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Better evidence: Assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

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Better evidence: Assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

Article

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Abstract

Objective: Evidence-based clinical resources (EBCRs) have the potential to improve diagnostic and therapeutic accuracy. The majority of U.S. teaching medical institutions have incorporated them into clinical training. Many EBCRs are subscription-based, and their cost is prohibitive for most clinicians and trainees in low- and middle-income countries. We sought to determine the utility of EBCRs in an East African medical school.

Setting: The University of Rwanda (UR), a medical school located in East Africa.

Participants: Medical students and faculty members at UR.

Interventions: We offered medical students and faculty at UR free access to UpToDate, a leading EBCR and conducted a cohort study to assess its utility. Students completed two surveys on their study habits and gave us permission to access their activity on UpToDate and their grades.

Results: Of the 980 medical students invited to enroll over two years, 547 did (56%). Of eligible final-year students, 88% enrolled. At baseline, 92% of students reported ownership of an internet-capable device, and the majority indicated using free online resources frequently for medical education. Enrolled final-year students viewed, on average, 1.24 topics per day and continued to use UpToDate frequently after graduation from medical school. Graduating class exam performance was better after introduction of UpToDate than in previous years.

Conclusions: Removal of the cost barrier was sufficient to generate high uptake of a leading EBCR by senior medical students and habituate them to continued usage after graduation.

Strengths and limitations of this study

- This is the first reported prospective cohort study of health professionals and trainees in Africa. Unlike previously conducted cross sectional studies, it will allow longitudinal tracking to investigate the learning behaviors of students and young physicians as they begin their career.
- This is the first study to link usage of online educational resources to performance in medical school examinations in Africa.
- Our ability to precisely track online usage of UpToDate eliminates recall bias that is likely to significantly impact findings of studies of educational interventions that are based on self-reporting.
- Given the observational nature of our study, we cannot make causal claims on the relationship between student use of UpToDate and their performance on medical school examinations.
- The relatively short follow-up period discussed in this paper limits our ability to understand the long term impact of offering UpToDate access to African health trainees.

Introduction

The velocity of growth of the clinical evidence base is staggering: In the last three years alone, over 16,000 unique clinical studies posted new results on ClinicalTrials.gov.¹ There is more information emerging every year than any one person could ever retain. In response, educators in the United States (U.S.) have called for a shift in the basic paradigm of medical education, deemphasizing the passive presentation of material and promoting problem-solving skills and the ability to find information and adapt it to the clinical situation at hand.² The Liaison Committee on Medical Education (LCME) mandates that self-directed learning be part of every accredited school's curriculum, and the American Board of Internal Medicine recently announced that maintenance of certification exams for internists and nephrologists will be open-book.^{3,4} The historical focus on memorization is giving way to an emphasis on knowing how to find information, synthesize it, and apply it clinically. Clinicians who have not developed these skills during medical school or clinical training are at a disadvantage, which, ultimately, means their patients are at a disadvantage.

The ability to access and synthesize clinical information effectively and efficiently is particularly crucial for clinicians in low- and middle-income countries (LMICs). The health workforce shortage and absence of specialists forces clinicians to care for more patients with a broader range of complaints than their counterparts in high-income countries. Rwanda, a country of 11 million people, had, until recently, a total of 15 anesthesiologists, 25 obstetricians, and zero neurologists.^{5,6} In addition, a study of 21 hospitals in LMICs documented substantial knowledge gaps among physicians.⁷ Constraints in medical education in these countries are likely responsible for both workforce and knowledge gaps. In 2011, the Sub-Saharan African Medical

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School Study group surveyed 146 of 168 medical schools in the region and found widespread shortages in qualified faculty and infrastructure.⁸

To address the challenge of the rapidly expanding evidence base in medicine, several organizations in high-income countries have created evidence-based clinical resources (EBCRs) – regularly updated, expert-authored, online tools that synthesize the primary literature to guide clinical decision making. Over the years, UpToDate, which was founded at Harvard Medical School in 1992, has emerged as a leading EBCR in high-income countries, and several studies have documented its utility: Use of UpToDate has been associated with improved examination performance among internal medicine residents, as well as lower mortality at U.S. hospitals.^{9,10} As of February 2018, 90% of teaching U.S. medical institutions and 100% of the top 20 U.S. medical schools (as ranked by U.S. News & World Report) subscribed to UpToDate.^{11,12,13} Despite the high demand for UpToDate in U.S. medical education, none of the 168 medical schools in sub-Saharan Africa subscribe to its services, partly because of the high subscription cost. An individual physician subscription to UpToDate in Rwanda costs \$299 per year; Rwanda spent \$52 per capita on healthcare in 2014.¹⁴

Given their utility in high-income countries, access to EBCRs could help address some of the challenges faced by clinicians in LMICs. We hypothesize that access to better evidence could improve the knowledge base of these clinicians, increase their perception of self-efficacy, and create a professional habit of seeking evidence at the point of care. This could be particularly beneficial for clinicians caring for a large number of complex patients without access to specialists. We have previously reported on a program which provides donated UpToDate subscriptions to clinicians in LMICs, in which we found that most use UpToDate with high

frequency and many report changing their clinical decision making as a result of having access to UpToDate.¹⁵

We postulated that medical school is the optimal moment to introduce EBCRs to LMIC physicians-in-training, as it is *de facto* the first locus of professional habit formation, and often their last formal one, as many clinicians in LMICs do not receive post-graduate education. Additionally, providing access to EBCRs to medical students in LMICs is a matter of equity: students who have worked hard to care for their community in LMICs should have the same opportunity to learn and provide quality care as their counterparts in U.S. medical schools.

Methods

Setting

The University of Rwanda (UR) is the only medical degree-granting school in Rwanda at this time and is a public university. 76% of students at UR are recipients of bursaries from the Government of Rwanda.¹⁶ Medical students enter UR after successful completion of high school and, during the study period, completed a 6-year medical education curriculum consisting of two years of pre-clinical education followed by 4 years of clinical education in the wards.

Intervention

In the fall of 2014, the authors formed an agreement with Wolters Kluwer, the parent company of UpToDate, to facilitate the donations of UpToDate subscriptions to medical students in sub-Saharan Africa. With appropriate IRB approval, medical students and faculty at the University of Rwanda were invited by email to enroll in our study. "Faculty member" was defined as anyone who teaches undergraduate medical students, which meant that residents were considered faculty. Undergraduate medical students, who unlike U.S. medical students are admitted to

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medical school after high school at age 18, were invited to enroll as well. Students were invited in cohorts that spanned the different years of medical school (see Supplementary Appendix 2). Enrollment was voluntary and not mandated by faculty or the curriculum. Each participant received a free 5-year individual subscription to UpToDate, which allowed them to access the website from any computer or mobile device. The authors undertook no recruitment or training efforts. Data reported in this paper was generated in 2015–2017.

Evaluation

Students were asked to complete an online baseline survey to document their study habits before provision of UpToDate and an Annual Evaluation survey. We chose questions around students' baseline utilization of the Internet in medical education, as others have identified access to devices and the Internet as potential barriers to EBCR utilization.¹⁷ Students' responses over time were linked using their name and email. All participant activity on the UpToDate website and mobile application was tracked remotely and linked to survey responses. An anonymized dataset of all student grades for the graduating classes of 2012-2017 was obtained to assess the impact of UpToDate on class examination performance. Lastly, to understand student usage of UpToDate over time, we plotted the average number of topics viewed per month by active users. To characterize a stable cohort of users over time, we plotted the average number of topics viewed by students in their final year who enrolled before March 1st 2016. Supplementary Appendix 1 describes the statistical approach of the data analysis, which was performed on Stata SE 14 and Microsoft Excel.

Patient and public involvement

Patients were not the subject of this study. A medical student at UR (BN) is a co-author of this study and brought the student perspective into the interpretation of the data.

Results

Of the 980 students and 1,084 faculty invited to enroll into the study during the 2015-2017 study period, 547 (56%) students and 325 (29%) faculty did. The highest enrollment rate (87%) was observed among students in their final (sixth) year of medical school, who are called "Doctorate 4" or Doc4 students at UR (Supplementary Appendix 2). In our baseline survey, 92% of student respondents overall and 96% of Doc4 students reported ownership of at least one internet-capable device (Figure 1a). Free electronic resources—primarily Medscape, Google, and Wikipedia—were used frequently for the purposes of medical education (Figure 1b). A small percentage reported frequent usage of UpToDate at baseline.

All users who completed the enrollment survey had an individual UpToDate account created for them and received an email with instructions on how to set up their UpToDate password. Of those who activated their UpToDate account, 76% of faculty and 64% of students viewed, on average, at least one UpToDate topic per week; 13% of faculty and 23% of students viewed, on average, one topic or more per day. In a multivariate linear regression looking at variables associated with UpToDate usage frequency, student year at enrollment was the only significantly associated variable (Table 1). Figure 2 shows average UpToDate usage by year of student at enrollment.

One year after enrollment, 52% of students completed the annual evaluation; 74% of Doc4 students did so. Both graduates, who had enrolled into the study as Doc4 students, and continuing students reported increased usage of UpToDate. Continuing students also reported decreased use of Google and Wikipedia (Figure 3).

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To assess the effect of providing UpToDate to students on their educational performance, we plotted the average grades of each graduating class from 2012 to 2017 (599 students in total) and compared the pre-UpToDate period (2012-2015; average grade 68) to the post-UpToDate period (2016-2017; average grade 75) (Figure 4). Both a simple t-test as well as a two-way ANOVA showed a statistically significant difference (Table 2). In 2017, a student who scored 68 would have ranked at the 16th percentile of the class, while a student scoring 75 would have ranked at the 66th percentile.

We used remote tracking to assess Doc4 student usage over time and found that it spiked in May 2016, as students prepared for their graduation exams in June. Usage fell significantly during summer vacation, but rose again in September and October, as the new graduates began their careers as physicians, either in residency or in independent practice. A similar pattern of usage over time was seen among faculty (Figure 5). elie

Discussion

Our findings represent the first prospective cohort study of medical students in Africa and suggest that access to devices and the internet might not be a significant barrier for African medical students wishing to access online resources. Our findings align with observations from a 2016 in Zimbabwe and contrast two earlier studies in Nigeria published in 2004 and 2008 that suggest lack of access to internet.^{18,19,20} The differences might be related to the passage of time or resource availability differences between Rwanda and Nigeria. The findings suggest that, in Rwanda, our focus should not be on securing devices but on securing access to the latest online tools and evidence.

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Our study also shows that students, especially final-year students, used a leading EBCR frequently when the cost barrier was removed. This was achieved with no provision of internetcapable devices, no subsidizing of mobile internet data, no dedicated training activities on EBCR use, and no curricular integration of EBCRs. Overall, our findings suggest that removing the cost barrier to access of EBCRs can generate uptake among a subset of medical students in Africa. The low uptake of UpToDate by junior UR students could be related to the basic science focus of their curriculum, which makes UpToDate's clinical content less relevant.

The introduction of an EBCR during the last year of medical school may lead to habit formation. Among students receiving an EBCR subscription in their final year, usage was sustained for the one and a half year period monitored after graduation. Additionally, self-reported usage of nonvalidated sources such as Google and Wikipedia fell among students within a year of UpToDate provision. In 2013, Gawande argued that habit change and formation in healthcare is a complex process that can often take decades.²¹ He also argued that some habits form quickly and that those might be the ones that make a physician's workflow faster and more efficient. Our study suggests that UpToDate may fall into this category of tools and habits that facilitate faster, more efficient work.

The temporal association of free access to UpToDate with an improvement of the overall examination performance of the graduating class may be causal or due to another explanation, as discussed below. It is consistent, however, with previous reports of associations between UpToDate usage and performance in exams by residents in the U.S. and Japan, and practicing physicians in the U.S.

Limitations

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Our study is subject to selection bias given its observational nature. It is possible that students with regular access to email were more likely to respond to our email-based invitation, thus biasing the response set, especially with respect to use of electronic resources and internet access. The high enrollment rate among Doc4 students mitigates this effect to some extent. The use of a historical control to assess the impact of UpToDate's introduction on student grades also has several limitations. First, no causal arguments can be made, given the fact that different exams were used each year and different students took them. While UpToDate may have helped students prepare for their exams more efficiently and increase their knowledge base, it is also possible that the exams in 2016 and 2017 were easier than those of years past or that the students were independently academically superior to the previous classes. Second, it is possible that test answers may not be contained/addressed in UpToDate, although the UR faculty among the authors of this paper do not believe that to be the case.

Next steps

Due to its longitudinal nature, this study has the potential to offer additional insights on the changes in learning behaviors of African health trainees over time. Qualitative research on this student cohort could help elucidate the drivers of different study behaviors, and the perceived impact of resources such as UpToDate on clinician's knowledge base and self-efficacy. Future research might explore other EBCRs and features that impact uptake and utility. We focused on UpToDate because of the body of literature that supports its value in high-income countries. However, we hypothesize that a suite of EBCRs and learning tools, possibly in multiple languages, might be helpful for trainees in LMICs. Given the relatively easy scalability of software-based tools, we believe that we can continue to decrease the barriers for trainees in LMICs to access the best available evidence at the frontline of care delivery. Our vision is that

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this work can prepare and inform how the next generation of clinicians in LMICs practices evidence-based medicine. Although our research focused on LMICs, disparities in access to high-quality EBCRs might exist within U.S. medical education as well, which can also be an area of future research and programming. As medicine continues to evolve rapidly and medical education shifts its focus from memorization to critical processing of information, we must ensure that all learners have equitable access to the best information available.

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Ethical Approval: The research described here was approved by the Harvard Medical School Institutional Review Board and the University of Rwanda Institutional Review Board.

Data sharing: No additional data available.

Contributorship: YV, KR, KW, RK, FM, RCM, TW, RW designed the study and co-wrote its protocol. JDK, AE, BN implemented the study at the University of Rwanda. YV analyzed the data and drafted this manuscript. All authors edited the manuscript. RW oversaw the entire design, implementation, and analysis of the study.

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Figure legends:

Figure 1: Baseline survey of Rwandan medical students. (A) shows the percentage of students at UR reporting that they own a particular internet-capable device or use it in medical education. "Any device" refers to any of the following: tablet, smartphone, laptop, desktop. (B) shows the percentage of students indicating that they use a specific resource to study for coursework or prepare for examinations. n = 547 UR students and 157 MUHAS students.

Figure 2: Predictor of UpToDate usage. (A) shows the average daily usage (ADU) during the study period by UR students broken down by class year at enrollment. Students who did not log onto their accounts after enrolling into the study were assigned a daily topic viewing frequency of zero. n = 547 UR students.

Figure 3: Changes in the usage of electronic resources. Figures show the percentage of respondents who reported using a particular resource "almost every day" at enrollment and one year later at the time of annual evaluation. Shading added to highlight responses for UpToDate. (A) shows responses of UR users who had graduated at the time of annual evaluation and were practicing physicians. (B) shows responses of UR clinical students (Doc1 at time of enrollment) who were still in school at the time of annual evaluation. n = 62 UR graduates, and 66 UR students.

Figure 4: Impact of EBCR provision on class exam performance at UR. (A) shows the average grades of graduating Doc4 students over time. Each dot represents one student and

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shows the average of their grades in the following eight exams: written & clinical exams in internal medicine, pediatrics, obstetrics & gynecology, and surgery. (B) shows the average grades of students pre-UpToDate (2012-2015) and post-UpToDate (2016-2017). The p-value represents a two-sided heteroscedastic t-test. The error bars represent standard error of the mean.

Figure 5: EBCR utilization over time by UR students and faculty. Lines show the average number of topics viewed per user per month by each user group. Only users who enrolled before 03/01/16 are included in this analysis (n = 185 faculty, 70 Doc4 students). Call-outs are added to describe events in the careers of Doc4 students

Table 1

	Coefficients	P-value
Cohort	-0.04	0.21
Year at enrollment	0.12	< 0.001
Own any device	0.07	0.29
Own smartphone	-0.03	0.49
Hours devoted to school	0.00	0.91
Google use frequency	-0.02	0.30
UpToDate use frequency	0.00	0.70

Table 1: Multivariate linear regression with UpToDate usage as the dependent variable.

The table shows a multivariable linear regression with average daily topic viewing frequency (natural logarithm transform) as the dependent variable. The dependent variable was calculated as "number of UpToDate topics viewed" / "days with an active subscription" for each user. It was set to zero for users who did not log on to UpToDate. The dependent variable was transformed with the equation Y' = ln(Y+1) to approximate normality. The independent variables were set as follows: "Cohort" was set to 1 for students enrolling in 2015-2016 and 2 for student enrolling in 2016-2017. "Year at enrollment": PCL1 was set to 1, PLC2 was set to 2, Doc1 was set to 3, Doc3 was set to 5 and Doc4 was set to 6. "Own any device" and "Own smartphone" were set to 0 if the student did not report ownership and to 1 if they did. "Hours devoted to school" is a sum of student reported hours spent in the classroom, in clinical activities, and on studying. "Google use frequency" and "UpToDate use frequency" were set based on student responses at the time of enrollment (before UpToDate subscriptions were given to them). They were set to 4 if student replied "almost every day", 3 if "a few times per week", 2 if "a few times per month", 1 if "a few times per year" and 0 if "Never" or "I don't know this resource." P-value bolded if < 0.05.

Table 2

Independent variable	Partial SS	P-value
UpToDate offered ^b	4197	< 10 ⁻⁴
Year of exam	6196	< 10 ⁻⁴

Table 2: Two-way ANOVA with average Doc4 grade as dependent variable. The table shows a two way ANOVA test with average Doc4 grade as dependent variable and year of exam and UpToDate provision as independent variables. n = 599 Doc4 students over 6 years. ^b UpToDate offered was set to 0 for 2012-2015 and 1 for 2016-2017.

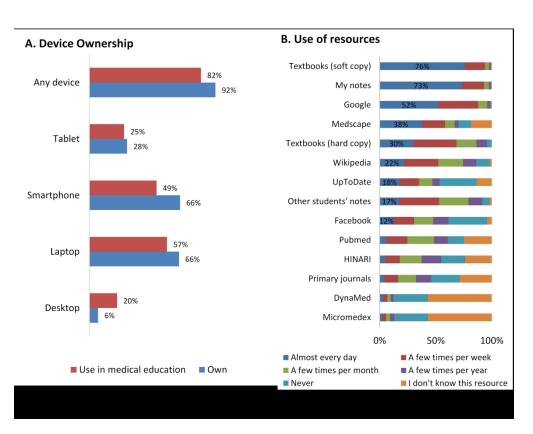
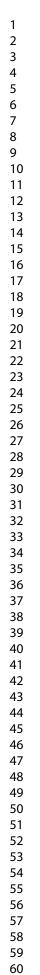


Figure 1: Baseline survey of Rwandan medical students. (A) shows the percentage of students at UR reporting that they own a particular internet-capable device or use it in medical education. "Any device" refers to any of the following: tablet, smartphone, laptop, desktop. (B) shows the percentage of students indicating that they use a specific resource to study for coursework or prepare for examinations. n = 547 UR students and 157 MUHAS students.



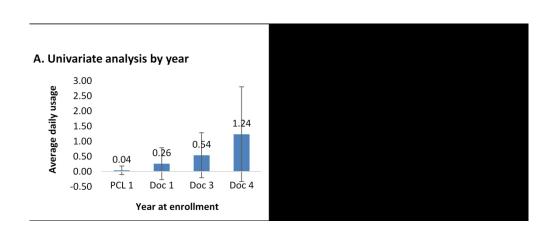
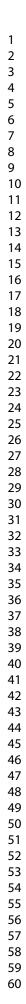


Figure 2: Predictor of UpToDate usage. (A) shows the average daily usage (ADU) during the study period by UR students broken down by class year at enrollment. Students who did not log onto their accounts after enrolling into the study were assigned a daily topic viewing frequency of zero. n = 547 UR students



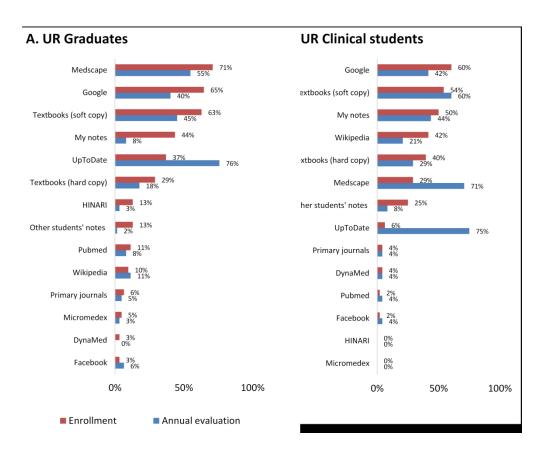


Figure 3: Changes in the usage of electronic resources. Figures show the percentage of respondents who reported using a particular resource "almost every day" at enrollment and one year later at the time of annual evaluation. Shading added to highlight responses for UpToDate. (A) shows responses of UR users who had graduated at the time of annual evaluation and were practicing physicians. (B) shows responses of UR clinical students (Doc1 at time of enrollment) who were still in school at the time of annual evaluation. n = 62 UR graduates, and 66 UR students.

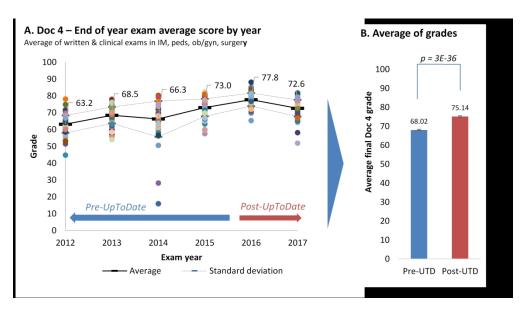


Figure 4: Impact of EBCR provision on class exam performance at UR. (A) shows the average grades of graduating Doc4 students over time. Each dot represents one student and shows the average of their grades in the following eight exams: written & clinical exams in internal medicine, pediatrics, obstetrics & gynecology, and surgery. (B) shows the average grades of students pre-UpToDate (2012-2015) and post-UpToDate (2016-2017). The p-value represents a two-sided heteroscedastic t-test. The error bars represent standard error of the mean.

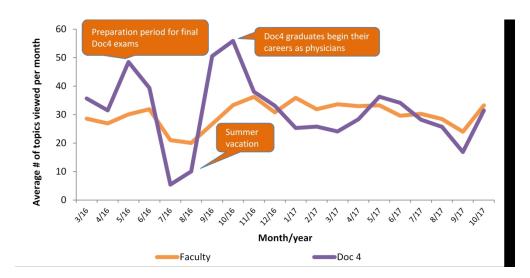


Figure 5: EBCR utilization over time by UR students and faculty. Lines show the average number of topics viewed per user per month by each user group. Only users who enrolled before 03/01/16 are included in this analysis (n = 185 faculty, 70 Doc4 students). Call-outs are added to describe events in the careers of Doc4 students

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Supplementary Appendix

Supplementary Appendix 1 – Supplementary Methods

Data analysis

To understand EBCR usage patterns by students and faculty, we calculated for each user the number of topics viewed. Any action resulting in the opening of a new UpToDate card (with a distinct title) was counted as a new topic. Viewing of the same topic in the same session was counted only once. A session was defined as the time period using UpToDate, initiated by a unique log-on of a user to the UpToDate website, mobile site, or mobile application and terminated when the user logged off, closed the application, or remained inactive for more than 3 hours. To calculate the average daily usage (ADU), the number of topics viewed was divided by the number of days that the user had an active account. The number of days with an active account was defined as the interval between the users' first-ever log-on and the end of the study period (10/31/2017). To identify predictors of high usage frequency, I conducted a multivariable linear regression after applying the natural log transform to ADU values to approximate normality.

To understand the impact of UpToDate on the overall exam performance of the graduating class at UR, we calculated the average grade of each graduating student for 2012-2017 by averaging their performance in all of their graduation exams. These were written and clinical exams in the following subjects: internal medicine, surgery, obstetrics & gynecology, and pediatrics. To assess the impact of UpToDate, I performed two tests: First, we performed a two-sided heteroscedastic t-test between grades assigned before UpToDate provision (2012-

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2015) and grades assigned after (2016-2017). To control for variability due to the year of exam administration, we performed a two-way Analysis of Variance (ANOVA) test with year of exam and UpToDate provision as the independent variables and average exam grade as the dependent variable.

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Role	Academic year	Class at time of enrollment	Eligible	Completing enrollment	% completing enrollment
Students	2015-2016	PCL1 (1st year)	271	92	34%
		Doc1 (3rd year)	125	90	72%
		Doc4 (6th year)	86	84	98%
	2017 2017	PCL1 (1st year)	102	24	24%
		Doc1 (3rd year)	205	102	50%
	2016-2017	Doc3 (5th year)	89	74	83%
		Doc4 (6th year)	102	81	79%
	Total - students		980	547	56%
Faculty	Continuous enrollment		1084	325	29%

Supplementary appendix 2: Participant enrolment

Supplementary Appendix 2: Participant enrollment. Table shows the number of eligible students and faculty by role, academic year at time of enrollment, and class at time of enrollment. Table also shows the number of students and faculty who completed enrollment, and the percentage of eligible students who completed enrollment.

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Better evidence: A Prospective Cohort Study Assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

Article

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Abstract

Objective: Evidence-based clinical resources (EBCRs) have the potential to improve diagnostic and therapeutic accuracy. The majority of U.S. teaching medical institutions have incorporated them into clinical training. Many EBCRs are subscription-based, and their cost is prohibitive for most clinicians and trainees in low- and middle-income countries. We sought to determine the utility of EBCRs in an East African medical school.

Setting: The University of Rwanda (UR), a medical school located in East Africa.

Participants: Medical students and faculty members at UR.

Interventions: We offered medical students and faculty at UR free access to UpToDate, a leading EBCR and conducted a cohort study to assess its uptake and usage. Students completed two surveys on their study habits and gave us permission to access their activity on UpToDate and their grades.

Results: Of the 980 medical students invited to enroll over two years, 547 did (56%). Of eligible final-year students, 88% enrolled. At baseline, 92% of students reported ownership of an internet-capable device, and the majority indicated using free online resources frequently for medical education. Enrolled final-year students viewed, on average, 1.24 topics per day and continued to use UpToDate frequently after graduation from medical school. Graduating class exam performance was better after introduction of UpToDate than in previous years.

Conclusions: Removal of the cost barrier was sufficient to generate high uptake of a leading EBCR by senior medical students and habituate them to continued usage after graduation.

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Strengths and limitations of this study

- This is the first reported longitudinal prospective cohort study of health professionals and trainees in Africa.
- This is the first study to link usage of online educational resources to performance in medical school examinations in Africa.
- Our ability to precisely track online usage of UpToDate eliminates recall bias that is likely to significantly impact findings of studies of educational interventions that are based on self-reporting.
- Given the observational nature of our study, we cannot make causal claims on the relationship between student use of UpToDate and their performance on medical school examinations.
- The relatively short follow-up period discussed in this paper limits our ability to understand the long term impact of offering UpToDate access to African health trainees.

Introduction

The velocity of growth of the clinical evidence base is staggering: In the last three years alone, over 16,000 unique clinical studies posted new results on ClinicalTrials.gov.¹ There is more information emerging every year than any one person could ever retain. In response, educators in the United States (U.S.) have called for a shift in the basic paradigm of medical education, deemphasizing the passive presentation of material and promoting problem-solving skills and the ability to find information and adapt it to the clinical situation at hand.² The Liaison Committee on Medical Education (LCME) mandates that self-directed learning be part of every accredited school's curriculum, and the American Board of Internal Medicine recently announced that maintenance of certification exams for internists and nephrologists will be open-book.^{3,4} The historical focus on memorization is giving way to an emphasis on knowing how to find information, synthesize it, and apply it clinically. Clinicians who have not developed these skills during medical school or clinical training are at a disadvantage, which, ultimately, means their patients are at a disadvantage.^{5, 6, 7}

The ability to access and synthesize clinical information effectively and efficiently is particularly crucial for clinicians in low- and middle-income countries (LMICs). The health workforce shortage and absence of specialists forces clinicians to care for more patients with a broader range of complaints than their counterparts in high-income countries. Rwanda, a country of 11 million people, had, until recently, a total of 15 anesthesiologists, 25 obstetricians, and zero neurologists.^{8,9} In addition, a study of 21 hospitals in LMICs documented substantial knowledge gaps among physicians.¹⁰ Constraints in medical education in these countries are likely responsible for both workforce and knowledge gaps. In 2011, the Sub-Saharan African Medical

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School Study group surveyed 146 of 168 medical schools in the region and found widespread shortages in qualified faculty and infrastructure.¹¹

To address the challenge of the rapidly expanding evidence base in medicine, several organizations in high-income countries have created evidence-based clinical resources (EBCRs) - regularly updated, expert-authored, online tools that synthesize the primary literature to guide clinical decision making. Over the years, UpToDate, which was founded at Harvard Medical School in 1992, has emerged as a leading EBCR in high-income countries, and several studies have documented its utility: Use of UpToDate has been associated with improved examination performance among internal medicine residents, as well as lower mortality at U.S. hospitals.5, 6 As of February 2018, 90% of teaching U.S. medical institutions and 100% of the top 20 U.S. medical schools (as ranked by U.S. News & World Report) subscribed to UpToDate.^{12,13,14} Despite the high demand for UpToDate in U.S. medical education, none of the 168 medical schools in sub-Saharan Africa subscribe to its services, partly because of the high subscription cost. An individual physician subscription to UpToDate in Rwanda costs \$299 per year; Rwanda spent \$52 per capita on healthcare in 2014.¹⁵ Additionally, cost of internet access can be prohibitively high in some LMICs; at the time of publication, mobile internet in Rwanda cost approximately \$0.05 per megabyte.¹⁶

Given their utility in high-income countries, access to EBCRs could help address some of the challenges faced by clinicians in LMICs. We believe that access to better evidence could improve the knowledge base of these clinicians, increase their perception of self-efficacy, and create a professional habit of seeking evidence at the point of care. This could be particularly beneficial for clinicians caring for a large number of complex patients without access to specialists. We have previously reported on a program which provides donated UpToDate

subscriptions to clinicians in LMICs, in which we found that most use UpToDate with high frequency and many report changing their clinical decision making as a result of having access to UpToDate.17

While EBCRs have traditionally been developed for physicians in practice, there are reasons to believe that their introduction to medical students would be beneficial. First, medical school is de *facto* the first locus of professional habit formation, and often their last formal one, as many clinicians in LMICs do not receive post-graduate education. Additionally, providing access to EBCRs to medical students in LMICs is a matter of equity: students who have worked hard to care for their community in LMICs should have the same opportunity to learn and provide quality care as their counterparts in U.S. medical schools. In this article, we hypothesized that removing the cost barrier to accessing EBCR will lead to high student uptake and possibly lead to an improvement in educational outcomes. N.C.

Methods

Setting

The University of Rwanda (UR) was the only medical degree-granting school in Rwanda at the time this study launched and is a public university. 76% of students at UR are recipients of bursaries from the Government of Rwanda.¹⁸ Medical students enter UR after successful completion of high school and, during the study period, completed a 6-year medical education curriculum consisting of two years of pre-clinical education followed by 4 years of clinical education in the wards.

Intervention

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In the fall of 2014, the authors formed an agreement with Wolters Kluwer, the parent company of UpToDate, to facilitate the donations of UpToDate subscriptions to medical students in sub-Saharan Africa. With appropriate IRB approval, medical students and faculty at the University of Rwanda were invited by email to enroll in our study. "Faculty member" was defined as anyone who teaches undergraduate medical students, which meant that residents, as well as staff physicians, were considered faculty. Undergraduate medical students, who unlike U.S. medical students are admitted to medical school after high school at age 18, were invited to enroll as well. Students were invited in cohorts that spanned the different years of medical school (see Supplementary Table 1). Enrollment was voluntary and not mandated by faculty or the curriculum. Each participant received a free 5-year individual subscription to UpToDate, which allowed them to access the website from any computer or mobile device. The authors undertook no recruitment or training efforts. Data reported in this paper was generated in 2015–2017. Of note, all participants in the study will be able to apply for an annually renewable, indefinite, donated subscription to UpToDate after the completion of the study.

Evaluation

Students were asked to complete an online baseline survey to document their study habits before provision of UpToDate and an Annual Evaluation survey. We chose questions around students' baseline utilization of the Internet in medical education, as others have identified access to devices and the Internet as potential barriers to EBCR utilization.¹⁹ Students' responses over time were linked using their name and email. All participant activity on the UpToDate website and mobile application was tracked remotely and linked to survey responses. An anonymized dataset of all student grades for the graduating classes of 2012-2017 was obtained to assess the impact of UpToDate on class examination performance. Lastly, to understand student usage of UpToDate

over time, we plotted the average number of topics viewed per month by active users. To characterize a stable cohort of users over time, we plotted the average number of topics viewed by students in their final year who enrolled before March 1st 2016.

To understand EBCR usage patterns by students and faculty, we calculated for each user the number of topics viewed. Any action resulting in the opening of a new UpToDate card (with a distinct title) was counted as a new topic. Viewing of the same topic in the same session was counted only once. A session was defined as the time period using UpToDate, initiated by a unique log-on of a user to the UpToDate website, mobile site, or mobile application and terminated when the user logged off, closed the application, or remained inactive for more than three hours. To calculate the average daily usage (ADU), the number of topics viewed was divided by the number of days that the user had an active account. The number of days with an active account was defined as the interval between the users' first-ever log-on and the end of the study period (10/31/2017). To identify predictors of high usage frequency, we conducted a multivariable linear regression after applying the natural log transform to ADU values to approximate normality.

To understand the impact of UpToDate on the overall exam performance of the graduating class at UR, we calculated the average grade of each graduating student for 2012-2017 by averaging their performance in all of their graduation exams. These were written and clinical exams in the following subjects: internal medicine, surgery, obstetrics & gynecology, and pediatrics. To assess the impact of UpToDate, we performed two tests: First, we performed a two-sided heteroscedastic t-test between grades assigned before UpToDate provision (2012-2015) and grades assigned after (2016-2017). To control for variability due to the year of exam

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administration, we performed a two-way Analysis of Variance (ANOVA) test with year of exam and UpToDate provision as the independent variables and average exam grade as the dependent variable.

Data analysis was performed on Stata SE 14 and Microsoft Excel.

Patient and public involvement

Patients were not the subject of this study. Given the setting of the study at a medical school, it was not feasible to include a patient partner. A medical student at UR (BN) is a co-author of this study and brought the student perspective into the interpretation of the data.

Results

Of the 980 students and 1,084 faculty invited to enroll into the study during the 2015-2017 study period, 547 (56%) students and 325 (29%) faculty did. The highest enrollment rate (87%) was observed among students in their final (sixth) year of medical school, who are called "Doctorate 4" or Doc4 students at UR (Supplementary Table 1). In our baseline survey, 92% of student respondents overall and 96% of Doc4 students reported ownership of at least one internet-capable device (Figure 1a). Free electronic resources—primarily Medscape, Google, and Wikipedia—were used frequently for the purposes of medical education (Figure 1b). A small percentage reported frequent usage of UpToDate at baseline.

All users who completed the enrollment survey had an individual UpToDate account created for them and received an email with instructions on how to set up their UpToDate password. Of those who activated their UpToDate account, 76% of faculty and 64% of students viewed, on average, at least one UpToDate topic per week; 13% of faculty and 23% of students viewed, on average, one topic or more per day. In a multivariate linear regression looking at variables

associated with UpToDate usage frequency, student year at enrollment was the only significantly associated variable (Table 1). Figure 2 shows average UpToDate usage by year of student at enrollment.

One year after enrollment, 52% of students completed the annual evaluation; 74% of Doc4 students did so. The low response rates could be attributed to lack of positive incentives to complete the survey or to students not checking their email to see that the evaluation survey was due. Both graduates, who had enrolled into the study as Doc4 students, and continuing students reported increased usage of UpToDate. Continuing students also reported decreased use of Google and Wikipedia (Figure 3).

To assess the effect of providing UpToDate to students on their educational performance, we plotted the average grades of each graduating class from 2012 to 2017 (599 students in total) and compared the pre-UpToDate period (2012-2015; average grade 68) to the post-UpToDate period (2016-2017; average grade 75) (Figure 4). Both a simple t-test as well as a two-way ANOVA showed a statistically significant difference (Table 2). In 2017, a student who scored 68 would have ranked at the 16th percentile of the class, while a student scoring 75 would have ranked at the 66th percentile.

We used remote tracking to assess Doc4 student usage over time and found that it spiked in May 2016, as students prepared for their graduation exams in June. Usage fell significantly during summer vacation, but rose again in September and October, as the new graduates began their careers as physicians, either in residency or in independent practice. A similar pattern of usage over time was seen among faculty (Figure 5).

Discussion

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Our findings represent the first prospective cohort study of medical students in Africa and suggest that access to devices and the internet might not be a significant barrier for African medical students wishing to access online resources. Our findings align with observations from a 2016 study in Zimbabwe and contrast two earlier studies in Nigeria published in 2004 and 2008 that suggest lack of access to internet.^{20,21,22} The differences might be related to the passage of time or resource availability differences between Rwanda and Nigeria. The findings suggest that, in Rwanda, our focus should not be on securing devices but on securing access to the latest online tools and evidence.

Our study also shows that students, especially final-year students, used a leading EBCR frequently when the cost barrier was removed. This was achieved with no provision of internetcapable devices, no subsidizing of mobile internet data, no dedicated training activities on EBCR use or evidence searching, and no curricular integration of EBCRs. Overall, our findings suggest that removing the cost barrier to access of EBCRs can generate uptake among a subset of medical students in East Africa. The low uptake of UpToDate by pre-clinical UR students could be related to the basic science focus of their curriculum, which makes UpToDate's clinical content less relevant.

The introduction of an EBCR during the last year of medical school may lead to habit formation. Among students receiving an EBCR subscription in their final year, usage was sustained for the one and a half year period monitored after graduation. Additionally, self-reported usage of nonvalidated sources such as Google and Wikipedia fell among students within a year of UpToDate provision. In 2013, Gawande argued that habit change and formation in healthcare is a complex process that can often take decades.²³ He also argued that some habits form quickly and that those might be the ones that make a physician's workflow faster and more efficient. Our study

suggests that UpToDate may fall into this category of tools and habits that facilitate faster, more efficient work.

The temporal association of free access to UpToDate with an improvement of the overall examination performance of the graduating class may be causal or due to another explanation, as discussed below. It is consistent, however, with previous reports of associations between UpToDate usage and performance in exams by residents in the U.S. and Japan, and practicing physicians in the U.S.

Limitations

Our study is subject to selection bias given its observational nature. It is possible that students with regular access to email were more likely to respond to our email-based invitation, thus biasing the response set, especially with respect to use of electronic resources and internet access. The high enrollment rate among Doc4 students mitigates this effect to some extent. The use of a historical control to assess the impact of UpToDate's introduction on student grades also has several limitations. First, no causal arguments can be made, given the fact that different exams were used each year and different students took them. While UpToDate may have helped students prepare for their exams more efficiently and increase their knowledge base, it is also possible that the exams in 2016 and 2017 were easier than those of years past or that the students were independently academically superior to the previous classes. The cause of the overall increase in student scores before UpToDate was introduced is unclear and could be related to changes in educational methods or examinations, although we do not have evidence for either of those. In addition, the reason for the decline in of students' scores from 2016 to 2017 is unknown, and could be statistically random or indicative of a trend. Further follow up will be required to answer this question.

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Second, it is possible that test answers may not be contained/addressed in UpToDate, although the UR faculty among the authors of this paper do not believe that to be the case.

Next steps

Due to its longitudinal nature, this study has the potential to offer additional insights on the changes in learning behaviors of African health trainees over time. Qualitative research on this student cohort could help elucidate the drivers of different study behaviors, and the perceived impact of resources such as UpToDate on clinician's knowledge base and self-efficacy. Future research might explore other EBCRs and features that impact uptake and utility. We focused on UpToDate because of the body of literature that supports its value in high-income countries. However, we hypothesize that a suite of EBCRs and learning tools, possibly in multiple languages, might be helpful for trainees in LMICs. Given the relatively easy scalability of software-based tools, we believe that we can continue to decrease the barriers for trainees in LMICs to access the best available evidence at the frontline of care delivery. Our vision is that this work can prepare and inform how the next generation of clinicians in LMICs practices evidence-based medicine. Although our research focused on LMICs, disparities in access to high-quality EBCRs might exist within U.S. medical education as well, which can also be an area of future research and programming. As medicine continues to evolve rapidly and medical education shifts its focus from memorization to critical processing of information, we must ensure that all learners have equitable access to the best information available.

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Competing interests: None declared

Ethical Approval: The research described here was approved by the Harvard Medical School Longwood Medical Area Institutional Review Board and the College of Medicine and Health Sciences University of Rwanda Institutional Review Board.

Data sharing: No data are available.

Contributorship: YV, JR, KW, RK, FM, RCM, TW, RW designed the study and co-wrote its protocol. JDK, AE, BN implemented the study at the University of Rwanda. YV analyzed the

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data and drafted this manuscript. All authors edited the manuscript. RW oversaw the entire design, implementation, and analysis of the study.

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Figure legends:

Figure 1: Baseline survey of Rwandan medical students. (A) shows the percentage of students at UR reporting that they own a particular internet-capable device or use it in medical education. "Any device" refers to any of the following: tablet, smartphone, laptop, desktop. (B) shows the percentage of students indicating that they use a specific resource to study for coursework or prepare for examinations. n = 547 UR students and 157 MUHAS students.

Figure 2: Predictor of UpToDate usage. (A) shows the average daily usage (ADU) during the study period by UR students broken down by class year at enrollment. Students who did not log onto their accounts after enrolling into the study were assigned a daily topic viewing frequency of zero. n = 547 UR students.

Figure 3: Changes in the usage of electronic resources. Figures show the percentage of respondents who reported using a particular resource "almost every day" at enrollment and one year later at the time of annual evaluation. Shading added to highlight responses for UpToDate. (A) shows responses of UR users who had graduated at the time of annual evaluation and were practicing physicians. (B) shows responses of UR clinical students (Doc1 at time of enrollment) who were still in school at the time of annual evaluation. n = 62 UR graduates, and 66 UR students.

Figure 4: Impact of EBCR provision on class exam performance at UR. (A) shows the average grades of graduating Doc4 students over time. Each dot represents one student and

shows the average of their grades in the following eight exams: written & clinical exams in internal medicine, pediatrics, obstetrics & gynecology, and surgery. (B) shows the average grades of students pre-UpToDate (2012-2015) and post-UpToDate (2016-2017). The p-value represents a two-sided heteroscedastic t-test. The error bars represent standard error of the mean.

Figure 5: EBCR utilization over time by UR students and faculty. Lines show the average number of topics viewed per user per month by each user group. Only users who enrolled before 03/01/16 are included in this analysis (n = 185 faculty, 70 Doc4 students). Call-outs are added to describe events in the careers of Doc4 students

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Table 1

Coefficients	P-value
-0.04	0.21
0.12	< 0.001
0.07	0.29
-0.03	0.49
0.00	0.91
-0.02	0.30
0.00	0.70
	-0.04 0.12 0.07 -0.03 0.00 -0.02

Table 1: Multivariate linear regression with UpToDate usage as the dependent variable.

The table shows a multivariable linear regression with average daily topic viewing frequency (natural logarithm transform) as the dependent variable. The dependent variable was calculated as "number of UpToDate topics viewed" / "days with an active subscription" for each user. It was set to zero for users who did not log on to UpToDate. The dependent variable was transformed with the equation Y' = ln(Y+1) to approximate normality. The independent variables were set as follows: "Cohort" was set to 1 for students enrolling in 2015-2016 and 2 for student enrolling in 2016-2017. "Year at enrollment": PCL1 was set to 1, PLC2 was set to 2, Doc1 was set to 3, Doc3 was set to 5 and Doc4 was set to 6. "Own any device" and "Own smartphone" were set to 0 if the student did not report ownership and to 1 if they did. "Hours devoted to school" is a sum of student reported hours spent in the classroom, in clinical activities, and on studying. "Google use frequency" and "UpToDate use frequency" were set based on student responses at the time of enrollment (before UpToDate subscriptions were given to them). They were set to 4 if student replied "almost every day", 3 if "a few times per week", 2 if "a few times per month", 1 if "a few times per year" and 0 if "Never" or "I don't know this resource." P-value bolded if < 0.05.

Table 2

Independent variable	Partial SS	P-value
UpToDate offered ^b	4197	< 10 ⁻⁴
Year of exam	6196	< 10 ⁻⁴

Table 2: Two-way ANOVA with average Doc4 grade as dependent variable. The table shows a two way ANOVA test with average Doc4 grade as dependent variable and year of exam and UpToDate provision as independent variables. n = 599 Doc4 students over 6 years. b UpToDate offered was set to 0 for 2012-2015 and 1 for 2016-2017.

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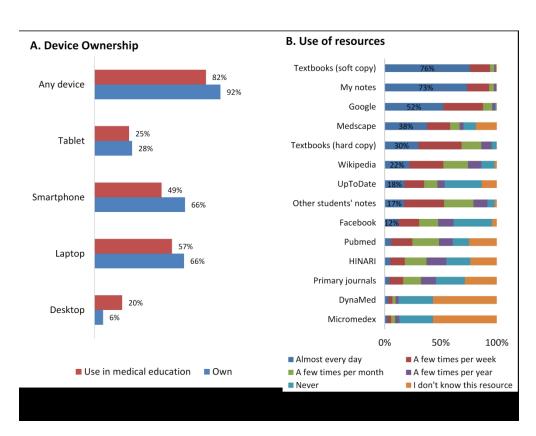


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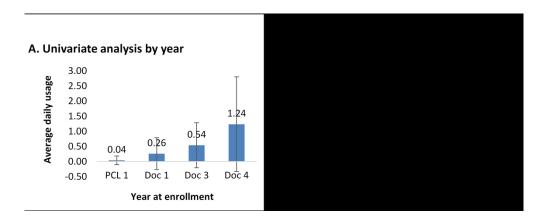


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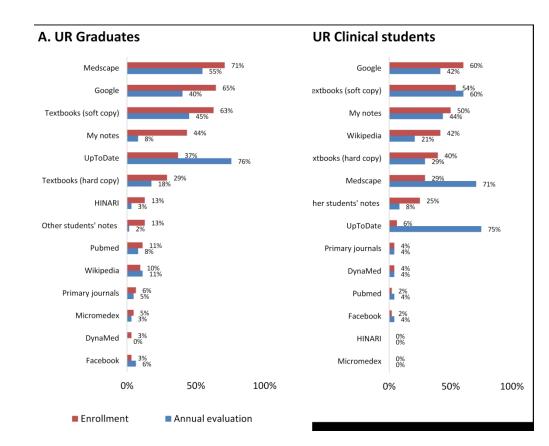
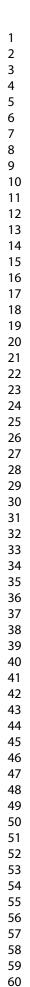


Figure 3: Changes in the usage of electronic resources. Figures show the percentage of respondents who reported using a particular resource "almost every day" at enrollment and one year later at the time of annual evaluation. Shading added to highlight responses for UpToDate. (A) shows responses of UR users who had graduated at the time of annual evaluation and were practicing physicians. (B) shows responses of UR clinical students (Doc1 at time of enrollment) who were still in school at the time of annual evaluation. n = 62 UR graduates, and 66 UR students.



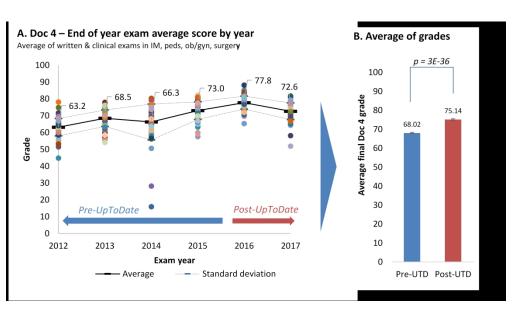


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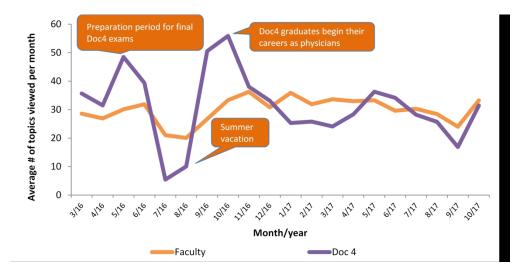


Figure 5: EBCR utilization over time by UR students and faculty. Lines show the average number of topics viewed per user per month by each user group. Only users who enrolled before 03/01/16 are included in this analysis (n = 185 faculty, 70 Doc4 students). Call-outs are added to describe events in the careers of Doc4 students

Better evidence: A prospective cohort study assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

Supplementary Appendix

Supplementary Table 1: Participant enrolment

Role	Academic year	Class at time of enrollment	Eligible	Completing enrollment	% completing enrollment
2015-2016 Students 2016-2017 Total - stude		PCL1 (1st year)	271	92	34%
	2015-2016	Doc1 (3rd year)	125	90	72%
	Doc4 (6th year)	86	84	98%	
	PCL1 (1st year)	102	24	24%	
	2016 2017	Doc1 (3rd year)	205	102	50%
	2010-2017	Doc3 (5th year)	89	74	83%
		Doc4 (6th year)	102	81	79%
	nts	980	547	56%	
Faculty	Continuous e	nrollment	1084	325	29%

Supplementary Table 1: Participant enrollment. Table shows the number of eligible students and faculty by role, academic year at time of enrollment, and class at time of enrollment. Table also shows the number of students and faculty who completed enrollment, and the percentage of eligible students who completed enrollment.

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STROBE Statement-Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstrac
		Study design indicated in the title
		(b) Provide in the abstract an informative and balanced summary of what was done
		and what was found. Page 2, abstract
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
		Page 3, introduction
Objectives	3	State specific objectives, including any prespecified hypotheses. Page 6, last
		paragraph of "Introduction"
Methods		
Study design	4	Present key elements of study design early in the pape.r Abstract
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
		exposure, follow-up, and data collection. Page 6, Methods ("Setting" and
		"Intervention")
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of
		participants. Describe methods of follow-up. Methods ("Intervention")
		(b) For matched studies, give matching criteria and number of exposed and
		unexposed. Not a matched study
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effec
		modifiers. Give diagnostic criteria, if applicable. Page 22, legend of Table 1
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement). Describe comparability of assessment methods if there
		more than one group. Page 22, legend of Table 1
Bias	9	Describe any efforts to address potential sources of bias, Page 8 "Data analysis"
Study size	10	Explain how the study size was arrived at. Study size was determined based on
		number of students enrolled at UR
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why Not applicable
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		Page 8 "Data analysis"
		(b) Describe any methods used to examine subgroups and interactions. Not
		applicable
		(c) Explain how missing data were addressed. Not applicable. No statistical
		inference was performed for students who did not complete the 1-year follow u
		survey
		(d) If applicable, explain how loss to follow-up was addressed. Not applicable
		(<u>e</u>) Describe any sensitivity analyses. Not applicable
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially
		eligible, examined for eligibility, confirmed eligible, included in the study,
		completing follow-up, and analysed. Supplementary Table 1
		(b) Give reasons for non-participation at each stage. Students were invited to
		participate and voluntarily opted in. Reasons for non-participation were not
		documented.

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Page 6, Methods ("Setting" and "Intervention")
		(b) Indicate number of participants with missing data for each variable of interest.
		Page 9, results
		(c) Summarise follow-up time (eg, average and total amount). Page 6, Methods
Outrouve late	1.5*	("Setting" and "Intervention")
Outcome data	15*	Report numbers of outcome events or summary measures over time. Page 10, "Results"
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and
		their precision (eg, 95% confidence interval). Make clear which confounders were
		adjusted for and why they were included. Page 22, Table 1 legend
		(b) Report category boundaries when continuous variables were categorized. Not
		applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period. Not applicable
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and
		sensitivity analyses Page 7, Methods ("Data analysis")
Discussion		
Key results	18	Summarise key results with reference to study objectives. Page 10, "Discussion"
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias. Page 11,
		"Limitations"
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,
		multiplicity of analyses, results from similar studies, and other relevant evidence.
		Page 10, "Discussion"
Generalisability	21	Discuss the generalisability (external validity) of the study results. Page 12, "Next
		steps"
Other information		4
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based. Page 13,
		"Funding"

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Better evidence: A Prospective Cohort Study Assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

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Better evidence: A Prospective Cohort Study Assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

Article

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Abstract

Objective: Evidence-based clinical resources (EBCRs) have the potential to improve diagnostic and therapeutic accuracy. The majority of U.S. teaching medical institutions have incorporated them into clinical training. Many EBCRs are subscription-based, and their cost is prohibitive for most clinicians and trainees in low- and middle-income countries. We sought to determine the utility of EBCRs in an East African medical school.

Setting: The University of Rwanda (UR), a medical school located in East Africa.

Participants: Medical students and faculty members at UR.

Interventions: We offered medical students and faculty at UR free access to UpToDate, a leading EBCR and conducted a cohort study to assess its uptake and usage. Students completed two surveys on their study habits and gave us permission to access their activity on UpToDate and their grades.

Results: Of the 980 medical students invited to enroll over two years, 547 did (56%). Of eligible final-year students, 88% enrolled. At baseline, 92% of students reported ownership of an internet-capable device, and the majority indicated using free online resources frequently for medical education. Enrolled final-year students viewed, on average, 1.24 topics per day and continued to use UpToDate frequently after graduation from medical school. Graduating class exam performance was better after introduction of UpToDate than in previous years.

Conclusions: Removal of the cost barrier was sufficient to generate high uptake of a leading EBCR by senior medical students and habituate them to continued usage after graduation.

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Strengths and limitations of this study

- This is the first reported longitudinal prospective cohort study of health professionals and trainees in Africa.
- This is the first study to link usage of online educational resources to performance in medical school examinations in Africa.
- Our ability to precisely track online usage of UpToDate eliminates recall bias that is likely to significantly impact findings of studies of educational interventions that are based on self-reporting.
- Given the observational nature of our study, we cannot make causal claims on the relationship between student use of UpToDate and their performance on medical school examinations.
- The relatively short follow-up period discussed in this paper limits our ability to understand the long term impact of offering UpToDate access to African health trainees.

Introduction

The velocity of growth of the clinical evidence base is staggering: In the last three years alone, over 16,000 unique clinical studies posted new results on ClinicalTrials.gov.¹ There is more information emerging every year than any one person could ever retain. In response, educators in the United States (U.S.) have called for a shift in the basic paradigm of medical education, deemphasizing the passive presentation of material and promoting problem-solving skills and the ability to find information and adapt it to the clinical situation at hand.² The Liaison Committee on Medical Education (LCME) mandates that self-directed learning be part of every accredited school's curriculum, and the American Board of Internal Medicine recently announced that maintenance of certification exams for internists and nephrologists will be open-book.^{3,4} The historical focus on memorization is giving way to an emphasis on knowing how to find information, synthesize it, and apply it clinically. Clinicians who have not developed these skills during medical school or clinical training are at a disadvantage, which, ultimately, means their patients are at a disadvantage.^{5, 6, 7}

The ability to access and synthesize clinical information effectively and efficiently is particularly crucial for clinicians in low- and middle-income countries (LMICs). The health workforce shortage and absence of specialists forces clinicians to care for more patients with a broader range of complaints than their counterparts in high-income countries. Rwanda, a country of 11 million people, had, until recently, a total of 15 anesthesiologists, 25 obstetricians, and zero neurologists.^{8,9} In addition, a study of 21 hospitals in LMICs documented substantial knowledge gaps among physicians.¹⁰ Constraints in medical education in these countries are likely responsible for both workforce and knowledge gaps. In 2011, the Sub-Saharan African Medical

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School Study group surveyed 146 of 168 medical schools in the region and found widespread shortages in qualified faculty and infrastructure.¹¹

To address the challenge of the rapidly expanding evidence base in medicine, several organizations in high-income countries have created evidence-based clinical resources (EBCRs) - regularly updated, expert-authored, online tools that synthesize the primary literature to guide clinical decision making. Over the years, UpToDate, which was founded at Harvard Medical School in 1992, has emerged as a leading EBCR in high-income countries, and several studies have documented its utility: Use of UpToDate has been associated with improved examination performance among internal medicine residents, as well as lower mortality at U.S. hospitals.5, 6 As of February 2018, 90% of teaching U.S. medical institutions and 100% of the top 20 U.S. medical schools (as ranked by U.S. News & World Report) subscribed to UpToDate.^{12,13,14} Despite the high demand for UpToDate in U.S. medical education, none of the 168 medical schools in sub-Saharan Africa subscribe to its services, partly because of the high subscription cost. An individual physician subscription to UpToDate in Rwanda costs \$299 per year; Rwanda spent \$52 per capita on healthcare in 2014.¹⁵ Additionally, cost of internet access can be prohibitively high in some LMICs; at the time of publication, mobile internet in Rwanda cost approximately \$0.05 per megabyte.¹⁶

Given their utility in high-income countries, access to EBCRs could help address some of the challenges faced by clinicians in LMICs. We believe that access to better evidence could improve the knowledge base of these clinicians, increase their perception of self-efficacy, and create a professional habit of seeking evidence at the point of care. This could be particularly beneficial for clinicians caring for a large number of complex patients without access to specialists. We have previously reported on a program which provides donated UpToDate

subscriptions to clinicians in LMICs, in which we found that most use UpToDate with high frequency and many report changing their clinical decision making as a result of having access to UpToDate.17

While EBCRs have traditionally been developed for physicians in practice, there are reasons to believe that their introduction to medical students would be beneficial. First, medical school is de *facto* the first locus of professional habit formation, and often their last formal one, as many clinicians in LMICs do not receive post-graduate education. Additionally, providing access to EBCRs to medical students in LMICs is a matter of equity: students who have worked hard to care for their community in LMICs should have the same opportunity to learn and provide quality care as their counterparts in U.S. medical schools. In this article, we hypothesized that removing the cost barrier to accessing EBCR will lead to high student uptake and possibly lead to an improvement in educational outcomes. N.C.

Methods

Setting

The University of Rwanda (UR) was the only medical degree-granting school in Rwanda at the time this study launched and is a public university. 76% of students at UR are recipients of bursaries from the Government of Rwanda.¹⁸ Medical students enter UR after successful completion of high school and, during the study period, completed a 6-year medical education curriculum consisting of two years of pre-clinical education followed by 4 years of clinical education in the wards.

Intervention

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In the fall of 2014, the authors formed an agreement with Wolters Kluwer, the parent company of UpToDate, to facilitate the donations of UpToDate subscriptions to medical students in sub-Saharan Africa. With appropriate IRB approval, medical students and faculty at the University of Rwanda were invited by email to enroll in our study. "Faculty member" was defined as anyone who teaches undergraduate medical students, which meant that residents, as well as staff physicians, were considered faculty. Undergraduate medical students, who unlike U.S. medical students are admitted to medical school after high school at age 18, were invited to enroll as well. Students were invited in cohorts that spanned the different years of medical school (see Supplementary Table 1). Enrollment was voluntary and not mandated by faculty or the curriculum. Each participant received a free 5-year individual subscription to UpToDate, which allowed them to access the website from any computer or mobile device. The authors undertook no recruitment or training efforts. Data reported in this paper was generated in 2015–2017. All study subjects will be eligible for getting free UpToDate access after the 5 years of the study through a donation program that UpToDate has created for all medical doctors practicing in resource limited settings. This donation program is available to any medical provider in a low and middle income country and gives free, unlimited access to UpToDate without a time limit. Donations have to be renewed annually. Hence, all study subjects will be able to get free UpToDate access after this study concludes, for as long as they practice medicine in a resource limited setting. The donation program details can be found here: https://www.globalhealthdelivery.org/uptodate/apply.

Evaluation

Students were asked to complete an online baseline survey to document their study habits before provision of UpToDate and an Annual Evaluation survey. We chose questions around students'

baseline utilization of the Internet in medical education, as others have identified access to devices and the Internet as potential barriers to EBCR utilization.¹⁹ Students' responses over time were linked using their name and email. All participant activity on the UpToDate website and mobile application was tracked remotely and linked to survey responses. An anonymized dataset of all student grades for the graduating classes of 2012-2017 was obtained to assess the impact of UpToDate on class examination performance. Lastly, to understand student usage of UpToDate over time, we plotted the average number of topics viewed per month by active users. To characterize a stable cohort of users over time, we plotted the average number of topics viewed by students in their final year who enrolled before March 1st 2016.

Data analysis

To understand EBCR usage patterns by students and faculty, we calculated for each user the number of topics viewed. Any action resulting in the opening of a new UpToDate card (with a distinct title) was counted as a new topic. Viewing of the same topic in the same session was counted only once. A session was defined as the time period using UpToDate, initiated by a unique log-on of a user to the UpToDate website, mobile site, or mobile application and terminated when the user logged off, closed the application, or remained inactive for more than three hours. To calculate the average daily usage (ADU), the number of topics viewed was divided by the number of days that the user had an active account. The number of days with an active account was defined as the interval between the users' first-ever log-on and the end of the study period (10/31/2017). To identify predictors of high usage frequency, we conducted a multivariable linear regression after applying the natural log transform to ADU values to approximate normality.

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To understand the impact of UpToDate on the overall exam performance of the graduating class at UR, we calculated the average grade of each graduating student for 2012-2017 by averaging their performance in all of their graduation exams. These were written and clinical exams in the following subjects: internal medicine, surgery, obstetrics & gynecology, and pediatrics. To assess the impact of UpToDate, we performed two tests: First, we performed a two-sided heteroscedastic t-test between grades assigned before UpToDate provision (2012-2015) and grades assigned after (2016-2017). To control for variability due to the year of exam administration, we performed a two-way Analysis of Variance (ANOVA) test with year of exam and UpToDate provision as the independent variables and average exam grade as the dependent variable.

Data analysis was performed on Stata SE 14 and Microsoft Excel.

Patient and public involvement

Patients were not the subject of this study. Given the setting of the study at a medical school, it was not feasible to include a patient partner. A medical student at UR (BN) is a co-author of this study and brought the student perspective into the interpretation of the data.

Results

Of the 980 students and 1,084 faculty invited to enroll into the study during the 2015-2017 study period, 547 (56%) students and 325 (29%) faculty did. The highest enrollment rate (87%) was observed among students in their final (sixth) year of medical school, who are called "Doctorate 4" or Doc4 students at UR (Supplementary Table 1). In our baseline survey, 92% of student respondents overall and 96% of Doc4 students reported ownership of at least one internet-capable device (Figure 1a). Free electronic resources—primarily Medscape, Google, and

Wikipedia—were used frequently for the purposes of medical education (Figure 1b). A small percentage reported frequent usage of UpToDate at baseline.

All users who completed the enrollment survey had an individual UpToDate account created for them and received an email with instructions on how to set up their UpToDate password. Of those who activated their UpToDate account, 76% of faculty and 64% of students viewed, on average, at least one UpToDate topic per week; 13% of faculty and 23% of students viewed, on average, one topic or more per day. In a multivariate linear regression looking at variables associated with UpToDate usage frequency, student year at enrollment was the only significantly associated variable (Table 1). Figure 2 shows average UpToDate usage by year of student at enrollment.

One year after enrollment, 52% of students completed the annual evaluation; 74% of Doc4 students did so. The low response rates could be attributed to lack of positive incentives to complete the survey or to students not checking their email to see that the evaluation survey was due. Both graduates, who had enrolled into the study as Doc4 students, and continuing students reported increased usage of UpToDate. Continuing students also reported decreased use of Google and Wikipedia (Figure 3).

To assess the effect of providing UpToDate to students on their educational performance, we plotted the average grades of each graduating class from 2012 to 2017 (599 students in total) and compared the pre-UpToDate period (2012-2015; average grade 68) to the post-UpToDate period (2016-2017; average grade 75) (Figure 4). Both a simple t-test as well as a two-way ANOVA showed a statistically significant difference (Table 2). In 2017, a student who scored 68 would have ranked at the 16th percentile of the class, while a student scoring 75 would have ranked at the 66th percentile.

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We used remote tracking to assess Doc4 student usage over time and found that it spiked in May 2016, as students prepared for their graduation exams in June. Usage fell significantly during summer vacation, but rose again in September and October, as the new graduates began their careers as physicians, either in residency or in independent practice. A similar pattern of usage over time was seen among faculty (Figure 5).

Discussion

Our findings represent the first prospective cohort study of medical students in Africa and suggest that access to devices and the internet might not be a significant barrier for African medical students wishing to access online resources. Our findings align with observations from a 2016 study in Zimbabwe and contrast two earlier studies in Nigeria published in 2004 and 2008 that suggest lack of access to internet.^{20,21,22} The differences might be related to the passage of time or resource availability differences between Rwanda and Nigeria. The findings suggest that, in Rwanda, our focus should not be on securing devices but on securing access to the latest online tools and evidence.

Our study also shows that students, especially final-year students, used a leading EBCR frequently when the cost barrier was removed. This was achieved with no provision of internetcapable devices, no subsidizing of mobile internet data, no dedicated training activities on EBCR use or evidence searching, and no curricular integration of EBCRs. Overall, our findings suggest that removing the cost barrier to access of EBCRs can generate uptake among a subset of medical students in East Africa. The low uptake of UpToDate by pre-clinical UR students could be related to the basic science focus of their curriculum, which makes UpToDate's clinical content less relevant.

The introduction of an EBCR during the last year of medical school may lead to habit formation. Among students receiving an EBCR subscription in their final year, usage was sustained for the one and a half year period monitored after graduation. Additionally, self-reported usage of nonvalidated sources such as Google and Wikipedia fell among students within a year of UpToDate provision. In 2013, Gawande argued that habit change and formation in healthcare is a complex process that can often take decades.²³ He also argued that some habits form quickly and that those might be the ones that make a physician's workflow faster and more efficient. Our study suggests that UpToDate may fall into this category of tools and habits that facilitate faster, more efficient work.

The temporal association of free access to UpToDate with an improvement of the overall examination performance of the graduating class may be causal or due to another explanation, as discussed below. It is consistent, however, with previous reports of associations between UpToDate usage and performance in exams by residents in the U.S. and Japan, and practicing physicians in the U.S.

Limitations

Our study is subject to selection bias given its observational nature. It is possible that students with regular access to email were more likely to respond to our email-based invitation, thus biasing the response set, especially with respect to use of electronic resources and internet access. The high enrollment rate among Doc4 students mitigates this effect to some extent. The use of a historical control to assess the impact of UpToDate's introduction on student grades also has several limitations. First, no causal arguments can be made, given the fact that different exams were used each year and different students took them. While UpToDate may have helped students prepare for their exams more efficiently and increase their knowledge base, it is also

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possible that the exams in 2016 and 2017 were easier than those of years past or that the students were independently academically superior to the previous classes. The cause of the overall increase in student scores before UpToDate was introduced is unclear and could be related to changes in educational methods or examinations, although we do not have evidence for either of those. In addition, the reason for the decline in of students' scores from 2016 to 2017 is unknown, and could be statistically random or indicative of a trend. Further follow up will be required to answer this question.

Second, it is possible that test answers may not be contained/addressed in UpToDate, although the UR faculty among the authors of this paper do not believe that to be the case.

Next steps

Due to its longitudinal nature, this study has the potential to offer additional insights on the changes in learning behaviors of African health trainees over time. Qualitative research on this student cohort could help elucidate the drivers of different study behaviors, and the perceived impact of resources such as UpToDate on clinician's knowledge base and self-efficacy. Future research might explore other EBCRs and features that impact uptake and utility. We focused on UpToDate because of the body of literature that supports its value in high-income countries. However, we hypothesize that a suite of EBCRs and learning tools, possibly in multiple languages, might be helpful for trainees in LMICs. Given the relatively easy scalability of software-based tools, we believe that we can continue to decrease the barriers for trainees in LMICs to access the best available evidence at the frontline of care delivery. Our vision is that this work can prepare and inform how the next generation of clinicians in LMICs practices evidence-based medicine. Although our research focused on LMICs, disparities in access to high-quality EBCRs might exist within U.S. medical education as well, which can also be an

area of future research and programming. As medicine continues to evolve rapidly and medical education shifts its focus from memorization to critical processing of information, we must ensure that all learners have equitable access to the best information available.

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Ethical Approval: The research described here was approved by the Harvard Medical School Longwood Medical Area Institutional Review Board and the College of Medicine and Health Sciences University of Rwanda Institutional Review Board.

Data sharing: No data are available.

Contributorship: YV, JR, KW, RK, FM, RCM, TW, RW designed the study and co-wrote its protocol. JDK, AE, BN implemented the study at the University of Rwanda. YV analyzed the data and drafted this manuscript. All authors edited the manuscript. RW oversaw the entire design, implementation, and analysis of the study.

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Figure legends:

Figure 1: Baseline survey of Rwandan medical students. (A) shows the percentage of students at UR reporting that they own a particular internet-capable device or use it in medical education. "Any device" refers to any of the following: tablet, smartphone, laptop, desktop. (B) shows the percentage of students indicating that they use a specific resource to study for coursework or prepare for examinations. n = 547 UR students and 157 MUHAS students.

Figure 2: Predictor of UpToDate usage. (A) shows the average daily usage (ADU) during the study period by UR students broken down by class year at enrollment. Students who did not log onto their accounts after enrolling into the study were assigned a daily topic viewing frequency of zero. n = 547 UR students.

Figure 3: Changes in the usage of electronic resources. Figures show the percentage of respondents who reported using a particular resource "almost every day" at enrollment and one year later at the time of annual evaluation. Shading added to highlight responses for UpToDate. (A) shows responses of UR users who had graduated at the time of annual evaluation and were practicing physicians. (B) shows responses of UR clinical students (Doc1 at time of enrollment) who were still in school at the time of annual evaluation. n = 62 UR graduates, and 66 UR students.

Figure 4: Impact of EBCR provision on class exam performance at UR. (A) shows the average grades of graduating Doc4 students over time. Each dot represents one student and

shows the average of their grades in the following eight exams: written & clinical exams in internal medicine, pediatrics, obstetrics & gynecology, and surgery. (B) shows the average grades of students pre-UpToDate (2012-2015) and post-UpToDate (2016-2017). The p-value represents a two-sided heteroscedastic t-test. The error bars represent standard error of the mean.

Figure 5: EBCR utilization over time by UR students and faculty. Lines show the average number of topics viewed per user per month by each user group. Only users who enrolled before 03/01/16 are included in this analysis (n = 185 faculty, 70 Doc4 students). Call-outs are added to describe events in the careers of Doc4 students

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Table 1

Coefficients	P-value
-0.04	0.21
0.12	< 0.001
0.07	0.29
-0.03	0.49
0.00	0.91
-0.02	0.30
0.00	0.70
	-0.04 0.12 0.07 -0.03 0.00 -0.02

Table 1: Multivariate linear regression with UpToDate usage as the dependent variable.

The table shows a multivariable linear regression with average daily topic viewing frequency (natural logarithm transform) as the dependent variable. The dependent variable was calculated as "number of UpToDate topics viewed" / "days with an active subscription" for each user. It was set to zero for users who did not log on to UpToDate. The dependent variable was transformed with the equation Y' = ln(Y+1) to approximate normality. The independent variables were set as follows: "Cohort" was set to 1 for students enrolling in 2015-2016 and 2 for student enrolling in 2016-2017. "Year at enrollment": PCL1 was set to 1, PLC2 was set to 2, Doc1 was set to 3, Doc3 was set to 5 and Doc4 was set to 6. "Own any device" and "Own smartphone" were set to 0 if the student did not report ownership and to 1 if they did. "Hours devoted to school" is a sum of student reported hours spent in the classroom, in clinical activities, and on studying. "Google use frequency" and "UpToDate use frequency" were set based on student responses at the time of enrollment (before UpToDate subscriptions were given to them). They were set to 4 if student replied "almost every day", 3 if "a few times per week", 2 if "a few times per month", 1 if "a few times per year" and 0 if "Never" or "I don't know this resource." P-value bolded if < 0.05.

Table 2

Independent variable	Partial SS	P-value
UpToDate offered ^b	4197	< 10 ⁻⁴
Year of exam	6196	< 10 ⁻⁴

Table 2: Two-way ANOVA with average Doc4 grade as dependent variable. The table shows a two way ANOVA test with average Doc4 grade as dependent variable and year of exam and UpToDate provision as independent variables. n = 599 Doc4 students over 6 years. b UpToDate offered was set to 0 for 2012-2015 and 1 for 2016-2017.

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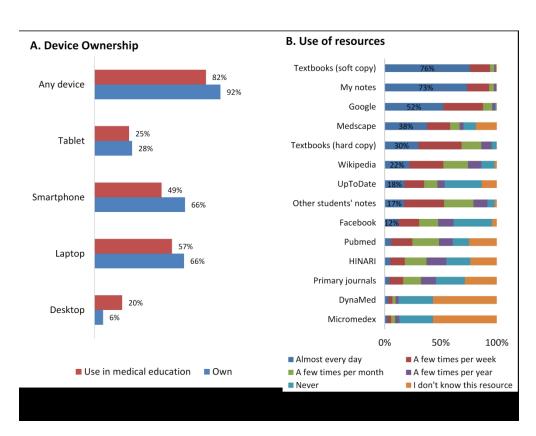


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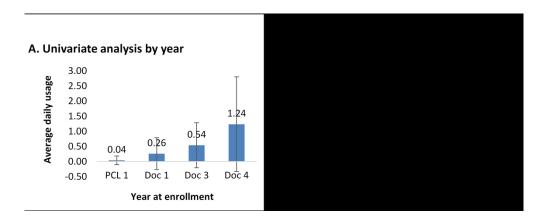


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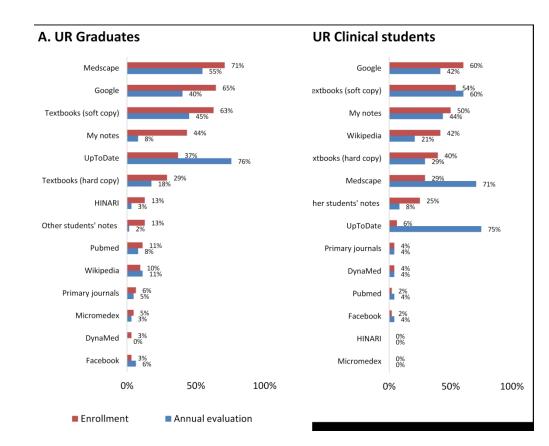
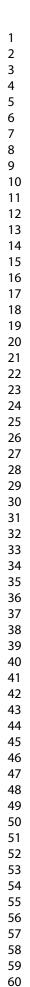


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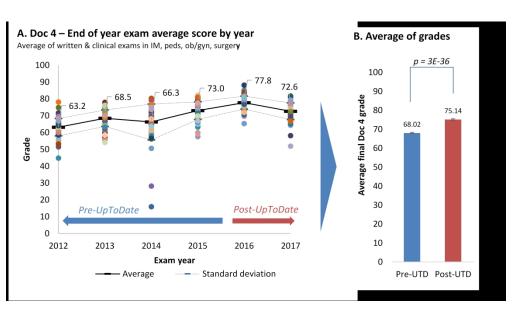


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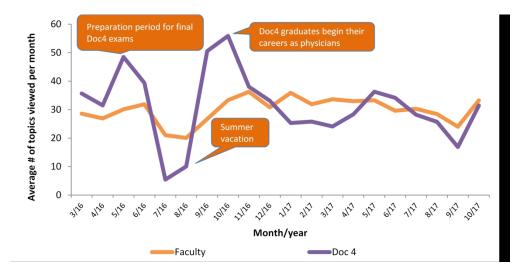


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Better evidence: A prospective cohort study assessing the utility of an Evidence-Based Clinical Resource at the University of Rwanda

Supplementary Appendix

Supplementary Table 1: Participant enrolment

Role	Academic year	Class at time of enrollment	Eligible	Completing enrollment	% completing enrollment
Students	2015-2016	PCL1 (1st year)	271	92	34%
		Doc1 (3rd year)	125	90	72%
		Doc4 (6th year)	86	84	98%
	2016-2017	PCL1 (1st year)	102	24	24%
		Doc1 (3rd year)	205	102	50%
		Doc3 (5th year)	89	74	83%
		Doc4 (6th year)	102	81	79%
	Total - students		980	547	56%
Faculty	Continuous e	nrollment	1084	325	29%

Supplementary Table 1: Participant enrollment. Table shows the number of eligible students and faculty by role, academic year at time of enrollment, and class at time of enrollment. Table also shows the number of students and faculty who completed enrollment, and the percentage of eligible students who completed enrollment.

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STROBE Statement-Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstrac
		Study design indicated in the title
		(b) Provide in the abstract an informative and balanced summary of what was done
		and what was found. Page 2, abstract
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
		Page 3, introduction
Objectives	3	State specific objectives, including any prespecified hypotheses. Page 6, last
		paragraph of "Introduction"
Methods		
Study design	4	Present key elements of study design early in the pape.r Abstract
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
		exposure, follow-up, and data collection. Page 6, Methods ("Setting" and
		"Intervention")
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of
		participants. Describe methods of follow-up. Methods ("Intervention")
		(b) For matched studies, give matching criteria and number of exposed and
		unexposed. Not a matched study
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effec
		modifiers. Give diagnostic criteria, if applicable. Page 22, legend of Table 1
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement). Describe comparability of assessment methods if there
		more than one group. Page 22, legend of Table 1
Bias	9	Describe any efforts to address potential sources of bias, Page 8 "Data analysis"
Study size	10	Explain how the study size was arrived at. Study size was determined based on
		number of students enrolled at UR
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why Not applicable
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		Page 8 "Data analysis"
		(b) Describe any methods used to examine subgroups and interactions. Not
		applicable
		(c) Explain how missing data were addressed. Not applicable. No statistical
		inference was performed for students who did not complete the 1-year follow u
		survey
		(d) If applicable, explain how loss to follow-up was addressed. Not applicable
		(<u>e</u>) Describe any sensitivity analyses. Not applicable
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially
		eligible, examined for eligibility, confirmed eligible, included in the study,
		completing follow-up, and analysed. Supplementary Table 1
		(b) Give reasons for non-participation at each stage. Students were invited to
		participate and voluntarily opted in. Reasons for non-participation were not
		documented.

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Page 6, Methods ("Setting" and "Intervention")
		(b) Indicate number of participants with missing data for each variable of interest.
		Page 9, results
		(c) Summarise follow-up time (eg, average and total amount). Page 6, Methods
Outrouve late	1.5*	("Setting" and "Intervention")
Outcome data	15*	Report numbers of outcome events or summary measures over time. Page 10, "Results"
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and
		their precision (eg, 95% confidence interval). Make clear which confounders were
		adjusted for and why they were included. Page 22, Table 1 legend
		(b) Report category boundaries when continuous variables were categorized. Not
		applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period. Not applicable
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and
		sensitivity analyses Page 7, Methods ("Data analysis")
Discussion		
Key results	18	Summarise key results with reference to study objectives. Page 10, "Discussion"
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias. Page 11,
		"Limitations"
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,
		multiplicity of analyses, results from similar studies, and other relevant evidence.
		Page 10, "Discussion"
Generalisability	21	Discuss the generalisability (external validity) of the study results. Page 12, "Next
		steps"
Other information		4
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based. Page 13,
		"Funding"

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.