

Results

- Over 4 years total direct medical costs for 1,000 suspected SLE pts tested with MAP are \$58,919,462 versus \$61,174,818 by SDT (Table 3)
- Reduced inpatient hospital admissions are the biggest driver of cost savings (\$581,728 in year 1)
- Over 4 years, incremental savings using MAP versus SDT are \$2,255,356 (\$0.05 per member per month)
- The most sensitive clinical parameter is % of diagnosable SLE among those suspected of SLE (Figure 3)
- The most sensitive cost parameter is the incremental cost of MAP + SDT vs SDT alone, with a reduction in cost savings of \$20 per \$100 increase in the incremental cost of the test (Figure 4)

Figure 2: One-way sensitivity analysis

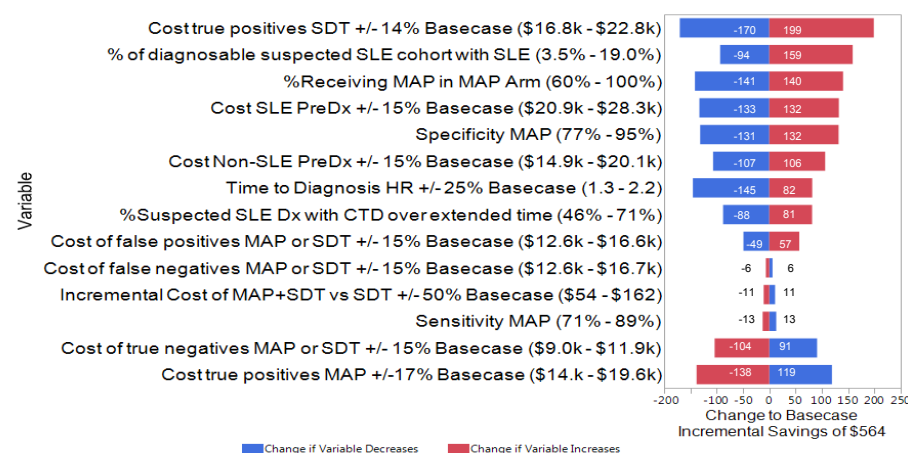


Figure 3: Change to incremental saving per unit increase of variable

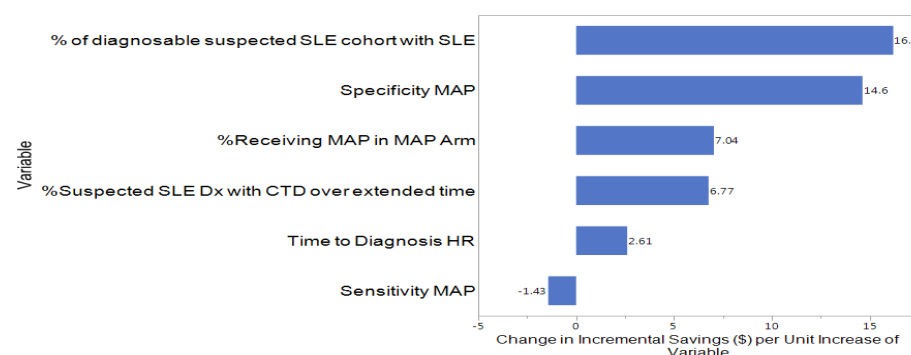
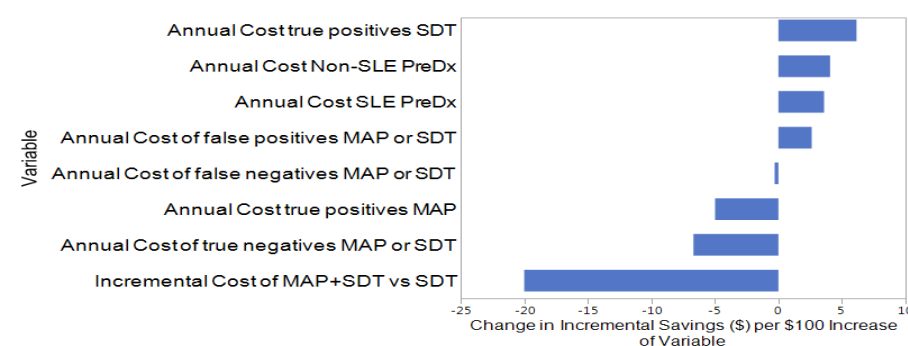


Figure 4: Change to incremental saving per \$100 increase of variable



Conclusion

- This is the first analysis of the budget impact associated with the diagnostic pathway of SLE using SDTs alone compared to a diagnosis made with a proprietary MAP. This allows clinicians and payers to assess expected clinical benefits of earlier SLE diagnosis
- The potential cost savings associated with use of MAP testing to diagnose SLE is clear, with an estimated savings of \$2,255,356 in total direct costs over a 4 year time horizon and \$711 (per suspected SLE patient) in year 1 projected for a commercial health plan with 1 million covered lives

AN EVALUATION OF THE ECONOMIC IMPACT OF EARLIER SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) DIAGNOSIS USING COMPLEMENT C4D ACTIVATION PRODUCTS IN A MULTIVARIATE ASSAY PANEL (MAP)

Ann E. Clarke¹, Thomas F. Goss², Andrew Piscetello³, Tarun Chandra³, Tyler O'Malley⁴, Thierry Dervieux⁴ and Tami Powell⁴

¹University of Calgary, ²Boston Healthcare Associates, ³EmpiriQA LLC, ⁴Exagen Diagnostics, Inc.

Abstract

PURPOSE: Diagnosis (dx) of systemic lupus erythematosus (SLE) is made via a combination of clinical and laboratory examinations; the sensitivity and specificity (S&S) of standard diagnostic tests (SDTs) (i.e.: ANA and antibodies to dsDNA, Smith, Ro/SSA, La/SSB, centromere, Jo-1, Scl-70, and CCP), are reported to be 83% & 76%, respectively (Putterman et al, 2014). A multivariate assay panel (MAP) combining biomarkers, complement C4d activation products on erythrocytes & B cells, with SDTs, yields improved dx performance with a S&S of 80% & 86%, respectively (Putterman et al, 2014). We evaluated the payer budget impact of SLE dx using MAP compared to SDTs.

METHODS: We modeled a health plan of 1 million enrollees, with 0.1% suspected of SLE. SLE dx among suspected SLE patients was 9.2% (Dijkstra et al, 1999). The MAP arm assumed 80% / 20% of suspected SLE patients were tested with MAP/SDTs, compared to 100% SDT testing in SDT arm. Based on improved MAP performance, the hazard ratio for the assumed dx rate compared to SDTs was 1.74, (71, 87, 90, and 91% of the suspected who develop SLE will be diagnosed in years 1 – 4 compared to 53, 75, 84, and 88% with SDTs). Increased MAP performance relative to SDTs should result in earlier dx of SLE, reduction in disease severity at dx, and a longer period of time in less severe disease states (Oglesby et al, 2014) with associated lower costs. Pre-SLE dx claims-based cost data was used to estimate recurring direct costs for undiagnosed patients, and a weighted average of post-dx direct cost data for mild, moderate, and severe SLE were obtained from the literature (Garris et al, 2013) for SDTs, which was re-weighted to reflect the MAP scenario (Table 1)

RESULTS: Total 4-year pre- and post- dx direct medical cost for suspected SLE patients tested with MAP were \$58,919,462 compared to \$61,174,818 by SDTs (Table 3). Total 4-year average cost savings per suspected SLE patient tested with MAP were \$2,256 (Table 3). Reduced inpatient hospital admissions were the biggest driver of cost savings (\$581,728 in yr 1). In a one-way sensitivity analysis, the percentage of SLE dx among those suspected of SLE and specificity of MAP had the largest impact on average annual cost savings (respective savings of \$16 and \$15 per 1% absolute increase in percentage of SLE among those suspected of SLE and MAP specificity).

CONCLUSION: Incorporating MAP into SLE dx results in total 4-year direct cost savings of \$2,255,356 (\$2,256 per suspected SLE patient) and year 1 savings of \$711 per suspected SLE patient. Further, by facilitating earlier dx of SLE at a less severe disease state, it is anticipated that MAP will enhance patient outcomes.

Background and Objectives

- SLE is diagnosed via a combination of clinical and laboratory examinations. Due to the lack of published conditional sensitivity and specificity (S&S) for SDTs the model used ANA, antibodies to dsDNA, smith, SS-B/La Scl-70, CENP, Jo-1, CCP as reported to be 83% & 76% (Putterman et al, 2014)
- MAP combines complement C4d activation products, EC4d & BC4d, with antibodies to ANA by ELISA and HEp-2 IFA, dsDNA, dsDNA (w/ Crithidia confirmation), Smith, SS-B/La, Scl-70, CENP, Jo-1, CCP, and yields improved diagnostic performance with a S&S of 80% & 86% (Putterman et al, 2014, Ramsey-Goldman et al, 2017 and Wallace et al, 2016)
- Analysis estimates the budget impact to a US commercial payer for SLE diagnosis via MAP versus SDT

Methods

- Analysis conducted in accordance with the ISPOR task force on budget impact models (Sullivan et al, 2014)
- Cost year used is 2017, all costs are inflated by 3% per year to reflect standardized costs in 2017
- 1 million enrollees in a U.S. Commercial Health Plan is used, 0.1% are suspected of having SLE
- 2 yr pre-dx cost data from MarketScan commercial medical and pharmacy longitudinal claims data analysis (Figure 1)
- 4 yr post-dx cost data sourced literature; inclusion based on availability of parameters and study design
- Clinical and cost parameters included in the base case model are included in Table 1 and Table 2, respectively

A one-way sensitivity analysis was performed using plausible ranges or each variable (Figure 2); variables were normalized by assessing per unit increase of clinical variable (Figure 3) and per \$100 increase of cost variables (Figure 4)

References

Dijkstra et al. Scand J Rheumatol 1999; 28:33-37; Garris et al. J Med Econ 2013; 16(5):667-77; Kawatkar et al: American College of Rheumatology 2012; 64(11):1649-1656; Li et al. Arthritis Rheum 2009; 61(6):755-63; McDonald et al. The Ocular Surface 2016; 14(2):144-167; Putterman et al. Lupus Sciences & Medicine 2014; 1:e000056; Ramsey-Goldman R et al. Lupus Science & Medicine; 2017;4(1):e000236; Sullivan et al. Value Health. 2014;17(1):5-14; Wallace DJ et al. Lupus Sci Med. 2016;3(1):e000127

Table 1: Clinical Parameters used in MAP arm and SDT arm

Parameter - % Suspected SLE Pts	MAP + SDT Arm	SDT Arm	Sources/Notes on derivation
Diagnosed with definitive CTD over extended time horizon	58%	58%	Dijkstra et al, 1999
Diagnosed with definitive CTD within 2 years	50%	44%	SDT: Dijkstra et al, 1999 MAP: Assumed
% diagnosable with SLE	9.2%	9.2%	Dijkstra et al, 1999
% diagnosable with RA or Sjorgen's	48.8%	48.8%	Derived from Dijkstra et al, 1999
Ratio of RA to Sjorgen's	1.44	1.44	Dijkstra et al, 1999. RA & SS represent CTD's with high and low post-dx costs, respectively
Sensitivity	80%	83%	Putterman et al, 2014
Specificity	86%	76%	Putterman et al, 2014
Diagnosed with definitive CTD within Year 1	71%	53%	Hazard ratio of 1.74 for the assumed dx rate applied
Diagnosed with definitive CTD within Year 2	87%	75%	
Diagnosed with definitive CTD within Year 3	90%	84%	
Diagnosed with definitive CTD within Year 4	91%	88%	

Figure 1: Selection Criteria for Incident SLE cases to assess pre-diagnosis costs via a claim analysis

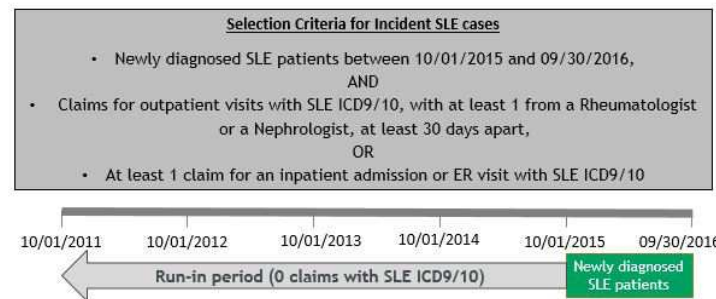


Table : Cost Parameters used in MAP arm and SDT arm

Parameter	MAP + SDT Arm	SDT Arm	Sources/Notes on derivation
SLE negative pre-dx costs factor	0.7114	0.7114	Newly diagnosed costs w/out nephritis and matched control (Li et al, 2009)
Incremental cost of MAP vs SDT	\$108	N/A	Medicare Allowable CY 2017
Avg pre-dx Cost per pt without SLE/yr ^a	\$17,495	\$17,495	MarketScan Data Claims Analysis
Avg pre-dx Cost per pt with SLE/yr	\$24,593	\$24,593	MarketScan Data Claims Analysis
Avg per pt cost for mild SLE/yr	\$7,021	\$7,021	Garris et al, 2013
Avg per pt cost for moderate SLE/yr	\$14,516	\$14,516	Garris et al, 2013
Avg per pt cost for severe SLE/yr	\$47,252	\$47,252	Garris et al, 2013
Avg per year post-dx cost for SDT TP ^b	N/A	\$19,577	Garris et al, 2013
Avg per year post-dx cost for MAP TP ^b	\$16,803	N/A	Garris et al, 2013
Avg per year post-dx cost for MAP TN	\$10,375	N/A	Kawatkar et al, 2012 and McDonald et al, 2016. Assume TN managed as a mix of RA/SS
Avg per year post-dx cost for MAP FP	\$14,441	N/A	Garris et al, 2013. Assume FP managed like SLE, RA managed like Mild/Moderate/Severe SLE and SS managed like Mild SLE
Avg per year post-dx cost for MAP FN	\$14,516	N/A	Garris et al, 2013. Assume FN managed similarly to Moderate Disease severity

^aPre-dx costs for SLE negative pts are based on the factor of 0.7114 (Li et al, 2009)

^bCosts and proportions of pts diagnosed as true positives and true negatives as per MAP were sourced from Garris et al (2013). SDT: Mild SLE: 26% at \$7,021, Moderate SLE: 52% at \$14,516, Severe SLE: 22% at \$47,252. MAP: Costs for all severity grades of SLE are equivalent to those in the SDT arm, however weights are adjusted: Mild SLE: 35%, Moderate SLE: 50%, Severe SLE: 15%

TN=True Negative; TP=True Positive; FN=False Negative; FP=False Positive

RA=Rheumatoid Arthritis; SS=Sjogren's syndrome

Table 3: Pre-diagnosis cost savings in MAP vs. SDT, Total and Average Direct Costs for Suspected SLE Patients in Plan

Cost per Year	Pre-diagnosis cost savings between MAP + SDT & SDT Arms							Pre and Post Diagnosis Direct Costs		
	Hospital Inpatient Visits	Emergency Room Visits	Outpatient Office Visits	Outpatient Radiology Procedures	Outpatient Lab Procedures	Outpatient Pharmacy Prescriptions	Other Outpatient Cost ^a	SDT	MAP +SDT	Cost Savings between MAP + SDT and SDT
Year 1	\$581,728	\$41,354	\$75,668	\$66,422	-\$17,787	\$336,716	\$502,990	\$16,144,023	\$15,433,347	\$710,676
Year 2	\$375,056	\$26,662	\$48,785	\$42,824	\$44,397	\$217,090	\$324,292	\$15,298,148	\$14,641,559	\$656,589
Year 3	\$187,089	\$13,300	\$24,336	\$21,362	\$22,146	\$108,291	\$161,766	\$14,941,507	\$14,450,654	\$490,853
Year 4	\$85,341	\$6,067	\$11,101	\$9,744	\$10,102	\$49,397	\$73,790	\$14,791,139	\$14,393,902	\$397,237
Total (Yr 1-4)	\$1,229,214	\$87,382	\$159,890	\$140,353	\$58,585	\$711,493	\$1,062,839	\$61,174,818	\$58,919,462	\$2,255,356

Limitations

- Shifts in severity at diagnosis with MAP are assumed, in the future these should be studied in the clinical setting
- A number of parameters in the model have been observed directly with the use of MAP testing, but have been estimated based on peer-reviewed published data, which the authors believe to be representative and generalizable
- The cost of treating SLE is likely to change given recent approvals of new treatments and a number that are in late stages of clinical development. This model does not accommodate for potential future changes in SLE treatment patterns