Clinical Translation of Recommendations from Randomized Clinical Trials on Patching Regimen for Amblyopia

Ya-Ping Jin, MD, PhD,[1,2] Amy H. Y. Chow,[3] Linda Colpa, OC(C),[4] Agnes M. F. Wong, MD, PhD[1,4]

Purpose: To investigate whether the evidence-based recommendations by the Pediatric Eye Disease Investigator Group (PEDIG) as initial treatment of amblyopia have been implemented into clinical practice and to discuss the necessary steps in translating evidence-based knowledge to inform clinical decision making.

Design: Retrospective cohort study.

Participants: Children with amblyopia seen from 2007 through 2009 by academic and community ophthalmologists in a large urban center in North America that serves a population of more than 8 million. Using PEDIG criteria, moderate amblyopia was defined as visual acuity between 20/40 and 20/80 and severe amblyopia was defined as visual acuity between 20/100 and 20/400.

Intervention: Patching of the sound eye.

Main Outcome Measures: The number of prescribed patching hours daily and the amblyopic eye visual acuity expressed as logarithm of the minimum angle of resolution (logMAR).

Results: For moderate amblyopia, the cohort (n = 71) was prescribed a mean of 3.2 hours of daily patching (95% confidence interval [CI]: 2.8–3.6 hours), which is significantly greater than the recommended 2 hours of daily patching for initial treatment. Only 24% (95% CI, 16%–35%) of them were prescribed the recommended initial patching hours. The amblyopic eye acuity on the 3- to 6-month visit in the cohort (0.23 logMAR) was similar to that of the 4-month visit in the PEDIG cohort (0.24 logMAR; $P = 0.74$). For severe amblyopia, the cohort (n = 52) was prescribed a mean of 3.9 hours of daily patching (95% CI, 3.5–4.3 hours), which is significantly lower than the recommended 6 hours of daily patching for initial treatment. Only 12% (95% CI, 5%–23%) of them were prescribed the recommended initial patching hours. The amblyopic eye acuity at the 7- to 12-month visit in the cohort (0.44 logMAR) was comparable with that of the 4-month visit in the PEDIG cohort (0.40 logMAR; $P = 0.35$).

Conclusions: The evidence-based recommendations for amblyopia management have not been translated widely into changes in clinical practice in a large urban center in North America, although there is a general move from full-time to part-time patching since the PEDIG results were published. Using a well-established framework for knowledge translation, the *Knowledge-to-Action Cycle*, the necessary steps required to implement new knowledge into actual clinical practice are discussed.

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One of the central challenges faced by medicine today is that, although a great deal of effort and resources have been devoted to medical research, there is a gap in implementing results from medical research into everyday clinical practice and health decision making.[1] It has become increasingly clear that a systematic approach that involves all stakeholders is essential to bridge the gap between knowledge and action. In the last decade, the science and practice of knowledge translation and implementation has made significant progress.[2] This study examined one of these efforts—the Amblyopia Treatment Studies conducted by the Pediatric Eye Disease Investigator Group (PEDIG)—by evaluating whether PEDIG recommendations have been translated into actual clinical practice. The necessary steps that are required for implementing the current best evidence into clinical practice are discussed by using a well-established knowledge translation framework known as the *Knowledge-to-Action Cycle*,[3] using amblyopia management as an example.

Amblyopia is a unilateral (or less commonly, bilateral) visual impairment that cannot be attributed to a structural abnormality of the eye as a result of abnormal visual development during childhood (e.g., eye misalignment, unequal or significant refractive errors). It is a significant public health problem because the impairment often persists into adulthood,[4] making it the leading cause of monocular vision loss, with a prevalence of 3% to 5%.[5,6] Patching of the fellow (nonamblyopic) eye has remained the mainstay of treatment for centuries. Until recently, there was no consensus as to how many hours of patching should be prescribed. To address this issue, the PEDIG was formed in

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1997 as a collaborative network dedicated to facilitating multicenter clinical research in strabismus, amblyopia, and other eye disorders that affect children. Funded by the National Eye Institute, the PEDIG has more than 60 sites with more than 120 pediatric ophthalmologists and pediatric optometrists in the United States, Canada, and the United Kingdom participating. Through the Amblyopia Treatment Studies,[7–14] the PEDIG found that for patients with moderate amblyopia, 2 hours of daily patching produced a similar amount of visual acuity improvement as 6 hours of daily patching.[8] For severe amblyopia, 6 hours of daily patching produced a similar magnitude of visual acuity improvement as full-time patching.[9] Consequently, 2 hours of daily patching for initial treatment of moderate amblyopia and 6 hours of daily patching for initial treatment of severe amblyopia are recommended.

Since the publication of the PEDIG findings in 2003,[8,9] a few studies have been conducted to assess their clinical impact using questionnaires, with several hypothetical scenarios presented.[15–18] These studies found that PEDIG recommendations have made an important but modest impact on clinical decisions. However, questionnaires are subject to many potential biases[19] and may not reflect the actual clinical practice of ophthalmologists when they are faced with real patients. This study examined whether PEDIG recommendations for patching regimens for amblyopia have been translated into actual clinical practice in a large urban center in North America. Future areas of research and efforts where gaps still exist between knowledge and action are discussed.

Patients and Methods

The medical records of patients referred to the orthoptic service at The Hospital for Sick Children in Toronto for amblyopia from January 1, 2007, through December 31, 2009, were reviewed retrospectively. The orthoptic service receives more than 4300 referrals annually from approximately 60 ophthalmologists (academic or community based) practicing in the greater Toronto area and neighboring cities (the so-called Greater Golden Horseshoe) with a population of more than 8 million.[20] Children 7 years of age or younger with a visual acuity between 20/40 and 20/400 (0.3–1.3 logarithm of the minimum angle of resolution [logMAR]) in the amblyopic eye, 20/40 (0.3 logMAR) or better in the fellow eye, and an interocular acuity difference of 0.3 logMAR or more were included. Those with visual acuity between 20/40 and 20/80 (0.3–0.6 logMAR) in the amblyopic eye were classified as having moderate amblyopia, and those with visual acuity between 20/100 and 20/400 (0.7–1.3 logMAR) in the amblyopic eye were classified as severe amblyopia, as set arbitrarily by the PEDIG studies. Strabismic amblyopia was defined as amblyopia in the presence of eye misalignment at distance or near fixation, or both. Anisometropic amblyopia was defined as amblyopia in the presence of a difference in refractive error between the 2 eyes of 0.50 diopter (D) or more of spherical equivalent or 1.50 D or more of difference in astigmatism in any meridian. Mixed amblyopia was defined as amblyopia in the presence of a combination of strabismus and anisometropia. Patients with any ocular cause for reduced visual acuity, high myopia (≥−6.00 D), or prior intraocular surgery were excluded. These inclusion and exclusion criteria were identical to those used in PEDIG studies.[8,9] The study protocol was approved by the Research Ethics Board at The Hospital for Sick Children.

Data on demographics, cause of amblyopia, visual acuity in both eyes on each visit, the test used for visual acuity assessment, refractive error, prescribed therapy (patching or pharmacologic penalization), and referring physicians were collected. Visual acuity assessed with Snellen-type scales (Snellen, Early Treatment Diabetic Retinopathy Study chart, HOTV, Sheridan Gardiner single letters, Cardiff, Teller acuity tests) was converted to logMAR scale. Patients with visual acuity assessed with non-Snellen scales (e.g., central, steady, maintained, fixed and followed, count fingers, hand movements) were excluded. Children who were lost to follow-up, those who were still undergoing treatment (and thus final visual outcome was not available), as well as those who were prescribed atropine penalization or combined patching and penalization on any visit during the study period also were excluded.

The main study outcomes were the number of prescribed daily patching hours and the visual acuity in both eyes at each visit. Final treatment conclusion was defined as the visit when the acuity of the amblyopic eye returned to within 0.1 logMAR of the fellow eye or when the amblyopic eye acuity failed to improve further after 3 consecutive visits. The baseline characteristics were compared using the 2-sample *t* test for continuous variables. For categorical variables, the chi-square test or Fisher exact test was used. The differences between the number of patching hours prescribed for the cohort and that recommended by PEDIG were evaluated using the 1-sample *t* test. The changes in prescribed patching hours and in visual acuity on follow-up visits were assessed with analysis of variance. The treatment compliance rate was computed as a percentage of self-reported patching hours compared with the amount of prescribed patching hours per week. Full compliance was defined as a compliance rate between 80% and 100%, overpatching was defined as a compliance rate of more than 100%, and underpatching was defined as a compliance rate of less than 80%.

Results

A total of 360 patient records were reviewed. After applying the inclusion and exclusion criteria, 123 patients were included. Seventy-one children were in the moderate group and 52 were in the severe group (see Fig 1, available at http://aaojournal.org). The top 2 reasons for exclusion were interocular acuity difference of less than 0.3 logMAR (n = 70; 19%) and acuity measured with a non-Snellen scale (n = 55; 15%). Of the 123 patients included, 41% were managed by 5 full-time academic ophthalmologists and 59% were managed by 20 community ophthalmologists. The demographics of the patients are shown in Table 1. The mean age of the cohort was slightly younger than that of the PEDIG cohort, and the cohort had more patients with strabismic amblyopia.

Moderate Amblyopia

On the initial visit, children in the cohort were prescribed a mean of 3.2±1.6 hours (95% confidence interval [CI], 2.8–3.6 hours) of daily patching, which was significantly greater than the recommended 2 hours ($P<0.0001$; Fig 2). Twenty-four percent (95% CI, 16%–35%) of patients were prescribed 2 hours of daily patching, 11% were prescribed fewer than 2 hours, and 65% were prescribed more than 2 hours. On the 13- to 18-month visit, patching was reduced by 1 hour compared with the initial visit ($P<0.05$; Fig 2). The prescribed number of patching hours at the initial visit for strabismic amblyopia (2.9±1.3 hours) were slightly fewer than that for anisometropic eyes (3.4±2.3 hours) and eyes with mixed amblyopia (3.7±1.7 hours), but the difference was not statistically significant ($P = 0.25$).

The mean visual acuity of the amblyopic eye on the 3- to 6-month visit was 0.23±0.23 logMAR, which was similar to that

Table 1. Comparisons of Baseline Characteristics between Our Cohort in Toronto and the Cohort in PEDIG

	Moderate		Severe	
	Toronto	*PEDIG (2 h of daily patching)*	*Toronto*	*PEDIG (6 h of daily patching)*
n	71	95	52	85
Gender, Female [n (%)]	34 (48)	42 (44)	28 (52)	41 (48)
	$P = 0.64$		$P = 0.52$	
Age in years [n (%)]				
<3	8 (11)	2 (2)	12 (23)	5 (6)
3 to <4	20 (28)	15 (16)	9 (17)	21 (25)
4 to <5	16 (23)	26 (27)	17 (33)	24 (28)
5 to <6	17 (24)	29 (31)	8 (15)	23 (27)
6 to ≤7	10 (14)	23 (24)	6 (12)	12 (14)
Mean (SD)	4.5 (1.3)	5.1 (1.1)	4.2 (1.4)	4.7 (1.1)
	$P<0.01$		$P = 0.02$	
Cause of amblyopia				
Strabismus	39 (55)	29 (31)	29 (56)	25 (29)
Anisometropia	15 (21)	34 (36)	8 (15)	30 (35)
Mixed	17 (24)	32 (34)	15 (29)	30 (35)
	$P<0.01$		$P<0.01$	
Visual acuity in amblyopic eye, logMAR				
Mean (SD)	0.44 (0.11)	0.48 (0.10)	0.92 (0.18)	0.89 (0.18)
	$P = 0.02$		$P = 0.35$	
Visual acuity in fellow eye, logMAR				
Mean (SD)	0.08 (0.09)	0.07 (0.10)	0.12 (0.11)	0.12 (0.12)
	$P = 0.51$		$P = 1.00$	
Interocular acuity difference, logMAR				
Mean (SD)	3.7 (0.8)	4.1 (1.1)	8.0 (2.0)	7.7 (2.3)
	$P = 0.01$		$P = 0.44$	
Refractive error in amblyopic eye, D				
Mean (SD)	3.82 (2.62)*	4.06 (3.20)	2.94 (2.60)*	4.98 (2.86)
	$P = 0.64$		$P<0.01$	
Refractive error in fellow eye, D				
Mean (SD)	3.17 (2.47)*	2.96 (2.44)	2.36 (2.31)*	3.18 (2.39)
	$P = 0.62$		$P = 0.10$	

D = diopter; LogMAR = logarithm of the minimum angle of resolution; PEDIG = the Pediatric Eye Disease Investigator Group; SD= standard deviation.
*With missing values: n = 52 for moderate group and n = 35 for severe group.

of the PEDIG cohort at the 4-month visit[8] (0.24±0.13 logMAR; $P = 0.74$; Fig 3). The average follow-up time to final treatment conclusion was 19 months (range, 2–75 months). The mean visual acuity in the fellow eye on the final visit (0.05±0.10 logMAR) was slightly better than that on the initial visit (0.08±0.10 logMAR; $P = 0.04$). Reverse (occlusion) amblyopia did not develop in any patients. Underpatching was found in 20% to 30%, overpatching was found in 10% to 20%, and full compliance was found in 50% to 60% over the follow-up period (Fig 4A, available at http://aaojournal.org).

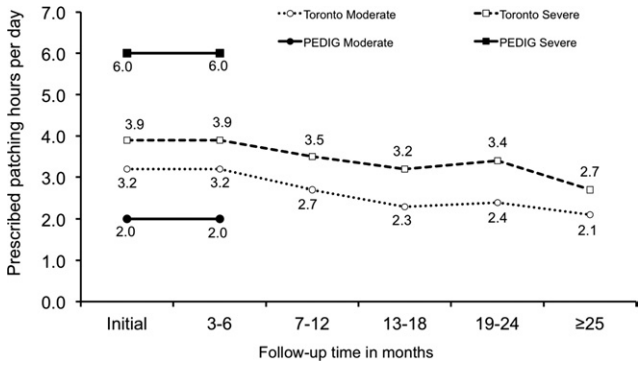

Figure 2. Graph showing patching hours prescribed in the study cohort (dotted lines) from January 1, 2007, through December 31, 2009, compared with the suggested patching hours recommended by the Pediatric Eye Disease Investigator Group (PEDIG; solid lines).[8,9]

Severe Amblyopia

At the initial visit, children in the cohort were prescribed a mean of 3.9±1.5 hours (95% CI, 3.5–4.3 hours) of daily patching, which was significantly fewer than the 6 hours recommended ($P<0.0001$; Fig 2). Twelve percent of patients (95% CI, 5%–23%) were prescribed 6 hours of daily patching, 83% of patients were prescribed fewer than 6 hours, and 6% of patients were prescribed more than 6 hours. On the 13- to 18-month visit, patching hours were virtually unchanged as compared with the initial visit ($P = 0.12$; Fig 2). Similar to the moderate group, the number of prescribed patching hours for strabismic amblyopia (3.6±1.6 hours) was slightly fewer than that for anisometropic eyes (4.8±2.1 hours) and eyes with mixed amblyopia (4.1±0.9 hours), but again, the difference was not statistically significant ($P = 0.11$).

The mean visual acuity of the amblyopic eye at the 3- to 6-month visit was 0.51±0.25 logMAR, which was worse than that

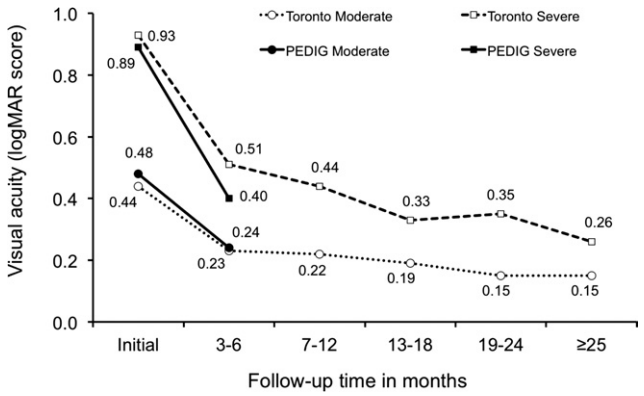

Figure 3. Graph showing visual acuity in the amblyopic eye in the study cohort (dotted lines) and in the Pediatric Eye Disease Investigator Group (PEDIG) cohorts (solid lines).[8,9] logMAR = logarithm of the minimum angle of resolution.

of the PEDIG cohort at the 4-month visit[9] (0.40±0.24 logMAR; $P = 0.02$; Fig 3). At the 7- to 12-month visit, however, the mean visual acuity improved to 0.44±0.28 logMAR, which was comparable with that of the PEDIG cohort at 4 months (0.40±0.24 logMAR; $P = 0.35$; Fig 3). The average follow-up time to final treatment conclusion was 21 months (range, 3–77 months). The mean visual acuity in the fellow eye on the final visit (0.06±0.11 logMAR) was slightly better than that at the initial visit (0.12±0.11 logMAR; $P<0.01$). No patients demonstrated reverse amblyopia.

Underpatching increased from 26% to 27% in the first 12 months to approximately 41% at the 13- to 24-month follow-up ($P = 0.08$; Fig 4B, available at http://aaojournal.org). Overpatching remained at approximately 14% to 18% in the first 24 months. Full compliance decreased from 55% to 61% in the first 12 months to 45% to 46% at the 13- to 24-month follow-up.

Discussion

This study investigated whether PEDIG recommendations for amblyopia patching regimens have been implemented into clinical practice in a large urban center in North America. The study found that only 24% of patients with moderate amblyopia were prescribed the recommended initial 2 hours of daily patching and only 12% with severe amblyopia were prescribed the recommended initial 6 hours of daily patching. Using the same inclusion and exclusion criteria as PEDIG studies, the present study excluded 237 (66%) of 360 patient records reviewed. The top 2 reasons for exclusion were an interocular acuity difference of less than 0.3 logMAR (n = 70; 19%) and acuity measured with a non-Snellen scale (n = 55; 15%). The exclusion of these patients was inevitable to allow a direct comparison with PEDIG studies to draw valid conclusions regarding the clinical translation of PEDIG results. This also highlights a potential drawback of clinical trials because a large number of patients may not be eligible when stringent criteria are used, hence reducing the generalizability of their findings in actual clinical practice. The mean age of the cohort was slightly younger than that of the PEDIG cohort because the present study included more patients younger than 3 years of age from whom Snellen scale acuity could be obtained (e.g., Teller and Cardiff tests), whereas PEDIG required patients to be able to read HOTV optotypes. The proportion of patients with different causes of amblyopia also was different. More than half of the cohort had strabismic amblyopia, whereas the causes of amblyopia were distributed equally in the PEDIG cohorts. This may be because strabismic amblyopia typically is identified at younger ages. The distribution in the current study, however, was similar to those reported in other large population-based studies.[21]

Earlier reports[15–18] have found that the impact of the PEDIG findings on clinical practice has been modest, with 12% to 40% pediatric ophthalmologists having adopted the recommendations. In a 2010 study, Newsham[18] found that only 15% of orthoptic department heads in the United Kingdom had changed their practice in accordance with PEDIG recommendations. However, all previous studies[15–18] used questionnaires with several hypothetical scenarios presented, which are subject to many well-documented potential biases.[19] For example, respondents may alter their responses systematically in the direction they perceive to be desired by the investigator, which may not reflect their actual clinical behaviors. In addition, 2 studies[16,17] examined respondents' practice within 1 year of publication of the PEDIG studies,[8,9] which may not have allowed enough time for dissemination of new information to the medical community. To the best of the authors' knowledge, this study is the first to investigate the actual number of patching hours prescribed by ophthalmologists in both academic and community settings 4 to 6 years after the publication of the PEDIG findings. These results show that the PEDIG recommendations have not been translated widely into a change in clinical practice, although there is a general move from full-time to part-time patching since the PEDIG results were published.

Knowledge-to-Action Gap in Amblyopia Treatment

Although a tremendous amount of medical research has been conducted, one of the greatest current challenges in medicine is that there is a gap in applying research evidence to the process of making informed clinical decisions. This is evident across all groups of decision makers (including health care providers, patients, managers, and policy makers) in both primary and specialty care across all disciplines. For example, despite extensive research showing that antibiotics are ineffective for treating viral infections and that misuse of antibiotics has contributed to the development of antibiotic resistance, physicians continue to prescribe antibiotics inappropriately for the common cold.[22] Indeed, it has been reported that patients in the United States received less than 55% of recommended care (acute, chronic, and preventive).[23] Although producing evidence from clinical research through publication in academic journals is a necessary first step to improve care, it often is not sufficient on its own to change behaviors that lead to optimal care. Recognition of the significance and scope of this issue has led to increasing interest in knowledge translation.

What is knowledge translation? In the United States, knowledge translation also is known as dissemination, dif-

fusion, and knowledge transfer, whereas in the United Kingdom and Europe, it is commonly referred to as implementation science or research uptake. For many, the term *knowledge translation* (and its synonyms) refers to the bench-to-bedside transfer of knowledge from basic sciences to produce new clinical approaches for prevention, diagnosis, and treatment of diseases.[24] For others, it refers to putting research into action by ensuring that new research knowledge and approaches actually affect patient care.[1] The distinction between these 2 definitions is important because most people have the former definition in mind. Using the former definition, the PEDIG studies have produced a wealth of evidence for the effective treatment of amblyopia. In what follows, the discussion focuses on knowledge translation using the latter definition, that is, what do we need to do to change decision-making behaviors so that patients with amblyopia ultimately will benefit from this new knowledge?

It would be helpful to begin answering this question using an established conceptual framework. One such framework, called the Knowledge-to-Action Cycle,[3] provides a model that builds on the commonalities of several theories of knowledge translation.[25] In this model, translating knowledge to action is an iterative, dynamic, and complex process that involves all stakeholders, including patients, health care providers, managers, and policy makers. It requires that appropriate implementation strategies be considered and planned out from the very beginning. The Knowledge-to-Action Cycle consists of 2 components: knowledge creation and the action cycle (Fig 5, available at http://aaojournal.org).[3] Knowledge creation comprises 3 phases. The first phase is knowledge inquiry, which includes the completion of primary research studies such as those conducted by PEDIG.[7–14] The second phase, knowledge synthesis, brings together research findings that may exist globally and reflects the totality of current evidence. Systematic reviews, such as the Cochrane database of systematic reviews on interventions for strabismic amblyopia[26] and refractive amblyopia,[27] are examples of knowledge synthesis. In the third phase, creation of knowledge tools, the knowledge is distilled further to provide explicit recommendations that ideally should be clear, concise, and user friendly. Examples of knowledge tools include the American Academy of Ophthalmology Preferred Practice Pattern Guidelines for Amblyopia 2007 (an up-to-date version will appear in 2012),[28] and Guidelines for the Management of Amblyopia developed by the Royal College of Ophthalmologists in the United Kingdom.[29]

The action cycle consists of 7 phases, which can occur sequentially or simultaneously and can be influenced by new knowledge creation at any point.[30] The 7 phases (Fig 5, available at http://aaojournal.org) are: (1) identify knowledge-to-action gaps; (2) adapt knowledge to the local context; (3) assess barriers to knowledge use; (4) select, tailor, and implement knowledge translation interventions; (5) monitor knowledge use; (6) evaluate knowledge use outcomes; and (7) sustain knowledge use. To illustrate this cycle, consider a local group that includes pediatric ophthalmologists (academic and community based), orthoptists, school nurses, teachers, care givers in daycare centers, parents, and children with amblyopia. This group completes a local audit and finds that less than 25% of children with amblyopia (results from the current study) are prescribed patching that is in accordance with PEDIG recommendations. The group adapts the evidence to their context (e.g., working hours of both parents) and identifies the barriers to implement the evidence. The barriers may include a lack of awareness or familiarity with the new knowledge and the lack of longer-term follow-up data from PEDIG studies.[15] Furthermore, clinicians may find that important issues such as compliance, dose response, and age of patients have not been addressed adequately by PEDIG. The group develops a multicomponent strategy that could include printed educational materials for clinicians; educational meetings and outreach visits; audit and feedback; interventional education programs for parents, caregivers, and patients; as well as multifaceted interventions combining clinician, patient, and public education in a variety of venues and formats. To access whether the strategy for knowledge translation is effective, the group analyzes the clinical and administrative databases. The outcomes of interest may include the number of patching hours, visual outcomes, quality of life, parent and patient satisfaction, compliance, as well as the strength of group's collaboration. This example emphasizes the partnership required for the practice of knowledge translation and the need to address issues that are relevant to all stakeholders.

In summary, the work by PEDIG has led to robust evidence for the optimal management of amblyopia. However, the PEDIG recommendations have not been translated widely into changes in clinical practice. This calls for a systematic approach to put what we have learned from PEDIG into action. Although knowledge translation as a discipline is still evolving, both in name and in scope, it is clear that knowledge creation (through primary studies, meta-analyses, and practice guidelines) on its own does not automatically lead to changes in decision making or behaviors. In addition, the proposed Knowledge-to-Action Cycle framework itself needs to be tested and validated through further research. Successful changes in amblyopia management, and in any medical decision in general, require not only the translation of clinical science, but also require close collaboration with other disciplines—such as epidemiology, behavioral science, psychology, communication, social marketing, economics, and political science—to close the knowledge-to-action gap. Realizing the importance of knowledge translation and taking steps toward implementing new knowledge to effect real changes are essential for the betterment of health in our patients.

References

1. Sung NS, Crowley WF Jr, Genel M, et al. Central challenges facing the national clinical research enterprise. JAMA 2003; 289:1278–87.
2. Straus SE, Tetroe J, Graham ID. Knowledge to action: what it is and what it isn't. In: Straus SE, Tetroe J, Graham ID, eds. Knowledge Translation in Health Care: Moving from Evidence to Practice. Chichester, West Sussex, UK: Wiley-Blackwell; 2009. Chapter 1.

3. Graham ID, Logan J, Harrison MB, et al. Lost in knowledge translation: time for a map? J Contin Educ Health Prof 2006; 26:13–24.
4. Hillis A, Flynn JT, Hawkins BS. The evolving concept of amblyopia: a challenge to epidemiologists. Am J Epidemiol 1983;118:192–205.
5. Buch H, Vinding T, La Cour M, Nielsen NV. The prevalence and causes of bilateral and unilateral blindness in an elderly urban Danish population. The Copenhagen City Eye Study. Acta Ophthalmol Scand 2001;79:441–9.
6. Attebo K, Mitchell P, Cumming R, et al. Prevalence and causes of amblyopia in an adult population. Ophthalmology 1998;105:154–9.
7. Holmes JM, Beck RW, Repka MX, et al, Pediatric Eye Disease Investigator Group. The Amblyopia Treatment Study visual acuity testing protocol. Arch Ophthalmol 2001;119: 1345–53.
8. Repka MX, Beck RW, Holmes JM, et al, Pediatric Eye Disease Investigator Group. A randomized trial of patching regimens for treatment of moderate amblyopia in children. Arch Ophthalmol 2003;121:603–11.
9. Holmes JM, Kraker RT, Beck RW, et al, Pediatric Eye Disease Investigator Group. A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. Ophthalmology 2003;110:2075–87.
10. Holmes JM, Beck RW, Kraker RT, et al, Pediatric Eye Disease Investigator Group. Impact of patching and atropine treatment on the child and family in the Amblyopia Treatment Study. Arch Ophthalmol 2003;121:1625–32.
11. Repka MX, Cotter SA, Beck RW, et al, Pediatric Eye Disease Investigator Group. A randomized trial of atropine regimens for treatment of moderate amblyopia in children. Ophthalmology 2004;111:2076–85.
12. Holmes JM, Edwards AR, Beck RW, et al, Pediatric Eye Disease Investigator Group. A randomized pilot study of near activities versus non-near activities during patching therapy for amblyopia. J AAPOS 2005;9:129–36.
13. Pediatric Eye Disease Investigator Group. A randomized trial of near versus distance activities while patching for amblyopia in children aged 3 to less than 7 years. Ophthalmology 2008; 115:2071–8.
14. Pediatric Eye Disease Investigator Group, Repka MX, Kraker RT, Beck RW, et al. A randomized trial of atropine vs patching for treatment of moderate amblyopia: follow-up at age 10 years. Arch Ophthalmol 2008;126:1039–44.
15. Wygnanski-Jaffe T, Levin AV. The effect of the randomized trial of patching regimens for treatment of moderate amblyopia on pediatric ophthalmologists: 3-year outcome. J AAPOS 2007;11:469–72.
16. Wygnanski-Jaffe T. The effect on pediatric ophthalmologists of the randomized trial of patching regimens for treatment of moderate amblyopia. J AAPOS 2005;9:208–11.
17. Khazaeni L, Quinn GE, Davidson SL, Forbes BJ. Amblyopia treatment: 1998 versus 2004. J Pediatr Ophthalmol Strabismus 2009;46:19–22.
18. Newsham D. The effect of recent amblyopia research on current practice in the UK. Br J Ophthalmol 2010;94:1352–7.
19. Choi BC, Pak AW. A catalog of biases in questionnaires. Prev Chronic Dis [serial online] 2005;2:A13. Available at: http://www.cdc.gov/pcd/issues/2005/jan/04_0050.htm. Accessed August 5, 2012.
20. Ontario. People and Culture—Population Densities. Available at: http://www.ontario.ca/en/about_ontario/EC001035.html. Accessed May 16, 2012.
21. Shaw DE, Fielder AR, Minshull C, Rosenthal AR. Amblyopia—factors influencing age of presentation. Lancet 1988;2:207–9.
22. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev 2005;(4):CD003539.
23. McGlynn EA, Asch SM, Adams J, et al. The quality of health care delivered to adults in the United States. N Engl J Med 2003;348:2635–45.
24. Woolf SH. The meaning of translational research and why it matters. JAMA 2008;299:211–3.
25. Estabrooks CA, Thompson DS, Lovely JJ, Hofmeyer A. A guide to knowledge translation theory. J Contin Educ Health Prof 2006;26:25–36.
26. Taylor K, Elliott S. Interventions for strabismic amblyopia. Cochrane Database Syst Rev 2011;(8):CD006461.
27. Taylor K, Powell C, Hatt SR, Stewart C. Interventions for unilateral and bilateral refractive amblyopia. Cochrane Database Syst Rev 2012;4:CD005137.
28. American Academy of Ophthalmology Pediatric Ophthalmology/Strabismus Panel. Preferred Practice Pattern Guidelines. Amblyopia. San Francisco, CA: American Academy of Ophthalmology. 2007. Available at: http://one.aao.org/CE/PracticeGuidelines/PPP.aspx. Accessed May 16, 2012.
29. Paediatric Subcommittee of the Royal College of Ophthalmologists of the United Kingdom. Guidelines for the Management of Amblyopia. Available at: http://rcophth-website.www.premierithosting.com/docs/publications/GuidelinesfortheManagementofAmblyopia.pdf Accessed May 16, 2012.
30. Straus SE, Tetroe J, Graham I. Defining knowledge translation. CMAJ 2009;181:165–8.

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[1] Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Canada.

[2] Dalla Lana School of Public Health, University of Toronto, Toronto, Canada.

[3] Department of Human Biology, University of Toronto, Toronto, Canada.

[4] The Hospital for Sick Children, Toronto, Canada.

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Correspondence:
Ya-Ping Jin, MD, PhD, Department of Ophthalmology and Vision Sciences, University of Toronto, Room 562, Health Sciences Building, 155 College Street, Toronto, Ontario M5T 3M7, Canada. E-mail: Yaping.Jin@utoronto.ca.