Cost BLCM Workshop - Welcome and Intro

Sonja Hartnack Valerie Hungerbühler

2021-07-13

Welcome

Please introduce yourself

app.klicker.uzh.ch/join/ouw

Learning aims

By attending this training, participants will:

- Perceive the logic of latent class models and their applicability in diagnostic accuracy studies in veterinary medicine
- Get acquainted with BLCMs basic principles & challenges
- Perform hands-on training on Se/Sp estimation with BLCMs
- Understand the importance of standards for reporting of diagnostic accuracy studies that use BLCMs (STARD-BLCMs)

University of Zurich[UZH]

Funded by the HORIZON 2020 Framework Programme of the European Union

Schedule today

Date	Start	End	Speaker(s)	Title
Wednesday 14 July 2021			Lecture Room Y17-M-05	
	9:00	10:15	Sonja Hartnack & Valerie Hungerbühler	Welcome & Introduction
	10:15	11:15	Sonja Hartnack	Brief historical sketch of BLCMs
	11:15	11:45	Coffee break	
	11:45	12:20	Sonja Hartnack & Valerie Hungerbühler	Hands-on Hui-Walter models I
	12:20	12:55	Sonja Hartnack	Hands-on Hui-Walter models II
	12:55	14:00	Lunch Break	
	14:00	14:30	Sonja Hartnack	Conditional dependencies
	14:30	15:00	Sonja Hartnack & Valerie Hungerbühler	Hands-on exercises
	15:00	15:30	Sonja Hartnack & Valerie Hungerbühler	Hands-on exercises
	15:30	16:00	Coffee break	
	16:00	16:30	Sonja Hartnack & HARMONY consortium	Question rounds to core group experts
	16:30	17:00	Sonja Hartnack	MCMC modeling

Schedule tomorrow

Date	Start	End	Speaker(s)	Title
Thursday 15 July 2021			Lecture Room Y17-M-05	
	9:00	10:15	Sonja Hartnack	Diagnostics (DIC, pscrf, autocorrelation)
	10:15	11:15	Sonja Hartnack & Valerie Hungerbühler	Exercises
	11:15	11:45	Coffee break	
	11:45	12:20	Sonja Hartnack	Covariates
	12:20	12:55	Sonja Hartnack & Valerie Hungerbühler	Hands- on BLCMs with covariates I
	12:55	14:00	Lunch Break	
	14:00	14:30	Sonja Hartnack	Hands-on BLCMs with covariates II
	14:30	15:00	Sonja Hartnack & Valerie Hungerbühler	Hands-on BLCMs with covariates III
	15:00	15:30	Sonja Hartnack & HARMONY consortium	Question rounds to core group experts
	15:30	16:00	Coffee break	
	16:00	16:30	Sonja Hartnack	General aspects of diagnostic test evaluation
	16:30	17:00	Sonja Hartnack & Valerie Hungerbühler	Group work and paper discussion

Schedule Friday

Date	Start	End	Speaker(s)	Title
Friday 16 July 2021			Lecture Room Y17-M-05	
	9:00	10:15	Sonja Hartnack	STARD guidelines
	10:15	11:15	Sonja Hartnack & Valerie Hungerbühler	Group work evaluation of a paper with STARD guidelines
	11:15	11:45	Coffee break	
	11:45	12:20	Sonja Hartnack	Sensitivity analysis
	12:20	12:55	Sonja Hartnack & Valerie Hungerbühler	Hands-on sensitivity anaylsis I
	12:55	14:00	Lunch Break	
	14:00	14:30	Sonja Hartnack & Valerie Hungerbühler	Hands-on sensitivity anaylsis II
	14:30	15:00	Sonja Hartnack	Final remarks & closure

Some Housekeeping

- Please sign the attendance sheet every day
- Please wear masks inside all buildings
- Please keep distance 1.5 m
- In case you get sick with COVID-19 symptoms, please leave

Some Housekeeping

Please fill in the google doc for the reimbursement:

`https://forms.gle/PKgm5wZdko5fmFMm7`

WLAN

Information for Guests

The University of Zurich provides several options for our guests to connect to the Internet:

1. eduroam WLAN

Most universities and research institutions use eduroam. Members of such institutions have Internet access in the public areas of UZH via the eduroam WLAN network. We recommend testing eduroam access at your home university in advance to ensure that the configuration is correct.

2. Internet Access for Guests via UZH WLAN

As a guest at UZH, you can access the Internet everywhere where there is WLAN access: Simply select the uzh-guest WLAN network. After doing so, accept the Terms of Service and fill in the registration form with your mobile phone number. You will subsequently receive an access code by text message, which allows you to unlock Internet access.

This option is available for all cell phone carriers that allow the receiving of SMS in Switzerland.

Evaluation of diagnostic test accuracies

Evaluation of diagnostic test accuracies

JOURNAL OF
MEDICAL VIROLOGY

LETTER TO THE EDITOR | Free Access

Should RT-PCR be considered a gold standard in the diagnosis of COVID-19?

Moustapha Dramé MD, PhD, Maturin Tabue Teguo MD, PhD, Emeline Proye MD, Fanny Hequet MD, Maxime Hentzien MD, PhD, Lukshe Kanagaratnam MD, PhD, Lidvine Godaert MD, PhD

First published: 08 May 2020 | https://doi.org/10.1002/jmv.25996 | Citations: 31

Evaluation of diagnostic test accuracies

JOURNAL OF
MEDICAL VIROLOGY

LETTER TO THE EDITOR | Free Access

Performance of VivaDiag COVID-19 IgM/IgG Rapid Test is inadequate for diagnosis of COVID-19 in acute patients referring to emergency room department

Irene Cassaniti, Federica Novazzi, Federica Giardina, Francesco Salinaro, Michele Sachs, Stefano Perlini, Raffaele Bruno, Francesco Mojoli, Fausto Baldanti ... See all authors

First published: 30 March 2020 | https://doi.org/10.1002/jmv.25800 | Citations: 61

Evaluation of diagnostic test accuracies

- «. . . indeed, when an existing test is considered as a reference, this suggests that the test in question is always correct, and that all misclassifications (false negatives, false positives) are due to the new test. . . »
- «Consequently, the new test will **never** be able to achieve sensitivity of 100%, since it is considered responsible for all misclassifications.»

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Recap on diagnostic test accuracies

Sensitivity & Specificity

- Sensitivity is the ability of a diagnostic test, to correctly classify infected individuals
- Specificity is the ability of a diagnostic test, to correctly classify healthy individuals

	Infected	Healthy	
Test (+)	80	5	85
Test (-)	20	95	115
	100	100	200

- Se 80% and Sp of 95%

Recap on diagnostic test accuracies

Sensitivity & Specificity

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	Infected	Healthy	
Test (+)	80	5	85
Test (-)	20	95	115
	100	100	200

- Se and Sp?

Recap on diagnostic test accuracies

Sensitivity & Specificity

- Sensitivity is the ability of a diagnostic test, to correctly classify infected individuals
- Specificity is the ability of a diagnostic test, to correctly classify healthy individuals

	Test 2 (+)	Test 2 (-)	
Test 1 (+)	80	5	85
Test 1 (-)	20	95	115
	100	100	200

- Se_1, Se_2 and Sp_1, Sp_2?

Evaluation of diagnostic test accuracies in the absence of a true gold standard

JOURNAL OF
MEDICAL VIROLOGY

LETTER TO THE EDITOR | Open Access

Bayesian latent class models to estimate diagnostic test accuracies of COVID-19 tests

Sonja Hartnack ✉, Paolo Eusebi, Polychronis Kostoulas

First published: 08 August 2020 | https://doi.org/10.1002/jmv.26405

University of Zurich

Historical sketch LCM

- 1980 Hui-Walter paradigm

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Population 1

		T2+	T2-
D+	T1+	P1*Se1*Se2	P1*Se1*(1-Se2)
	T1-	P1*(1-Se1)*Se2	P1*(1-Se1)*(1-Se2)

		T2+	T2-
D-	T1+	(1-P1)*(1-Sp1)*(1-Sp2)	(1-P1)*(1-Sp1)*Sp2
	T1-	(1-P1)*Sp1*(1-Sp2)	(1-P1)*Sp1*Sp2

Terminology *latent*

- The true infection status of an individual is unobserved, hence *latent*
- Instead of individuas being explicitely classified as *infected* or *uninfected*, each individual is assumed to have a probability of infection, given the combination of an observed diagnostic test outcome, knowledge on sensitivity and specificity and prior knowledge of disease prevalence in the population of interest (Cheung et al. 2021).
- In a BLCM *latent* does mean soemthing different as in a "latent herpes infection".

Historical sketch LCM

- 1980 Hui-Walter paradigm

Population 1	
T1+T2+:	P1*Se1*Se2+(1-P1)*(1-Sp1)*(1-Sp2)
T1+T2-:	P1*Se1*(1-Se2)+(1-P1)*(1-Sp1)*Sp2
T1-T2+:	P1*(1-Se1)*Se2+(1-P1)*Sp1*(1-Sp2)
T1-T2-:	P1*(1-Se1)*(1-Se2)+(1-P1)*Sp1*Sp2

- 5 parameter and 3 degrees of freedom
- Non identifiable model

Historical sketch LCM

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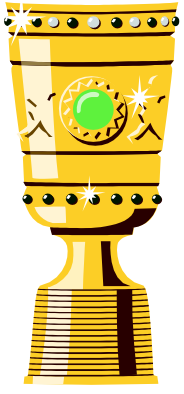
Population 1	
T1+T2+:	P1*Se1*Se2+(1-P1)*(1-Sp1)*(1-Sp2)
T1+T2-:	P1*Se1*(1-Se2)+(1-P1)*(1-Sp1)*Sp2
T1-T2+:	P1*(1-Se1)*Se2+(1-P1)*Sp1*(1-Sp2)
T1-T2-:	P1*(1-Se1)*(1-Se2)+(1-P1)*Sp1*Sp2
Population 2	
T1+T2+:	P2*Se1*Se2+(1-P2)*(1-Sp1)*(1-Sp2)
T1+T2-:	P2*Se1*(1-Se2)+(1-P2)*(1-Sp1)*Sp2
T1-T2+:	P2*(1-Se1)*Se2+(1-P2)*Sp1*(1-Sp2)
T1-T2-:	P2*(1-Se1)*(1-Se2)+(1-P2)*Sp1*Sp2



Identifiable model!

6=6

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TABLE 2. Maximum Number of Estimable Parameters and Number of Parameters to Be Estimated in the Absence of Conditional Independence and Under Conditional Independence as a Function of the Number of Tests per Subject

Number of Tests	Maximum Number of Estimable Parameters	Parameters to be Estimated Under Conditional Dependence	Parameters to Be Estimated Under Conditional Independence
1	1	3	3
2	3	7	5
3	7	15	7
4	15	31	9
5	31	63	11
h	$2^h - 1$	$2^{h+1} - 1$	$2h + 1$

Berkvens D et al. (2006) Estimating Disease Prevalence in a Bayesian Framework Using Probabilistic Constraints. doi: 10.1097/01.ede.0000198422.64801.8d

Historical sketch BLCM

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- 1995 Joseph et al. Bayesian estimation of disease prevalence and the parameters of diagnostic tests in the absence of a gold standard
  - prevalence $\pi = P(D+)$, sensitivity $Se_i = P(T_i + | D+)$, specificity $Sp_i = P(T_i - | D-)$
  - prior beta distributions $\pi \sim Beta(a_\pi, b_\pi)$, $Se_i \sim Beta(a_{Se_i}, b_{Se_i})$,$Sp_i \sim Beta(a_{Sp_i}, b_{Sp_i})$
  - $posterior \propto likelihood \cdot prior$

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- 2017 Kostoulas et al. STARD-BLCM: Standards for the Reporting of Diagnostic accuracy studies that use Bayesian

BLCM are endorsed by OIE

2.2.2. Samples from animals of unknown status

When the so-called reference standard is imperfect, which is the rule with any diagnostic tests, estimates of DSe and DSp for the candidate assay based on this standard will be flawed. A way to overcome this problem is to perform a latent class analysis of the joint results of the two tests assuming neither test is perfect.

Latent-class models do not rely on the assumption of a perfect reference test but rather estimate the accuracy of the candidate test and the reference standard with the joint test results (Branscum et al., 2005; Enøe et al., 2000; Georgiadis et al., 2003; Hui & Walter, 1980). If a Bayesian latent class analysis is used, prior knowledge about the performance of the reference test and the candidate test can be incorporated into the analysis.

Because these statistical models are complex and require critical assumptions, statistical assistance should be sought to help guide the analysis and describe the sampling from the target population(s), the characteristics of other tests included in the analysis, the appropriate choice of model and the estimation methods based on peer-reviewed literature (see *Terrestrial Manual* Chapter 3.6.5 [footnote [14]] for details).

Cheung et al., 2021

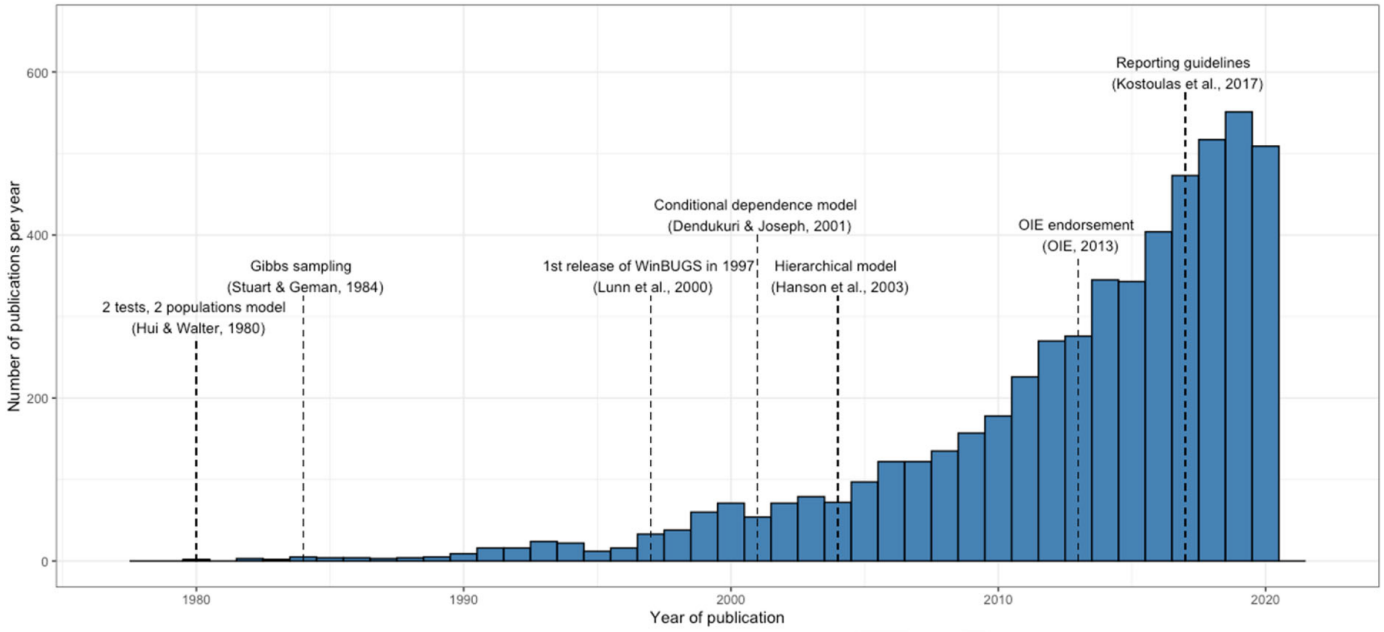

Fig. 2

Frequency histogram of the number of peer-reviewed articles published on latent class analysis when there is an imperfect reference test

End of intro

Any questions so far?