Capacity building in screening and treatment of diabetic retinopathy in Asia-Pacific region

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The focus of capacity building for screening and treatment of diabetic retinopathy (DR) is on health professionals who are nonophthalmologists. Both physicians and nonphysicians are recruited for screening DR. Although there is no standardization of the course syllabus for the capacity building, it is generally accepted to keep their sensitivity >80%, specificity >95%, and clinical failure rate <5% for the nonophthalmologists, if possible. A systematic literature search was performed using the PubMed database and the following search terms: diabetic retinopathy, diabetic retinopathy screening, Asia, diabetic retinopathy treatment, age-related macular degeneration, capacity building, deep learning, artificial intelligence (AI), nurse-led clinic, and intravitreal injection (IVI). AI may be a tool for improving their capacity. Capacity building on IVIs of antivascular endothelial growth factors for DR is focused on nurses. There is evidence that, after a supervision of an average of 100 initial injections, the trained nurses can do the injections effectively and safely, the rate of endophthalmitis ranges from 0.03 to 0.07%, comparable to ophthalmologists. However, laws and regulations, which are different among countries, are challenges and barriers for nonophthalmologists, particularly for nonphysicians, for both screening and treatment of DR. Even if nonphysicians or physicians who are nonophthalmologists are legally approved for these tasks, sustainability of the capacity is another important challenge, this may be achieved if the capacity building can be part of their career development. Patient acceptability is another important barrier for initiating care provided by nonophthalmologists, particularly in Asia. There are also collaborations between national eye institutes of high-income countries, nongovernment organizations, and local eye institutes to improve both the quality and quantity of ophthalmologists and retinal specialists in low-income countries in Asia. This approach may require more labor, cost, and time consuming than training nonophthalmologists.

Key words: Capacity building, diabetic retinopathy screening, diabetic retinopathy treatment, health workforce, nurse-led intravitreal injection

Health workforce crisis has long been identified by the World Health Organization (WHO) as one of the major health problems in the world. Millions more of health professionals, such as medical doctors and nurses, are needed to achieve universal health coverage by 2030, which is the goal of WHO.[1] Human Resource for Health Action Plan of WHO proposed the interventions which should be interlinked in five areas: education, partnership, leadership, financing, and policy to solve this crisis.[2] An example of linked interventions was an effort to establish long-term health links which represented international partnership between developed and developing countries. These links were often dedicated to a specific intervention, such as capacity building of health professionals.[2]

For building capacity in health care, skills development has been the main avenue and the four contributing themes are identified: (a) at individual level: growth in knowledge, skills, and professional relationship of workers, (b) at institutional level: harmonized curricular for training institutes, (c) at country level: clinical guideline developed and implemented nationally, and (d) at regional level: fellowship examination and annual congress running.[3]

The VISION 2020 LINKS program, launched in 2004 by the International Centre for Eye Health, was a well-recognized example of intervention links for the purpose of capacity building of eye care in Africa.[4] This program takes on the regional level theme of capacity building in eye care between the College of Ophthalmology of Eastern, Central, and Southern Africa and the Royal College of Ophthalmologists in the United Kingdom with the aims to increase the quantity and quality of eye care training.

In Asia-Pacific region, where half of the world's population resides and more than half of the countries have low or middle incomes, it is critical to understand the current and

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projected needs for eye care services.[5] This is essential for strategic planning for the development of appropriate eye health resources and health policies to potentially overcome the shortage of eye care workforce in this region. The needs for eye care were proposed in refractive services, cataract surgery services, and annual eye examination services, where the high prevalence of diabetes was the driving factor underlying them.[5] The burden of providing such eye care services highlights the need for new strategies for improvements in primary care and capacity building for eye care professionals including ophthalmologists, ophthalmic nurses, ophthalmic technicians, and even nonophthalmic health professionals.

Diabetes is a major health crisis in countries across levels of their incomes in the world.[6] While regular eye examination in patients with diabetes[7] and timely treatment of diabetic retinopathy (DR)[8] are keys to successfully reduce the risk of blindness from the disease, a shortage of eye care workforce compared to the growing number of patients with diabetes is one of the factors contributable to the global blindness due to diabetes. Capacity building in screening and treatment of DR may be pieces of the puzzle to unlock the keys to reduce the risk of blindness for patients with diabetes in this region and in the world.

Method of Literature Search

A systematic literature search was performed using the PubMed database for articles in English published since 2000 with the following search terms: diabetic retinopathy, diabetic retinopathy screening, Asia, diabetic retinopathy treatment, age-related macular degeneration, capacity building, deep learning, artificial intelligence, nurse-led clinic, and intravitreal injection.

Capacity Building in DR Screening

Capacity building of health professionals

The shortage of ophthalmologists and retina specialists in Asia-Pacific countries[9] has already led to engaging health professionals who are nonophthalmologists for screening of DR in many countries. Capacity building on these professionals is essential for the effectiveness of the screening. Table 1 summarizes published studies on DR screening protocols

and their effectiveness when the screenings were deployed by nonophthalmologists.

In Australia, Askew and colleagues[10] reported training two general practitioners with online upskilling program offered by the University of Queensland Discipline of General Practice and accredited by the Royal Australian and New Zealand College of Ophthalmologists Queensland Faculty to conduct DR screening. The training was 9 hours long, and an agreement of more than 75% compared with two ophthalmologists in interpretation of at least 30 retinal photographs was required to achieve accreditation achievement.

In Singapore, both physicians and nonphysicians were deployed as screeners in the DR screening program. Bhargava and colleagues[11] reported that the physicians and nonphysicians were trained in different courses and evaluated in different systems. The five family physicians were trained by a retinal specialist for DR grading on retinal photographs for a two-hour period and accredited every two years. This training for family physicians was short because of their busy schedules. Meanwhile, the five nonphysician graders (NPG), who worked at the Ocular Grading Center of the Singapore Eye Research Institute, were trained and evaluated by the University of Melbourne using a high reliability index (κ=0.8) as a benchmark. The NPGs underwent 1 year of rigorous training and had regular yearly auditing.

Rani and colleagues[12] including Ramasamy and colleagues,[13] in India, described a novel model of Diabetic Retinopathy Capacity Building for eight optometrists for screening of DR. This model which was set up for both hospital- and community-based service delivery included training and certification on the screening, and learning referral guidelines for DR. The training included a 7-month course of fellowship in DR and a 1-day orientation workshop organized by cofacilitators who were mentors on DR screening guidelines across India. It was taught by an experienced vitreoretinal surgeon and divided into three phases: Phase 1, a 1-month observation at the retinal clinics; Phase 2, a 4-month hands-on training in comprehensive eye examination including assessment of the fundus, fundus photography, optical coherence tomography (OCT), fundus fluorescein angiography, and B- scan ultrasonography, and Phase 3, a 2-month service

Table 1: A summary of screening personnel, protocols, and effectiveness in previous studies regarding diabetic retinopathy screening

Studies	Camera model	Screening personnel	Standard reference	Number of photos read	Number of unreadable photos	Prevalence of DR	Sensitivity	Specificity
Askew et al.[10]	Canon nonmydriatic CR-1	2 GP	Ophthalmologists	158	39%	7%	87%	95%
Bhargava et al.[11]	Canon CR-DGi with a 10-D SLR back	5 NPG 5 FP	Retinal specialists	706	0%	17% (NPG) and 12.3% (FP)	69.8% (NPG) and 44.7% (FP)	94.4% (NPG) and 92.4% (FP)
Rani et al.[12] and Ramasamy et al.[13]	3 Nethra-Forus Royal	8 optometrists	Retinal specialists	150	0%	NA	95%	79%
Bhalla et al.[14]	NA	578 PCP	NA	NA	NA	NA	NA	NA
Ruamviboonsuk et al.[15]	NA	3 Photographers 3 Nurses	Retinal specialists	400	1.3%	27.2%	85%	85%

DR=diabetic retinopathy, GP=general practitioner, NPG=nonphysician grader, FP=family physician, PCP=primary care physicians, NA=not available

delivery for the DR screening program in communities. An online educational portal was created to administer weekly assessments through quizzes and assignments. A minimum of 75% marks was required to achieve certification.

Bhalla and colleagues[14] initiated another capacity-building program, Certificate Course in Evidence Based Management of Diabetic Retinopathy, for 578 primary care physicians (PCP) across India in the management of diabetes including DR screening. The program was an on-the-job training course and was conducted as once-a-month contact session, with hands-on-skill training and an exit examination. The course included didactic lectures, case studies, and instructional videos. A minimum of 50% score of exit examination was required for certification at the end of the course. This unique course has been adopted by the Ministry of Health in Afghanistan, and Myanmar.

The screening program for DR in Thailand is governed directly by the Ministry of Public Health using grading of retinal photographs by either ophthalmologists or a trained nonophthalmologist personnel to detect referable DR.[16] The training courses were conducted at national level with more than 1,000 trainees across the 13 health regions in the country. Their performances were monitored at the level of 85% sensitivity and specificity using grading by retinal specialists as the gold standard.[15] The Ministry of Public Health also issued an indicator of at least 60% of patients with diabetes screened for DR in the national program.

British Diabetic Association, the audit standards for DR screening, recommended an acceptance for DR screening at a sensitivity of >80%, a specificity of >95%, and clinical failure rate should be less than 5%.[17] Although the results from many studies could not achieve such values, they showed the acceptable levels of sensitivities and specificities for DR screening in the real world where resources were limited.

While almost all these programs were adopted at either institutional or national level, there are some capacity building programs developed at international level; some were links between developed and developing countries within Asia-Pacific region.

Nongovernment organizations (NGOs) play important roles for capacity building for DR screening in many countries in Indochina, the area between India and China composed of Vietnam, Laos, Cambodia, and Myanmar. Sight For All (SFA), an NGO based in Australia, supports initiatives for DR management in these countries, including training retinal specialists and providing necessary equipment, such as indirect ophthalmoscopes, fundus cameras, OCT devices, surgical microscopes and vitrectomy devices, and retinal lasers.[18] The aim is to set up retina units for management of retinal diseases including DR, which can be run in long term by local major eye institutes in these countries. For example, almost 40 secondary eye centers for screening and treatment of DR have been established in Myanmar in collaboration with SFA and the Australian government. Similar projects for capacity building are conducted in Cambodia and Laos.

World diabetes foundation (WDF), another NGO in collaboration with Project Orbis, supports DR programs in Vietnam. These programs do not only include the use of telemedicine but also include training personnel at different levels for both diagnosis and treatment of DR.[19] The targeted population in this collaboration is approximately 120,000 patients with diabetes across the targeted areas and approximately 4,500 patients are expected to have laser treatment.[19] WDF also conducts another project in rural Myanmar in a smaller scale aimed at 10,000 patients for screening, and 1,250 patients for treatment with laser.[20]

There are limitations in capacity building of nonophthalmologists to read retinal photographs for screening DR. The training courses are scattered in many countries without standard course syllabus. Regular edits on the grading by the nonophthalmologists as well as refresher courses are required. The capacity building on training to increase the number of ophthalmologists and retinal specialists in low-income countries is a lot more difficult. To achieve successful implementation of capacity building for DR screening, long-term strategic planning on continuing education is essential.

Capacity Improvement of the screening using AI

Recently, DL, a new branch of machine learning in AI, has emerged as a disruptive tool for screening DR with robust performance.[21] The accuracies, including sensitivity and specificity, of the DL algorithms from many retrospective studies were found to be at least as good as or even better than human graders.[22,23] In addition, the sensitivity of a DL model was found to be >20% higher than the graders who regularly read retinal photographs for detecting referrals in a national screening program for DR.[24]

The robust performance of AI for DR screening was carried over and proven in a few prospective studies[25,26] with proposals to deploy DL, as either autonomous grading tool or assistant to human graders, into the real-world workflow of DR screening. A cost-minimization analysis found that deploying experienced human graders to filter all referrals identified by DL from its initial grading in the DR screening workflow was more cost saving than without the filtering.[27]

Interestingly, in a qualitative analysis on a prospective study of AI for DR screening where the trained human graders were to provide the reading results from DL to patients immediately at the point of care, the graders appreciated a potential of improvement of their capacity on gradings retinal photographs by assistance of the DL. They could learn from comparisons of results from their own interpretation of retinal photographs to the results obtained from DL. This demonstrated a possibility that AI may be used to enhance capacity building for DR screening by providing feedback of screening results for the graders.[28]

Although studies on AI in ophthalmology have been proliferating in areas other than DR,[29-32] the roles of DL are mostly investigated in terms of its efficacies in screening and monitoring disease, and determination of disease prognosis, few evaluated AI on the roles of capacity building or capacity improvement. Apart from the potential to improve capacity on grading retinal photographs, using AI may give personnel more time for capacity building in other tasks for improving DR screening, such as administration, calling patients who missed appointments, running campaign to increase uptake, etc.

Capacity building in treatment: Training nonphysician personnel for intravitreal injections

Background and evolution of nurse-led intravitreal injection (IVI)

Treatment for visual threatening DR comprises IVI of antivascular endothelial growth factor (anti-VEGF) for diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR), while laser photocoagulation and vitrectomy are recommended therapy for PDR and PDR associated with sequelae from neovascularization.[16] Panretinal laser photocoagulation and vitrectomy are normally conducted by ophthalmologists specializing in vitreoretinal surgery. The IVI of anti-VEGF was solely administered by ophthalmologists until 2006 when pivotal trials demonstrated the efficacy of IVI of ranibizumab in improving visual outcome of wet age-related macular degeneration (wAMD) and United States (US) Food and Drug Administration approved the treatment.[33,34] Since then, there has been an increase in number of patients requiring this route of drug delivery. In the United Kingdom (UK), it has been estimated that there are about 26,000 new cases of wAMD each year.[35-38] In the US, the estimated number of people with AMD is expected to escalate from 2.07 million to 5.44 million by 2050, with a nearly six-fold rise in the number of expected cases from 2010 to 2050, according to the data from National Eye Institute.[39] Although clinical management of wAMD places an increasing burden on the hospital eye service, burden from DR is even greater due to the number and the wider span of life of patients with diabetes.[16] Indications for IVI of anti-VEGF was later expanded to treat various ocular and retina diseases including diabetic-related eye diseases, retinal vein occlusion (RVO), and other neovascularization-related eye diseases. As such, IVI has become one of the most common operations performed on outpatient basis by ophthalmologists and this posed an enormous burden in ophthalmology practice worldwide.

Two major medications used for IVI are anti-VEGF agents (bevacizumab, ranibizumab, aflibercept) and corticosteroids. While IVI of anti-VEGF is used widely for neovascularization-related ocular diseases, the indications of intravitreal corticosteroid injection and intravitreal corticosteroid implants are limited to DME, macular edema related to RVO, and inflammatory eye diseases.[16] There have been attempts to find an initiative to alleviate the burden associated with delivering the intravitreal pharmacotherapy, especially in countries where a shortage of ophthalmologists exist.[35] A conventional model of nursing work has been altered noticeably in recent years with the introduction of extended roles in many surgical specialties. Nurses in ophthalmology have a long history of adopting innovative approaches as an independent operator after rigorous and careful training to improve service delivery.[40] Currently, nurse-driven anti-VEGF services have become the norm in various eye units across many high-income countries. After the first publication of nurse-led IVI by Varma and colleagues in 2013, many similar reports have emerged constantly. Most of them were from European countries, such as UK,[8,35,36,40-44] Denmark,[45] Norway,[46,47] and Spain[44]; a few were from countries outside Europe, such as New Zealand[48] and Singapore.[49,50] Table 2 demonstrates a summary of the literature review of studies related to nurse-led IVI. These studies may be used for evaluation of safety and efficacy related to the injections which were shifted from being given in an "operating theatre by doctors" into a "clean room by nurses."

In the UK where the shortage of ophthalmologists was aggravated by the UK medical training policy in reducing the number of ophthalmologists in training, transformational change was evident by having nurses as substitutes for ophthalmologists in some outpatient operations including Nd: YAG laser capsulotomy, minor eyelid surgery, and intravitreal injection.[35,40] In early 2013, the Royal College of Ophthalmologists guidance on IVI was updated to include endorsement of appropriately trained nonmedical staff for the injection.[51] Meanwhile, there has not been any revision of the summary of product characteristics supplied by manufacturers of any anti-VEGF medications; restrictive IVI guideline from American Academy of Ophthalmology, which indicates that IVI administration is limited to a qualified ophthalmologist, is still applied.[52]

The endorsement of nurse-led IVI in the UK, however, have already led this practice into the real-world situations where many hospitals do not have adequate numbers of ophthalmologists to meet the requirement for the modern anti-VEGF era.

Among clinical staffs in eye care team, the nurse practitioners were considered in a position to undertake IVI lists. This deployment of nurses exclusively for administering the IVI services is found in eye units across the UK.[35] However, although the IVI performed by nurses should be independent without medical staffs being present as supervisors in the injection room, there must always be a retina specialist available on site as a consultant when needed. Thus, it is advisory to have nurse-led IVI sessions run collateral to ophthalmologist clinics. Currently, the workload of nurse-led IVI ranges from 40 to 100% of eye clinic capacity.[8,35,42]

In general, the strict training course for nurse practitioners before undertaking the IVI procedure includes a full day training and workshop, an observation of the injections, patient preparation, injections under direct supervision, competency assessment of injections without supervision after a certain number of injections under supervision, and continuing audit assessment [Fig. 1]. The continuous audit was based on safety aspects and nurse practice was routinely reviewed to evaluate complication rates and patients' satisfaction to assure safety and efficacy of the nurse-led IVI practice compared to audit standards. In addition to conventional IVI procedure amidst an increasing demand of IVI, some eye center has begun using inVitria® (FCI Ophthalmics, Pembroke, MA), an intravitreal injection assistive device, to help nurse-led IVI to deliver faster, safe, and accurate injections without compromising on patient comfort.[42,53-55] Besides the training course, the selected nurses are required to achieve best practice, including business case submission and clinical governance approval encompassing legal issues (vicarious liability, appropriate indemnity cover, consent form, patient information booklet).[35,40]

According to the studies related to the nurse-led IVI, advantages of this potentially disruptive initiative include: (1) improved patient access to IVI,[8,38,42] (2) reduced patient waiting time and improved compliance,[42,44,49] (3) injection cost saving,[42,49] and (4) decreased the burden of injections performed by ophthalmologists and allowing them to pay attention to the more complicated eye diseases.[42,49] Endophthalmitis rate after nurse-led IVI ranges from 0.03 to 0.07%, and this was comparable to the endophthalmitis rate of IVI performed

Table 2: A summary of literature review for nurse-led intravitreal injection

Country	Author (Publishing year)	Exact number of initial injections supervised by a consultant ophthalmologist	Number of nurses performing IVI	Number of nurse-led IVI (duration in months)	Anti-VEGF used	Indications	Endophthalmitis after nurse injections	Other visually significant complications[a]
UK	Varma et al.[40] (2013)	25	4	1,400 (5 months)	RNZ	Wet AMD	None	None
UK	DaCosta et al.[35] (2014)	100 (After 20 direct supervision)	3	4,000 (24 months)	RNZ	Wet AMD	None	None
UK	Simcock et al.[8] (2014)	20	2	10,006 (66 months)	RNZ	Wet AMD	4 (0.04%)	None
UK	Michelotti et al.[42] (2014)	200[b] with inVitria® assist	4	3,355 (18 months)	RNZ > AFB	Mostly wet AMD	None	None
UK	Mall et al.[36] (2015)	NA	More than 4[c]	NA	NA	NA	NA	NA
UK	Gallagher et al.[43] (2017)	50[b]	NA	100 (7 months)	NA	NA	NA	NA
UK	Mohamed et al.[41] (2018)	NA	NA	34 injections as compared to 27 injections by physicians (NA)	NA	NA	NA	NA
UK	Raman et al.[44] (2021)	20	2	1,006 (33 months)	Dexamethasone implant	NA	None	None
Denmark	Hasler et al.[45] (2015)	NA[d]	4	12,542 (60 months)	RNZ	CNV, RVO, DME, PDR, CSC	4 (0.03%)	NAe
Norway	Austeng et al.[46] (2016) Bolme et al.[47] (2020)	100	6	163 injections as compared to 155 injections by physicians (12 months)	BVZ, RNZ, AFB	AMD, RVO, DME	1 (0.6%)	1 uveitis case
New Zealand	Samalia et al.[48] (2016)	50[b]	3	2,900 (18 months)	BVZ, RNZ, AFB	AMD, PCV, diabetic eye disease, RVO	2 (0.07%)	2 cases of vitreous hemorrhage
Singapore	Teo et al.[49] (2020)	100 (including 50 injections by close supervision)	4	8,599 (8 months)	NA	AMD, DME, others	None	None

aVision threatening complications from nurse injections include endophthalmitis, retinal detachment, lens damage, loss of central artery perfusion, uveitis, or vitreous hemorrhage. bUnder direct supervision. cInclude one orthoptist and three nurses. dAt least 8-10 injections performed under direct supervision. eAdverse effects from the procedure were not clarified either by physicians or by nurses: one by anterior uveitis, one by traumatic cataract, 1 by vitreous hemorrhage, and one by rhegmatogenous retinal detachment. IVI=Intravitreal injections, RNZ=Ranibizumab, AFB=Aflibercept, BVZ=Bevacizumab, AMD=Age-related macular degeneration, CNV=Choroidal neovascularization, RVO=Retinal vein occlusion, DME=Diabetic macular edema, PDR=Proliferative diabetic retinopathy, CSC=Central serous chorioretinopathy, PCV=Polypoidal choroidal vasculopathy
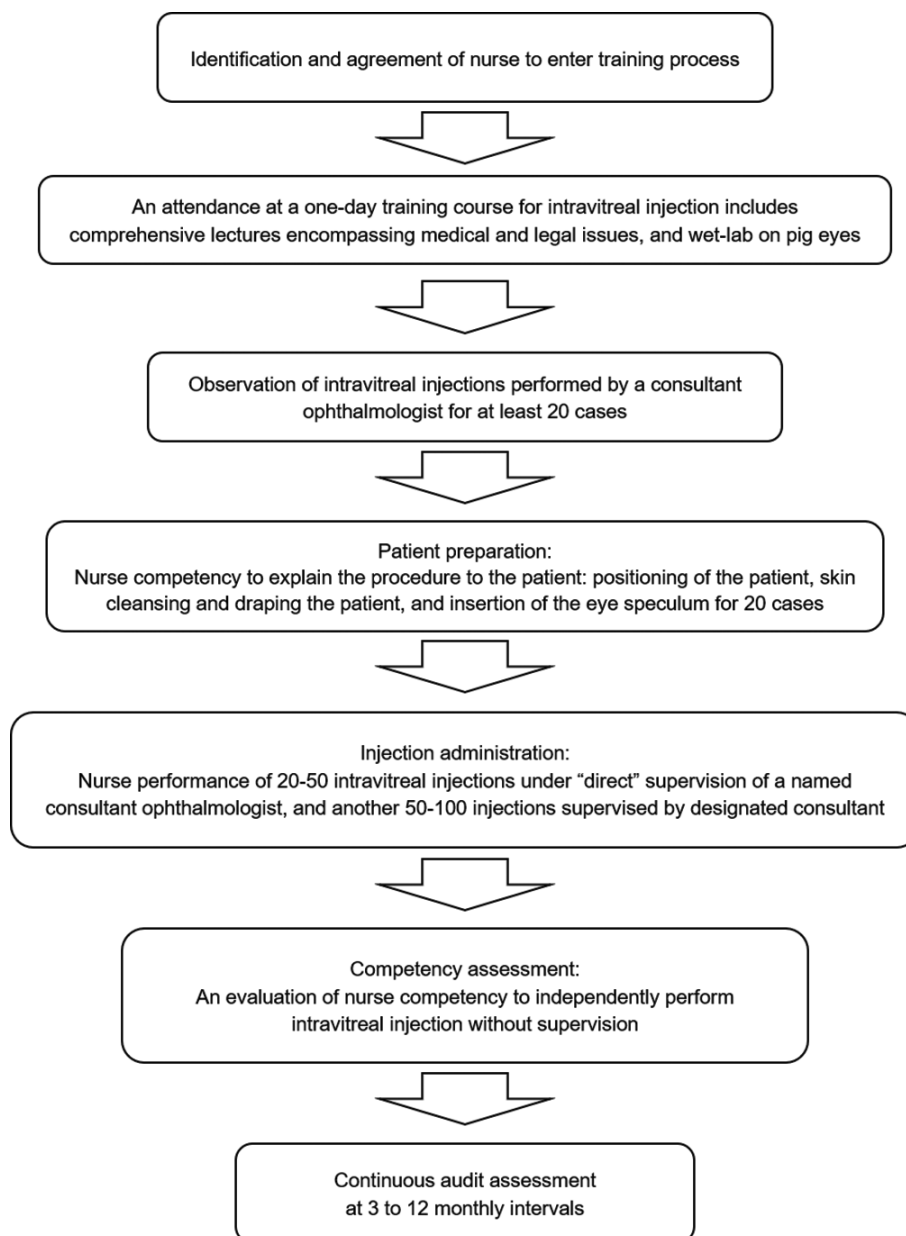
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┌─────────────────────────────────────────────────────┐
│  Identification and agreement of nurse to enter       │
│  training process                                     │
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│  An attendance at a one-day training course for        │
│  intravitreal injection includes comprehensive         │
│  lectures encompassing medical and legal issues,       │
│  and wet-lab on pig eyes                               │
└─────────────────────────────────────────────────────┘
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┌─────────────────────────────────────────────────────┐
│  Observation of intravitreal injections performed      │
│  by a consultant ophthalmologist for at least          │
│  20 cases                                             │
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                        ▼
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│  Patient preparation:                                  │
│  Nurse competency to explain the procedure to the      │
│  patient: positioning of the patient, skin cleansing   │
│  and draping the patient, and insertion of the eye     │
│  speculum for 20 cases                                │
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│  Injection administration:                             │
│  Nurse performance of 20-50 intravitreal injections    │
│  under "direct" supervision of a named consultant      │
│  ophthalmologist, and another 50-100 injections        │
│  supervised by designated consultant                   │
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│  Competency assessment:                                │
│  An evaluation of nurse competency to independently    │
│  perform intravitreal injection without supervision    │
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┌─────────────────────────────────────────────────────┐
│  Continuous audit assessment                           │
│  at 3 to 12 monthly intervals                         │
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Figure 1: Overview of training procedures of nurse-led intravitreal injection

by ophthalmologists.[8,45,48] In addition, for qualitative evaluation, the majority of patients reported satisfaction with the nurse-led IVI service, based on the positive outcomes from the questionnaire.[35,41,43,44,47,49] Bolme and colleagues conducted a randomized single-masked noninferiority study of IVI rendered by nurses and ophthalmologists in Norway; they concluded that the task shifting of IVI to nurses can be performed without increased risk to damage to visual function. Sixty percent of patients did not know whether it was a physician or a nurse who performed the injection.[47]

Application and expansion of nurse-led intravitreal injection

Clinical staffs in eye care team other than nurses for IVI
Among clinical staffs in eye care team, ophthalmic nurse practitioners were regarded the most appropriate to expand their role to IVI practice.[43] Thus, most studies implemented

this new task service to different groups of nurses: senior and experienced nurses[35,36,40,44] or nurses proficient in minor ophthalmic procedures.[8,48] Mall and colleagues reported the utilization of orthoptists at Frimley Park Hospital and Oxford Eye Hospital for delivering IVI as part of their macular services.[36] Nevertheless, other allied staffs in the eye care team such as optometrists and orthoptists may not be familiar with aseptic technique, administration of injections, and safe disposal of sharp medical instruments, given that these procedures are not typically required for their regular professional practice. Thus, caution must be taken when recruiting personnel for this delicate and meticulous task.[37]

Medication options for IVI
Although the product characteristics supplied by manufacturers of commercially available anti-VEGF agents (i.e., ranibizumab,

aflibercept) provide limitation of IVI therapy to be performed only by a qualified physician, not other trained nonmedical staff, in the UK, Royal College of Ophthalmologists guidance on IVI has allowed trained nonmedical personnel to undertake the task.[51] Ranibizumab was the most commonly used medication injected by nurses [Table 2]. Recently, IVI medications other than anti-VEGF including dexamethasone implant (Ozurdex®) was supported by The Royal College of Ophthalmologists guidelines on intravitreal injection for the delivery by nonmedical staffs in 2018. The procedure of injection of the dexamethasone implant into vitreous cavity was not viewed as different from IVI if it was provided by nonmedical staffs.[44] Nevertheless, it should be noted that IVI performed by nurses remains off-label even though licensed drugs are used. A detailed consent form and patient information leaflet stated that the injections performed by trained nurses are necessary as part of the procedure to avoid medico-legal issues. While there was no study on IVI bevacizumab, which is an off-label drug according to the National Institute for Health and Care Excellence, in the UK, there were studies in other countries in Europe, i.e., Norway and New Zealand, where the injection by nurses began to undertake for various retinal disorders.[46,48] This may potentially be the major challenge to overcome for vicarious liability of the IVI given by nurses.

Asian perspectives

The traditional roles of the clinical staffs in eye care team are different between Europe and Asia. While appropriately trained ophthalmic nurses can replace ophthalmologists in many care settings in Europe, such roles of ophthalmologists and nurse are distinctly demarcated in Asia, where patients may prefer treatments given by ophthalmologists. As a result, IVI services administered by nurses are likely to slowly gain acceptance for building their capacity to treat patients with DR in Asia. A study regarding nurse-led IVI in Asia came from Singapore, where at least two tertiary eye centers have implemented this procedure.[49,50] Teo and colleagues conducted a study to evaluate a nurse-led IVI program for retinal diseases in the Singapore National Eye Centre. After 8,599 injections for retinal disorders (including wet AMD and DME) were carried out by four well-trained nurses over the periods of 8 months, the authors concluded that nurse-led IVI is a safe, acceptable, and cost-saving procedure.

In Thailand, the standard treatment of anti-VEGF injections given by ophthalmologists has also been approved and treatment with bevacizumab is included in the Thai National List of Essential Medicine. The treatment is available to all three government health insurance schemes: universal coverage, social security, and civil servants, in Thailand.[16] Although the problem of shortage of workforce of ophthalmologists in remote locations exists,[9] the well-established national screening programs for DR conducted by trained nonophthalmologist personnel in all district hospitals in Thailand can detect referrals and refer them to the provincial hospitals where ophthalmologists and retinal specialists practice. Most of the IVI in the country is provided by retinal specialists who are distributed in all provincial hospitals. They prefer to perform the IVI themselves, and the volume of the procedure at present is still manageable.

A large volume of patients is referred to tertiary care centers where there are residency training programs. In these centers, large IVI clinics typically run on a capacity of more than 30–40 injections per day and IVI procedures have been provided by well-trained ophthalmology residents. Physician in training was found to perform IVI with generally acceptable safety and efficacy.[45] In our institute, first-year residents of ophthalmology are routinely and rigorously trained to perform IVI; after completing 50 supervised procedures within 2 weeks, each of the residents underwent a competency evaluation by a vitreoretinal consultant so that they can independently perform IVI by themselves.

Although nurses became the main responsible personnel in the task of IVI in many European countries, the role of them in substituting physicians for treating diseases may be far from reach in many countries in Asia, where the symbolic importance of doctors in the eyes of patients is evident. In Thailand, in addition, Thailand Nursing and Midwifery Council has just imposed a new rule, according to the Rules of the Nurse Council of Thailand, B.E. 2564 (2021), to prohibit nurses from injecting any kind of contrast media into patients' bodies. In countries with this similar rule or situation, it is even more difficult to persuade nurses to perform IVI. Furthermore, more and more nurses are responsible for quality management or taking up administrative roles at the price of clinical care. However, given safety profile and cost effectiveness of this modality proven by many studies, we believe that nurse-led IVI can serve as another effective treatment model for a country in need.

Conclusion

Capacity building of health professionals who are not ophthalmologists for screening and treatment of DR has been evaluated as a strategy which may help improving health force crisis to reduce blindness from diabetes. Family physicians, PCP, and general practitioners are among nonophthalmologist physicians, whereas ophthalmic nurses, general practice nurses, and technicians are among nonphysicians, who are trained for DR screening at institutional or national level.

Although there is no standardization of the course syllabus for capacity building in DR screening, it is generally accepted to keep sensitivity >80%, specificity >95%, and clinical failure rate <5% for the nonophthalmologists, if possible. There are also collaborations between national eye institutes of high-income countries, NGOs, and local eye institutes to improve both quality and quantity of ophthalmologists and retinal specialists in low-income countries in Asia. This approach will also improve eye care for DR; however, it may be more labor-, cost-, and time-consuming than training nonophthalmologists.

Recently, AI was found to have robust performance for screening patients with DR who should be referred to be managed by ophthalmologists. Although it seems that AI may be deployed to replace the task of screening DR by nonophthalmologists, it can also be a tool to improve capacity of health professionals or to allow them to have more time for capacity building in other areas of DR screening or other eye care services.

Several countries in Europe and Asia train and deploy nurses to perform intravitreal injection of anti-VEGF agents for treatment of DME and other macular diseases. After supervisions of an average of 100 initial injections, the trained

nurses can do the injections safely and effectively comparable to ophthalmologists. However, laws and regulations that are different among countries are challenges and barriers for nonophthalmologists, particularly for nonphysicians, not only to provide treatment but also to screen DR.

Even if nonophthalmologists are legally approved for the tasks, sustainability of the built capacity is another important challenge; this may be achieved if the capacity building can be part of their career development. Patient acceptability is another important barrier for initiating care provided by nonophthalmologists.

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Conflicts of interest

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