(Quake Check Box, Quake Global, Inc, San Diego, CA).

The error rate decreased from 5.3 errors per 1000 skin specimens at baseline to 1.9 errors per 1000 specimens after the intervention (χ^2 (1, n = 11,118; 5383) = 9.55; P = .001) (Table II). Most specimen errors were related to anatomic site. The greatest error reduction occurred with PDSA 1. Value stream mapping of RFID tracking data identified inefficient specimen routing from our community clinic to central processing. Process streamlining eliminated 1.5 hours and unnecessary hand-offs (Supplemental Fig 2; available via Mendeley at https://doi.org/10.17632/hrd3swhyxm.1).

This study shows technology- and workflow-based improvements that led to a reduction in specimen errors. Our interventions focused on communication, process standardization, task automatization, and specimen integrity.

The greatest error rate reduction occurred in PDSA cycle 1, likely due to the ease of implementation. The interventions in subsequent PDSA cycles were more technologically complex with greater training requirements. The extent of the benefits may not have been fully captured in the short follow-up timeframe.

RFID technology has not been reported in the dermatology literature, although use by other specialties shows favorable outcomes. We instituted RFID in a 2-step method. The semiautomated accessioning functionality implemented in PDSA 3 showed a larger impact on error rate due to errors related to manual accessioning.

These interventions may serve as best practices for other high-volume dermatology practices. RFID technology can have large upfront costs, although this may be offset by increased workflow efficiency and task automatization. The impact of each intervention is difficult to determine when bundled. Only recorded errors were captured; near misses went unaccounted for. A stewardship program was established to review adverse events and provide staff education.

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Cyclic calcipotriene 0.005% foam and 1% 5-fluorouracil cream after cryotherapy in treatment of hyperkeratotic actinic keratosis: A retrospective study

To the Editor: Traditional treatments for actinic keratoses include cryotherapy, 5-fluorouracil cream, imiquimod, diclofenac, ingenol mebutate gel, and photodynamic therapy.[1,2] Recent research suggests topical vitamin D3 as possibly efficacious by mounting a robust antitumor immunoresponse via T-cell recruitment.[3] We hypothesized that these treatments may be synergistic and that vitamin D3 would enhance the efficacy of 5-fluorouracil cream in hyperkeratotic actinic keratoses treatment after cryotherapy.

This retrospective chart review from 2016-2018 included 175 patients with actinic keratoses treated with cryotherapy (group 1, n = 50), cryotherapy followed by cyclic 1% 5-fluorouracil cream (group 2, n = 50), cryotherapy followed by cyclic 1% 5-fluorouracil cream and calcipotriene 0.005% foam (vitamin D3) (group 3, n = 50), and cryotherapy followed by cyclic vitamin D3 (group 4, n = 25). Patients in groups 2, 3, and 4 were instructed to apply

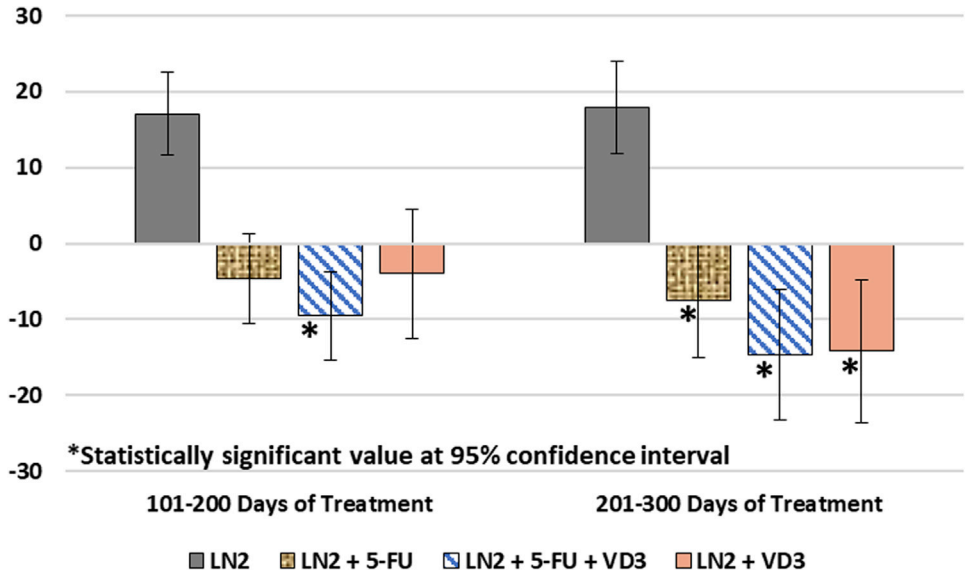

Fig 1. Mean change in actinic keratosis counts at 101 to 200 days and 201 to 300 days of treatment. *LN2*, Cryotherapy; *5-FU*, 5-fluorouracil cream; *VD3*, vitamin D3.

Table I. Comparison of mean changes in actinic keratosis counts at 101 to 200 days and 201 to 300 days of treatment

Number of days of treatment	Treatments compared with LN2	*P* value
101−200 days of treatment	LN2 + 5-FU	.40
	LN2 + 5-FU + VD3	.008*
	LN2 + VD3	.78
201−300 days of treatment	LN2 + 5-FU	.19
	LN2 + 5-FU + VD3	.006*
	LN2 + VD3	.02*

LN2, Cryotherapy; *5-FU*, 5-fluorouracil cream; *VD3*, vitamin D3.
*Statistically significant value at 95% confidence level.

topicals off label in 3-week cycles for 5 nights on the face and 7 nights elsewhere, off for 2 weeks, and then repeat.[4] They were also instructed to apply zinc healing cream as needed and sunblock every morning for the 3 weeks. Actinic keratoses were noted by location at baseline, 101 to 200 days, and 201 to 300 days. Any patient-reported irritation was recorded.

An analysis of covariance compared posttreatment counts with the cryotherapy control group at 95% confidence, whereas Tukey contrasts compared the efficacy between groups. Group 2 showed statistically significant actinic keratoses reduction (−7.54) by 201 to 300 days ($P = .047$). Group 3 showed statistically significant actinic keratoses reduction at 101 to 200 days (−9.55; $P = .002$) and 201 to 300 days (−14.70; $P = .001$), but only a marginal difference in lesion clearance was noted between groups 3 (−14.70; $P = .001$) and 4 (−14.18; $P = .004$) at 201 to 300 days (Fig 1). Statistically significant actinic keratoses reduction from group 1 was observed in group 3 ($P = .008$) only at 101 to 200 days, but both groups 3 ($P = .006$) and 4 ($P = .02$) showed statistically significant actinic keratoses reduction compared with group 1 at 201 to 300 days (Table I and Supplemental Table I, available via Mendeley at https://data.mendeley.com/datasets/pr3879pfsx/1).

Cryotherapy followed by cyclic vitamin D3 (group 4) resulted in a decrease in actinic keratoses similar to that of group 3 by 201 to 300 days. Less irritation was reported in group 3 (5 patients, 10%) than group 2 (15 patients, 30%), whereas group 4 had the lowest irritation rate (2 patients, 8%), with reported symptoms including nonpersistent redness, dryness, and itching. No pain, scabbing, or blisters were noted. Irritation appeared to resolve within each 3-week cycle.

The addition of vitamin D3 to 5-fluorouracil cream after cryotherapy in actinic keratoses treatment may improve efficacy and expedite onset of action, possibly through induction of antitumor T-cell immunity and tissue-resident memory cell formation.[3] In fact, twice-daily topical calcipotriol plus 5-fluorouracil cream for 4 days on the face and scalp has previously been shown to decrease subsequent squamous cell carcinoma development for 3 years.[5]

Interpretation of our results is limited by the nonrandomized, retrospective nature of the study. Larger, prospective, multicenter, randomized,

placebo-controlled trials with cyclic vitamin D3 and 5-fluorouracil cream after cryotherapy for hyperkeratotic actinic keratoses treatment are needed to confirm these findings. Similarly, monotherapy studies with cyclic topical calcipotriene 0.005% foam for actinic keratoses treatment may be warranted to confirm any association of improved efficacy and decreased irritation and possible effect on subsequent squamous cell carcinoma development.

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A retrospective cohort study confirms that prophylactic vaccination is underused in patients on tumor necrosis factor inhibitors

To the Editor: Biologics place patients at increased risk for infection.[1] The medical boards of the National Psoriasis Foundation, the American College of Rheumatology, and the European League Against Rheumatism advocate influenza, pneumococcal, and varicella zoster vaccines for this high-risk patient population.[2-4] Unfortunately, low use of pneumococcal vaccine among Veterans Affairs patients prescribed tumor necrosis factor inhibitors (TNFi) has been noted.[5]

We performed a retrospective cohort study accessing the MarketScan Commercial Claims and Encounters Database (IBM, Armonk, NY) containing data from >150 million Americans to explore vaccine use in TNFi-treated patients. We used National Drug Codes to identify commercially insured patients, aged 18 to 60 years, prescribed adalimumab, etanercept, or infliximab continuously for ≥6 months between 2014 and 2016. National Drug Codes or Current Procedural Terminology (American Medical Association, Chicago, IL) entries, or both, for influenza, varicella zoster, or pneumococcal pneumonia vaccines were used to classify individuals as vaccinated or unvaccinated. *International Classification of Disease* 9 and 10 codes were used to identify patients diagnosed with influenza, varicella zoster, or pneumococcal pneumonia and capture those hospitalized for relevant infections. Infection rates and frequency of subsequent hospitalization were compared between vaccinated and unvaccinated patients. Odds ratios were constructed for each comparison.

Included were 89,098 patients prescribed TNFi for ≥6 months (19,878 on adalimumab, 12,167 on etanercept, and 57,053 on infliximab). Only a fraction of the patients were vaccinated for influ-

Table I. Vaccination rate of patients on biologic therapy from 2014 to 2016*

Vaccination	Vaccine received	Number	% of total
Influenza vaccination	In 2014	31,117	34.92
	In 2015	32,854	36.87
	In 2016	35,344	39.67
Zoster vaccination	In 2014-2016	2963	3.33
Pneumococcal	In 2014-2016	9406	10.56

*Number and rates of patients who received influenza, zoster and pneumococcal vaccination from 2014-2016.