Improving Hydroxychloroquine Dosing and Toxicity Screening at a Tertiary Care Ambulatory Centre: A Quality Improvement Initiative

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ABSTRACT

Objectives: Hydroxychloroquine (HCQ) is a commonly used weight-based medication with a risk of retinal toxicity when prescribed at doses above 5 mg/kg/day. The objectives of our study were: (1) To characterize the frequency of inappropriate HCQ dosing and retinopathy screening and (2) to improve guideline-based management by implementing quality improvement (QI) strategies.

Methods: A retrospective chart review was performed to obtain baseline analysis of HCQ dosing, weight documentation, and retinal toxicity screening to characterize current practices. The primary aim was to increase the percentage of patients appropriately dosed from 30% to 90% over a ten-month period. The secondary aim was to increase the percentage of documented retinal screening from 59% to 90%. The process measure was the number of patients with a documented weight in the chart. The balancing measure was the physician's perceived increase in time spent with each patient due to implemented interventions.

QI methodology was used to implement sequential change ideas: (1) HCQ weight-based dosing charts to facilitate prescription regimens, (2) addition of scales to patient rooms to facilitate weight documentation, and (3) electronic medical record 'force function' involving weight documentation and auto-dosing prescription.

Results: The percentage of patients being weighed increased from 40% to 92% after ten months. Appropriate HCQ dosing improved from 30% to 89%. Retinal screening documentation improved by 33%.

Conclusion: Dosing charts in clinic rooms, addition of weight scales, and EMR force function auto-dosing prescriptions significantly improved appropriate HCQ dosing practices. These interventions are generalizable and can promote safe and guideline-based care.

INTRODUCTION:

Hydroxychloroquine (HCQ) is used widely to treat inflammatory arthritis and connective tissue disease. In rare instances, HCQ can lead to vision-threatening retinopathy. A 2014 case-control study showed that retinal toxicity is not as rare as previously thought among long-term users of the drug, with an overall prevalence of 7.5% in patients taking HCQ greater than 5 years(1). More recent publications have identified an increasing number of patients with advanced HCQ retinopathy(2, 3). Therefore, it is important for rheumatologists, dermatologists, ophthalmologists, and primary care physicians to understand the prevalence and risk factors associated with this adverse event. In response to this, there have been several detailed publications and guidelines from the American Association of Ophthalmology and the British Society of Rheumatology focusing on the recommendations for appropriate HCQ dosing and toxicity monitoring(4, 5).

The risk of toxicity is greatly dependent on daily dose, which is calculated using body weight. Traditional dosing was based on a maximum of HCQ 6.5mg/kg of ideal body weight (IBW), rather than actual body weight (ABW), as this was considered safe for most adults to reduce the risk of retinal toxicity(6). However, more recent evidence suggests that dosing based on ABW is more predictive of toxicity and is more accurate over a broad range of body sizes(1, 4). Melles et al. suggested 5 mg/kg of ABW/day corresponded approximately to a dose of 6.5mg/kg of IBW/day given the average body habitus in their North American study population(1). Therefore, this change in prescribing recommendation for HCQ may be more practical in rheumatology clinics, as it has been shown that calculating doses of HCQ based on IBW is not undertaken on the majority of patients(2). Since HCQ retinopathy is not reversible and cellular damage may progress even after the drugs are stopped, screening guidelines were also updated to provide clarity on the diagnostic tests required from ophthalmologists and suggested more frequent monitoring schedules(4, 5).

Despite new guidelines, there remains a lack of adherence to safe and effective dosing standards. Several North American and European studies have reported that between 37-56% of patients are still receiving doses in excess of the recommended maximum(7-9). Gianfrancesco et al. have demonstrated that the percentage of individuals receiving doses in excess of guideline recommendations has decreased over time, but 30% of patients still receive doses above 5mg/kg. Risk factors for receiving higher doses included female sex, low body weight (<68kg), African American race, mild liver disease, and public insurance payer (10). Retinopathy screening guidelines are only being met in 82-87% of patients on average(11, 12), with one center reporting screening rates as low as 49%(13). Prior literature has identified barriers to uptake of new clinical guidelines by clinicians, including lack of awareness, lack of agreement with the evidence, external barriers, and clinical inertia (10, 14, 15) . It is clear that additional steps are needed to improve guideline adherence and promote evidence-based care.

Therefore, the objective of this study was to characterize the frequency of appropriate weight-based HCQ dosing and retinal toxicity screening at an academic ambulatory care hospital in Toronto, Canada and to implement quality improvement (QI) strategies aimed at improving these outcomes.

METHODS:

The Model for Improvement framework developed by the Institute for Healthcare Improvement was used for project development. There are 3 fundamental components: 1) developing a specific and timely aim; 2) choosing a family of outcome, process, and balancing measures; and 3) selecting interventions that focus on the underlying causes of the targeted quality gap. The interventions are then regularly refined by using Plan-Do-Study-Act (PDSA) cycles to develop and test change ideas (16).

Ethics approval for this study was obtained from the Women's College Hospital Ethics Assessment Process for Quality Improvement Projects (REB # 2017-0137-E).

Baseline Analysis

A retrospective chart review for baseline analysis was performed for a three-month period, in the year prior to the study. Variables assessed were HCQ prescription dosing, patient weight documentation, retinal toxicity screening documentation, and risk factor assessment. Charts from all four general rheumatologists at this ambulatory hospital were reviewed from consecutive patient encounters. Charts were selected for baseline analysis if a patient was being initiated on or continuing HCQ during the clinical visit, regardless of diagnosis. A total of 70 charts, an average of 18 charts per rheumatologist, were reviewed.

The percentage of patients with appropriate HCQ dosing was determined at weekly intervals and was graphed on statistical process control (SPC) charts. Appropriate dosing was strictly defined as HCQ ≤ 5mg/kg of actual body weight as documented in the chart. If a patient's weight was not documented in the electronic medical record (EMR), they were classified as 'inappropriately dosed.' The percentage of patients with a documented weight in the EMR and appropriate yearly retinal screening were also determined at weekly intervals and graphed on SPC charts. Demographic data, rheumatological diagnosis, and other high-risk features for HCQ toxicity were also collected.

Given the baseline results, the primary aim was to increase the percentage of patients being appropriately dosed from 30% to 90% over a ten-month period. The secondary aim was to increase the percentage of patients with documented retinal screening from 59% to 90%. A target

of 90% was chosen to keep the outcome measures realistic, accounting for some error in actual practice; recognizing that rheumatologists may choose to intentionally go above the recommended guidelines in some cases; and recognizing that patients may not get screened regardless of the efforts of their rheumatologist.

Root Cause Analysis

An Ishikawa diagram was created to understand root causes for inappropriate HCQ dosing and toxicity screening after speaking to relevant stakeholders including ten patients, twelve rheumatologists, three ophthalmologists/optometrists, and five family doctors (Figure 1). Stakeholders were interviewed after the baseline analysis and prior to the first intervention. The causes identified for inappropriate dosing and screening were: 1) HCQ available only in 200mg tablets and difficulty quickly determining intermediate prescription doses, 2) patient and physician lack of awareness of dosing and screening guidelines, 3) weights not documented in patient charts to allow for appropriate dosing, 4) lack of time in a busy clinic to obtain weights and calculate dose, and 5) lack of government coverage for eye exams for patients <65 years old without a ministry form.

PDSA Cycles

Iterative PDSA cycles were used to refine 3 change ideas to help address the causes of inappropriate dosing and toxicity screening. Each of the change ideas was derived based on the most commonly identified barriers and feasibility of implementation within our clinics. The same four rheumatologists were involved with all three interventions and the study did not impact any other clinicians.

PDSA 1: HCQ Dosing Charts (Week 0)

To address the difficulty in quickly determining intermediate prescription doses, a user-friendly HCQ dosing chart was placed in each clinic room (Figure 2). The dosing chart helped simplify the

process by providing the clinician with alternative dosing regimens between 200mg to 400mg based on weight.

PDSA 2: Weight Scales (Week 10)

To address the lack of weight documentation, five weight scales were added to clinic rooms to help facilitate the weighing of patients during clinical encounters.

PDSA 3: EMR-Based Force Function (Week 33)

To facilitate weight-based prescriptions, an EMR-based force function was developed to require a documentation of weight within the last 12 months in all patients being prescribed HCQ, regardless of whether it was a new or repeat prescription (Figure 3a). The EMR was also modified to provide an auto-dosed prescription for HCQ based on the documented weight (Figure 3b).

Family of measures

The primary outcome measure was the percentage of patients prescribed an appropriate daily dose of HCQ (based on 5 mg/kg of actual body weight). The secondary outcome measure was the percentage of patients with documented annual retinal screening.

The process measure was the percentage of patients with a documented weight in the EMR in the last 12 months.

The balancing measure was physician satisfaction and perceived increase in time spent with each patient due to the implemented interventions, as determined by physician survey. Physician satisfaction was assessed by means of a 5-point Likert scale asking physicians to rate each intervention for its helpfulness in appropriately prescribing HCQ and ease of integration into their

usual clinic routine. Most satisfied was 5 points and least satisfied was 0 points. They were also asked to estimate the approximate increase in time spent with each patient due to the interventions.

Data Analysis

Each week, 10 consecutive charts of patients prescribed HCQ were reviewed to determine weight documentation, appropriate dosing, and retinal screening. Audits were performed by one investigator to ensure consistency. Two months following the implementation of the forced-function intervention, an anonymous paper survey was provided to all rheumatologists to assess satisfaction and collect information related to the balancing measure. The survey process was conducted using a Likert Scale and included one reminder.

Outcomes and process measures were plotted weekly on p-type SPC charts to analyze data over time, provide feedback, and determine statistically significant ("special cause") variation.

RESULTS

Baseline analysis

During the baseline period, there were 70 unique patient charts assessed. Appropriate HCQ dosing was found in 30% of patients, while weight was documented in 40% of patients. Retinal screening was documented for 59% of patients. SPC charts did not show any special cause variation in these measures prior to implementation of the QI interventions (Figures 4-6).

Outcome measures

There were 92 patient charts reviewed during PDSA-1, 230 charts reviewed during PDSA-2, and 117 charts reviewed during PDSA-3. The percentage of patients being appropriately dosed on HCQ

increased from 30% to 89% over the 10-month intervention period (Figure 4). There is evidence of special cause variation after the first and third intervention, as witnessed by a shift after weeks 0 and 33, respectively. This suggests that change was not due to chance alone.

The percentage of patients with documentation of retinal screening increased from 59% to 91% over the 10-month period (Figure 5). There is evidence of special cause variation after the first intervention due to a shift.

Process measures

The percentage of patients with a documented weight over the last 12 months increased from 40% to 92% (Figure 6). There is evidence of special cause variation after both the first and third interventions.

Balancing measures

All rheumatologists rated their satisfaction and integration of the HCQ dosing charts as ≥ 4. The average increased time spent was reported as one minute per patient. The weighing scales were viewed as less helpful with two rheumatologists rating it 3 and two as 4. It added on average two minutes per patient. The forced function EMR intervention was viewed favourably by all rheumatologists with a score ≥ 4 for satisfaction and integration. It added 1.5 minutes on average per patient.

DISCUSSION

Guideline-based management is important to ensure safe and effective care. This study focused on improving appropriate HCQ dosing and retinal screening, given its identification as a significant issue in the field of rheumatology and ophthalmology over the last several years. A multifaceted QI

intervention was noted to be effective and feasible, increasing appropriate HCQ dosing and toxicity screening to 90% at our institution over ten months.

Based on our analysis, the introduction of the HCQ dosing charts in each clinic room significantly improved appropriate HCQ dosing by 38%. The root cause analysis suggested that the time, difficulty, and effort it took to calculate intermediate-dosing regimens was a major barrier to appropriately dosing HCQ. Therefore, the dosing chart successfully acted as a low-effort, high-yield tool assisting the rheumatologist by providing prescription regimens based on the patient's weight.

The EMR force function was also effective at significantly improving appropriate HCQ dosing. Based on the Hierarchy of Intervention Effectiveness, force functions that mandate users to complete a task in a certain way have the highest likelihood of creating desired change compared to rules, checklists, or education(17). Since there was no option to bypass this EMR feature, it ensured that there was a documented weight prior to prescribing HCQ. Having pre-set dosing regimens in the EMR, based on the HCQ dosing chart, also assisted clinicians in choosing the correct dose. However, despite the force function, 100% compliance with dosing guidelines was not achieved. This may be because the rheumatologist chose to prescribe a higher dose based on the diagnosis or clinical presentation, or that they prescribed HCQ manually without using the EMR, thereby bypassing our force function.

Although the addition of weight scales in clinic rooms did not result in any significant improvement, it may have aided in uptake by increasing stakeholder buy-in, as witnessed by sustained improvement in our SPC charts. Our second aim of improving retinal screening also had significant improvements after the first (HCQ dosing charts) and third (EMR forced function) intervention. Although there was no directed intervention targeting improving retinal screening

documentation, it is likely that implementation of all change ideas served as a reminder during clinical encounters, helping to improve this outcome. Reassuringly, physician satisfaction was high following the implementation of these interventions and there were no obvious unintended consequences to the interventions.

Our results align with previous studies that have detailed the inappropriate dosing and toxicity screening patterns for HCQ(7-13). However, to our knowledge, only one previous study has implemented a QI strategy to improve these practices. Jessee et al. demonstrated that grand round lectures, modifications of EMR templates, and email reminders improved compliance with HCQ dosing from 63% to 72%. However, compliance remained poor at only 44% in patients weighing <80kg(7). Our current study differed by using QI methodology, including PDSA cycles and weekly data analysis via SPC charts, as well as high-effectiveness interventions such as force functions rather than education. Unlike the Jessee et al study, we also examined balancing measures to ensure that the interventions were not disturbing the clinical flow.

There are a number of strengths to note in this study. Our interventions, especially the HCQ dosing chart, are simple and can be easily integrated into other rheumatology clinics to help achieve similar results. The use of SPC charts allowed data to be analyzed in real time so that further interventions could be designed and implemented. Using a survey to understand physician satisfaction helped mitigate any barriers to successful implementation of the interventions.

As with any QI study, limitations include potential confounding variables. For example, rheumatologists may have made efforts to improve their practices after learning about our study, independent of the actual interventions. However, in our analysis, the use of process measures and statistical process charts helped to minimize the impact of confounding variables. For example, we

can correlate the timing of interventions and improvement in process measures with our outcomes. In addition, we did not collect data about potential flares from HCQ dose reduction, so we cannot comment on potential flare risk by following the guidelines.

Stakeholder engagement through close collaboration with rheumatologists, trainees, administrative personnel, and EMR developers was essential in the successful implementation of the project. Determining balancing measures and mitigating issues early was of the utmost importance. We expect our results to be sustainable over time; given the simplicity of use and the fact that weight documentation is now required to prescribe HCQ, the interventions have become regular practice at our institution. The generalizability of this study allows for all interventions to be adapted for use at other clinics and hospitals, further promoting guideline-based and safe care.

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Figure Legend:

Figure 1 - Ishikawa diagram showing root causes for inappropriate hydroxychloroquine dosing and toxicity screening

Figure 2 - Hydroxychloroquine dosing chart used in intervention 1

Figure 3 – A) Forced function weight documentation in the EMR whenever hydroxychloroquine was prescribed and B) Auto-dosing prescriptions in the EMR based on patient weight.

Figure 4 - Percentage of patients with appropriate dosing of hydroxychloroquine at baseline and over ten months of the QI intervention.

Figure 5 - Percentage of patients with appropriate retinal screening documentation at baseline and over ten months of the QI intervention

Figure 6 - Percentage of patients with recorded weights in the EMR at baseline and over ten months of the QI intervention

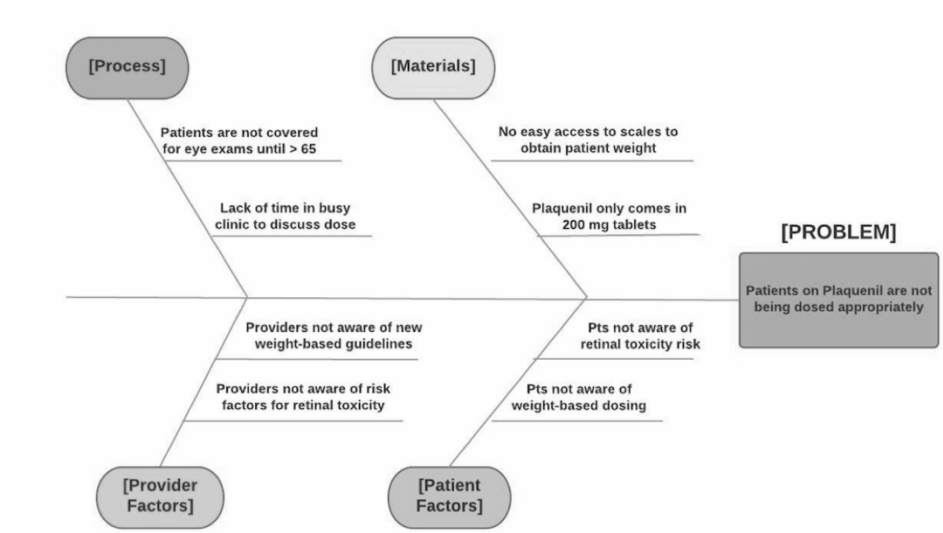

Figure 1 - Ishikawa diagram showing root causes for inappropriate hydroxychloroquine dosing and toxicity screening

228x123mm (200 x 200 DPI)

Hydroxychloroquine Dosing Chart

Use the table below to determine the recommended dosing regimen for hydroxychloroquine with examples of how this could be prescribed.

NB: Dosing regiment based on 5mg/kg of hydroxychloroquine as per 2016 AAO guidelines.

Weight	Equivalent Daily Dose	Example Dosing Regimens
80 kg or more (175 lbs or more)	400 mg	200mg BID x 7 days
70 – 79 kg (154 – 174 lbs)	342 mg	200mg BID x 6 days
65 – 69 kg (143 – 153 lbs)	315 mg	200mg and 400mg alternating days
55 – 64 kg (121 – 142 lbs)	285 mg	200 mg BID x 5 days
50 – 54 kg (110 – 120 lbs)	257 mg	200mg daily x 5 days and 400mg daily x 2 days
49 kg or less (109 lbs or less)	200 mg	200 mg daily x 7 days

Figure 2 - Hydroxychloroquine dosing chart used in intervention 1

164x106mm (200 x 200 DPI)

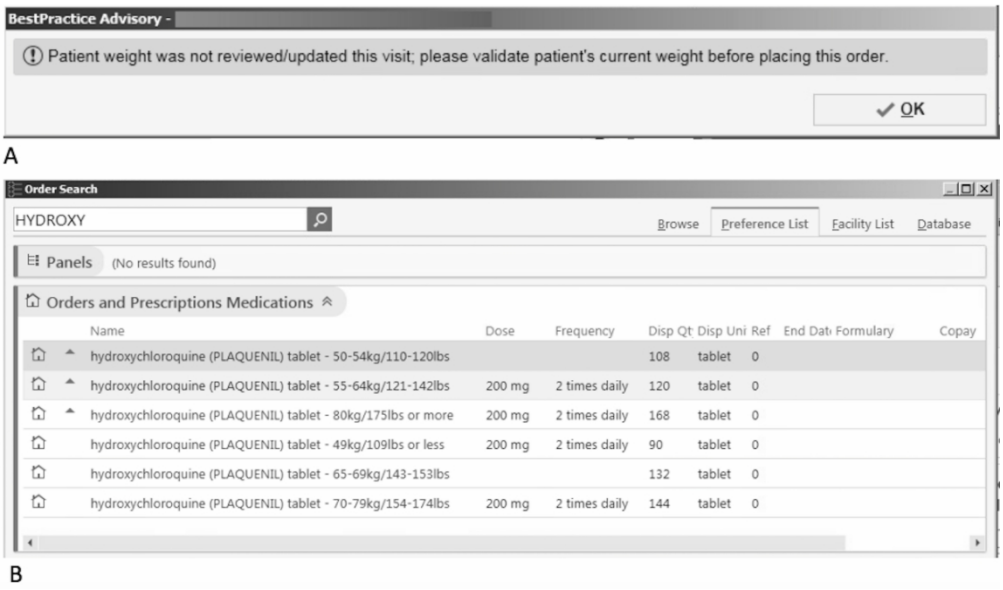

Figure 3 – A) Forced function weight documentation in the EMR whenever hydroxychloroquine was prescribed and B) Auto-dosing prescriptions in the EMR based on patient weight.

317x185mm (200 x 200 DPI)

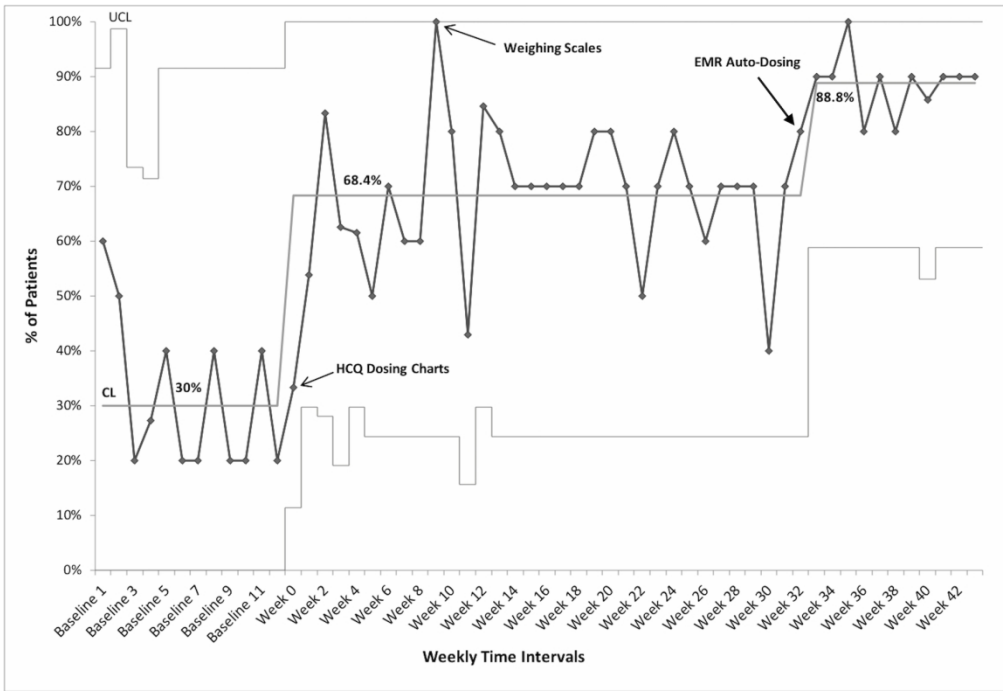

Figure 4 - Percentage of patients with appropriate dosing of hydroxychloroquine at baseline and over ten months of the QI intervention.

240x165mm (200 x 200 DPI)

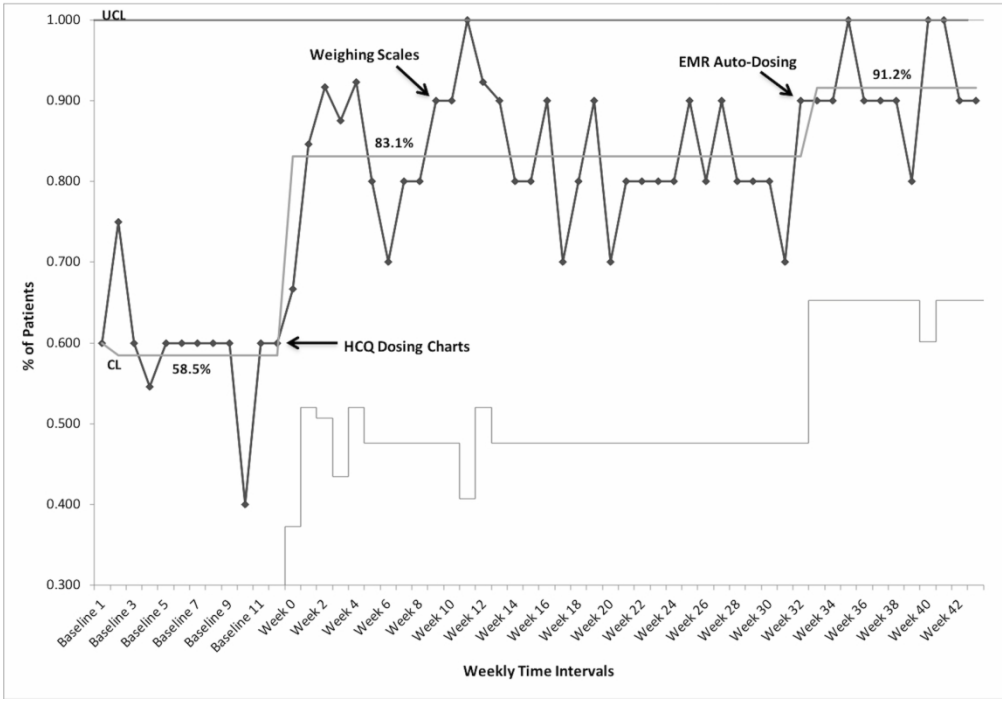

Figure 5 - Percentage of patients with appropriate retinal screening documentation at baseline and over ten months of the QI intervention

237x165mm (200 x 200 DPI)

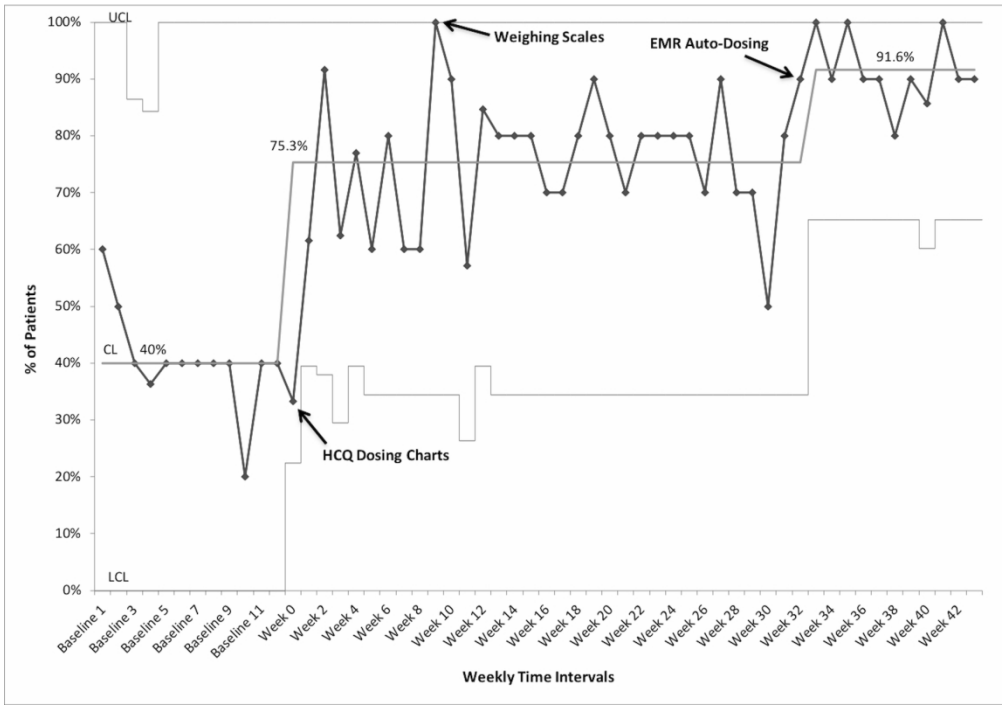

Figure 6 - Percentage of patients with recorded weights in the EMR at baseline and over ten months of the QI intervention

235x165mm (200 x 200 DPI)