IN THIS ISSUE:

FEATURE ARTICLE
Digital Pathology: An Innovative Approach to Medical Education
Leonisa Sagun and Randell Arias

ORIGINAL ARTICLES
Interobserver Variability of Gleason Score and Completeness of Histopathology Report in Prostatic Adenocarcinoma in Prostate Needle Biopsy Specimens among General Pathologists in a Multi-institutional Setting
Anne Lizbeth Valdez and Jeffrey So

Commercially Bottled Purified Water as an Alternative Instrument Feed Water in Automated Time-Resolved Fluorescent Immunoassay for TSH, 17-OHP and IRT in Neonatal Screening
Emilio Villanueva III, Roel Martin Bumalay, John Michael Rivera

BRIEF COMMUNICATIONS
External Quality Assessment Scheme for Transfusion Transmissible Infections among Blood Service Facilities in the Philippines, 2017
Kenneth Aristotle Punzalan, Rhoda Yu, Iza Mae Chamen

IMAGES IN PATHOLOGY
Ameloblastic Fibro-Odontoma
Jay Hansel Tabije, Leila Salera, Jose Angelo Militante
THE PHILIPPINE BOARD OF PATHOLOGY

announces the dates of the

2019 DIPLOMATE EXAMINATIONS

CLINICAL PATHOLOGY
FEBRUARY 24, 2019 (SUNDAY)

ANATOMIC PATHOLOGY
MARCH 10, 2019 (SUNDAY)

APPLICATION DEADLINE
DECEMBER 14, 2019 | 5:00 PM

For particulars, please call the PSP secretariat:

Tel. No.: 920-3192 | 738-6814;
Mobile no.: 0922-851-7379 | 0926-067-6283

* This advertisement is a complimentary service of the PJP for member societies/organizations.
The Philippine Journal of Pathology (PJP) is an open-access, peer-reviewed, English language, medical science journal published by the Philippine Society of Pathologists, Inc. Committee on Publications. It shall serve as the official platform for publication of high quality original articles, case reports or series, feature articles, and editorials covering topics on clinical and anatomic pathology, laboratory medicine and medical technology, diagnostics, laboratory biosafety and biosecurity, as well as laboratory quality assurance. The journal's primary target audience are laboratorians, diagnosticians, laboratory managers, pathologists, medical technologists, and all other medical and scientific disciplines interfacing with the laboratory. The PJP follows the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals, EQUATOR Network Guidelines, and COPE Guidelines. The PJP does not charge any article processing or submission fees from authors. It does not charge any subscription fees or download fees to access content.
Greetings to our PJP readers,

This is now our 2nd issue for 2018 and the 5th issue since 2016. I hope everyone is pleased with our issues and I hope our pathologists, especially our trainees, are inspired to write articles, submit their researches and case reports. This journal is your venue for your works to be seen and read.

Please take time to read our journal and be inspired to contribute.

Bernadette R. Espiritu, MD, FPSP, MMHoA, MIAC
President, Philippine Society of Pathologists, Inc.
Editorial

Just Before Dawn

Publication is research work’s endpoint. Unless we publish our work (i.e., “to make public”), our outputs will not be included in the body of scientific literature, will neither be cited nor acknowledged, will be lost knowledge and information, and ultimately cannot be built upon by future researchers. Publication is permanence and is an imperative for a professional society like the Philippine Society of Pathologists.

For us Filipino pathologists, the publication of our local data, is an issue that can be addressed systematically, purposefully, and comprehensively.

First, there must be recognition from our leaders on the need for evidence on which to base our practice as laboratorians and laboratory managers, and, from there, investment of time, effort, and funding.

Second, there must be concrete planning of the steps to take, to get us from the status quo to what should be. The Committee on Research of PSP and Board of Pathology are in the best position to do this, through purposeful capacity building of our young pathologists on the necessary research competencies—from grant proposal writing to research methodologies, from data analysis to research writing—to generate the results that we need. We can consider publication and not mere completion of research, as a requirement for residents and diplomates.

Third, the society can support the research consortia being organized by the pathology training institutions, in order to stimulate research questions and catalyze collaborations. I must thank PSP for her recognition of PJP as a high-quality platform for pathology research and her continued support to the operations of the journal. But the society can do more, by investing in medium- and long-term research agenda setting, as well as, looking into establishment of grant schemes to motivate our pathologists-in-training to go into research.

Thomas Fuller, a historian and theologian, was the first one to have said that “the night is darkest, just before dawn,” which reminds us that things get worse, before they get better, and more importantly, that even in adverse circumstances, there is hope.

We are on our way. We will get there.

Amado O. Tandoc III, MD, FPSP
Editor-in-Chief

https://doi.org/10.21141/PJP.2018.008
Asia Pacific International Academy of Pathology
Junior Academy
&
Philippine Society of Pathologists, Inc.
(Spearheaded by the PSE Central Luzon Chapter)

14TH MIDYEAR CONVENTION
“Pathologists Conquering the Challenges of the Millennium”

27-29 November 2018
Xenia Hotel, Clark Freeport Zone, Pampanga

REGISTRATION FORM

Name: __________________________
LAST NAME: __________________________
FIRST NAME: __________________________
MIDDLE NAME: __________________________

☐ Consultant ☐ Resident ☐ Non-member

Hospital Affiliation: __________________________
Address: __________________________
Home/Mailing Address: __________________________

Landline Number: __________________________
Fax Number: __________________________
Mobile Number: __________________________
Email Address: __________________________

Pre-Registration
(an or before September 21, 2018)
Consultants: Php 6,000
Residents: Php 4,000
Non-Members: Php 6,500

Registration
(after September 21, 2018)
Consultants: Php 6,500
Residents: Php 4,500
Non-Members: Php 7,500

Foreign Delegates
Consultants: USD 200
Residents: USD 150
Non-Members (AAIAP): USD 220

REGISTRATION IS LIMITED TO 300 DELEGATES ONLY

PAYMENTS:
All checks, bank drafts or money orders should be made payable to Philippine Society of Pathologists, Inc. Payments may be deposited to BPI Philippine Heart Center Branch Savings Accnt no. 4253 0472-27. Please fax deposit slip with the supplied registration form to tel/fax (02) 920-3192 or email to pspc1930@yahoo.com and please present the ORIGINAL slip to the registration booth.

REFUND:
Requests for refund shall be submitted in writing to the Registration Committee thru the PSP Secretariat not later than November 15, 2018. No requests for refund shall be granted beyond said date. Refund shall only be 50% of the paid value to cover for handling and processing.

* This advertisement is a complimentary service of the PJP for member societies/organizations.
NOVEMBER 27
TUESDAY
08:30-08:40 Opening Remarks
  Dr. Remoutedte Espiritu
  PSP President

08:40-08:50 Opening Remarks
  Puay Hoon Tan
  Convener, AAPAP

08:50-10:00 Molecular Pathology for Anatomical Pathologists
  Stephen Fox

10:00-10:30 Coffee Break

10:30-11:10 Difficult Issues in Papillary Lesions of the Breast
  Puay Hoon Tan

11:10-11:50 The Role of IHS in Breast Cancer Management
  Gary Tien

11:50-12:30 PD1: Assessment in Non-small Cell Lung Cancer
  Stephen Fox

12:30-1:00 Lunch Break

01:00-02:00 What WHO 2016 has Not Solved for Adult Gliomas
  Ho-Kueing Hg

02:00-02:50 Can Pediatric Low Grade Gliomas Really Be Diagnosed By Microscopy Alone?
  Ho-Kueing Hg

02:50-03:30 Sclerosing Breast Lesions
  Gary Tien

03:30-04:00 Coffee Break

04:00-04:40 Fibroepithelial Lesions - A 2018 Update
  Puay Hoon Tan

04:40-05:20 How Can A Regular Lab Do Molecular Diagnostics of Pediatric Brain Tumors?
  Ho-Kueing Hg

06:30 Fellowship Night
  Theme: Filipino Cultural Night

NOVEMBER 28
WEDNESDAY
09:00-09:40 Algorithmic Approach for the Diagnosis of Fungal Infections
  Isaac Solaman

09:40-10:20 Effective Utilization of Molecular Diagnostics in Infectious Disease Pathology
  Isaac Solaman

10:20-11:00 Endometrial Hyperplasia to Carcinomas
  Nolia Kayani

11:00-11:30 Coffee Break

11:30-12:10 Cytology and Pathology of Salivary Gland Tumors
  Jen-Fan Hang

12:10-12:50 Emerging and Re-emerging Viral Infections in the 21st Century
  Isaac Solaman

12:50-02:00 Lunch Break

02:00-02:40 Updates of WHO Classification and AJCC Staging of Head and Neck Tumors
  Jen-Fan Hang

02:40-03:20 Mesenchymal Tumors of the Uterus
  Nolia Kayani

03:20-04:00 Common Ovarian Surface Epithelial Tumors: Histological and Immunohistochemical Assessment
  Nolia Kayani

04:00-04:10 Closing Remarks
  Course Directors

NOVEMBER 29
THURSDAY
08:30-09:15 Investing in People: Knowing the Standards in Personnel Management
  Ms. Maridet Distor

09:15-10:00 Risk Management in the Laboratory
  Mr. Brian Eclatant

10:00-10:30 Coffee Break

10:30-11:00 Change Management
  Aly. Josephine Fernandez

11:00-11:45 Workshop: Application of Change Management Tools

11:45-12:30 Lunch Break

  Ms. Pyla Tan

01:45-02:45 Workshop: ROI: Break Even Points and More

02:45-03:30 Part II. Financial Management and Metrics: Supply Chain Management
  Ma. Carla G. Namon

03:30-03:45 Coffee Break

03:45-04:30 Part III. Financial Decision Making for the Pathologists- Financial Strategies for Laboratoriests
  Mr. Luis Bernas

04:30-5:00 Closing Ceremonies

14th MIDYEAR CONVENTION
ORGANIZING COMMITTEE

OVERALL CHAIRMAN:
Ricardo E. Eclatant, MD, FSPS

IAP – Edna May Lasap-Go, MD, FSPS
CP – Maria A. Orilaza, MD, FSPS
Montasser S. Chichoco, MD, FSPS
Marjory G. Gapala, MD, DPSP
Sheridan Steven C. Aquino, MD, FSPS
Frances A. Sauto-Sanchez, MD, FSPS
Ma. Theresa T. Enrique, MD, FSPS
Ronald C. Cabuday, MD, FSPS
Emil Bryan M. Garcia, MD, FSPS
Gil Bryan B. Galvan, MD, FSPS
Michelle T. Miranda, MD, FSPS
Joel T. Tisac, MD
Kathryn I. Leyte, MD, FSPS
Nick R. Fernandez, MD, FSPS
Aerenif May H. Rafanan, MD, FSPS
Robert R. Reyes, MD

FINANCE:
DOCUMENTATION:
PUBLICITY:
HOSPITALITY:
SENIOR HOUSE OFFICERS:

RECOGNIZING THE FOLLOWING:
Edith S. Yna, MD, FSPS
Bernadette R. Espiritu, MD, FSPS
Herbert G. Pascual, MD, FSPS
Kalingtan R. Gutierrez, MD, FSPS
Joyelyn Mya R. Caja, MD, FSPS
Januario D. Veloso, MD, FSPS
Richard Victor O. Quimbo, MD, DPSP
Ayan T. Koa, MD, FSPS

PHILIPPINE SOCIETY OF PATHOLOGISTS, INC.
114 Malakas Street, Diliman, Quezon City
Email: pspinc1950@yahoo.com
Telephone Number: +63 (02) 920-3192, 738-6814
Cellphone Number: 0922-851-7379

For further inquiries please contact:
Dr. Ricardo Eclatant @ +639189047921

* This advertisement is a complimentary service of the PJP for member societies/organizations.
ABSTRACT

Pathology, a basic science course in medical schools, is a highly visual subject that requires examination of tissues using a microscope. With progressive technological advancements, the use of time-tested optical microscopes in teaching is seemingly slowly replaced by virtual microscopy that many medical schools in developed countries have proved its numerous advantages. In our setting, digital pathology is not yet fully integrated into medical schools. Although a few medical institutions in the country may have started this technology, there is still a lot to explore with virtual microscopy that will unlock its full potential of revolutionizing medical education in the future.

Key words: digital pathology, virtual microscopy, medical education, pathology education

INTRODUCTION

Pathology is the medical discipline that provides a scientific foundation for medical practice. It is a required basic science course in medical school, and is often the first introduction to human disease processes. Compared with other basic sciences, pathology is a visual subject that is based in part on histopathologic examination of tissues which is important to understanding basic mechanisms of disease processes.

The microscope has been the most widely used instrument in pathology education and until now, is still a mainstay in the classrooms and laboratories of pathologists. However, pathology is under a digital revolution enabled by virtual microscopy – the practice of converting glass microscope slides to high-resolution, whole-slide digital images that some recent studies have demonstrated a decrease in the use of traditional microscopes in medical schools, mainly as a result of current developments in the curriculum as well as some disadvantages of the technique itself.

Whole slide imaging (WSI), also known as digital pathology or virtual pathology, is a technology that involves high-speed, high-resolution digital acquisition of images representing entire stained tissue sections from glass slides in a format that allows them to be viewed by a pathologist on a computer monitor, where the image – often referred to as the ‘whole slide image’ or digitized slide’ can be magnified and navigated spatially in much the same way as standard microscopy. In addition, the digital slide images can be viewed across a network, including the Internet, using specialized viewing software – a potential area for accurate and timely diagnosis in actual pathology practice compared with traditional methods.

Significant technological advancements of digitizing slides and the development of workflow tools that facilitate remote viewing and analysis are likewise enabling pathologists to substantially change how they learn and practice their profession. With the emergence of digital pathology over the past several years, there is
an opportunity to revolutionize the way teaching and learning are done in medical schools in the country and would create opportunities beyond classroom teaching.

TRENDS IN IMPLEMENTATION

Digital pathology has already been implemented in many medical schools in the United States and other developed countries and has been shown to provide advantages compared with the usual traditional method of teaching histology and pathology courses.\(^5\)\(^6\)\(^7\)\(^8\) A few of the developing countries has utilized the digital pathology in the form of telepathology in clinical practice.\(^9\)\(^10\) Telepathology is the electronic multimedia communication across a network of pathology-related information, between 2 or more locations for use – cases between pathologists and/or qualified laboratory personnel, and may include involvement by clinicians and/or patients.\(^1\) Several journals reported the use of digital pathology in the form of telepathology in education,\(^1\)\(^2\)\(^9\)\(^10\)\(^11\) second-opinion consultations,\(^1\)\(^3\)\(^14\) and primary diagnosis.\(^1\)\(^5\)\(^16\)\(^17\) Success in the implementation of virtual microscopy has been documented in graduate education in medical,\(^1\)\(^8\)\(^19\)\(^20\) dental\(^1\) and veterinary schools.\(^2\) In addition, the US Food and Drug Administration approval of whole slide imaging (Philips IntelliSite Pathology Solution) for primary diagnosis in surgical pathology in 2017 marked a significant evolution of digital pathology.\(^2\)\(^5\) If the current trend continues, the implementation of virtual microscopy may eventually make the time-tested microscope a relic in medical education, and possibly in pathology laboratories.

THE LEARNING ENVIRONMENT

The general pathology course in medical education includes different elements, each with different learning goals. In our experience, these elements include lectures, virtual microscopy lessons and small group discussions. The virtual microscopy session involves 1 teacher per 12 students wherein selected microscopy specimens are scrutinized and allowing students to interact actively. The small group discussions include case studies wherein theory from lectures are combined with information from textbooks, microscopy and clinical data (clinical correlation). Proper alignment of these study elements would allow microscopy to be seamlessly integrated in all aspects of the course, improving microscopy knowledge and performance of the students. From this pioneering experience, we utilized digital pathology in classroom teaching that favors student-centered, self-directed learning. This new framework based on platforms familiar with twenty-first century students will change how they learn pathology – a transition from seeing actual gross and microscopic specimens to looking at images from Web-based resources.

### Table 1. Benefits of digital pathology/virtual microscopy versus traditional microscopy

<table>
<thead>
<tr>
<th>Digital Pathology/Virtual Microscopy</th>
<th>Traditional Microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Images can be standardized</td>
<td>Variability of histologic sections</td>
</tr>
<tr>
<td>Image quality can be maintained indefinitely</td>
<td>Variability of histologic sections</td>
</tr>
<tr>
<td>Multiple annotation can be done</td>
<td>None (except, pointer an/or pen marks)</td>
</tr>
<tr>
<td>Easier storage and retrieval</td>
<td>Requires physical space for storage of both microscopes and glass slide sets</td>
</tr>
<tr>
<td>Images of rare cases can be stored indefinitely</td>
<td>Glass slides of rare cases cannot be duplicated and made available</td>
</tr>
<tr>
<td>Cost-effective over time</td>
<td>Maintenance and replacement of microscopes and glass slide sets are costly</td>
</tr>
<tr>
<td>Convenient for both teacher and student</td>
<td>Time-consuming during preparation and actual lecture</td>
</tr>
</tbody>
</table>

### PRACTICAL BENEFITS OVER CONVENTIONAL MICROSCOPY

There are many advantages to using digital pathology or virtual microscopy than with traditional microscope glass slides (Table 1). Digital images can be standardized, with the potential for image enhancement, so that all students will study the exact same tissue section. Microscopic sections on glass slides show variability with regards to quality and content\(^2\) which may often be incomplete and not identical leading to discrepancies in testing and scores of students. These variabilities can be substantially eliminated with digital imaging. Compared to glass slides that are prone to fading, breaking and loss over time, the quality of the image can also be indefinitely maintained with digital pathology.\(^2\)\(^5\) In addition, rare cases of glass slides cannot be duplicated and made available for the students.

Another very helpful aspect of virtual microscopy is that digital images of microscopic glass slides on a computer screen have panning and zooming capabilities simulating moving the stage and the low to high power magnification of an optical microscope.\(^2\) The digital image has a thumbnail image from which the students can always refer to when viewing the digital slides at a higher magnification for proper orientation of histologic sections (Figure 1).\(^3\)

Aside from these benefits, the time used for setting up the educational sessions and actual teaching process are much less compared to traditional microscopy, hence giving students more time to learn. The use of the microscopes is often limited to the working hours of the faculty, requiring the students to be physically at school for self review.19

With digital pathology where whole-slide images are loaded onto a web-based server, study can occur wherever and whenever the student wishes.25 Finally, storage and maintenance of microscopes and glass slides sets are cumbersome and require significant expenses.2 Digital images can be easily stored in server memory or computer disks which provides smooth retrieval.

**IMPACT ON STUDENT LEARNING**

The possibility of providing students with all the information they need electronically has been an idealized concept for many years.27 Web-based resources including social media have shown benefits to supplement education in a cost-effective way. This was certainly one of the reasons for the positive attitude of the students toward digital pathology. Several studies have proven that the majority of students believe that the use of digital slides enhanced their ability to learn.24,28

Virtual microscopy has not only been reported to improve the student learning process, but it has also been shown to improve their cooperation skills, communication abilities and self-confidence.29 However, some students still find it important for them to be proficient in using the traditional method of viewing the glass slides. The sense of fulfillment of manually operating the microscope – focusing the image, navigating the slides and changing objectives – cannot be satisfied by digital slides. In our setting, the extent of what digital pathology can offer for student learning has yet to be explored which includes remotely reviewing the digital images anytime, anywhere.

**IMPACT ON TEACHING**

The transition from conventional to virtual microscopy presents certain challenges for teachers. The methods of preparing and delivering the lessons changed. Teachers could now prepare lessons at home on a personal computer without requiring access to a microscope.

In addition, there will no longer be any time-consuming, hands-on microscope work during lessons which could create more time for reviewing specimens with the students.27 Digital pathology has enabled each teacher or course director to customize a collection of scanned slide specimens to suit particular needs. Teachers regarded this flexibility as a positive aspect of virtual microscopy.27

**CHALLENGES IN IMPLEMENTATION**

Implementing digital microscopy in medical education may not pose crucial challenges as in diagnostic practice. Unlike in medical education, digital microscopy in the actual practice of pathology requires several important considerations, of which quality slides that are cut and stained properly are a crucial step.

Aside from these, barcode labelling of slides for accurate identification of data entry into database, slide scanning, integration of the scanned data and image-viewing applications into the laboratory and hospital’s information system and the technological infrastructure enabling image transfers must be taken into account.26

Digital slides used in teaching are customized according to the topic of discussion. These may not necessarily come from the original scanned glass slides from the Histopathology Section, but may be retrieved from image-viewing applications or pre-loaded digital images by the system provider.
Establishing a digital microscopy laboratory is initially an expensive project, but may eventually become economical than traditional microscopy which relates to additional costs in the storage and maintenance of microscopes and glass slides sets. Dee et al., calculated the cost of a microscope laboratory for 50 students to be about $100,000 per year, which approaches the complete start-up costs for virtual microscopy, including purchase of a virtual slide scanner.  

In low resource areas such as in our setting, the challenges are more apparent. Access to the Internet on academic networks is often slow and expensive. Aside from the cost, other barriers include the limited student access to computer workstations especially after class hours, technical aspects such as unreliable electrical power and adverse weather events which could disrupt telecommunications. 

Teacher-student interaction is also a concern. It would seem like virtual microscopy would decrease the dynamic interaction between teachers and students. However, in truth, this technology enabled the students to learn pathology in a more interactive and stimulating manner. 

**OPPORTUNITIES FOR DIGITAL PATHOLOGY IN EDUCATION**

Although the classroom offers a high utility environment for digital pathology in medical education, many other education-related areas also benefit from the use of digital pathology, including decision support, digital slide conferences, proficiency testing and quality assurance. The possibility of creating a repository of digital slides by pathologists over time can be helpful in decision support. 

The accessibility of digital pathology makes it easier to present in seminars, symposia and conferences. Of these scientific presentations, clinicianopathologic conference, tumor boards and morbidity/mortality/autopsy audits are among the most commonly encountered meetings by a medical student. Digital slide conferences conducted via the Internet allow multiple participants to view the digital slides simultaneously, and in real-time. 

Digital pathology can be utilized in training and education in the form of proficiency testing in other fields of anatomic pathology. It has been shown that proficiency testing in gynecologic cytopathology (“virtual Pap tests”) is feasible. Similar with proficiency testing, the cost and difficulty of glass slides logistics in quality assurance (QA) practices is one of the drawbacks of traditional microscopy. With digital pathology, it is simple to make digital slides accessible to other facilities and organizations for QA programs. 

Finally, digital pathology can be utilized in other learning courses such as microbiology, hematology, histology, cytology and clinical microscopy (urine and body fluids) and integrated in online platforms showing educational videos and slide navigation of particular topics in medicine. 

**CONCLUSION**

Digital pathology is a powerful educational tool that could effectively replace the traditional standard methods of teaching and learning pathology. It provides mobility and convenience to medical students and teachers alike. While majority of the medical schools in the country still consider microscopes and glass slides inevitable in pathology education, we believe that in the coming years, digital pathology will be eventually integrated not only in pathology and histology curricula, but also in other courses requiring microscopy. It will potentially revolutionize medical education and create several opportunities beyond classroom teaching. 

**STATEMENT OF AUTHORSHIP**

All authors certified fulfillment of ICMJE authorship criteria. 

**AUTHOR DISCLOSURE**

The authors declared no conflict of interest. 

**FUNDING SOURCE**

None. 

**REFERENCES**


Disclaimer: This journal is OPEN ACCESS, providing immediate access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge. As a requirement for submission to the PJP, all authors have accomplished an AUTHOR FORM, which declares that the ICMBIE criteria for authorship have been met by each author listed, that the article represents original material, has not been published, accepted for publication in other journals, or concurrently submitted to other journals, and that all funding and conflicts of interest have been declared. Consent forms have been secured for the publication of information about patients or cases; otherwise, authors have declared that all means have been exhausted for securing consent.
CALL FOR PARTICIPATION

29-30 January 2019, Zamboanga City

15th National Medical Writing Workshop &
8th WriteShop for Young Researchers

APPLICATION EXTENDED
Deadline: 22 October 2018

For more information, visit
www.pchrd.dost.gov.ph

* This advertisement is a complimentary service of the PJP for member societies/organizations.
Interobserver Variability of Gleason Score and Completeness of Histopathology Report in Prostatic Adenocarcinoma in Prostate Needle Biopsy Specimens among General Pathologists in a Multi-institutional Setting

Anne Lizbeth Valdez and Jeffrey So

St. Luke’s Medical Center, Quezon City, Philippines

ABSTRACT

Introduction. Gleason score, the most widely used grading system for prostatic adenocarcinoma, is the most powerful predictor of patient’s clinical outcome and is used to customize treatment strategies. It possesses an inherent degree of subjectivity, as inter-observer and intra-observer variability does exist. Moreover, there are currently no structured histopathology report guidelines for prostate needle biopsies in our setting, making relevant information overlooked by pathologists and interpretation of report between laboratories challenging.

Objective. With these in mind, we sought to study the interobserver variability of Gleason score and completeness of histopathology report in prostate needle biopsy specimens.

Methodology. A set of 19 prostate needle biopsy slides was sent to 18 general pathologists from different institutions in the Philippines for histopathologic analysis of Gleason scores and completeness of reporting. The interobserver agreement of each pathologist will be evaluated using Spearman’s rank correlation coefficient.

Results. Overall, there was moderate correlation between the interobserver’s Gleason score and Gleason grade group. Low to moderate correlation was seen in primary grade while negligible correlation was seen in secondary grade. Best agreement was seen in poorly differentiated neoplasms. Undergrading was more common than overgrading. Most respondents gave an incomplete histopathology report.

Conclusion. There is an overall moderate correlation between Gleason score. A non-standardized histopathology report is currently used, leaving out relevant histopathologic findings.

Key words: prostate, prostate cancer, urology

INTRODUCTION

Gleason score is the most widely used grading system for prostatic adenocarcinoma. Inevitably, like all other grading systems, it is flawed by some degree of interobserver and intraobserver variability.1 Although this grading system has undergone significant revisions for the past years, it still continues to have deficiencies that can potentially impact patient care.

Gleason score is the most powerful predictor of patient’s clinical outcome and is a major determinant in customizing treatment strategies that is most appropriate for a patient. It is utilized to tailor-fit post biopsy treatment, plan for the type of radiation therapy and whether to administer hormonal therapy with radiation therapy. Patients with Gleason scores of <6 may benefit from watchful waiting and surveillance as initial management.1 The presence of high-grade Gleason pattern (Gleason pattern 4 or 5) harbors the greatest risk for metastasis and treatment failure. Thus, discordance in Gleason scoring, albeit small, will have a dramatic effect on risk stratification and clinical management.
It has been observed that general pathologists more frequently underscore than over score, with a natural tendency to assign low Gleason pattern in such small core needle biopsies. In a study done by RV Singh et al.,2 Gleason score 7 was identified as an area of difficulty as 14 of 63 readings (22%) were underscored. The differences centered on the assessment of small areas of fused and separate glands and fused small irregular glands. This has led to the inappropriate assignment of Gleason score 6 and probable suboptimal patient management as a consequence. In the same study, assignment of Gleason pattern 4 and 5 as distinction between few tiny poorly formed glands versus cords and nests of malignant cells were particularly challenging. As a result, sheets of cells with ill-defined lumina were inappropriately given as Gleason pattern 5 instead of pattern 4. These discrepancies suggest that misperceptions among each Gleason pattern in the scheme exist, especially for “borderline” cases, which exhibit features intermediate between 2 patterns. In another study by Coard,3 the greatest discordance is seen in distinguishing Gleason score 6 from 7 in biopsy specimens with less than 30% tumor volume. This has led to the conclusion that assignment of Gleason scores in core needle samples, in contrast to TURP and radical prostatectomy specimens, poses a diagnostic dilemma as these samples contain low tumor volume.4,5 Several data support that for needle biopsy grading, pathologist training and experience can influence the degree of interobserver agreement.6,7 In one study,7 41 general pathologists exhibited moderate interobserver agreement with a kappa coefficient of 0.435, while substantial interobserver agreement with a kappa coefficient of 0.6-0.7 was seen among 9 of 10 urologic pathologists. Interest in urologic pathology, particularly in Gleason scoring, resulted in participation of general pathologists in educational courses and subspecialty training, which however is not readily available in our setting. Other sources of grading variation in core needle samples include difficulty in appreciation of infiltrative growth pattern, tissue sampling error and artificial tissue distortion.

A structured histopathology report for prostate needle biopsy has an essential role in conveying the result to clinicians. The report should be uniform and formatted to provide compete, clear and unambiguous data. The inclusion of tumor volume and presence of extraprostatic extension, perineural and lymphovascular invasion, prostatic intra-epithelial neoplasia and intraductal carcinoma in prostate needle biopsy reports are equally essential as the Gleason score, and must be reported when present since these are associated with adverse clinical outcome.8 Moreover, these pathologic findings are being utilized in common nomograms used to guide clinical decision making and therefore must be reported when present. In one study by Kryvenko et al.,1 analysis of needle biopsy cores showed that the number of positive cores, tumor volume and perineural invasion predicts presence of extraprostatic extension, seminal vesicle invasion and positive surgical margins in radical prostatectomy specimens. In the same study, they concluded that biopsy specimens with perineural invasion is significantly associated biochemical recurrence.

With these in mind, our study intends to 1) determine the interobserver agreement of the respondent pathologists in Gleason grading of prostatic adenocarcinoma in terms of: primary grade, secondary grade, Gleason score and Gleason Grade Group; and 2) describe the completeness of reporting of histopathology results by respondent pathologists in terms of inclusion of tumor volume and mention of presence of extraprostatic extension, perineural and lymphovascular invasion, prostatic intra-epithelial neoplasia and intraductal carcinoma.

METHODOLOGY

Board certified fellows or diplomats in anatomic pathology by the Philippine Society of Pathologists who acquired no formal training in uropathology and practicing as a general pathologist were recruited for this study. Information on respondents’ age, number of years in practice, current affiliation/s and other demographic profiles were not collected. They were invited to take part in the study via phone calls, letters and emails. Our study welcomed 18 pathologists from all over the Philippines, including areas outside Metro Manila such as Ilocos Norte, Cagayan, Isabela, Zamboanga, Cebu and Davao. A set of 19 slides diagnosed by a uropathologist with prostatic adenocarcinoma at St. Luke’s Medical Center Quezon City was sent to the respondent pathologists. These cases were seen by a second pathologist from the same institution who concurred with the diagnosis. The slides were selected by the original sign-out pathologist to roughly represent the spectrum of Gleason scores based on the 2015 Modified Gleason Grading System and no effort was made to select particularly difficult cases. The slides, in hematoxylin and eosin preparation, was of uniform and adequate quality and was assessed prior to shipping to ensure proper and careful examination. Also sent along with the slides was a copy of the questionnaire and endorsement letter.

The questionnaire had assigned codes (P1-P18) to maintain the respondent’s anonymity while the endorsement letter contained a brief description of the study. Each slide was given a code number (1-19) to maintain patient’s anonymity and to ensure that these could not be identified by the respondent pathologists. Each respondent was instructed to give a complete diagnosis as they normally would with their own cases. He/she reviewed the slides without the knowledge of the previous Gleason scores. The interobserver agreement was evaluated using Spearman’s rank correlation coefficient. Agreement was calculated for primary grade, secondary grade, Gleason score and Gleason grade group (based on 2015 ISUP and 2016 WHO grading system). The completeness of reporting of each pathologist was evaluated by the mention or failure to mention of tumor volume, extraprostatic extension, perineural and lymphovascular invasion, prostatic intra-epithelial neoplasia and intraductal carcinoma. Institutional Review and Ethics Research Committee approval was secured prior to the commencement of this study.
RESULTS

To assess for interobserver agreement, a mathematical consensus was first calculated (Table 1). The overall percentage of Gleason score agreement for all respondents is 43.0% (10.5% to 68.4%) (Table 2). The maximum number of readings were in the Gleason score 7 (33.9%; n=78/342) and least in Gleason score 2-4 (3.2%; n=11/342).

The distribution of percentage agreement for Gleason score with consensus score was computed (Table 3). 43% (n=147/342) of all assigned Gleason scores were in exact agreement with the consensus score. 72.8% and 83.6% of the assigned Gleason score were within ±1 and ±2 of the consensus score, respectively. Agreement was best in Gleason 9 (75%; n=25/33) and worst with Gleason 3 (0%; n=0/18) and Gleason 8 (30%; n=30/100). Overall, undergrading was seen in 30.4% while overgrading was seen in 26.9% of the readings. Most commonly undergraded is Gleason score 8 (46/100; 46%) while Gleason score 6 is most commonly overgraded (43/114; 38%).

Interobserver Spearman’s rank correlation coefficient for primary grade, secondary grade Gleason score and Gleason grade group were computed (Table 4). Majority had moderate to low correlation (64.7%; n=198/306) in the primary grade while majority had negligible correlation (61.4%; n=188/306) for secondary grade. Likewise, moderate correlation (35.9%; n=110/306) was seen in the majority of the Gleason scores and moderate correlation (39.2%; n=120/306) with the Gleason grade group.

A total of 8 respondents (44.4%; n=8/18) mentioned at least 1 other histopathologic finding (Table 5).

DISCUSSION

Agreement was best seen in Gleason score 9. This is may be due to the straightforward identification of sheets, cords and solid nests of infiltrative neoplastic cells and necrosis and the large tumor volume of such poorly differentiated neoplasms.
CONCLUSION

Overall, tumor heterogeneity giving rise to various patterns/mimickers and the presence of morphologically borderline tumors complicates Gleason scoring. We strongly believe that subjectivity will always be present in any grading system and that a good agreement can only be achieved by understanding the definition of each pattern in the scheme, as well as the pitfalls, in the updated Gleason grading system. In addition, our study puts emphasis that a complete histopathologic report is an important contributor to the success of patient management. The need to identify relevant histopathologic findings, which are often overlooked, greatly impact patient management.

ACKNOWLEDGMENTS

The authors extend their gratitude to the consultants of St. Luke’s Medical Center Quezon City Institute of Pathology, all the respondent pathologists of this study for sharing their knowledge, and to the staff of the Histopathology Section of St. Luke’s Medical Center Quezon City for their kind assistance during the collection of test materials.

STATEMENT OF AUTHORSHIP

All authors certified fulfillment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

The authors declared no conflict of interest.

FUNDING SOURCE

None.

REFERENCES


Disclaimer: This journal is OPEN ACCESS, providing immediate access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge. As a requirement for submission to the PJP, all authors have accomplished an AUTHOR FORM, which declares that the ICMJE criteria for authorship have been met by each author listed, that the article represents original material, has not been published, accepted for publication in other journals, or concurrently submitted to other journals, and that all funding and conflicts of interest have been declared. Consent forms have been secured for the publication of information about patients or cases; otherwise, authors have declared that all means have been exhausted for securing consent.
Objective. The study was undertaken to determine if commercially bottled purified water can be used as substitute instrument feed water for three (3) newborn screening immunoassays.

Methodology. A total of 294 control samples and 300 patient samples were included in this study. Accuracy and precision studies using control samples, and parallel testing using patient samples, were done to compare the use of clinical laboratory reagent water (CLRW) and commercially bottled purified water (CBPW) in the performance of automated time-resolved fluorescent immunoassay of thyroid stimulating hormone (TSH), 17α-OH-progesterone (17-OHP) and immunoreactive trypsinogen (IRT).

Results. The use of CBPW as instrument feed water for measurements of TSH, 17-OHP and IRT levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS has an acceptable accuracy and precision compared to using CLRW. The parallel testing using patient samples showed that, overall, the performance of using CBPW in automated time-resolved fluorescent immunoassay for TSH, 17-OHP, and IRT is acceptable, compared with using CLRW as instrument feed water.

Conclusion. Commercially bottled purified water can be used as substitute when setting up a laboratory water purification system is too expensive for a laboratory, or as back up to clinical laboratory reagent water when there is breakdown of the installed water purification system to be used as instrument feed water in automated time-resolved fluorescent immunoassay of TSH, 17-OHP and IRT in NBS using AutoDELFIA (Perkin-Elmer).

Key words: fluorescent antibody technique, immunoassay, neonatal screening, clinical laboratory reagent water

INTRODUCTION

The Newborn Screening Study Group (NSSG) first conceptualized newborn screening (NBS) in the Philippines in 1996. The initial objectives of the Philippine Newborn Screening Project (PNBSP) were to establish the incidence data of six metabolic conditions – congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), galactosemia (GAL), phenylketonuria (PKU), homocystinuria (HCY), and glucose-6-phosphate dehydrogenase (G6PD) deficiency, and to make recommendations for the adoption of newborn screening nationwide. This project has been successful as a newborn screening bill was introduced and was signed into law in 2004 as Republic Act 9288 or Newborn Screening Act of 2004. This law requires that every newborn must be given access to NBS by the attending or assisting health practitioner. Later on, there was discontinuation of screening for homocystinuria as a cost-cutting measure due to non-detection of cases, and inclusion of screening for maple syrup urine disease (MSUD) as part of the six basic screened disorders. Additional disorders were included in the expanded NBS (eNBS) in 2014. It included screening for cystic fibrosis (CF), biotinidase deficiency (BTND), hemoglobinopathies (HBP), amino acid
metabolism disorders (AAD), acylcarnitine metabolism disorders (ACD), fatty acid oxidation disorders (FAO), and urea cycle disorders (UCD).

NBS for primary CH is done through determining the TSH level on a dried blood spot (DBS). Infants with significantly elevated DBS TSH indicate risk for primary CH. An elevated serum TSH and a low serum FT4 confirm primary CH. The 17α-OH-progesterone (17-OHP), a precursor of cortisol, is increased in the 2 most common types of CAH, i.e., 21- and 11β-hydroxylase deficiencies. Therefore, measuring the 17-OHP levels on DBS is a useful NBS method for the detection of CAH. Infants with moderate to severe elevation of 17-OHP, and those who have mild elevation of 17-OHP and are low birth weight must undergo confirmatory tests with plasma 17-OHP, sodium, potassium, cortisol and glucose. Screening for CF entails for initial measurement of IRT levels on DBS. An elevated IRT level signifies an increased risk of CF. The neonate then undergoes confirmatory testing with either a sweat test for chloride or a DNA test for CFTR mutations. Since the initiation of the NBS in the Philippines, fluorescent immunoassay is the recommended laboratory method for NBS of CH, CAH, and CF.

Automated methods for detecting TSH and 17-OHP use solid phase time-resolved fluorescent immunoassay. Solid-phase methods utilize a washing step to separate the bound analyte, which is immobilized by the antibody attached to a solid support, from the unbound, which is washed away. The presence of analyte is then detected by labeled indicator reagents using different techniques. The TSH and IRT assays are based on a direct sandwich technique where two monoclonal antibodies recognize separate antigenic determinants on the TSH molecule. The fluorescence signal is proportional to the TSH concentration in the sample. The 17-OHP assay, on the other hand, is based on the competitive binding of Europium-labeled 17-OHP, and 17-OHP in the sample to 17-OHP-specific antibodies. The fluorescence signal is inversely proportional to the 17-OHP concentration in the sample. Excess, unbound labeled indicator reagents will be washed by another washing step before instrument reading.

Clinical laboratory reagent water (CLRW) should be pure enough to satisfy the requirements of most clinical laboratory testing. CLRW must have resistivity ≥ 10 MΩ·cm referenced to 25°C, total heterotrophic plate count <10 CFU/mL, total organic carbon <300 ng/g, and particulate content sizes of <0.22 μm. The CLRW are prepared though different available laboratory water purification systems. The automated method for time-resolved fluorescent immunoassay utilizes this CLRW as instrument feed water for internal washing, rinsing and dilution.

Commerically bottled purified water (CBPW) refers to water that is marketed for drinking. Manufacture of CBPWs is regulated by law and should follow standards prior to commercial release for consumption. The Department of Health Administrative Order 10 series of 2017 requires the following physico-chemical and microbiologic standards: CBPW must have resistivity ≥0.2 MΩ·cm referenced to 25°C, total heterotrophic plate count <500 CFU/mL, and organic chemicals <0.0002 to 1mg/L, depending on the particular organic chemicals. There is no specified standard for total organic carbon and particulate content sizes.

The objective of this study is to determine if CBPW, particularly Wilkins distilled water, can be used as a substitute when setting up a laboratory water purification system is too expensive for a laboratory, or as back up to CLRW when there is breakdown of water purification systems, in the performance of automated time-resolved fluorescent immunoassay of TSH, 17-OHP, and IRT using AutoDELFIA (Perkin-Elmer) for NBS.

The study is limited to the evaluation of the above-mentioned analytes. These are the only analytes measured by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS in the Philippines.

**METHODOLOGY**

A total of 294 control samples and 300 patient samples were included in this study. There were 61 low and 61 high TSH controls, 55 low and 55 high 17-OHP controls, 31 low and 31 high IRT controls, 100 TSH patient samples, 100 17-OHP patient samples, and 100 IRT patient samples. A single analyst did the sample preparation and operation of the instrument to control for possible inter-analyst variability in technique. A single reagent kit lot was used to control for possible inter-lot variability in the chemical reactions. Finally, a single automated time-resolved fluorescent immunoassay instrument using AutoDELFIA (Perkin-Elmer) was used to control for possible inter-machine variability in instrument performance. The type of water used, i.e. CLRW or CBPW (using Wilkins distilled water), was the experimental intervention for this study.

There were two phases of the study; first is the accuracy and precision studies. The accuracy of using CBPW in measuring control samples was compared to the reference method, i.e., using CLRW as instrument feed water. Mean and deviation were the statistic used to evaluate accuracy. A deviation less than [10%] and/or t-test between two independent means with t < Critical indicates an acceptable accuracy. The precision of CBPW compared to the precision of the CLRW in measuring control samples. Standard deviation (SD) and Coefficient of variation (CV) were the statistic used to evaluate accuracy. A CV less than [10%] and/or F-test between two variances with F < Critical indicates an acceptable precision.

The second part of the study is the parallel testing using patient samples. Bland-Altman analysis, Passing Bablok regression, and kapa statistic are used to evaluate the performance of using CBPW compared to using CLRW as instrument feed water. A bias less than [10%], slope of between 0.90 to 1.10, linearity of 0.975 to 1.000, and kapa greater than 0.90 indicates an acceptable comparable performance of using CBPW in automated time-resolved fluorescent immunoassay.
RESULTS

Accuracy and Precision Studies

A total of 294 control samples were included in this phase. The results are summarized in Table 1. There were no significant mean differences in the measurements of the 17-OHP, TSH, and IRT levels of low and high control samples between CLRW and CBPW ($t < \text{Critical t}$). The percent deviations of CBPW from CLRW were less than $|10\%|$ for all analytes and control levels. There was no significant difference in variances in the measurements of the 17-OHP, TSH, and IRT levels of low and high control samples between CLRW and CBPW ($F < \text{Critical F}$), and the CV of CBPW were less than $|10\%|$ for all analytes and control levels. This indicates that using CBPW as instrument feed water for measurements of the 17-OHP, TSH, and IRT levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS has an acceptable accuracy and precision.

Parallel Testing of Patient Samples

A total of 300 patient samples were included in this phase. The results of Bland-Altman analysis and Passing Bablok regression analysis are summarized in Table 2. Generally, CBPW gives higher results than CLRW, with % bias less than $|10\%|$ for all analytes, and the slope and linearity are within 0.90 to 1.10 and 0.975 to 1.000, respectively.

Evaluation of the Bland-Altman plot and Passing Bablok regression line (Figures 1-6) shows that values near the cut-off values for 17-OHP, TSH, and IRT are within the agreement limits, and are close to the best fitted line, respectively. This may indicate that using CBPW as an alternative to CLRW would not misclassify the result of the screening test.

In NBS, it is the delineation of a positive versus a negative screen which is more critical than the actual quantitative value; therefore, the agreement in terms of $\kappa$ of the screening status of both methods is more significant to evaluate. Based on $\kappa$ statistic, there is a perfect level of agreement in the identification of positive screen between CBPW and CLRW (Tables 3-5).

The parallel testing showed that overall, the performance of using CBPW in automated time-resolved fluorescent immunoassay for TSH, 17-OHP, and IRT is acceptable, compared with using CLRW as instrument feed water.

DISCUSSION

Time-resolved fluorescent immunoassay is widely used for measurement of various hormones in biological specimens. As a solid-phase method, a washing step is needed in order to remove unbound analytes, and unbound labeled indicator reagents that may create background noise to the signal detected by the instrument. CLRW are used as instrument feed water in automated instruments for this purpose.

<table>
<thead>
<tr>
<th>Table 1. Evaluation of accuracy and precision of CBPW in comparison to CLRW as instrument feed water for measurements of the 17-OHP, TSH, and IRT levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statistic</strong></td>
</tr>
<tr>
<td><strong>Control Level</strong></td>
</tr>
<tr>
<td>17-OHP</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Parallel testing of CBPW and CLRW as instrument feed water for measurements of the 17-OHP, TSH, and IRT levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statistic</strong></td>
</tr>
<tr>
<td>Count</td>
</tr>
<tr>
<td>Bias</td>
</tr>
<tr>
<td>Slope</td>
</tr>
<tr>
<td>Linearity</td>
</tr>
</tbody>
</table>
Figure 1. Bland-Altman plot of CBPW and CLRW as instrument feed water for measurements of the 17-OHP levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS. (Note: Red line indicates cut-off value).

Figure 2. Passing Bablok regression line of CBPW and CLRW as instrument feed water for measurements of the 17-OHP levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS. (Note: Red line indicates cut-off value).

Figure 3. Bland-Altman plot of CBPW and CLRW as instrument feed water for measurements of the TSH levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS. (Note: Red line indicates cut-off value).

Figure 4. Passing Bablok regression line of CBPW and CLRW as instrument feed water for measurements of the TSH levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS. (Note: Red line indicates cut-off value).

Figure 5. Bland-Altman plot of CBPW and CLRW as instrument feed water for measurements of the IRT levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS. (Note: Red line indicates cut-off value).

Figure 6. Passing Bablok regression line of CBPW and CLRW as instrument feed water for measurements of the IRT levels by automated time-resolved fluorescent immunoassay using AutoDELFIA (Perkin-Elmer) in NBS. (Note: Red line indicates cut-off value).
CBPW may have met the specifications for CLRW when it was bottled by the manufacturer, however, it is recommended that laboratories must validate that the bottled water is fit for its intended purpose in their setting.14

In this study, we have validated the use of CBPW, and have observed that it has no significant difference in the performance of automated time-resolved fluorescent immunoassay for TSH, 17-OHP, and IRT compared with using CLRW as instrument feed water.

**CONCLUSION**

Based on our findings, we conclude that CBPW can be used as substitute to CLRW as instrument feed water in automated time-resolved fluorescent immunoassay of TSH, 17-OHP, and IRT in NBS using AutoDELFIA (Perkin-Elmer).

**STATEMENT OF AUTHORSHIP**

All authors certified fulfillment of ICMJE authorship criteria.

**AUTHOR DISCLOSURE**

The authors declared no conflict of interest.

**FUNDING SOURCE**

None.

REFERENCES


ABSTRACT

The External Quality Assessment Scheme (EQAS) evaluates the performance of participating laboratories through an external agency by which known blinded samples are sent to participants for analysis, and their performance evaluated and monitored.

The Transfusion Transmissible Infections – National Reference Laboratory provides an external quality assessment scheme for transfusion transmissible infections to blood service facilities in the Philippines with the aim of raising the standards of quality testing in infectious diseases in blood units and as a mandatory requirement in the licensing of laboratories.

In the 2017 test event, 180 participants were given an EQAS panel composed of the HVHT4120 serology program and the MLRA415 malaria program. Results were submitted through an online informatics system managed by OneWorld Accuracy Canada using the ISO 13528:2008 Robust Statistics method (Huber’s Method). Results were analyzed and evaluated with the reference result of the NRL to which non-concordant results would be marked aberrant.

From the 14,392 generated results from the HVHT4120 program and 885 generated results from the MLRA415 program, 51 (0.35%) results and 86 (9.72%) results were reported as aberrant respectively. The aberrant results reported were either due to random or systematic errors.

Analyzed data from this test event are used for the continuous improvement of their competencies and the renewal of their license to operate as required by the Department of Health.

Key words: quality assurance, blood donor serology, transfusion transmissible infections, proficiency testing

INTRODUCTION

The quality management system model developed by the Clinical and Laboratory Standards Institute (CLSI), lists assessment an important element of the 12 quality system essentials and defines it as a tool for examining laboratory performance and comparing it to standards, benchmarks or the performance of other laboratories. An external quality assessment scheme (EQAS) is a method by which an independent external agency uses known samples with undisclosed results and is commonly used to establish inter-laboratory comparability.

In the Philippines, participation in an external quality assessment scheme for transfusion transmissible infections is a mandatory requirement for the licensure of blood service facilities and aims to raise the standards on the quality testing of blood units.

This activity evaluated the performance of the blood service facilities in the Philippines by analyzing the results of the external quality assessment scheme conducted by the Transfusion Transmissible Infections – National Reference Laboratory in 2017.
METHODOLOGY

Panel Composition
The TTI EQAS 2017 test event consisted of two panels, the HVHT4120 for blood donor serology, and the MLRA415 for malaria slide microscopy. The HVHT4120 consisted of twenty (20) pooled plasma samples obtained from blood donors from different regions of the country. Each pooled sample was prepared by mixing similar volumes of at least two samples that had similar antibody and antigen profiles. All samples were subjected to filtration prior to aliquoting. The samples were aliquoted, and their homogeneity confirmed. The serology profile for HIV, HBV, HCV, Syphilis of each sample were identified nationwide using a chemiluminescence assay (ChLIA), enzyme immunoassay (EIA), Rapid Plasma Reagin (RPR), Particle Agglutination (PA) and a Differentiation/Supplemental Assay (SA).

Program code MLRA415 consists of five (5) blood smears. The samples were obtained from Malaria patients in Palawan and prepared by the NRL for Malaria and other Parasites of the Research Institute for Tropical Medicine.

Participants
The multimarker blood serology EQAS panel ID HVHT4120 and malaria microscopy EQAS panel ID MLRA415 were distributed to 180 participants nationwide. These participants enrolled for the EQAS 2016 test event with a corresponding registration fee to cover expenses for the test event.

Majority of the participants were private institutions (44%) followed closely by government institutions (42%) and the remainder are from the different Philippine Red Cross chapters (14%). Figure 1 shows the distribution of participants by region.

Data Analysis
ISO 13528:2005 Robust Statistics method (Huber’s Method) was used to identify outlying results (numerical test results found to be statistically different from other test results reported by participants that tested the same sample in the same assay) for the created peer groups. A peer group is defined as a set of laboratories that utilize the same test format and assay test kit for screening TTI. The said method uses the mean as an estimator and outlying test results were removed from statistical calculation. Qualitative results of the BSF were compared with the qualitative reference results of the NRL Discrepancy between the two results would mark a result aberrant.

RESULTS AND DISCUSSION

A total of 14,392 results were generated from 75 assays for the HVHT4120 panel and 885 results were generated from 1 assay for the MLRA415 panel.

Data entry errors: Two participants reported a “reactive” test result but submitted a “negative” assay interpretation.

False positive results: Nine participants reported false reactive results on known negative samples.

False negative results: Five participants reported false negative results on initial testing.

Educational sample (HIV and HCV): Two participants reported false negative results on the HIV and HCV sample with one of the participants having reported a “reactive” test result but submitted a “negative” assay interpretation. One participant had reported a reactive HBsAg result.

Educational sample (HIV p24 Antigen): Two participants reported a “reactive” result using a 3rd generation HIV assay. Eleven participants reported a “negative” result using a 4th generation HIV assay with one participant having reported a “reactive” test result but submitted a “negative” assay interpretation. Three participants reported an “inconclusive” test result using a 4th generation HIV assay. Three participants reported a reactive HBsAg result on the HIV p24 antigen sample.

Of the total number of results generated in the HVHT4120 panel, 51 results (0.35%) were reported as aberrant.

On rating the performance of the participants, the following criteria must be met to be classified as an unsatisfactory performer in the HVHT4120 initial panel:
(a) at least one false negative result;
(b) at least twenty percent (20%) false positive results.

![Figure 1. Regional distribution of participants.](http://philippinejournalofpathology.org | Vol. 3 No. 2 November 2018)
In accordance with these criteria, corresponding participants were given an investigation checklist to assist them in identifying errors and make the necessary corrective actions and/or troubleshooting methods. A 2nd set of the HVHT4120 panel were given to participants for retesting if the identified unsatisfactory performance was due to a testing error. Participants with aberrant results due to transcription errors were only given an investigation/troubleshooting checklist and a written recommendation. Three (10) participants were given a second set of samples wherein one participant had reported a false negative result and one participant did not submit their results.

Of the total number of results generated in the MLRA415 panel, 86 results (9.72%) were reported as aberrant.

Figure 2 shows the distribution of grades of the participants. They have been evaluated and graded as follows:

- **Excellent** – 100% acceptable results on the initial panel (all final results were correctly identified in comparison with the reference results);
- **Very Satisfactory** – Less than 100% acceptable results on the initial panel without being given a second panel for retesting;
- **Satisfactory** – 100% acceptable results on retesting of the second panel; or had an aberrant result in the initial panel due to a clerical error, given that the participant was able to identify this error through the EQAS investigation checklist;
- **Poor** – Participant did not follow minimum requirements of testing as per DOH Circular No. 2013-0132 or less than 100% acceptable results on retesting of the second panel; or had an aberrant result in the initial panel due to a clerical error which the participant had failed to identify in the EQAS investigation checklist.

**CONCLUSION**

EQAS is an essential element of the quality system and plays a vital role in facilitating optimal patient care. The transfusion transmissible infections EQAS directed for blood service facilities was designed to assess the entire phase of testing and monitor the quality of laboratory results. This also enables the participants to compare their performance with other laboratories and this can aid them in detecting potential problems which present opportunities for improvement.

**RECOMMENDATION**

The participants should regularly review their results as part of quality improvement regardless of their rating. Participants should take responsibility in implementing the necessary corrective action as part of the quality assurance program in their laboratory.

**ACKNOWLEDGMENTS**

The authors thank the TTI-NRL staff, Dr. Catherine Masangkay and Dr. Socorro Lupisan of the Research Institute for Tropical Medicine (RITM), the Health Facility Development Bureau, the Health Facility Services and Regulatory Bureau, the Department of Health – National Voluntary Blood Services Program, the National Council for Blood Services – Technical Committee, the Department of Parasitology (RITM), Philippine Red Cross – National Blood Center (Port Area), Asian Hospital and Medical Center, OneWorld Accuracy – Canada and Joe Vincini from NRL – Australia.

We would also thank all participating Blood Service Facilities for their support.

**STATEMENT OF AUTHORSHIP**

All authors certified fulfillment of ICMJE authorship criteria.

**AUTHOR DISCLOSURE**

The authors declared no conflict of interest.

**FUNDING SOURCE**

None.
REFERENCES


Second Asia Pacific Molecular Brain Tumor Course
Gold Coast, Australia | May 18-19, 2019

(http://www.hkiap.org/braintumor/)

Arie Perry
UCSF
WHO 2016 Consensus Group

David Ellison
St. Jude, Memphis
WHO 2016 Consensus Group

Alfred Lam
Griffith University
(Pituitary)

H K Ng
The Chinese University of Hong Kong
WHO 2016 Consensus Group

(contact: hkng@cuhk.edu.hk)


* This advertisement is a complimentary service of the PJP for member societies/organizations.
Ameloblastic Fibro-odontoma

Jay Hansel Tabije,1 Leila Salera,2 Jose Angelo Militante1

1Oral and Maxillofacial Surgery and Implantology, St Jude Hospital and Medical Center, Philippines
2College of Dentistry, University of the East Manila, Philippines

Key words: ameloblastic, fibroma, odontoma

INTRODUCTION

A seven-year-old male was referred for consult at the oral & maxillofacial surgery & implantology section of the hospital due to a large asymptomatic left maxillary mass resulting to a noticeable facial asymmetry. Clinical examination showed a solitary bony hard swelling on the left posterior maxilla exhibiting buccal and palatal expansion. Tooth mobility of the left premolars and absent permanent molar are likewise noted (Figure 1). CT scan showed an enlarging mass on the left posterior maxilla exhibiting an amorphous ovoid opacity surrounded by a defined radiolucent border overlying the crown of a permanent molar displacing the maxillary

Figure 1. Clinical appearance. Mass producing facial asymmetry on left side of the patient, intra oral finding showing an evident bony hard mass on the posterior region of the left maxilla with noticeable altered eruption pattern of the left permanent molars.
sinus floor without perforating it. (Figure 2) Based on the initial diagnostics considered impressions where ameloblastic fibro-odontoma and calcifying epithelial odontogenic tumor. Patient was admitted, prepared, once cleared underwent surgical enucleation of the mass under GETA via an intra-oral Lefort 1 incision, the mass was then submitted for histopathologic examination. 11 months after the operation (Figure 3), both clinical and radiographic findings show no sign of recurrence.

Histologic examination revealed a benign tumor composed of ameloblastic islands amidst a cellular fibrous background (Figure 4), and areas showing dentin formation. (Figure 5). Histomorphologic features were consistent with an ameloblastic fibro-odontoma.

As listed in the updated 2017 WHO classification of benign odontogenic tumors and cyst, a handful are considered calcifying types of epithelial or mixed lesions. In a review by Augello et.al. regarding AFO the prevalence is set at 1-3.4% among odontogenic tumors with no gender predilection equally found on either jaw but is seen more occurring in the molar regions also associated with an impacted tooth. Generally seen with a mean age of 11.5 years which together with the complaint of an asymptomatic growing mass together with the distinct calcification on diagnostic imaging can be considered an important criterion for considering AFO. AFO is currently recognized as part of the histologic spectrum of developing odontomas, although it is argued that in some cases of AFO neoplastic changes may be possible specially with large AFO.

AFO has histologic features identical to ameloblastic fibroma (AF) with a hard tissue component consisting of dental hard structures. The AF component is the “soft tissue” component, while the “hard tissue” component contains a calcifying component composed of enamel and dentin structures. AFO is described in its WHO (World Health Organization) classification as a lesion similar to AF, and both have been defined as hamartomatous lesions, believed to be stages of odontoma formation. Similar to what most authors suggest this case of a large AFO was primarily managed conservatively with enucleation, reserving more ablative surgery for rare cases of recurring AFO as well as confirmed malignant transformations.

Figure 2. Coronal cut CT scan showing impacted permanent molar and large amorphous opacity surrounded by a defined radiolucency.

Figure 3. Clinical appearance 11 months post-operatively showing improvement in facial symmetry and defect on the operative site with no clinical sign of recurrence.

Figure 4. Ameloblastic islands in a fibromyxoid background (H & E, 40x).
ETHICAL CONSIDERATION

Patient consent was obtained before submission of the manuscript.

STATEMENT OF AUTHORSHIP

All authors certified fulfillment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

The authors declared no conflict of interest.

FUNDING SOURCE

None.

REFERENCES

# Principles of Transparency & Best Practice in Scholarly Publishing

Committee on Publication Ethics (COPE), the Directory of Open Access Journals (DOAJ), the Open Access Scholarly Publishers Association (OASPA), and the World Association of Medical Editors (WAME) are scholarly organizations. All have seen increases in the number, and range in quality, of membership applications. Our organizations have collaborated to identify Principles of Transparency & Best Practice for Scholarly Publications. These principles form the basis of the criteria by which suitability for membership is assessed by COPE, DOAJ and OASPA, and part of the criteria on which membership applications are evaluated by WAME.

## Website

<table>
<thead>
<tr>
<th>Website</th>
<th>Name of Journal</th>
<th>Peer Review Process</th>
<th>Ownership and Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Journal's website, including the text that it contains, shall demonstrate that care has been taken to ensure high ethical and professional standards. It should: – contain an ‘Aims &amp; Scope’ statement and the readership clearly defined. – include a statement on what a journal will consider for publication including authorship criteria e.g. not multiple submissions, redundant publications) – ISSN displayed clearly (separate for print and electronic). It must not: – contain information that might mislead readers or authors. – attempt to mimic another journal/publisher’s site.</td>
<td>The Journal name shall be unique. It must not: – be one that is easily confused with another journal. – mislead potential authors and readers about the Journal’s origin or association with other journals.</td>
<td>Journal content must be clearly marked as whether peer reviewed or not. Peer review is defined as obtaining advice on individual manuscripts from reviewers expert in the field who are not part of the journal’s editorial staff. The journal’s website should: – clearly describe this process, as well as any policies related to the journal’s peer review procedures including the method of peer review used.</td>
<td>Information about the ownership and/or management of a journal should be clearly indicated on the journal’s website. Publishers should not: – use organizational or journal names that would mislead potential authors and editors about the nature of the journal’s owner.</td>
</tr>
<tr>
<td>WEBSITE</td>
<td>NAME OF JOURNAL</td>
<td>PEER REVIEW PROCESS</td>
<td>OWNERSHIP AND MANAGEMENT</td>
</tr>
<tr>
<td>A</td>
<td>The Journal name shall be unique. It must not: – be one that is easily confused with another journal. – mislead potential authors and readers about the Journal’s origin or association with other journals.</td>
<td>Journal content must be clearly marked as whether peer reviewed or not. Peer review is defined as obtaining advice on individual manuscripts from reviewers expert in the field who are not part of the journal’s editorial staff. The journal’s website should: – clearly describe this process, as well as any policies related to the journal’s peer review procedures including the method of peer review used.</td>
<td>Information about the ownership and/or management of a journal should be clearly indicated on the journal’s website. Publishers should not: – use organizational or journal names that would mislead potential authors and editors about the nature of the journal’s owner.</td>
</tr>
<tr>
<td>GOVERNING BODY</td>
<td>EDITORIAL TEAM/CONTACT INFORMATION</td>
<td>COPYRIGHT AND LICENSING</td>
<td>AUTHOR FEES</td>
</tr>
<tr>
<td>Journals shall have editorial boards or other governing bodies whose members are recognized experts in the subject areas included within the journal’s scope. The journal’s website should: – show full names and affiliations of the journal’s editorial board or other governing body.</td>
<td>Journals shall provide the full names and affiliations of the journal’s editors on the journal website as well as contact information for the editorial office, including a full address.</td>
<td>The policy for copyright shall be clearly stated in the author guidelines and the copyright holder named on all published articles. The journal’s website should: – show licensing information clearly described in guidelines. Licensing terms shall be indicated on all published articles, both HTML and PDFs. If authors are allowed to publish under a Creative Commons license then any specific license requirements shall be noted. Any policies on posting of final accepted versions or published articles on third party repositories shall be clearly stated.</td>
<td>Any fees or charges that are required for manuscript processing and/or publishing materials in the journal shall be clearly stated. This must be: – in a place that is easy for potential authors to find prior to submitting their manuscripts for review OR – explained to authors before they begin preparing their manuscript for submission. – if no such fees are charged that should also be stated.</td>
</tr>
</tbody>
</table>

Each organization also has its own, additional criteria which are used when evaluating applications. The organizations will not share lists of publishers or journals that failed to demonstrate that they met the criteria for transparency and best practice. This is the third version of a work in progress (published January 2018); the first version was posted on the COPE website on January 2014 and a second version in June 2015. We encourage its wide dissemination and continue to welcome feedback on the general principles and the specific criteria.
In the event that a member organization is found to have violated these best practices, or other specific requirements of the organization, OASPA/DOAJ/COPE/WAME shall in the first instance try to work with them in order to address any concerns that have been raised. In the event that the member organization is unable or unwilling to address these concerns, their membership in the organization may be suspended or terminated. All of the member organizations have procedures for dealing with concerns raised about member journals.
SPECIAL OFFER FOR PSP MEMBERS:

ASCP International Physician Membership
$50 USD with code PSPASCP
www.ascp.org/psp_ipath

International Resident Membership FREE
www.ascp.org/psp_ires

* This advertisement is a complimentary service of the PJP for member societies/organizations.
PSP
PRO PHOTOMICROSCOPY CONTEST 2018
MARK JASON G. ORDENES

Urine, Total magnification used: 400x and 100x
Case of a 2-year-old male with a complaint of painful urination.

SECOND PLACE

THADDEUS C. HINUNANGAN
“LAST EXIT TO LEYTE”

A 22-year-old male dies of pneumonia, but an autopsy revealed Schistosoma japonicum ova, inducing pipe stem fibrosis in the liver. The young man may have passed, but this undeniable reminder of a neglected tropical disease remains.
FAYE VICTORIA A. DE LOS REYES
This photomicrograph depicts the ventral sucker and part of the uterus of the Clonorchis sinensis. The numerous eggs shown is a reminder of the burden of disease in East and Southeast Asia that is caused by this organism despite being only 2.5 cm in its full adult size.

MARIA CECILIA M. DAÑGUILAN
Fine-needle aspiration biopsy of a pulmonary mass showed papillae lined by columnar cells with nuclear grooves and pseudoinclusions resembling papillary thyroid carcinoma. Granular cytoplasmic staining with Napsin A is seen in tumor cells exhibiting prominent nuclear pseudoinclusions.
Ruby O. Rusia-Uy
Gram stain of cervicovaginal smear
What am I? It depends...
To a kid, a teddy bear.
To an animal lover, a koala or a tarsier.
To a parasitologist, a scolex.
To a mystery hunter, an ET or an alien.
What do you think am I?
Just a bunch of squamous epithelial cells,
says a pathologist.

Louis Alvin Maranan
Incidental finding on a section of lung tissue exhibiting a Coccidioides immitis spherule within a multinucleated giant cell.
Bright yellow flecks of hematoidin crystals are strewn across this colonic wall in a patient with aortoenteric fistula redolent of a madman/genius post-impressionist painter’s most iconic work ‘The Starry Night’.

The picture depicts an endometrial tissue in secretory phase composed of layers of long, tortuous to serrated glands looking like gummy worms, lined by cells with short rounded nuclei with some subnuclear vacuoles and intraluminal secretions. These are supported by a fairly loose stroma.
This image depicts crystals from a parotid cyst smear.

FRANZ JOBERT L. SEBASTIAN

What a big surprise when on Valentine’s Day! I saw this heart-shaped image from a gram stain of synovial fluid knee aspirate from an arthritic patient. I went home with a happy heart because I see love even at work.

EVELINA N. LAGAMAYO

“A HEART DOWN ON ITS KNEES”
OTHANIEL PHILIP R. BALISAN

“PURPLE RAIN”

These cytological smear shows a flurry of purple ‘blobs’ or benign mesothelial cells which is a usual diagnostic stumbling block for the uninitiated.

AARON PIERRE P. CALIMAG

“KAPIT LANG”

This photo is from a renal allograft with acute T-cell mediated rejection with a chronic active component. There are areas of inflammation, sclerosis, and hemorrhage. It shows that despite how everything else falls apart around you, you still manage to muster the strength to hold on.
This is a photomicrograph (40x magnification) of a worm taken from a stool sample from an adult male that was initially suspected as a parasite. On further investigation, it turned out to be a larvae of drain flies (Order: Diptera, Family: Psychodidae) that bred in his toilet bowl. Fake (and very fortunate) news, indeed.

A microscopic sneak peak of the universe, of its countless galaxies and stars, hiding within us.
THIRD PLACE

NIKKO PAOLO R. CABLAO
"BON VOYAGE!"
A photomicrograph of lymphovascular space invasion from an invasive mammary carcinoma in a 50-year-old female. A ball of tumor cells is seen inside a blood vessel all set for an adventure to the great unknown. Any guesses where these guys could end up?

ANDREA R. VILLARUEL
“SO CLASSICAL... IT LOOKS UNUSUAL!”
Tumors want to be diagnosed. Look at the wild animal stripes in this cerebellopontine angle schwannoma. Sometimes... the horses are zebras!
GLENN NATHANIEL SAN DIEGO VALLOSO
Olympus 5-header microscope with camera under oil-immersion objective. Narrative of the image: An excised, solitary, slow-growing, painless, firm single nodular neck mass from an adult male.

DEMIE DANE C. SANORIA
Granulosa Cell Tumors form characteristic “Cal Exner Bodies”, comprised of a single layer of granulosa cells forming “gland-like” structures containing acidophilic material. Green hues and filters were added to contrast with the purple staining nuclei and pinkish material contained within these structures, resembling rose bushes in a luminescent garden.
CHRISTINE MAE OLIVAR
“TOGE”
Toge sa kanyang dumi!
Dahan-dahan lumalaki.
Kumekembot unti-unti,
Para maging ispageti.

Hatching of Ascaris lumbricoides
Olympus CX23, 100x magnification

CRISTON VAN C. MANASAN
“PAP ON PAPS”
Papillary Thyroid Carcinoma
on Papanicolaou Stain

ChRiSTiNE  MAE  OLIVAR
“PAP ON PAPS”
Papillary Thyroid Carcinoma
on Papanicolaou Stain

CRiSTON  V AN  C. MANASAN
“PAP ON PAPS”
Papillary Thyroid Carcinoma
on Papanicolaou Stain
GABRIEL M. OZOA
“COBBLESTONES”
A breast mass from a young adult female.

JOEANNE SALISE
“WAVES”
Angry waves in the ocean.
A stormy daylight.
The predator is not here.
But the creatures are in fear.

(Cytology of subependymal giant cell astrocytoma)
LESTER FLOYD D. ZAMORA
“THE SINISTER SMILE OF PAIN”
The sinister smile that can make even the strongest woman bow down in pain - Oh! how could you endometriosis?

FIRST PLACE
OLIVER D. PINTOR
“PIXIE DUST”
Details of the microscope and technique:
Human urine uric acid crystals under an Olympus CX31-P Polarizing Microscope, 40x magnification.
“The human body is made from a sprinkle of love, a dash of hope, and a little bit of pixie dust...
JOSEPH MICHAEL R. ESPRITU
“VARYING SHADES OF BLUE”
The interplay of different stains: Masson trichrome and H&E with Alcian blue, bequeaths beautiful hues of this simple hyaline cartilage. Notice the beautiful blue hue of the left section elicited by Masson trichrome; while on the right, the Alcian blue outlines the lacunae on an H&E background.

VICTORIA E. CRUZ
This is a smear from a fine needle aspiration biopsy of a pre-auricular mass. The smear consists of bland epithelial cells entangled with a fibrillar matrix. Diagnosis: Pleomorphic Adenoma.
Mary, quite contrary, how does your garden grow?'
Antibiotic use, uncontrolled diabetes, and elevated estrogen, among other things.

Spot the Hidden Mickey!
**Instructions to Authors**

The Philippine Journal of Pathology (PJP) is an open-access, peer-reviewed, English language, medical and health science journal that is published continuously online and semi-annually in print by the Philippine Society of Pathologists, Inc. (PSP, Inc). All manuscripts must be submitted through the PJP Official Website (Open Journal Systems) [http://philippinejournalofpathology.org]. All other correspondences and other editorial matters should be sent via electronic mail to philippinepathologyjournal@gmail.com.

Articles and any other material published in the PJP represent the work of the author(s) and do not reflect the opinions of the Editors or the Publisher. Articles that do not subscribe to the Instructions to Authors shall be promptly returned.

**ARTICLE SECTIONS**

The PJP welcomes manuscripts on all aspects of pathology and laboratory medicine, to include cytology, histopathology, autopsy, forensic pathology, clinical chemistry, clinical microscopy, medical microbiology, parasitology, immunology, hematology, blood banking, medical technology, laboratory diagnostics, laboratory biosafety and biosecurity, laboratory management, and quality assurance.

The PJP accepts original articles, review articles, case reports, feature articles, brief communications, autopsy cases, editorials, or letters to the Editor.

**Original articles**

The research must have received institutional review board approval that is explicitly stated in the methodology. The abstract should contain no more than 200 words with a structured format consisting of the objectives, methodology, results and conclusion. A manuscript for original articles should not exceed 25 typewritten pages (including tables, figures, illustrations and maximum of 30 references) or 6000 words.

**Reviews**

Review articles, both solicited and unsolicited, provide information on the “state of the art.” PJP reviews not only summarize current understanding of a particular topic but also critically appraise relevant literature and data sources, describe significant gaps in the research, and future directions. The abstract should be from 50 to 75 words and should not be structured. A manuscript for reviews should not exceed 15 typewritten pages (including tables, figures, illustrations and maximum of 15 references) or 4000 words.

**Case Reports**

This type of article pertains to single or multiple reports of well-characterized cases that are highly unusual, novel, or rare; or that represent an unexpected or uncommon association of two or more diseases or disorders that may represent a previously unsuspected causal relationship; or that are underreported in the literature. The abstract should be from 50 to 75 words and should not be structured. A manuscript for case reports should not exceed 10 typewritten pages (including tables, figures, illustrations and maximum of 15 references) or 3000 words.

**Feature articles**

The PJP may feature articles, either as part of an issue theme or a special topic on pathology by a local or international expert or authority. The abstract should be from 50 to 75 words and should not be structured. A manuscript for feature articles should not exceed 25 typewritten pages (including tables, figures, illustrations and maximum of 30 references) or 6000 words.

**Autopsy Vault**

The PJP highly welcomes articles on autopsy protocols of cases. The article must include a summary presentation of the history, evaluation and work-up, clinical course of a case, followed by the autopsy procedure performed, gross and microscopic findings, discussion, learning points and conclusion. The PJP recognizes the instructional and educational value of articles under this section. The abstract should be from 50 to 75 words and should not be structured. A manuscript for the Autopsy Vault should not exceed 25 typewritten pages (including tables, figures, illustrations and maximum of 30 references) or 6000 words.

**Images in Pathology**

Images of unique, interesting, or highly educational cases encountered in hematology, cytology, histopathology, or medical microbiology, may be submitted under this section, and may include photomicrographs, gross pictures, machine read-outs, among others. A brief history, the photograph(s) and short discussion of the case. No abstract is required. A manuscript for Images in Pathology should not exceed 500 words, with maximum of 10 references. This is distinct from the Case Report which is a full write up.

**Brief Communications**

Brief Communications are short reports intended to either extend or expound on previously published research or present new and significant findings which may have a major impact in current practice. If the former, authors must acknowledge and cite the research which they are building upon. The abstract should be from 50 to 75 words and should not be structured. A manuscript for brief communications should not exceed 5 typewritten pages (including tables, figures, illustrations and maximum of 10 references) or 1500 words.

**Editorials**

Recognized leaders in the field of pathology and laboratory medicine may be invited by the Editor-in-Chief/Editorial Board to present their scientific opinion and views of a particular topic within the context of an issue theme or issues on scholarly publication. No abstract or keywords necessary.

**Letters to the Editor**

The PJP welcomes feedback and comments on previously published articles in the form of Letters to the Editor. No abstract or keywords are necessary. A Letter to the Editor must not exceed 2 typewritten pages or 500 words.

**Special Announcements**

Special announcements may include upcoming conventions, seminars or conferences relevant to pathology. The Editors shall deliberate and decide on acceptance and publication of special announcements. Please coordinate with the Editorial Coordinator for any request for special announcements.

**COVER LETTER**

A cover letter must accompany each manuscript citing the complete title of the manuscript, the list of authors (complete names, position/designation and institutional affiliations), with one (1) author clearly designated as corresponding author, providing his/her complete institutional mailing address, institutional telephone/fax number, and work e-mail address. The PJP Cover Letter Template must be used.
For submissions to the PJP to be accepted, all authors must read and sign the PJP Author Form consisting of: (1) the Authorship Certification, (2) the Author Declaration, (3) the Statement of Copyright Transfer, and (4) the Statement of Disclosure of Conflicts of Interest. The completely accomplished PJP Author Form shall be scanned and submitted along with the manuscript. No manuscript shall be received without the PJP Author Form.

**GENERAL FORMATTING GUIDELINES**

- Authors must use the standard PJP templates for each type of manuscript. These templates are aligned with the most current versions of the EQuaToR Network guidelines and checklists (http://equatornetwork.org).
- The paper should be encoded on the template using Microsoft Word (2007 version or later version), single-spaced, 2.54 cm margins throughout, on A4 size paper. Preferred fonts may include Century Gothic (template default), Times New Roman, or Arial.
- The manuscript should be arranged in sequence as follows: (1) Title Page, (2) Abstract, (3) Text, (4) References, (5) Tables, and (6) Figures & Illustrations.
- All the sheets of the manuscript should be labelled with the page number (in Hindu-Arabic Numerals) printed on the upper right corner.
- References should contain directly to the work being reported. Within the text, references should be indicated using Hindu-Arabic numerals in superscripts.

**SPECIFIC FORMATTING GUIDELINES**

**Title and Authors**

- The title should be as concise as possible.
- A running title (less than 50 characters) shall also be required. The running title is the abbreviated version of the title that will be placed in the header. The running title should capture the essence of the manuscript title.
- The full name of the author(s) directly affiliated with the work should be included (First name, Middle initial and Last name). The order of authorship shall be the prerogative of the author(s).
- There are 4 criteria for authorship (ICMJE recommendations). These are captured in the PJP Author Form.
  - Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
  - Drafting the work or revising it critically for important intellectual content; AND
  - Final approval of the version to be published; AND
  - Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- The highest educational attainment or title of the authors should be included as an attachment whenever appropriate (MD, PhD, et cetera).
- Name and location of no more than one (1) institutional affiliation per author may be included.
- If the paper has been presented in a scientific forum or convention, a note should be provided indicating the name of the forum or convention, location (country), and date of its presentation.

**Abstract**

- For manuscripts under the “Original Article” section: the abstract should contain no more than 300 words with a structured format consisting of the following standard headings: objective/s, methodology, results and conclusion.
- For manuscripts under the “Feature Article,” “Review Article,” “Case Report,” “Brief Communications,” and “Autopsy Vault” sections: the abstract should be no more than 200 words and need not be structured.
- Letters to the Editor and editorials do not require an abstract.

**Keywords**

At least three (3) keywords but no more than six (6), preferably using terms from the Medical Subject Headings (MeSH) list of Index Medicus, should be listed horizontally under the abstract for cross-indexing of the article.

**Text**

- The text should be organized consecutively as follows: Introduction, Methodology, Results and Discussion, Conclusion (IMRaD format), followed by Disclosures, Acknowledgments and References.
- All references, tables, figures and illustrations should be cited in the text, in numerical order.
- All abbreviations should be spelled out once (the first time they are mentioned in the text) followed by the abbreviation enclosed in parentheses. The same abbreviation may then be used subsequently instead of the full names.
- All measurements and weights should be in System International (SI) units.
- Under Methodology, information should be provided on institutional review board/ethics committee approval or informed consent taking (if appropriate).
- Acknowledgements to individuals/groups of persons, or institution/s who have contributed to the manuscript but did not qualify as authors based on the ICMJE criteria, should be included at the end of the text just before the references. Grants and subsidies from government or private institutions should also be acknowledged.

**References**

- References in the text should be identified by Hindu-Arabic Numerals in superscript on the same line as the preceding sentence.
- References should be numbered consecutively in the order by which they are mentioned in the text. They should not be alphabetized.
- All references should provide inclusive page numbers.
- Journal abbreviations should conform to those used in PubMed.
- A maximum of six authors per article can be cited; beyond that, name the first three and add “et al.”
- The style/punctuation approved by PJP conforms to that recommended by the International Committee of Medical Journal Editors (ICMJE) available at http://www.icmje.org. Examples are shown below:

**One to Six Authors**

Instruction to Authors

Tables
• Cite all tables consecutively in the text and number them accordingly.
• Create tables preferably using Microsoft Excel with one table per worksheet.
• Tables should not be saved as image files.
• The content of tables should include a table number (Hindu-Arabic) and title in capital letters above the table.
• Place explanatory notes and legends, as well as definitions of abbreviations used below the table. For legends, use small letters (i.e., a, b, c, d).
• Each table must be self-explanatory, being a supplement rather than a duplicate of information in the text.
• Up to a maximum of five (5) tables are allowed.

Figures and Graphs
• Figures or graphs should be identified by Hindu-Arabic Numerals with titles and explanations underneath.
• The numbers should correspond to the order in which the figures/graphs occur in the text.
• Figures & graphs should not be saved as image files.
• For illustrations and photographs, see next section.
• Provide a title and brief caption for each figure or graph. Caption should not be longer than 15-20 words.
• All identifying data of the subject/s or patient/s under study such as name or case numbers, should be removed.
• Up to a maximum of five (5) figures and graphs are allowed.

Illustrations and Photographs
• Where appropriate, all illustrations/photographic images should be at least 800 x 600 dpi and submitted as image files (preferably as .png, .jpeg or .gif files).
• For photomicrographs, the stain used (e.g. H & E) and magnification (e.g. X400) should be included in the description.
• Computer-generated illustrations which are not suited for reproduction should be professionally redrawn or printed on good quality laser printers. Photocopies are not acceptable.
• All letterings for illustration should be of adequate size to be readable even after size reduction.
• Place explanatory notes and legends, as well as definitions of abbreviations used below the illustration/photograph.
• Up to a maximum of five (5) illustrations/photographs are allowed.

N.B.: For tables, figures, graphs, illustrations and photographs that have been previously published in another journal or book, a note must be placed under the specific item stating that such has been adapted or lifted from the original publication. This should also be referenced in the References portion.

EDITORIAL PROCESS (Figure 1)
• The Editorial Coordinator shall review each submission to check if it has met aforementioned criteria and provide feedback to the author within 24 hours.
• Once complete submission is acknowledged, the manuscript undergoes Editorial Board Deliberation to decide whether it shall be considered or not for publication in the journal. Within five (5) working days, authors shall be notified through e-mail that their manuscript either (a) has been sent to referees for peer-review or (b) has been declined without review.
• The PJP implements a strict double blind peer review policy. For manuscripts that are reviewed, authors can expect a decision within ten (10) working days from editorial deliberation. There may be instances when decisions can take longer; in such cases, the Editorial Coordinator shall inform the authors.
• The editorial decision for manuscripts shall be one of the following: (a) acceptance without further revision, (b) acceptance with minor revisions, (c) major manuscript revision and resubmission, or (d) non-acceptance.
• Accepted manuscripts are subject to editorial modifications to bring them in conformity with the style of the journal. Copyediting and layout shall take five (5) working days, after which the manuscript is published online.
• All online articles from the last six (6) months shall be collated and published in print as a full issue.

EDITORIAL OFFICE CONTACT INFORMATION:
The Philippine Journal of Pathology
2nd Floor, Laboratory Research Division
Research Institute for Tropical Medicine
Filinvest Corporate City
Alabang, Muntinlupa City 1781
Editor-in-Chief: Amado O. Tandoc III, MD, FPSP
Teletelx number: (+632)8097120
E-mail: philippinejournalofpathology@gmail.com
Website: http://philippinejournalofpathology.org

http://philippinejournalofpathology.org | Vol. 3 No. 2 November 2018
Figure 1. Editorial Process Flow.
PJP AUTHOR FORM

For submissions to the PJP to be accepted, all authors must read and sign this PJP Author Form consisting of: (1) the Authorship Certification, (2) the Author Declaration, (3) the Statement of Copyright Transfer, and (4) the Statement of Disclosure of Conflicts of Interest. The completely accomplished PJP Author Form shall be scanned and submitted along with the manuscript. No manuscript shall be received without the PJP Author Form.

COMPLETE TITLE OF MANUSCRIPT

________________________________________________________________________________________________________________________
________________________________________________________________________________________________________________________
________________________________________________________________________________________________________________________

AUTHORSHIP CERTIFICATION

☐ In consideration of our submission to the Philippine Journal of Pathology (PJP), the undersigned author(s) of the manuscript hereby certify, that all of us have actively and sufficiently participated in (1) the conception or design of the work, the acquisition, analysis and interpretation of data for the work; AND (2) drafting the work, revising it critically for important intellectual content; AND (3) that we are all responsible for the final approval of the version to be published; AND (4) we all agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

AUTHOR DECLARATIONS

☐ The undersigned author(s) of the manuscript hereby certify, that the submitted manuscript represents original, exclusive and unpublished material. It is not under simultaneous consideration for publication elsewhere. Furthermore, it will not be submitted for publication in another journal, until a decision is conveyed regarding its acceptability for publication in the PJP.

☐ The undersigned hereby certify, that the study on which the manuscript is based had conformed to ethical standards and/or had been reviewed by the appropriate ethics committee.

☐ The undersigned likewise hereby certify that the article had written/informed consent for publication from involved subjects (for case report/series only) and that in case the involved subject/s can no longer be contacted (i.e., retrospective studies, no contact information, et cetera), all means have been undertaken by the author(s) to obtain the consent.

AUTHOR STATEMENT OF COPYRIGHT TRANSFER

☐ Furthermore, the undersigned author(s) recognize that the PJP is an OPEN-ACCESS publication which licenses all published manuscripts to be used for building on and expanding knowledge, for non-commercial purposes, so long as the manuscripts are properly cited and recognized (Attribution-NonCommercial-ShareAlike 4.0 International Creative Commons License [CC BY-NC-SA 4.0]). The undersigned author(s) hereby, transfer/assign or otherwise convey all copyright ownership of the manuscript to the PJP.

AUTHOR DISCLOSURE OF CONFLICTS OF INTEREST

In order to ensure scientific objectivity and independence, the PJP requires all authors to make a full disclosure of areas of potential conflict of interest. Such disclosure will indicate whether the person and/or his/her immediate family has any financial relationship with pharmaceutical companies, medical equipment manufacturers, biomedical device manufacturers, or any companies with significant involvement in the field of health care. Place all disclosures in the table below. An extra form may be used if needed. Examples of disclosures include but not limited to: ownership, employment, research support (including provision of equipment or materials), involvement as speaker, consultant, or any other financial relationship or arrangement with manufacturers, companies or suppliers. With respect to any relationships identified, author(s) must provide sufficiently detailed information to permit assessment of the significance of the potential conflict of interest (for example, the amount of money involved and/or the identification of any value of goods and services).

<table>
<thead>
<tr>
<th>AUTHOR NAME</th>
<th>RELATIONSHIP</th>
<th>MANUFACTURER/ SUPPLIER/ COMPANY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All disclosures shall remain confidential during the review process and the nature of any final printed disclosure will be determined by the PJP. If there are no conflicts of interest to disclose, the author(s) should check the box below.

☐ I/We do not have any conflicts of interest to disclose.

Author Name

Signature

Date (MM/DD/YYYY)

http://philippinejournalofpathology.org | Vol. 3 No. 2 November 2018
ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking “No” means that you did the work without receiving any financial support from any third party — that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check “Yes”.

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work’s sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.


This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.

Grant: A grant from an entity, generally (but not always) paid to your organization

Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting, lectures, speakers bureaus, expert testimony, employment, or other affiliations

Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.

Other: Anything not covered under the previous three boxes

Pending: The patent has been filed but not issued

Issued: The patent has been issued by the agency

Licensed: The patent has been licensed to an entity, whether earning royalties or not

Royalties: Funds are coming in to you or your institution due to your patent
ICMJE Form for Disclosure of Potential Conflicts of Interest

**Section 1. Identifying Information**

1. Given Name (First Name)  
2. Surname (Last Name)  
3. Date  
4. Are you the corresponding author? [ ] Yes [ ] No  
5. Manuscript Title  
6. Manuscript Identifying Number (if you know it)

**Section 2. The Work Under Consideration for Publication**

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?  
Are there any relevant conflicts of interest? [ ] Yes [ ] No

**Section 3. Relevant financial activities outside the submitted work.**

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the “Add +” box. You should report relationships that were present during the 36 months prior to publication.  
Are there any relevant conflicts of interest? [ ] Yes [ ] No

**Section 4. Intellectual Property -- Patents & Copyrights**

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? [ ] Yes [ ] No 

http://philippinejournalofpathology.org | Vol. 3 No. 2 November 2018
ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above
Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☐ Yes, the following relationships/conditions/circumstances are present (explain below):
☐ No other relationships/conditions/circumstances that present a potential conflict of interest

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement
Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Generate Disclosure Statement

Evaluation and Feedback
Please visit http://www.icmje.org/cgi-bin/feedback to provide feedback on your experience with completing this form.
PATIENT CONSENT FORM

For case report and image submissions to the PJP to be accepted, the author/s must ensure that patients or patients’ legal guardian/relative have provided informed consent to publish information about them in the journal. The completely accomplished PJP Patient Consent Form shall be scanned and submitted along with the manuscript. No case report and image shall be received without the PJP Consent Form.

Name of person described in article or shown in photograph:________________________

Subject matter of photograph or article (brief description):
__________________________________________________________________________________
__________________________________________________________________________________

(The Subject matter of the photograph or article is hereafter termed as the “INFORMATION.”)

Title of article:
__________________________________________________________________________________
__________________________________________________________________________________

I, ______________________________________ , give my consent for this information about MYSELF/MY CHILD OR WARD/MY RELATIVE relating to the subject matter above to appear in the Philippine Journal of Pathology (PJP) subject to its publication policies and ethical standards.

I have seen and read the material to be submitted to the PJP and thoroughly understand the following:
• The Information will be published in the PJP without my name. It is the obligation of the PJP to make all attempts, within its reasonable jurisdiction and authority, to ensure my anonymity.
• The Information may also be placed on the PJP website.
• The PJP shall not allow the Information to be used for advertising or packaging or to be used out of context (i.e., used to accompany an entirely different article or topic).
• I can withdraw my consent at any time before publication, but once the Information has already been sent to press, it is my understanding that it will not be possible to revoke the consent.

Signed:__________________________________ Date:______________________

Witness:
Signed:__________________________________ Date:______________________
# Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Guide questions / description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>DOMAIN 1: RESEARCH TEAM AND REFLEXIVITY</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Interviewer/facilitator</td>
<td>Which author(s) conducted the interview or focus group?</td>
</tr>
<tr>
<td>2</td>
<td>Credentials</td>
<td>What were the researcher’s credentials? E.g. PhD, MD</td>
</tr>
<tr>
<td>3</td>
<td>Occupation</td>
<td>What was their occupation at the time of the study?</td>
</tr>
<tr>
<td>4</td>
<td>Gender</td>
<td>Was the researcher male or female?</td>
</tr>
<tr>
<td>5</td>
<td>Experience and training</td>
<td>What experience or training did the researcher have?</td>
</tr>
<tr>
<td></td>
<td>Relationship</td>
<td>Was a relationship established prior to study commencement?</td>
</tr>
<tr>
<td>6</td>
<td>Participant knowledge of the interviewer</td>
<td>What did the participants know about the researcher? e.g. personal goals, reasons for doing the research</td>
</tr>
<tr>
<td>7</td>
<td>Interviewer characteristics</td>
<td>What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic</td>
</tr>
<tr>
<td></td>
<td><strong>DOMAIN 2: STUDY DESIGN</strong></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Methodological orientation and Theory</td>
<td>What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis</td>
</tr>
<tr>
<td>9</td>
<td>Participant selection</td>
<td>How were participants selected? e.g. purposive, convenience, consecutive, snowball</td>
</tr>
<tr>
<td>10</td>
<td>Method of approach</td>
<td>How were participants approached? e.g. face-to-face, telephone, mail, email</td>
</tr>
<tr>
<td>11</td>
<td>Sample size</td>
<td>How many participants were in the study?</td>
</tr>
<tr>
<td>12</td>
<td>Non-participation</td>
<td>How many people refused to participate or dropped out?</td>
</tr>
<tr>
<td></td>
<td>Setting</td>
<td>Where was the data collected? e.g. home, clinic, workplace</td>
</tr>
<tr>
<td>13</td>
<td>Description of sample</td>
<td>What are the important characteristics of the sample? e.g. demographic data, date</td>
</tr>
<tr>
<td>14</td>
<td>Setting of data collection</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Presence of non-participants</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Interview guide</td>
<td>Were questions, prompts, guides provided by the authors? Was it pilot tested?</td>
</tr>
<tr>
<td>17</td>
<td>Repeat interview</td>
<td>Were repeat interviews carried out? If yes, how many?</td>
</tr>
<tr>
<td>18</td>
<td>Audio/visual recording</td>
<td>Did the research use audio or visual recording to collect the data?</td>
</tr>
<tr>
<td>19</td>
<td>Field notes</td>
<td>Were field notes made during and/or after the interview or focus group?</td>
</tr>
<tr>
<td>20</td>
<td>Duration</td>
<td>What was the duration of the interviews or focus group?</td>
</tr>
<tr>
<td>21</td>
<td>Data saturation</td>
<td>Was data saturation discussed?</td>
</tr>
<tr>
<td>22</td>
<td>Transcripts returned</td>
<td>Were transcripts returned to participants for comment and/or correction?</td>
</tr>
<tr>
<td></td>
<td><strong>DOMAIN 3: ANALYSIS AND FINDINGS</strong></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Data analysis</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Number of data coders</td>
<td>How many data coders coded the data?</td>
</tr>
<tr>
<td>25</td>
<td>Description of the coding tree</td>
<td>Did authors provide a description of the coding tree?</td>
</tr>
<tr>
<td>26</td>
<td>Derivation of themes</td>
<td>Were themes identified in advance or derived from the data?</td>
</tr>
<tr>
<td>27</td>
<td>Software</td>
<td>What software, if applicable, was used to manage the data?</td>
</tr>
<tr>
<td>28</td>
<td>Participant checking</td>
<td>Did participants provide feedback on the findings?</td>
</tr>
<tr>
<td>29</td>
<td>Quotations presented</td>
<td>Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number</td>
</tr>
<tr>
<td>30</td>
<td>Data and findings consistent</td>
<td>Was there consistency between the data presented and the findings?</td>
</tr>
<tr>
<td>31</td>
<td>Clarity of major themes</td>
<td>Were major themes clearly presented in the findings?</td>
</tr>
<tr>
<td>32</td>
<td>Clarity of minor themes</td>
<td>Is there a description of diverse cases or discussion of minor themes?</td>
</tr>
</tbody>
</table>

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
### CARE Checklist (2013) of Information to include when Writing a Case Report

<table>
<thead>
<tr>
<th>Topic</th>
<th>Item no.</th>
<th>Checklist item description</th>
<th>Reported on page no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td>1</td>
<td>The words “case report” should be in the title along with the area of focus</td>
<td></td>
</tr>
<tr>
<td>Key Words</td>
<td>2</td>
<td>2 to 5 key words that identify areas covered in this case report</td>
<td></td>
</tr>
<tr>
<td>Abstract</td>
<td>3a</td>
<td>Introduction—What is unique about this case? What does it add to the medical literature?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3b</td>
<td>The main symptoms of the patient and the important clinical findings</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3c</td>
<td>The main diagnoses, therapeutics interventions, and outcomes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3d</td>
<td>Conclusion—What are the main “take-away” lessons from this case?</td>
<td></td>
</tr>
<tr>
<td>Introduction</td>
<td>4</td>
<td>One or two paragraphs summarizing why this case is unique with references</td>
<td></td>
</tr>
<tr>
<td>Patient Information</td>
<td>5a</td>
<td>De-identified demographic information and other patient specific information</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5b</td>
<td>Main concerns and symptoms of the patient</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5c</td>
<td>Medical, family, and psychosocial history including relevant genetic information (also see timeline)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5d</td>
<td>Relevant past interventions and their outcomes</td>
<td></td>
</tr>
<tr>
<td>Clinical Findings</td>
<td>6</td>
<td>Describe the relevant physical examination (PE) and other significant clinical findings</td>
<td></td>
</tr>
<tr>
<td>Timeline</td>
<td>7</td>
<td>Important information from the patient’s history organized as a timeline</td>
<td></td>
</tr>
<tr>
<td>Diagnostic Assessment</td>
<td>8a</td>
<td>Diagnostic methods (such as PE, laboratory testing, imaging, surveys)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8b</td>
<td>Diagnostic challenges (such as access, financial, or cultural)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8c</td>
<td>Diagnostic reasoning including other diagnoses considered</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8d</td>
<td>Prognostic characteristics (such as staging in oncology) where applicable</td>
<td></td>
</tr>
<tr>
<td>Therapeutic Intervention</td>
<td>9a</td>
<td>Types of intervention (such as pharmacologic, surgical, preventive, self-care)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9b</td>
<td>Administration of intervention (such as dosage, strength, duration)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9c</td>
<td>Changes in intervention (with rationale)</td>
<td></td>
</tr>
<tr>
<td>Follow-up and Outcomes</td>
<td>10a</td>
<td>Clinician and patient-assessed outcomes (when appropriate)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10b</td>
<td>Important follow-up diagnostic and other test results</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10c</td>
<td>Intervention adherence and tolerability (How was this assessed?)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10d</td>
<td>Adverse and unanticipated events .</td>
<td></td>
</tr>
<tr>
<td>Discussion</td>
<td>11a</td>
<td>Discussion of the strengths and limitations in your approach to this case</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td>Discussion of the relevant medical literature</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11c</td>
<td>The rationale for conclusions (including assessment of possible causes)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11d</td>
<td>The primary “take-away” lessons of this case report</td>
<td></td>
</tr>
<tr>
<td>Patient Perspective</td>
<td>12</td>
<td>When appropriate the patient should share their perspective on the treatments they received</td>
<td></td>
</tr>
<tr>
<td>Informed Consent</td>
<td>13</td>
<td>Did the patient give informed consent? Please provide if requested</td>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at [http://equator-network.org](http://equator-network.org).
The complete checklists and full guidelines are available at http://equator-network.org for various types of studies, from clinical trials and observational studies to reviews and case reports.

### PRISMA 2009 Checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analyses

<table>
<thead>
<tr>
<th>Section / Topic</th>
<th>Item no.</th>
<th>Checklist item</th>
<th>Reported on page no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
<td></td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td></td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>17</td>
<td>Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>18</td>
<td>For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>19</td>
<td>Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>20</td>
<td>For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>21</td>
<td>Present results of each meta-analysis done, including confidence intervals and measures of consistency.</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>22</td>
<td>Present results of any assessment of risk of bias across studies (see Item 15).</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>23</td>
<td>Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
<td></td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>24</td>
<td>Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).</td>
<td></td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>25</td>
<td>Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).</td>
<td></td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>26</td>
<td>Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
<td></td>
</tr>
<tr>
<td>FUNDING</td>
<td>27</td>
<td>Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.</td>
<td></td>
</tr>
</tbody>
</table>


EQUATOR stands for Enhancing the QAUality and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
### STROBE Statement - Checklist of Items that should be included in Reports of Observational Studies

<table>
<thead>
<tr>
<th>Section / Topic</th>
<th>Item no.</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE</strong></td>
<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
</tr>
<tr>
<td><strong>OBJECTIVES</strong></td>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
</tr>
</tbody>
</table>
| **Participants**| 6        | (a) **Cohort study**—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  
(b) **Case-control study**—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  
(c) **Cross-sectional study**—Give the eligibility criteria, and the sources and methods of selection of participants |
| **Variables**   | 7        | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| **Data Sources / measurement** | 8*       | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| **Bias**        | 9        | Describe any efforts to address potential sources of bias |
| **Study Size**  | 10       | Explain how the study size was arrived at |
| **Quantitative variables** | 11       | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| **Statistical methods** | 12       | (a) Describe all statistical methods, including those used to control for confounding  
(b) Describe any methods used to examine subgroups and interactions  
(c) Explain how missing data were addressed  
(d) **Cohort study**—If applicable, explain how loss to follow-up was addressed  
(e) **Case-control study**—If applicable, explain how matching of cases and controls was addressed |
| **Participants**| 13*      | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed  
(b) Give reasons for non-participation at each stage  
(c) Consider use of a flow diagram |
| **Descriptive data** | 14*      | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders  
(b) Indicate number of participants with missing data for each variable of interest  
(c) **Cohort study**—Summarise follow-up time (eg, average and total amount) |
| **Outcome data** | 15*      | (a) **Cohort study**—Report numbers of outcome events or summary measures over time  
(b) **Case-control study**—Report numbers in each exposure category, or summary measures of exposure  
(c) Cross-sectional study—Report numbers of outcome events or summary measures |
| **Main Results**| 16       | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included  
(b) Report category boundaries when continuous variables were categorized  
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| **Other analyses** | 17       | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **DISCUSSION**  |          | | |
| **Key Results** | 18       | Summarise key results with reference to study objectives |
| **Limitations** | 19       | Discuss limitations of the study, taking into account sources of potential bias or imprecision. |
| **Interpretation** | 20       | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| **Generalisability** | 21       | Discuss the generalisability (external validity) of the study results |
| **Funding**     | 22       | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

* Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.


---

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
STARD 2015 Checklist of Essential Items for Reporting Diagnostic Accuracy Studies

<table>
<thead>
<tr>
<th>Section and Topic</th>
<th>No.</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE OR ABSTRACT</strong></td>
<td>1</td>
<td>Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)</td>
</tr>
<tr>
<td><strong>ABSTRACT</strong></td>
<td>2</td>
<td>Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td>3</td>
<td>Scientific and clinical background, including the intended use and clinical role of the index test</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Study objectives and hypotheses</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td>5</td>
<td>Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>6</td>
<td>Eligibility criteria</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Where and when potentially eligible participants were identified (setting, location and dates)</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Whether participants formed a consecutive, random or convenience series</td>
</tr>
<tr>
<td><strong>Test Methods</strong></td>
<td>10a</td>
<td>Index test, in sufficient detail to allow replication</td>
</tr>
<tr>
<td></td>
<td>10b</td>
<td>Reference standard, in sufficient detail to allow replication</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Rationale for choosing the reference standard (if alternatives exist)</td>
</tr>
<tr>
<td></td>
<td>12a</td>
<td>Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory</td>
</tr>
<tr>
<td></td>
<td>12b</td>
<td>Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory</td>
</tr>
<tr>
<td></td>
<td>13a</td>
<td>Whether clinical information and reference standard results were available to the performers/readers of the index test</td>
</tr>
<tr>
<td></td>
<td>13b</td>
<td>Whether clinical information and index test results were available to the assessors of the reference standard</td>
</tr>
<tr>
<td><strong>Analysis</strong></td>
<td>14</td>
<td>Methods for estimating or comparing measures of diagnostic accuracy</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>How indeterminate index test or reference standard results were handled</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>How missing data on the index test and reference standard were handled</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>Intended sample size and how it was determined</td>
</tr>
<tr>
<td><strong>RESULTS</strong></td>
<td>19</td>
<td>Flow of participants, using a diagram</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Baseline demographic and clinical characteristics of participants</td>
</tr>
<tr>
<td></td>
<td>21a</td>
<td>Distribution of severity of disease in those with the target condition</td>
</tr>
<tr>
<td></td>
<td>21b</td>
<td>Distribution of alternative diagnoses in those without the target condition</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>Time interval and any clinical interventions between index test and reference standard</td>
</tr>
<tr>
<td><strong>Test Results</strong></td>
<td>23</td>
<td>Cross tabulation of the index test results (or their distribution) by the results of the reference standard</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>Any adverse events from performing the index test or the reference standard</td>
</tr>
<tr>
<td><strong>DISCUSSION</strong></td>
<td>26</td>
<td>Study limitations, including sources of potential bias, statistical uncertainty, and generalisability</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>Implications for practice, including the intended use and clinical role of the index test</td>
</tr>
<tr>
<td><strong>OTHER INFORMATION</strong></td>
<td>28</td>
<td>Registration number and name of registry</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>Where the full study protocol can be accessed</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>Sources of funding and other support; role of funders</td>
</tr>
</tbody>
</table>

This STARD list was released in 2015. The 30 items were identified by an international expert group of methodologists, researchers, and editors. The guiding principle in the development of STARD was to select items that, when reported, would help readers to judge the potential for bias in the study, to appraise the applicability of the study findings and the validity of conclusions and recommendations. The list represents an update of the first version, which was published in 2003.


**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at [http://equator-network.org](http://equator-network.org).
### CHEERS Checklist - Items to include when Reporting Economic Evaluations of Health Interventions

<table>
<thead>
<tr>
<th>Section / Item</th>
<th>Item no.</th>
<th>Recommendation</th>
<th>Reported on page no. / title no.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE AND ABSTRACT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.</td>
<td></td>
</tr>
<tr>
<td>Abstract</td>
<td>2</td>
<td>Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.</td>
<td></td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background and objectives</td>
<td>3</td>
<td>Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.</td>
<td></td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target population and subgroups</td>
<td>4</td>
<td>Describe characteristics of the base case population and subgroups analysed, including why they were chosen.</td>
<td></td>
</tr>
<tr>
<td>Setting and location</td>
<td>5</td>
<td>State relevant aspects of the system(s) in which the decision(s) need(s) to be made.</td>
<td></td>
</tr>
<tr>
<td>Study Perspective</td>
<td>6</td>
<td>Describe the perspective of the study and relate this to the costs being evaluated.</td>
<td></td>
</tr>
<tr>
<td>Comparators</td>
<td>7</td>
<td>Describe the interventions or strategies being compared and state why they were chosen.</td>
<td></td>
</tr>
<tr>
<td>Time horizon</td>
<td>8</td>
<td>State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.</td>
<td></td>
</tr>
<tr>
<td>Discount rate</td>
<td>9</td>
<td>Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.</td>
<td></td>
</tr>
<tr>
<td>Choice of health outcomes</td>
<td>10</td>
<td>Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.</td>
<td></td>
</tr>
<tr>
<td>Measurement of effectiveness</td>
<td>11a</td>
<td>Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.</td>
<td></td>
</tr>
<tr>
<td>Assumptions and conversion</td>
<td>11b</td>
<td>Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.</td>
<td></td>
</tr>
<tr>
<td><strong>RESULTS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimating resources and costs</td>
<td>13a</td>
<td>Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td></td>
</tr>
<tr>
<td>Assumptions</td>
<td>13b</td>
<td>Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td></td>
</tr>
<tr>
<td>Currency, price date, and conversion</td>
<td>14</td>
<td>Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.</td>
<td></td>
</tr>
<tr>
<td><strong>DISCUSSION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimating resources and costs</td>
<td>15</td>
<td>Describe and give reasons for the specific type of decision analytical model used. Providing a figure to show model structure is strongly recommended.</td>
<td></td>
</tr>
<tr>
<td>Assumptions</td>
<td>16</td>
<td>Describe all structural or other assumptions underpinning the decision-analytical model.</td>
<td></td>
</tr>
<tr>
<td>Estimating resources and costs</td>
<td>17</td>
<td>Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.</td>
<td></td>
</tr>
</tbody>
</table>

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.

http://philippinejournalofpathology.org | Vol. 3 No. 2 November 2018
## ARRIVE

### The ARRIVE Guidelines

**Animal Research: Reporting of In Vivo Experiments**

<table>
<thead>
<tr>
<th>Section / Topic</th>
<th>Item no.</th>
<th>Checklist Item</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td>3a</td>
<td>Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale.</td>
</tr>
<tr>
<td></td>
<td>3b</td>
<td>Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td>5</td>
<td>Dilucidate the nature of the ethical review permissions, relevant licences (e.g. Animal [Scientific Procedures] Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.</td>
</tr>
<tr>
<td></td>
<td>6a</td>
<td>For each experiment, give brief details of the study design including:</td>
</tr>
<tr>
<td></td>
<td>6b</td>
<td>a. The number of experimental and control groups.</td>
</tr>
<tr>
<td></td>
<td>6c</td>
<td>b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when).</td>
</tr>
<tr>
<td></td>
<td>6d</td>
<td>c. The experimental unit (e.g. a single animal, group or cage of animals).</td>
</tr>
<tr>
<td></td>
<td>7a</td>
<td>A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out.</td>
</tr>
<tr>
<td></td>
<td>7b</td>
<td>For each experiment and each experimental group, including controls, provide precise details of all procedures carried out.</td>
</tr>
<tr>
<td></td>
<td>7c</td>
<td>a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used [including monitoring], surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s).</td>
</tr>
<tr>
<td></td>
<td>7d</td>
<td>b. When (e.g. time of day).</td>
</tr>
<tr>
<td></td>
<td>7e</td>
<td>c. Where (e.g. home cage, laboratory, water maze).</td>
</tr>
<tr>
<td></td>
<td>8a</td>
<td>d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used).</td>
</tr>
<tr>
<td></td>
<td>8b</td>
<td>a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range).</td>
</tr>
<tr>
<td></td>
<td>8c</td>
<td>b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naive, previous procedures, etc.</td>
</tr>
<tr>
<td><strong>RESULTS</strong></td>
<td>11a</td>
<td>Provide details of:</td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td>a. Housing (type of facility e.g. specific pathogen free [SPF], type of cage or housing; bedding material; number of cage companions; tank shape and material etc. for fish).</td>
</tr>
<tr>
<td></td>
<td>11c</td>
<td>b. Husbandry conditions (e.g. breeding programme, light/dark cycle, temperature, quality of water etc for fish, type of food, access to food and water, environmental enrichment).</td>
</tr>
<tr>
<td></td>
<td>12a</td>
<td>c. Welfare-related assessments and interventions that were carried out prior to, during, or after the experiment.</td>
</tr>
<tr>
<td></td>
<td>12b</td>
<td>a. Specify the total number of animals used in each experiment, and the number of animals in each experimental group.</td>
</tr>
<tr>
<td></td>
<td>12c</td>
<td>b. Explain how the number of animals was arrived at. Provide details of any sample size calculation used.</td>
</tr>
<tr>
<td></td>
<td>12d</td>
<td>c. Indicate the number of independent replications of each experiment, if relevant.</td>
</tr>
<tr>
<td></td>
<td>13a</td>
<td>a. Give full details of how animals were allocated to experimental groups, including randomisation or matching if done.</td>
</tr>
<tr>
<td></td>
<td>13b</td>
<td>b. Describe the order in which the animals in the different experimental groups were treated and assessed.</td>
</tr>
<tr>
<td><strong>DISCUSSION</strong></td>
<td>18a</td>
<td>b. Describe any modifications to the experimental protocols made to reduce adverse events.</td>
</tr>
<tr>
<td></td>
<td>18b</td>
<td>c. Describe any implications of your experimental methods or findings for the replacement, refinement or reduction (the 3Rs) of the use of animals in research.</td>
</tr>
</tbody>
</table>

The ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines were developed as part of an NC3Rs initiative to improve the design, analysis and reporting of research using animals – maximising information published and minimising unnecessary studies. The guidelines were published in the online journal PLOS Biology in June 2010 and are currently endorsed by scientific journals, major funding bodies and learned societies. More information can be found on www.nc3rs.org.uk/ARRIVE

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
### Revised Standards for Quality Improvement Reporting Excellence
(SQUIRE 2.0)

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Guide questions / description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE AND ABSTRACT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Title</td>
<td>Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patient-centeredness, timeliness, cost, efficiency, and equity of healthcare)</td>
</tr>
</tbody>
</table>
| 2 | Abstract | a. Provide adequate information to aid in searching and indexing  
| | | b. Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions |
| **INTRODUCTION** | WHAT DID YOU START? | |
| 3 | Problem Description | Nature and significance of the local problem |
| 4 | Available knowledge | Summary of what is currently known about the problem, including relevant previous studies |
| 5 | Rationale | Informal or formal frameworks, models, concepts, and/or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work |
| 6 | Specific aims | Purpose of the project and of this report |
| **METHODS** | WHAT DID YOU DO? | |
| 7 | Context | Contextual elements considered important at the outset of introducing the intervention(s) |
| 8 | Intervention(s) | a. Description of the intervention(s) in sufficient detail that others could reproduce it  
| | | b. Specifics of the team involved in the work |
| 9 | Study of the Intervention(s) | a. Approach chosen for assessing the impact of the intervention(s)  
| | | b. Approach used to establish whether the observed outcomes were due to the intervention(s) |
| 10 | Measures | a. Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability  
| | | b. Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost  
| | | c. Methods employed for assessing completeness and accuracy of data  
| | | a. Qualitative and quantitative methods used to draw inferences from the data  
| | | b. Methods for understanding variation within the data, including the effects of time as a variable |
| 11 | Analysis | | |
| 12 | Ethical Considerations | Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest |
| **RESULTS** | WHAT DID YOU FIND? | |
| 13 | Results | a. Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project  
| | | b. Details of the process measures and outcomes  
| | | c. Contextual elements that interacted with the intervention(s)  
| | | d. Observed associations between outcomes, interventions, and relevant contextual elements  
| | | e. Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).  
| | | f. Details about missing data |
| **DISCUSSION** | WHAT DOES IT MEAN? | |
| 14 | Summary | a. Key findings, including relevance to the rationale and specific aims  
| | | b. Particular strengths of the project |
| 15 | Interpretation | a. Nature of the association between the intervention(s) and the outcomes  
| | | b. Comparison of results with findings from other publications  
| | | c. Impact of the project on people and systems  
| | | d. Reasons for any differences between observed and anticipated outcomes, including the influence of context  
| | | e. Costs and strategic trade-offs, including opportunity costs |
| 16 | Limitations | a. Limits to the generalizability of the work  
| | | b. Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis |
| 17 | Conclusions | c. Efforts made to minimize and adjust for limitations  
| | | a. Usefulness of the work  
| | | b. Sustainability  
| | | c. Potential for spread to other contexts  
| | | d. Implications for practice and for further study in the field  
| | | e. Suggested next steps |
| **OTHER INFORMATION** | | |
| 18 | Funding | Sources of funding that supported this work. Role, if any, of the funding organization in the design, implementation, interpretation, and reporting |

---

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
SPRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

<table>
<thead>
<tr>
<th>Section / Topic</th>
<th>Item no.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADMINISTRATIVE INFORMATION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym</td>
</tr>
<tr>
<td>Trial registration</td>
<td>2a</td>
<td>Trial identifier and registry name. If not yet registered, name of intended registry</td>
</tr>
<tr>
<td></td>
<td>2b</td>
<td>All items from the World Health Organization Trial Registration Data Set</td>
</tr>
<tr>
<td>Protocol version</td>
<td>3</td>
<td>Date and version identifier</td>
</tr>
<tr>
<td>Funding</td>
<td>4</td>
<td>Sources and types of financial, material, and other support</td>
</tr>
<tr>
<td>Roles and responsibilities</td>
<td>5a</td>
<td>Names, affiliations, and roles of protocol contributors</td>
</tr>
<tr>
<td></td>
<td>5b</td>
<td>Name and contact information for the trial sponsor</td>
</tr>
<tr>
<td></td>
<td>5c</td>
<td>Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities</td>
</tr>
<tr>
<td></td>
<td>5d</td>
<td>Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background and rationale</td>
<td>6a</td>
<td>Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention</td>
</tr>
<tr>
<td></td>
<td>6b</td>
<td>Explanation for choice of comparators</td>
</tr>
<tr>
<td>Objectives</td>
<td>7</td>
<td>Specific objectives or hypotheses</td>
</tr>
<tr>
<td>Trial design</td>
<td>8</td>
<td>Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)</td>
</tr>
<tr>
<td><strong>METHODS: PARTICIPANTS, INTERVENTIONS, AND OUTCOMES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study setting</td>
<td>9</td>
<td>Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>10</td>
<td>Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)</td>
</tr>
<tr>
<td>Interventions</td>
<td>11a</td>
<td>Interventions for each group with sufficient detail to allow replication, including how and when they will be administered</td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td>Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)</td>
</tr>
<tr>
<td></td>
<td>11c</td>
<td>Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)</td>
</tr>
<tr>
<td></td>
<td>11d</td>
<td>Relevant concomitant care and interventions that are permitted or prohibited during the trial</td>
</tr>
<tr>
<td>Outcomes</td>
<td>12</td>
<td>Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended</td>
</tr>
<tr>
<td>Participant timeline</td>
<td>13</td>
<td>Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)</td>
</tr>
<tr>
<td>Sample size</td>
<td>14</td>
<td>Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations</td>
</tr>
<tr>
<td>Recruitment</td>
<td>15</td>
<td>Strategies for achieving adequate participant enrolment to reach target sample size</td>
</tr>
<tr>
<td><strong>METHODS: ASSIGNMENT OF INTERVENTIONS (FOR CONTROLLED TRIALS)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allocation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sequence generation</td>
<td>16a</td>
<td>Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions</td>
</tr>
<tr>
<td>Allocation concealment mechanism</td>
<td>16b</td>
<td>Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned</td>
</tr>
<tr>
<td>Implementation</td>
<td>16c</td>
<td>Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions</td>
</tr>
<tr>
<td>Blinding (masking)</td>
<td>17a</td>
<td>Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how</td>
</tr>
<tr>
<td></td>
<td>17b</td>
<td>If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial</td>
</tr>
</tbody>
</table>

http://philippinejournalofpathology.org | Vol. 3 No. 2 November 2018
METHODS: DATA COLLECTION, MANAGEMENT, AND ANALYSIS

| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity; if known. Reference to where data collection forms can be found, if not in the protocol |
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) |

METHODS: MONITORING

| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial |
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor |

ETHICS AND DISSEMINATION

| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) |
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site |
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |

APPENDICES

| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons “Attribution-NonCommercial-NoDerivs 3.0 Unported” license.

EQUATOR stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
<table>
<thead>
<tr>
<th>Section / Topic</th>
<th>Item no.</th>
<th>Checklist item</th>
<th>Reported on page no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE AND ABSTRACT</td>
<td>1a</td>
<td>Identification as a randomised trial in the title</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)</td>
<td></td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>2a</td>
<td>Scientific background and explanation of rationale</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2b</td>
<td>Specific objectives or hypotheses</td>
<td></td>
</tr>
<tr>
<td>METHODS</td>
<td>3a</td>
<td>Description of trial design (such as parallel, factorial) including allocation ratio</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3b</td>
<td>Important changes to methods after trial commencement (such as eligibility criteria), with reasons</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4a</td>
<td>Eligibility criteria for participants</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4b</td>
<td>Settings and locations where the data were collected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>The interventions for each group with sufficient details to allow replication, including how and when they were actually administered</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6a</td>
<td>Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6b</td>
<td>Any changes to trial outcomes after the trial commenced, with reasons</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7a</td>
<td>How sample size was determined</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7b</td>
<td>When applicable, explanation of any interim analyses and stopping guidelines</td>
<td></td>
</tr>
<tr>
<td>Randomisation:</td>
<td>8a</td>
<td>Method used to generate the random allocation sequence</td>
<td></td>
</tr>
<tr>
<td>Sequence generation</td>
<td>8b</td>
<td>Type of randomisation; details of any restriction (such as blocking and block size)</td>
<td></td>
</tr>
<tr>
<td>Allocation concealment mechanism</td>
<td>9</td>
<td>Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned</td>
<td></td>
</tr>
<tr>
<td>Implementation</td>
<td>10</td>
<td>Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions</td>
<td></td>
</tr>
<tr>
<td>Blinding</td>
<td>11a</td>
<td>If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how</td>
<td></td>
</tr>
<tr>
<td>Statistical methods</td>
<td>12a</td>
<td>Statistical methods used to compare groups for primary and secondary outcomes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12b</td>
<td>Methods for additional analyses, such as subgroup analyses and adjusted analyses</td>
<td></td>
</tr>
<tr>
<td>RESULTS</td>
<td>13a</td>
<td>For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome</td>
<td></td>
</tr>
<tr>
<td>Participant flow</td>
<td>13b</td>
<td>For each group, losses and exclusions after randomisation, together with reasons</td>
<td></td>
</tr>
<tr>
<td>Recruitment</td>
<td>14a</td>
<td>Dates defining the periods of recruitment and follow-up</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14b</td>
<td>Why the trial ended or was stopped</td>
<td></td>
</tr>
<tr>
<td>Baseline data</td>
<td>15</td>
<td>A table showing baseline demographic and clinical characteristics for each group</td>
<td></td>
</tr>
<tr>
<td>Numbers analysed</td>
<td>16</td>
<td>For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups</td>
<td></td>
</tr>
<tr>
<td>Outcomes and estimation</td>
<td>17a</td>
<td>For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17b</td>
<td>For binary outcomes, presentation of both absolute and relative effect sizes is recommended</td>
<td></td>
</tr>
<tr>
<td>Ancillary analyses</td>
<td>18</td>
<td>Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory</td>
<td></td>
</tr>
<tr>
<td>Harms</td>
<td>19</td>
<td>All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)</td>
<td></td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>20</td>
<td>Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses</td>
<td></td>
</tr>
<tr>
<td>Limitations</td>
<td>21</td>
<td>Generalisability (external validity, applicability) of the trial findings</td>
<td></td>
</tr>
<tr>
<td>Generalisability</td>
<td>22</td>
<td>Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence</td>
<td></td>
</tr>
<tr>
<td>OTHER INFORMATION</td>
<td>23</td>
<td>Registration number and name of trial registry</td>
<td></td>
</tr>
<tr>
<td>Registration</td>
<td>24</td>
<td>Protocol</td>
<td></td>
</tr>
<tr>
<td>Protocol</td>
<td>25</td>
<td>Where the full trial protocol can be accessed, if available</td>
<td></td>
</tr>
<tr>
<td>Funding</td>
<td>26</td>
<td>Sources of funding and other support (such as supply of drugs), role of funders</td>
<td></td>
</tr>
</tbody>
</table>

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmaceutical treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming; for those and for up to date references relevant to this checklist, see www.consort-statement.org.

---

**EQUATOR** stands for Enhancing the QUAlity and Transparency Of health Research. It is an international initiative that started in 2008 whose main objective is to improve the reliability and value of scholarly publication of health research through promotion of transparent, complete, and accurate reporting. The Network promotes standards, guidelines and checklists of reporting requirements for various types of studies, from clinical trials and observational studies to reviews and case reports.

The complete checklists and full guidelines are available at http://equator-network.org.
Getting Started

- From the PJP website (http://www.philippinejournalofpathology.org), navigate to ‘For Authors’. (add screenshot of PJP landing page, circle ‘for authors’ on right column).

Select ‘FOR AUTHORS’.

Information For Authors

Interested in submitting to this journal? We recommend that you review the About the Journal page for the journal’s section policies, as well as the Author Guidelines. Authors need to register with the journal prior to submitting or, if already registered, can simply log in and begin the five-step process.
Getting Started

- Log in
- New user:
  - If you are a new user of the PJP website, please register by clicking the link ‘Not a user, Register with this site’.
  - Complete the online form then select ‘Register’. A confirmation email with your username and password will be sent to your email address.
• Existing user:
  o Log in to your OJS account using the username and password from original registration.
  o If you have forgotten your log in details, please click the ‘Forgot the password?’ and an email will be sent to your registered email address.

The Submission Process

• To start the submission process, click ‘New Submission’

Step 1: Starting the submission

• From the drop-down menu, please select the most appropriate section to describe your submission article type. If you are not sure what section to select, click ‘About’ to find out more information.
Please ensure the items listed in the checklist are ready then tick each box.

![Submission Checklist](image-url)
- Read the ‘Copyright Notice’ and add comments to the editor (optional). Select ‘Save and continue’.

### Step 2: Uploading the Submission

- Please follow the instructions on this page to upload your file, then select ‘Save and continue’. This is where you upload the **manuscript only**. (You will be asked to upload other required documents at Step 4.)
Step 3: Entering the Submission’s Metadata

- Complete author(s)’s information as much as you can. Fields marked with * are mandatory. If you have more than one author for your submission, click ‘Add author’ for each of these.

- Please note the system will automatically select the first-recorded author as the principal contact for editorial correspondence. If you want to change this, choose the following option listed at the bottom of the author details for the author you want to be the principal contact.
Complete ‘Title’, ‘Abstract’, ‘Indexing’ and ‘Supporting Agencies’ of your submission. Select ‘Save and continue’. These can be pasted from a word document.
Once all files are uploaded, if you need to you can edit or delete them by clicking the links. To continue to next step, select ‘Save and continue’.
Step 5: Confirming the Submission

- Please check that all required files have been uploaded and are listed on the ‘File Summary’. Select ‘Finish Submission’ to submit your manuscript.

- The principle contact of the submission will then receive an acknowledgement email.

Dear xxx:

Thank you for submitting the manuscript, "xxxxxx" to Philippine Journal of Pathology. With the online journal management system that we are using, you will be able to track its progress through the editorial process by logging in to the journal web site:

Manuscript URL:  
http://philippinejournalofpathology.org/index.php/PJP/...........  
Username: xxxxxx

If you have any questions, please contact me. Thank you for considering this journal as a venue for your work.

Amado O. Tandoc III, MD, DPSP  
Philippine Journal of Pathology

http://philippinejournalofpathology.org

Status of Submission

- During the review and editing process, the principal contact can log in to the PJP website to check the status of the submission. Follow the log in instructions on Page (?) and then click the ‘Active’ tab.

<table>
<thead>
<tr>
<th>ID</th>
<th>MM-DD</th>
<th>SEC</th>
<th>AUTHORS</th>
<th>TITLE</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>02-05</td>
<td>ORL</td>
<td>Smith</td>
<td>TEST SUBMISSION</td>
<td>IN EDITING</td>
</tr>
</tbody>
</table>

Start a New Submission  
CLICK HERE to go to step one of the five-step submission process.
You will receive an email from the Editor-in-Chief after the peer review process which will indicate the outcome of the review and provide the reviewer’s comments.

Dear xxx:

Your manuscript "xxxxxx" submitted to Philippine Journal of Pathology has undergone peer review. The manuscript has been accepted subject to major / minor revisions.

Please find attached the comments from the peer reviewers. Please take the following actions:
1. Review the manuscript according to the reviewers’ comments using the track changes facility in Word.
2. Provide a response to each of the reviewers’ comments in a separate Word document.
3. Upload both the revised manuscript and the response to the reviewers’ comments.

The due date for these revisions is Friday, xx month. If you have any queries regarding this please contact me.

Thank you and kind regards,

Amado O. Tandoc III, MD, DPSP
Philippine Journal of Pathology

Please make the required changes to manuscript and in a separate file provide responses to each of the reviewer’s comments.

These can then be uploaded onto the system.

- Login (see instructions on Page (?))
- Click ‘Active’ tab.
- Click on your submission listed below ‘TITLE’.
- Select the ‘Review’ tab.
- In the ‘Editor Decision’ section at the bottom of the page, you can upload your revised manuscript and responses to reviewer’s comments.
- Once you have uploaded your files, you can view them at the ‘Author’s Version’ section.
GET PUBLISHED IN THE NEW PHILIPPINE JOURNAL OF PATHOLOGY!

The Philippine Journal of Pathology (PJP) is an open-access, peer-reviewed, English language, medical science journal published by the Philippine Society of Pathologists, Inc. It shall serve as the official platform for publication of high quality original articles, case reports or series, feature articles, and editorials covering topics on clinical and anatomic pathology, laboratory medicine and medical technology, diagnostics, laboratory biosafety and biosecurity, as well as laboratory quality assurance.

The journal’s primary target audience are laboratorians, diagnosticians, laboratory managers, pathologists, medical technologists, and all other medical and scientific disciplines interfacing with the laboratory. For instructions and more information, visit our Official Website at:

http://philippinejournalofpathology.org