ACD ANNUAL REPORT 2018

Our Mission

The ACD is the only patient advocacy group that is devoted to Cerebral Creatine Deficiency Syndromes (CCDS).

We are committed to meet our goals, which are “to provide patient, family and public education; to advocate for early intervention through newborn screening, and to promote and fund medical research for treatments and cures for Cerebral Creatine Deficiency Syndromes.”

The ACD sets these goals to bring the CCDS Community together as one strong voice, to be united in our efforts, to urge allied medical professions to test for CCDS, and to promote scientific research of CCDS.

It is through our mission that we are “building strength and changing lives.”

President's Letter

Dear CCDS Stakeholders,

In 2018, the ACD and CCDS community celebrated huge milestones. 2018 marked a turning point and set the bar high for continued CCDS awareness, advocacy and research efforts. Through your help and continued support, ACD was able to accelerate many tangible results for CCDS. Here is a look back at some of the 2018 highlights:

In 2018, ACD continued to promote CCDS awareness and education. Efforts included participating in 23 CCDS informative sessions and the production of the first CCDS Educational Video, featuring testimonials from leading CCDS experts and patients. To date, this video has received over 1,400 views! In July of 2018, the ACD hosted the first CCDS Scientific and Patient Symposium in Austin, Texas. This was an incredible event that brought together researchers, physicians, industry and families to collaborate on CCDS advancements. This event surpassed all expectations with over 200 attendees, including families and professionals from seven countries. The ACD was also able to provide PatientStrong™ Travel Grants to five families to help them attend the conference. It was an amazing opportunity to meet other CCDS families and develop life-long relationships in the community.

Newborn screening has been a very important part of the ACD mission. In 2018, ACD representatives organized a newborn screening committee dedicated to newborn screening advocacy efforts. This committee continues to press RUSP (Recommended Uniform Screening Panel) RUSP to recommend GAMT through collaboration with state like Missouri, Texas, New York, Georgia and Minnesota. We are incredibly pleased to announce that Utah, and now New York, are both actively screening for GAMT in every newborn baby born in their state and Michigan will begin screening in 2019.

ACD's commitment to CCDS research soared in 2018. The first ACD Research Grant of $10,000 was awarded to Dr. Matthew Skelton, from Cincinnati Children's Hospital. This grant funded Dr. Skelton and his team in their efforts to study the effects of creatine on early brain development. Participating in the CCDS Patient Insights Network (PIN), a patient registry platform hosted by Invitae, and contributing valuable data are the most important way we, as a CCDS community, can take charge and help initiate research. The ACD set a precedent in 2018 by being the first patient advocacy group to integrate genetic data into their patient registry. ACD's participation in the Patient Data Sharing Program allows registry participants to share de-identified genetic health information to help advance CCDS research.

The ACD Board of Trustees added a new member, Laura Trutoiu, as Director of Research in 2018. The Board meets weekly to review ongoing strategic goals and progress and works closely with

ambassadors and volunteers to accomplish these goals. We also rely on the expertise of our Scientific Medical Advisory Board (SMAB), comprised of leading CCDS experts who are dedicated to helping us advance our efforts. In 2018, we are pleased to have Saadet Andrews, Gajja Salomons and Adreas Shultze join the SMAB.

This past 2018 fundraising campaigns were critical in generating the financial support to implement many of our programs. From small donations, in-kind donations, underwriting and corporate giving, these gifts helped us raise over $140,000. Without these contributions we would not be able to complete these achievements or host our 2018 CCDS Scientific + Patient Symposium.

On behalf of the ACD Board of Trustees, I am honored to present the ACD's Annual Report for fiscal year 2018. As CCDS needs grow, it will require us to be stronger, work harder, and stretch ourselves even further. Based on our progress this past year, I am certain we will succeed.

Thank you for your continued support.

Whitnie Strauss

The Importance of Cerebral Creatine Deficiency Syndromes (CCDS)

Let us take a moment to understand this disease. CCDS are inborn errors of metabolism, which interrupt the formation or transportation of creatine. Creatine is necessary to increase adenosine triphosphate (ATP) which provides energy to all cells in the body. Creatine is essential to sustain the high energy levels needed for muscle and brain development.

There are three Cerebral Creatine Deficiency Syndromes with complicated medical names for some to remember. So, we refer to them by acronyms.

Arginine: Glycine Amidinotransferase Deficiency or AGAT

AGAT is involved in the first step of creatine formation. Mutations found in the AGAT gene impair the body's production of creatine. There are fewer than twenty AGAT cases reported, to date.

Guanidinoacetate Methyltransferase Deficiency or GAMT

GAMT is a mutation in the gene that makes the enzyme that creates creatine, resulting in a shortage of creatine. GAMT is the most severe of the three CCDS due to an elevation of guanidinoacetate (which is neurotoxic) in addition to creatine deficiency, and there are more than 100 cases reported in medical literature.

Creatine Transporter Defect or CTD

CTD is a mutation in the creatine transporter gene. This mutation results in a blockage in the transportation of creatine to the brain and muscles. CTD is the most common CCDS. It is estimated to account for about 2% of all unexplained X-linked intellectual disabilities.

Symptom(s)

The most common symptom of CCDS is a global delay. Speech delay may be particularly severe, and intellectual disability of variable severity is typically present in older children and adults. Other additional symptoms may include seizure disorders, muscle weakness, autistic-like behaviors, movement disorders, gastrointestinal problems and failure to thrive.

Treatment(s)

Treatment with oral supplementation is available and effective if initiated early for AGAT and GAMT patients. To date, this type of therapy has not shown to improve outcomes in individuals with CTD.

Education and Awareness

The ACD is the only non-profit patient advocacy group raising CCDS education and awareness.

Rare Disease Partners

As part of its commitment to patient and public education, the ACD maintains ongoing relationships with several rare disease and advocacy partners. Our collaboration continues with organizations like: the National Organization for Rare Disease (NORD), Global Genes, EveryLife Foundation, Child Neurology Foundation (CNF), and ThinkGenetic. These partnerships help build a solid foundation in which ACD can better serve our patient population, to increase CCDS knowledge within the medical community and, in general, the public at large.

Medical and Scientific Conferences

ACD feels that with a continued presence at strategic medical and scientific conferences we can increase CCDS awareness and promote earlier screening and diagnostics for GAMT, AGAT and CTD patients. By attending and exhibiting at conferences, such as the Child Neurology Society and the American College of Medical Genetics and Genomics, Society of Inherited Metabolic Disorders (SIMD), and Gatlinburg conferences we are able to make face-to-face contact with thousands of physicians who are in a position to screen and treat CCDS patients.

Educational Sessions

ACD has increased education efforts through targeted speaking opportunities. Speaking at and attending two Mountain State Regional Genetics Network conferences (Austin and San Antonio, TX), Primary Children's Hospital Grand Rounds (Salt Lake City, UT), and Rare on the Road (Salt Lake City, UT) provides an important opportunity to educate a wider network of physicians about the early signs and symptoms and diagnostic process. Increased education has been instrumental in helping CCDS families find answers and due to these efforts we have seen a drastic increase in newly diagnosed families in 2018.

Website and Social Media

ACD continues to utilize the website www.creatineinfo.org and our social media channels to increase educational and key messaging.

2018 Social Media Highlights

- 1,062 Facebook likes and followers
- Facebook Total Post organic reach: 123,811
- 179 Instagram followers
- 105 Twitter followers

Educational Video Production

The ACD produced our first educational video that is a sharable educational tool to be used across a variety of platforms. The 2018 CCDS Scientific + Patient Symposium was a perfect setting to create this Creatine Deficiency Educational Video that we hope serves to help advocate for newborn screening and treatments for years to come.

The CCDS Educational Video has received over 1,400 views and is proving to be a wonderful resource for friends, families and physicians to better understand CCDS. The video can be viewed at: https://creatineinfo.org/creatine-deficiency-educational-video/#more-6672

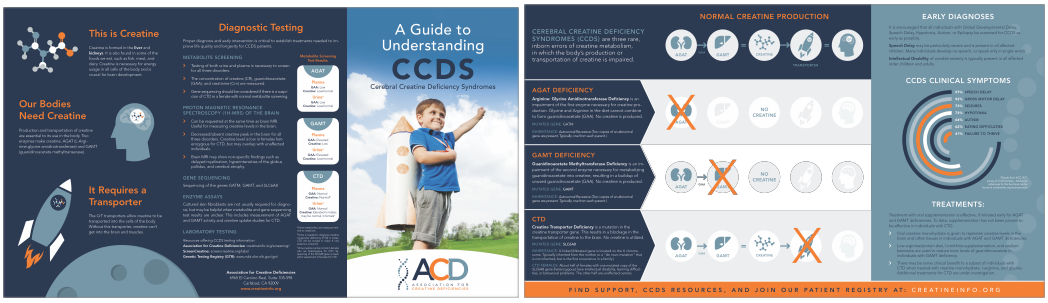
ACD is extremely proud of this video and we thank all of the families, physicians, and researchers who participated, as well as Lumos Pharma for sponsoring this project.

CCDS Day and Rare Disease Day

CCDS Day (Feb. 1) and Rare Disease Day (Feb. 28) continue to be important days for the CCDS community to unite under our shared cause. These awareness days bring critical attention to GAMT, AGAT and CTD. It is so important to continue participating in awareness days to join forces to give these rare disorders a louder voice. We've seen a huge increase in participation and are excited that these days are receiving global recognition.

Other Opportunities

The ACD developed a comprehensive CCDS overview in 2018 that details all three CCDS disorders. This important educational aid provides important early detection and screening information, in addition citing clinical symptoms that could lead to an earlier diagnosis.



> Her doctors and therapists are amazed at how rapidly she has progressed. And we are thrilled with the happy girl who is full of life and out to conquer the world!
>
> Mother of a daughter diagnosed with GAMT

Advocacy

The ACD is the only patient advocacy group in the United States that devotes their efforts to changing the lives of people living with CCDS. Along with education and awareness, the ACD is passionate about advocating the rights of individuals with CCDS.

Newborn Screening

The ACD is pleased to report tremendous momentum in GAMT newborn screening in 2018. The state of New York began testing for GAMT in October 2018. Almost 400,000 babies are born in New York each year. Michigan approved the addition of GAMT in 2018 and is set to begin testing within the first quarter of 2019. Michigan has 115,000 births each year. Including the state of Utah, which began testing in 2015, there will soon be over 565,000 babies tested for GAMT annually in the U.S.

In 2018, a family in the United Kingdom began a petition to request the addition of GAMT to the UK's newborn screening. Hana Young, midwife, and mother of a child diagnosed with GAMT, was highlighted by the BBC, speaking on the importance of catching this devastating disorder early on in life. Read the article here: https://www.bbc.co.uk/news/health-46456984

The Robinson family spoke in front of the Missouri newborn screening committee in November of 2018 to recommend the addition of GAMT to their list of screened disorders and highlighted the importance of early detection of the disorder. Members of our SMAB, Dr. Nicola Longo and Dr. Andreas Schulze, also represented ACD by speaking on our behalf in the states of New York and Missouri.

The ACD plans to aggressively advocate in many more states in 2019, including Georgia, Missouri, Wisconsin, Ohio, and Minnesota.

Rare Disease Partners

As part of our responsibility to advocate for CCDS, the ACD has partnerships with Global Genes, NORD, Child Neurology Foundation, EveryLife Foundation, and ThinkGenetic. These relationships are incredibly important to building an extensive network of Rare Disease advocates who can provide an even greater platform to provide resources, share communication, petition on behalf and represent for our CCDS patients and community.

> Our community is strong together. Knowledge is power. There's always something we can do.
>
> Mother of a son with CTD.

Medical and Scientific Research

Patient Registry

In 2018, the ACD was pleased to announce that they teamed up with ClinVar to add important gene variant information to their already growing ACD Patient Registry with Invitae. ClinVar is a freely accessible, public archive of reports of the relationships among human variations and phenotypes hosted by the National Center for Biotechnology Information (NCBI) and funded by the Intramural National Institutes of Health (NIH). ClinGen investigators work closely with NCBI regarding the development and functionality of ClinVar and to support data deposition from many sources, and ClinGen curation efforts will improve the CCDS data within ClinVar.

CARE Grant

The first ACD C.A.R.E (Corporate Alliance for Research and Education) Grant of $10,000 was awarded to Dr. Matthew Skelton, from Cincinnati Children's Hospital. This grant funded Dr. Skelton and his team in their efforts to study the effects of creatine on early brain development.

> Milestones came, milestones went. Some were met. Some…well. We realized may never happen. We grieved many times as I'm positive each of you has done.
>
> Mother and grandmother of daughter and grandson diagnosed with CTD

“Research for CCDS in 2018”

Update by: Laura Trutoiu, Director of Research

At the ACD, we believe that a thriving research community is how we are going to bring treatments and therapies to our loved ones. Research happens at the basic science level, at the lab bench, in experiments with animal models, in natural history studies and surveys, in pre-clinical research, and eventually in clinical experiments. I joined the ACD in June 2018 as the Director of Research with the mission of supporting, enabling, and driving research in CCDS. As a parent, I strongly believe that we have to be actively engaged in research to find cures. By coming together as a community and participating in surveys, studies, research meetings, and by sharing our experience with CCDS we are pushing the boundaries of knowledge and making progress towards cures.

I am hopeful to see growth in 2019 and numerous research projects for creatine deficiencies. In 2018, our Scientific and Medical Advisory Board (SMAB) grew significantly and currently has eleven outstanding scientists and physicians dedicated to research and finding treatments for CCDS. Many of our SMAB researchers published important papers in 2018 that pushed the boundary of what we know about CCDS. At the symposium in Austin, we awarded our first research grant to Professor Matthew Skelton to support his ongoing work on mouse models for CTD. Similarly important, the symposium led to productive conversations and ideas for studies that we hope to pursue.

As a metric for research, albeit a limited measure, in the graph below you can see the number of publications per year on PubMed, the top database search engine for medical references, with keywords like GAMT, AGAT, SLC6A8. Though not all of these publications are necessarily on CCDS (for example, AGAT can be mentioned in publications that may not necessarily reference creatine deficiency) the graph provides an interesting perspective on where we are. Our goal for 2019 is to foster and support more research that leads to treatments and therapies. To research treatments, we must all participate in research, in the patient registry, and surveys.

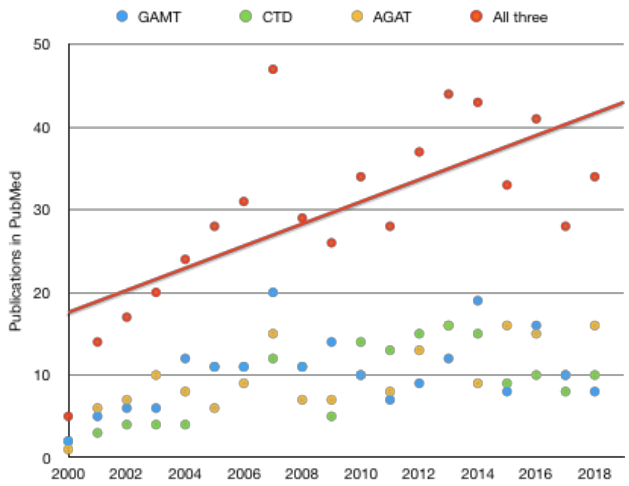


Figure 1: Number of PubMed articles by year with keywords like GAMT, AGAT, and CTD. Please note that not all keywords reference CCDS.

A highlight for 2018 that we are particularly proud of is partnering with ClinGen to share genomic and phenotypic data to inform variant classification and gene–disease relationships for CCDS. We are grateful to be early partners with ClinGen and one of three patient orgs (together with Cardio-Facio-Cutaneous Syndrome (CFC) International, and CureCADASIL) currently in the project. Furthermore, the partnership has led to establishing a CCDS variant curation expert panel which you can read about below.

For 2019, we look forward to supporting and driving more research partnerships with academia and industry alike. A specific goal is to engage the research community by gathering, through surveys, patient experience data from our CCDS community. Your participation in research projects will help us achieve this goal!

The Clinical Genome Resource (ClinGen) initiates a CCDS variant curation expert panel headed by Jenny Goldstein, PhD, CGC, and Saadet Andrews, MD, PhD, FCCMG

Figuring out whether or not a variant in a gene is causing disease can be a challenge for molecular genetic laboratorians and researchers. In 2015, the American College of Medical Genetics (ACMG) and Association for Molecular Pathology (AMP) published guidelines to help molecular genetic laboratories determine the clinical impact of genetic variants, allowing a variant to be classified as pathogenic (disease-causing), likely pathogenic, unknown significance, likely benign, or benign. While the ACMG/AMP guidelines have been tremendously helpful, the guidance provided is general and does not address specific genes and diseases. The Clinical Genome Resource (ClinGen), an NIH-funded project dedicated to creating a publically available resource that defines the clinical relevance of genes and variants for use in precision medicine and research, is assembling groups of experts and curators to adapt the ACMG/AMP guidelines for specific genes. These groups, called Variant Curation Expert Panels (VCEPs), use their guidelines to classify variants within their genes of interest and to submit their classifications to the publicly available ClinVar database (https://www.ncbi.nlm.nih.gov/clinvar/). ClinVar serves as a repository for genetic variants and their classifications, based on information submitted by clinical laboratories, researchers, and patients, as well as the ClinGen VCEPs. Since the FDA approved ClinGen's VCEP process in December 2018, all variants submitted to ClinVar from ClinGen VCEPs are tagged to indicate that they are part of an FDA recognized database. One of the most recently-formed ClinGen VCEPs is dedicated to adapting the ACMG/AMP guidelines for interpretation of variants in the three CCDS genes (*GATM*, *GAMT*, and *SLC6A8*) and submitting their classifications into ClinVar. This group, which is chaired by Dr. Saadet Andrews and Dr. Yiumo Chan, is made up of some of the world experts in CCDS patient care, diagnostics, research, and treatment, and has already made significant progress in writing variant interpretation guidelines for the three genes. It is hoped that these guidelines will help to reclassify the many variants of unknown significance in these genes for clinical diagnosis of CCDS. This will also facilitate the interpretation of molecular genetic test results in newborns identified by newborn screening for GAMT deficiency in the pre-symptomatic stage of the disease.

We planned the space. You brought the fun!

CCDS Scientific + Patient Symposium
Austin, Texas
KidsCamp, 2018

Patient and Family Supportive Services

The ACD's website is an essential platform for CCDS information. Our patient and family supportive services can be obtained by visiting our site www.creatineinfo.org. For 2018, we have brought together areas of interest for supportive services. We listen to the needs of our community and take every means to produce helpful and beneficial information for daily use.

PatientStrong™

Travel Grant Program

ACD is excited to have launched the PatientStrong™ Grant Program in 2018. This program was established to assist CCDS patients and in 2018 helped several families to attend the 2018 Symposium. ACD's PatientStrong™ Outreach Fundraiser helps support these awards.

Captain Creatine

ACD introduced Captain Creatine, one of the newest members of the ACD Team, to the CCDS community in November. He battles CCDS one day at a time and everyone is able to follow him on his journey.

CCDS Patient Growth

In 2018, ACD saw a 50% increase in newly diagnosed families. That is an incredible growth rate for a rare disease community! We believe this is due to increased awareness in the medical community, and through social media efforts to be found by these families.

“There is currently no cure for Ben... The last week in June I’ll be riding my bycicle from Cincinnati to Cleveland, Ohio to raise awareness of this disorder and to raise funds for the ACD.

-Chuck, Ride for Ben

Ride for Ben raised $5,425 to support ACD’s mission programs.

Fundraising

The ACD is a 501(c)(3) charitable non-profit organization which can provide valuable services to the CCDS community only because of the generosity of our contributors.

Special Events and Corporate giving are essential to raising CCDS awareness and funds needed to continue the ACD's mission.

The following is a list of sources, which provided funding for 2018:

Contributors

Corporate:

United Way
Microsoft
Mode-ology
Rare Care Foundation
Smith-Cooper International

Sponsors:

Lumos Pharma
Thisbe& Noah Scott Foundation
AlzChem
Sema4
Solace Nutrition
Arborvitae Biologics
Big Sky Oral and Facial Surgery
Xtraordinaire
Global Genes
EveryLife Foundation
Think Genetic
NORD
Global Genes

Special Events:

Amazon Smile
Holiday Hero's Outreach
Ride for Ben
Savage Racing
Rohan's Research Blend Tea (Friday Afternoon)
Reid's Blend Coffee (Greater Goods)
PatientStrong™

Ultragenyx
Rare Care Foundation
TriWest, LTD.
Progressive Leasing
Southern Rock, LLC
Egg Traders
Miracle Clay
Elison Orthodontics
Ott Painting, Inc.
KidSpark

We gratefully acknowledge these generous donors, each playing a vital role, in carrying out our mission to serve CCDS patients and families.

And to all our donors, sponsors and volunteers across the country who helped our various events, it is with sincere gratitude that we thank you for your continued support and generosity.

Our Board

The ACD was founded in 2012 by parents with children diagnosed with a CCDS. The ACD was established to raise awareness and education of CCDS among the medical community, and the general public, and to advocate on behalf of the families and patients living with CCDS.

The ACD aims to bring the CCDS community together as one strong voice to promote newborn screening and medical treatments and one-day cures for CCDS.

Together we are "building strength and changing lives."

2018 Board of Trustees:

Whitnie Strauss
President, Trustee

Heidi Wallis
Vice President, Trustee

Linda Cooper
Director of Special Initiatives, Trustee

Kim Tuminello
Director of Advocacy, Trustee

Melissa Parker
Director of Finance, Trustee

Laura Trutoiu
Director of Research, Trustee

2018 ACD Scientific Medical Advisory Board:

Dr. Nicola Longo, M.D., Ph.D.
Dr. Bruce Barshop, M.D., Ph.D.
Dr. Saadet Andrews, M.D., Ph.D., FCCMG, FRCPC
Dr. Andreas Schulze, M.D., Ph.D.
Dr. Sylvia Stockler, M.D.
Dr. Sarah Young, Ph.D.
Dr. Denise Morita, M.D.
Dr. Ton DeGrauw, M.D., Ph.D.
Dr. Yiumo Chan, Ph. D
Dr. Gajja Salomons, Ph. D.
Dr. Matthew Skelton, Ph.D.

ACD 2018 Financial Accounting

Statement of Financials
January – December 2018
Balance

Assets

Current Assets	$117,527.23

Liabilities & Equity

Equity

Opening Balance Equity	$23,919.12
Retained Earnings	$93,572.62
Net Income	$35.49
Total Equity	**$117,527.23**

Total Liability & Equity

As of December 31, 2018	$117.527.23

Statement of Financials
January – December 2018
Profit & Loss

Ordinary Income/Expense

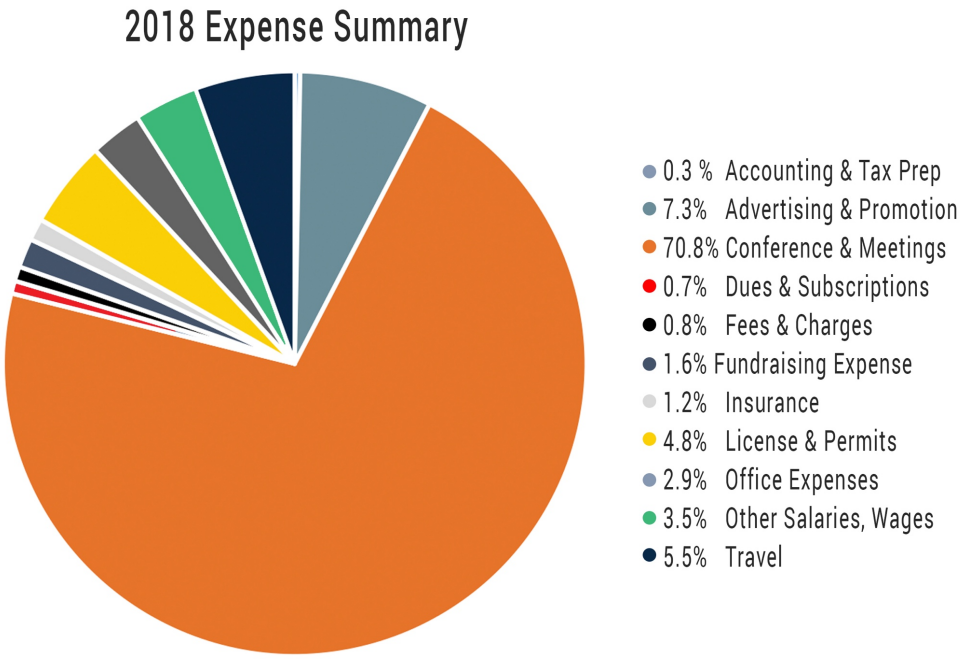
Income

General	$86,683.39
Grants	$13,500.00
Newborn Screening	$9,599.80
Research	$33,440.16
Unapplied Cash Payment Income	$0.00
Total Income:	**$143,233.35**
Gross Profit	**$143,233.35**

Expense

Accounting & Tax Prep	$520.00
Advertising	$10,489.86
Conference(s)	$101,396.85
Dues & Subscriptions	$1,076.76
Fees & Charges	$1,196.49
Fundraising Expense	$2,352.90
Insurance	$1,830.00
License & Permits	$6,922.00
Office Equipment & Supplies	$4,276.68
Other Salaries, Wages	$5,109.57
Travel	$7,946.75
Uncategorized Expense	$0.00
Total Expense	$143,187.86
Net Operating Income	**$35.49**
Net Income	**$35.49**

Expense Summary
January-December 2018



2018 Financials prepared by: Marlo Scarlet, MS Consulting