1	A bootstrap method for comparing correlated kappa
2	coefficients
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6	(Received 00 Month 200x; In final form 00 Month 200x)
7	Cohen's kappa coefficient is traditionally used to quantify the degree of agreement between two raters
8	on a nominal scale. Correlated kappas occur in many settings (e.g. repeated agreement by raters on
9	the same individuals, concordance between diagnostic tests and a gold standard) and often need to
10	be compared. While different techniques are now available to model correlated κ coefficients, they
11	are generally not easy to implement in practice. The present paper describes a simple alternative
12	method based on the bootstrap for comparing correlated kappa coefficients. The method is illustrated
13	by examples and its type I error studied using simulations. The method is also compared to the
14	generalized estimating equations of second order and the weighted least-squares methods.
15	Keywords: Cohen's kappa, comparison, bootstrap

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17 1 Introduction

The kappa (κ) coefficient proposed by Cohen [1] in 1960 is widely used to as-18 sess the degree of agreement between two raters on a binary or nominal scale. 19 It corrects the observed percentage of agreements between the raters for the ef-20 fect of chance. Thus, a value of 0 implies no agreement beyond chance, whereas 21 value of 1 corresponds to a perfect agreement between the two raters. Correа 22 lated kappas can occur in many ways. For example, two raters may assess the 23 same individuals at various occasions or in different experimental conditions 24 and it may be of interest to test for homogeneity of the kappas. Alternatively, 25 each member of a group of raters may be compared to an expert in assessing 26 the same items on a nominal scale. Are there differences between the indi-27 vidual kappas obtained? The same problem arises when comparing several 28 diagnostic tests on a binary scale (negative/positive) with respect to a gold 29 standard. Fleiss [2] developed a method based on the chi-square decomposition 30 for comparing two or more κ coefficients but only applicable to independent 31 samples. McKenzie et al. [3] proposed an approach based on resampling for 32 the comparison of two correlated κ coefficients. With the advent of generalized 33 linear mixed models, it is now possible to model the coefficient κ as a function 34 of covariates. Williamson et al. [4] used the generalized estimating equations 35 of second order (GEE2) to model correlated kappas. Lipsitz et al. [5] proposed 36 an empirical method to model independent κ coefficients. Finally, Barnhart 37

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and Williamson [6] used the weighted least-squares approach (WLS) to model 38 correlated κ coefficients with respect to categorical covariates. All modeling 30 techniques represent a considerable progress but they require adequate model 40 specifications and expert programming skills. Currently, no simple method can 41 be found in the literature for comparing several correlated κ coefficients. The 42 present paper describes a practical and feasible alternative to the modeling 43 techniques by expanding the resampling method based on bootstrap proposed 44 by McKenzie et al. [3]. The original method is exposed in Section 2 and the 45 extension detailed in Section 3. Simulations of the type I error are given in 46 Section 4 for different levels of the kappa coefficient and different sample sizes. 47 Results are compared to those obtained by the GEE2 and the WLS methods. 48 The bootstrap, GEE2 and WLS methods were applied to two examples in 49 Section 5. Finally, results are discussed in Section 6. 50

51 2 Bootstrapping two correlated kappas

Suppose that two raters classify n subjects on a binary or nominal scale at two different occasions or in two different experimental settings. Let $\hat{\kappa}_1$ and $\hat{\kappa}_2$ be the kappa coefficients obtained. Since the two agreements are assessed on the same subjects, $\hat{\kappa}_1$ and $\hat{\kappa}_2$ are correlated. Are they statistically different? Let H_0 : $\kappa_1 = \kappa_2$, the null hypothesis to be tested. The bootstrap method consists in drawing q samples (1000 is generally sufficient [3]) of size n with ⁵⁸ replacement. For each generated sample, the κ coefficient between the 2 raters ⁵⁹ is estimated in the two settings and their difference $\hat{\kappa}_d = \hat{\kappa}_2 - \hat{\kappa}_1$ calculated. ⁶⁰ McKenzie et al. [3] suggested to determine the bootstrap two-sided $(1 - \alpha)$ -⁶¹ confidence interval for the $\hat{\kappa}_d$ differences, whence rejecting the null hypothesis ⁶² if the confidence interval did not include 0. This approach is equivalent to ⁶³ using a Student's t-test and to reject H_0 at the α -significance level if

$$|t_{obs}| = \left|\frac{\overline{\kappa}_d}{SE(\kappa_d)}\right| \ge Q_t(1 - \alpha/2; q - 1) \tag{1}$$

where $\overline{\kappa}_d$ and $SE(\kappa_d)$ are respectively the mean and standard deviation of the q bootstrapped kappa differences and $Q_t(1 - \alpha/2; q - 1)$ is the upper $\alpha/2$ percentile of the Student's t distribution on q-1 degrees of freedom. Otherwise, H_0 is not rejected.

68 3 Extension to several correlated kappas

Suppose we want to compare $G \ge 2$ correlated kappa coefficients $(\kappa_1, \dots, \kappa_G)$ i.e., to test the null hypothesis H_0 : $\kappa_1 = \dots = \kappa_G$ against the alternative hypothesis H_1 : $\exists k \neq l \in \{1, \dots, G\}$: $\kappa_k \neq \kappa_l$. As before, the bootstrap method will consist in drawing q samples of size n with replacement from the original data. Then, for each bootstrapped sample $(j = 1, \dots, q)$, let $\widehat{\kappa}_j = (\widehat{\kappa}_{1(j)}, \dots, \widehat{\kappa}_{G(j)})'$ be the vector of the G kappa coefficients obtained. The

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null and alternative hypotheses can be rewritten in matrix form as follows: $H_0: C\kappa = 0$ versus $H_1: C\kappa \neq 0$, where $\kappa = (\kappa_1, \dots, \kappa_G)'$ and C the $(G-1) \times G$ patterned matrix

78 Then, the test statistic is

$$T^{2} = (\boldsymbol{C}\overline{\boldsymbol{\kappa}})'(\boldsymbol{C}\boldsymbol{S}\boldsymbol{C}')^{-1}\boldsymbol{C}\overline{\boldsymbol{\kappa}}$$
(2)

⁷⁹ distributed as Hotelling's T^2 , where $\overline{\kappa}$ and S are respectively the sample mean ⁸⁰ vector and covariance matrix of the q bootstrapped vectors $\hat{\kappa}$. The null hy-⁸¹ pothesis will be rejected at the α -level if

$$T^{2} \ge \frac{(q-1)(G-1)}{(q-G+1)}Q_{F}(1-\alpha;G-1,q-G+1)$$
(3)

where $Q_F(1-\alpha; G-1, q-G+1)$ is the upper α -percentile of the F distribution on G-1 and q-G+1 degrees of freedom. Otherwise, H_0 will not be rejected. Note that, since "q-G+1" will be large in general, the left-hand side of equation 3 can be approximated by $Q_{\chi^2}(1-\alpha; G-1)$, the $(1-\alpha)$ th percentile of the chi-square distribution on G-1 degrees of freedom. If c_g denotes the gth row of matrix C, simultaneous confidence intervals for individual contrasts $c'_g \kappa \ (g = 1, \dots, G-1)$ given by

$$\boldsymbol{c}_{g}^{\prime}\boldsymbol{\overline{\kappa}} \pm \sqrt{\frac{(q-1)(G-1)}{(q-G+1)}}Q_{F}(1-\alpha;G-1,q-G+1)\sqrt{\boldsymbol{c}_{g}^{\prime}\boldsymbol{S}\boldsymbol{c}_{g}}$$
(4)

⁸⁹ can be used for multiple comparison purposes.

90 4 Simulations

The method described in Section 3 was applied to simulated data sets in order 91 to study the behavior of the type I error (α) of the homogeneity test for G = 3. 92 Each simulation consisted in applying the bootstrap method to 3000 data sets 93 generated under the null hypothesis H_0 : $\kappa_1 = \kappa_2 = \kappa_3$ and to determine 94 the number of times H_0 was rejected. The simulated data set was based on 95 4 binary random variables X, Y, Z and V. The agreement between X and 96 $Y(\kappa_{XY}), X \text{ and } Z(\kappa_{XZ}) \text{ and } X \text{ and } V(\kappa_{XV}) \text{ were compared using the}$ 97 bootstrap method with q = 2000 iterations. Simulations were repeated for 3 98 sample sizes (50, 75 and 100) and 5 levels of agreement ($\kappa=0$, 0.2, 0.4, 0.6 99 and 0.8). To obtain a given level of agreement (κ), 2 vectors of size n from 100 binary random variables (U and W) were generated. Then, a vector of size n101

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with uniform random numbers between 0 and 1 was generated. Each time the 102 random uniform number was less than or equal to the given level of agreement 103 (κ) , the value of W was changed into the value of U, otherwise it remained 104 unchanged. The kappa coefficient was derived from the 2×2 table obtained 105 by cross-classifying the vectors U and W. The codes for the simulations were 106 written in R language using uniform random number generator with seed 107 equal to 2. The method of generalized estimating equations of second order 108 (GEE2) [4] and the weighted least square approach (WLS) [6] were also applied 109 to the 3000 simulated data sets. Results are summarized in Table 1. It is seen 110 that type I error rates obtained with the bootstrap method are slightly but 111 systematically higher than the expected 5% nominal level. While the GEE2 112 approach appears to be optimal, the bootstrap was better than the WLS, at 113 least for elevated κ values. However, the bootstrap method may be preferred 114 to the GEE2 approach because of the ease of implementation in all settings as 115 compared to the GEE2 method, which requires the writing of a lengthy and 116 specific program for each particular problem. 117

118 5 Examples

119 5.1 Deep venous thrombosis

A study was conducted on 107 patients in the medical imaging department of the university hospital (unpublished data) to compare deep venous thrombosis

				κ level		
Sample size	Method	0	0.2	0.4	0.6	0.8
50	$\operatorname{Bootstrap}^{\operatorname{a}}$	0.065	0.069	0.061	0.076	0.056
	GEE2	0.067	0.061	0.063	0.052	0.044
	WLS	0.0027	0.037	0.062	0.0769	0.064
75	$\operatorname{Bootstrap}^{\operatorname{a}}$	0.070	0.061	0.061	0.063	0.063
	GEE2	0.046	0.058	0.057	0.051	0.040
	WLS	0.0030	0.040	0.060	0.071	0.069
100	$\operatorname{Bootstrap}^{\operatorname{a}}$	0.089	0.065	0.064	0.061	0.058
	GEE2	0.057	0.054	0.050	0.053	0.040
	WLS	0.0027	0.037	0.055	0.064	0.064
2 2222						

Table 1. Type I error for the comparison of G = 3 correlated kappa coefficients, according to κ level and sample size (figures are based on 3000 simulations each)

^a q = 2000

(DVT) detection using a multidetector-row computed tomography (MDCT) 122 and ultrasound (US). The study also looked at the benefit of using spiral 123 (more images and possibility of multiplanar reconstructions) with respect 124 to sequential technique (less slices, less irradiation). Images were acquired 125 in the spiral model (ankle to inferior vena cava) and reconstructed in 5 mm 126 thickness slices every 5 mm, 20 mm and 50 mm. Two radiologists (one junior 127 and one senior) assessed for each patient and each experimental setting (5/5,128 5/20 and 5/50 slices) the presence of DVT. The aim of the study was to 129 compare agreement of the different MDCT slices with the US method. Only 130 data of the senior radiologist will be presented here (see Table 2). 131

Table 2. Cross-classification of DVT detection (0=absence, 1=presence) using different MDCT slices (5/5, 5/20 and 5/50 mm) and US in 107 patients by a senior radiologist (unpublished data)

	MDCT slices							
	o/o mm		5/2	0/ 20 mm		5/ 55 mm		
US	0	1	0	1	0	1	Total	
0	96	1	95	2	96	1	97	
1	0	10	1	9	2	8	10	
Total	96	11	96	11	98	9	107	
		0.05		0.04		0.00		
	$\kappa_{5/5}$	= 0.95	$\kappa_{5/20}$	$\kappa_{5/20} = 0.84$		$\kappa_{5/50} = 0.83$		

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The observed kappa coefficients (\pm SE) were 0.95 \pm 0.053, 0.84 \pm 0.089 and 133 0.83 ± 0.098 for 5/5, 5/20 and 5/50 mm slices, respectively. The bootstrap 134 approach with 2000 iterations led to a Hotelling's T^2 value of 1.46 (p=0.48) 135 indicating no evidence of a difference between the κ coefficients at the 5% sig-136 nificance level. The bootstrap estimates of bias were 0.003, 0.008 and 0.009 for 137 the 5/5, 5/20 and 5/50 mm slices, respectively. According to the rule described 138 in Efron [9], the bias can be ignored. The differences between the κ generated 139 by the 2000 iterations of the bootstrap are represented in Figure 1 with the 140 95% confidence ellipse for the difference vector ($\kappa_{5/5} - \kappa_{5/20}, \kappa_{5/5} - \kappa_{5/50}$). 141



Figure 1. Kappa differences $(\kappa_{5/5} - \kappa_{5/50})$ versus $\kappa_{5/5} - \kappa_{5/20})$ generated by the bootstrap (q=2000) with 95% confidence interval.

It is seen that the origin (0,0) is well inside the confidence region, as expected.

144 5.2 Diagnosis of depression

McKenzie et al. [3] compared for illustrative purposes the agreement between two different screening tests (Beck Depression Inventory (BDI) and General Health Questionnaire (GHQ)) and the diagnosis of depression including DSM-III-R Major depression, dysthymia, adjustment disorder with depressed mood and depression not otherwise specified (NOS). The study consisted in determining presence or absence of depression in 50 patients. Data are summarized in Table 3. McKenzie et al. found that the 95% bootstrap confidence

Table 3. Depression (0=absence, 1=presence) assessed in 50 patients according to two screening tests (BDI and GHQ) and to a medical diagnosis

	BDI		GHQ		
Depression diagnosis	0	1	0	1	Total
0	35	2	34	3	37
1	6	7	2	11	13
Total	41	9	36	14	50
	$\kappa_{BDI} = 0.54$		κ_{GHG}	p = 0.75	

interval based on the percentiles for the difference between the two kappas 152 did include 0. The kappa coefficients were 0.54 ± 0.14 between diagnosis of 153 depression and BDI and 0.75 ± 0.11 between diagnosis of depression and 154 GHQ, respectively. The bootstrap method described in Section 3 resulted 155 in a T^2 value of 2.19 (p=0.14) confirming the findings of McKenzie [3]. The 156 bootstrap estimates of bias were 0.008 and 0.009 for BDI and GHQ methods, 157 respectively, and could be ignored. Figure 2 displays the kappa values for 158 BDI and GHQ generated by the bootstrap method (q = 1000) with the 159 corresponding 95% confidence interval. 160

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Figure 2. Kappa values of BDI and GHQ for the diagnosis of depression generated by the bootstrap (q=1000) with 95% confidence interval

162 5.3 Application of WLS and GEE2 approaches

The weighted least squares method developed by Barnhart and Williamson [6] and the GEE2 approach of Williamson et al. [4] were also applied to both datasets. As seen in Table 4, these approaches led to the same conclusions as the bootstrap procedure for both examples.

167 6 Discussion

The comparison of two or more correlated kappa coefficients is a frequently encountered problem in real life practice and there is no simple handy test to solve it. The bootstrap method described in this work provides an estimate of

Table 4. Comparison of the bootstrap, the GEE2 and the weighted least squares (WLS) approaches applied to the radiology data (unpublished) and the depression data of McKenzie [3]

	Bootstrap			GEE2			WLS		
	κ	SE	p-value	κ	SE	p-value	κ	SE	p-value
DVT radiology data									
$5/5 \mathrm{~mm}$	0.95	0.056	0.48	0.95	0.048	0.56	0.95	0.053	0.46
$5/20 \mathrm{~mm}$	0.84	0.096		0.84	0.060		0.84	0.089	
$5/50 \mathrm{~mm}$	0.83	0.108		0.83	0.063		0.83	0.098	
Depression data									
BDI	0.54	0.144	0.14	0.54	0.115	0.13	0.54	0.141	0.13
GHQ	0.75	0.114		0.75	0.128		0.75	0.107	

the mean and the variance-covariance matrix of correlated kappa coefficients 171 and hence a way to test their homogeneity by means of the Hotelling's T^2 . 172 This extension of the resampling method proposed by McKenzie et al. [3] 173 provides an alternative to the existing advanced techniques of modeling κ 174 coefficients. Furthermore, it can be used for the comparison of other correlated 175 agreement or association indexes, like the intraclass kappa coefficient [7] and 176 the weighted kappa coefficient [8] for example. The weighted least squares 177 method developed by Barnhart and Williamson [6] and the GEE2 approach of 178 Williamson et al. [4] led to the same conclusions as the bootstrap procedure 179 for both examples, although estimates of the κ coefficients obtained with the 180

bootstrap method were slightly biased. However, Efron [9] suggested that if the 181 estimate of the bias (bias) is small compared to the estimate of the standard 182 error (\hat{SE}) , i.e. $\hat{bias}/\hat{SE} \leq 0.25$, the bias can be ignored. Otherwise, it may 183 be an indication that $\hat{\kappa}$ is not an appropriate estimate of the parameter κ . 184 The bootstrap approach also yields slightly higher standard errors than the 185 WLS and the GEE2 methods, as it was expected from the results of the 186 simulations. Indeed, the type I errors obtained with the bootstrap method were 187 more liberal than those with the GEE2 method, in particular if the sample 188 size (n) was small with respect to the number (G) of kappas to be compared. 189 This finding confirms the remark made by McKenzie [3] et al. Nevertheless, 190 the type I error obtained by the bootstrap remains acceptable although it is 191 recommended to use more than 1000 bootstrap iterations when the number of 192 κ coefficients to be compared is greater than 2. The method outlined in Section 193 3 can be easily implemented in many statistical packages and programming 194 languages since the method merely requires the generation of random uniform 195 numbers and simple matrix calculations. By contrast, modeling techniques 196 require specific programming for each problem encountered in practice. Their 197 use is nevertheless highly recommended when it comes to account for many 198 covariates. A function for the bootstrap method was developed in R language 199 and is available on request from the first author. 200

²⁰¹ The authors are grateful to Dr B. Ghaye, senior radiologist at the university

²⁰² hospital, for providing the medical imaging data.

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