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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 26184
Title: Dried blood spots, valid screening for viral hepatitis and human immunodeficiency virus in real-life
Reviewer's code: 02363520
Reviewer's country: United States
Science editor: Jing Yu
Date sent for review: 2016-04-05 09:29
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

General Comments – Given the importance of the influence of DBS processing, sample input volume, and elution the DBS method should be described more in detail. – The selection and inclusion criteria of the population or subjects studied need further explanation. – In this context. Most subjects seem to be known positive patients, and thus appear to be somewhat at variance with the intended claim to test difficult to reach populations not yet tested. – The justification for the underlying prevalence of 30% has to be explained. – Another aspect is the differentiation and assessment against detection of primary infections, which particularly play a role in risk groups. – The overall classification of the sensitivity, for instance with respect to rapid point of care or self testing which may have similar use, may be extended. Specific questions to the manuscript. Page 5, last paragraph: Patient selection should be described more in detail. What were the criteria for selection of the subjects? Page 6, to the M&M section: Given the subsequent discussion on the sample volume it should be described in more detail how the sample volume was determined. The DBS-processing method is not described in sufficient detail. How exactly the factor come about?

Page 7, to sample size and power estimation: How is the expected prevalence of 33% based on? Page 9, to Hepatitis B: From <175 IU/ml to the test cutoff of about <0.1 IU / ml there is a very broad range. In this area, one would actually expect a reliable positive test result. Otherwise the question would arise whether weak positives can be detected at all. Can this figure be shown more limited? Page 10 1st paragraph regarding: "CMIA median 6.19, range 1.1-10.1". One can imagine that values only slightly >1 s/co in Architect Anti-HBc as shown here can be false negative after dilution by the elution of DBS. This should be further explained. Also for Fig. 2 the HBV algorithmus does not include clarification of the aHBc results to exclude false positives? Page 10, 3rd paragraph: Anti-HBs was positive in plasma (1.08-9.44 mIU/ml) but negative in DBS (0-0.3 mIU/ml). According to the Architect test interpretation criteria, only aHBs values ≥ 10.00 mIU/mL are considered reactive. Therefore, this appears to be only seemingly a discrepancy. Page 10, 4th paragraph: 79 where plasma was positive (median 9.9 mIU/ml, range 1-75) and DBS negative (median 0.01 mIU/ml, range 0-0.93). The question arises whether this is not a value range, which is negative after the dilution in the eluent DBS. This should be explained further. Page 11, last paragraph to sentence: "The low sensitivity, for the serological markers; anti-HBs and anti-HBc in DBS versus plasma, found in our study is in contrast to recent studies using automated platforms". This may be an combined effect of different starting titers of the sample and different dilution factors by elution. Can the discussion be extended to? Page 12, 1st paragraph to sentence: "We speculate if an indicator for the amount of blood collected on the paper could be developed to insure that enough blood is present for sampling (e.g. weight, haemoglobin etc). This would also us allow to calculate a quantitative antiHBs /ml of serum from DBS, to be used in outreach vaccination trials." The increase of the sample input volume, e.g. as mentioned above from approximately 75 ul to 100 ul seems to be to be rather small compared against the dilution effect of the elution (factor 23) and differences in this dilution factor. This should be explained more. Page 13, 1st paragraph to sentence: "We therefore suggest that treatment na?ve patients that are anti-HCV positive/HCVRNA negative in DBS screening (suggesting past HCV infection) should have their status confirmed by a subsequent venous blood sample." This may not be the only constellation, since single negative HCV-RNA results may not determine the infection status due

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COMMENTS TO AUTHORS

Mossner et al. investigates the sensitivity and specificity of a Dried Blood Spot (DBS) screening for HIV, HBV and HCV in patients in drug treatment centers. The authors find that DBS had a high sensitivity >96% and a high specificity 98% for all three infections; however, the antiHBc and antiHBs showed low sensitivities in DBS (42% and 68%, respectively). Chronic infections such as HIV, HBV and HCV remains major sources of mortality and morbidity. However, due to their mild symptoms during early phases of infection, most of infected people are not aware of infection status. Developing a low-cost medically scalable diagnostic tool for testing chronic infections such as HIV, HBV and HCV, is of great importance and has substantial public health implications. Evaluating the feasibility using DBS as diagnostic tool is especially important in a resource limited settings. Thus, this manuscript addresses an important question, and the results are promising in many ways. It is well written. The methodology and analysis are well documented and the results are analyzed rigorously. Therefore, I recommend publication.