the most widely used illicit substance in the world. Results from the 2008 Belgian Health Interview Survey indicated that 14% of the population aged 15–64 years used cannabis at least once in their life, while 5% (one-third of them) indicated that they have used cannabis in the past 12 months and 3% in the past 30 days. Thirty percent of this last category indicated that they smoked it intensively (minimum 20 out of the 30 days). The mean age of first-time use of cannabis was 18 years and 11 months.[1]

The prevalence of driving under the influence of drugs such as cannabis has also been studied in recent years. An attitude measurement on traffic safety performed by the Belgian Road Safety Institute (BIVV) in 2009 showed that 13% and 0.76% of the Belgian driving population had declared to have been driving under influence of alcohol or drugs, respectively.[2]

Results of the DRUID project have shown that 0.5% of randomly selected drivers in Belgium tested positive for cannabis (0.35% for single use, 0.14% combined with alcohol, medicines, or other illicit drugs).[3] The estimated prevalence of cannabis in the general driving population in Europe was 1.32% for single use.[4]

Figures from a study on seriously injured drivers indicated that in Belgium 10% was positive for cannabis (8% in combination with other psychoactive substances, 2% for single use).[5] The prevalence in the five other participating countries (Denmark, Finland, Italy, Lithuania, and the Netherlands) ranged from 0.8% to 6.6%.[6]

A case–control study in Belgium estimating accident risk for alcohol, medicines, and illegal drugs, demonstrated a concentration-dependent crash risk for tetrahydrocannabinol (THC) positive drivers. In general, cannabis caused an increase in accident risk with an odds ratio of 13.4.[7]

Risk analysis based on the overall DRUID case–control data showed that the risk associated with cannabis seems to be similar to the risk when driving with a low alcohol concentration (between 0.1 and 0.5 g/L), which is about 1–3 times that of sober drivers.[8]

Meta-analyses performed by Asbridge,[9] Li *et al.*,[10] and Elvik[11] also suggest that cannabis use by drivers is associated with a significantly increased risk of being involved in motor vehicle crashes.

* *Correspondence to: T. Van der Linden, National Institute of Criminalistics, Vilvoordsesteenweg 100, 1120 Brussels, Belgium. E-mail: trudyvdlinden@gmail.com*

a *Department of Clinical Chemistry, Microbiology and Immunology, Ghent University, De Pintelaan 185, 9000 Ghent, Belgium*

b *Belgian Road Safety Institute, Haachtsesteenweg 1405, 1130 Brussels, Belgium*

c *National Institute of Criminalistics and Criminology, Vilvoordsesteenweg 100, 1120 Brussels, Belgium*

Much of the early research assessing the effects of cannabis on driving performance was done by laboratory and driving simulator studies. The results of these studies are generally consistent: at increased doses, cannabis impairs the psychomotor skills necessary for safe driving.[12–19]

Fergusson and Horwood[20] found that the risk of crash involvement increased significantly as self-reported frequency of cannabis use in the past year increased.

Evaluation of drug use based on the subject's self-report is the most widely used practice for epidemiological research in addiction, as it has two very clear advantages: low cost and the possibility of collecting an abundance of information from many people.[21] However, the validity of estimations based on their use has frequently been questioned. There has been a certain tendency to believe that results from self-reported use are only the tip of the iceberg of real consumption and that therefore, the studies estimating the highest prevalence were the most valid, although this affirmation has also been questioned.[22]

Drug use is frequently considered within a social-cultural framework as improper, shameful, dangerous, and even illegal, so that the subject's own report on it may be subject to deception, hiding, and other types of bias in the response.[23]

The purpose of this study was to compare the number of drivers who declared to have used cannabis with the results of toxicological analysis of an oral fluid sample and blood sample. Is the self-report of cannabis use by drivers biased? To what extent is there a correlation between both types of information on use (self-report versus toxicological analyses)?

Method

Participants

Between 2008 and 2009, 2957 respondents driving a personal car or van participated in a roadside survey.

Sixty-seven percent (1989) of the drivers were male and 32.7% (967) female. Almost 58% of the drivers could be categorized in the age group 25–34 (20.7%) or in the group 35–49 (37.2%). The percentage of respondents in the categories 25–34 and 50+ were 11.4 and 30.0, respectively.

Variables and instruments

Two techniques were used (1) self-report, based on a self-administered questionnaire, and (2) analysis of blood and oral fluid samples to measure use of cannabis.

Self-report. A questionnaire was given to the respondents of the roadside survey to report their use of drugs and medicines during the previous two weeks and indicate the time of last intake.

The following data were recorded: type of vehicle; gender; age; education level; results of breathalyzer test, drug control or other observations by police; and self-reported drug, alcohol, and medicine use.

The respondents were asked to fill in their questionnaire while waiting for the oral fluid sample to be collected. Questions could be asked of the research staff when topics were not clear. No interviewing was done. The surveys were guided by a member of the research team or a trained student.

Toxicological analysis. Each volunteer was asked to provide a blood sample (5-ml tube with sodium fluoride and potassium oxalate) and an oral fluid sample collected with the StatSure™ Saliva Sampler™. The collection device consisted of a cellulose pad on a plastic stick. When approximately 1-ml sample had been collected, an indicator on the stick turned blue. The stick was then sealed in a tube containing 1-ml of buffer. The oral fluid samples were weighted to correct differences in sample volume.[24]

A total of 2750 drivers provided both a blood and an oral fluid sample, while 199 drivers only provided an oral fluid sample and 8 drivers only completed a questionnaire.

Samples were transported under cooled conditions to the laboratory where the toxicological analyses for 11 illicit psychoactive substances and metabolites† were performed.

In oral fluid, THC was analyzed using liquid-liquid extraction (LLE) followed by ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS).[25] Blood samples were initially screened for using ELISA and confirmed using LLE followed by gas chromatography–mass spectrometry (GC/MS).[26] All the blood samples for which the corresponding oral fluid sample was positive for THC as well as 300 for which the corresponding oral fluid sample was negative for THC were screened with ELISA (IDS Elisa One-Step Cannabis (Cat No. TH-96-CE-U), targeting delta9-tetrahydrocannabinol (THCCOOH)).‡

The cut-off for THC was set at 1 ng/ml for both matrices. For THCCOOH in blood, a cut-off of 5 ng/ml was used.

Survey procedure

The research procedure consisted of two independent phases: the first was a random alcohol control performed by the police. After the police procedure, the stopped drivers were asked whether they wanted to participate in the DRUID research. If they refused, a refusal form with their demographic data was filled in to be able to calculate a response rate. The second phase was the DRUID research itself, which took place in a motorhome. The drivers were informed about the objective and the content of the research, asked to fill in a questionnaire, and to give an oral fluid sample and a blood sample. Drivers who didn't want to participate in the study where asked to only fill in the questionnaire. If they refused, a refusal form was filled in to be able to calculate a response rate. Respondents who participated in the study were given compensation in form of a gift voucher for €20. Surveys lasted 90 minutes at one location.[3]

The project was conducted according to the guidelines laid down in the Declaration of Helsinki and was approved by the Ethics Committee of Ghent University Hospital (Belgian registration number B67020073143).

The respondents were assured confidentiality. Anonymity was guaranteed by linking toxicological and questionnaire data through numbers.

Data analysis

Percentages of positive findings and concentration ranges were calculated using Microsoft Office Excel 2010. Statistical analysis was made using IBM SPSS Statistics 21.

†6-acetylmorphine, amphetamine, benzoylecgonine, cocaine, MDA, MDEA, MDMA, methamphetamine, morphine, THC, and THCCOOH.

‡Concentration (ng/ml) that gives a positive response (equivalent to xx ng/mL of THCCOOH): 11-nor-delta-9THC-9-COOH = 4100; Delta-9-THC = 7; Delta-8-THC = 5; 11-nor-delta-8-THC-9COOH = 87.5; 11-nor-delta-9-THC-9-COOH-glucuronide = 50; 11-Hydroxy-delta-9-THC = 21.9; Cannabinol = 2.7; Cannabidiol = 0.002

The following data were calculated: ratio of positive toxicological result/self-report use by category of 'time of intake'; diagnostic values (sensitivity, specificity, accuracy), and kappa statistics.

The evaluation of the results is based on classification into the following categories:

- True positive (TP): number of cases with a positive self-report and a positive confirmation analysis
- True negative (TN): number of cases with a negative self-report and a negative confirmation analysis
- False positive (FP): number of cases with a positive self-report and a negative confirmation analysis
- False negative (FN): number of cases with a negative self-report and a positive confirmation analysis

Since, according our cut-off and the Model 1 formula of Huestis, [27] we expected THC to be positive in blood for up to 5 h after intake, positive self-report was defined as those respondents who declared to have used cannabis 'less than 4 hours ago'.

For THCCOOH in blood and THC in oral fluid these limits are set to '< 24 hours' and '<12 hours', respectively.

Using these classifications, the following parameters for the evaluation can be calculated:

Sensitivity is the proportion of positive cases (= subjects with THC/THCCOOH in blood or oral fluid) that are correctly identified by the test (= self-report of cannabis use).

$$Sensitivity = \frac{TP}{TP + FN} \quad (1)$$

Specificity is the proportion of negative cases (= subjects with no THC/THCOOH in blood or oral fluid) that are correctly identified by the test (= self-report of no cannabis use).

$$Specificity = \frac{TN}{TN + FP} \quad (2)$$

Accuracy is the proportion of correctly identified positive and negative results from all the test results.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (3)$$

Sensitivity, specificity, and accuracy performance values of 80% or more were set as a desirable target value.

Cohen's Kappa measures the agreement between two raters who each classified N items into C mutually exclusive categories. The equation for κ is:

$$K = \frac{\Pr(a) - \Pr(e)}{1 - \Pr(e)} \quad (4)$$

where $\Pr(a)$ is the relative observed agreement among raters, and $\Pr(e)$ is the hypothetical probability of chance agreement, using the observed data to calculate the probabilities of each observer randomly saying each category. If the raters were in complete agreement then $\kappa = 1$. If there was no agreement among the raters other than what would be expected by chance (as defined by $\Pr(e)$), $\kappa = 0$.

Interpretation of Kappa is rather arbitrary. Landis and Koch characterized values < 0 as indicating no agreement and 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1 as almost perfect agreement.[28] Fleiss's equally arbitrary guidelines characterized Kappa over 0.75 as excellent, 0.40 to 0.75 as fair to good, and below 0.40 as poor.[29]

Three box-and-whisker plots were drawn (one for each analyte), to show the distribution of the non-zero concentrations by self-reported time after intake. The box in these box-and-whisker plots represents those cases between the 75th and 25th percentile (Q3–Q1), whilst the line that bisects the box is the median concentration of the cases. The whiskers that protrude from the box extend to 1.5 times 'Q3-Q1' or, if no case has a value in that range, to the minimum or maximum values. If the data are distributed normally, approximately 95% of the cases are expected to lie between the whiskers. Outliers, denoted by a point, are defined as cases that do not fall within the whiskers. Extreme outliers are denoted by asterisks and represent cases that have values more than three times 'Q3-Q1' beyond the limits of the box.

Results

Table 1 shows the relationship between the time after intake and the ratio of positive toxicological result versus self-reported use.

Out of the 81 people who declared to have used cannabis, 34 were found positive for THC in oral fluid. The ratio of positive toxicological result versus self-reported use was highest at '<1 h' and '<12 h', with a decline after 12 h.

For blood results, only 8 out of 81 self-reported users were found positive for THC; 27 were positive for THCCOOH. The ratio of positive toxicological results versus self-reported use for THCCOOH is the highest at '<1 h' (0.8), showing a decreasing trend with increasing time after intake. The ratio for THC is indicating a peak at 4 h, a possible outlier at 12 h and the same decreasing trend at 24 h and more after intake as THCCOOH in blood and THC in oral fluid.

For five self-reported users, only oral fluid results were available, since either no blood sample was taken, or not enough

Table 1. Self-reported cannabis use and positive toxicological results per time category of intake

	Total	<1 h	<4 h	<12 h	<24 h	>24 h	unknown
Total number of subjects who self-reported cannabis use	81	5	3	10	7	46	10
Number of positives in saliva for THC (cut-off: 1 ng/ml) among the subjects who self-reported cannabis use	34	4	1	8	3	15	3
Number of positives in blood for THC (cut-off: 1 ng/ml) among the subjects who self-reported cannabis use	8	1	2	0	1	4	0
Number of positives in blood for THCCOOH (cut-off: 5 ng/ml) among the subjects who self-reported cannabis use	27	4	2	5	3	11	2
Number of subjects who self-reported cannabis use while no THC or THCCOOH were detected in blood or oral fluid	43	1	1	2	3	29	7

sample was left for THC and THCCOOH analysis. They were only included in the oral fluid analysis.

Figure 1 gives an overview of the distribution of THC concentrations in oral fluid and THC and THCCOOH concentrations in blood. It shows that, as is generally known, THC concentrations are higher in oral fluid than in blood. Generally speaking, higher THC concentrations are found in oral fluid for the time categories '<1 h' and '<4 h', a decline after 12 h is noticeable and stable for the categories that follow. THCCOOH concentrations are quite equal for all time categories with a small decrease in the category '<12 h'. For THC in blood, the low number of positive findings (n = 8) might give a biased idea. The concentrations seem to be increasing until '<24 h' and then rapidly declining.

The cases with negative self-report but positive toxicological results were investigated using the formulas of Huestis[27] to estimate the time of intake. Out of 48 cases in total, only four datasets were complete with both THC and THCCOOH results. The calculated time ranged between 0.7 and 2.1 hours (CI: 0.3–4.7 h) according to model 1 and between 1.3 and 2.6 h according to model 2 (CI: 0.5–7.0 h).

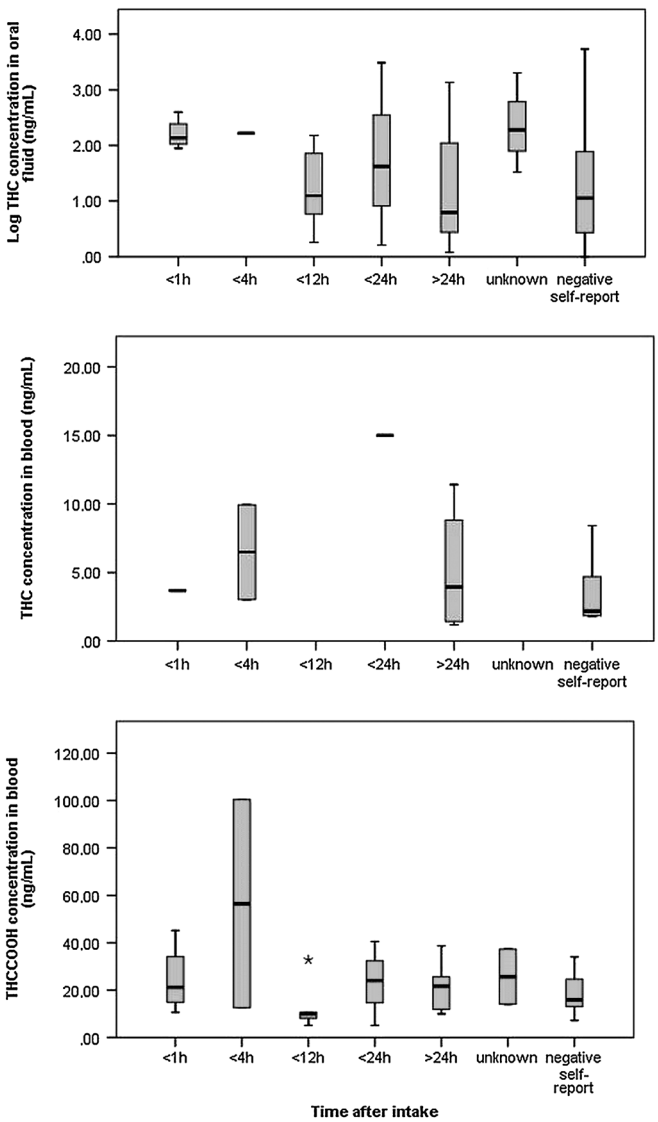

Figure 1. Distribution of analyte concentrations by time after intake.

Table 2 gives an overview of the diagnostic values and the Kappa statistics calculated for the self-report versus toxicological analysis, with the toxicological results considered as the reference method.

Sensitivity is low for all three analytes, only higher than 50% for THCCOOH in blood. Specificity ranges from 94% for THC in blood to almost 100% for THC in oral fluid.

Kappa statistics can be read as fair for THC in oral fluid and in blood and moderate for THCCOOH in blood.

Of the 47 false positives in oral fluid (positive self-report but negative oral fluid results), one respondent who declared to have smoked cannabis less than 4 h previous tested positive for THC and THCCOOH in blood. One person categorized in '<24 h' and two in '>24 h' were positive for THCCOOH in blood.

Of the 33 false positives for THC in blood (positive self-report but negative for THC in blood), almost 70% had concentrations of THC in oral fluid and/or THCCOOH in blood above the cut-off. The same trend could be seen for the false positives for THCCOOH.

Discussion

Concentrations of THC depend on dose and type of use (occasional or chronic). Also, after cannabis inhalation, contamination of THC in the oral cavity appears. These facts may explain the rather irregular pattern of the ratio between self-reported use and toxicological findings in the first hours, and a declining trend after 12 h, as expected with plasma concentrations.

A study in 2003 compared self-report data and oral fluid testing in patients treated for drug addiction. Findings indicated a high level of consistency between self-reported drug use and oral fluid testing. However, agreement varied by drug type and respondents commonly reported consumption that screening failed to identify. Inconsistencies appeared to relate to a number of factors and were not necessarily a function of deliberate

Table 2. Diagnostic values and kappa statistics for self-reported cannabis use (<4 h for THC in blood, <12 h for THC in oral fluid and <24 h for THCCOOH in blood) by laboratory test

	THC oral fluid (cut-off: 1 ng/ml)	THC blood (cut-off: 1ng/ml)	THCCOOH blood (cut-off: 5 ng/ml)
TP	13	3	14
TN	2829	64	57
FP	5	4	3
FN	47	5	11
Total	2894	76	85
Sensitivity	0.22	0.38	0.58
Specificity	0.998	0.94	0.95
Accuracy	0.98	0.88	0.84
Kappa	0.33	0.34	0.56

TP = positive self-report + positive toxicological analysis
TN = negative self-report + negative toxicological analysis
FP = positive self-report + negative toxicological analysis
FN = negative self-report + positive toxicological analysis
Sensitivity: proportion of subjects in whom THC/THCCOOH was detected in OF/blood that self-reported cannabis use
Specificity: proportion of subjects in whom no THC/THCCOOH was detected in OF/blood, that self-reported no cannabis use
Accuracy: proportion of subjects who accurately self-reported cannabis use

distortion by the drug user.[30] This study was conducted on new treatment patients, which is a different population compared to randomly selected drivers.

A study in 2009 compared self-report of cannabis use by university students with detection in urine. Sensitivity of the self-report was 91.8%, the specificity was 89.6%.[31]

One of the key elements of a questionnaire is the way of interviewing: orally or with a written questionnaire. Who is responsible for the interview: an expert, a student…? In our study, interrogation was not performed by expert interviewers and there was little interaction between respondents and the study team. Future research might benefit from having well-trained interviewers who work in drug advisory clinics. Getting into dialogue with the respondents could reduce the number of incomplete questionnaires. But it still has to be kept in mind that a roadside setting is different from drug advisory clinics where fear of retribution is less and cooperation is part of the treatment.

Also the illegal nature of drug abuse, privacy, face-saving, and possible criminal sanctions are all factors associated with social pressure, largely affecting the reliability of self-report outcomes. However, in Belgium, cannabis possession of less than three grams for one's own use is not prosecuted, so users might be more willing to declare use than in other countries.

Although it was explained to the respondents of the roadside survey that there was no data transmission from the study to the police, there could have been a bias: people were maybe more reluctant to share information with the police nearby. Since a consent form had to be signed, some respondents could not reconcile this with the guaranteed anonymity. Also some participants asked to be updated on the test results, indicating that the term 'anonymity' was not always fully understood.

The preceding police procedure might have induced restlessness in some respondents, which did not attenuate completely once they were completing the questionnaire, even though confidentiality was observed. Those participants might have volunteered more out of fear than for altruistic reasons or for a reward. This could explain the conclusion we made from our data, that respondents gave a more 'socially desirable' answer, for example, reporting use more than 24 h ago, while in fact biological analysis suggest use within a period of 4 h. It has to be taken into account that since seven of the self-reported users did not provide a blood sample (five gave an oral fluid sample, two only filled in the questionnaire), and the already low number of positives in blood, making assumptions based on blood results should be done carefully. Especially because Van der Linden *et al.*[24] demonstrated that there was a higher percentage of drug-positive drivers in a group of respondents who did not provide a blood sample compared to the group who gave a blood and oral fluid sample.

The following remarks could be made regarding the false positive results. The person with self-reported use less than 1 h before, with negative results for THC in oral fluid, but THC and THCCOOH in blood, might be missed as positive in oral fluid due to a sampling problem. Of all the negative saliva samples whose corresponding blood was analyzed (300 in total), this respondent was the only one found positive in blood. The calculated time after intake with the formulas of Huestis[27] suggests recent intake.

The three positive self-reports with negative result for THC in blood, categorized in '<1 h' were positive for THC in oral fluid and THCCOOH in blood. This could suggest chronic use (indicated by the residual THCCOOH in blood), with very recent last intake.

The positive self-reports with negative result for THCCOOH might suggest more occasional use, since there was no residual THCCOOH in blood.

Data on the five false negatives (no self-reported use, but positive toxicological results) for whom blood concentrations and the formulas of Huestis[27] time of intake were estimated, suggest that these respondents had smoked very recently and hence probably didn't give a correct answer to the questionnaire.

Subjects were asked to report their use within the past 14 days, subdivided into several categories (<1 h, <4 h, <12 h, <24 h, >24 h, unknown). It has to be noted that '>24 h' was a widely defined category.

Looking at the distribution of the concentrations, it could be noted that maybe some respondents gave a 'socially desirable' answer, stating 'I smoked cannabis >24 h ago', while in fact it was more recently.

Kappa statistics are fair to moderate and specificity is very high. But since sensitivity and prevalence of use in the general driving population (0.5%)[3] are low, positive predictive values (PPV)[§] calculated through the theorem of Bayes, in which PPV is directly proportional to the prevalence, are low. For instance, using the values for sensitivity and specificity for THC in blood, a prevalence of 38% is needed to have a positive predictive value of 80%.

Future roadside studies based solely on self-report might not be worthwhile as the prevalence of recent drug use is severely underestimated. Objective measurements on biological samples give more accurate information. On the other hand, such questionnaire data could be used to gather extra information (like time of last use and route of administration) for traffic statistics.

Conclusion

Although in other settings the use of self-report turned out to be a good indicator of cannabis use, the presented data suggest that self-report is not the ideal measurement to detect driving under the influence of cannabis. The idea of a possible retribution or penalty associated with a positive answer might have a great impact on how the questionnaire is completed. Analysis of biological samples is more accurate.

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[§]PPV = (*sensitivity*prevalence*)/(*sensitivity*prevalence* + (1 - *specificity*)(1 - *prevalence*))

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