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POLICY FORUM

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Materiality of evidence-based policy making for child and adolescent psychiatry in Japan

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Abstract: The Japanese government established the Children and Family Agency in April 2023 and is trying to promote evidence-based policymaking (EBPM). However, the current state of child and adolescent psychiatry in Japan demonstrated some difficulties. School refusal and suicide problems are increasing after the coronavirus disease-2019 (COVID-19) pandemic. These issues need to be addressed, thereby warranting various policies to be developed and implemented. Increasing the number of inpatient medical institutions and establishing a community-based data accumulation system that enables data and knowledge sharing among professionals is essential to improve child and adolescent psychiatric care. Furthermore, EBPM is needed to effectively develop a policy, and specialized experts are necessary to organize data and critically review evidence.

***Keywords*:** child, mental health, EBPM, policymaking

Introduction

The Japanese government is trying to promote evidence-based policymaking (EBPM). The Cabinet Office defined EBPM as the practice of basing policy planning on evidence, with clear policy objectives, rather than relying on *ad hoc* episodes (Cabinet Office) (*1*). EBPM has several issues, such as organizing data into analyzable formats and avoiding a half-hearted approach to policy formation. This study emphasizes the importance of systematically reviewing information and sharing tools based on information for children's mental health. It also indicates a dialogue between medical professionals, such as child and adolescent psychiatrists, psychologists, and social workers, policymakers, policy formation experts, economists, and educators. Such a discussion would ensure that evidence is rigorously analyzed, translated, and successfully shared.

EBPM emphasizes the importance of transitioning from the "equality for everyone" approach to the "resource allocation based on needs" approach. This transition is essential to address the growing disparity in education among Japanese children. Overall, this study provides a detailed examination of the various issues related to child poverty and childcare policies in Japan. It highlights the need to use EBPM to develop informed decisions, as well as the importance of systematically reviewing and sharing information, the challenges in child and adolescent psychiatry, and the need to transition from the "equality for everyone" approach to the "resource allocation based on needs" approach.

Some studies discuss EBPM for children's mental health. The American child welfare system identifies this area and discusses the use of decision-analytic models to advance child welfare policy and practice (*2*). Canadian child mental health policy researchers hope to use the best available research evidence to develop policy to address important public issues (*3*). Children are recognized to be more vulnerable to abuse and neglect and are, thus, more likely to experience negative health and mental health outcomes. Therefore, this study discusses the EBPMs that prevent child maltreatment and reduce negative mental health outcomes for young people who are victims (*4*).

Serious issues in children's mental health in Japan

The current state of children's mental health in Japan has some issues. For example, school refusal and suicide problems are increasing after the coronavirus disease-2019 (COVID-19) pandemic. In FY2021, the number of elementary and junior high school children who did not attend school increased for the ninth year to 240,000, the highest number ever. The Ministry of Education, Culture, Sports, Science and Technology emphasizes that the environmental changes and various restrictions on school life caused by COVID-19 have affected friendships and other relationships, thereby motivating students to attend school becomes difficult.

Serious issues in Japanese society included suicide in

512 children under 18 years of age in 2022. Of the 512 children, 352 were high school students (up 38 from the previous year), accounting for 70% of the total, and up 39 from 473 in 2009. Additionally, 143 children were junior high school students (decreased by five children) and 17 were elementary school students (increased by six children). The previous record reported 499 children who committed suicide in 2008, including 339 high school, 146 junior high school, and 14 elementary school students. Suicides among children have been increasing in recent years while the birth rate is decreasing (*5*). The number of child suicides has increased in recent years and the problem is becoming more serious.

Neurodevelopmental disorders are increasing rapidly, with autism diagnoses rising from 1 in 5,000 in 1975 to 1 in 59 in 2018 (*6*). Meanwhile, attention deficit hyperactivity disorder (ADHD) is the most prevalent childhood psychiatric disorder in children under 18 years of age, with a rate of 5.29% (*7*). The "Administrative Evaluation of Support for Persons with Developmental Disabilities – Monitoring" of the Ministry of Internal Affairs and Communications recommended that in specialized medical institutions, the waiting list for the initial consultation for children suspected of having a developmental disability is getting longer. For example, more than half of the medical institutions (14/27 hospitals) had a waiting time of > 3 months, with the longest waiting time being approximately 10 months in terms of waiting time for an initial consultation, and > 50 patients in approximately 40% of the medical institutions (12/27 hospitals) are waiting for an initial consultation, with the maximum waiting time being 316 patients. Japan's Ministry of Internal Affairs and Communications has issued recommendations to medical institutions for improvement.

Some diseases have increased with the COVID-19 Pandemic. Studies reported increased restriction and anxiety about eating behavior in individuals with anorexia nervosa under the spread of COVID-19 (*8*). Many patients presented with medical instability following restrictive diets and required acute hospitalization to correct malnutrition but often had difficulty finding a hospital that has a child and adolescent psychiatric unit.

The reason for recognizing children with such diverse issues is that development of mental illness begins in adolescence (*9*). However, the medical field of child and adolescent psychiatry in Japan faces a shortage of child and adolescent psychiatrists which necessitates multi-professional support. One child psychiatrist at the Japanese Council of Child and Adolescent Mental Health Institutions treated an average of 132 outpatients (maximum 360 outpatients) and five inpatients (maximum 19 inpatients), spending ≥ 60 min for the initial visit and 30-60 min for the follow-up visit. Additionally, 80% of child psychiatrists worked in maternal and child health, welfare, education, justice, and training (*10*). This significantly exceeded the consultation time of a regular psychiatrist in Japan, thereby causing depopulation of child psychiatry in terms of overwork and cost-effectiveness. Additionally, more inpatient hospital beds were needed to provide comprehensive treatment for psychiatric difficulties beyond developmental problems, such as depression, suicide, and eating disorders.

Japanese social costs for children's well-being

Japan established the Children and Family Agency in April 2023. This study discusses research and policy issues related to child mental health. A study by the Nippon Foundation reported the social loss caused by child poverty amounting to 42.9 trillion yen (*11*). The economic loss suffered by society, even in a single school year of a current 15-year-old, reaches approximately 2.9 trillion yen if child poverty is left unchecked, which increases the government's financial burden by 1.1 trillion yen. Child poverty is becoming increasingly critical in Japan. Looking at the child poverty rates of seven major countries (2012), Japan's child poverty rate stands at 16.3%, following the United States at 20.8% and Italy at 17.2%.

The Nomura Research Institute estimated Japan's economic losses related to developmental disabilities to amount to approximately 2.3 trillion yen, including 1.3 trillion yen for autism spectrum disorder (ASD) and 1.0 trillion yen for ADHD. Economic loss in this case includes direct costs, such as medical expenses and social service costs, as well as indirect costs, such as losses due to low income and non-employment (*12*).

Abused children can suffer lifelong physical and mental health problems (*13,14*). The Ministry of Health, Labor and Welfare is taking a seamless and comprehensive approach to prevent child abuse, from preventing the occurrence of abuse to early detection and early response, as well as protection and support for the independence of abused children (*15*). The social cost of child abuse is 1.6 trillion yen annually, of which 0.1 trillion yen is direct costs (money paid by the government as a budget such as operating expenses of support organizations) and 1.5 trillion yen is indirect costs (money expected to be lost due to abuse) (*16*). Various policies will need to be developed and implemented to address these issues.

Insufficient evidence for EBPM of child and adolescent psychiatry in Japan

The Child and Adolescent Mental Health Registry of the National Center for Global Health and Medicine (NCGM) collects clinical activity in child psychiatry. A few cohort studies focused on general child populations but collected information in a limited geographical area, and the data collected were not consistent. Thirty-eight hospitals of

the Japanese Council of Child and Adolescent Mental Institution have statistics on the number of people by age group of first outpatient visits and diagnoses (n = 13,059) and new admissions (n = 2,955) in FY2021 (*17*). Neurodevelopmental disorders, such as ASD and ADHD, accounted for half of the total in the outpatient setting. Schizophrenia was less common in contrast to adults. Abuse accounted for 12% of these cases while truancy accounted for 30%. Neurodevelopmental disorders in residential treatment accounted for half the cases, with an increasing proportion of life-threatening eating disorders. Of these, abuse accounted for 27%, and truancy accounted for 49%. The average length of stay in residential treatment was 126.1 days.

Therefore, evidence for practicing EBPM in children's mental health in Japan is lacking. Training specialists and having a system to support people with developmental disabilities in the community who want to be seen is essential to address the problem of their waiting lists. Expanding specialized hospitals that can provide inpatient treatment is also essential, as problems other than developmental disabilities, such as suicide, depression, and anorexia, also need to be addressed. Evidence on how much and in what areas the limited number of child psychiatric facilities should be established to address these issues is lacking. Adverse childhood experiences have a significant impact on children's lives. A continuous support system, including maternal and child health care to adolescent mental health care, must be established.

The need for the children's mental health registry system to support EBPM

The Japanese child and adolescent psychiatric field should conduct real-world surveys to gather evidence of children's mental health and need to construct a statistical maintenance system. Thus, developing an implementation system that does not increase the burden of real-world clinical practice and the necessity of bridging treatment of mental disorders with maternal and child health and child welfare fields are important (*3,4,18*). Additionally, the need for a statistical system and promotion of its use should ensure ease of access, protection of personal data, promotion of its use in health, social care, and education, and budgetary incentives. Smart statistical operations are systems that are directly connected to electronic medical records, such as J-DREAMS by NCGM and publication of information and open data for statistical systems (*19*).

Nudge plan for EBPM of child and adolescent psychiatry

The Children and Family Agency will provide services for all children and families. These policies could include mental health services for children and their families, such as those with developmental disorders, depression, suicide, and eating disorders. However, challenges remain, such as lack of a specific budget for professional development, which could hinder the agency's effectiveness and children's mental and physical health.

Establishing an information network across various systems related to children, as mentioned earlier, is essential to overcome these challenges. This network will facilitate sharing of data and knowledge among professionals in different fields such as maternal and child health, education, medical care, welfare, and justice. Furthermore, providing adequate training for professionals is crucial to ensure that they can provide evidence-based care.

Establishment of the Children and Family Agency is a crucial step toward addressing increasing issues related to child poverty and mental health in Japan. However, addressing the challenges in child and adolescent psychiatry, establishing an information network, and providing adequate training for professionals is necessary to ensure its success. Department of Child and Adolescent Psychiatry Kohnodai Hospital, NCGM, at the Council for Measures for Children in Need of Protection, are committed to building and implementing a network of regional cooperation that promotes collaboration between specialized organizations, such as medical care, education, welfare, maternal and child health care, justice, and corrections, in Ichikawa City. This network aims to develop a system in which no one organization is the only center of the community using Guidelines for the Establishment and Operation of a Response and Collaboration System for Problem Behaviors in Children and Adolescents with Mental disorders. NCGM believes that maternal and child health and education facilities can serve as a regional safety net for vulnerable children.

Department of Child and Adolescent Psychiatry Kohnodai Hospital, NCGM are planning three nudge steps (activities, output, and outcome) for EBPM of child and adolescent psychiatry (Figure 1).

Step 1. Making system for EBPM of children's mental health – "Activities" pertains to the following three aspects:

i) Training and quality improvement for professionals focusing on children's mental health in model regions;

ii) Collecting medical information from existing psychiatric care for children and adolescents (*e.g.,* if there is registry data for children's mental health that already exists, it should be utilized); and

iii) Gathering data on medical care, welfare, education, and maternal and child health at the municipal level (*e.g.*, through the Council for Measures for Children in Need of Protection).

Step 2. Making data of EBPM – "Output" covers these three main points:

i) Merging various data, such as medical care, welfare, education, and maternal and child health;

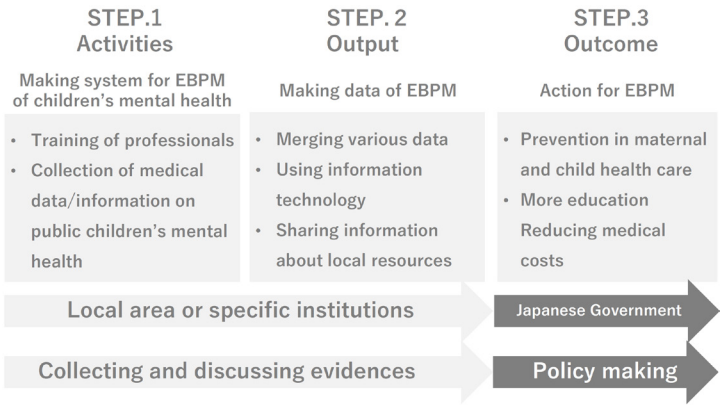

Figure 1. Nudge plan for EBPM of children's mental health in Japan. EBPM, evidence-based policymaking.

ii) Using tools, such as information technology, and linking electronic medical records. Sharing information about local resources, including counseling services; and

iii) Creating connections between different systems, such as associating maternal and child health with compulsory education.

Step 3. Action for EBPM – "Outcome" aims the following four main points:

i) Preventing maternal isolation in maternal and child health care and early intervention in the community;

ii) More educational opportunities;

iii) Reducing medical costs for children with mental problems such as neurodevelopmental disorders; and

iv) Making new policies to promote children's well-being.

Conclusion

Child and adolescent psychiatry plays a crucial role in promoting healthy emotional development in children by collaborating with local specialized institutions, such as education, welfare, maternal and child health, and the judiciary. However, specialized child and adolescent psychiatrists are significantly short, which makes it challenging to address psychiatric issues beyond developmental problems, such as depression, suicide, and eating disorders, in Japan. Increasing the number of medical institutions that have training programs for medical residents and specific psychiatric wards for child and adolescent psychiatry is essential to overcome this issue. Moreover, EBPM is crucial for effective policy formation. Organizing data into analyzable formats, critically reviewing and translating evidence using specialized experts, and establishing an information network to share data and knowledge among professionals in various fields related to children are necessary to achieve this goal. Establishing a community-based data accumulation system is essential for future projects to improve children's mental health. This system will facilitate the sharing of data and knowledge among professionals in different fields, such as maternal and child health, education, medical care, welfare, and justice, and enable evidence-based care.

In conclusion, increasing the number of inpatient medical institutions and establishing a community-based data accumulation system that enables data and knowledge sharing among professionals is essential to improve child and adolescent psychiatric care. Furthermore, EBPM is needed to effectively develop a policy, and specialized experts are necessary to organize data and critically review evidence.

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ORIGINAL ARTICLE

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Evaluation of interventions to improve clinical practices for hypertension in health facilities in rural Zambia: A cross-sectional study

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Abstract: Responding to high disease burden of Hypertension (HTN), the Ministry of Health in Zambia considers improving services related to HTN a national priority. Therefore, this study evaluated the interventions for HTN pharmaceutical treatment by training of health staffs and procurement of necessary medical devices. We investigated service provision in the outpatient department (OPD) visits among patients aged 40 years and above in randomly selected health facilities in Chongwe district, between May and December 2017, before and after the interventions. The proportion of OPD visits that included standard clinical practices for HTN services significantly increased post-intervention: 45.8% to 71.9% for blood pressure screening, 26.8% to 31.8% for HTN diagnosis, and 14.2% to 20.9% for HTN medication. The proportion of OPD visits at which HTN medication was prescribed increased significantly post-intervention among patients with Grade 2 HTN or above, from 68.3% to 86.0%. The estimated district-wide monthly cost for HTN services in USD was $1,905 at baseline and increased to $2,643 post-intervention. These results suggest that improving HTN service provision is feasible and affordable at the district level. However, because a large number of individuals in need of HTN medication did not access a health facility, further investigation is required to estimate the expected effects and costs under improved access in the future.

***Keywords*:** hypertension, non-communicable diseases, Africa

Introduction

Non-communicable diseases (NCDs), including cardiovascular diseases (CVDs), are a major cause of mortality around the world; approximately 35 million people die every year from NCDs including CVDs. One of the major contributing factors to the high prevalence of CVDs is Hypertension (HTN) (*1*). In low- and middle-income countries, 80% of these deaths occur in individuals aged less than 70 years (*2,3*). Total deaths from NCDs are projected to increase by more than 17% over the next 10 years, constituting a substantial financial burden on national economies (*3,4*). In response to this situation, the World Health Organization (WHO) adopted a resolution based on the 2011 United Nations (UN) Declaration on NCDs at the 66th World Health Assembly (*5*), endorsing new health goals to enable a 25% reduction in avoidable mortality from NCDs by 2025 (*6*). In addition, NCD-related indicators were added to several targets in Goal 3 of the UN's Sustainable Development Goals (*7,8*), and the WHO published NCD related policy documents such as the Global NCD Action Plan 2013-2020 (*9*), and the Package of Essential Non-communicable Disease Interventions for primary health care in low-resource settings (*10,11*).

In African countries, there is an increased demand for quality NCD health services (*12*). In Zambia, 18% of deaths among people aged 30 to 70 years in 2017 were due to four main NCDs (cardiovascular diseases, cancers, chronic respiratory diseases and diabetes) (*13*), accounting for approximately 20,000 deaths. A sample vital registration with verbal autopsy (SAVVY) conducted in 2015 reported that cardiovascular diseases accounted for 12.1% of total causes of death (*14*). In addition, the WHO STEPwise approach to Surveillance (STEPs) in 2017 revealed a large number of people with risk factors leading to major NCDs such as HTN; 19.1% of the adult population (20.5% of men and 17.6% of women) had elevated blood pressure (BP), defined as systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg (*15*). In this context, the Zambian Ministry of Health (MoH) has designated improved health services for HTN and other NCDs, as a priority in the National

Health Strategic Plan 2017-2021 (*16*). However, the necessary information to understand the actual capacity of health facilities and related costs for treating hypertensive patients in Zambia is lacking. Therefore, the feasibility and affordability of implementing the NCD-related services stipulated in the Basic Health Care Package, which is a set of essential health care services for everyone, were unknown.

With support from the Japanese International Cooperation Agency (JICA), the Zambian MoH has endeavored to improve HTN-related services at the primary healthcare level, in the rural Chongwe district, by increasing health staff capacity, procuring necessary medical equipment, and developing clinical guidelines for HTN. Chongwe district is located 50 km away from the Zambian capital city of Lusaka and is a middle-sized rural district with a population of 177,491, according to the Zambian National Census (*17*). To evaluate the service provision for HTN on a health facility basis, the project conducted operational research using medical record data from selected health facilities in the Chongwe district. The objective of this study is to provide useful information for the development of health policies in Zambia for HTN services by analyzing, one, the outcomes of interventions designed to improve service provision for HTN and, two, the related costs at the primary healthcare level.

Patients and Methods

Study sites, population, and data collection

This was a repeated cross-sectional study based on medical record data from randomly selected health facilities in Chongwe District. The target population for this study was patients aged greater or equal to 40 years, who visited an outpatient department (OPD) at a targeted health facility in the Chongwe district. WHO (*9,10*) recommends routine BP screening for persons in this age group as they are a high-risk population for cardiovascular diseases, and Zambia's 2016 Standard Treatment Guideline (STG) (*18*) followed this guideline. Individuals who resided outside Chongwe district or refused to participate in the study were excluded.

Chongwe district has three types of health facilities, varying by catchment population and function: first-level hospitals, rural health centers, and health posts. The number of each type of health facility at the beginning of the study period was 1, 12, and 11, and the catchment populations were approximately 180,000, 8,000-12,000, and 2,000-4,000, respectively (*17*).

An *a priori* power analysis was conducted to determine the minimum sample and cluster sizes required to find significant differences in the proportions of HTN diagnoses, pre- and post-intervention. Power was set at 0.8, with an alpha level of 0.05, and the proportion of HTN diagnoses was assumed to be 20% before and 30% post-intervention. Based on this analysis, a minimum of 300 pre- and post-intervention visits per health facility were required to ensure adequate power. The average number of visits to rural health centers and health posts by the target population was assumed to be 50 and 100 per month, respectively, based on the data obtained from the abovementioned medical records. Therefore, two health facilities per type were selected to collect the necessary samples over four months. Thus, targeted facilities were randomly selected for each facility type using computer-generated random numbers as follows: one first-level hospital (1 of 1), one urban health center (1 of 1), two rural health centers (2 of 11), and two health posts (2 of 11).

For data collection, surveyors visited the targeted health facilities twice: just before the intervention and four months after the intervention. Using a structured data collection template developed for this research, the data were obtained retrospectively for the past four months from all medical records, that recorded OPD visits among the target population. This template covered demographic information, HTN status, and items related to standard clinical practices for HTN services, including BP screening, HTN diagnosis, and prescription of HTN medication. All data were collected over 8 months from May to December 2017, as the 2016 data from the Chongwe District Health Office indicated that the number of OPD visits for HTN did not have seasonal fluctuations. In addition, each OPD visit for HTN services was categorized as "first visit" or "revisit". Revisits were defined as multiple OPD visits for HTN treatment within the past 3 months at the targeted health facilities. Other cases were defined as first visits.

Interventions

Interventions to strengthen HTN service provision at the health facility level were implemented throughout the Chongwe district, as part of the Project for Strengthening Basic Health Care Services Management for Universal Health Coverage (the BHC for UHC Project) beginning from September 2017. These interventions consisted of HTN service training for health staff. Previously, standardized training materials for HTN services were not available in Zambia. Therefore, we spent a year developing a national training course with the MoH and experts in Zambia, by referring to Zambia's 2016 Standard Treatment Guideline (STG) (*18*) and WHO's Package of Essential Non-communicable (PEN) disease interventions for primary health care in low-resource settings (*10*). The training materials included an overview, prevention, screening, and treatment of CVDs. The risk assessment of HTN was guided only by the BP level to simplify the HTN management protocol considering the local capacity in Zambia. The training materials included lectures, case studies, demonstrations, and practicums. A two-day off-site training was provided

to 109 health staff, responsible for HTN services at primary health facilities in the Chongwe district, by nine Zambian specialists in internal medicine, who in turn had received three days of off-site training to become trainers. All essential medical equipment and medicines for HTN services were available in Chongwe district during the study period.

Analytic approach

Analysis of staff performance

The primary outcome of this study was to understand the quality of clinical practice, based on consistency with the established criteria for BP screening and prescription of HTN medications. These outcomes were calculated by analyzing data obtained from observations during set periods (pre-intervention, the first four months from May to August; and post-intervention, the second four months from September to December) and by comparing the results of the two observation periods.

BP was measured by auscultatory methods using a BP machine or sphygmomanometer, with the patient in the sitting position, with the back and the legs supported. Loss of follow-up was frequent and the diagnosis of HTN could not be re-confirmed during additional visits, as recommended by the WHO HEARTS Technical Package (*19*).

According to the STG (*18*), all adult patients aged greater or equal to 40 years who visit an OPD should undergo BP screening. Therefore, the quality of the BP screening was evaluated by dividing the number of BP screenings performed, by the total number of OPD visits by the target population. The number of visits that included BP screening was determined by the number of OPD visits during which BP was measured, as noted in the medical records. The quality of practice for HTN treatment was represented by the number of HTN medications among patients diagnosed with grade 2 (mild; systolic BP ≥ 160 mmHg or diastolic BP ≥ 100 mmHg) or grade 3 HTN (moderate; systolic BP ≥ 180 mmHg or diastolic BP ≥ 110 mmHg). HTN treatment was defined as the prescription of HTN medication in the medical records. According to STG (*18*), HTN medication should be prescribed to patients with grade 1 HTN (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg) if the HTN level persists for 3 months, even after lifestyle modification through counseling by nurses or clinical officers. Counseling addressed the four risk factors for CVDs: unhealthy diet, harmful use of alcohol, tobacco use, and insufficient physical activity. In contrast, pharmaceutical treatment should be considered immediately for all patients with grade 2 or 3 HTN. Compatibility with HTN treatment criteria was difficult to judge in patients with grade 1 HTN because many medical records had no clear history of lifestyle modifications, even when patients received relevant instructions from their clinicians during consultation. Therefore, the quality of staff performance in terms of HTN medications was investigated only for OPD visits of patients diagnosed with grade 2 HTN or above.

In addition, the proportions of other HTN practices were calculated, to evaluate the effects of the abovementioned interventions in HTN services. HTN practices included HTN diagnosis and treatment, which are the standard practice components outlined in the STG (*18*). HTN diagnoses were counted, if the BP range exceeded the criteria of grade 1 HTN according to the STG (*18*), that is, systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg.

Analysis of HTN medication use

The use of HTN medications was calculated based on the data obtained from the data collection registry. The number of pills prescribed was not properly recorded in the patients' medical records, so it was assumed that patients received 30 pills per visit. This was in accordance with the STG instructions, that patients with HTN should receive pills at monthly follow-ups (*18*). To calculate costs, the unit prices for key HTN drugs were obtained from the Medical Store Limited (MSL) Catalogue 2016 (Table 1). The incremental consumption and costs of HTN medications were estimated for the post-intervention period and compared with those of the pre-intervention period. The expected monthly use and costs of these medications were estimated for Chongwe district under the assumption, that the results from one health facility would be applicable to other facilities of the same type.

Analysis of HTN service costs

The unit costs of OPD services obtained from a previous study conducted in Chongwe District (*20*), were used

Table 1. Unit costs of HTN medications

Medications	Strength	Pack size, pills	Pack cost, USD
Nifedipine	20 mg	1,000	9.25
Amiloride + hydrochlorothiazide (Moduretic)	5 mg/50 mg	1,000	3.01
Enalapril	10 mg	1,000	2.67
Atenolol	50 mg	1,000	1.78
Propranolol	40 mg	1,000	2.53
Frusemide	40 mg	1,000	3.01

Source: The Medical Store Limited (MSL) Catalogue 2016. HTN, hypertension.

Table 2. Unit costs (excluding variable costs) by health facility type

Types	OPD costs, USD	Laboratory costs, USD
First Level Hospital	14.1	3.4
Health Center (urban and rural)	2.6	1.75
Health Post	3.3	0.3

Source: Study on the Unit Costs of Health Services Provided at Hospitals and Health Centres in Lusaka and Southern Provinces, Zambia (*Ref. 20*). OPD, outpatient department.

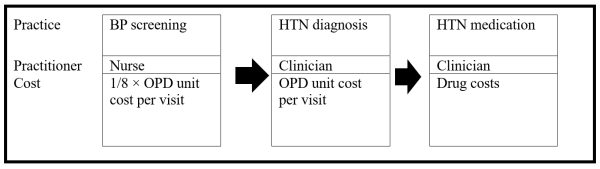

Figure 1. Practice flow for HTN service. Formula: HTN service cost = (OPD unit cost) × (number of visits with BP screening) × 0.125 + (OPD unit cost) × (number of visits with HTN diagnosis) + ∑{(unit cost of HTN medication) × (number of visits with HTN medication prescription) × (number of prescriptions for HTN medications per visit)}. BP, blood pressure; HTN, hypertension; OPD, outpatient department.

to estimate the labor and capital costs per OPD, and the laboratory visits (Table 2). Fixed costs included capital and labor costs for HTN services, and variable costs included costs for drugs, reagents, and other necessary consumables for HTN services. The total costs for HTN clinical services (BP screening, HTN diagnosis, and medication), including variable costs, were calculated for each health facility type using Figure 1 and the formula given below. The unit cost of BP screening was estimated to be one-eighth of the OPD unit cost, as the time spent on BP screening was found to be one-eighth of the total OPD consultation, on average, in a time-motion survey conducted during this study. While the practitioners for different services in Chongwe district varied, the service providers at health facilities were generally clinical care officers, rather than medical doctors. According to previous research (*20*), the salaries of clinical care officers and nurses were similar, and it was assumed that the unit cost per BP screening depended only on the differences in the time spent for each practice. The costs of each HTN service components were summed for the pre- and post-intervention periods for each health facility type, and the unit cost per OPD visit for HTN services was calculated, as the total costs divided by the number of HTN diagnoses. The total costs for HTN services in Chongwe district were estimated from the costs for each facility type, under the assumption that the average costs for HTN services at one health facility would be applicable to other facilities, of the same type. Finally, to evaluate the cost-effectiveness of prescribing HTN medications for eligible patients, the incremental number of HTN medication prescriptions for those with HTN grade 2 or above, was estimated for the Chongwe district as a whole, and the costs per HTN treatment were calculated.

Statistics

All variables were analyzed using STATA version 14 and Microsoft Excel 2013. Statistical differences were evaluated using a multilevel regression model with restricted maximum likelihood estimation (REML) and Kenward-Roger correction for small samples (*21*). Statistical significance was set at p-values of < 0.05. Discounts and inflation were not considered in the cost estimations because the research period was less than one year. Costs were reported in USD using the currency exchange rate as of June 2016 (1 USD = 10.59 Zambian Kwacha).

Ethics

Ethics approval was obtained from the University of Zambia Biomedical Research Ethics Committee (No. 006-04-17) and the Ethics Committee of the National Center for Global Health and Medicine in Japan (No. 3288). The study used only patient information available in the medical records, hence, written consent was not obtained from individual participants. Instead, a participation information sheet explaining the study objectives and research methods was attached to the walls at all target sites during the study period. The staff measuring BP explained the information sheet verbally, allowing the patients to opt out of participation in the study. If the patients wanted to stop participation at any time during the study, they could contact the heads of the nearest target health facility or directly call the office of the principal investigator, to convey their intention.

Results

Characteristics of OPD visits

Descriptive statistics for OPD visits among the included patients during the study period are shown in Table 3. The total number of visits was 3,774 and the average patient age was 55.0 years. There were no refusal cases. These values were similar in the pre- and post-intervention periods. Men accounted for 41.3% of the sample population. The number of OPD visits by health facility type was 1,373 for the first-level hospital, 1,733 for the three targeted health centers, and 668 for the two targeted health posts.

Practices of the HTN services

Table 4 describes the key HTN services (BP screening, HTN diagnosis, and prescription of HTN medications) provided by the staff. The proportion of OPD visits at which key services were provided increased significantly

Table 3. Characteristics of OPD visits, pre- and post-intervention

Characteristics	Full study period	Pre-intervention	Post-intervention
Total visits, *n*	3,774	1,770	2,004
Average age, years (95% CI)	55.0 (54.7–55.4)	54.9 (54.3–55.4)	55.2 (54.6–55.7)
% male (95% CI)	41.3% (40.0–42.8)	42.5% (40.2–44.8)	40.1% (38.0–42.3)
Revisits for HTN, *n*	421	216	205
First Level Hospital visits, n	1,373	609	764
Health Center visits, *n*	1,733	848	904
Health Post visits, *n*	668	332	336

CI, confidence interval; HTN, hypertension.

Table 4. Visits with HTN clinical practices, pre- and post-intervention

Visits	Full study period	Pre-intervention	Post-intervention	*p* value
Total visits, *n*	3,774	1,770	2,004	N/A
BP screening visits, *n* (%)	2,250 (59.6%)	810 (45.8%)	1440 (71.9%)	< 0.05
HTN diagnosis visits, *n* (%)	1,111 (29.4%)	474 (26.8%)	637 (31.8%)	< 0.05
HTN medication visits, *n* (%)	670 (17.8%)	252 (14.2%)	418 (20.9%)	< 0.05

BP, blood pressure; HTN, hypertension.

Table 5. Visits with HTN medications by HTN grade, pre- and post-intervention

HTN grade	Pre-intervention		Post-intervention		*p* value
	Total visits, *n*	HTN medication visits, *n* (%)	Total visits, *n*	HTN medication visits, *n* (%)	
Unknown	960	27 (2.8%)	960	27 (2.8%)	< 0.05
Normal	336	21 (6.3%)	336	21 (6.3%)	0.934
Grade 1	218	55 (25.2%)	218	55 (25.2%)	0.890
Grade 2	136	68 (50.0%)	136	68 (50.0%)	< 0.05
Grade 3	120	81 (67.5%)	120	81 (67.5%)	< 0.05

HTN, hypertension.

after the interventions, from 45.8% to 71.9% for BP screening, from 26.8% to 31.8% for HTN diagnosis, and from 14.2% to 20.9% for prescription of HTN medication. The results were similar after stratification by the first visit and the revisit (Supplemental Tables S1 and S2, *https://www.ghmopen.com/site/supplementaldata.html?ID=83*).

Table 5 presents details of HTN medications prescribed at OPD visits in the pre- and post-intervention periods. The proportion of OPD visits at which HTN medication was prescribed did not differ significantly pre- and post-intervention among patients with normal BP or grade 1 HTN. In contrast, this proportion increased significantly from 68.3% to 86.0% among patients with grade 2 HTN or above after the interventions, as more health staff began following the HTN medication protocols given in the STG (*18*). As shown in Supplemental Tables S3 and S4 (*https://www.ghmopen.com/site/supplementaldata.html?ID=83*), these results were similar after stratification by first visit and revisit. However, the proportion of OPD visits at which HTN medication was prescribed without BP screening increased significantly after the interventions, even among first visits, despite being against the standard protocols (*18*).

HTN medication use

Types of HTN medication

Table 6 and Figure 2 show additional details of the HTN medications by drug type. While the proportion of OPD visits at which nifedipine or moduretic were prescribed increased significantly after the intervention, prescriptions of atenolol, propranolol, or frusemide significantly decreased. This may provide evidence for improved compliance with the standard HTN medication protocol (*18*) used in HTN training.

Estimated use of HTN medications

Supplemental Tables S5, S6, and S7 (*https://www.ghmopen.com/site/supplementaldata.html?ID=83*) describe the average monthly use and costs of HTN medications in first-level hospitals, health centers, and health posts, respectively. The l monthly average costs for HTN medications for each health facility before and after the interventions were $9.95 and $15.55 for the first level hospital, $1.06 and $4.44 for health centers, and $0.08 and $0.81 for health posts, respectively. As

Table 6. Visits with HTN drugs, pre- and post-intervention

Drugs	Pre-intervention		Post-intervention		*p* value
	n	%	*n*	%	
Nifedipine	126	50.0%	331	79.2%	< 0.05
Moduretic	73	29.0%	181	43.3%	< 0.05
Atenolol	60	23.8%	35	8.4%	< 0.05
Propranolol	24	9.5%	9	2.2%	< 0.05
Enalapril	6	2.4%	46	11.0%	< 0.05
Furosemide	57	22.6%	50	12.0%	< 0.05
Total	252		418		

HTN, hypertension.

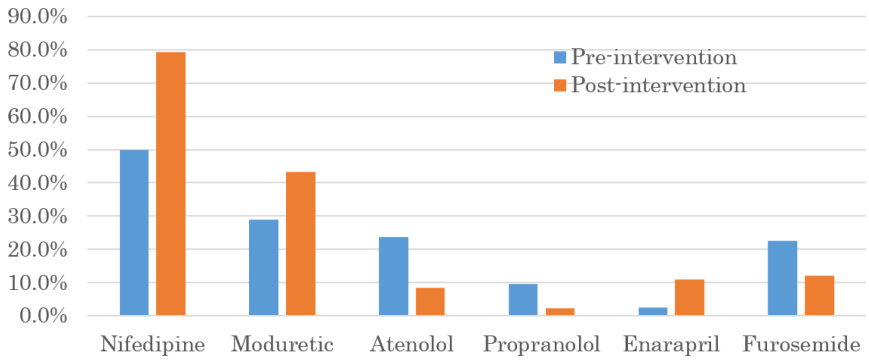

Figure 2. Percentage of outpatient department visits receiving each type of HTN medication among visits receiving any HTN medication, pre- and post-intervention.

Table 7. Estimated monthly average use and costs of HTN drugs in the Chongwe district

Drugs	Unit price, USD/pill	Pre-intervention		Post-intervention	
		Pills used, *n*	Cost, USD	Pills used, *n*	Cost, USD
Nifedipine 20 mg	0.00925	1,462.5	13.53	6,352.5	58.76
Moduretic	0.00301	1,256.8	3.81	4,669.3	14.15
Atenolol	0.00178	1,012.5	1.80	397.5	0.71
Propranolol	0.00253	540	1.37	247.5	0.63
Enalapril	0.00267	45	0.12	712.5	1.90
Furosemide	0.00301	832.5	2.51	465	1.40
Total			23.13		77.54

Assumptions for analysis: Unit prices for each drug were obtained from the Medical Store Limited Catalogue 2016. Material costs were calculated under the assumption, that a one month supply of drugs was prescribed (30 pills per visit). There are 12 health centers, 11 health posts and one first level (district) hospital in Chongwe. HTN, hypertension.

shown in Table 7, the estimated monthly average costs of HTN medications in Chongwe district were $23.59 pre-intervention and $77.8 post-intervention.

Estimated cost of HTN services

Supplemental Tables S8, S9, and S10 (*https://www.ghmopen.com/site/supplementaldata.html?ID=83*) describe the monthly average costs for HTN services in Chongwe district by health facility type. The monthly average costs (variable costs) for HTN services pre- and post-intervention were $1331.67 ($9.79) and $1,363.24 ($15.36) for the first-level hospital, $40.25 ($1.17) and $87.83 ($4.44) for Health Centers, and $8.29 ($0.08) and $21.41 ($0.89) for health points, respectively. Table 8 shows the fixed and variable unit costs per OPD visit with an HTN diagnosis: $16.95 and $17.51 for the first-level hospital; $3.38 and $3.91 for health centers; and $3.67 and $4.20 for health posts, respectively. As shown in Table 9, the estimated monthly average costs (variable costs) for HTN services in Chongwe District were $1,904.62 ($23.89) pre-intervention and $2,643.46 ($69.53) post-intervention. Table 8 also describes the estimated post-intervention unit cost per HTN medication prescription, among OPD visits with HTN of grade 2 or above. The incremental number of visits at which HTN medications were prescribed among patients with grade 2 or 3 HTN and the incremental post-intervention costs were 120.0 visits and $738.84, respectively. Therefore, the post-intervention unit cost required to prescribe HTN

Table 9. Estimated monthly average costs for HTN service and number of OPD visits with medication prescription in the Chongwe district

Values	Pre-intervention costs, USD	Post-intervention costs, USD	Incremental cost, USD
Total Cost	1,904.62	2,643.46	738.84
Fixed Cost	1,880.73	2,572.93	693.20
Variable Cost	23.89	69.53	45.64
No. of OPD visits with HTN treatment and HTN grade 2 or above	63.1	183.1	120.0
Medication prescription cost per visit			6.16

Assumptions for analysis: Fixed cost includes capital costs and labor costs for HTN service. Variable cost includes costs for drugs, reagents, and other necessary consumables for HTN services. There are 12 health centers, 11 health posts, and one first level (District) hospital in Chongwe. HTN, hypertension.

Table 8. Unit cost per visit with an HTN diagnosis, by health facility type

Types	Pre-intervention cost, USD	Post-intervention cost, USD
First Level Hospital	16.95	17.51
Health Center (urban and rural)	3.38	3.67
Health Post	3.91	4.20

HTN, hypertension.

medication for one person with HTN grade 2 or above was $6.16 per visit.

Discussion

We conducted training on HTN service provision for health staff in Chongwe district and evaluated the effects on the quality of clinical practices for HTN services. The results showed that proportion of eligible people who received BP screening and HTN drug therapy for secondary prevention significantly improved post-intervention. Additionally, the rates of key HTN service practices (HTN diagnosis and treatment) designated by Zambia's STG (*18*) significantly increased during the post-intervention period. While it was difficult to set the expected cutoffs of these indicators owing to the lack of any guidelines and previous data, the significant increases suggest that training led to improvements in HTN practices in terms of identifying more HTN cases and providing treatment. These indicators for evaluating staff performance in HTN service provision were selected by considering the NCD Global Monitoring Framework (*22*), which includes the target of "at least 50% of eligible people receive drug therapy and counseling to prevent heart attacks and strokes". While a population-level study was not feasible due to limited resources and because counseling history was not evaluated, HTN medications for grade 2 and grade 3 HTN patients at the facility level were assessed in this study. The key HTN practices of BP screening, HTN diagnosis, and HTN treatment were monitored as measures of health system performance, similar to the indicators referred to as the HTN care cascade in a previous study (*23*).

There are several challenges in achieving high-quality HTN services. First, BP screening rates were suboptimal, even after the interventions. Although Zambian guidelines indicate that BP screening should be conducted for all OPD patients aged greater or equal to 40 years (*18*), the prevalence of these practices was still as low as 71.9%. Second, pharmacological HTN treatment was received by 80% of patients with grade 2 HTN and 94.3% of those with grade 3 HTN. Moreover, the proportion of HTN medications among patients with normal BP did not significantly change, and 4.2% of patients with normal BP received HTN drugs even after intervention. We observed that some healthcare staff prescribed medications only for HTN-related symptoms. Even in first-visit cases, this proportion did not significantly change (Supplemental Table S3, *https://www.ghmopen.com/site/supplementaldata.html?ID=83*). These results suggest that there is scope for improvement in the HTN service quality. Third, the number of Revisits was similar throughout the study period, despite the fact that the number of patients receiving HTN medications significantly increased. This finding indirectly suggests a high follow-up dropout rate because the number of revisits should accumulate if all patients taking HTN medications receive follow-up, as recommended. Therefore, the capacity of health staff should be increased, and the health system should be strengthened to allow such patients to regularly visit health facilities. Finally, our results suggest that health facilities were not accessed by a large proportion of the population who required HTN medication. Considering that 19.1% of the adult population in Zambia has elevated BP[13] and 15% of the total population in the Chongwe district was greater or equal to 40 years during the study period (*24*), approximately 6,000 adults requiring HTN medication and monthly follow-up was expected in the sampled district. However, there were only an estimated 418 monthly OPD visits by patients with elevated BP in Chongwe district post-intervention, suggesting that many people in need of HTN medication did not access the health facilities. Therefore, community awareness of HTN should be improved to encourage the extensive use of HTN services.

There have been concerns about the incremental costs of HTN treatment owing to the increased number

of patients with HTN visiting health facilities as a result of improved awareness. The budget impact of these interventions could be substantial given that NCDs are generally chronic diseases that require long-term treatment. Our analysis showed that the estimated monthly costs required for Chongwe District were $1,905 ($23.90, variable costs) pre-intervention and $2,643 ($69.50, variable costs) post-intervention. As all fixed costs and most variable costs are covered by the Zambian government, Chongwe District is responsible for only a portion of the variable costs. Therefore, the estimated costs of HTN services appear affordable based on this research, even after the interventions, considering that the provisions in the 2018 Chongwe District Health Office budget was approximately $270,000 (*25*). Post-intervention incremental costs per visit, excluding intervention costs, were estimated at $6.16. These figures should still be fairly affordable, given that the Zambian gross domestic product was $1,509.80 per capita in 2017 (*26*). Therefore, policymakers should secure the necessary budget to cover the costs of HTN services according to these estimates for interventions to improve the performance of HTN clinical practices.

This study has several limitations. First, the BP data in the medical records may not be reliable due to various reasons discussed below. There may be concerns regarding the skills of health workers in measuring BP using sphygmomanometers, especially before the intervention. However, most health staff already knew how to manually screen for BP because they had been trained to use a stethoscope and sphygmomanometer in other programs, including those for HIV/AIDS and maternity services. Therefore, an increase in BP screening and HTN diagnosis may reflect an improvement in the knowledge of HTN management. In addition, the appropriateness of the BP measurement procedure could not be monitored during each patient visit. The training course covered the methods of BP measurement by the BP monitoring machine as well as the sphygmomanometer, including practices to make sure that patients wait at least five minutes after sitting, that BP is measured twice in one-two minute intervals, and that the average BP is calculated. However, we could not monitor the details of the procedure, even post-intervention, owing to the limited resources available for this research. Therefore, we could not ensure that accurate BPs measurements were obtained and recorded in medical records. However, patients usually needed to wait for a minimum of 30 minutes before receiving consultation in Zambian health facilities, and almost all health staff members were familiar with the sphygmomanometer during training. Therefore, we surmise that the BP data is reliable.

Second, we randomly selected six health facilities of different types to ensure generalizability within the Chongwe district. However, our results may not be fully applicable to other regions of Zambia, such as urban areas or districts further away from the capital city. Further research is required to investigate the generalizability of the present results to other regions of Zambia.

Third, because the follow-up of individual patients with HTN was difficult owing to the poor quality of medical records, health staff performance was evaluated based on OPD visits. Individual patient records should be analyzed to fully evaluate the quality of HTN service provision, as appropriate practices for HTN patients vary between the first and subsequent visits. In addition, BP screening should be conducted for all OPD patients, and HTN medications should be prescribed for all patients diagnosed with grade 2 HTN or higher according to the Zambian treatment guidelines. Therefore, the staff performance of these practices could be evaluated by the OPD visit history, regardless of the first visit or revisit status. In addition, only visits by patients diagnosed with grade 2 or 3 HTN were evaluated for the provision of HTN medications, as the unavailability of individual histories made it difficult to judge compatibility with treatment criteria among patients with grade 1 HTN.

Fourth, the duration of the study was only eight months. While the samples of OPD visits were sufficient for the analysis of staff performance to assess the short-term effects of training on the capacity to manage HTN, the study was not long enough to observe follow-ups for patients diagnosed with HTN, and to evaluate the durability of training effects. A longer study period is necessary to develop more effective strategies to strengthen HTN services from a long-term perspective. However, we found that the improvement of HTN practice was not sufficient even four months after pre-intervention, including the prescription of medications for grade 2 & 3 HTN and unnecessary medication for people with normal BP. We believe that these findings could be useful when considering the points of emphasis during the training for HTN. In addition, cost analysis, including intervention costs, was not considered because the intervention effects were evaluated only for the first four months post-intervention. Post-intervention incremental costs could be lower, if the follow-up period is longer.

Fifth, the unit-cost data obtained from previous research had several limitations, including missing data and small sample sizes. We found that the MSL Catalogue prices were lower than the market prices. A unit cost survey should be conducted using larger samples in Zambia to improve generalizability, and the results of the present analysis may require adjustment if the unit cost data change in the future.

Finally, this study did not evaluate the effectiveness of HTN treatment on patients' clinical presentations, such as BP level, complications, and mortality. Geldsetzer *et al.* (2019) evaluated health system management performance for HTN in 44 low- and middle-income countries using an HTN care cascade, including HTN

diagnosis and HTN treatment, and the final indicator for evaluating performance was the outcome of treatment to control HTN. The clinical effects need to be scrutinized for different HTN risks. To truly evaluate the cost-effectiveness of HTN interventions, further studies should utilize data on clinical effects together with the costs and utility values for mathematical modeling (*e.g.*, a Markov model). The aim should be to project HTN management costs and secure utility values in the Zambian setting to arrive at policy implications for NCD strategies at the primary level, similar to Robberstad *et al.*'s study on the cost-effectiveness of HTN in Tanzania (*27*). Furthermore, although there are evidence-based clinical guidelines for HTN in Zambia, the sustainability of local-level applications is challenging due to limited resources to ensure quality services. Therefore, cost-effective health system modifications, such as integration with other chronic diseases, such as HIV, should also be addressed, similar to those introduced by Gimbel in Mozambique (*28*).

Conclusion

This study used medical records to investigate the staff performance in delivering HTN services at health facilities in rural Zambia. The rate of adherence to standard clinical practices among health staff at the target sites increased after the implementation of interventions, that included training and procurement of necessary medical devices. However, the quality of HTN services, including risk screening and pharmacological treatment, can be improved. To improve and sustain the quality of their performance, program managers should consider additional interventions, such as periodical training, mentorship, and online education.

The estimated monthly cost of HTN services was $2,643 for the target district, post-intervention. As most of the expenditures were fixed costs covered at the national level, the district-level costs amounted to $69.53. Therefore, when implementing interventions, policymakers should secure a budget to cover the costs of HTN services based on the results of research to improve the performance of clinical practices for HTN at the facility level. However, a large proportion of the population in need of HTN medication did not access any health facilities during the study period, indicating that, outreach to improve community awareness of HTN is necessary to increase access to HTN services among eligible individuals. Further investigation is necessary to examine the expected effects and costs for providing HTN services.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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Unit costs of health services provided at hospitals and health centres in two provinces of Zambia

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Abstract: In Zambia, information on cost of services provided at health facilities are deficient. This study aims to contribute to fill this knowledge gap by estimating the unit costs of health services provided at different levels of health facilities. This costing exercise used cross-sectional data for the year 2016. Fourteen facilities were purposefully selected to represent different levels of health facilities and mix of characteristics. We used an accounting-based approach to calculate the unit costs of health services. Specifically, we employed the top-down approach to allocate total overhead costs incurred over to different services that were provided at the facility. Full costs of health facilities varied substantially between different levels, and even between facilities within the same level (particularly between health centres). The compositions of cost items within any facility were largely dominated by labour and material costs, each of which contributing approximately half the shares, whilst the proportion of capital costs remained small irrespective of the levels. Unit costs of outpatient services in the health centres ranged from ZMW 15 (USD 1.3) to ZMW 30 (USD 2.7) without medical consumables, while inpatient costs were between ZMW250 (USD 22.2) and ZMW 1,300 (USD 115.6) per admission and ZMW 140 (USD 12.4) to ZMW 500 (USD 44.4) per bed-day. Unit costs between services provided at the same facility exhibit fairly comparable pattern. The findings from this study provides useful information of unit costs for referencing in future studies. Further, the variations of unit costs among facilities with different characteristics provides policy relevant information for health administrators and policy makers.

***Keywords*:** unit costs, health services, top-down, Zambia

Introduction

The Ministry of Health in Zambia (MOH) launched the National Health Care Package (NHCP) in 2016 which specified the basic and essential health care packages to be provided at different levels of health care. Zambia spends between 7 and 8% of its total national budget on health. In 2020, the total health expenditure amounted to USD 1,017 million which was about 5.6% of gross domestic product (GDP), and health allocation from the government's domestic revenue was USD 442 million, approximately 7% of general government expenditure and 2.4% of GDP (*1*). This falls short of the recommended government health expenditure (*i.e.*, at least 5% of GDP) (*2*), and remains unknown what extra resources are needed in providing services included in the NHCP since the package was not costed. Cost information of health services provide critical intelligence for health administrators for planning and budgeting process. Without such information, planners are not able to make appropriate budgeting and allocate health resources to health facilities and services in an efficient way. In Zambia, health care costs have not been examined rigorously, up-to-date information on unit costs of health services are critically deficient.

Unit costs of health services are context-specific that is affected by multiple factors, and hence is not appropriate to assume the same cost information to be applicable from other countries. Therefore, it is critical to calculate the costs of health services in Zambia. Cost information can be used in various aspects of policy decisions: allocating resources to health facilities and services, calculating user fees where relevant, assessing relative efficiency of health care services in economic evaluation, and overall budgeting (*3-6*). In Zambia, information on unit costs could potentially be used for the costing of NHCP, National Health Strategic Plans (NHSP), National Health Insurance (NHI) services

and Medium Term Budget Frameworks (MTBF) particularly for services provided at the first level and below for which information is critically missing.

This study was conducted as part of an overarching technical assistance project undertaken by the MOH in collaboration with Japan International Cooperation Agency, which aimed to develop the managerial capacity of provincial and district health authorities in selected geographic areas: Lusaka and Chongwe Districts from Lusaka Province, and Choma and Kalomo districts of Southern Province (*7*). The aim of the study was twofold: first to estimate the unit costs of health services provided at different levels of health facilities in the target districts; and secondly, to compare the unit costs between facilities that have different characteristics. The study sample was purposefully selected to cover different levels and mix of characteristics including urban *vs.* rural, large *vs.* small, and high *vs.* low-volume caseload of specific services (birth, diagnostic services, *etc.*) at different levels. One health post, eight health centres, three first-level hospitals and two third-level hospitals were selected for the cost analysis. Table 1 lists the health facilities that were included. The study was cross-sectional using data from the year 2016. The currency rate adopted was 1 USD = 11.25 Zambian Kwacha (ZMW) in June 2016.

Materials and Methods

There are broadly two approaches that have been popularly used to estimate costs within healthcare: top-down and bottom-up (*8*). Top-down assigns and allocates total overhead costs incurred over a given time period to different services that are provided at a facility using a predefined set of rules (*9,10*). Bottom-up approach relies on detailed activity and input data at the service provider level to estimate unit costs (*11*). While an alternative bottom up method has been reported to produce more accurate estimates (*12*), it is also considered more time demanding, specific to the setting and expensive to undertake (*13,14*). In the context of this study, we opted for the top-down approach. Under this approach, there were various steps involved in the assignment and allocation of costs into various cost centres including administrative services, ancillary services, patient services and non-patient services. Figure 1 provides the sequence of how costs were assigned and allocated to different cost centres.

The analytical process comprised three steps: defining cost centres; determining direct costs; and allocating direct costs to intermediate and final cost centres.

Step1: Defining cost centres

This process was conducted by discussing with various stakeholders including officials from the District Health Offices (DHOs) such as the Planners, Human Resource Officers and Information Officers, and members from the hospitals (Administrators and Information Officers). Table 2 provides the list of identified cost centres.

Step 2: Determining direct costs

In this step, each cost item was assigned to a specific cost centre by certain rules to establish the "total direct cost" of each cost centre. Some of the cost items were straight forward in assigning to a cost centre, while others were more complicated. For instance, the cost of a drug that was used for anti-retroviral treatment (ART) were assigned to the cost centre "ART service". On the other hand, when assigning the cost of utility such as electricity and water, it was not immediately obvious how much of the total amount was used for which cost centre. For such items, a certain rule must be predefined how to assign the costs to each cost centre (*e.g.*, proportionally based on the floor space of each cost centre). The following sections divide the cost items into three broad categories (*i.e.*, labour cost, material

Table 1. Health facilities included in the study

Province	District	Health facility	Type of facility
National	Lusaka	UTH, Paediatrics Hospital	Third-level
	Lusaka	UTH, Women & Newborn Hospital	Third-level
Lusaka	Lusaka	Chilenje Hospital	First-level, urban
	Chongwe	Chongwe Hospital	First-level, peri-urban
	Lusaka	Mtendere Health Centre	Urban, large
	Chongwe	Chongwe Health Centre	Urban, medium-size
	Chongwe	Kanakantapa Health Centre	Zonal, medium-size
	Chongwe	Shiyala Health Post	Rural, small
Southern	Kalomo	Kalomo Hospital	First-level, rural
	Choma	Shampande Health Centre	Urban, medium-size, lab high-volume
	Choma	Mapanza Health Centre	Zonal, medium-size
	Choma	Popota Health Centre	Rural, small
	Kalomo	Chilala Health Centre	Zonal, medium-size
	Kalomo	Kanchele Health Centre	Rural, small, birth high-volume

UTH: University Teaching Hospital.

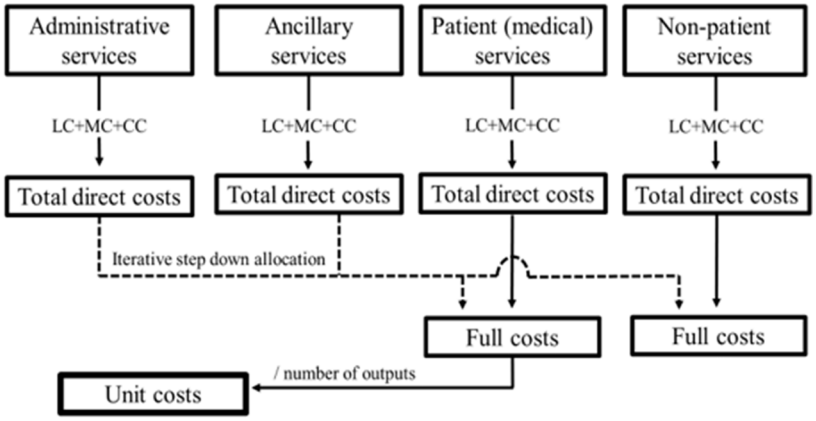

Figure 1. Conceptual framework of assignment and allocation of health facility costs.

Table 2. List of cost centres

Service	Health centre/health post	First level	Third level (paediatrics)	Third level (women & new born)
Admin	Administration	Administration	Administration	Administration
	General work	Human resource	Human resource	Human resource
		HMIS	HMIS	HMIS
		Account	Account	Account
		Procurement	Procurement	Procurement
Ancillary	Pharmacy	Pharmacy	Pharmacy	Pharmacy
	Laboratory	Laboratory	Laboratory	Laboratory
	Labour room	Labour room	Radiology	Labour room
	Operating room	Operating room		Operating room
		Radiology		Ultrasound
Patient (outpatient)	OPD general	OPD general	OPD paediatrics	ANC/PNC
	ART	ART		PMTCT
	ANC/PNC	ANC/PNC		Neonatal
	Under five	Family planning		
	Family planning	Nutrition		
	Nutrition	TB		
	TB	Surgery		
	Surgery	Dental		
	Dental	Physiotherapy		
	Physiotherapy			
Patient (inpatient)	IPD general	IPD general (male)	IPD paediatrics	Obstetrics
	Obstetrics	IPD general (female)	PICU	Gynaecology
	Paediatrics	Obstetrics	Nutrition	Neonatal
		Paediatrics	TB	NICU
			Special (kidney)	
Non-patient	Environ. health	Environ. health		
	Outreach	Outreach		

ANC: antenatal care; ART: anti-retroviral therapy; HMIS: health management and information system; IPD: inpatient department; NICU: neonatal intensive care unit; OPD: outpatient department; PICU: paediatric intensive care unit; PMTCT: prevention of mother to child transmission; PNC: postnatal care; TB: tuberculosis.

cost and capital cost) and provide details of how each cost item was assigned.

Labour costs included salary of staff members at health facilities, allowances (housing, transport, hardship, *etc.*) and also daily subsistence allowance (DSA). Salaries were standardised for cadres, so we obtained information about the position of each staff member from the health facilities and matched with the salary specified in the standard salary scale of the MOH. Information on allowances were obtained from the Human Resource section of the DHOs or hospitals. Information on DSA was a major challenge as such information was not recorded in official document or data base. We obtained this information through interviews with individual staff members and In-Charges from the health facilities.

Staff members at health facilities were typically involved in multiple tasks that cut across different cost centres. It was therefore not straight forward to assign individual labour costs to different cost centres. To work out the proportion of contributions of individuals to each cost centre, we interviewed the In-Charges from

each facility or department to provide an estimate of the proportion of time each staff member spent for each service (cost centre). This was not an easy undertaking as such an exercise is prone to a major recall bias. In many cases, estimating the proportion of time spent for each cost centre proved difficult. If the estimates did not seem plausible, we interviewed the individual staff members to verify the estimates provided by the In-Charges. Further, in some cases, adjustments were made by pooling and splitting the total time spent proportions within each of the four-broad cost centre classification (*i.e.*, administrative, ancillary, outpatient, inpatient and non-patient services) based on common units such as number of visits, tests, bed-days, *etc*. This adjustment implicitly assumed that the time spent on each unit of output within the broader cost centre classification was the same regardless of the services provided. This issue was a challenge particularly for smaller facilities (as the staff members were more likely to be engaged in multiple services) than larger ones (where staff members were more specialised and assigned to a specific service centre).

Material costs comprised drug, vaccine, medical and non-medical supplies (< ZMW 1,000 (USD 88.9)), utility, fuel, maintenance of building and equipment. Data for each item came from different sources that are summarised in Supplemental Table S1 (*https://www.ghmopen.com/site/supplementaldata.html?ID=87*).

Amongst the material cost items, utility, fuel, general supplies and general maintenance costs were all assigned to "administration" that became subjects for further allocation to other cost centres in the subsequent steps. Drugs, vaccines and medical supplies were directly assigned to the relevant cost centres where those items were actually used (ancillary, outpatient, inpatient and non-patient services). While the issuance of those items was generally recorded in the stock control cards, information where those items were actually used was almost totally missing. Therefore, the assignment of those items had to rely on certain assumptions. A physician (YY) from the research team was tasked to develop a matrix that specified which drug and supply items were likely to have been used in which cost centres. Based on the matrix, the total quantity of each drug and item was proportionally assigned to each identified cost centre based on the number of outputs (test, visit, and bed-day). On the other hand, the cost centres were self-evident for some drugs and supplies such as those for ART, TB treatment or malaria diagnosis.

One major challenge related to the quantification of drug consumption was that many stock control cards did not specify the number of tablets, capsules or blisters per container/package. The actual and calculated quantities varied by a factor of 10 or 100 if the correct units were not used. We minimised such errors by asking the pharmacists, referring to the Medical Stores Limited (MSL) catalogue and comparing with the actual number of patients. Prices of drugs were mostly available from the MSL catalogue. In case the price of a drug was not listed in the catalogue, we referred to the International Medical Products Price Guide to obtain the reference price, with preference put on price from South Africa.

Capital costs comprise building, medical and non-medical equipment (≥ ZMW 1,000 (USD 88.9)) amounts above this threshold are considered capital cost) and transport facilities. As capital assets are purchased at one point of time but used over several years, allocation of costs required some computations. We calculated the cost of capital assets for 2016 by means of annuitisation using the following formula (*15*):

$$K = \frac{E(1-(1+r)^{-i})}{r}$$

where K is the cost of a capital asset, E is the equivalent annual cost of the asset (we have solved for this), r is the interest rate and i is the number of useful years of that asset. We assumed 3% for r and obtained information of i from the "Estimated useful lives of depreciable hospital assets" (*16*).

Obtaining price information of capital assets at the time of acquisition proved problematic. Therefore, we decided to use the replacement costs of the assets during the study year (2016). We used the market price of equipment collected in 2017, which was inflation-adjusted for year 2016. Construction costs of building was not available, so we obtained the standard construction cost of a standard health centre to calculate the average cost per square meter from the Department of Physical Plant and Medical Equipment, MOH (calculated as ZMW 350 (USD 31.1) per m^2 in 2017, which was adjusted for inflation). Land cost was not included in the cost estimation as it was very difficult to obtain information of price and difficult to determine the land area of health facilities.

Cost of transport facilities were assigned to "administration". Equipment costs were assigned directly to the cost centre where each equipment was used. Information of the presence and quantity of equipment was obtained from inventory list where applicable, but most information was collected by the enumerators through direct observation and physical counting. Building cost was proportionally assigned to each cost centre based on floor spaces occupied by each cost centre. Floor space of each cost centre was physically measured by the enumerators.

Step 3: Allocating direct costs to intermediate and final cost centres

Once all cost items were assigned to one of the cost centres, the next step was to allocate the overhead costs to the intermediate and final cost centres. A stepdown

method with iteration was employed for this process (*15*). The iterative stepdown approach allocates each overhead cost item (*i.e*., administrative and ancillary services) to all relevant cost centres that benefit from those services based on a pre-defined set of criteria. The criteria for the allocation of each overhead cost item are provided in Supplemental Table S2 (*https://www.ghmopen.com/site/supplementaldata.html?ID=87*).

Step 4: Full cost determination and unit cost calculation

After the allocation of overhead costs, full costs were determined for each cost centre of ancillary services, patient services and non-patient services in the following forms: *i*) with and without variable costs (*i.e.*, drugs, vaccines and medical supplies), *ii*) with and without allocation of costs of ancillary services (for patient and non-patient services).

Unit costs were calculated for all patient services (and for selected ancillary services) by dividing the full costs by the corresponding volume of outputs. The unit of outputs for each service were: *i*) number of visits (for outpatient services), *ii*) number of admissions and bed-days (for inpatient services), *iii*) number of tests, imaging and examination (for laboratory, radiology and ultrasound)

Results

Descriptive statistics of health facilities

Table 3 provides general information of each health facility showing the level of health care, the number of staff attached to the facility and the volume of health services provided in terms of outpatient visits, admissions and laboratory tests conducted.

Full cost and cost breakdown

Figure 2 provides the full costs of health facilities. Full costs of health facilities varied substantially between different levels, first level hospitals incurred higher

Table 3. General information of health facilities

Level of facility	Name of facility	Number of staff	Total number of outpatient visits	Total number of inpatient admissions	Total number of lab tests
Third	UTH (women & newborn)	489	23,041	41,396	39,509
	UTH (paediatrics)	439	30,925	25,079	25,642
First	Chilenje Hospital	167	249,648	6,289	80,902
	Chongwe Hospital	121	23,796	6,042	11,796
	Kalomo Hospital	59	87,975	4,595	15,690
Primary	Mtendere HC	122	222,625	2,501	28,599
	Chongwe HC	29	91,087	307	17,961
	Kanakantapa HC	20	26,465	413	3,774
	Shampande HC	53	52,799	664	40,510
	Mapanza HC	14	29,780	635	4,140
	Chilala HC	9	26,358	641	3,776
	Popota HC	8	12,257	110	1,384
	Kanchele HC	4	34,433	718	5,625
	Shiyala HP	3	6,062	29	3,080

UTH: University Teaching Hospital; HC: health centre; HP: health post.

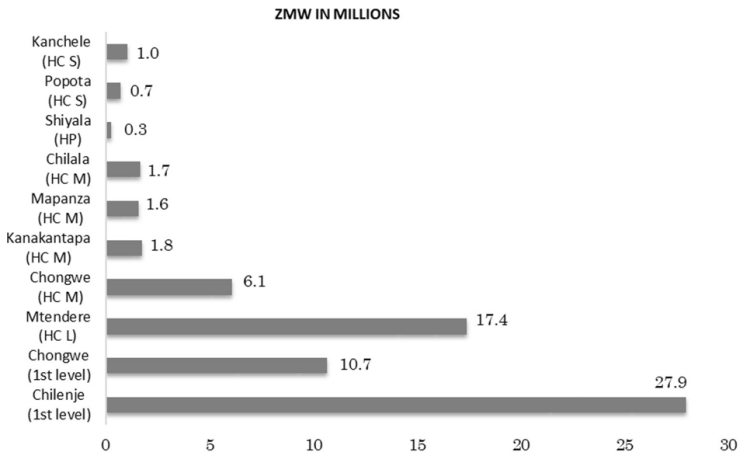

Figure 2. Total costs by facility.

costs and rural health centres the lowest.

A large portion of facility costs at all levels comprised labour and material costs, each of which contributing half the shares, whilst the proportion of capital costs remained small (Supplemental Figure S1, (*https://www.ghmopen.com/site/supplementaldata.html?ID=87*).

However, there were some notable differences between the share of labour and material costs in some facilities. Figure 3 provides the share of each cost item.

A larger portion of costs at Chongwe Hospital and Popota HC comprised labour costs (65%-75%), while material costs dominated in Chongwe HC and Kanchele HC (around 67%). The share of capital costs was generally small at around 10%, yet with variations between 3% and 17%.

Unit cost of health services

The unit costs of health centres and health posts are provided in Tables 4 and 5 for Lusaka and Southern Provinces, respectively. The unit cost of nutritional services at Mtendere HC in Lusaka Province was ZMW 828 (USD 73.6) per patient visit, which was considerably higher than those of other HCs in the same province. The unit cost of surgeries at Mtendere was also higher compared to Chongwe and Kanakantapa HC. Although there were no comparators among HCs, the unit cost of physiotherapy at Mtendere HC seemed substantially high, which was ZMW 1,455 (USD 129.3) per patient visit (this was also substantially higher than the first-level hospitals provided in Table 6 below). Regarding the inpatient care, the unit cost of delivery at Kanakantapa HC was twice as high as that of Mtendere HC and was one and a half times as high as that of Shiyala HP. The unit costs between three HCs and Shiyala HP were more or less similar.

With respect to the HCs in the Southern Province, the unit costs were relatively comparable to those in the Lusaka Province, except for Kanchele HC. Most unit costs, except for ART and surgery, at Kanchele HC were the lowest of all HCs and HPs examined in this

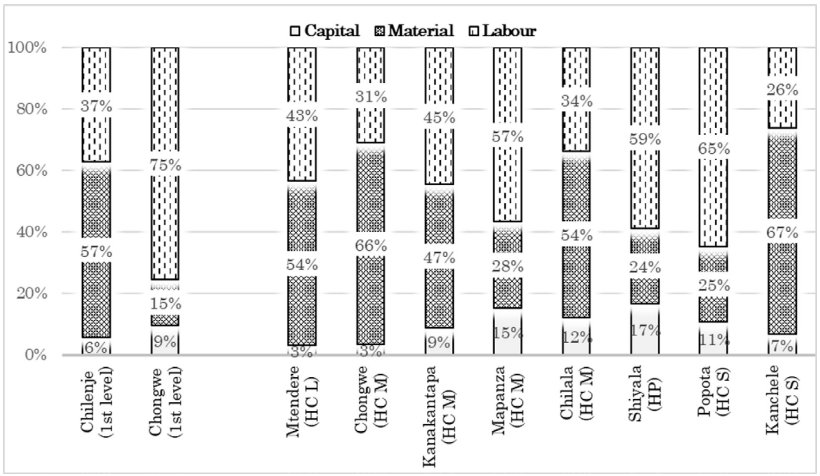

Figure 3. Facility Cost structure based on major line items.

Table 4. Unit costs of services at health centres/posts in Lusaka Province (ZMW)

Service	Unit	Mtendere HC	Chongwe HC	Kanakantapa HC	Shiyala HP
Laboratory	Test	13* (17)**	16 (18)	19 (23)	3 (8)
OPD general	Visit	24 (45)	25 (37)	27 (45)	33 (41)
ART	Visit	19 (105)	17 (103)	18 (125)	59 (78)
ANC/PNC	Visit	55 (58)	26 (28)	22 (24)	30 (36)
Under five	Visit	26 (34)	17 (33)	15 (24)	26 (33)
FP	Visit	24 (36)	17 (25)	15 (25)	26 (33)
Nutrition	Visit	828 (828)	17 (18)	15 (16)	26 (26)
TB	Visit	34 (151)	34 (149)	72 (188)	19 (135)
Surgery	Visit	355 (384)	107 (160)	257 (270)	-
Dental	Visit	89 (92)	-	-	-
Physiotherapy	Visit	1,455 (1,455)	-	-	-
IPD general	Admission/ bed-day	-	440 (490)/409 (455)	449 (471)/263 (276)	-
Obstetrics	Admission/ bed-day	372 (392)	-	780 (791)	468 (523)
Paediatrics	Admission/ bed-day	-	356 (397)/340 (380)	406 (419)/200 (206)	-

OPD: outpatient department; ART: anti-retroviral therapy; ANC: antenatal care; PNC: post-natal care; FP: family planning; TB: tuberculosis; IPD: inpatient department; HC: health centre; HP: health post. *Unit costs without variable costs (*i.e.*, drugs and medical supplies). **Unit costs with variable costs in parentheses. The currency rate was 1 USD = 11.25 Zambian Kwacha

study. For instance, laboratory services at Kanchele HC costed only ZMW 3 (USD 0.27) per test, which was just about 10% of that at Mapanza HC. The unit cost of general OPD was ZMW 15 (USD 1.33) per visit, which was a-third of those in other HCs such as Mtendere, Kanakantapa, or Popota.

The unit costs of first-level hospitals are provided in Table 6. By comparing the results with Tables 6 and 7, the unit costs of outpatient services at HCs and first-level hospitals were comparable, whereas costs of inpatient services were generally higher at first-level hospitals.

A comparison between Chilenje Hospital and Chongwe Hospital revealed that the unit costs at Chilenje Hospital were generally lower than those at Chongwe Hospital. For instance, the general OPD and family planning (FP) in Chongwe hospital costed more than three times of those at Chilenje Hospital. Unit costs at Kalomo Hospital lay somewhere in-between Chilenje and Chongwe Hospitals including laboratory services, OPD general, ART, dental care. On the other hand, some services were considerably more costly at Kalomo Hospital such as TB and surgery while others were less particularly inpatient services.

The unit costs of third-level hospitals are provided in Table 7. Regardless of nature of services, the unit costs at the UTH were higher than those of the HCs or first-level hospitals, with a few exceptions. For instance, the unit costs of ANC/PNC services at the UTH Women and Newborn Hospital were more than six times higher than that of HCs or first-level hospitals. The inpatient TB care at the UTH Paediatrics costed the highest of all unit costs per admission estimated in this study, which was ZMW 5,789 (USD 514.6) per admission. The paediatric intensive care unit (PICU) costed the highest per bed-day, which was ZMW 1,162 (USD 103.3).

Table 5. Unit costs of services at health centres in Southern Province (ZMW)

Service	Unit	Mapanza HC	Chilala HC	Shampande HC	Popota HC	Kanchele HC
Laboratory	Test	28* (31)**	18 (21)	9 (-)	3 (7)	2 (3)
OPD general	Visit	24 (33)	19 (33)	14 (24)	34 (46)	6 (15)
ART	Visit	16 (-)***	17 (99)	27 (32)	-	8 (120)
ANC/PNC	Visit	47 (51)	29 (32)	24 (26)	31 (33)	10 (13)
Under five	Visit	18 (23)	12 (23)	13 (22)	29 (43)	6 (16)
FP	Visit	18 (30)	11 (41)	13 (22)	29 (45)	6 (7)
Nutrition	Visit	18 (18)	12 (13)	13 (14)	29 (29)	6 (6)
TB	Visit	16 (131)	18 (134)	13 (168)	26 (141)	7 (123)
Surgery	Visit	98 (116)	67 (148)	149 (171)	87 (237)	67 (202)
Dental	Visit	-	-	-	-	-
Physiotherapy	Visit	-	-	-	-	-
IPD general	Admission/ bed-day	451 (526)/243 (283)	498 (579)/79 (91)	-	-	317 (338)/119 (127)
Obstetrics	Admission/ bed-day	516 (533)	744 (767)	905 (927)	659 (668)	143 (155)
Paediatrics	Admission/ bed-day	451 (528)/223 (262)	276 (284)/223 (229)	-	-	209 (224)/72 (77)

OPD: outpatient department; ART: anti-retroviral therapy; ANC: antenatal care; PNC: post-natal care; FP: family planning; TB: tuberculosis; IPD: inpatient department; HC: health centre. *Unit costs without variable costs. **Unit costs with variable costs in parentheses. ***Information on ART drug consumption was not available. The currency rate was 1 USD = 11.25 Zambian Kwacha.

Table 6. Unit costs of services at first-level hospitals (ZMW)

Service	Unit	Chilenje Hospital	Chongwe Hospital	Kalomo Hospital
Laboratory	Test	12* (-)**	34 (-)	27 (-)
Radiology	Imaging	-	118 (135)	153 (156)
OPD general	Visit	28 (49)	141 (184)	75 (114)
ART	Visit	23 (155)	127 (205)	15 (81)
ANC/PNC	Visit	53 (57)	-	17 (18)
FP	Visit	42 (43)	92 (161)	17 (33)
Nutrition	Visit	72 (72)	-	11 (76)
TB	Visit	96 (225)	83 (199)	51 (121)
Surgery	Visit	413 (615)	627 (666)	1160 (1459)
Dental	Visit	93 (177)	137 (143)	68 (69)
Physiotherapy	Visit	219 (219)	111 (111)	260 (260)
IPD general (male)	Admission/ bed-day	995 (1,147)/187 (216)	1,329 (1,415)/487 (519)	383 (795)/138 (287)
IPD general (female)	Admission/ bed-day	893 (1,045)/152 (177)	1,134 (1,208)/484 (516)	386 (494)/243 (311)
Obstetrics	Admission/bed-day	351 (433)	660 (685)	267 (392)/178 (261)
Paediatrics	Admission/bed-day	938 (957)/289 (294)	1,127 (1,165)/516 (534)	791 (1142)/301 (435)

OPD: outpatient department; ART: anti-retroviral therapy; ANC: antenatal care; PNC: post-natal care; FP: family planning; TB: tuberculosis; IPD: inpatient department. *Unit costs without variable costs (*i.e.*, drugs, vaccines and medical supplies). **Unit costs with variable costs in parentheses. The currency rate was 1 USD = 11.25 Zambian Kwacha.

Table 7. Unit costs of services at third-level hospitals (ZMW)

Service	Unit	UTH Women & Newborn	UTH Paediatrics
Laboratory	Test	19*	19
Radiology	Imaging	-	88
Ultrasound	Examination	21	-
OPD paediatrics	Visit	-	239
ANC/PNC	Visit	313	-
PMTCT	Visit	617	-
Neonatal	Visit	671	-
IPD paediatrics	Admission/bed-day	-	1,360/405
PICU	Admission/bed-day	-	3,760/1,162
Nutrition	Admission/bed-day	-	1,482/99
TB	Admission/bed-day	-	5,789/367
Special (paediatrics)	Admission/bed-day	-	1,281/361
Obstetrics	Admission/bed-day	808/237	-
Gynaecology	Admission/bed-day	775/226	-
Neonatal	Admission/bed-day	833/231	-
NICU	Admission/bed-day	2,031/722	-

UTH: University Teaching Hospital; OPD: outpatient department; ANC: antenatal care; PNC: post-natal care; PMTCT: prevention of mother to child transmission; IPD: inpatient department; PICU: paediatric intensive care unit; TB: tuberculosis; NICU: neonatal intensive care unit. *Unit costs without variable costs (*i.e.*, drugs, vaccines and medical supplies). The currency rate was 1 USD = 11.25 Zambian Kwacha.

Discussion

Overall, the relative levels of unit costs between services provided at the same facility exhibited reasonably comparable pattern, albeit with some notable exceptions. For instance, unit costs without drugs and consumables for ANC/PNC, family planning, nutrition and TB were fairly similar within the same facility (an example of a notable exception includes nutrition in Mtendere HC), and the unit costs of OPD general tended to be higher. Among outpatient services, unit cost of surgery was consistently on the higher end followed by TB and ART if drugs were included. Inpatient services costed more than outpatient services as expected. This is consistent with other studies that have generally reported that inpatient departments consumed more resources than outpatient services (*4,17*).

It is plausible to conclude from these findings that resource allocation pattern within a facility was generally comparable to other facilities. For some notable exceptions, such as nutrition and physiotherapy in Mtendere HC, resources may have been disproportionately assigned to those services. For such irregular unit cost patterns within the same facility, it is recommended to review the balance between the resources allocated to those services and the actual number of patients utilising those services in comparison to other services. In some cases, discontinuing the provision of an expensive service may be considered by merging the service provision with another facility at the same or higher levels.

On the other hand, findings from the comparison of unit costs between facilities were mixed. Some services exhibited similar unit costs within the same levels, whilst others differed substantially. For instance, unit costs without drugs and consumables for ART at health centres mostly fell in the range between ZMW 16 (USD 1.42) and 19 (USD 1.69). On the other hand, unit costs of outpatient surgery without drugs and consumables at health centres varied between ZMW 46 (USD 4.09) and ZMW 355 (USD 284). The reasons behind the substantial heterogeneity of unit costs between the same level of facilities can be multi-faceted, including difference in the number and compositions of staff members, size of facilities, number of patients, quality of care, amongst others (*3,18,19*).

Among the health centres, unit costs of services at Kanchele HC in Kalomo District were mostly lower than any other health centres. Kanchele is known as the hub for delivery in the Southern part of Kalomo District that managed 559 delivery cases in 2016 with just three professional staff members (midwife, nurse and environmental health technologist). The number of deliveries was considerably larger than others given the capacity of the facility. The relative quantity of outputs given the available input resources could be the main driver of the lower unit costs. In other words, efficiency is likely the key driver of the varied levels of unit costs between facilities at the same level. However, the term "efficiency" used here solely reflects the relationship between outputs and inputs that do not reflect quality and performance. In less densely populated rural areas, the establishment of a stand-alone facility can be warranted if access to health care will be significantly compromised in absence of that, even if the catchment population may be small. Such facilities may likely have higher unit costs of services, as the denominator of unit costs (*i.e.*, number of patient visits) will be smaller for the capacity. Similarly, the higher unit costs of Chongwe Hospital may be explained by the smaller number of patients given the district's proximity to Lusaka that may be more convenient to access for a sizable portion of the district's population. Nonetheless,

it is recommended to review the resource allocated if a particular service or facility has substantially higher unit costs than others, including number of staff and skill mix, capital assets and others. However, the reallocation of resources should be performed with caution so that the equitable access to health services would not be significantly compromised.

It is generally expected that the unit costs of services become higher as the level of facility moves up the hierarchy. This is not surprising given that facilities at higher levels deal with more severe and complex cases and require more intensive resources such as specialists. Comparing the overall unit costs between health centres, first-level hospitals and UTH, it is obvious that the overall levels of unit costs become higher as the levels become higher. The pattern is particularly prominent for inpatient services as the patients' severity levels can become substantially greater at higher levels requiring more complex, resource-intensive and specialised services. There is a similar pattern for outpatient services, though to a lesser extent than inpatients.

From the estimates, it is evident that unit costs at UTH are many-folds more expensive than those at lower levels. Although this may be caused by a combination of multiple factors, the higher costs should not be driven by the extensive resources directed towards treating less severe cases that can be managed at lower levels. Here, UTH has been arguably quoted as accepting all referral cases from Lusaka area that could have been managed by first-level hospitals. In this regard, the upgrade of five health centres in Lusaka to first-level hospitals was a significant step forward to improve the efficiency of service delivery. However, it is critical to have guidelines to foster appropriate decision-making for referrals to make the most out of this opportunity.

On the other hand, facilities at the lowest level may not necessarily have the lowest unit costs in providing the services. Shiyala HP was at the lowest level among the facilities included in this analysis. If we compare the unit cost estimates, they were generally more costly than health centres. This may be a case where economies of scale had a role to play. The relatively higher unit costs may be improved by gaining economies of scale through merger with other facilities. However, as mentioned earlier, such rearrangements should be carefully weighed against the potential compromise in efficiency and equitable access to health services (*20*).

Although this study was conducted to examine health facilities at different levels and characteristics using most detailed data that were available at the time of study, it is not without limitations. Here we describe the main challenges that we faced in estimating each of the three cost items: labour, material and capital costs. Whilst labour costs comprised nearly half the total cost of health facilities, service-specific costs of labour were estimated by the time spent by staff members on each service at the facilities. It proved difficult for each staff member to recall the time spent for each service accurately, particularly for smaller and lower level facilities where individuals were more involved in multiple tasks than more specialised facilities at larger and higher levels. Therefore, we obtained the information of time spent in broader groupings such as ancillary services, outpatient services and inpatient services, and apportioned the staff time in each group to specific services by the relative size of outputs within the same service groups. This assumed that the time required to provide a unit output in each group (*e.g.*, one outpatient visit) was the same for all services in the group, and the relative difference in unit costs between those services were driven by the different resource use related to materials and capital assets.

Similar to labour costs, material costs comprised close to another half of the full costs of health facilities. The majority of material costs were drugs that were largely procured centrally and distributed to the health facilities nation-wide. While we obtained the quantity of drug consumptions from the stock records and prices from the price catalogue prepared centrally, some of the drugs were purchased at the district levels as emergency procurement. Those drugs were procured from the private vendors which may or may not have been procured at the same price levels. Further, some drugs that were consumed in health facilities were not on the price list of the government, for which we obtained information from the international price database. These limitations may have had over or under estimated the overall drug costs, but given the very small portion of drugs where we needed to refer to international sources and that the emergency drug procurement was capped at 4% of the district budget that is already small, the impact on the unit costs was deemed negligible.

Reliable information on the price of capital assets was deficient, particularly for buildings. For equipment, we obtained various quotations that were obtained by the MOH for different purposes and assumed replacement costs in the base year. For buildings, we obtained a standard construction cost for a standard health facility provided by the MOH, and calculated the cost per square meters that were applied for the size of buildings. If a building had multiple floors, the area of each floor was added up to obtain the total square meters of the building. Although assuming the size of building as the only determining factor of the costs can be an over-simplification, the proportion of building in the full facility costs was small compared to other cost items (*i.e.*, labour, material and equipment) that is unlikely to have substantially distorted the estimation of the unit costs.

Despite the limitations, this study is likely the most accurate unit cost estimates of services provided

at health facilities in Zambia to date. We compared the unit cost estimates with those estimated by econometrical means by the WHO-CHOICE study (*21*). Supplemental Table S3 (*https://www.ghmopen.com/site/supplementaldata.html?ID=87*) provides a rough comparison of unit costs at different levels of health facilities. Estimates for health centres are rather comparable between the two, although the estimates from WHO-CHOICE appear to be on the lower end. However, the estimated unit costs by this study for hospitals are significantly higher than those of WHO-CHOICE, particularly for IPD and tertiary hospitals (*i.e.*, USD 21.92-112.71 *vs.* USD 6.06, respectively). Given the significant resources that are used at higher level hospitals, the WHO-CHOICE estimates may be underestimating the true costs. While the reasons for the differences remain to be studied, this potentially points to the need to update the country-specific estimates with primary data obtained from the facilities. Further, although this study provides the cost estimates in 2016 value for Zambia that may seem somewhat dated, they still remain the best estimates with adequate inflation adjustments to date. Given the general lack of literature on unit costs of health services in Africa, especially in recent years, it can provide some indications of unit costs in peer countries with similar health systems and income levels. Particularly in conducting economic evaluations of various health services in Zambia, the estimated unit costs can serve as a superior alternative source to WHO-CHOICE 2021 update, which provided estimates in 2010 value requiring a more rigorous adjustment for inflation.

Conclusion

This study provides the unit costs of health services that are provided in two provinces of Zambia. Apart from the use of unit cost information in future studies, the variations of unit costs among facilities with different characteristics provided policy relevant information to be considered by health administrators and policy makers. Nonetheless, although this study discussed potential issues that may explain the differences in the level of unit costs, those issues need to be confirmed by additional specialised analyses that investigate each specific issue more intensively (*e.g.*, efficiency, economies of scale).

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BRIEF REPORT

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Analysis of infantile hemangioma without proliferation after birth

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Abstract: Infantile hemangiomas (IHs) are the most common benign tumors of infancy, occurring in approximately 5-10% of the population. Among what appear to be typical IHs with proliferative and involuting phases, we noticed that there are also IHs that are already present at birth and regress without proliferating. We therefore aimed to determine the frequency and clinical characteristics of this type of IH. A retrospective study was conducted on 176 lesions of 137 Japanese patients with IH. As a result, six lesions (3.4%) in three patients with IH (2.1%) were already present at birth and lacked subsequent proliferation. Analysis of the clinical characteristics of IHs without proliferation revealed that they are significantly less common in the head and neck region, which is the preferred site of the tumor, than typical IHs with proliferation (0% *vs.* 42.9%, $p < 0.05$ by Fisher's exact test). This suggests that when the clinical course of IH is uncommon, their distribution can also be atypical. Furthermore, all of the IHs without proliferation were superficial types, and there were no deep types in this cohort. This study demonstrates that the clinical course of IH can be diverse, and that very rarely there can be a type of IH that does not grow after birth. It may be necessary to consider conducting a detailed interview for the growth history at the first visit for the possibility of such a type of IH without proliferation, as it is likely that they can be followed up without the need for treatment.

Keywords: pathogenesis, cause, subtype

Introduction

Infantile hemangiomas (IHs) are the most common benign tumors in infancy, occurring in approximately 5-10% of the population (*1*). The typical clinical course is either absent at birth or with precursor lesions, such as erythematous telangiectasias or macules. The lesions thereafter show tumor growth (*i.e.,* proliferation phase) for several months, and in the involuting phase, they gradually disappear over several years. The site of predilection is the head and neck region (*2*). Low birth weight, multiple pregnancies, preterm delivery, progesterone therapy, and family history of IH have all been reported to be associated with the incidence of IH (*1*).

The detailed pathogenesis of IH has yet to be elucidated, but a number of hypotheses exist to explain its unique clinical presentation (*3*). For example, the first hypothesis is placental cell embolism. The gene expression pattern of IH differs from that of endothelial cells in the surrounding skin, resembling the pattern of endothelial cells comprising fetal microvessels in the human placenta (*4*). A second hypothesis is related to hypoxia: Local hypoxia associated with glucose transporter (GLUT)-1 and indoleamine 2,3-dioxygenase may be involved in the pathogenesis (*1*). A third hypothesis concerns endothelial progenitor cells and stem cells. Endothelial progenitor cells derived from IHs have been shown to cause IH-like lesions in immunocompromised mice (*5*).

In addition, according to our previous study, IH is less common in the jaw and cheek regions among the head and neck area, which are less prone to external stimuli (*6*). We therefore hypothesized that physiological events, including perinatal hypoxia or mechanical stress during delivery, may be one of the triggers of hemangioma formation. Recently, among what appear to be typical IHs, we have also noticed that there are IHs that were already present at birth, that do not enlarge thereafter, and then spontaneously involute. Here, we aim to determine the frequency and clinical characteristics of this type of IH.

Patients and Methods

Clinical assessment and patient material

This retrospective study was approved by the Research Ethics Committee of Wakayama Medical University (No. 2730) in accordance with the Declaration of Helsinki. The informed consent was obtained from the

patients' guardians. IH infants who visited Wakayama Medical University Hospital between January 2017 and June 2020 were included in the study. All patients were diagnosed based on clinical symptoms, imaging findings (*e.g.,* ultrasound and MRI), or histopathological findings. Cases with unknown onset were excluded.

The following variables from medical records and clinical photographs were collected for our analysis: date of onset, gender, number of lesions, distribution (head and neck, limbs, trunk), family history, gestational week, birth weight, and clinical subtypes (*7*). The clinical subtype was defined by the depth of soft tissue involvement. Superficial-type IHs involving the skin surface have elevated, lobulated, bright red appearance. Deep-type IHs arise from the reticular dermis and/or subcutaneous layers, and appear as bluish subcutaneous nodules or tumors. Mixed-type IH has features of both subtypes.

Statistical analysis

Statistical analysis was performed using Fisher's exact test for comparison of frequencies; $p < 0.05$ was considered statistically significant.

Results and Discussion

Clinical characteristics of IH patients included in this study

Clinical data were collected on 176 lesions in 137 IH patients (87 females and 50 males). Their mean age at first visit was 2.94 months. The distribution of the 176 lesions was 73 in the head and neck (41%), 42 in the extremities (24%), and 61 in the trunk (35%). No segmental IH was included. The clinical subtypes of the 176 lesions were 113 superficial (64%), 17 deep (10%), and 46 mixed (26%). Multiple lesions were detected in 24 patients (14%). Among the 137 patients, only 5 (4%) had apparent family history. Information on gestational week was available for 74 patients based on medical record, and 14 cases were born earlier than 37 weeks. According to data on birth weight for 70 patients, 15 had low birth weight (< 2,500 g). Because this was retrospective study, information on gestational age or birth weight was sometimes lacking in medical records.

Clinical pictures of IH without proliferation

In our cohort, of the 176 lesions in 137 patients with IH, six lesions (3.4%) in three patients with IH (2.1%) were already present at birth and did not show subsequent proliferation. The information on the presence or absence of proliferation after birth was based on parental observation, but most cases in the present cohort were thought to have proliferative tendencies. The 137 IH patients were then classified into two groups according to the presence or absence of tumor proliferation: Patients with IH already present at birth and without subsequent proliferation (IH without proliferation, $n = 3$), and those with typical IH present at or after birth and subsequently proliferated (IH with proliferation, $n = 134$).

Representative clinical pictures of patients with IH lesions already present at birth and without subsequent proliferation are shown in Figures 1-3. Case 1 was born at 40 weeks and five days with hemangioma of the vulvar region (Figure 1A). Diagnosis of IH was confirmed histopathologically based on the neoplastic proliferation of disorganized vascular channels (Figure 1B) and positive GLUT-1 staining (Figure 1C). Case 2 had a lesion on the thigh (Figure 2), while Case 3 showed multiple IHs on the hand, lower leg, abdomen, and back (Figure 3, A-D).

Each of these patients had typical clinical presentation of IH, but did not proliferate during at least five months of follow-up, and spontaneous involution was confirmed (Table 1), except for the thigh lesion of case 2 and the hand lesion of case 3 which treated with pulsed dye laser

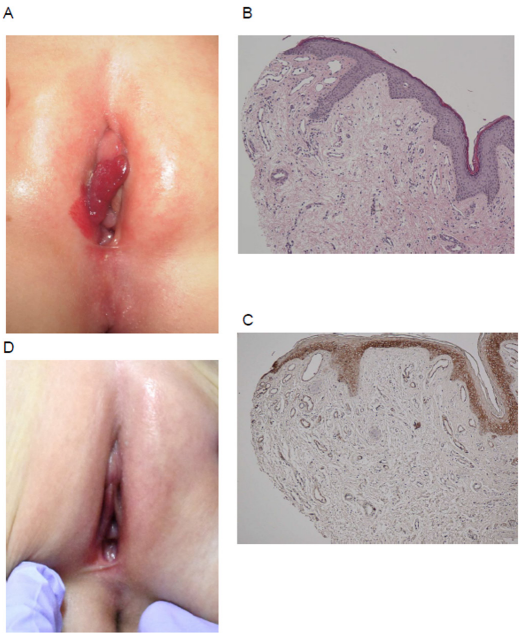

Figure 1. Clinical manifestation of Case 1 without proliferation on the vulva. (A) Clinical finding at the first visit, **(B)** Histological findings of biopsy specimen showing proliferation of disorganized vascular channels, **(C)** GLUT-1 staining, **(D)** involution at 12 months after the first visit.

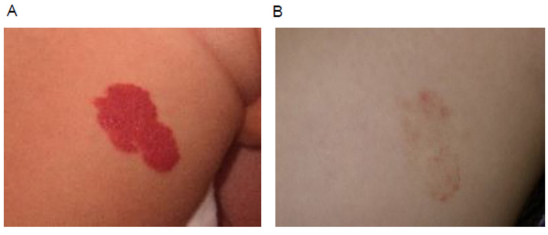

Figure 2. Clinical manifestation of Case 2 without proliferation on the right thigh. (A) Clinical finding at the first visit, **(B)** involution at 10 months after the first visit.

before involuting phase.

Usually, such IH cases without proliferation are considered to be abortive IH, minimal growth IH, or rapidly involuting congenital hemangioma (RICH) as differential diagnosis (*8,9*). However, the clinical presentation and clinical course of the three patients were different.

Analysis of clinical characteristics of IH without proliferation

Differences between the two groups in gender, distribution, clinical subtype, family history, gestational week, and birth weight were analyzed (Table 2). As a result, the distribution of IHs with proliferation was in the head and neck in 73 lesions, the trunk in 58 lesions, and the extremities in 39 lesions (Table 3). As mentioned above, IH was more common in the head and neck region (*10*), but IH without proliferation tended to be found in the other areas, indicating a statistically significant difference in the frequency of head and neck lesions between the two groups (42.9% *vs.* 0%, $p = 0.036$ by Fisher's exact test). IH without proliferation is more likely to occur outside the head and neck region.

Thus, our analysis suggests that when the clinical course of IH is uncommon, the distribution may also be atypical. In our previous study, IH appearing after birth was shown to tend to have multiple lesions more frequently than IH present at birth, suggesting that IH present at birth is caused by local triggers (*7*). In addition to local triggers, multiple IHs appearing after birth may be caused by systemic factors, such as cytokines involved in systemic neovascularization or sensory nerve growth after birth. Actually, several cytokines (bFGF, IFN-γ, IGF-I, and TGF-β1) were higher in the patients with multiple lesions than in those with a single lesion, with statistically significant difference (*11*). The pathogenesis

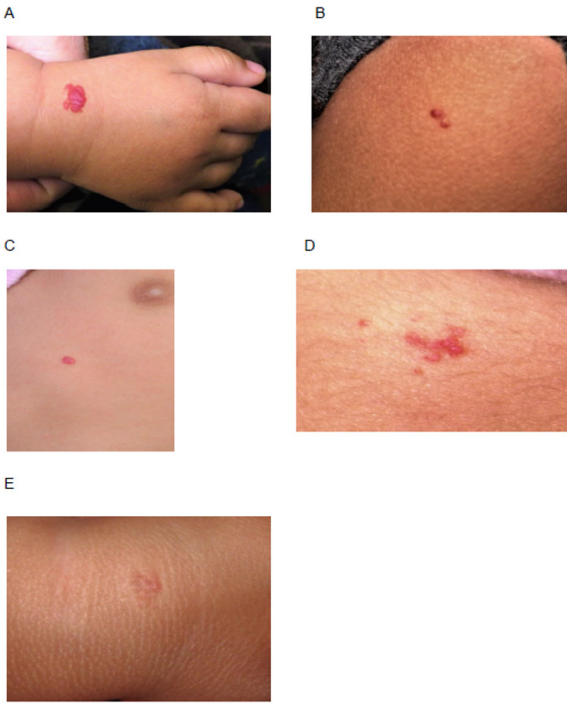

Figure 3. Clinical manifestation of Case 3 without proliferation. (A) right hand at the first visit, **(B)** left lower leg, **(C)** right upper abdomen, and **(D)** back, **(E)** disappearance of right hand lesion at 5 months after the first visit.

Table 2. Clinical characteristics of infantile hemangioma patients included in this study

Characteristics	Number of cases
Gender	
Female	87
Male	50
Distribution	
Head and neck	73
Limbs	42
Trunk	61
(Multiple)	(24)
Clinical type	
Superficial	113
Deep	17
Mixed	46
Family histories	
+	5
–	129
Unknown	3
Gestational week	
< 37 weeks	14
≥ 37 weeks	60
Unknown	63
Birth weight	
Mean weight (kg)	2.84
Low birth weight	15
Proliferation	
+	134
–	3

Table 3. Correlation of onset with distribution

Distribution	Without proliferation	With proliferation	All
Head and neck	0 (0%)	73 (42.9%)	73
Trunk and limbs	6 (100%)	97 (57.1%)	103
All	6	170	176

Table 1. Clinical characteristics of infantile hemangioma without proliferation

Cases	Gestational week	Birth weight	Age at the first visit	Follow-up period	Involution
Case 1	40w, 5d	3,170g	12 months	12 months	+
Case 2	Unknown	Unknown	2 months	10 months	+
Case 3	Unknown	Unknown	11 months	5 months	+

Table 4. Correlation of onset with clinical subtypes

Subtypes	Without proliferation	With proliferation	All
superficial	5	108	113
deep	0	17	17
mixed	1	45	46
All	6	170	176

of IH without proliferation in the present study may be different from such typical IHs, and tumor growth may have already begun before birth, and the tumor may be at its maximum size at birth. However, because gestational weeks were not significantly different between the two groups, the detailed etiology is still to be clarified.

Furthermore, the clinical subtypes of IH lesions without proliferation were five superficial-type (83%), none of deep-type, and one of mixed-type (17%), while those with proliferation were 108 superficial-type (64%), 17 deep-type (10%), and 45 mixed-type (26%). The superficial-type was the most common in both groups, whereas the deep-type was found only in IH with proliferation (Table 4). The deep-type may be difficult to recognize on the day of birth because of the lack of color change on the surface, and this result should be verified through further case series.

Conclusion

This study demonstrates that the clinical course of IH can be diverse, and that very rarely there may be a type of IH that does not grow after birth. It may be necessary to consider conducting a detailed interview for the growth history at the first visit for the possibility of such a type of IH without proliferation, as it is likely that they can be followed up without the need for treatment.

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BRIEF REPORT

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Validity of vaccination information in the COVID-19 surveillance system in Japan: Implications for developing efficient and highly valid data collection systems in future pandemics

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Abstract: Japan's government developed the Health Center Real-time Information-sharing System on COVID-19 (HER-SYS), the national COVID-19 surveillance system, which relies on manual data entry. Following the COVID-19 vaccination campaign, physicians were mandated to report COVID-19 cases with vaccination history *via* HER-SYS. However, concerns have arisen regarding the accuracy of this vaccination history. This study aimed to assess the validity of vaccination history recorded in HER-SYS. We used data from HER-SYS provided by three municipalities. The study cohort comprised COVID-19 cases registered in HER-SYS from February 2021 to March 2022. The validity of vaccination history in HER-SYS was assessed by cross-referencing with the Vaccination Record System (VRS) of these municipalities. We calculated sensitivity to gauge the extent of missing data in HER-SYS, and positive predictive value (PPV) to evaluate the accuracy of data entered into HER-SYS. Of the 19,260 COVID-19 cases included in the study cohort, HER-SYS and VRS identified 3,257 and 8,323 cases, respectively, as having the first-dose vaccination history. Cross-referencing identified 3,093 cases as true positives in HER-SYS. The sensitivity was 37.2% (95% confidence interval [CI]: 36.1−38.2) and the PPV was 95.0% (95% CI: 94.2−95.7). Collection of vaccination data by HER-SYS was found to be inadequate to obtain information on vaccination history of COVID-19 cases. This suggests that real-time data linkage across different systems such as HER-SYS and VRS would reduce the burden of manual data entry during the pandemic and lead to appropriate infection control measures based on more accurate information.

***Keywords*:** COVID-19, surveillance system, vaccine, validation, linkage

Introduction

Coronavirus disease (COVID-19) has become a global pandemic since the first reported case in Wuhan, China, in December 2019 (*1*). In Japan, COVID-19 monitoring commenced on February 1, 2020 in accordance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (*2*). Under the act, reporting for *Designated Infectious Disease* cases typically involves the use of a handwritten *Report Form*, which must be completed by a physician diagnosing the infectious diseases. These reports are then sent to the Public Health Center in each municipality *via* fax, where Public Health Center officials enter this information into the National Epidemiological Surveillance of Infectious Disease (NESID) database to monitor trends in infectious disease outbreaks (*3*). COVID-19 monitoring was initiated utilizing this *Report Form,* along with other *Designated Infectious Diseases* (*4*). However, as the number of COVID-19 cases has increased, there was concern that entering information into the NESID would not keep pace. Therefore, the Health Center Real-time Information-sharing System on COVID-19 (HER-SYS) was developed in May 2020, as a system that allows each medical facility to report information on the online *Report Form* to the Public Health Center (*5*). HER-SYS data have been used to determine the number of COVID-19 cases in Japan, provide information to the advisory board of the Ministry of Health, Labour and Welfare (MHLW) against COVID-19, and perform epidemiological studies (*6*-*8*).

In the initial stage of its operation, the HER-SYS had approximately 120 entry items per COVID-19 case, including health status and medical information (*9*). However, as COVID-19 cases increased rapidly, extremely busy medical facilities could no longer cope with entering these items. In September 2020, a notification was issued to give top priority to the

input of approximately 40 items, including items in the *Report Form* and the current health status of COVID-19 patients (*e.g.*, awaiting test results, recuperating at home, recuperating at a hotel, hospitalization, death, *etc.*) (*10*). Subsequently, in February 2021, when the COVID-19 vaccination campaign began, additional entry items for COVID-19 vaccination history were added to the *Report Form* (*11*). Consequently, physicians faced an increased burden of manually inputting these types of information. However, the quality of the information within HER-SYS had not previously been reported.

Conversely, the national COVID-19 vaccination registry, the Vaccination Record System (VRS) is a cloud-based system developed by the Digital Agency to record individuals' COVID-19 vaccination status for the smooth of the COVID-19 vaccination campaign in each municipality (*12*). In addition, the number of vaccinations based on VRS is utilized for COVID-19 vaccination policymaking and summarized on the MHLW website (*13*). In the VRS, the vaccination information is recorded at the COVID-19 vaccination facility using an electronic device to read the vaccination coupon. Although more accurate vaccination information is stored in the VRS than in the HER-SYS, these national systems were developed independently and are not linked. If VRS data were re-used as the vaccination status information in HER-SYS, it could not only facilitate efficient data collection to alleviate the burden on physicians during a pandemic but also enhance data accuracy. Therefore, the objective of this study was to quantitatively evaluate the validity of vaccination history information in the HER-SYS data by cross-referencing with VRS.

Materials and Methods

Data source

We used HER-SYS and VRS data from three municipalities (one in Chugoku- and two in Kanto-region) in Japan. These municipalities participated in the Vaccine Effectiveness, Networking, and Universal Safety (VENUS) Study (*14*), which links resident VRS and HER-SYS data to individuals using anonymous residential identifiers for secondary data use. The data period used in this study was from the date of the addition of the vaccination history section (February 10, 2021) in HER-SYS to the latest data provided (municipality A: February 10, 2021 to March 29, 2022; municipality B: February 10, 2021 to March 22, 2022; municipality C: February 10, 2021 to December 31, 2021). HER-SYS data included the following items related to each vaccination dose: vaccination status ("vaccinated", "unvaccinated", "not entered", or "unknown"), vaccination date, age at vaccination, vaccine manufacturer, and type (messenger ribonucleic acid, viral vector, *etc.*). On the other hand, the VRS data included the following items for each vaccination dose: vaccination history registration date, vaccination date, vaccination municipality code, vaccination site, vaccine manufacturer, and vaccine lot number. We utilized the VRS data as the gold standard for this validation study.

The Kyushu University Institutional Review Board for Clinical Research approved this study (No. 2021-399). The requirement for individual informed consent was waived based on the Japanese ethical guidelines, as this study secondary used routinely collected anonymized data by the municipalities.

Study cohort

The study cohort was defined as residents registered in HER-SYS, which consisted of patients with COVID-19, during the data period. The cohort entry date was defined by the registration date in HER-SYS was defined as a cohort entry date. Residents without an anonymized identifier that uniquely identified an individual within the municipality were excluded from the study. The data source profile was detailed in the previous article, with approximately 10% of COVID-19 patients excluded due to missing the unique identifier (*14*).

Comparing vaccination status in HER-SYS with that in VRS

To assess the validity of vaccination status information of the study cohort in HER-SYS, we extracted their VRS data. The vaccination status of the study cohort entered in HER-SYS was compared with their vaccination status recorded in the VRS prior to their cohort entry date. A flowchart of the study procedure is shown in Figure 1.

Statistical analysis

The sensitivity of the vaccination status for each vaccination dose in the HER-SYS data was calculated to evaluate the degree of omission of vaccination history in the HER-SYS data. The positive predictive value (PPV) of the vaccination status for each vaccination dose was calculated to evaluate the correctness of the information entered into HER-SYS. We also estimated the 95% confidence intervals (CIs) of sensitivity and PPV using Wilson's confidence intervals (*15*). Sensitivity was calculated as the proportion of the population with "vaccination status: vaccinated" entered in the HER-SYS data out of the vaccinated population in the VRS among the study cohort. PPV was calculated as the proportion of the vaccinated population in the VRS out of the population with "vaccination status: vaccinated" entered in HER-SYS. We also conducted subgroup analyses by municipality, fiscal quarter, and age for the primary outcome of each vaccination dose.

Additional analyses were conducted to assess the correctness of the vaccination date field in HER-SYS in addition to the vaccination status field. The PPV was

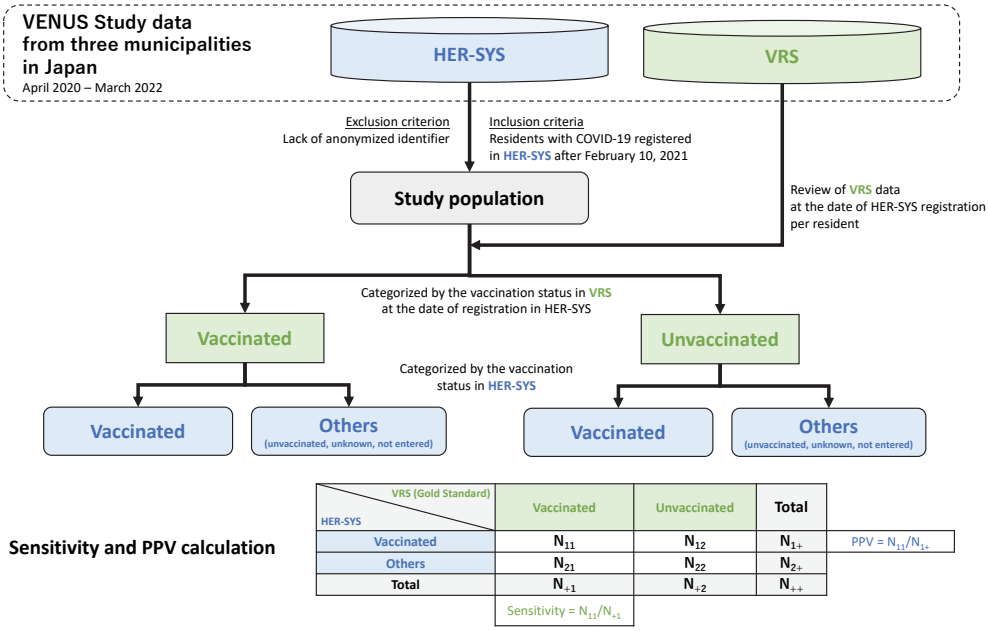

Figure 1. Study flow of assessment of the validity of vaccination status in the HER-SYS. HER-SYS, Health Center Real-time Information-sharing System on COVID-19; VRS, Vaccination Record System; PPV, positive predictive value.

calculated as the proportion of concordant HER-SYS vaccination status and date records with the VRS in the population where the HER-SYS fields "vaccination status: vaccinated" and "vaccination date" were entered. We also assessed the correctness of the vaccination date and vaccine manufacturer fields in HER-SYS, in addition to the vaccination status field. The PPV was calculated as the proportion of concordant HER-SYS and VRS vaccination status, vaccination date, and vaccine manufacturer data in the population in which the HER-SYS vaccination status, vaccination date, and vaccine manufacturer fields were entered.

The analysis was conducted using R Version 4.1.0. (R Foundation for Statistical Computing, Vienna, Austria).

Results and Discussion

A total of 19,260 residents were identified from HER-SYS as the study cohort. Table 1 shows the characteristics of the study cohort. Table 2 shows sensitivity and PPV of vaccination status for each vaccination dose including the main and subgroup analyses. The sensitivities of the main analysis were between 30% and 40%, but those of the subgroup analyses by municipality ranged from 18.0% to 72.1%. Most PPVs in the main and subgroup analyses were greater than 90%. Table 3 shows the PPVs of the combination of vaccination status, date, and manufacturer for each vaccination dose, which were lower than the PPV for vaccination status alone.

There are several possible reasons for the low sensitivity. First, the vaccination history information in the HER-SYS was based on patient self-reports. Patients have to remember their vaccination history if they do not have their vaccination certificate. As vaccination doses increase, it would be difficult to accurately recall the previous vaccination date. Second, there were many data entry items in HER-SYS that were entered by staff in medical facilities, and even when the number of entry items was reduced based on priority, there were still approximately 40 items per COVID-19 case, excluding vaccination history information (*9*). Third, it would have been challenging to collect information from patients with COVID-19 in a limited time when medical facilities and healthcare systems were overwhelmed by the increase in COVID-19 cases. These factors may have

Table 1. Demographics of the study cohort

Characteristics	Number of individuals	Proportion (%)
Total	19,260	100
Sex		
Male	9,932	51.6
Female	9,328	48.4
Age*		
< 15	3,533	18.3
15–65	13,257	68.8
≥ 65	2,343	12.2
Unknown	127	0.7
Municipality		
Municipality A	6,100	31.7
Municipality B	9,100	47.3
Municipality C	4,060	21.1
Quarter registered in HER-SYS		
2021-First	834	4.3
2021-Second	1,744	9.1
2021-Third	4,934	25.6
2021-Fourth	303	1.6
2022-First	11,445	59.4

HER-SYS, Health Center Real-time Information-sharing System on COVID-19. *Age at the date of HER-SYS registration.

Table 2. Sensitivity and PPV of vaccination status in the HER-SYS

	N_{11}	N_{+1}	N_{1+}	Sensitivity (95% CI)	PPV (95% CI)
All					
First dose	3,093	8,323	3,257	37.2 (36.1–38.2)	95.0 (94.2–95.7)
Second dose	2,821	7,797	2,934	36.2 (35.1–37.3)	96.1 (95.4–96.8)
Third dose	235	741	253	31.7 (28.5–35.2)	92.9 (89.0–95.5)
Subgroup					
Municipality					
A					
First dose	667	3,609	694	18.5 (17.2–19.8)	96.1 (94.4–97.3)
Second dose	650	3,528	665	18.4 (17.2–19.7)	97.7 (96.3–98.6)
Third dose	66	366	70	18.0 (14.4–22.3)	94.3 (86.2–97.8)
B					
First dose	2,119	4,270	2,205	49.6 (48.1–51.1)	96.1 (95.2–96.8)
Second dose	2,042	4,090	2,121	49.9 (48.4–51.5)	96.3 (95.4–97.0)
Third dose	169	375	183	45.1 (40.1–50.1)	92.3 (87.6–95.4)
C					
First dose	307	444	358	69.1 (64.7–73.3)	85.8 (81.8–89.0)
Second dose	129	179	148	72.1 (65.1–78.1)	87.2 (80.8–91.6)
Third dose	0	0	0	Null	Null
Quarter					
2021-First					
First dose	0	1	1	0.0 (0.0–79.3)	0.0 (0.0–79.3)
Second dose	0	1	1	0.0 (0.0–79.3)	0.0 (0.0–79.3)
2021-Second					
First dose	12	47	12	25.5 (15.3–39.5)	100 (75.8–100.0)
Second dose	0	0	0	Null	Null
2021-Third					
First dose	394	836	445	47.1 (43.8–50.5)	88.5 (85.2–91.2)
Second dose	157	424	186	39.4 (34.9–44.1)	89.8 (84.6–93.4)
2021-Fourth					
First dose	34	204	36	16.7 (12.2–22.4)	94.4 (81.9–98.5)
Second dose	26	181	29	14.4 (10.0–20.2)	89.7 (73.6–96.4)
Third dose*	0	0	0	Null	Null
2022-First					
First dose	2,653	7,235	2,763	36.7 (35.6–37.8)	96.0 (95.2–96.7)
Second dose	2,628	7,186	2,718	36.6 (35.5–37.7)	96.7 (95.9–97.3)
Third dose	235	741	253	31.7 (28.5–35.2)	92.9 (89.0–95.5)
Age					
< 65					
First dose	2,634	6,788	2,788	38.8 (37.7–40.0)	94.5 (93.6–95.3)
Second dose	2,410	6,361	2,515	37.9 (36.7–39.1)	95.8 (95.0–96.5)
Third dose	159	527	175	30.2 (26.4–34.2)	90.9 (85.7–94.3)
≥ 65					
First dose	459	1,535	469	29.9 (27.7–32.2)	97.9 (96.1–98.8)
Second dose	411	1,436	419	28.6 (26.3–31.0)	98.1 (96.3–99.0)
Third dose	76	214	78	35.5 (29.4–42.1)	97.4 (91.1–99.3)

N_{11}, numerator; N_{+1}, sensitivity denominator; N_{1+}, PPV denominator; PPV, positive predictive value; HER-SYS, Health Center Real-time Information-sharing System on COVID-19; CI, confidence interval. *The fields for third-dose vaccination history were added to a report form for COVID-19 cases in November 2021.

Table 3. PPV of the combinations of vaccination status, date, and vaccine manufacturer in the HER-SYS

	N_{11}	N_{1+}	PPV (95% CI)
Vaccination status and vaccination date			
First dose	1,166	1,438	81.1 (79.0–83.0)
Second dose	1,150	1,367	84.1 (82.1–86.0)
Third dose	169	200	84.5 (78.8–88.9)
Vaccination status, date, and vaccine manufacturer			
First dose	841	1,341	62.7 (60.1–65.3)
Second dose	830	1,323	62.7 (60.1–65.3)
Third dose	142	200	71.0 (64.4–76.8)

N_{11}, numerator; N_{1+}, PPV denominator; PPV, positive predictive value; HER-SYS, Health Center Real-time Information-sharing System on COVID-19; CI, confidence interval.

contributed to inaccurate or missing HER-SYS data.

The variation in sensitivity among municipalities (18.5%, 49.6%, and 69.1%) may have been influenced by differences in the number of COVID-19 cases, medical and human resources, and strategies against COVID-19 in each region and municipality (*16-18*). Approximately 500 Public Health Centers in municipalities played a major role in COVID-19 measures, and there were instances when staff entered information on COVID-19 cases instead of medical institutions. These centers have provided various services, such as health consultations, health status monitoring of COVID-19 patients, adjustment of hospital admission and recuperation at hotels, and active epidemiological investigation, which are important infection control measures in Japan. However, the role of Public Health Centers is not limited to COVID-19 measures but also includes other services, such as infectious disease control measures, mental health, food hygiene, environmental hygiene, and many other functions. Some COVID-19 measures have been strengthened and improved through outsourcing relative to their situation (*19*). However, when COVID-19 cases increased dramatically during the Delta variant wave in July 2021 (the fourth wave) and the Omicron variant wave in January 2022 (the fifth wave), it is considered that the burden significantly exceeded the prepared functions and resources in each municipality. These factors may have contributed to the differences in sensitivity results between municipalities.

One of Japan's neighboring countries, Taiwan, has established an excellent healthcare system that uses personal identification numbers as a common identifier for insurance cards (*20,21*). The development of such a system played an important role in COVID-19 measures, allowing for medical information to be easily shared across hospitals and clinics. A system that linked travel history and medical records was developed in the early stages of the pandemic; this system notified medical personnel of potential COVID-19 cases, thereby aiding the prevention of the spread of infection (*20*). Furthermore, introducing a mask distribution system based on personal identification numbers allowed all citizens to obtain masks fairly (*22*). In Japan, the linking and development of services based on personal identification numbers, known as "My number", is ongoing (*23*). Further, the VRS, which collects vaccination information on COVID-19, has been developed to link to personal identification numbers so that vaccination information can be shared among municipalities even if a resident moves to another municipality. In addition, each individual can obtain a vaccination certificate for the COVID-19 vaccine linked to their identification number (*24*). From October 20, 2021, an "Identification Number Card" can be used as a health insurance card (*23*). Using this card, medical facilities can share medical treatment and prescription drugs with each other, and patients can personally check previous medical history. The development of such infrastructure and the linking of various services using personal identification numbers could improve the quality of medical care and public health.

To prepare for the next pandemic, we recommend that it is necessary to go beyond the legal framework and develop national systems with real-time data linkage for primary data use. In the COVID-19 pandemic, HER-SYS and VRS were developed and operated independently of each other because HER-SYS is a system based on the Infectious Diseases Act and VRS is a system based on the Immunization Act. Therefore, COVID-19 vaccination history was registered in VRS by barcode scanning when individuals were vaccinated but it was manually entered in HER-SYS when COVID-19 occurred. If the vaccination history data in VRS had been linked and cross-referenced to HER-SYS, in real time, manual data entry would not have been required, thus more accurate data would have been obtained.

HER-SYS ceased operation in March 2024 (*5*), but individual patient-level data from HER-SYS for secondary use have been available since April 2024 and can be linked to three national healthcare claims databases: National Database (NDB), Diagnosis Procedure Combination Database, and Long-Term Care Claims Database (*25*). VRS was discontinued on April 2, 2024 (*26*). Currently, counts of vaccinations in VRS are available for download from the MHLW website (*13*). In addition, the National Vaccine Database (VDB), which contains all routine vaccination histories, is under construction, and linkage between the VDB and the NDB is also planned (*27*). Therefore, VDB and HER-SYS will be linked *via* NDB in the near future. However, the linkage between these national databases has been developed for secondary data use, not for primary data use. If these national systems are linked in real time, more specific information (*e.g.*, vaccination coverage by subgroup of specific diseases, quantitative analysis of the effectiveness and safety of each vaccine, *etc.*) can be evaluated in near real time. This real-time evidence will be of great benefit to frontline health care providers, health policy makers, researchers, and industry.

While this study provides valuable insights, there are some limitations that need to be acknowledged. Firstly, the generalizability of the results to the overall population of Japan is limited owing to the use of data from only three municipalities. Moreover, the sensitivity of the subgroup analysis tended to differ between municipalities. Secondly, the study cohort only included individuals who could be assigned an anonymized identifier, not all individuals registered in the HER-SYS. The HER-SYS and VRS in the VENUS Study data were linked using information such as name and age. If incorrect information was entered, the individual would not be included in the study cohort. However, because the number of such cases constituted less than 10% of the entire HER-SYS population, the impact on the results

of this study was not expected to be significant. Thirdly, the period evaluated in this study was limited. We used data through to the end of March 2022, but after June 30, 2022, the content of the *Report Form* was simplified (*28*), and on August 4, 2022, the number of items was further reduced to seven (*29*). Furthermore, after September 26, 2022, the individuals for whom the report should be submitted were restricted to patients aged ≥ 65 years, those who need hospitalization, have a higher risk of developing severe COVID-19, and are pregnant, although the *Report Form* returned to that as of June 30, 2022 (*30*). Further research is required to determine the impact of changes in reporting methods after the study period on the validity of input information.

In conclusion, we quantitatively demonstrated the incomplete vaccination history information in the HER-SYS. This study highlights the critical importance of data linkage to access high-quality information during a pandemic. Moreover, linking data across national systems would reduce the burden of manual data entry and lead to appropriate infection control measures based on more accurate information. We hope that the results of this study will provide insight and help develop surveillance systems for future pandemics.

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Direct aortic suture technique for anomalous systemic arterial supply to the basal lung: A retrospective cohort study

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Abstract: Anomalous systemic arterial blood supply to the basal lung (ABLL) is a rare congenital malformation. Although surgical resection is the standard treatment, the surgical techniques for aberrant arteries remain poorly discussed. Herein, we evaluated the efficacy of our direct suture closure technique in preventing aneurysmal changes in aberrant artery stumps through a retrospective review of the medical records of patients who underwent surgical resection of ABLL at our institution between January 2013 and January 2023. The diagnosis of ABLL was based on enhanced computed tomography (CT) findings. To treat ABLL, we performed lateral thoracotomy through the 5th intercostal space *via* a ~10 cm skin incision. After anatomical pulmonary resection, the aortic stump of the aberrant artery was sutured directly with a felted non-absorbable thread. In one patient, we further examined the postoperative blood flow using 4D-flow magnetic resonance imaging. Overall, 5 consecutive patients, including four (80%) females with a median age at operation of 59-year-old, were assessed. The median operative time was 166 min, and the median blood loss was 34 ml. There were no cases of perioperative mortality or morbidity, and the median hospital stay was 8 days. No vortex flow was observed in 4D-flow evaluation of blood flow. Histological changes were observed in the aberrant artery, including fibrous intimal thickening, atherosclerosis, intramural thrombus, and collection of foam cells and lymphocytes. Thus, we present this technique as a safe treatment for ABLL that allows for the preservation of blood flow and complete resection of abnormal vessels.

***Keywords*:** direct aortic suture technique, anomalous systemic arterial supply to the basal lung, pulmonary sequestration, 4D-flow MRI, aberrant artery

Introduction

Pulmonary sequestration (PS) is a rare congenital malformation first described by Pryce in 1946. PS is subdivided into two types: intrapulmonary and extrapulmonary fractionation (*1*). The condition initially classified as Conventional Pryce type III, defined as an anomalous systemic arterial supply to the basal lung (ABLL), is now considered an independent disease (*2*). The presentation of this disease varies widely, with patients ranging from asymptomatic hemoptytic, requiring emergency surgery. However, surgical resection and/or endovascular treatment is generally recommended after diagnosis in all cases (*3*). PS is rare, with an incidence of only 0.15-1.7% among all congenital malformations (*4*). Therefore, surgical techniques and postoperative complications remain poorly discussed.

Damage to the lungs can cause secondary infection and hemoptysis (*5*), therefore, pulmonary resection is essential. Distinct from usual pulmonary resection, in PS surgical methods to treat aberrant arteries must be performed in addition to lung resection. Division of the aneurysmal aberrant artery has been described as having a high risk of rupture during surgical dissection or re-aneurysmal changes of the arterial stump following surgery (*6*). The effects of endovascular treatment, such as embolization or stent grafting, on aberrant arteries from the descending aorta have previously been demonstrated (*7,8*).

Recently, thoracoscopic surgery has been proven to be a minimally invasive alternative to conventional thoracotomy. In this technique, the aberrant artery can be resected using a stapler during thoracoscopic surgery (*9,10*). Previous reports have also described endovascular treatment of aberrant arteries performed prior to lung resection (*7-9,11*). Various methods for this technique have been reported by many institutions. The bifurcations and roots of aberrant arteries can be observed as slightly saccular protrusions from the descending aorta. This sac-shaped protruding stump can lead to turbulent blood flow in the descending aorta.

However, no consensus has yet been reached regarding the treatment of aberrant artery stumps.

In our department, which includes both cardiovascular and thoracic surgeons, during surgical management of such patients, we apply a side clamp to the descending aorta after anatomical lung resection, and use felt for direct suture closure of the resected stump. In the present study, we evaluated the results of surgical cases managed using this novel technique. Throughout the study period, we assessed the perioperative clinical course, pathology of the aberrant artery, and blood flow in the descending aorta after resection in 5 patients. Further, we examined postoperative blood flow using 4D-flow magnetic resonance imaging (MRI) in one patient.

Study design for direct aortic suture technique

Ethical considerations

This study was approved by the Institutional Review Board of the Hamamatsu University School of Medicine (approval number 23-126). The need for informed consent was waived due to the retrospective study design.

Data analysis

Herein, we retrospectively reviewed the medical records of patients who underwent surgical resection of ABLL at our institution between January 2013 and January 2023, and further extracted the relevant clinical data. The diagnosis of ABLL was made based on the findings of enhanced computed tomography (CT), according to the conventional Pryce classification type III, which require that abnormal arteries return only to the PS and intrapulmonary sequestration shared visceral pleura with the normal lung. The resection range was defined as the area of the normal pulmonary artery bifurcation, inflow of the aberrant artery, destructive changes, and secondary infection. Patients who received oxygen therapy or were unable to tolerate general anesthesia due to organ failure were excluded.

Surgical technique

Lateral thoracotomy was performed through the 5th intercostal space. A skin incision of approximately 10 cm was made for segmentectomy or lobectomy. The aberrant arteries were dissected 2 cm apart, and resected using a staple. After anatomical lung resection, a side-biting clamp was placed on the descending aorta around the aberrant artery in the same surgical view, and the staple was removed by clamping the descending aortic staple transection. Felt-reinforced mattress sutures were then placed to close the stump of the aberrant artery, passing through the aortic wall just beside the aberrant artery take-off (Figure 1).

4D-flow magnetic resonance imaging

A 3-Tesla magnetic resonance scanner (Discovery MR750 or MR750w; GE Healthcare, Waukesha, Wis, USA) was used for 4D-MRI. Contrast-enhanced 3D magnetic resonance angiography was performed first to define the shape of the aortic wall. Subsequently, a bolus injection of 0.1 mmol/kg gadolinium chelate (Omniscan; Daiichi Pharma Co., Japan) was administered at an injection rate of 2.0 mL/s, followed by saline (20 mL) at the same injection rate. Respiration compensated for retrospective cardiac gating was used for 4D-flow imaging. Raw data were transferred to a personal computer for postprocessing and flow visualization in the Digital Imaging and Communications in Medicine (DICOM) format. The flow analysis software Flova (R'Tech Co, Hamamatsu, Japan) was used to visualize intraaortic flow information at a spatial resolution of 2 × 2 × 2 mm.

Clinical Characteristics of 5 ABLL patients

Five consecutive patients were assessed in this study. The median age at operation was 59-year-old, and 4 of the 5 patients (80%) were female. The only male patient was a current smoker. Four patients presented with symptoms, including repeated pneumonia from childhood in two patients, and epigastric pain and hemoptysis each in one patient. The respiratory function measured in elective operation cases was within the normal limits. Respiratory function could not be evaluated in one patient who required emergency surgery due to hemoptysis. The number of aberrant arteries was usually one, and only one case showed two aberrant arteries.

Perioperative outcome included postoperative blood flow

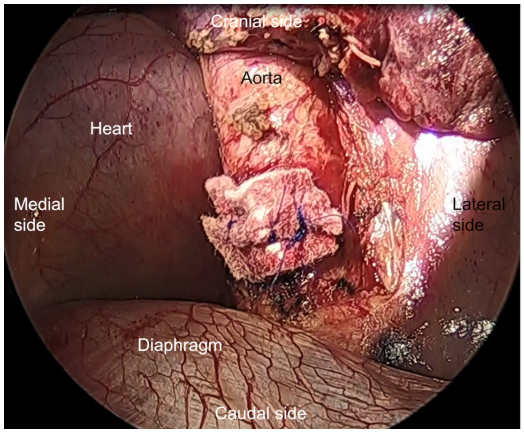

Figure 1. Intraoperative findings after lung resection and direct suture of the aorta. The stump of abnormal vessel was enclosed using felt and non-absorption thread.

We performed segmentectomy in three patients and lobectomy in two patients. The median operative time was 166 min, and the median blood loss was only 34 ml. There were no cases of perioperative mortality or morbidity. The median hospital stay was 8 days (range 5-13 days). One month after surgery, the descending aorta was smooth, and no internal vortex flow was observed on 4D-flow evaluation of blood flow (Figure 2).

Histopathological examination of aberrant artery

Histopathological examination revealed fibrous intimal thickening in three patients, atherosclerosis in three patients, intramural thrombus in two patients, and collection of foam cells and lymphocytes in one patient. Inflammatory cell infiltration was observed in 4 patients, bronchial epithelial metaplasia in 3, hemorrhage in 3, and chronic inflammation in 2.

Clinical outcome of direct aortic suture technique

In the present study, we found that the walls of aberrant arteries invariably show pathological changes that may underlie future aortic problems. Our direct suturing technique enables complete removal of the modified tissue, allowing the creation of a smooth aortic internal surface. In our study, absence of a protruding remnant or vortex flow was observed on 4D flow MRI in the one patient who underwent this analysis. As the exposure of the descending aorta is excellent after anatomical lung resection, this method can be performed safely through the same surgical field without prolonging the operative time or increasing blood loss. All patients, including those who underwent emergency surgery, were discharged within a short period without experiencing postoperative complications.

Histopathological changes in aneurysms of aberrant arteries

Several studies have previously demonstrated the formation of aneurysms in aberrant arteries (*11-14*). However, the mechanisms by which aberrant arteries form aneurysms remain unclear. However, pathological changes in aberrant arteries may be one such mechanism. Aneurysms of aberrant arteries caused by arteritis or arteriosclerosis in childhood have long been reported (*4*), and enlarged aberrant arteries were further observed inside a PS that had lost its normal structure due to chronic inflammation and interstitial fibrosis (*15*). Various histological changes, including those described previously, were observed in this study. Although there have been no prior case reports of clinical problems linked to treatment, Shibano *et al.* reported concerns regarding reaneurysm formation on the stump of an aberrant artery (*5*).

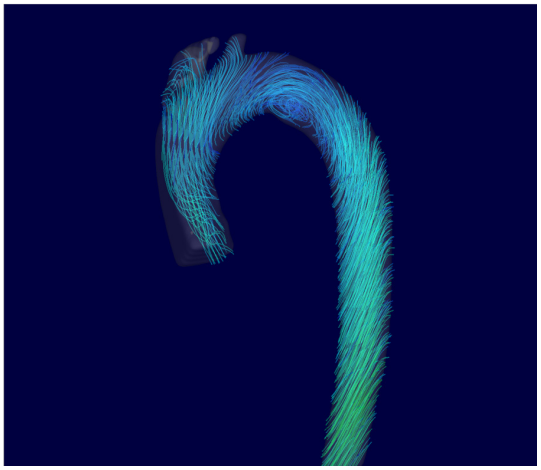

Figure 2. Results of postoperative 4D-flow magnetic resonance imaging (MRI) in the patient.

Postoperative blood flow in the aorta

Another concern which should be considered in cases of remnant protrusion is the turbulent flow within the protrusion. In a previous study, we showed that wall shear stress (WSS) is low in saccular aneurysms with a sac depth/width ratio > 0.8, which is caused by vortex flow within the aneurysms (*16*). The aberrant arterial remnant after stapling had this shape. A low WSS promotes atherosclerosis, and may cause aneurysm formation (*17*). Malek *et al.* previously demonstrated the biological responses to low WSS and the morphological transformation of endothelial cells (*18*). Overall, we believe that our method may help prevent histological changes by maintaining laminar blood flow in the aorta.

Limitation

This study has several limitations which should be mentioned. First, this method can only be performed in cases in which the lesion is located on the left side. Second, only five cases were performed at a single institution; thus, the number of cases was small, and the long-term results for more than ten-years remain unknown. Third, our method is not a procedure that can readily be performed by thoracic surgeons alone, but instead requires joint collaboration with cardiovascular surgeons. Furthermore, previous studies have demonstrated the incidence of intraoperative bleeding from aberrant arteries (*10*).

In conclusion, the present study showed that our direct suture closure technique is safe for ABLL. This procedure allows the complete resection of abnormal vessels and avoids vortex flow in the descending aorta, which may prevent future aortic complications.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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Pain relief effect of metoclopramide *vs*. sumatriptan for acute migraine attack: A single-center, open-label, cluster-randomized controlled non-inferiority trial

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Abstract: Triptans are recommended as a treatment for moderate to severe migraines; however, barriers to administration include contraindications or possible side effects. In contrast, metoclopramide, which is frequently used as an antiemetic in the emergency department setting, has shown efficacy in alleviating migraine pain. This study investigated the non-inferiority of intravenously (IV) administered metoclopramide 10 mg compared with subcutaneously (SQ) administered sumatriptan 3 mg for alleviating migraine pain. In this single-center, open-label, cluster-randomized controlled trial, patients presenting to the emergency department with migraine attacks were allocated to either the IV metoclopramide 10 mg group or the SQ sumatriptan 3 mg group. The primary outcome was change in numerical rating scale (NRS) score for headache at 1 h after baseline. The non-inferiority margin was set as −1.0 NRS points. Thirty-six patients were enrolled over a period of 3 years, starting from July 2019. Reduction in NRS at 1 h was 4.1 (95% confidence interval [CI]: 2.8, 5.4) in the metoclopramide group and 5.2 (95% CI: 4.2, 6.1) in the sumatriptan group, with a mean difference of −1.1 (95% CI: −2.7, 0.4), indicating that metoclopramide was not non-inferior to sumatriptan. Four patients required rescue medication: 3 (18%) in the metoclopramide group and 1 (7%) in the sumatriptan group ($p = 0.34$). There were no serious adverse events in either group. One hour after metoclopramide administration, migraine pain was reduced compared with baseline, but metoclopramide did not demonstrate non-inferiority for alleviating acute migraine pain compared with sumatriptan.

***Keywords*:** emergency department, pain management, primary headache

Introduction

Migraine is one of the most common diseases among young and middle-aged people and is the world's second leading cause of disability, according to the Global Burden of Disease 2019 (*1*). The annual prevalence of migraine in Japan is 8.4% (*2*), and the number of patients who are transported to emergency departments (EDs) for migraine attacks is high. Previous studies have reported the analgesic effects of various medications, including nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, triptans, antiemetics (*e.g*., metoclopramide, prochlorperazine), antipsychotics (*e.g*., chlorpromazine, haloperidol), and ergotamine (*3,4*). However, consistent results have not been obtained in comparative studies of these drugs (*3,4*).

Although clinical guidelines recommend triptans as first-line therapy for moderate to severe migraine attacks (*5*), some doctors hesitate to use triptans in the ED setting because of contraindications, including history of ischemic disease and uncontrolled hypertension, or possible side effects such as chest pressure. Additionally, in Japan, the injectable formulation of sumatriptan has been discontinued, making it urgent to find an effective injectable treatment for migraines that can be used in emergency departments.

Metoclopramide, a dopamine antagonist, is frequently used for patients with nausea in ED settings in Japan because of its effectiveness, low cost, and few contraindications. Metoclopramide has long been used for nausea associated with migraine headaches, and past studies have shown that it can improve pain in migraine headaches. It was also reported that metoclopramide is effective as a single agent in the treatment of migraine headaches due to its dopamine antagonist effect (*6*). A meta-analysis of studies comparing metoclopramide with placebo showed that metoclopramide was more likely to provide a significant reduction in migraine pain (odds ratio 2.84, 95% confidence interval 1.05 to 7.68) (*7*). Previous studies have compared the efficacy of metoclopramide and sumatriptan. Friedman *et al*. found no significant difference between intravenous (IV) metoclopramide (up to 80 mg) and subcutaneous (SQ) sumatriptan (6 mg) in terms of pain improvement after 2

h (*8*). Talabi *et al*. compared intravenous metoclopramide (20 mg) and sumatriptan (6 mg) for the treatment of migraine and found that metoclopramide was superior in reducing pain at 1 h post-administration (*9*). However, it should be noted that the dosages of the medications used in those previous studies were higher than the dosages commonly used in Japan (*i.e.*, metoclopramide 10 mg, sumatriptan 3 mg).

In the present study, our objective was to assess whether IV metoclopramide 10 mg is non-inferior to SQ sumatriptan 3 mg for alleviating acute migraine pain in the ED setting.

Study design

This single-center, prospective, open-label, cluster-randomized controlled, non-inferiority trial was conducted over a 3-year period from July 1, 2019 to June 30, 2022 in the ED of the Center Hospital of the National Center for Global Health and Medicine in Japan, where about 11,000 patients are emergently transported each year. The study was approved by the certified review board of the National Center of Global Health and Medicine (NCGM) (Approved number: NCGM-C-003164-03) and conducted in accordance with the Declaration of Helsinki. The trial registration number is jRCTs031190007.

Patients

Patients emergently transported to the ED for headache were eligible for participation if they satisfied the criteria for migraine according to the International Classification of Headache Disorders of the International Headache Society, third edition (*10*), had moderate to severe headache intensity, were between the ages of 20 and 65 years, and provided written informed consent. Exclusion criteria are listed in the protocol paper (*11*).

Interventions

After providing informed consent, participants were allocated to one of the two treatment groups according to the month (see *randomization and data collection* below). Participants in the metoclopramide group received IV metoclopramide 10 mg and those in the sumatriptan group received SQ sumatriptan 3 mg.

Outcomes

The primary outcome was change in headache pain intensity at 1 h after baseline, evaluated according to NRS score. Secondary endpoints were change in NRS score 30 min after medication administration, headache relief 1 h after medication administration (defined as the patient's description of headache from severe or moderate to either mild or none), and adverse events.

Randomization and data collection

Metoclopramide and sumatriptan have different routes of administration, so for patient safety in the busy ED, randomization was performed on a monthly basis and neither physicians nor participants were blinded. The monthly allocation was carried out using computer-generated random numbers. The time of medication administration was considered Time 0, and pain intensity was assessed using NRS at Time 0 and again at 30 min and 1 h. Patients were asked to rate their pain on a scale between 0 and 10, with 0 representing no pain and 10 representing the worst pain imaginable. Pain intensity was also assessed according to four rankings (none, mild, moderate, and severe) at Time 0 and 1 h.

Sample size and statistical analysis

A previous study indicated an expected reduction in NRS pain score of 6 and 5 for participants in the metoclopramide and sumatriptan groups, respectively (*8*). Based on previous data, we set the standard deviation as ±3 NRS points. The non-inferiority cutoff was set as −1.0 NRS points, based on findings from a previous study that a between-group difference of 1.3 NRS points is a valid and reproducible minimum clinically significant change in the ED setting (*12*). Thus, a sample size of 37 per group was calculated to be sufficient, with a one-sided α of 0.025 and a power of 0.8. Taking potential dropout rates into account, the sample size for each group was set at 40. All randomized participants who satisfied the inclusion criteria and signed the informed consent form were included in the intention-to-treat (ITT) set. For the primary outcome, we reported the within-group improvement in NRS pain score between baseline and 1 h. Student's t-test was used to compare mean differences in NRS score and the lower one-sided 95% confidence interval (CI). A two-sided p value of < 0.05 was considered to indicate significance.

Key research findings

Patient background

Participant enrollment began in July 2019 and continued for 36 months. During the study period, a total of 1,025 patients with acute headache were screened, and migraine was diagnosed in 104 patients. A total of 36 patients satisfied the eligibility criteria and consented to participate in this study; 19 and 17 were randomized to the metoclopramide group and the sumatriptan group, respectively. In the metoclopramide group, 1 participant was discharged before the 1-h follow-up, and thus the data from only 18 participants were included for the analysis of the primary outcome. The target number of patients was 80, but due to the COVID-19 epidemic, we

Table 1. Baseline characteristics, headache severity at baseline

Characteristics	Metoclopramide (*n* = 19)	Sumatriptan (*n* = 17)	*p* value
Median age, y [IQR]	28 [24, 40]	29 [24, 41]	0.95
Female sex, *n* (%)	22 (58%)	12 (71%)	0.43
Median attack duration, h [IQR]	7 [3, 24]	5 [2, 10.5]	0.22
Self-medicated prior to ED visit, *n* (%)	10 (53%)	10 (58%)	0.71
Baseline NRS score, mean (SD)	5.9 (2.7)	6.9 (1.7)	0.18

ED, emergency department; NRS, numerical rating scale for pain, ranging from 0 (no pain) to 10 (worst pain imaginable); IQR, interquartile range; represents 25th, 75th percentile; SD, standard deviation.

determined that it would be difficult to reach the target, even if the study period were extended.

Table 1 shows the baseline characteristics, the headache severity at baseline. There were no differences between the two groups in terms of age or sex. More than half of the patients in both groups self-medicated prior to visiting the ED. The baseline NRS score (standard deviation) was 5.9 (± 2.7) in the metoclopramide group, and 6.9 (± 1.7) in sumatriptan group ($p = 0.18$).

Improvement in NRS after 30 min and 1 hour post-medication

The mean NRS score at 30 min was 3.3 (± 2.9) in the metoclopramide group and 3.6 (± 1.9) in the sumatriptan group, while the scores at 1 h were 1.9 (± 2.8) and 1.8 (± 1.8), respectively (Figure 1). The mean differences in reduction of NRS score from baseline to 1 h were −4.1 (± 2.6) in the metoclopramide group and −5.2 (± 1.8) in the sumatriptan group.

NRS scores were significantly reduced 1 h after administration of the treatment medications in both groups. However, metoclopramide was not statistically non-inferior to sumatriptan, given that the 95% confidence interval (CI) lower boundary of the absolute difference in mean NRS reduction was smaller than the inferiority margin of −1.0 (absolute difference −1.1; one-sided 95% CI −2.7). On the other hand, the proportion of patients whose pain disappeared one hour after medication was 50% in the metoclopramide group, compared to 35% in the sumatriptan group (Supplemental Table S1, *https://www.ghmopen.com/site/supplementaldata.html?ID=92*).

Comparison with previous studies

Compared with previous studies, the mean baseline NRS score prior to medication administration was lower in the present study. In the sample-size calculation based on a previous study, the mean baseline NRS score was over 8, and the reduction in NRS score for the metoclopramide group at 1 h was assumed to be 6 points (*8*). However, in the present study, the mean baseline NRS score was 6.4, which was lower than that in the previous study. The difference in baseline NRS scores between the previous study and the present study may

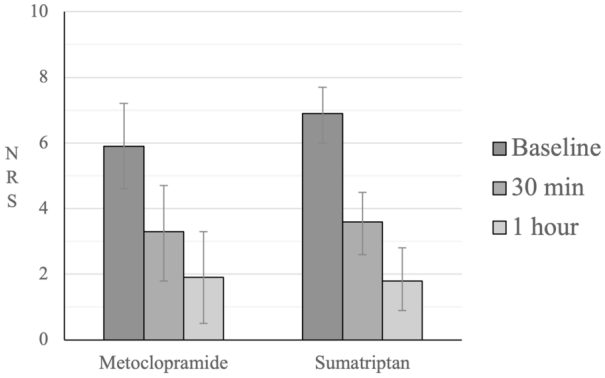

Figure 1. Numerical rating scale (NRS) scores for headache. The graph represents NRS before medication, 30 minutes after medication, and 1 hour after medication. Bars represent the 95% confidence intervals. Both groups showed a temporal decrease in NRS scores after medication, with no significant differences observed between the groups at each time point.

have implications for the interpretation of the results. In a study by Talabi *et al*., metoclopramide demonstrated a greater decrease in visual analog scale scores compared with sumatriptan, but there were differences between the two groups in terms of patient age and baseline pain scales (*9*). Additionally, both groups received a higher dose than we used in our study. Meanwhile, in studies investigating the optimal dosage of metoclopramide for migraine treatment, no significant increase in pain improvement effect was observed with doses of 20 mg or 40 mg compared with 10 mg (*13*). In a previous study comparing subcutaneous injections of 3 mg and 6 mg sumatriptan for the treatment of migraine attacks, there was no significant difference between the two groups in terms of the proportion of subjects who were pain-free 1 h after administration or in reduction in pain intensity (*14*).

Adverse events

There were no serious adverse events in either group. No side effects were reported in the metoclopramide group but 1 patient (5.6%) in the sumatriptan group complained of nausea after administration, but the nausea resolved spontaneously.

In this study, there were no serious adverse events or chest symptoms, which might be a concern with sumatriptan, in either group. In addition, other side

effects were minimal, with only one participant in the sumatriptan group experiencing worsened nausea. The limited occurrence of side effects can be attributed to several factors, including the relatively small sample size, lower dosage compared with previous studies, and the short duration of observation. It has been previously reported that side effects called "triptan sensations", which include paresthesia and chest symptoms, are dose related (*15*).

Limitations

There are several limitations to this study. First, because of the COVID-19 epidemic, the study was terminated before the target sample size was reached; therefore, the sample size was small and the statistical power was insufficient. Despite randomization, there was a difference of more than 1.0 in the baseline mean NRS scores between the two groups. Second, blinding was impractical due to differences in administration methods. Third, this study was conducted at a single center, which may limit the generalizability of the findings. Finally, we did not evaluate the persistence of the pain-improving effect.

In conclusion, 1 h after metoclopramide administration, migraine pain was reduced compared with baseline, but metoclopramide did not demonstrate non-inferiority or inferiority for pain relief of acute migraine pain compared with sumatriptan, and thus the results are inconclusive.

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Scaling-up hepatitis B testing and treatment and adapting response during COVID-19: Experience of the demonstration pilot in Central Luzon Region, Philippines

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Abstract: This study aimed to describe the experience of scaling up hepatitis B virus (HBV) testing and treatment services during the COVID-19 pandemic in Central Luzon, Philippines. In 2019, service delivery networks (SDN) were established across all health system levels, linking tertiary and secondary care to primary units. Routine screening began at primary healthcare facilities, increasing HBV case detection. Community outreach improved public screening. However, the pandemic severely disrupted services, leading to the implementation of telephone hotlines and courier services for chronic treatment support. A pilot project review from August 2019 to September 2020 revealed that over 50,000 individuals were screened, with over a thousand testing positive for HBV. Thirteen percent of positive cases were eligible and enrolled for treatment. The pilot demonstrated successful scaling of HBV testing and treatment and the ability to adapt service delivery during the pandemic.

***Keywords*:** HBV, service delivery network, COVID-19

Introduction

Hepatitis B, caused by the hepatitis B virus (HBV), can result in acute or chronic illness, with chronic cases leading to liver cirrhosis or cancer (*1*). In the Philippines, the prevalence of Chronic Hepatitis B (CHB) is approximately 9.6%, affecting around 10 million individuals (*2*). From 2013 to 2017, 14,082 confirmed cases were reported, with 1,163 cases in Central Luzon, Philippines from 2015 to 2018 (*3*).

The urgency to control Hepatitis B is underscored by its high prevalence and alignment with the United Nations' Sustainable Development Goals (SDGs). Goal 3, Target 3.3 aims to end epidemics, including viral hepatitis, by 2030. In response, the Philippines initiated a National Viral Hepatitis Task Force in 2013, collaborating with the World Health Organization and endorsing the Regional Action Plan for Viral Hepatitis in 2015 (*4*).

In 2017, the Department of Health institutionalized a policy to control viral hepatitis, prioritizing access to effective treatment. The Department Memorandum Number 2019-0062 released in 2019 outlined the "Integration of Chronic Hepatitis B Management in Selected Health Facilities in National Capital Region and Central Luzon: Demonstration Project", serving as an evaluation summary for the Hepatitis B Demonstration Project in Central Luzon (Figure 1).

Implementation

The World Health Organization Philippines supported a community-based, people centered delivery of Hepatitis B services to 2 local government units (LGU) of Central Luzon. The objectives of the Project were to *i*) to document acceptability of Hepatitis B service delivery and referral model including packages of services, recording and reporting system and monitoring of cascade of services; *ii*) to establish baseline information on cascade of care (screening, treatment eligibility, treatment coverage) for Chronic Hepatitis B infection; and *iii*) to evaluate the Hepatitis B Service Delivery and Referral model for planning on sustainability and implementation expansion. The Project consisted of two phases, pre-implementation phase and implementation phase. Training materials were also developed and

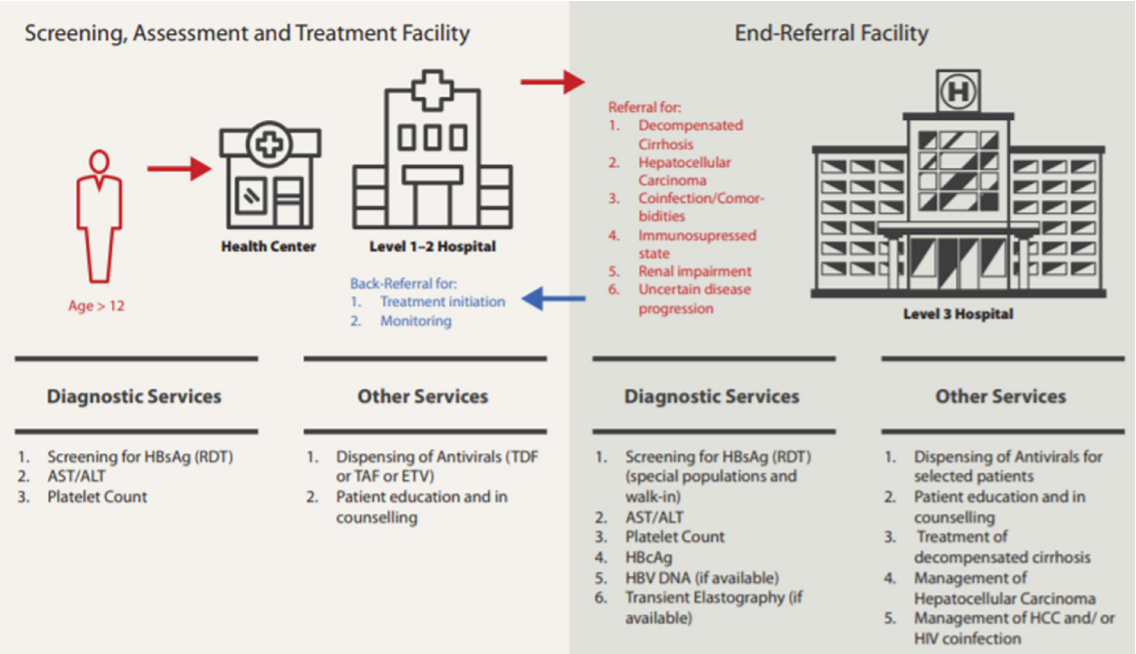

Figure 1. Hepatitis B Service Delivery Model in Central Luzon, Philippines.

reproduced soft copies distributed for each service facility and incorporated were the Information, Education and Communication (IEC) materials.

Pre-implementation phase

In the pre-implementation phase, rapid assessment of the present capacity in terms of facility readiness like the laboratory, human resources, patient flow, available IEC materials, recording and reporting platforms and existing referral network. The following programs that contribute to finding the missing millions in the country were also reviewed informally and these are Prevention of Mother-to-Child Transmission services of the Safe Motherhood Program, National Voluntary Blood Donation Program, HIV, STI Program, Infection prevention and control practices in hospitals and rural health units including those with birthing facilities.

Implementation phase

The implementation of the program initially began in the province of Bataan and Angeles City, Pampanga in August 2019. In December 2019 the Project was expanded to include DOH Hospitals in Talavera and Cabanatuan City, which are both located in the Province of Nueva Ecija.

The interim guidelines on Hep B diagnosis and treatment provides the specifics of a technical guide on diagnosis, treatment and management. It also included monitoring guidelines for those HBV positive on treatment and of those not eligible for treatment. Cirrhosis and hepatocellular carcinoma are included in the monitoring of hepatitis B progression.

Both Screening, Assessment and Treatment Facilities (SATF) and End Referral Facilities (ERF) provides testing and treatment. However, assessment for eligibility for treatment are not always present in every SATF, hence the service delivery network (SDN) addresses the completion of the full cascade of services except for the HBV DNA test.

ERF is level 3 referral facility provides the full cascade of services plus other tests to diagnose cirrhosis and hepatocellular carcinoma and management of complicated and or decompensated Chronic Hepatitis B.

Initiation of treatment by the physician in SATF or ERF and refill of monthly medicines was done initially during the first few months until patient is considered stable with treatment and a quarterly refill was done. With the announcement of COVID-19 pandemic, treatment follow-up became erratic and monitoring of treatment response was not regularly done. Those Hepatitis B patients not on treatment were lost to follow-up and will need to be tracked in the community. However, the COVID-19 situation in Central Luzon limits the health workers to work on regular programs and the patients are as well not confident to make a follow-up monitoring of their Hep B status especially so that they are not symptomatic.

Key findings

From August 2019 to September 2020, the demonstration sits in Central Luzon reported 36,300 clients who were screened for HBsAg, of these, 1,252 were positive. Seventy-seven percent (969/1,252) were registered in the masterlist for further assessment (Figure 2). Out of these

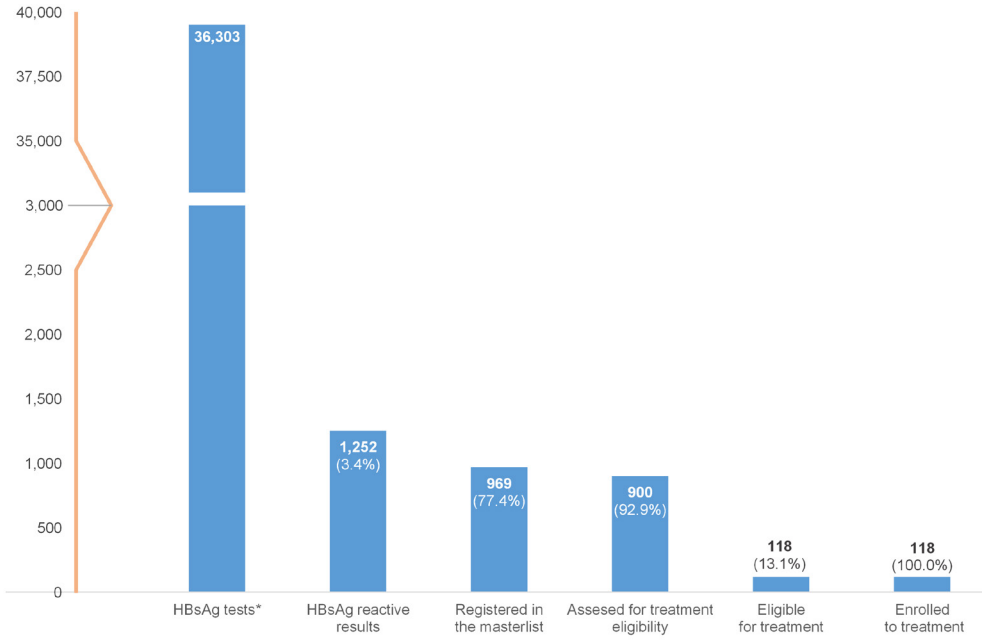

Figure 2. Hepatitis B cascade of services in Demonstration Sites in Central Luzon, August 2019 to September 2020. *Note*: *HBsAg tests were aggregate counts and was not case-based. Double reporting may be possible if one person got tested in multiple laboratories or at multiple times during the reporting period. Counts reported do not represent the final number and subject to change after the inclusion of late reports and review of cases.

969 patients, 900 (93%) were assessed for eligibility for treatment and 118 (13%) were found to be eligible for treatment. Thirteen percent (118) of the clients who were assessed were eligible for treatment. All of whom were initiated with Tenofovir-based antiviral treatment. Among those who were enrolled in treatment, 64% were on treatment, 32% were lost to follow-up and 4% were reported dead. All 118 (100%) eligible were enrolled and initiated on treatment. The remaining 782 patients who were assessed for treatment but were not found to be eligible for treatment need to be monitored further. Also, the 96 positive patients who were not assessed need to be traced and assessed for treatment.

In 2020, the COVID-19 pandemic has had a major impact on the continuity of delivery of essential health services including Hepatitis B. While the health services are being challenged because of COVID-19, Hepatitis B services were continuously provided by SATF and ERF. This demonstration project has provided important insights in terms of the acceptability of a Hepatitis B service delivery model in the Philippines. While a nationwide implementation is highly encouraged, several recommendations are also made to improve the program:

i) Streamlining the monitoring and evaluation through integration of the viral hepatitis module in the existing One HIV/AIDS and STI Information System (OHASIS) which has a data validation, deduplication, and data presentation mechanisms. A strong disease surveillance system is necessary to provide data on incidence and prevalence of HBV and HCV so that policy makers can implement effective primary prevention, screening and treatment strategies. It is also recommended to include monitoring indicators for disease progression for those not eligible for treatment and monitoring indicators for treatment response for those undergoing treatment.

ii) Increase access points nation-wide through a phased implementation model such as sustaining the expansion to all DOH Hospitals, established HIV treatment facilities and those health facilities ready as SATF and ERF.

iii) A platform for the capacity-building of the healthcare providers should also be ready and should consider the inclusion in the DOH Academy. Due to the COVID-19 pandemic, face to face training is unlikely to be held soon. It is recommended that training modules on management of hepatitis B and programmatic topics such as monitoring, and reporting be developed and delivered *via* online training platforms. This may be developed in coordination with the Health Human Resources Development Bureau (HHRDB), the Hepatology Society of the Philippines (HSP) and WHO.

iv) Intensify awareness campaign on the prevention of transmission of hepatitis, and the importance of access to hepatitis testing and availability of deleted treatment and other services for those who test reactive.

In conclusion, the Hepatitis B pilot project demonstrated a model for scaling up HBV testing and treatment services within the context of the Philippines' healthcare system. By established SDN linking tertiary, secondary, and primary care units, the project successfully increased routine HBV screening and detection. This project highlighted the acceptability of a Hepatitis B service delivery model for the Philippines and recommended integrating the hepatitis into the

existing health information system for streamlined monitoring and evaluation, expanding access points nationwide, developing online training modules for health service providers, and intensifying awareness campaigns on hepatitis prevention and treatment.

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2020 and 2021 web-based training program on children's mental health during the COVID-19 pandemic

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Abstract: COVID-19 adversely affected mental health care and service delivery globally. Continuing its thrust on improving child and adolescent mental health, the National Center for Global Health and Medicine conducted a training program in collaboration with the University of the Ryukyus, University of the Philippines Manila, the National Center for Mental Health, and the Philippine Society of Child and Adolescent Psychiatry in 2020 and 2021 to discuss the situation, challenges, and good practices in mental health treatment, care, and promotion for children and adolescents during the COVID-19 pandemic. Composed of 15 on-demand lectures and a webinar on three general mental health themes, the training identified the need for strengthening the provision of care not only in specialized health facilities but also in empowering communities in addressing children and adolescent mental health concerns. Collaboration between different stakeholders is needed to ensure child and adolescent well-being during public health emergencies.

***Keywords*:** COVID-19, mental health, child, adolescent, Philippines, Japan

Introduction

Adolescence is a crucial phase in the physical, emotional, and social development of an individual (*1*) and it also coincides with the stage where mental health conditions begin to manifest (*2*). Mental health problems affect children and adolescents globally (*2*) with mental disorders as the third leading cause of disability-adjusted life years (DALY) among children in the Western Pacific Region. Additionally, suicide remains high in the region.

The COVID-19 pandemic exacerbated mental health challenges and disrupted mental health care and service delivery globally (*3*). Despite a lower risk of COVID-19 infection among children and adolescents, associated factors such as school closures and economic hardship experienced by the family during lockdowns pose significant threats to their mental well-being (*4*). Due to the pandemic, the need for mental health support for children and adolescents has increased, emphasizing the crucial role of engaging stakeholders in education and health to address these concerns effectively.

Children and adolescents with mental health

problems are also a cause of concern in the Philippines (*5*), with a reported 16% prevalence of mental disorders (*6*) and 16.8% prevalence of attempted suicide (*7*). The pandemic further exacerbated the situation, as evidenced by the 200% increase in calls to suicide prevention and crisis intervention hotlines (*8*), higher levels of stress, moderate to severe depression and psychological impact and anxiety (*9,10*).

Training program objectives

Given the increase in mental health concerns during the pandemic, the National Center for Global Health and Medicine (NCGM) organized a training program for children's mental health, specifically focusing on the challenges brought by the COVID-19 pandemic. Building on previous initiatives (*11,12*), NCGM, in collaboration with the University of the Ryukyus, the University of the Philippines Manila (UPM), the National Center for Mental Health (NCMH), and the Philippine Society of Child and Adolescent Psychiatry (PSCAP), conducted additional training programs in 2020 and 2021, reflecting a continued commitment to enhance child and adolescent mental health. The programs, entitled, "*Project to reinforce medical treatment, care, and the promotion of mental health among children and adolescents*" in 2020 and "*Project to reinforce medical treatment, care, and promotion of mental health among children and adolescents during the COVID-19 pandemic*" in 2021, aimed to discuss the current situation, challenges, and good practices in mental health treatment, care, and promotion for children and adolescents in the time of COVID-19.

Training program design

Training content

The training programs were shifted to web-based on-demand training in 2020 and 2021 to adapt to travel constraints brought about by the pandemic. The 2020 program covered 15 topics under three themes: *i*) child and adolescent mental health during the COVID-19 pandemic, *ii*) child and adolescent mental health in the school setting, and *iii*) special topics such as child abuse, pharmacotherapy, community mental health, and disaster psychiatry (Table 1). Each topic was composed of a prerecorded lecture and a pre-and post-lecture evaluation. Lectures were available on-demand through Moodle, and accessible to registered participants from January 4 to February 28, 2021. Two interactive sessions restricted to training participants – an introductory session on the training and a webinar on education in the new normal – were also conducted through Zoom. Lectures were subsequently made available to the public in 2021 through Youtube and the NCGM Clinical Center for Children's Mental Health homepage (*13*). The last webinar was held on February 17, 2022 through Zoom to share experiences on children and adolescent mental health while working in healthcare facilities during the COVID-19 pandemic and provide a global perspective on mental health during the pandemic.

Participants

Teachers, health personnel, academics, and researchers were invited to participate through email from December 18, 2020 to January 28, 2021. The email, which described the objectives, content, and schedule of the web-based training program, also included the registration link. Data privacy protection measures were implemented and a certificate was provided to participants who completed the program.

Similar to previous activities, the invitation to the webinar held on February 17, 2022 was extended to

Table 1. Lectures included in the 2020 web-based on-demand training program

Topics	Lecture
Child And Adolescent Mental Health During the COVID-19 Pandemic	Child Mental Health During COVID-19 (Japan) Extending Child Community Mental Health Care During the COVID-19 Pandemic (Philippines) Care for Children During the Pandemic (Philippines)
Child And Adolescent Mental Health in the School Setting	School Closure During the COVID-19 Pandemic (Japan) Education in the New Normal: Learning and Psychosocial Challenges to Students in the Philippines (Philippines) Development of a Mental Health Literacy Teaching Material for Schools in the Philippines
Special Topics on Child And Adolescent Mental Health	Online Sexual Exploitation in the Philippines Current Situation of Child Abuse in Japan Current issues Pharmacotherapy in Japan Traditional Practices in Managing Children's Illness "Folk sector" involvement in community mental health Promotion of community mental health: an example in the remote island of Okinawa Needs and global strategy of community mental health Disaster Psychiatry in Japan (Nuclear Power Plant Accidents) Disaster Psychiatry in Japan (Earthquake)

psychiatrists, psychologists, teachers, school health personnel, academics, and researchers in the field of child and adolescent mental health. Participants who accomplished a pre-test and a post-test was provided with a certificate of attendance.

Training outcomes

On-demand lectures and synchronous sessions in 2021

A total of 202 people registered in the training program (Table 2), with 27 (13.37%) completing selected lectures and five participants (2.5%) completing all sessions. The majority of participants who only viewed selected lectures accessed the sessions consecutively while 20% only viewed sessions that they wanted. The session with the most recorded views was "Child Mental Health During COVID-19 (Japan)", followed by the session "Extending Child Community Mental Health Care During the COVID-19 Pandemic (Philippines)", and "The Care for Children During the Pandemic (Philippines)". The synchronous sessions on education in the new normal was attended by 15 participants. The average pre-test score was 42.9% while the average post-test score was 83.3%, resulting in a 40.4% score improvement.

Webinar in 2022

The webinar was attended by a total of 259 participants, with 63 accomplishing both the pre- and post-tests. The average score for the pre-test was 66.7% while the average post-test score was 77.8%, showing an 11.1% improvement in the average score. An evaluation of the webinar revealed an outstanding rating in terms of content, delivery, and logistical preparation.

Participants stated their appreciation for the insightful discussion on global mental health and the strategies implemented by countries like Japan in response to the COVID-19 pandemic. The comparative analysis of best practices between Japan and the Philippines provided an opportunity to examine good practices that can be adapted to local settings. Notably, participants highlighted the significance of addressing suicidal behaviors among children and adolescents, emphasizing the importance of identifying red flags among students and how to address these. For future webinars, participants recommended a variety of topics such as awareness of different disabilities, stress and burnout management, internet addiction, coping skills, counseling strategies for students with mental health issues, psychological first aid, resilience for children, and self-care and support for children. Some participants also suggested discussing the mental health programs that were developed and implemented by the Philippine government, as well as strategies that will support students as they return to school during the COVID-19 pandemic. Another major theme that the participants recommended was mental health in the workplace, recognizing that teaching and non-teaching personnel are also experiencing stress, burnout, and other mental health problems like their students.

Table 2. Profession of the Participants in the web-based on-demand training program

Profession	Frequency	Percent
Teacher	132	63.16
Medical Doctor	38	18.18
Nurse	22	10.53
Psychologist	3	1.44
Faculty member	3	1.44
Dean	2	0.96
Guidance Counselor	2	0.96
School personnel	2	0.96
Educator	1	0.48
Psychiatrist	1	0.48
Dentist	1	0.48
Clinical Instructor	1	0.48
Public Health Program Manager	1	0.48
Total	209	100.0

School closures during the COVID-19 pandemic affected mental health status and health service delivery

Both Japan and the Philippines implemented physical distancing measures to mitigate the spread of COVID-19, which disrupted daily life and interpersonal interactions. Schools in both countries were forced to close and shift to online learning. Philippine schools adopted alternative modes of learning, including online and modular approaches while Japanese schools gradually reopened in June 2020 with a staggered schedule, adopting online teaching systems. Minimum health measures, such as mask-wearing and limiting social activities, were implemented, and various school events such as school trips and forest schools, as well as sports events and school festivals were canceled.

Child and adolescent mental health during the COVID-19 pandemic

Although children and adolescents had lower COVID-19 infection rates than adults, they also faced significant challenges due to the pandemic (*4*). Females and individuals aged 12 to 21 years in the Philippines exhibited stress, depression symptoms, and anxiety (*9*). Japanese students had reduced physical activity and struggled with finding interests during extended school closures. Physical and psychological effects, including increased screen time, needed attention and monitoring (*14*).

The added stressors in the household due to the pandemic such as disruption in livelihood and social isolation, can increase the tensions at home, putting

children at a higher risk for abuse and neglect (*15*) and isolation from important child protection services (*16*). The same increasing trend in abuse and neglect were observed in both countries (*17,18*) with online sexual exploitation increasing by 264% in the Philippines (*18*). Children also spent more time indoors during the pandemic, resulting in less physical activity, increased pathological internet use, and binge eating behaviors.

Resources for mental health during the COVID-19 pandemic

The stay-at-home measures posed challenges to service delivery during the pandemic. In Japan, a decrease in outpatient consultations was observed when comparing the current figures with pre-pandemic data (*19*) while the number of children with anorexia nervosa requiring hospitalization increased by 104%. Telemedicine services were implemented to address the challenges posed by the restrictions on hospital and home visits.

The increase in mental health problems among children and adolescents also emphasizes the lack of mental health professionals in both Japan and the Philippines, which has been a long-standing problem even pre-pandemic (*12*). To augment the mental health services available to the Filipino public and raise awareness during the pandemic, government, non-government, and professional societies established telemedicine platforms, helplines, and mental health promotion campaigns.

In conclusion, the online training program provided an opportunity to share the current situation, challenges, and good practices in mental health treatment, care, and promotion for children and adolescents in Japan and the Philippines during the COVID-19 pandemic. It also provided an opportunity to share best practices for child and adolescent mental health care and promotion in a post-COVID-19 society. The COVID-19 pandemic exacerbated mental health problems among children and adolescents, with mitigation measures disrupting the routine of children and adolescents and subsequently increasing risk of their exposure to violence and developing mental health problems. The pandemic emphasizes the need for strengthening care not only in specialized health facilities but also by empowering communities to address mental health concerns of children and adolescents. Collaboration between health facilities, schools, local government, different stakeholders, and families, is crucial to ensure the well-being of children and adolescents during public health emergencies.

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Quality improvement of the national examination for nurses and midwives in Lao People's Democratic Republic

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Abstract: The quality of national licensing examinations is critical to ensuring a competent health workforce. This communication analyzes the process of improving examination questions for nurses and midwives in the Lao People's Democratic Republic (Lao PDR). Following the Ministry of Health's 2014 amendment to the Law on Health Care and the 2015 approval of the Strategy on Healthcare Professional Licensing and Registration System, a national licensing examination was initiated. Supported by the Japan International Cooperation Agency, the Nursing and Midwifery Board has conducted the annual examination since 2019, with 2,000 candidates participating to date. A continuous quality improvement cycle involving statistical analysis, revision, and new question creation has been implemented. Results showed significant improvement in key indicators such as correct answer rates and point-biserial correlations. These efforts highlight the importance of continuous quality improvement and collaboration between educators and clinicians, providing a model for enhancing healthcare professional licensing examinations.

***Keywords*:** national examination, license, regulation, nursing, midwifery

Introduction

The performance of healthcare systems hinges on healthcare providers' knowledge, skills, and motivation. Recognizing this, the World Health Organization has advocated for competency-based national licensing and relicensing assessments for graduates from both public and private institutions (*1*). In addition, the Association of Southeast Asian Nations (ASEAN) Mutual Recognition Arrangement, signed in 2016, has catalyzed the development of registration, licensing, and continuing education systems for healthcare professionals in member states (*2*). In response, the Lao People's Democratic Republic (Lao PDR) Ministry of Health (MoH) amended *the Law on Health Care* in 2014 to mandate a national licensing examination for healthcare professionals (*3*). Following this, the MoH endorsed *the Strategy on Healthcare Professional Licensing and Registration System in Lao PDR 2016–2025* (Strategy) in 2015, including a national licensure examination for healthcare professionals as a core pillar (*4*). To implement the Strategy, the MoH sought technical cooperation from the government of Japan, leading to the launch of the Project for Sustainable Development and Quality Assurance of Healthcare Professionals in Lao PDR by the Japan International Cooperation Agency (JICA) in 2018.

This paper aimed to analyze the process of improving the quality of examination questions for the national examination for nurses and midwives in Lao PDR, evaluate the effectiveness of these improvements, and discuss the implications for the future of healthcare professional licensing and regulation.

National licensing examination implementation

The Nursing and Midwifery Board (Board), under the Healthcare Professional Council (HPC), is the regulatory body of the Strategy. At the national examination's launch, the Board discussed and approved the examination outline, including the organizer, frequency, and venue, and conducted a pilot examination in September 2019. Since the following year, the Board has conducted the national examination annually, with 2,000

graduates participating to date. The national examination, held simultaneously over two days at nine educational institutions nationwide, is a written test consisting of multiple-choice questions (MCQs).

Nursing education and licensure in Lao PDR

Prior to the national examination, graduation from a nursing or midwifery educational institution was the sole requirement to practice as a nurse or midwife (*5*). Eligibility for the national examination requires completion of a higher diploma curriculum or above in nursing or midwifery. Nine public institutions offer these advanced diplomas, one offering a four-year bachelor's degree program and the others being three-year colleges or vocational schools (*5*). Despite a uniform syllabus and competency-based curriculum developed in 2015, teaching materials, including textbooks, were not standardized. Medical education, including nursing and midwifery, is conducted exclusively in Lao, the country's official language, reflecting its multi-ethnic makeup. Upgrading courses for nurses and midwives, although encouraged (*6*), are excluded from the national examination due to their clinical experience. Graduates from equivalent programs in neighboring countries are also eligible upon diploma submission. Application for the national examination coincides with the professional license application, and the certificate of passing the national examination serves as the license. Successful candidates generally undergo an eight-month professional internship program to cultivate practical skills.

Quality improvement cycle of national licensing examinations

Introduction of quality improvement cycle

Over the past three years of administering national examinations, a need to improve and ensure the quality of exam questions was recognized. Thus, we applied a continuous quality improvement cycle (Figure 1), applying quality improvement methods such as Plan-Do-Study-Act cycles (*7*), to enhance question quality. Post examination (Step 1), the Board evaluates the statistical analysis results of the questions (Step 2). A technical working group comprising faculty from educational institutions, clinical nurses, and midwives reviews and revises the examination blueprint and creates new questions (Step 3). The Board, with technical assistance from the Healthcare Professional Bureau, MoH, selects 240 questions each for nursing and midwifery, proofreading for consistency and readability (Step 4).

Quality improvement approach

Key approaches during the evaluation (Step 2),

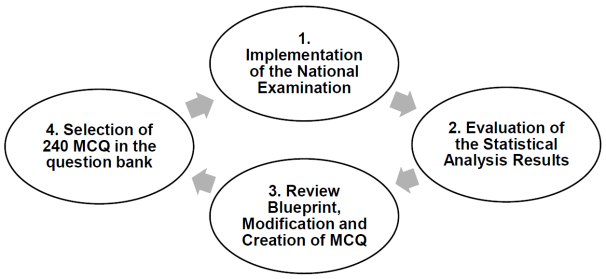

Figure 1. Quality Improvement Cycle of the National Examination in Lao People's Democratic Republic

modification, and creation (Step 3) include: 1. key validation, 2. question revision based on item analysis, and 3. new question creation based on lessons learned. Evaluation indices for MCQs include correct answer rate and point-biserial correlation. A low correct answer rate indicates difficulty beyond qualifying exam standards, while a negative point-biserial correlation suggests that low-performing students answered better than high-performing ones, impacting reliability (*8*). The analysis was performed using *Remark Office OMR Software* (Gravic, Inc., Pennsylvania, US).

Implementation of continuous quality improvement

Key validation of the exam questions occurs immediately post-examination and prior to scoring. Questions with significantly low correct answer rates or point-biserial correlations undergo qualitative review by the Board to determine exclusion, acceptance of multiple correct answers, or retention. Questions are modified based on the item analysis results during preparation for the subsequent national examination. Criteria include correct answer rate and point-biserial correlation, and questions with non-selected options are also revised. Distribution data of the examinees' responses guide modifications. Technical working group members perform comprehensive assessments for revision, ensuring plausible alternatives and sufficient information. New questions are created based on the lessons learned. Members modifying questions based on various data understand inappropriate questions and how to develop good questions. New questions require evidence-based development, improving quality and stability.

Achievements through quality improvement

The recent national examination showed significant improvements in the correct answer rate and point-biserial correlation (Table 1). The mean correct answer rate increased by approximately 10 points, and the mean point-biserial correlation increased by approximately 0.15. Notably, as defined by these criteria, the number of good questions doubled. These improvements correlated

Table 1. Changes in difficulty and quality of examination questions from the first to third national examination

Items	First National Examination (2020)	Second National Examination (2021)	Third National Examination (2022)
Means of Correct Answer Rate			
Nursing	49.03	46.59	60.17
Midwifery	55.61	55.06	65.00
Means of Point-Biserial Correlation			
Nursing	0.28	0.32	0.46
Midwifery	0.26	0.32	0.41
Number of Good Questions			
Nursing	91/240 (38%)	114/237 (48%)	178/238 (75%)
Midwifery	64/240 (27%)	111/235 (47%)	159/236 (67%)
Means of Examinees' Total Score			
Nursing	121.7/240 (51%)	117.4/237 (50%)	154.9/238 (65%)
Midwifery	134.4/240 (56%)	134.3/235 (57%)	168.6/236 (71%)

with the higher examinee performance, with the mean total scores increasing by over 30 points. Although passing criteria are undisclosed, improved question quality has enabled more reasonable passing criteria.

Behind the quality pursuit

Ensuring examination quality is crucial for state-administered credential qualifications. Continuous quality improvement in Lao PDR has enhanced examination question quality. Objective analytical data facilitated critical assessments and motivated those involved in examination administration. A continuous quality improvement cycle allows for responsive blueprint reviews, aligning with the population's health needs and healthcare policies (*9*).

The involvement of nursing and midwifery faculty in technical working groups ensured alignment with actual teaching content. The Board emphasized the examination aim of testing minimum knowledge and competence standards. Intensive meetings fostered communication and mutual learning among faculty members. Clinical nurses and midwives' participation incorporated practical clinical perspectives.

Keys for further improvement

Incorporating external professional organization perspectives could further improve examination quality. For example, the Japan Society of Midwifery Education qualitatively reviews exam questions post-examination, submitting reports to a regulatory body in Japan (*10*). Although releasing questions is restricted in Lao PDR, external review could address inappropriate questions. Continuing capacity-building efforts within the HPC is essential for effectively regulating healthcare professionals (*9*). Sustained governmental commitment is crucial for maintaining high standards in healthcare professional regulation post-project completion.

In conclusion, this paper highlights the success of a continuous quality improvement cycle in enhancing the national examination for nurses and midwives in Lao PDR. Significant improvements in question quality and examinee performance were achieved through rigorous evaluation, modification, and creation of exam content, with valuable contributions from nursing and midwifery faculty and clinicians. These advancements not only raise examination standards but also align closely with current educational and clinical practices. This approach serves as a model for improving healthcare professional licensing and regulation, emphasizing the importance of ongoing quality improvement in healthcare education. The sustained commitment of the regulatory body to these improvements is crucial for maintaining high standards in healthcare professional regulation.

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Case Reports	~3,000	~5	~30
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Comments			
Correspondence			
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